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World Health Organization

Technical Specifications Series for submission to WHO Prequalification – Diagnostic Assessment

TSS-4 In vitro diagnostic medical devices (IVDs) used for the detection of high-risk human papillomavirus (HPV) genotypes in cervical cancer screening

Technical Specifications Series for submission to WHO Prequalification – Diagnostic Assessment: In vitro diagnostic medical devices (IVDs) used for the detection of high-risk human papillomavirus (HPV) genotypes in cervical cancer screening

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The draft technical specifications document was posted on the WHO website for public consultation on 18 September 2017 for a 2-month commenting period. Various stakeholders, including manufacturers submitting to WHO Prequalification of IVDs, IVD manufacturing industry associations, various national and international regulatory bodies, and IVD standards organizations were informed of the consultation in order to solicit feedback.

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Abbreviations

ANOVA	analysis of variance
CIN	cervical intraepithelial neoplasia
HPV	human papillomavirus
IFU	instructions for use
IVD	in vitro diagnostic medical device
IU	international units
POC	point of care
ROC	receiver operated curve
spp.	species
TSS	Technical Specifications Series
US FDA	U.S. Food and Drug Administration
v/v	volume per volume
WHO	World Health Organization
w/v	weight per volume

A. Introduction

The purpose of this document is to provide technical guidance to in vitro diagnostic medical device (IVD) manufacturers that intend to seek WHO Prequalification of tests for the detection of human papillomavirus (HPV). This document is relevant to IVDs that detect HPV genotypes that are associated with cervical cancer *(1)*. Although this does not exclude those IVDs that may claim to detect other HPV associated cancers (e.g. anal cancer), IVDs will only be prequalified on the basis of evidence that pertains specifically to detection of HPV types associated with *cervical* cancer.

For the purpose of this document, the verbal forms used follow the usage described below:

- "shall" indicates that the manufacturer is required to comply with the technical specifications.
- "should" indicates that the manufacturer is recommended to comply with the technical specifications but it is not a requirement.
- "may" indicates that the technical specifications are a suggested method to undertake the testing but it is not a requirement.

A documented justification and rationale shall be provided by the manufacturer when the WHO Prequalification submission does not comply with the required technical specifications outlined in this document.

Minimum performance requirements for WHO Prequalification are summarized in this document, and where possible, are aligned with published guidance, standards and/or regulatory documents. Although references to source documents are provided, in some cases WHO Prequalification has additional requirements. A full list of the individual studies is provided in Section D.

- Part 1 lists the analytical studies that are required to assess the ability of the IVD to measure the relevant analyte(s).
- Part 2 lists the clinical studies that are required to support the clinical performance of an IVD, and demonstrate that reasonable steps have been taken to ensure that a properly manufactured IVD, being correctly operated in the hands of the intended user, will detect the target analyte and fulfil its indications for use.

Clinical utility studies, i.e. the effectiveness and/or benefits of an IVD, relative to and/or

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