Prequalification

WHO rotational fellowships: an update

WHO prequalification has a significant impact on regulatory capacity in Member States. Much of the capacity-building effect has been achieved through the rotational positions offered by the WHO Prequalification Team (PQT), featured in an earlier issue of this journal. This article provides an update on the rotational fellowships programme.

Background
Access to medical products of assured quality, safety and efficacy is one of the cornerstones of health care. The essential role of WHO prequalification in facilitating procurement of products of assured quality, safety and efficacy has been recognized (1). What is less well known is the significant capacity-building effect that prequalification has in WHO Member States.

Much of PQT’s capacity-building effect is due to the inclusive character of its work. Since its inception in 2001, the medicines prequalification programme has carried out its evaluations together with experts from around the world, bringing in the perspectives from both mature regulatory authorities and developing countries. In addition, PQT develops training programmes, conducts regulatory trainings in countries and in Copenhagen, supports regulatory collaborations, facilitates regulatory approvals, organizes consultations and provides technical advice.

An important part of this capacity-building framework are the rotational positions at PQT, a unique arrangement within WHO. These positions are offered to regulators who have had some initial exposure to PQT’s work. For medicines assessors, the bi-monthly assessment sessions in Copenhagen – where prequalification dossiers for pharmaceutical product are evaluated by regulatory experts from around the world – are the training ground from which rotational assessors are recruited after 1-2 years of participation.

Feedback obtained in 2012 indicated that the rotational fellowships enabled the regulators to become familiar with international standards and procedures and to build professional networks. After their return they implemented guidelines and procedures in line with WHO standards in their countries, with a positive

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Another round of feedback was sought from regulators who have held a rotational position at any time since 2014 as a basis for the update presented here.

An expanding network
Since 2006, a total of 37 rotations have taken place. Starting with medicines assessors, the programme was opened up to inspectors in 2014 and to vaccines assessors in 2015 (Table 1). The first pharmacovigilance rotation is expected to start in June 2016, and rotations for regulatory systems strengthening are also intended to be introduced.

At the time of writing 36 of the 37 regulators that have held a rotational post were still in professional contact with PQT; 28 were working at national medicines regulatory authorities (NMRAs) and eight at international organizations (Figure 1).

Given that English is the working language at WHO there has been a predominance of fellows from anglophone countries. However, participation from non-English-speaking countries has increased in recent years, with a total of five inspectors from China and Brazil and two assessors from the Democratic Republic of Congo (DRC) completing a rotation. This has helped to expand the PQT network. DRC became the second of six French-speaking countries to

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**Table 1. Rotational fellowships at WHO-PQT**

<table>
<thead>
<tr>
<th>Type of rotation</th>
<th>Duration</th>
<th>First rotation started</th>
<th>Total rotations to date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assessors (medicines)</td>
<td>3 months</td>
<td>November 2006</td>
<td>28</td>
</tr>
<tr>
<td>Inspectors</td>
<td>4 months</td>
<td>March 2014</td>
<td>7</td>
</tr>
<tr>
<td>Assessors (vaccines)</td>
<td>3 months</td>
<td>July 2015</td>
<td>2</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td><strong>37</strong></td>
</tr>
</tbody>
</table>

**Figure 1. Current places of work of former rotational fellows**

As at February 2016 (in brackets: number of regulators)

![World map showing current places of work of former rotational fellows](image)

UNFPA (1)
WHO-PQT (5)
USP (2)
ANVISA Brazil (1) (at WHO at the time of writing)
NMRAs of:
- Ethiopia (1)
- Tanzania (5)
- Uganda (4)
- Zimbabwe (3)
- Zambia (2)
- Botswana (1)
- South Africa (1)

NMRA, National medicines regulatory authority
USP, United States Pharmacopeia
UNFPA, United Nations Population Fund

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participate in the collaborative registration procedure for WHO-prequalified products (3) and the regulatory authority of the DRC hosted the 2015 annual meeting of focal points, which was combined with a PQT regulatory training attended by assessors from nine francophone African countries.

Benefits
PQT is benefiting from its growing network of experts as it is increasingly able to draw on the expertise of assessors and inspectors throughout the countries where WHO-prequalified medicines are used. After their rotations, the assessors continued to contribute to the assessment sessions held in Copenhagen and regional capacity-building events. The inspectors participated in PQT inspections and conducted supportive activities in their countries such as verification of corrective and preventive action (CAPA), investigation of complaints and monitoring of progress of local manufacturers after provision of PQT technical assistance.

The benefits for individual regulators and their organizations, as mentioned in the feedback received from the rotational fellows, are outlined below.

Convergence of standards
During their rotation, the regulators participated in a wide range of prequalification activities and were provided with a complete set of the WHO norms and standards that underpin prequalification. This enabled them to reconsider regulatory practices in their countries. A rotational inspector said: “I learned WHO GMP guidelines systematically. It could help me realize the gaps between WHO and China GMP guidelines. Hence, as I will be involved in the revision of China GMP for CFDA in the near future, I will know how to achieve the harmonization of these guidelines.”

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Box 1: ‘Critical mass’ for change
Capacity-building is a gradual process, as illustrated by these two examples of comments by rotational assessors about challenges experienced after their return.

The first rotational fellow from Zambia worked at WHO in 2010. As a result of his authority’s participation in WHO prequalification, including his rotational fellowship, the Medicines Committee of the Board directed the regulatory authority to urgently start applying unified standards. In his 2012 feedback he said:

“The difficult part during my subsequent work has been to achieve a complete overhaul of the registration system to bring it in line with international best practices. (…) This involves availability of resources and skilled staff, requiring a sound financial base.”

The first rotational fellow from Tanzania completed his rotation in 2007. In 2011 he became Director General of the regulatory authority, and two assessors who had completed rotational fellowships at PQT in 2008 and 2010 moved to senior management posts. A fourth assessor completed a rotation in 2015. He said:

“Coming back home from the fellowship was a smooth transition since the minimum framework for regulation of medicines was already in place, hence I did not experience much difficulty in implementation of best practices.”
Links with WHO
The rotational fellows attended the WHO induction course, visited all units within the Essential Medicines and Health Products Department and collaborated with other departments as needed. For example, the rotational inspector from Brazil provided input on the Zika virus disease emergency. The regulators appreciated the opportunity to get to know the work of WHO, be exposed to a different job environment and make contacts for future professional networking and information-sharing.

Sustained impact over time
The two rounds of feedback received from former rotational fellows suggest that implementation of WHO standards in countries has been progressing over time (see also examples in Box 1). In countries with less mature regulatory systems, a framework was put into place covering the main functions. Thus in DRC ministerial decrees on registration, sales and outlets of medicines were signed, guidelines on good manufacturing practice and marketing authorization applications were adopted, and a national medicines registration committee was formed. Consequently, most of the assessment procedures changed.

At authorities where a basic framework was already in place more advanced elements were added. In Botswana a guideline on Common Technical Document (CTD) format drafted by a returning rotational fellow was piloted and adopted within less than a year of his return. In Uganda submission of dossiers on active pharmaceutical ingredients (APIs) became a requirement for marketing authorization of medicines, with a former rotational assessor being appointed as the focal point for API evaluation. In Tanzania a rotational assessor introduced a shared repository of API assessment reports, saving evaluation time for relevant applications and allowing the evaluators to focus on issues related to the finished pharmaceutical products.

Building regulatory capacity in countries
All the respondents reported having shared their experience with other regulators, applicants and professional organizations during trainings, workshops and seminars. Review and discussion of particular applications were also an effective way to improve the review process, as suggested in this statement: “Assessors in my agency have learnt a lot from my experience gained during the rotation at WHO, so this has translated into quicker decision-making in terms of the right questions to ask applicants, and also in terms of registration of products.”

In the two rounds of feedback assessors from six countries said that they shared their knowledge and experience through peer review of assessment reports – an approach recommended in recent international guidance (4).

Reliance and work-sharing
Having worked with regulatory experts from all over the world, the regulators became more inclined to rely on other regulatory authorities’ decisions. Expedited review procedures for stringently assessed products were introduced in a number of countries. In terms of inspections, a rotational fellow stated: "Exposure to the WHO and its collaborating partners (...) will also aid further collaboration (...). For instance, having joint inspections for common products and sites at national and
regional level and sharing information (…) will save resources in terms of finances, technical staff and time.”

Work at WHO furthermore provided opportunities for involvement in advocacy at the international level to promote convergence, reliance and regional networks:

“I participated in the 17th ICDRA\(^1\) planning meeting (…) This is the first time ICDRA will be held in Africa. NAFDAC and other drug regulatory authorities in the region are expected to leverage this opportunity (…) by strengthening their medicines regulatory harmonization which was launched recently in Ghana.”

Progress in collaborative initiatives
Contributions to collaborative initiatives were mentioned more frequently in this round of feedback than in 2012, as for example in this statement:

“I wrote a proposal for strengthening joint GMP inspections within the EAC region with support from international agencies and experts, which was approved by the EAC and is currently under implementation.”

Former rotational fellows have been driving forces in collaborative projects. The three initiatives mentioned in their feedback have all progressed well in recent years:

• The East African Community (EAC) harmonization project has resulted in introduction of harmonized guidelines and requirements in EAC countries (5). Joint inspections are conducted, and the regulatory authorities have embarked on joint assessments of product dossiers.

• The Zazibona collaborative pathway for registration of essential medicines in Zambia, Zimbabwe, Botswana and Namibia (6) has enabled significant work-sharing. A former rotational fellow now working at PQT facilitates the information-sharing process. Since 2013 over a hundred submissions have been assessed, leading to 69 registrations in participating countries (7).

• The WHO collaborative registration procedure for WHO-prequalified products aims to shorten registration timelines through sharing of PQT assessment and inspection reports. A total of 110 marketing authorizations have been granted through this procedure since 2013 (3), the median time to registration was 78 days. Ten former rotational fellows have been serving as collaborative registration focal points at NMRAs.

Challenges
All the regulators felt that the rotations were too short to cover the full range of WHO activities on medicines regulation. They wished to continue being involved in prequalification activities, for example in evaluating applications for snake venoms, which are newly eligible for prequalification. Several suggested that a continuous development programme should be introduced. Considering the growing number of applications for biosimilars and vaccines, the wish was expressed that WHO should provide more support to NMRAs in these areas as well.

The regulators’ comments about challenges on their return were mainly related to the resource constraints that continue to affect many regulatory authorities in WHO Member States. One respondent mentioned the heavy work load, leaving little time to implement
change. Two noted the need to advocate for more staff and adequate salaries, and one mentioned the lack of a qualified laboratory and the difficulty of transforming the NMRA’s business model for more managerial and financial autonomy.

Applicant-related challenges were mentioned by one respondent, who said that numerous applications were still being submitted that were not in the CTD format, causing delays in registration.

**Conclusion**
The rotational fellowship programme at WHO-PQT continues to have a positive impact at regulatory authorities. It has strengthened the network of people who work together to improve medicines regulation from a public health perspective.

Given the increasing complexities of medicines regulation the World Health Assembly has urged WHO Member States to engage in networks, pool regulatory capacities and promote collaboration and information-sharing across countries (1). The PQT rotational fellowship programme provides a platform for learning and sharing of experience, bringing regulators together to deal with some of the challenges that medicines regulation will continue to pose globally and in each of their countries.

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