A rapid quality risk assessment mechanism for assessing needed pharmaceutical products that have not completed a stringent assessment

WHO prequalification of medicines for procurement by UN and other agencies has levelled the playing field and created a competitive supply of quality products in response to donor demand. However, there are still too few WHO-prequalified or stringently authorized finished products available on the market to ensure a sustainable supply of all medicines needed by treatment programmes.

Since 2009 the WHO Quality Assurance and Safety of Medicines Team (WHO-QSM) has hosted and coordinated a novel quality risk assessment mechanism on behalf of the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund): the Expert Review Panel (ERP). This expert group assesses the quality risks of pharmaceutical products that do not meet stringent quality requirements. Based on standardized and transparent criteria it then advises whether each product would be acceptable for procurement, for the next 12 months.

The ERP assessed a total of 310 dossiers of antiretrovirals, anti-tuberculosis products and antimalarials in its first six sessions; each session was completed within 4-6 weeks. The cost of ERP review is moderate as it is a one-off and abbreviated assessment. The outcomes have been crucial to securing a sustained supply of needed medicines, especially anti-TB products and some antimalarials.

The process has been well accepted by manufacturers and procurement agencies, and has promoted progression of medicines to prequalification. Of 115 eligible products assessed by the ERP in 2009 and 2010, 44 were subsequently prequalified by WHO or approved by a stringent regulatory authority. Agencies have harmonized their quality assurance policies and are using the mechanism jointly with the Global Fund. This has resulted in unified quality standards and efficiency gains for all stakeholders.

The ERP approach could be adapted for assessment of additional product categories such as life-saving antibiotics or zinc for the treatment of diarrhoea in children. But it should be borne in mind that ERP is not intended to replace WHO prequalification or stringent regulatory assessment.

Incentives for manufacturers to submit products to ERP for evaluation may remain limited for medicines that have a market outside donor-funded programmes. But this does not signify that such products need not adhere to stringent quality standards or that such standards should apply to donor-funded products only. On the contrary, WHO is working with manufacturers and regulators around the world to strengthen regulatory capacity in line with internationally accepted standards, so that all medicines are safe, effective and of good quality.
Quality policies in medicines procurement

**Stringent standards for key medicines**

Significant progress has been achieved in the last decade to increase access to medicines in low- and middle-income countries. The treatment of HIV, tuberculosis (TB) and malaria has attracted international funding, and competitively-priced medicines are now being sourced from emerging countries — especially India — and from some developing countries.

Today, donors and health care implementers rely on the stringent standards of the WHO Prequalification of Medicines Programme (WHO-PQP) and stringent regulatory authorities (SRAs) to ensure the quality of the products that they source from diverse regulatory environments. Likewise, the Medicines Patent Pool, which aims to bring down medicines prices through voluntary licensing of critical intellectual property from patent-holders, will require its licensees to submit their products to either PQP or to an SRA for evaluation.

The Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund) has played a leading role in promoting this development. Since its inception in 2002 it has defined a formal quality policy for pharmaceutical products for implementation by its grant recipients, requiring WHO prequalification or SRA-authorization of key products that are procured with its funds. As its funds account for a significant market share of key products, especially antiretrovirals (ARVs) and artemisinin-based combination therapies (ACTs), the policy has had a significant market impact.

**Alternative criteria to ensure continued supply**

Despite increasing demand from donors, WHO-prequalified or SRA-approved products are not available on the market for all needed medicines. To ensure a continued supply of needed products, alternative criteria must be applied to product selection that balance the benefit of treatment against the quality risks of products that do not yet meet stringent standards. This can be a complex process, with decisions often made on a case-by-case basis. Specialized agencies such as UNICEF and Médecins Sans Frontières (MSF) developed their own systems to perform such risk reviews, and the WHO Quality Assurance and Safety of Medicines Team (WHO-QSM) supported the Global Drug Facility (GDF) and UNITAID to do so. The members of the Interagency Pharmacist Group worked together by discussing the outcomes and challenges of their risk reviews on a confidential basis.

Having formally defined its alternative quality criteria, the Global Fund successively strengthened these over the years, thereby encouraging competition and promoting WHO prequalification of products. In 2008 it conducted a major policy review in wide consultation with stakeholders. The resultant, revised policy — effective since July 2009 — stipulates the application of stringent quality requirements to all ARVs, anti-TB products and antimalarials, and relies on a novel mechanism to ensure a continued supply of needed products not yet meeting these requirements: the Expert Review Panel (ERP). Based on some of the earlier risk assessment approaches developed by WHO and other agencies, this mechanism serves to assess product quality risks according to transparent criteria.
The Expert Review Panel (ERP)

The ERP is an independent technical body hosted by WHO, composed of external regulatory experts and coordinated by WHO-QSM which forms part of WHO’s Department of Essential Medicines and Health Products. To date, ERP has met twice a year to review submissions received in response to the Global Fund’s invitations to manufacturers to submit an expression of interest for product evaluation (EOIs), and to advise whether or not each of the products concerned can be considered acceptable for procurement during the following 12 months. Ad-hoc reviews can be arranged for urgently needed products, for both the Global Fund and other interested parties.

Manufacturers are requested to submit product data in questionnaire-type, abridged product dossiers, based on a format published in WHO technical guidance, and further developed by the Interagency Pharmacist Group, as part of its collaboration on quality risk reviews prior to the creation of the ERP. A manufacturer can provide cross-references to more detailed information that has already been submitted to WHO-PQP in a complete dossier.

The ERP coordinator manages the selection of ERP members, ensures that they remain current with the latest WHO-PQP and SRA guidelines, arranges timely review of submissions, and advises — based on the results of the reviews conducted by the ERP members — the Global Fund on the acceptability for procurement of each specific finished product.

Eligibility criteria for ERP review

To be eligible for ERP review, a product must be manufactured at a site and on a production line that complies with stringent Good Manufacturing Practice (GMP), as determined by WHO-PQP, an SRA or a member of the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (jointly referred to as PIC/S). Before ERP finalizes its advice, it verifies the GMP status of each product with the WHO-PQP inspectorate.

Secondly, a product dossier must already have been accepted for review, after screening for completeness, by WHO-PQP or an SRA. Most submissions received since 2009 had been submitted to WHO-PQP for evaluation, although approximately 40% of HIV-related products submitted to ERP had been submitted to the United States Food and Drug Administration for evaluation and tentative approval under the President’s Emergency Plan for AIDS Relief (commonly known as PEPFAR) but not to WHO-PQP.

Some needed products are not included on the EOIs for WHO prequalification and are also unlikely to be submitted for marketing approval in a country with an SRA. Medicines in this group include special strengths of anti-TB medicines used in India, and older, non-artemisinin-based antimalarials still used in certain regions and situations. The ERP will review such products even if they are not under assessment by a stringent body, as long as they are manufactured in compliance with international GMP standards.
**Transparent assessment criteria**

The ERP assesses four main quality elements, and categorizes each product in one of four risk categories (see Table 1).

**Table 1: Overview of ERP assessment criteria**

(Summarized: see Global Fund website for details<sup>9</sup>)

<table>
<thead>
<tr>
<th>Quality:</th>
<th>No objection to procurement (Risk category 1, applicable only to products under assessment by WHO PQP or an SRA)</th>
<th>No objection to procurement (Risk category 2, applicable only to products under assessment by WHO-PQP or an SRA)</th>
<th>Objection to procurement, but can be procured if benefit outweighs risk (Risk category 3)</th>
<th>Objection to procurement (Risk category 4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finished product manufacturing process and specifications</td>
<td>Acceptable specifications (in-house or compendial + additional in-house tests, and verified compendial /validated in-house methods). For sterile products, manufacturing processes are adequately validated</td>
<td>Acceptable specifications as per official monograph but missing certain additional in-house tests. For sterile products, manufacturing processes are adequately validated</td>
<td>Acceptable specification but analytical methods not sufficiently validated</td>
<td>Unacceptable specification or analytical validation for a critical test parameter. For sterile products, manufacturing process were not adequately validated</td>
</tr>
<tr>
<td>Stability and shelf life</td>
<td>The submitted data support the claimed shelf-life or an acceptable shelf life during which the product will comply with acceptable specifications</td>
<td>The submitted data support the claimed shelf-life or an acceptable shelf life during which the product will comply with compendial specifications</td>
<td>Shelf life is supported by insufficient stability data (e.g. submission of data on only one batch of a product with potential stability problems).</td>
<td>The available stability data does not allow any assignment of shelf life</td>
</tr>
<tr>
<td>Safety and efficacy: For generics: Evidence of therapeutic equivalence with a safe and effective comparator</td>
<td>Acceptable evidence of safety and efficacy OR demonstrated in vivo bioequivalence with an acceptable comparator product, OR (for oral products exempt from bioequivalence studies) acceptable multi-media dissolution data</td>
<td>Bioequivalence demonstrated or for biowaiver eligible oral products similarity in multi-media dissolution studies. The source of the comparator product is unknown or known to be outside of ICH OR comparator itself is a generic but prequalified by WHO or approved by SRA</td>
<td>Bioequivalence data not submitted, but for orally administered products, multi-media dissolution data show similarity (for non-oral products other in vitro data, as applicable, indicate similarity), AND/OR comparator is a generic product not prequalified or SRA-authorized</td>
<td>Efficacy and safety data not submitted, or unsatisfactory (e.g. several major deficiencies)</td>
</tr>
<tr>
<td>Source and quality of active pharmaceutical ingredients (API)</td>
<td>API has acceptable specifications and is manufactured at a GMP compliant facility as inspected by WHO, SRA or PIC's member inspectorate</td>
<td>API has acceptable specifications with no major quality concern and is manufactured at a licensed site with no known GMP issues</td>
<td>API has acceptable specifications but there are GMP issues</td>
<td>API specification not acceptable for a critical test parameter</td>
</tr>
</tbody>
</table>

As most innovator products have been assessed and registered in countries with an SRA, the ERP’s review mechanisms are geared towards rapid review of generic products, rather than of the safety and efficacy aspects of new molecules. The exception has been DHA-piperaquine, an ACT developed and
registered in China (which is not a country with an SRA as defined by the Global Fund\(^1\)). The ERP reviewed submissions from two manufacturers and assigned them to Risk Category 4 because the data provided was not sufficient to warrant assigning them to Risk Category 1, 2 or 3.

**Time-limited advice**

The ERP's advice regarding a product is valid for 12 months. During this time the product is expected to progress to WHO-prequalification or SRA-approval. For products in Risk Categories 1 or 2, manufacturers can apply for an extension by submitting an updated dossier and a progress report on the product's progression towards stringent approval.

Products in Risk Categories 1 or 2 are included on the Global Fund on-line product list,\(^10\) together with the date until which the ERP's advice will remain valid. Grant recipients can conclude procurement contracts until the last day of the validity period, for a maximum duration of one year.

**Use of ERP mechanism by agencies**

**Harmonization**

The Global Fund invites product dossiers for ERP review twice a year for medicines that are on WHO-PQP EOIs, and for which there are fewer than three WHO-prequalified or SRA-authorized finished products on the market. The ERP mechanism builds on the experience of the ad hoc quality risk reviews that WHO-QSM carried out before 2009 for GDF and UNITAID, and has created an opportunity for these organizations to harmonize their quality standards.

During 2009, the Global Fund and GDF organized separate quality risk reviews and, after a thorough review of the processes used, mutually recognized the outcomes of the ad hoc reviews that each agency had organized. From 2010 onwards, GDF and UNITAID have provided their input to the EOIs issued by the Global Fund for ERP review of medicines for TB and HIV/AIDS, respectively (Table 2). UNICEF has been reviewing dossiers as part of its ACT tender process with WHO, and will adapt this process to link it with the ERP procedure from 2012.
Table 2: Joint use of the ERP review mechanism by agencies

<table>
<thead>
<tr>
<th>Organization</th>
<th>Input to ERP EOI for ERP session:</th>
<th>GDF</th>
<th>Global Fund</th>
<th>UNITAID</th>
<th>UNICEF</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TB/HIV, TB, malaria</td>
<td>HIV</td>
<td>Malaria</td>
<td></td>
<td></td>
<td>UNFPA (reproductive health products)</td>
</tr>
<tr>
<td></td>
<td>WHO Department of Control of Neglected Tropical Diseases (albendazole, praziquantel)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>February 2009</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>x</td>
</tr>
<tr>
<td>June 2009</td>
<td>Session I</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>September 2009</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>x</td>
</tr>
<tr>
<td>October 2009</td>
<td>Session II</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>May 2010</td>
<td>Session III</td>
<td></td>
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<td></td>
<td></td>
<td>x</td>
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<tr>
<td>November 2010</td>
<td>Session IV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>x</td>
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<tr>
<td>December 2010</td>
<td>Session IV Supplement</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>March 2011</td>
<td>Session V</td>
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<tr>
<td>June 2011</td>
<td>Session V</td>
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<td></td>
<td></td>
<td></td>
<td>x</td>
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<tr>
<td>November 2011</td>
<td>Session VI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>x</td>
</tr>
<tr>
<td>Mid-2012</td>
<td>Session VII</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>x</td>
</tr>
</tbody>
</table>

**Process and timelines**

On receipt of submissions, the Global Fund liaises with manufacturers, screens dossiers for completeness and forwards the submissions to the ERP Coordinator ahead of each ERP session. For the first six ERP sessions, 79% of the submissions received were eligible and complete, and were forwarded for review.

In these first six sessions, the ERP assessed between 15 and 96 submissions per session. The median turn-around time from the start of the review until communication of final advice by the ERP Coordinator to the Global Fund was 35 calendar days (the range was 17–49 days). The session-based system has proved efficient, with predictable timelines for manufacturers and agencies.

**Outcomes of reviews**

In its first six sessions, the ERP assessed 310 submissions (involving 220 products), and had no objection to procurement for 74 products (see Figure 1).
Figure 1: ERP advice on 310 product dossiers reviewed (2009−2011)

Only products under assessment by WHO-PQP or an SRA can be categorized in Risk Categories 1 or 2 ("no objection"), and this was the case with two thirds of the ARVs, about one-third of the anti-TB products and less than one in eight of the antimalarials assessed.

Among the products not under stringent assessment, more than half of the anti-TB products and one-third of the antimalarials were considered acceptable for procurement in exceptional situations.

**Major deficiencies identified**

The ERP identified major deficiencies in 253 of the 310 submissions shown in Figure 1. Figure 2 shows the percentage of dossiers in each product category for which major deficiencies were identified. For some products, additional information was subsequently submitted by the manufacturer, so that ultimately they formed part of the group of 74 products, each of which was categorized in Risk Category 1 or 2, as shown in Figure 1 above.
As Figure 2 shows, for ARVs, problems related mostly to specifications and incomplete stability data. Anti-TB products were the only products for which GMP problems, with respect to active pharmaceutical ingredients (APIs), were identified. For antimalarials, unsatisfactory specifications, and problems with stability and efficacy data, were observed more frequently than for other medicines. As can be expected, insufficient or missing data were most common among products that were not under stringent assessment.

**Progression towards stringent approval**

Of the 115 products that the ERP reviewed between June 2009 and November 2010, 44 (38%) had become WHO-prequalified or SRA-authorized by March 2012 (see Figure 3). For products reviewed in 2011, it is too early to estimate the rate of progression; but already, by March 2012, two ARVs, one anti-TB product and two variations of anti-TB products had become prequalified, and others may follow.

Thirty-four of 56 favourably reviewed products — compared with 10 of 59 unfavourably reviewed products — progressed to stringent approval, meaning that categorization of a product in Risk Category 1 or 2 (which may be considered as a “positive” categorization) has a good predictive value. Most of the successful products progressed to become WHO-prequalified; some ARVs progressed to FDA tentative approval under PEPFAR, and many of these also became WHO-prequalified.
Figure 3: Progression of eligible ERP-reviewed products (2009–2010) to WHO prequalification or SRA approval

<table>
<thead>
<tr>
<th></th>
<th>ERP objection</th>
<th>No ERP objection</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARVs</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Anti-TB products</td>
<td>18</td>
<td>2 8</td>
</tr>
<tr>
<td>Antimalarials</td>
<td>25</td>
<td>2 3</td>
</tr>
</tbody>
</table>

Subsequently approved by WHO-PQP or SRA (as at March 2012): Yes No

The ten unfavourably reviewed products that progressed to stringent approval were all reviewed in the first two ERP sessions. Manufacturers thereafter submitted improved dossiers directly to a stringent assessment body without re-submitting them to ERP.

**Extension of ERP advice**

Four months before the expiry of the ERP advice, the Global Fund contacts manufacturers of products classified in Risk Categories 1 or 2, to request them to provide a progress report and additional product data. Based on this information, the ERP will consider extending its advice for another year. Of the 28 products relating to ERP sessions I to VI, the ERP granted an extension in 5 cases and a further 5 products became WHO-prequalified while extension was being considered. The remaining 18 were not granted an extension. Extension of ERP advice has thus been the exception rather than the norm.

**Procurement decisions**

Although the ERP advises on procurement of a product, donors and procurement entities are responsible for deciding on the use of that product in any treatment programme that they support.

The Global Fund lists products that have been categorized in Risk Categories 1 or 2 on its web site, for the information of grant recipients and other organizations. Nevertheless, grant recipients must obtain the Global Fund’s approval before procuring an ERP-reviewed product.

Products categorized in Risk Category 3 are not listed, and will be funded only if experts of the relevant WHO disease programme have confirmed that the treatment benefit in each specific context will outweigh the quality risk identified by the ERP. If not, grant recipients can either work with the Global Fund to identify an acceptable clinical alternative, or they can purchase the relevant product at their own risk and expense.

As an additional safeguard, batches of all ERP-reviewed products must pass random quality control testing before shipment.
Past procurement of ERP-reviewed products

Use by Global Fund grant recipients

Most of the ARVs and antimalarials and a significant proportion of the anti-TB medicines that have been reviewed by the ERP are procured with Global Fund grants. According to the Global Fund’s online Price and Quality Reporting database as at 31 October 2011, recipients had reported purchasing ERP-reviewed products worth USD 13.2 million since July 2009. In value terms, this corresponded to 13% of all first-line anti-TB products (including streptomycin), 5% of all antimalarials and 0.6% of all ARVs reported as procured. Second-line anti-TB products were approved by the Green Light Committee until the second half of 2011 and were therefore not reported as ERP-reviewed products.

The use of ERP-reviewed products has increased. During 2011 the Global Fund received 88 funding requests for ERP-reviewed anti-TB products and 32 funding requests for ERP-reviewed antimalarials (compared with 48 and 7 respectively in 2010). Two funding requests for ERP-reviewed ARVs were received in 2012: the first since June 2009. These figures reflect the availability of prequalified, SRA-authorized and ERP-reviewed products in each of the three disease categories:

- For ARVs, a wide choice of WHO-prequalified or SRA-authorized products is available. Few ERP-reviewed products are needed, with the exception of new paediatric formulations, or situations where stringently assessed products are not accessible due to patent issues.

- For anti-TB medicines, WHO-prequalified finished products are available, but ERP-reviewed products have been crucial in securing a continued, competitive supply. Requests are increasing for ERP-reviewed products for second-line treatment.

- For antimalarials, the numbers of WHO-prequalified and of ERP-reviewed product choices are the lowest. The Global Fund list of January 2012 listed 19 WHO-prequalified or SRA-authorized formulations, for 17 of which there was only one supplier. No ERP-reviewed product was listed for general use, although some non-artemisinin-based products can be procured under exceptional circumstances.

Quality control testing outcomes

In 2010 and 2011, the Global Fund and GDF jointly arranged for pre-shipment quality control testing of almost 800 batches of ERP-reviewed products by two competitively selected laboratories. All batches passed testing, although in a few cases, non-compliant results were initially reported due to methodological and interpretation issues. (Certificates of analysis for all batches tested are publicly available on the Global Fund website.) This experience suggests that quality problems at the pre-shipment stage in the supply chain are rare. It also underscores the importance of in-country quality monitoring. (Many quality problems may be identified only after the product has been received, stored and distributed in the destination country.) It demonstrates, too, that coordination and communication between manufacturers, procurement agencies, laboratories and recipients — for organizing efficient testing and correct interpretation of test results — are crucial.
Proven public health impact of ERP

Securing supply of needed products

The ERP mechanism has proved effective in supporting procurement of needed medicines for which the number of WHO-prequalified or SRA-authorized finished products is insufficient, thereby preventing treatment disruption and mitigating the risk of stock outs.

The impact has been greatest for anti-TB medicines. A core group of manufacturers has been submitting dossiers to ERP and working towards WHO prequalification, and two sources of finished products are now available for most medicines. This has helped to achieve shorter lead times and competitive prices. Moreover, a successful transition was made whereby GDF procurement policy was harmonized with that of the Global Fund. Some initial price increases did occur before a competitive supply of quality-assured products could be established, but this was in only a few cases. ERP review has also helped to secure a sustainable supply of some second-line products for which the production capacity of individual suppliers is limited.

A single process with unified requirements

Major procurement actors are harmonizing their quality assurance policies to incorporate the ERP process, which is both defined and flexible enough to result in useful procurement outcomes. This has resulted in efficiency gains not only for procurement agencies, but also for manufacturers, since they can now follow a single quality assurance process that has transparent, unified requirements.

Interim risk assessment leads to stringent approval

The ERP review mechanism has challenged initial concerns that it might duplicate prequalification and merely add another layer of procedures. On the contrary, ERP review complements WHO prequalification, as shown by the rates of progression in Figure 3 above.

The mechanism works best where it is linked to WHO prequalification, which — unlike marketing authorization in a country with an SRA — incorporates regular follow up and requalification in the destination countries.

Manufacturers have welcomed this process, which has helped them to bring needed products to market quickly, while progressing towards WHO prequalification. The intensive communication during each ERP session has in some cases laid the groundwork for speedy development of full dossiers for submission to WHO-PQP. Twelve of 19 anti-TB products and all three antimalarials which have been prequalified since 2009 had been submitted to the ERP.
Challenges

Incentives for ERP review

Incentives for meeting donors' stringent quality requirements are limited for manufacturers if they have markets other than donor-funded markets for their products. Moreover, donor-funded markets are often fragmented, with inaccurate forecasting and complex payment issues. If they are to justify investment in quality systems, manufacturers require a prospect of predictable sales over a period of several years and sometimes across product categories. Advance information on the magnitude of the quality investments that they may be required to make in order to meet international quality standards, and on potential, subsequent sales would be especially helpful for manufacturers. But these are influenced by many factors and therefore difficult to project.

Ongoing availability of quality-assured products

Unexpected quality issues can arise in connection with any of the quality elements of a product that have been assessed by the ERP. These can result in de-listing or downgrading of an ERP-reviewed product. For example, a notice of concern issued by WHO-PQP for an API recently affected the quality status of several anti-TB products from different suppliers. In 2011, WHO-PQP started to prequalify APIs, hopefully reducing the likelihood that this particular issue reoccurs. More generally, this example emphasizes the importance of diversified supply sources and of vigilance in procurement, to verify that the product purchased has the same specifications as the WHO-prequalified or ERP-reviewed product.

Future perspectives

ERP reviews of additional essential medicines

The ERP mechanism has been well accepted by manufacturers and procurement agencies, and clearly continues to be needed to support procurement of antimalarials, anti-TB products and reproductive health products, in compliance with quality assurance policies.

Donors, procurement agencies and implementers are also considering whether to introduce more stringent requirements, including for stringent follow-up in recipient countries, for other essential medicines. Obvious candidates include products on the WHO-PQP EOIs, such as life-saving antibiotics and zinc for treatment of diarrhoea in children.

Not all essential medicines needed by treatment programmes are currently on WHO-PQP’s EOI lists. If the ERP mechanism were to be used to ensure the quality of these medicines, methods would need to be designed to ensure regular follow-up. Currently, the ERP provides interim advice only. It is not designed to verify continued compliance of manufacturers with stringent quality standards on an ongoing basis.

For certain product groups, such as life-saving antibiotics that are vulnerable to emerging resistance, modification of ERP eligibility and assessment criteria might be justified, provided sufficient technical
rationale can be demonstrated. However, more work would be needed to group such products into risk-based categories, and to determine the technical criteria that the ERP should apply to each product group to mitigate any risks.

Cost recovery

Although ERP review has proved to be rapid and cost-effective, the cost will increase if dossiers for additional products are reviewed. The cost of administrative and communication support, which has so far been covered by the Global Fund, must also be considered. In future, a full cost recovery system may need to be envisaged if ERP review is to become a sustainable mechanism for wider use.

Replication of the ERP mechanism may seem an attractive prospect from the point of view ensuring continued supply of needed products across different therapeutic categories. However, this could lead to divergent standards and procedures, and potentially weaken the unified approach that has been the ERP’s major strength.

Beyond donor-funded programmes

Medicines quality has very real implications for patients and for public health. The ERP mechanism is a unique tool for supporting evidence-based decision-making in procurement of needed treatment options. It has also raised awareness of medicines quality issues among suppliers and recipients.

However, stringent quality assurance cannot and should not remain limited to donor-funded medicines. WHO is working with regulatory authorities around the world, to implement internationally accepted quality standards, so that all medicines are safe, effective and of good quality.

Acknowledgements

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References

1 Up to 30 June 2009, the Global Fund’s quality assurance policy defined an SRA as a member of ICH or PIC/S and, as of 1 July 2009, as a member, observer or associate of ICH through a legally binding mutual recognition agreement. ICH is the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use and PIC/S is the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (jointly referred to as PIC/S).


3 For more information on the Medicines Patent Pool, go to: http://www.medicinespatentpool.org/


8 For further information on PEPFAR, go to: http://www.fda.gov/InternationalPrograms/FDABeyondOurBordersForeignOffices/AsiaandAfrica/ucm119231.htm


11 The laboratories were WHO-prequalified. See http://apps.who.int/prequal/ for more information on WHO-PQP prequalification of laboratories and the list of laboratories prequalified by WHO-PQP to date.


