World Health Organization

# Abridged prequalification assessment

*Prequalification of in vitro diagnostics*

Abridged prequalification assessment: prequalification of in vitro diagnostics, PQDx_173, version 5

WHO/MHP/RPQ/PQT/2023.04



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## Contents

## 1. Introduction

World Health Organization (WHO) prequalification of in vitro diagnostics (IVDs) is coordinated through the Regulation and Prequalification Department. Focus is placed on IVDs for priority diseases and their suitability for use in resource-limited settings.

WHO prequalification of IVDs is a comprehensive quality assessment of individual IVDs through a standardized procedure aimed at determining whether a product meets WHO prequalification requirements.

An abridged prequalification assessment includes the following components:

- review of an abridged product dossier;
- performance evaluation, including operational characteristics;
- manufacturing site(s) inspection; and
- labelling review.

This document should be read in conjunction with the "*Overview of the WHO prequalification of in vitro diagnostics assessment"* document PQDx_007, as well as with the other relevant documents set forth in Section 7 below.

## 2. Intended Audience

This document has been prepared to provide manufacturers with information on the abridged prequalification assessment. Manufacturers wishing to apply for WHO prequalification of their product(s) should read this document before submitting the pre-submission form for prequalification.

## 3. Definitions

| | |
|---|---|
| Abridged WHO prequalification assessment | Prequalification assessment by WHO including review of an abridged product dossier, performance evaluation, manufacturing site inspection and labelling review. |

## 4. Abbreviations

| | |
|---|---|
| BLA | Biologics License Application |
| EC | European Commission |
| GHTF | Global Harmonization Task Force |
| HSA | Health Sciences Authority of Singapore |
| IFU | Instructions for use |
| IMDRF | International Medical Device Regulators Forum |
| IVD | In vitro diagnostic medical device |
| IVDD | Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices |

| | |
|---|---|
| IVDR | Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU |
| JMHLW | Japanese Ministry of Health, Labour and Welfare |
| PMA | Premarket Approval |
| QMS | Quality Management System |
| SMDR | Singapore Medical Device Register |
| SRA | Stringent Regulatory Authority |
| TGA | Australian Therapeutic Goods Administration |
| WHO | World Health Organization |
| WHOPAR | World Health Organization Public Assessment Report, which summarizes the findings of the prequalification assessment, but excludes confidential and proprietary information. |
| WHOPIR | World Health Organization Public Inspection Report, which summarizes the findings made during the inspection of the manufacturing site(s) as well as corrective actions taken in respect of the site(s) but excludes confidential and proprietary information. |

## 5. Rationale for abridged prequalification assessment

The rationale for abridged prequalification assessment is that a prior regulatory approval provides a level of assurance relating to a product's quality, safety and performance in countries where it is approved, but it cannot always provide the same assurance when the product is used in other jurisdictions, including resource-limited settings.

The aim of abridged prequalification assessment is to avoid duplication of effort and reduce the time taken to prequalify a product by focusing on aspects where WHO prequalification assessment brings added value. WHO will review the pre-submission form and supporting documentation to determine whether the product qualifies for an abridged prequalification assessment. Products that do not qualify for abridged prequalification assessment will require a full prequalification assessment.

WHO will apply the abridged prequalification assessment process, in accordance with this document, in the following instances:

1. if a regulatory version of the product submitted for WHO prequalification has previously been "stringently assessed" by one of the Recognized Stringent Regulatory Authorities (SRAs); or

2. if a regulatory version of the product submitted for WHO prequalification has not been stringently assessed by a Recognized SRA, but a stringently assessed regulatory version of the product also exists, and there are no substantial differences between the two regulatory versions.

WHO reserves the right to shift from an abridged prequalification assessment to a full prequalification assessment at any stage in the prequalification assessment process, if the manufacturer fails to submit satisfactory evidence supporting a previous stringent review and/or if the submitted evidence does not meet WHO's requirements for abridged prequalification.

## 6. Abridged prequalification assessment process

### 6.1. Eligibility for abridged prequalification assessment

When considering whether a product qualifies for an abridged prequalification assessment procedure, WHO takes into account the following two factors: (1) whether the regulatory version of the product submitted for WHO prequalification has been "stringently assessed" (as defined below) and approved by any of the stringent national regulatory authorities listed in Table 1 below (each such authority is hereinafter referred to as a "Recognized SRA") and, (2) if so, whether the regulatory version of the product submitted for WHO prequalification is the same (or is not substantially different) as the regulatory version that was stringently assessed and approved by the Recognized SRA.

For purposes of this document, the regulatory version of a product has been "stringently assessed" if the assessment has been performed by a Recognized SRA for the following relevant risk classes set forth in Table 1 below.

**Table 1- Recognized stringent assessment**

| Stringent Regulatory Authority (Recognized SRA) | Risk classes undergoing stringent assessment |
|---|---|
| European Union | Annex II, List A (IVDD), Class C and Class D (IVDR) |
| Food and Drug Administration of the United States of America | Class III |
| Health Canada | Class III and Class IV |
| Therapeutic Goods Administration, Australia | Class 3 and Class 4 |
| Ministry of Health, Labour and Welfare, Japan | Class III |
| Singapore Health Sciences Authority | Class C and Class D |

Based on these factors, a product is eligible for abridged prequalification assessment if one of the following conditions is met:

1. The regulatory version of the product submitted for WHO prequalification has previously undergone stringent assessment and approval by a Recognized SRA (as defined above); or
2. The regulatory version of the product submitted for WHO prequalification has not been stringently assessed and approved by a Recognized SRA, but a stringently assessed and approved regulatory version of the product also exists, and, in WHO's discretion, there are no substantial differences between the two regulatory versions (including, without limitation, substantial differences as to the product description, intended use, test procedure, labelling and instructions for use, quality management system, design, manufacturing site, key suppliers, verification/validation studies, and/or lot release criteria).

Conversely, a product is not eligible for abridged prequalification assessment if:

- The regulatory version of the product submitted for WHO prequalification has not previously undergone any stringent assessment and approval by a Recognized SRA, and no stringently assessed and approved regulatory version of the product exists. The foregoing includes cases where the regulatory version of the product:

A. has been previously assessed and approved by a Recognized SRA, but not according to an appropriate level of stringency (i.e., lower risk classification or different risk classes than those set forth in Table 1), and/or

B. has been previously assessed and approved by a regulatory authority other than a Recognized SRA listed in Table1; or

- The regulatory version submitted for WHO prequalification is different from the regulatory version that has previously undergone stringent assessment and approval by a Recognized SRA and, in WHO's discretion, there are substantial differences between the two regulatory versions.

Products which are determined by WHO not to be eligible for abridged prequalification assessment will be required to undergo a full prequalification assessment.

Figure 1 summarizes the eligibility requirements and decision process for abridged prequalification assessment.

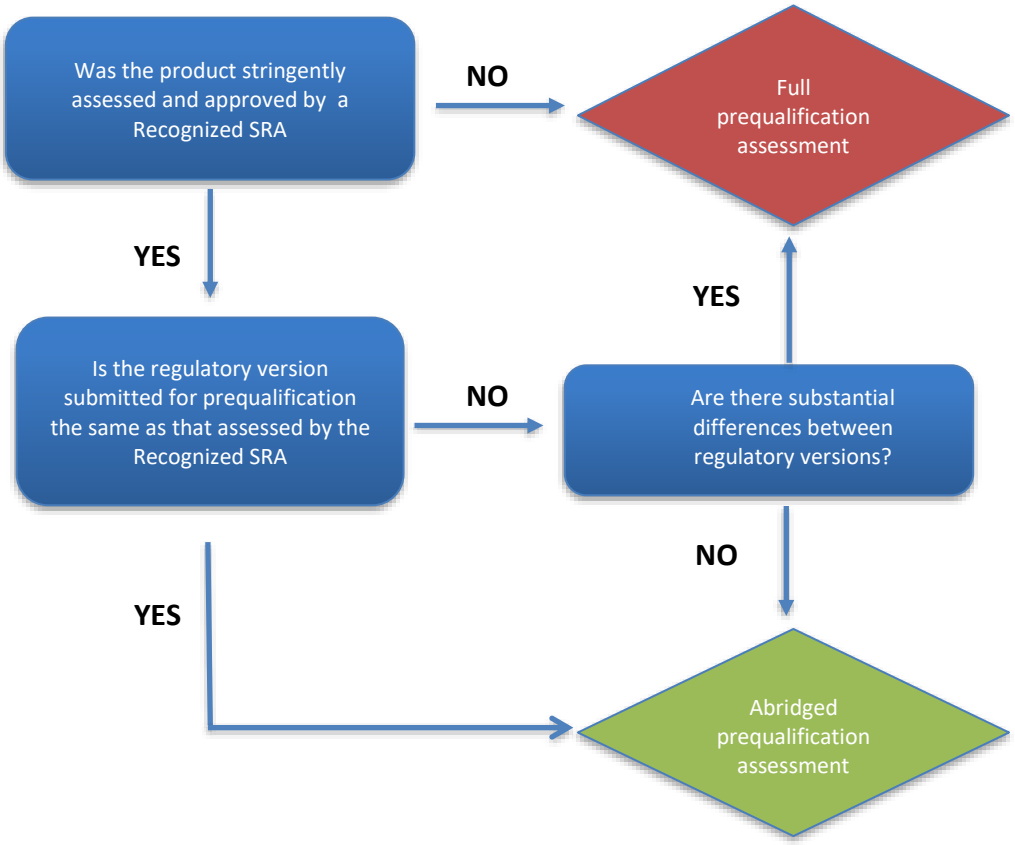


**Figure 1- Decision tree for abridged prequalification assessment**

Differences between a full and an abridged prequalification assessment.

The full prequalification assessment process includes the following components:

- review of a full product dossier;
- performance evaluation, including operational characteristics;
- manufacturing site(s) inspection; and
- labelling review.

By contrast, an abridged prequalification assessment process includes the following components:

- review of an abridged product dossier;
- performance evaluation, including operational characteristics;
- manufacturing site(s) inspection; and
- labelling review.

An abridged prequalification assessment considers available evidence that an eligible product meets certain WHO prequalification requirements as a result of the product's previous stringent regulatory assessment and approval. Table 2 lists the differences between a full prequalification assessment and an abridged prequalification assessment. Additional details are provided in Section 6.2 below.

**Table 2 - Differences between a full prequalification assessment and an abridged prequalification assessment**

| Prequalification stage | Full prequalification assessment | Abridged prequalification assessment |
|---|---|---|
| Review of a product dossier | Full product dossier | Abridged product dossier |
| Inspection of a manufacturing site | Manufacturing site(s) inspection | Manufacturing site(s) inspection |
| Performance evaluation, including operational characteristics | Yes | Yes |
| Labelling review | Yes | Yes |

## 6.2. Abridged prequalification assessment process

### *6.2.1. Pre-submission stage*

A prequalification pre-submission form must be submitted by the manufacturer to WHO. This form will serve to:

- provide information about the product submitted for prequalification;
- identify the regulatory version submitted for prequalification; and
- determine the differences between existing regulatory versions of the product.

Following its receipt of a pre-submission form, WHO will determine (i) whether there is acceptable evidence of prior stringent assessment and approval for the product submitted for prequalification, and (ii) whether the product is eligible for abridged prequalification assessment pursuant to the requirements contained or referenced in this document. For such evidence to be considered acceptable, the product must meet the requirements for placing a product on the market in the respective regulatory jurisdiction. Table 3 and 4 show acceptable evidence for abridged prequalification assessment.

### Table 3 - Acceptable evidence of stringent regulatory assessment for GHTF/IMDRF Class D IVDs

| Recognized SRA | Acceptable evidence of approval by the Recognised SRA |
|---|---|
| European Union | EC Full Quality Assurance Certificate and EC Design Examination Certificate, issued under Annex IV of Directive 98/79/EC<br>• EC Production Quality Assurance Certificate, issued under Annex VII of Directive 98/79/EC and EC Type-Examination Certificate, issued under Annex V of Directive 98/79/EC<br>Certificate issued under Annex IX of Regulation 2017/746<br>• Certificates issued under Annex X and XI of Regulation 2017/746 |
| Food and Drug Administration of the United States of America | Premarket Approval Letter (PMA) letter or Biologics License Application (BLA license) |
| Health Canada | Medical Device License |
| Therapeutic Goods Administration, Australia | TGA Full Quality Assurance Certificate and TGA Design Examination Certificate; or<br>TGA Production Quality Assurance Certificate and Type-Examination Certificate |
| Japan Ministry of Health, Labour and Welfare | JMHLW Minister's Approval<br>Registration to JMHLW of Manufacturer (seizogyo touroku)<br>Registration to JMHLW of Foreign Manufacturer (gaikoku seizogyosha touroku) |
| Singapore Health Sciences Authority | Listing on the Singapore Medical Device Register (SMDR) as Class D IVD. |

### Table 4 - Acceptable evidence of stringent regulatory assessment for GHTF/IMDRF Class C IVDs

| Recognized SRA | Acceptable evidence of approval by the Recognised SRA |
|---|---|
| European Union | EC Full Quality Assurance Certificate issued under Annex IV of Directive 98/79/EC<br>EC Production Quality Assurance Certificate issued under Annex VII of Directive 98/79/EC<br>EC Type-Examination Certificate issued under Annex V of Directive 98/79/EC<br>Certificate under Annex IX of Regulation 2017/746<br>Certificates under Annex X and XI of the Regulation 2017/746 |
| Food and Drug Administration of the United States of America | Premarket Approval Letter (PMA) letter or Biologics License Application (BLA license) |
| Health Canada | Medical Device Licence |
| Therapeutic Goods Administration, Australia | TGA Full Quality Assurance Certificate; or<br>TGA Production Quality Assurance Certificate and Type-Examination Certificate |
| Japan Ministry of Health, Labour and Welfare | JMHLW Minister's Approval |

| | |
|---|---|
| | Registration to JMHLW of Manufacturer (seizogyo touroku)<br>Registration to JMHLW of Foreign Manufacturer (gaikoku seizogyosha touroku) |
| Singapore Health Sciences Authority | Listing on the Singapore Medical Device Register (SMDR) as Class C IVD[1]. |

### *6.2.2. Decision to abridge the prequalification assessment*

WHO will determine if the product qualifies for abridged prequalification assessment pursuant to and in accordance with the requirements contained and/or referenced in this document, including but not limited to Section 6.1 above.

If any of conditions 1 or 2 set forth in Section 6.1 above are met, then WHO will perform an abridged prequalification assessment of the product in question. Conversely, if none of those conditions are met, or if any of the disqualifying conditions set forth in Section 6.1 are met, then WHO will perform a full prequalification assessment of the product in question.

WHO will notify the manufacturer in writing of its decision on whether or not the product in question will undergo an abridged manufacturing assessment.

NOTE: In some cases, a product may have multiple regulatory versions and associated approvals and more than one of the different types of evidence specified in Tables 3 and 4. Each of these approvals may support different aspects of WHO's requirements for prequalification, which could further facilitate the abridged prequalification assessment. Therefore, it is important for the manufacturer to submit to WHO all available evidence of previous and current stringent regulatory assessments and approvals.

### *6.2.3. Abridged product dossier review*

If the product qualifies for abridged prequalification assessment, the manufacturer must submit the abridged product dossier according to the requirements and provisions set forth in Annex 1: Abridged product dossier requirements. The assessment will be conducted in accordance with the WHO document "*Overview of the WHO prequalification of in vitro diagnostics assessment" document PQDx_007.*

### *6.2.4. Manufacturing site(s) inspection*

Under the abridged prequalification assessment, a manufacturing site inspection will take place. The on-site inspection time will be calculated and limited to those product- and user-specific processes that are a major focus of WHO prequalification inspections (e.g. processes related to risk management, in-use stability under poorly controlled conditions, impact on stability of transportation, information gathered from the market etc., user training and training material).
The inspection scope will not include an in-depth review of all Quality Management System (QMS) procedures and processes usually inspected, but instead will take into consideration the findings of the most recent regulatory audit report. There will be limited sampling of some of the general quality management processes and associated records and a follow-up on, or clarification of, individual findings identified during the previous inspection.

[1] Based on the full review by Singapore Health Sciences Authority.

If the product qualifies for abridged prequalification assessment, the manufacturer must submit an information package in order to assist WHO in preparing for the manufacturing site(s) inspection. The contents of the information package are as shown in Annex 1.

The manufacturing site inspection will normally be shorter in duration compared to a full prequalification assessment manufacturing site inspection. If time allows, a preliminary non-conformance report detailing issues of concern (if any) will be provided to the manufacturer on the final day of the inspection. A final inspection report, including the graded nonconformities will be issued to the manufacturer after the inspection of the manufacturing site(s).

All nonconformities must be corrected by the manufacturer through suitable corrective actions addressing the root cause of each nonconformity. The manufacturer will have the opportunity to submit up to two corrective action plans. Depending on the nature and number of nonconformities, objective evidence of the effective implementation of proposed corrective actions may be required. WHO will assess the information provided and decide whether the corrective action plan can be accepted. Conformity with prequalification requirements will be established based on assessment of such information. In some instances, the number and criticality of nonconformities may require that the effective implementation of proposed corrective actions needs to be verified in a follow up inspection, before the nonconformities can be closed off.

A statement on the compliance of the site inspected will be included in the WHO Public Inspection Report (WHOPIR), if the product successfully meets the WHO prequalification requirements. In certain cases, WHO may agree, in its sole discretion, to permit the manufacturer to correct specific nonconformities after prequalification, provided that the manufacturer commits in writing to address them by an agreed upon deadline. Such a "commitment to prequalification" will be verified during the re-inspection. Failure to comply with prequalification commitments within agreed deadlines will result in the delisting from the WHO list of prequalified IVDs. If the manufacturer does not meet WHO prequalification requirements or if any of the other conditions outlined in the document *"Overview of the WHO prequalification of in vitro diagnostics assessment"* document PQDx_007 Section 10.3 (Cancellation of the application) are met, the prequalification application will be cancelled.

### *6.2.5. Performance evaluation*

The purpose of the performance evaluation is to independently verify and evaluate the performance and operational characteristics of the product. It is carried out by specified WHO Collaborating Centre(s) or designated laboratory(ies) (collectively referred to as "evaluating site(s)"), using the WHO prequalification evaluation protocol. The product will be evaluated against pre-determined performance criteria established by WHO.

The manufacturer must choose one of the following two performance evaluation options, and must indicate its choice in the pre-submission form:

Option 1: Performance evaluation commissioned by WHO and carried out at an evaluating site listed by WHO. The manufacturer must indicate in the pre-submission form the choice to undergo a performance evaluation coordinated by WHO and performed by an evaluating site selected by WHO.

Option 2: Performance evaluation commissioned by the manufacturer and carried out at an evaluating site listed by WHO. The manufacturer must indicate in the pre-submission form the choice to have the performance evaluation performed by an independent laboratory selected

by the manufacturer from the list of prequalification evaluating sites.[2] If this option is chosen, the manufacturer will be responsible for paying the full cost of the performance evaluation (in addition to paying the applicable prequalification assessment fee) and for coordinating the performance evaluation directly with the evaluating site.

Regardless of the option chosen, the performance evaluation must be carried out in accordance with a publicly available WHO protocol developed in collaboration with international experts.
WHO will have absolute, exclusive, unfettered control over the manner in which the prequalification assessment process is carried out (including the performance evaluation and/or the publication of results of the prequalification assessment, regardless of the outcome).
A summary of the performance evaluation report/findings will be included in the WHO Prequalification Public Report (WHOPAR), if the product successfully meets the WHO prequalification requirements.

Irrespective of whether the product meets WHO prequalification requirements, a summary of the performance evaluation report may be published in a WHO composite report as part of the WHO technical series on the performance and operational characteristics of commercially available IVDs.
If the product fails to meet WHO prequalification acceptance criteria for performance evaluations, the application will be cancelled.

### *6.2.6. Labelling review*

The Instructions for use (IFU) version, labels and information intended for the end-user of the product which is submitted with the pre-submission form will be considered during the abridged prequalification assessment. The manufacturer must obtain WHO's written agreement prior to implementing any changes to this version of the labelling, otherwise, the application may be cancelled.

The product labelling will be reviewed as part of the pre-submission form, product dossier, performance evaluation and inspection of manufacturing site(s). The IFU is reviewed for clarity, correctness, consistency with the information submitted in the technical documentation and with international guidance and requirements, and suitability for the target user group in WHO Member States. The overall feedback on the labelling review will be provided to the manufacturer after all abridged prequalification assessment components have been completed. If requested by WHO, the manufacturer must amend the labelling before the product can be prequalified.

The agreed-upon product labelling will be included in the prequalification WHOPAR.

### *6.2.7. Prequalification decision*

WHO will determine whether the product meets the WHO prequalification requirements and can be included in the WHO list of prequalified IVDs. The decision to include the product in the WHO list of prequalified IVDs is made based upon information available to WHO at the time of the prequalification assessment, including information obtained as a result of the outcomes of the product dossier review, manufacturing site(s) inspection, the performance evaluation findings and the labelling review. This decision is subject to change on the basis of new information that may become available to WHO.

[2] The *List of WHO prequalification evaluating laboratories* is available at: https://extranet.who.int/pqweb/vitro-diagnostics/performance-evaluation-laboratories

### *6.2.8. Cancellation of Application*

If the manufacturer fails to meet WHO prequalification requirements or fails to provide any information or evidence requested by WHO within the specified time periods, or if any of the other situations outlined in Section 10.3 (Cancellation of application) of the document "*Overview of the WHO prequalification of in vitro diagnostics assessment"* document PQDx_007 occur, WHO reserves the right to cancel the manufacturer's application for prequalification of its product.

## 7. Relevant documents

This document must be read and understood in conjunction with other relevant documents of the In Vitro Diagnostic Assessment Team[3] including, without limitation, the following:

- Overview of the WHO prequalification of in vitro diagnostics assessment: Document PQDx_007
- Instructions for completion of the pre-submission form: Document PQDx_017
- Pre-submission form: Document PQDx_015
- Product dossier checklist: Document PQDx_049
- Instructions for compilation of a product dossier – IMDRF ToC: Document PQDx_018
- Information for manufacturers on the inspection of manufacturing site(s) (assessment of the quality management system): Document PQDx_014
- Labelling review for prequalification assessment: Document PQDx_361.

[3] Documents can be accessed through the WHO website: https://extranet.who.int/prequal/vitro-diagnostics/what-we-do

## Annex 1: Abridged product dossier and information package requirements

| Abridged product dossier content requirements |
|---|
| **1. ADMINISTRATIVE** |
| **1.1 Cover letter** |
| **1.2 Submission table of contents** |
| **1.3 List of terms/Acronyms** |
| **1.4 Application form/Administrative information** |
| **1.5 Listing of device(s)** |
| **1.6 QMS or other regulatory certificates** |
| **1.7 Free sale certificate/Certificate of marketing authorisation** |
| **1.8 User fees** |
| **1.12 Statements, Certifications, Declarations of conformity** |
| **2. SUBMISSION CONTEXT (Product Information)** |
| **2.4 Device description** |
| *2.4.1 Comprehensive device description and principle of operation* |
| **2.5 Indications for use and/or intended use** |
| *2.5.1 Intended use; Intended purpose; Intended user; Indications for use* |
| *2.5.2 Intended environment/setting for use* |
| **2.6 Global market history/(Commercial History)** |
| *2.6.1 Global market history* |
| *2.6.4 Evaluation/inspection reports* issued by the Recognized SRA, if available |
| **2.7 Other submission context information** |
| *2.7.1 Global prices* |
| **3. Analytical performance and other evidence** |
| **3.2 Risk management** |
| **3.5 Analytical performance** |
| 3.5.4.2 Precision of measurement (repeatability and reproducibility) - *If applicable, studies to establish repeatability undertaken by non-laboratory personnel are provided* (Note: *Precision in the hands of end users may be appraised by the manufacturer in the clinical studies, and thus may not be included in the analytical studies).* |
| **3.6 Other studies** |
| *3.6.4 Usability/Human factors* |
| *3.6.5 Stability of the IVD* |
| *3.6.5.1 Claimed shelf life* |
| *3.6.5.2 In-use stability* |
| *3.6.5.3 Shipping stability* |
| **5 LABELLING AND PROMOTIONAL MATERIAL** |
| **5.2 Product/package labels** |
| **5.3 Package insert/Instructions for use** |
| **5.6 Technical/operators manual** |
| **5.8 Other labelling and promotional materials** |

**Information package contents:**

| Element | Required documents for the manufacturing site(s) inspection |
|---|---|
| Quality Management System | |
| | Quality manual including staff organogram |
| | List of current quality management procedures |
| | Standard operating procedures for: |
| | ○ Complaint handling and vigilance |
| | ○ Control of nonconforming goods/processes |
| | ○ Change control/change notifications (product and processes) |
| | ○ Risk management |
| | ○ Supplier evaluation and control, verification of purchased product |
| | ○ Design and development |
| | Audit report of the most recent full regulatory inspection/audit and all subsequent surveillance inspections/audits |
| | Any valid quality management system certificate(s) (e.g. ISO 13485) |
| | Name and contact details of the responsible person at the site of manufacture regarding the inspection |
| Product | |
| | Labelling (instructions for use (IFU), component labels and box labels) |
| | Photographs of kit, box including contents, kit components |
| | Accessories (including photographs) |
| | Copy of current product regulatory approval certificate(s) |
| | Summary of changes initiated or applied to the product subsequent to the above regulatory approvals |
| Manufacturing | |
| | Full address, including latitude and longitude of the manufacturing facility(s) |
| | Site floor plan |
| | Manufacturing flowchart including in-process control points |
| | List of critical raw materials (including details of the supplier of each material) |
| | List of outsourced processes with direct product impact (e.g. outsourced manufacturing of components (conjugated antibodies, strips, reagents, outsourced laboratory testing, packaging, printing, etc.) including details of the supplier for each process |