PQTm Quality update

Lynda Paleshnuik
Lead quality assessor
OVERVIEW

• Preparing to submit your dossier
• PQTm quality guidelines including WHO publications
• Assessing and using the principle quality guidelines
• Additional guidance documents (published on website)
• Guideline revisions planned or in progress
• What’s new
PREPARING TO SUBMIT YOUR DOSSIER

The advancement of a dossier through the assessment process depends on a number of factors in the control of the manufacturers, including:

• preparation before submitting the dossier

  Especially important if you are new to PQ

  If you are experienced with PQTm, be aware of updates

• response time (applicant) after PQ questions are sent out

• communication – we are responsive to questions
COMMUNICATION

See Advice to Manufacturers

at:

“This note gives some examples of the type of guidance that PQTm can offer with respect to quality and BE.”
COMMUNICATION

From Advice to Manufacturers

The data required to prepare a dossier for submission is complex, and attention to the details of requirements is required to ensure a smooth passage through the assessment process. It is most important to ask for advice before starting any studies that will necessitate significant investment of time and/or resources.

Applicants should consult the PQTm website — since it contains extensive guidance — before requesting advice.
PREPARING TO SUBMIT YOUR DOSSIER

Make use of available tools to help advance your dossier:

- Prequalification website (new site 2017)
  https://extranet.who.int/prequal/

- Current Prequalification guidelines

- Screening checklist

Note that the new PQTm website has an excellent search function, e.g. the screening checklist comes up by searching « screening »
WHO PUBLISHED GUIDELINES


TRS available for download at:

who.int/medicines/publications/pharmprep/en/
WHO prequalification requirements for active pharmaceutical ingredients and finished pharmaceutical products

Guidelines on active pharmaceutical ingredient master file procedure (2008)

Guidelines on submission of documentation for a multisource (generic) finished pharmaceutical product for the WHO Prequalification of Medicines Programme: quality part (2012)

Guidelines on submission of documentation for a multisource (generic) finished product. Preparation of product dossiers in common technical document format (2011)

Guidelines on submission of documentation for prequalification of finished pharmaceutical products approved by stringent regulatory authorities (2014)

- Request to submit stability data with the submission of documentation for prequalification of finished pharmaceutical products (FPPs) approved by stringent regulatory authorities (SRAs) (1 March 2016)
- Clarification with respect to a stringent regulatory organization as applicable to the stringent regulatory authority (SRA) guideline (15 February 2017)

Guidelines on variations to a prequalified product (2013)

Procedure for assessing the acceptability, in principle, of active pharmaceutical ingredients for use in pharmaceutical products (2009)

Procedure for prequalification of pharmaceutical products (2011)
PQTm GENERIC GUIDELINES

• For multisource (generic) products the product dossiers have to meet the norms and standards as specified in:

• Preparation of Prequalification Product Dossier in CTD Format: TRS961An15 2011
  — How to format the dossier
  — The expected contents of modules including details of module1 (regional information)

• Guideline on submission of documentation for a multisource FPP: Quality Part TRS970An4 2012
  Comprehensive quality GL- detailed information on the technical requirements for the dossier to be submitted for quality assessment.
QIS/QOS-PD templates have been required as part of quality dossiers since March 2011:

— Quality Overall Summary-Product Dossier (QOS-PD)
— Quality Information Summary (QIS) - critical data only
— These should be submitted in Word format

Note: Current versions: QIS (12 July 2017), QOS-PD (10 March 2017)
— Updated versions are periodically published

Access through the PQTm website https://extranet.who.int/prequal/ to ensure the current guidelines/templates are used.

Also published on PQTm website:

- **Request to submit stability data** with the submission of documentation for prequalification of finished pharmaceutical products (FPPs) approved by stringent regulatory authorities (SRAs) (1 March 2016) (https://extranet.who.int/prequal/sites/default/files/documents/48%20Stability%20data%20SRA%20FPPs_March2016_0.pdf)

- **Clarification with respect to an SRA** as applicable to the stringent regulatory authority (SRA) guideline (15 February 2017) (https://extranet.who.int/prequal/sites/default/files/documents/75%20SRA%20clarification_February2017_0.pdf) – discussed further under REVISIONS
OTHER KEY PUBLISHED QUALITY GUIDELINES

• WHO guidelines on variations to a prequalified product: TRS 981, Annex 3 (2013)


WHO GUIDELINES vs PQ-specific GUIDELINES

NOTE: A general WHO quality guideline is published in TRS986 (2014):
- Guidelines on submission of documentation for a multisource (generic) finished pharmaceutical product: quality part

This GL is based on the PQ quality guidelines (TRS 970, Annex 4, 2012):
- Guidelines on submission of documentation for a multisource (generic) finished pharmaceutical product for the WHO Prequalification of Medicines Programme: quality part

Use the PQ quality GL to submit a dossier to PQ – this GL includes many PQ-specific requirements, i.e. specific instruction to enable applicants to meet PQ requirements.

**PREQUALIFICATION or PREQUALIFIED** is IN THE NAME in the key PQ QUALITY GLs
ASSESSING AND USING PQTm GUIDELINES

• All current guidelines and templates for PQTm should be assessed through the PQTm website https://extranet.who.int/prequal/

• Non-PQTm guidelines may provide supportive guidance

• BUT wherever there is conflict between PQTm guidelines and other GLs, **PQTm guidelines prevail** in PQTm
ADDITIONAL PQTm GUIDANCE – PUBLISHED ON THE PQTm WEBSITE

- Guidance on preparation of product information (PIL, SmPC, labels (October 2016)) and compilation of the WHOPAR including Scientific Discussion (Part 6)

- Associated templates for the above
ADDITIONAL PQTm GUIDANCE – PUBLISHED ON THE PQTm WEBSITE

Information on submitting zinc sulfate dossiers:

☐ Q and A for submission of zinc sulfate dossiers (August 2013)

☐ Advice on zinc acceptability study (10 Nov 2016) and study form (11 Nov 2016)

☐ Advice on selection of excipients for zinc products (October 2014) – choosing excipients that don’t affect absorption
ADDITIONAL PQTm GUIDANCE – PUBLISHED ON THE PQTm WEBSITE

Information on submitting other products:

- Magnesium sulfate injections Q&A (6 October 2014)
- Medroxyprogesterone acetate depot guidance (DMPA) (1 August 2015)
- FAQ for submission of reproductive health products (29 March 2017)
### SCREENING CHECKLIST – EXAMPLE SECTIONS

<table>
<thead>
<tr>
<th>Comment</th>
<th>15</th>
<th>If technology transfer is involved, has validation data been presented</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td><strong>Is there data or a protocol presented for prospective validation of 3 consecutive production scale batches (of the largest proposed production size)</strong></td>
</tr>
<tr>
<td>Comment</td>
<td>16</td>
<td>Does the manufacturer include in Section 2.3.R copies of executed biobatch and proposed blank master production record(s) for proposed production batch(es)</td>
</tr>
<tr>
<td></td>
<td>17</td>
<td>Is there data presented on validation of analytical procedures</td>
</tr>
<tr>
<td>Comment</td>
<td>18</td>
<td>Is there data on FPP batch sizes and composition of pilot and production scale as well as those used in bioequivalence and dissolution studies (e.g. 2.3.P.2.2.1)</td>
</tr>
<tr>
<td></td>
<td>19</td>
<td>Does the applicant indicate the full physical address of the FPP manufacturing site including Unit and Block numbers, where applicable</td>
</tr>
</tbody>
</table>

Copenhagen, Denmark  18-21 September 2017
GUIDELINE REVISIONS

Guidance documents that may be targeted for future revision:

• FDC guideline (2005)

• Requalification guideline (2010) – may be targeted for revision based on the experience obtained with the process
GUIDELINE REVISIONS

One important quality guideline is currently being updated:

WHO stability guidelines (TRS 953, Annex 2) 2009
- The parent stability GL referred to throughout the PQ quality GL
STABILITY GUIDELINE REVISION

- The WHO stability guideline (TRS 953) is in the revision process.
  
  Target for completion (final version): 2018

- Current status: the current draft is available on the WHO ECSPP Current Projects site:
  

- Current comment period ends 18 September 2017
SRA definition – EC SPP

New draft for comment was circulated 1 September 2017


• Commenting until 8 October 2017
SRA definition

The term and definition is used in 9 current WHO GLs including the principle PQTm quality GLs.

• Draft provides the “interim definition”, which is as per previous but includes, “as before 23 October 2015”.
SRA interim definition

Excerpt only: A regulatory authority which is:

a *member* of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), being the European Commission, the US Food and Drug Administration and the Ministry of Health, Labour and Welfare of Japan also represented by the Pharmaceuticals and Medical Devices Agency (*as before 23 October 2015*); or…
SRA draft:

- Provides the elements for a new concept
- States that NRA’s in interim definition are to be grandfathered (retained)
SRA draft states:

- Need for process to expand to add new NRA’s in a transparent process

- Use of WHO GBT to add/maintain list

- Include modular function - listed for specific function and/or product group

GBT=global benchmarking tool. See “Assessing National Medicines Regulatory Systems” at:

SRA definition – EC SPP

New draft for comment was circulated 1 September 2017


• Commenting until 8 October 2017

Note: moving away from “SRA” and also soliciting proposals for new term.
New PQTm website 2017
https://extranet.who.int/prequal/

- **Note** that you can tour the website – tour is only through the HOME page
Welcome to our New Website
Built based on your feedback

Procedures for WHO Prequalification
Learn about the application process for finished pharmaceutical products (FPPs), active pharmaceutical ingredients (APIs) and quality control laboratories (QCLs)

Prequalified Lists
See lists for FPPs, APIs and QCLs

Reports for Prequalified Products
Find WHO Public Assessment Reports (WHOPARs) & WHO Public Inspection Reports (WHOPIRs)

Guidance Documents
WHO Technical Report Series, WHO prequalification of medicines guidance & International Pharmacopoeia
UPDATES

Model dossier (MD)

The MD is an example medicine dossier. The product chosen for the MD is a prequalified solid oral product, Levonorgestrel 0.75 mg tablets.

The MD includes the completed quality templates (QIS, quality information summary and QOS-PD, quality overall summary-product dossier) and the corresponding data expected in CTD Module 3 for the example product.
UPDATES

Model dossier (MD)

The MD is fully downloadable (258MB) on the PQTm website:

https://extranet.who.int/prequal/content/medicines-fpps
Model dossier (MD)

Intended as:
- training tool for regulators
- guidance for applicants
- an example for organizations involved in harmonizing regulatory requirements

The MD has been used as a training tool during the PQTm annual training workshop for regulators in 2016 and 2017
SUMMARY

Prepare before submitting

Ensure the current GLs are used

Ensure GLs for PQTm are obtained through the PQTm website

Be aware of draft guidelines circulated for comment
Acronyms!

API: active pharmaceutical ingredient
APIMF: API master file
CTD: common technical document
EC SPP: expert committee on specifications for pharmaceutical preparations
FPP: finished pharmaceutical product
GL: guideline
ICH: International Council on Harmonization
FDC: fixed-dose combination
Acronyms!

PQTm: Prequalification Team - Medicines

PIL: patient information leaflet

QIS: quality information summary (required quality template)

QOS-PD: quality overall summary – product dossier (required quality template)

SmPC: summary of product characteristics

SRA: stringent regulatory authority

WHOPARs: WHO public assessment reports
Thank you for your attention