WHO Prequalification of medical products and health technologies

Ensuring the Quality of Priority Medicines –
Workshop for National Medicines Regulatory Authorities and Manufacturers of Anti-Tuberculosis and Neglected Tropical Disease Products

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Protecting and promoting public health
WHO Prequalification

Was created in response to procurement agencies and WHO Member States needs to ensure that products supplied through these agencies are consistently safe and effective under conditions of use in resource limited countries.
WHO Prequalification

In vitro Diagnostics

2010

HIV test kit evaluation

1988

Vector control: 2017

WHO Pesticide Evaluation Scheme (WHOPES) was set up in 1960

Vaccines 1987

Medicines 2001
Structure of the Prequalification Team

Prequalification Team

Coordinator’s office

Vx Assessment

Mx Assessment

Dx Assessment

Vx Assessments

Inspections

Administrative team
Structure of Department of Essential Medicines & Health Products

Essential Medicines and Health Product [EMP]

Policy, Access and Use [PAU]
Regulation of Medicines and other Health Technologies [RHT]
Public Health, Innovation and Intellectual Property [PHI]

Technologies Standards and Norms [TSN]
Regulatory Systems Strengthening [RSS]
Prequalification Team [PQT]
Safety and Vigilance [SAV]
5th Invitation to Manufacturers of Medicinal Products for Treatment of Neglected Tropical Diseases, to Submit an Expression of Interest (EOI) for Product Evaluation to the WHO Prequalification Team: medicines

To support national and global efforts to increase access to and the affordability of care and treatment of neglected tropical diseases, WHO invites manufacturers of selected pharmaceutical products to submit Expressions of Interest (EOI) for product evaluation.

14th Invitation to Manufacturers of Antituberculosis Medicines to Submit an Expression of Interest (EOI) for Product Evaluation to the WHO Prequalification Team: medicines

To support national and global efforts to increase access to and the affordability of care and treatment of tuberculosis, WHO, together with UNICEF, UNAIDS and UNITAID, invites manufacturers of selected pharmaceutical products to submit Expressions of Interest (EOIs) for product evaluation.
PQ Process Overview: Medicines

Assessment of API Master File

Verification of Compliance with GMP

Apply API Master File Procedure

Submission of Dossier

Prequalification of API

Prequalification of FPP (full assessment)

Verification of Compliance with GMP

Prequalification of FPP (abbreviated assessment)

WHO LIST OF PREQUALIFIED APIs

WHO LIST OF PREQUALIFIED MEDICINAL PRODUCTS
WHO PREQUALIFICATION TEAM

PQ process overview: Vaccines

1. Submission for prequalification of a vaccine approved by an SRA
2. Submission of dossier
3. Testing of Samples
4. Verify GMP compliance
5. Prequalification of vaccine (full assessment)
6. Prequalification of vaccine (abbreviated assessment)
7. Post-Prequalification Activities
   - NRA Maturity Level 3 (GBT)
   - WHO List of prequalified vaccines & immunization equipment & devices

World Health Organization
PQ process overview: IVDs

Full prequalification assessment

Pre-submission form

Priority product

Yes

No

Dossier review

Site inspection

Laboratory evaluation

Prequalification decision

Abbreviated prequalification assessment

Pre-submission form

Priority product

Yes

No

Decision on abbreviated PQ assessment

Abbreviated site inspection

Laboratory evaluation

Prequalification decision
WHO PREQUALIFICATION TEAM

PQ process overview: Vector control products

Pre-submission package for vector control product submitted to WHO

WHO pre-submission Coordination Committee determines product pathway

Product class WITH a WHO policy recommendation

Prequalification pathway

WHO List of prequalified products

New intervention pathway

Product class WITHOUT a WHO policy recommendation

Post-prequalification activities

WHO List of prequalified products
Prequalification by numbers:

At the close of 2016, the list of prequalified products* included:

**Medicines**
- 416 FPPs
- 100 APIs
- 41 Quality Control Labs

**Diagnostics**
- 64 IVDs
- 2 MC devices

**Vaccines**
- 147 Vaccines
- 310 Immunization equipment and devices

**Vector control**

* Numbers are not the cumulative PQed products since their inceptions
# Time to prequalification (FPPs)

## Full assessment route (median time, days)

<table>
<thead>
<tr>
<th>Year</th>
<th>WHO time</th>
<th>Total time to PQ</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>292</td>
<td>872</td>
</tr>
<tr>
<td>2011</td>
<td>261</td>
<td>790</td>
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<tr>
<td>2012</td>
<td>347</td>
<td>760</td>
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<td>2013</td>
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<td>598</td>
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<td>2014</td>
<td>207</td>
<td>721</td>
</tr>
<tr>
<td>2015</td>
<td>206</td>
<td>805</td>
</tr>
<tr>
<td>2016</td>
<td>223</td>
<td>889</td>
</tr>
</tbody>
</table>
Time to prequalification FPPs

SRA route (median time, days)

<table>
<thead>
<tr>
<th>Year</th>
<th>WHO time</th>
<th>Total time to PQ</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>83</td>
<td>134</td>
</tr>
<tr>
<td>2011</td>
<td>63</td>
<td>355</td>
</tr>
<tr>
<td>2012</td>
<td>65</td>
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<td>2013</td>
<td>15</td>
<td>97</td>
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<td>2014</td>
<td>14</td>
<td>117</td>
</tr>
<tr>
<td>2015</td>
<td>78</td>
<td>118</td>
</tr>
<tr>
<td>2016</td>
<td>37</td>
<td>148</td>
</tr>
</tbody>
</table>
### Prequalified NTD products

<table>
<thead>
<tr>
<th>WHO Ref Number</th>
<th>INN</th>
<th>Applicant</th>
<th>Dosage form</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>NT001 (a)</td>
<td>Diethylcarbamazine (citrate)</td>
<td>Sanofi-Aventis, France</td>
<td>Tablet 100mg</td>
<td>2016</td>
</tr>
<tr>
<td>NT002</td>
<td>Diethylcarbamazine (citrate)</td>
<td>Eisai Co Ltd, Japan</td>
<td>Tablet 100mg</td>
<td>2013</td>
</tr>
<tr>
<td>NT003</td>
<td>Praziquantel</td>
<td>Cipla Ltd, India</td>
<td>Tablet 600mg</td>
<td>2015</td>
</tr>
</tbody>
</table>

The aim of this 5th EOI is to ensure the availability of quality assured albendazole, diethylcarbamazine, ivermectin, mebendazole, praziquantel, miltefosine, sodium stibogluconate, paromomycin and azithromycin for the treatment of lymphatic filariasis (albendazole, diethylcarbamazine or ivermectin), onchocerciasis (ivermectin), transmitted helminthiasis (STH) (albendazole, mebendazole or ivermectin), schistosomiasis, cutaneous leishmaniasis (miltefosine, sodium stibogluconate), visceral leishmaniasis (miltefosine, sodium stibogluconate and paromomycin sulfate) and yaws (azithromycin). Dosage forms and strengths listed in this document have been identified by the Department for effective treatment of patients suffering from these disease in either in the WHO Model List of Essential Medicines 19th list, April 2016 series.

3 prequalified NTD medicines; 9 products in EOI
96 Prequalified TB products

1. Isoniazid/Pyrazinamide/Rifampicin
2. Kanamycin (sulfate)
3. Linezolid
4. Para-aminosalicylate (sodium)
5. Protionamide
6. Rifapentine
7. Streptomycin (sulfate) - Sterile

Less than 3 prequalified products

1. Isoniazid / Rifapentine,
2. Ethambutol hydrochloride tablet 100 mg (scored, dispersible); 50 mg (dispersible)
3. Isoniazid tablet 100 mg (scored, dispersible); 50 mg (dispersible)
4. Cycloserine capsule 125 mg
5. Levofloxacin tablet 100 mg (dispersible)
6. Moxifloxacin tablet 100 mg (dispersible)
7. Linezolid tablet 150 mg (dispersible)
PQT – revised fee model

background

• PQT fees: 1999 (vaccines); 2008 (IVDs); 2013 (medicines & APIs)

• January 2017; Revised fee model for vaccines, medicines and APIs.

• A revised fee model will be introduced for diagnostics in 2018.

• The model includes screening, application/evaluation fee, inspection fee and annual fee.
PQT – revised fee model: Criteria

- The fees are structured in consideration of the following:
  - type of product: API, FPP or Vaccine
  - Product complexity (vaccines only): Simple/Traditional or Combinations/Novel
  - assessment procedure: Screening (vaccines only); Abridged or full assessment of new application; Assessment of major variations (medicines only)
  - Inspections (vaccines only)
  - PQ enabled sales (vaccines only)

- Annual fee: Fixed for medicines and APIs, Tiers based for vaccines
PQT – revised fee model - determination of Tier

- There is one Tier per company and NOT per vaccine
- The Tier is based on:
  - prequalification-enabled vaccine sales (sales to UN agencies and GAVI, only).
    - prequalification-enabled vaccine sales (sales to UN agencies and GAVI, only).
    - average annual PQ-enabled sales of all prequalified vaccines from that manufacturer over the last three completed calendar years.

<table>
<thead>
<tr>
<th>Tier</th>
<th>Average annual PQ-enabled Sales over the last completed three-year period. (US$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>US$0 to US$1 million</td>
</tr>
<tr>
<td>2</td>
<td>&gt;US$1 million to US$20 million</td>
</tr>
<tr>
<td>3</td>
<td>&gt;US$20 million to US$300 million</td>
</tr>
<tr>
<td>4</td>
<td>&gt;US$300 million</td>
</tr>
</tbody>
</table>
### Table 1: Fees for FPP and API prequalification applications (effective 1 January 2017)

<table>
<thead>
<tr>
<th></th>
<th>Single Registration Fee Per Product</th>
<th>Annual Fee Per Product</th>
<th>Post-PQ Changes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Application Fee</td>
<td>Annual Fee</td>
<td>Major variation</td>
</tr>
<tr>
<td><strong>FPP – Full assessment</strong></td>
<td>$25,000</td>
<td>$20,000</td>
<td>$3,000</td>
</tr>
<tr>
<td><strong>FPP – Abridged assessment</strong></td>
<td>$6,000</td>
<td>$5,000</td>
<td>NA</td>
</tr>
<tr>
<td><strong>API</strong></td>
<td>$20,000</td>
<td>$8,000</td>
<td>$3,000</td>
</tr>
</tbody>
</table>

1 Refer to SRA-Approved Multisource (Generic) or Innovator FPPs procedure - https://extranet.who.int/prequal/content/abbreviated-assessment-multisource-generic-or-innovator-product-0

### Table 2: Fees for Vaccine prequalification applications (effective 1 January 2017)

<table>
<thead>
<tr>
<th></th>
<th>Single Registration Fee Per Product</th>
<th>Annual Fee Per Product</th>
<th>Site Audit</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Application Screening Fee Abridged assessment procedure</td>
<td>Tier 1</td>
<td>Tier 2</td>
</tr>
<tr>
<td><strong>Simple / Traditional Vaccines</strong></td>
<td>$2,500</td>
<td>$25,000</td>
<td>$100,000</td>
</tr>
<tr>
<td><strong>Combinations or Novel Vaccines</strong></td>
<td>$5,000</td>
<td>$65,500</td>
<td>$232,750</td>
</tr>
</tbody>
</table>

Waivers:

- Applicants of products that generate only small profits, who may be discouraged from applying or maintaining their products on the list should contact the PQT. This will be discussed and a way forward reached on a case by case basis.

- A deferment, reduction or waiver to the annual fee may be granted if the applicant presents evidence that there has not been any sales in the previous year and the current year up to the date of invoicing – 01 September.
PQT has a value for manufacturers

**Direct value**
- Access to donor-sponsored markets

**Indirect value**
- Having good quality product
- Test of access to global markets (e.g. USA and EU)
- Image (internal and external)
- Facilitated and faster regulatory approval in a range of countries and less inspections
- Free of charge learning process enhancing technical and organizational capabilities and chance to succeed with submissions to SRAs
- Possibility to be assisted by expert consultants (GMP, dossier)
- Higher margins (non-institutional markets)
- Contract manufacturing for local markets
- Promotion of prequalified APIs