

Prequalification Timeline Key Performance Indicators (KPIs)

1. Introduction

The purpose of this document is to provide background information relating to prequalification (PQ) timeline indicators. It also covers harmonization of PQ timeline calculation, and the method for computing WHO time, and defines the new set of key performance indicators (KPI) relating to PQ timeline.

This document should be read in conjunction with the summary table of **PREQUALIFICATION TIMELINE KPIs** presented separately, which contains details of targets.

See table in annex for the list of all indicators, including targets.

Key words

Application

An *application* expresses the intent of a manufacturer to participate in a given WHO process; it includes the submission of a *dossier* (see definition below).

Assessment

An *assessment* is a WHO process that consists of the evaluation of an *application* and concludes with a “pass/fail” decision.

Cohort

In this context of defining PQ timeline indicators, the word *cohort* is used to define a group of *products* at a given point in time, but does not necessarily imply that follow up over time is carried out.

Dossier

A *dossier* is a written document including all necessary evidence for WHO to make an informed decision. It is used in a broader sense than an actual regulatory dossier would be.

Product

A product is the subject of the *assessment*. In this context of defining PQ timeline indicators, the following products are considered:

- API: active pharmaceutical ingredient¹
- FPP: finished pharmaceutical product
- FVP: finished vaccine product
- IMD: immunization device
- IVD: in vitro diagnostic
- MCD: male circumcision device
- VCAI: vector control active ingredient
- VCP: vector control product.

¹ APIMF: active pharmaceutical ingredient master file, the API equivalent to a dossier, used in API and FPP prequalification.

2. Timeline Calculation

In the past, the process for calculating PQ timelines and WHO PQ time was different for IVDs, medicines and vaccines.

The harmonization of the PQ timeline calculation is based on the principle that time is allocated to either WHO or the manufacturer. Mutual stop-clock time is applicable only in exceptional situations, and if both WHO and the manufacturer agree on the stop-clock conditions.

The new algorithm proposed for determining WHO and manufacturer time is the following:

- Rule 1 – From acceptance for assessment to *dossier final decision*², the split between WHO time and manufacturer time applies only to the dossier review component.
- Rule 2 – If at the time of *dossier final decision* the inspection or, when applicable, the laboratory component, is still being performed, then after this point the split between WHO time and manufacturer time is counted only with respect to the longest-running component, i.e. the component that determines conclusion of the prequalification process, and therefore of the prequalification timeline.

This algorithm is based on the assumption that the dossier review is the principal component of the assessment. If another component cannot be finalized within the overall dossier review time, it is considered to be delaying the prequalification decision, and therefore should also be included in the timeline calculation.

The split between WHO and manufacturer time for the inspection and the laboratory components is also calculated starting from acceptance of the dossier for assessment, but is taken into account only for the calculation of the overall WHO PQ time, after the dossier component has been completed. In principle, all of the time occurring between acceptance for assessment and the actual inspection, or the laboratory evaluation, is counted as WHO time. However, if the manufacturer delays the inspection or the laboratory evaluation, the time between the initial date planned by WHO and the date proposed by the manufacturer is subtracted from WHO time related to the specific component.

This timeline calculation algorithm will be embedded in the new IT system. Potential implementation in the current systems should be evaluated, but is likely to be challenging.

See diagrams 1 & 2 in appendix for detailed figures explaining how timelines will be computed.

3. New Set of Performance Indicators

New performance indicators related to PQ timeline have been developed in addition to the current measurements: total PQ time split between WHO time and manufacturer time. The new set of PQ performance indicators includes both existing and new indicators. The purpose of these new indicators is to enable measurement of the progress of applications through the PQ pipeline more closely, rather than only measuring the timeline at the end of the PQ assessment. It also aims at monitoring the performance of the different components of PQ assessment. The components of PQ assessment are defined as: **dossier review**; **inspection** of the manufacturing site to verify good manufacturing practice or quality management system compliance — except for IMD — and **performance evaluation** (only for IVD) or **laboratory testing** (only for FVP).

² *Dossier final decision* is when all rounds of complete dossier review (i.e. for all sections of the dossier, if sections are reviewed separately) have been finalized.

A subset of the new set of indicators recently developed is proposed as **key performance indicators (KPIs)**, for the purpose of public reporting on PQ performance. These performance indicators are **application-based performance indicators**, which measure the trends in overall application progress through the PQ pipeline.

The concept of **first action** is also introduced, with different types of first action, defined as:

- **dossier first action**³: communicating the result of complete (i.e. all sections of the dossier, if sections are reviewed separately) initial dossier review to the manufacturer,
- **inspection first action**⁴: communicating the result of inspection (inspection report or desk review outcome) to the manufacturer,
- **laboratory first action**⁵: communicating the result of laboratory testing/performance evaluation to the manufacturer, if applicable.

The performance indicators become the **time to first action**, defined as the time from acceptance for assessment to each of the above first actions, calculated independently for each component. The aim is to measure WHO responsiveness, i.e. the time after which the manufacturer can expect first complete feedback, covering each assessment component.

In addition, the following *first action* will also be used:

- **screening first action**: requesting further information (if necessary), or communicating the acceptance/rejection of application for assessment decision (if no further information is requested).

This leads to the performance indicator **time to screening first action**, defined as the time from application submission to **screening first action**.

See *diagrams 3 & 4 in appendix* for detailed figures explaining how first actions will be computed.

Performance indicators are applicable to the following product types:

- **diagnostics (Dx)**: in-vitro diagnostics (IVDs), male-circumcision devices (MCDs)
- **medicines (Mx)**: finished pharmaceutical products (FPPs), active pharmaceutical ingredients (APIs)
- **vaccines (Vx)**: finished vaccine products (FVPs), immunization device (IMDs)
- **vector control (VCx)**: vector control products (VCPs), vector control active ingredients (VCAs).

Currently, prequalification of MCDs and IMDs is not subject to performance measurement related to PQ timeline. However they will be covered by the new IT system; performance measurement will start once the system has gone live. Most of the new indicators presented below will not be measurable under the current data management systems.

The targets for indicators have been set for 2018 and apply to all product types, unless specified otherwise. The targets may be revised one year after implementation, to include new targets from 2019 onwards, taking into account preliminary results.

³ *Dossier first action* is applicable to the review of full and abridged dossiers.

⁴ *Inspection first action* is only measured for initial inspections, i.e. inspections linked to a new PQ application.

⁵ *Laboratory first action* is only applicable to FVP and IVD.

Application-based performance indicators

This category consists of two types of indicator:

- those currently used to measure performance upon completion of prequalification assessment (for products that have attained prequalification), presented below under the *annual PQ cohort* headings,
- those for measuring performance of applications as they progress through the PQ pipeline, presented below under the *submission cohort*, *assessment cohort* and *change cohort* headings.

→ **Annual PQ cohort (products prequalified in a calendar year)**

Each of the indicators — presented in tables below — is calculated separately by product type⁶ and split between products assessed through the full assessment procedure and products assessed through the abridged assessment procedure.

- Products prequalified (i.e. the annual PQ cohort)

100	Number of products prequalified
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- Time to prequalification (from acceptance for assessment to prequalification)

110	Median WHO PQ time
111	Median manufacturer PQ time
112	Median total PQ time ⁷
KPI 1	% of products prequalified at or below target WHO PQ time

→ **Submission cohort (PQ applications submitted for PQ assessment in a calendar year)**

Each of the indicators — presented in tables below — is calculated separately by product type⁶ and split between products assessed through the full assessment procedure and products assessed through the abridged assessment procedure.

- PQ applications submitted for PQ assessment (i.e. the submission cohort)

200	Number of PQ applications submitted
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- Time to screening first action

210	Number of screening first actions
KPI 2	% of screening first actions taken at or below target time

⁶ Product types: API; FPP; FVP; IMD; IVD; MCD; VCAI; VCP.

⁷ Total PQ time is split between WHO PQ time and manufacturer PQ time; a mutual stop clock is applicable only in exceptional situations, if both WHO and the manufacturer agree on the stop-clock conditions.

→ **Assessment cohort (PQ applications accepted for PQ assessment in a calendar year)**

Each of the indicators — presented in tables below — is calculated separately by product type⁶ and split between products assessed through the full assessment procedure and products assessed through the abridged assessment procedure; the cohort is **followed for 3 years**.

- PQ applications accepted for PQ assessment (i.e. the assessment cohort)

300	Number of PQ applications accepted
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- Time to *dossier first action*

310	Number of dossier first actions
KPI 3.1	% of dossier first actions taken at or below target time

- Time to *inspection first action*

320	Number of inspection first actions
KPI 3.2	% of inspection first actions taken at or below target time

- Time to *laboratory first action*

330	Number of laboratory first actions
KPI 3.3	% of laboratory first actions taken at or below target time

→ **Change cohort (post-PQ change applications accepted for change assessment in a calendar year)**

Each of the indicators — presented in tables below — is calculated separately by product type⁶ and split according to the different types of post-PQ changes⁸.

- Post-PQ change applications accepted for change assessment (i.e. the change cohort)

400	Number of post-PQ change applications assessed
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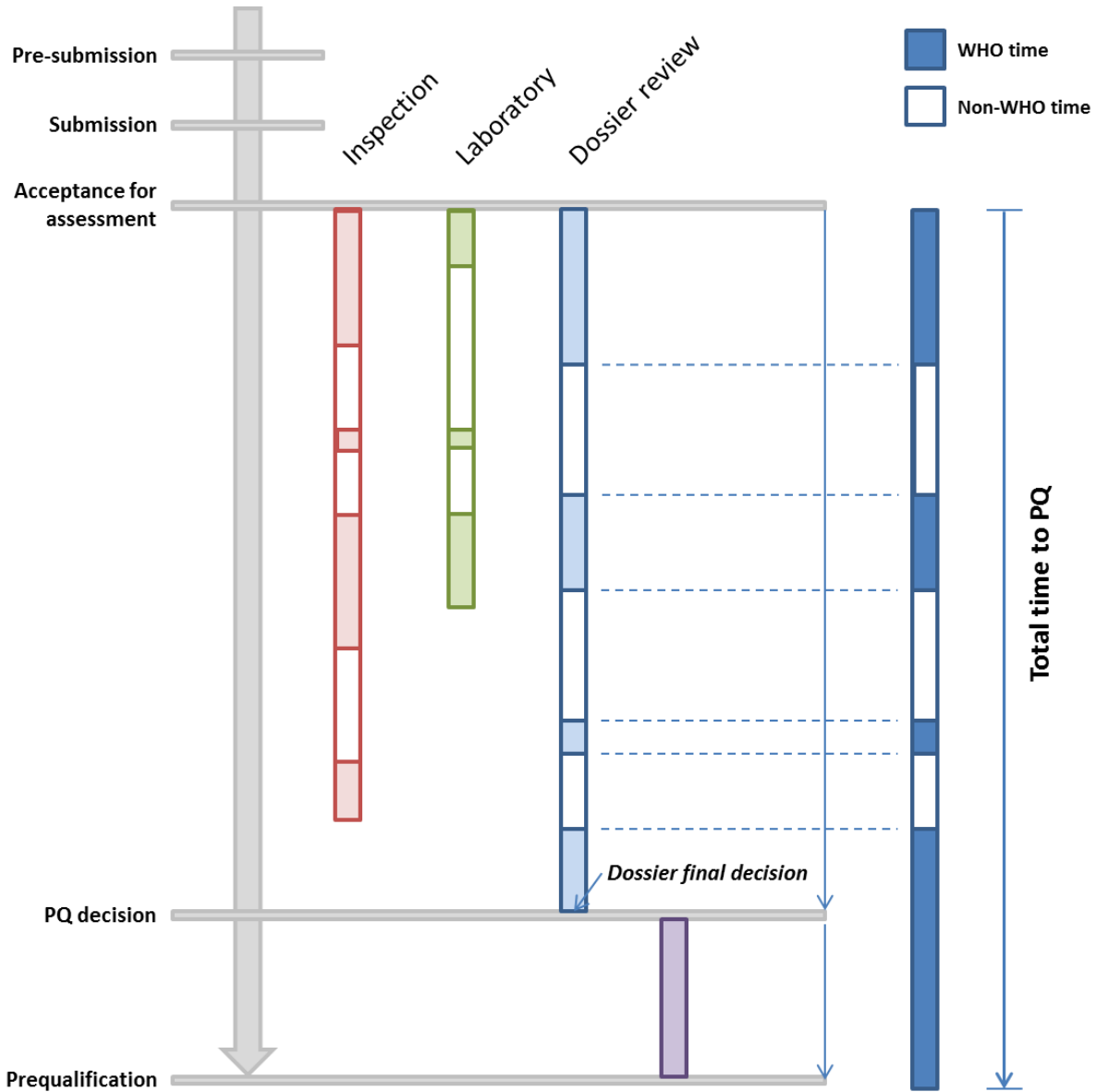
- Time to *post-PQ change first action*

410	Number of <i>post-PQ changes first actions</i>
KPI 4	% of <i>post-PQ change first actions</i> taken at or below target time

⁸ APIME: major/minor amendments, immediate/annual notifications; FPP: major/minor variations, immediate/annual notifications; FVP: variations with prior-approval, immediate/annual notifications; IVD: reportable/non-reportable changes.

4. Appendix

Diagram 1 - Rule 1 for timeline calculation:
Dossier review is the longest component of PQ assessment



**Diagram 2 - Rule 2 for timeline calculation:
Dossier review completed before the other component(s)**

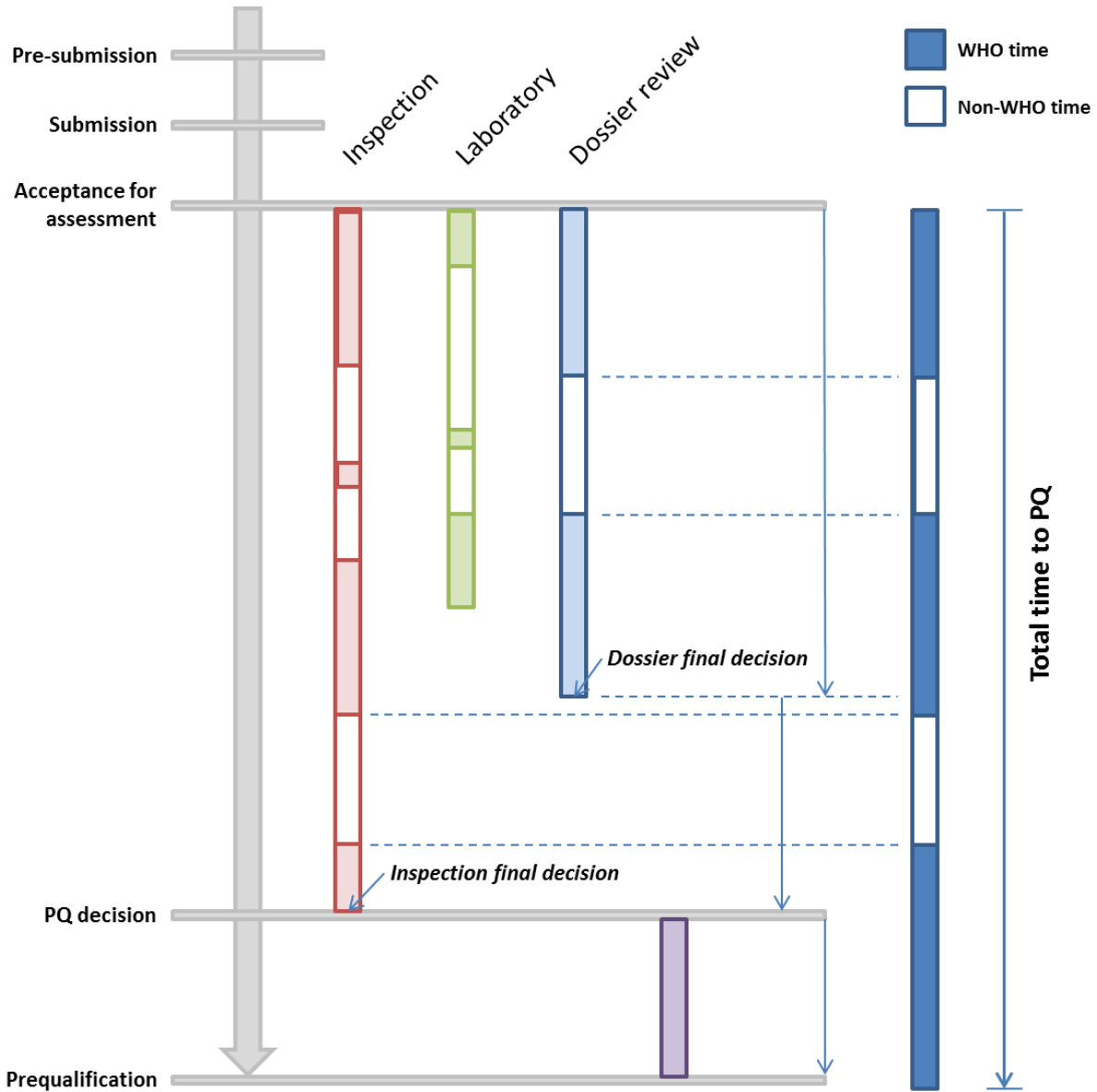


Diagram 3: First actions & final decisions

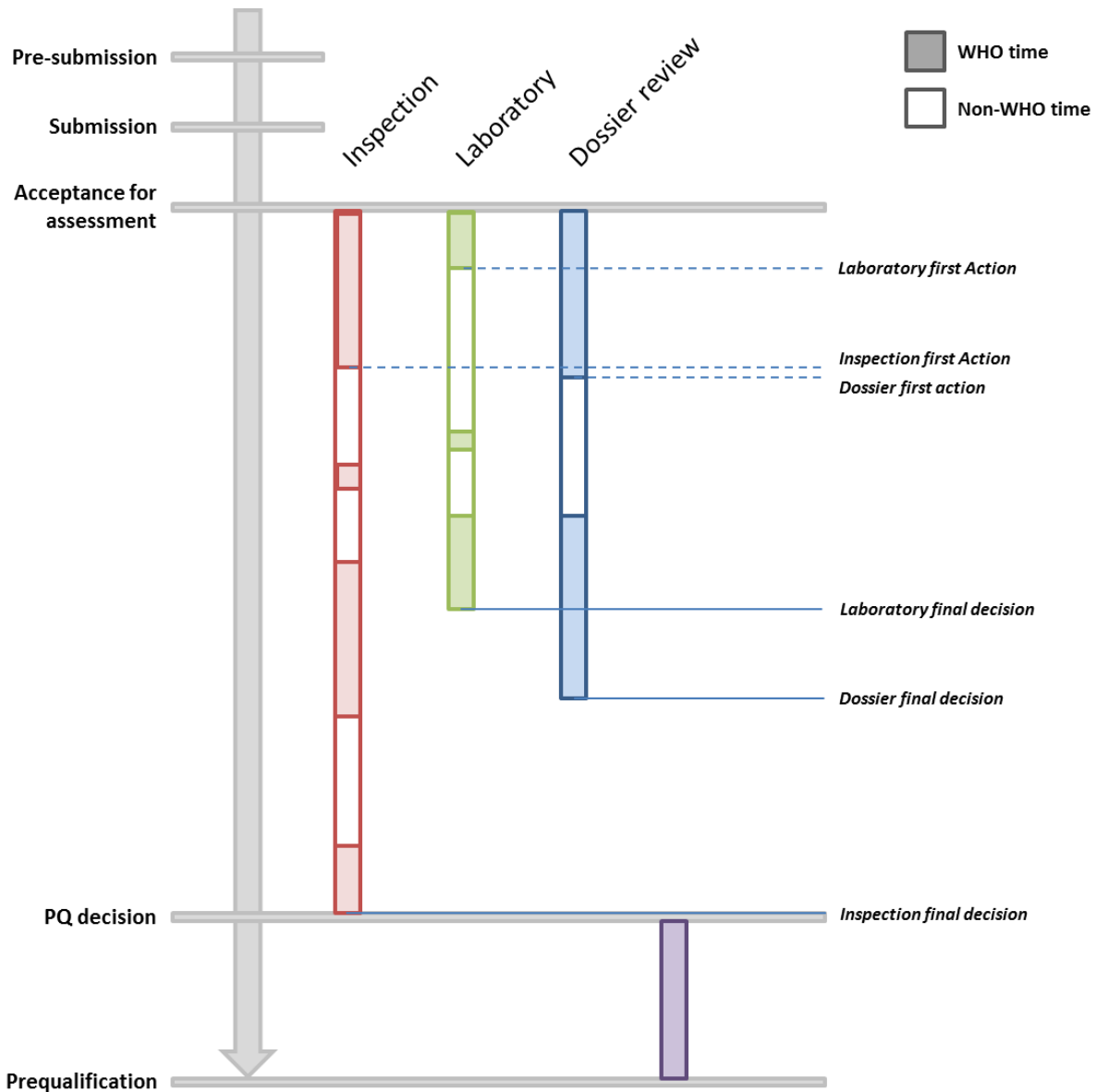


Diagram 4: Screening

