Q & A

CHANGE REQUEST FOR WHO PREQUALIFIED and EMERGENCY USE LISTED IN VITRO DIAGNOSTICS

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This document is only applicable for reportable changes to WHO prequalified and emergency use listed in vitro diagnostic products. See WHO document *Reportable Changes to WHO Prequalified & Emergency Use Listed In Vitro diagnostics* (PQDx_121).

Introduction

WHO is committed to supporting manufacturers in their efforts to maintain high-quality, safe, and effective diagnostic products. This Q&A document is intended to assist manufacturers in understanding WHO's expectations for their post-prequalification change applications for WHO-prequalified or EUL-listed in vitro diagnostics and medical devices.

The guidance provided herein is applicable only when the described scenarios are accurate and the associated risk assessments have been properly and comprehensively conducted. While the examples offer general guidance, they are only illustrative and cannot replace a thorough, product-specific risk assessment of each change.

Manufacturers are expected to apply their established risk assessment procedures as part of their quality management system, in accordance with the principles outlined in the WHO guidance document PQDx_121: Reportable Changes for Prequalified IVDs. The responsibility for evaluating, documenting, and reporting changes remains solely with the manufacturer.

Q1. What is the expected target time for the assessment of change requests?
Please refer to the WHO guidance "Prequalification assessment and change assessment target deadlines" (PQDx_300), available at: https://extranet.who.int/prequal/vitro-diagnostics/prequalification-guidance.

Q2. What is the expected timeline from submission to acceptance for a low-impact change?
Please refer to change request screening timelines in the WHO guidance "Prequalification assessment and change assessment target deadlines" (PQDx_300), available at: https://extranet.who.int/prequal/vitro-diagnostics/prequalification-guidance

Q3. Do I need to an electronic copy of the change request on CD/DVD or upload to the Diagnostics Inbox on Dropbox?
No. As of 1 June 2025 all applications should be done via the ePQS Portal, available at: https://extranet.who.int/prequal/epqs/epqs-portal

Q4. Are there special provisions for urgent changes - e.g., switching of a supplier due to unforeseen circumstances?
Exceptions are possible but limited and will be evaluated on a case-by-case basis.

Q5. Does approval of a change by a designated EU Notified Body meet the requirement of being an "NRA" in the context of abridged change assessments?
Yes. Provided the approval covers the considered change.

Q6. What provisions are in place for changes that may be considered moderate/high impact by the guidance, but the changes are not typically sent to NRAs- e.g. change in a supplier for a WHO-EUL device which has US FDA EUA clearance but typically only used for WHO?

If the product is WHO prequalified or EUL-listed, the manufacturer should follow the WHO provisions given in the reportable change guidance document *PQDx_121* under which such changes will be assessed by WHO.

Q7. If the change is approved by a designated EU Notified Body, does it get 'downgraded' to a low-impact change?

No. If the Change is approved by a Notified Body and/or other recognized NRA, the change can be considered for an abridged assessment. Nonetheless, the categorisation of changes should fulfil the guidance criteria independently of a previous regulatory approval.

Q8. Do you apply regulatory reliance?

Yes. If the manufacturer can provide objective evidence that the exact same proposed high/moderate impact change has previously undergone stringent assessment by a recognized National Regulatory Authority (NRA), as defined in *PQDx_173_Abridged prequalification assessment: prequalification of in vitro diagnostics (Section 6.1)*, the change request will be eligible for the abridged assessment pathway.

Q9. Should Change Requests eligible for an abridged assessment be submitted to WHO once the approval from authority is obtained?

It is under the manufacturer's responsibility to plan the change implementation, including the timing of submission to WHO. However, an abridged assessment can only be considered in cases where the manufacturer provides objective and sufficient evidence that the same change has been reviewed and approved by the recognized NRA.

Q10. Is the post PQ change abridged assessment applicable for both cases of prequalification dossier assessment (full or abridged assessment)?

Yes. The change request abridged assessment can be considered in all situations where the eligibility criteria are met, regardless of the initial PQ dossier assessment pathway.

Q11. How to decide whether a change's impact is high or moderate based on risk classification criteria?

The definitions of high/moderate and low-impact changes in the guidance are based on the potential impact of a change on the quality, function, performance, usability, safety, or the information provided with a prequalified or EUL-listed IVD. Manufacturers are expected to follow their established risk assessment framework, under their quality management system (QMS) to conduct a proper risk assessment of changes, following the principles outlined in the guidance. Examples of low-impact and high/moderate-impact changes are provided in the Appendix 1 of *PQDx_121* Guidance document.

Q12. Should minor changes in labelling be reported?

Yes. Change in the labelling or information mentioned in the WHO Public Report should be reported as they are used by procurers and stakeholders to make informed procurement

decisions. If a manufacturer modifies information provided on the packaging design or labels without notifying WHO, the public report will not be updated to reflect these changes. As a result, procurers may reject the product, assuming it is different from the prequalified or EUL-listed version.

Q13. When should changes be reported to WHO?

Submission of reportable changes to WHO and approval by WHO should occur prior to the release of the modified prequalified product, or any prequalified product manufactured under the modified conditions is placed on the market. A product that has undergone change without WHO prior approval would no longer be considered prequalified.

Q14. Is providing a quarter timepoint in the change planning acceptable?

Yes, this is acceptable. If a date is provided like e.g., Q2 2025, WHO will consider a timetable as of 30 June 2025.

Q15. Is it acceptable to have a grouping approach based on risk/manufacturability or is the requirement that it be one plan/report per product?

Yes. It can be accepted, provided that adequate information, justification and risk assessment is provided.

Q16. Are changes to second source suppliers reportable?

Changes conducted to second source suppliers of critical materials or processes should follow the same criteria defined for primary sources, as in *PQDx_121 Guidance document*. Furthermore, the need for informing about changes downstream shall be part of the quality agreement between manufacturer and critical suppliers as applicable.

Q17. Do new kit configurations and new product codes or catalogue numbers of a Prequalified or EUL listed IVDs need to be reported?

Yes. Only product codes and configurations specified in the prequalification/EUL Letter of Agreement, as well as in the List of WHO prequalified or EUL-listed IVDs are approved. Therefore, any addition of new product codes or kit configurations should be reported to WHO for approval.

Q18. Is introducing a similar nitrocellulose membrane and/or active ingredients from a new supplier considered a reportable change or a new product?

Manufacturers are expected to follow their established risk assessment framework under their quality management system, including design change procedure, and conduct a proper risk assessment of all changes, following the principles outlined in *PQDx_121 Guidance document*.

In general, WHO PQ team would consider that introducing a similar NC membrane from a new supplier as a reportable change rather than a new product, provided that no change in design or technology is introduced.

On the other hand, the introduction, or a change in active ingredients, e.g., a change in the number, type, specifications or attributes of capture antibodies or antigens (test line) are

likely to be considered as a new product. However, change in the active ingredient of a control line is likely to be considered as a reportable change.

In case of doubts, the manufacturer should seek guidance by contacting the WHO Prequalification team.

Q19. Is it a reportable change to introduce a new type of desiccant (e.g., Molecular Sieve, Clay, Activated Alumina) and/or changes to the weight of the desiccant, specimen transfer device/dropper, or aluminium/foil pouch?

Yes. The mentioned changes are reportable.

Q20. Are changes relevant to the pouch, packing material or the packing material supplier, to be reported to WHO?

Manufacturers are expected to follow their established risk assessment framework under their quality management system to conduct a proper risk assessment of all changes, following the principles outlined in PQDx_121 Guidance document.
In general, WHO would consider that:

- Changes in primary packaging (e.g., pouches, reagent bottles, etc.) are reportable as they affect the design of the product and would be considered in general moderate/high risk.
- Changes of suppliers of secondary packaging where there are no changes in the design of packaging are in general non-reportable and should be managed through the QMS of the manufacturer solely for their implementation. However, they become reportable if the manufacturer identifies potential new risks to the product.

Q21. Is the introduction of a new supplier for specimen transfer device/dropper, with the same specifications and quality standards a reportable change?

WHO would consider in general that a change in the supplier of a dropper is reportable if there is a change of manufacturer, reference, or product code or changes on accessories' labelling.
In case where the change is limited to a same material's distribution network (i.e., if the distributor changes and not the manufacturer of the accessory), this would not be considered reportable and should be managed within the manufacturer's QMS only.

Q22. Is the introduction of a new supplier for the desiccant with the same specifications and quality standards a reportable change?

The introduction of a new supplier for the desiccant, provided that the new desiccant has the same specifications and attributes and does not impact the labelling of the accessory, is not considered reportable and should be managed within the manufacturer's QMS solely. However, it would become reportable if the manufacturer identifies potential new risks to the product.

Q23. Do changes related to associated instruments need to be submitted?

The manufacturer should determine on a risk-based principle, whether the changes could affect the performance or intended use of the IVD, in line with the principles outlined in the PQDx_121 Guidance Document.

Based on these principles, in general, the following changes may be reportable:

- Change to the claimed instruments, automation process, including change or replacement by a new smaller/larger model or the change from a manual procedure to an automated procedure and associated instruments
- Changes in instrument compatibility (e.g., newly supported or obsolete platforms)
- Introduction of accessory components that interact with the IVD (e.g., new sample handling modules or readers)
- Modifications to calibration or maintenance or cleaning procedures that could affect test reliability or performance.
- Software or hardware updates to the instrument that could influence test accuracy, reliability, or user interface, or test protocol
- Change to interpretation algorithm(s) or software or modification that could impact performance or the assay cut off.
- Other changes to the instrument that would impact the test safety or performance.
- Where in general the instruments, by themselves, are not prequalified, so the following change are not reportable:
- Changes on their labelling and/or IFU (operation manual) as they are not included in the public report
- Change to their manufacturing process or facility.

Q24. Is having translations of the Prequalified English IFU a reportable change?

Yes, as it may require a change in the WHO public report. Refer to the reportable changes webpage for additional guidance: https://extranet.who.int/prequal/vitro-diagnostics/reportable-changes.

Q25. Will eCTD be implemented for IVD dossiers? Can different dossiers be submitted during a single login session?

eCTD does not apply to IVDs, only for medicines and vaccines prequalification. You can access the ePQS portal from this link: https://extranet.who.int/prequal/epqs/epqs-portal. The user can add more than one submission per login.

Q26. Will pre-notifications of upcoming changes (in order to plan assessment time) still be accepted via e-mail or is there also a space on the ePQS?

Manufacturers are welcome to inform WHO of potential changes via email diagnostics@who.int. However, the official change request assessment process is only initiated once a change request application is submitted through the ePQS portal and accepted by the WHO for review.

Q27. If the " implementation date" stated at the time of WHO change notification submission has already passed, but the WHO is still reviewing the change (assuming that all preparations for the implementation have been completed), can the manufacturer proceed with the implementation of the change? Or are there any specific actions that should be taken in this situation?

The manufacturing can start, but the change can only be implemented (changed products released to the market) after WHO approval.

Q28. Are ePQS portal credentials provided to each manufacturer?

Yes, with the two official contacts for the manufacturer included. Manufacturers should ensure that the contact details in the ePQS portal is correct. For further questions about the ePQS portal, please check the following webpage: https://extranet.who.int/prequal/epqs/epqs-portal

Please email diagnostics@who.int if you are unable to login or there is no record for your company.

Q29. In the portal, after successful submission of CR in Documents upload section, we are not receiving any confirmation mail or auto generated mail from WHO. How to confirm the submission of CR is done successfully?

Manufacturers will continue to receive an email from WHO confirming receipt of a submission along with invoice for the submission, if applicable. If you do not receive a confirmation email, please contact WHO to ensure your submission has been received.

Q30. As EU regulation MDR change, such as lancet, supplier change the label, but lancet itself has no change, is it reportable change?

Yes. Any change to the WHO public report, including component labels, is a reportable change. Refer to the reportable changes' webpage for additional details: https://extranet.who.int/prequal/vitro-diagnostics/reportable-changes.

Q31. Is there a specific period for CR applications in a calendar year.

Manufacturers can submit change request applications at any time.

Q32. What is the cost of the assessment fee?

WHO charges a nonrefundable fee of US$ 3,000 only for technical or abbreviated review. No fee is charged for administrative or EUL changes. More information regarding submission fees can be found in *PQDx_299*: *Prequalification fees: WHO prequalification of in vitro diagnostics* guidance document.

Q33. Are the responses submitted in Round 2 or Round 3 reviewed in the next assessment session?

Responses from manufacturers and aadditional information can be reviewed by WHO between assessment sessions. However, responses submitted close to the date of the bimonthly assessment sessions may be reviewed during the following session.

Q34. Is it possible to have multiple persons connected to the e-portal, for one manufacturer?

Yes. We recommend that manufacturers have at least two contacts included. For more information on ePQS, please see the following link about the ePQS portal: https://extranet.who.int/prequal/epqs/epqs-portal

Q35. Is it a reportable change if we change the supplier of nitrocellulose membrane for RDT kit? Or a new Prequalification or EUL application is needed?

In general, WHO PQ team would consider that introducing a similar NC membrane from a new supplier as a reportable change rather than a new product, provided that no change in design or technology is introduced. Please refer to the reportable changes for more detailed guidance: https://extranet.who.int/prequal/vitro-diagnostics/reportable-changes. If there are additional questions, please email diagnostics@who.int.

Q36. Is there a transition time from the old to the new guidance?

As of 1 June 2025, all manufacturers should submit change request applications solely in accordance with the new guidance and using the new submission form.

Q37. Is the portal also to be used to report changes for EUL products?

Yes. Changes to EUL-listed products should be submitted through the ePQS portal.

Q38. Do we need to submit changes just to fix a single typo in IFU?

Yes, but only if the typo affects information provided in the WHO public report. Any change to the WHO public report is a reportable change. Refer to the reportable changes for additional details: https://extranet.who.int/prequal/vitro-diagnostics/reportable-changes

Q39. Can we submit both low-impact and high impact change together?

Changes that are related to each other can be included into a single submission. In case of doubt, and to determine whether change applications can be grouped, manufacturers are encouraged to seek guidance by contacting the WHO Prequalification Team (diagnostics@who.int).

Q40. What type of change would trigger a WHO inspection?

Inspection Services review (desk review and if necessary onsite inspection) may be needed to ensure appropriate QMS implementation of the manufacturer of a PQ product. Changes in the manufacturing process may trigger an inspection, such as physical move/relocation of manufacturing site(s) or introduction of a new manufacturing site.

For the approval, a change application must be submitted with all relevant descriptions and supporting evidence. INS Services will review the submission and determine whether the information is sufficient to approve the change or if an on-site inspection is required. This outcome will be detailed in the WHO change decision letter.

The manufacturer is also advised to inform WHO in advance of such changes by contacting the WHO Prequalification team (diagnostics@who.int).