AT THE CORE of Quality

WHITE PAPER

High-Risk HPV Quality Controls are Needed to Uphold Clinical Laboratory Quality Standards

1. Scope

In the 1940s, the Pap Smear was introduced in clinic and quickly became the gold standard for cervical cancer screening in women. Unfortunately, at the time, the lack of acceptable quality standards and negligence in cytology laboratories gave rise to a significant number of misdiagnoses, alleged decreased life expectancy claims, and death[1]. These errors provoked the implementation of Clinical Laboratory Improvement Act (CLIA) in 1967 to introduce clinical laboratory regulations, and a second amendment in 1988 to hold hospital laboratories, independent laboratories, physician offices, and nursing homes accountable for these new standards[2].

As we enter a new era of cervical cancer screening, where Human Papillomavirus (HPV) extended genotyping diagnostic panels are becoming (if not already) a primary test method in clinic, it is critical to uphold quality standards to avoid reliving the malpractices that occurred in the past. Good quality assessment products should be used in conjunction with HPV extended genotyping panels to ensure proper assay verification/validation, laboratory personnel training, and regular quality control.

2. What Makes a Good Control

A reliable quality control should simulate the patient specimen and contain inactivated whole-genome/native pathogens in order to capture all possible assay targets. Using patient specimens as quality controls can be problematic because the samples have high variability and potential interference agents that can impact test reproducibility. Positive patient samples for uncommon high-risk HPV types may also not be easily accessible. Additionally, most synthetic and cell line-derived controls only contain a subset of possible HPV assay targets making them incompatible with certain HPV test platforms.

3. The Benefit of HPV Multiplex Controls

According to CAP and other accreditation bodies, molecular assays that simultaneously detect multiple pathogens/gene targets require the use of quality controls to ensure that all assay targets are properly detected[3]. Using a single control that contains all HPV assay targets is not recommended as the control cannot flag assay cross-reactivity. Instead, smaller multiplex formulations which contain a few high-risk HPV types are more advantageous as these samples behave as positive controls for certain assay channels while acting as negative controls for others. Furthermore, these samples provide laboratories with an economical solution to evaluate all assay targets rather than using multiple single analyte samples.

4. How Often Should Laboratories Run HPV Controls?

While ISO 15189, CLIA, and other regulatory guidelines mandate regular quality control, it is up to the laboratory manager to establish how frequently controls are run. Key opinion leaders typically recommend that external controls are run at least once a day (but preferably with each run) for high throughput instruments[4].

5. Microbix's HPV Controls

- Inactivated whole-genome samples that contain all common assay targets (E1, E6, E7, L1), episomal and integrated viral DNA, viral RNA, and proteins.
- Cross-platform compatible (verified with laboratory developed and commercial tests)
- Formulated in PreservCyt; stored at 2-8°C; 1-year shelf-life.
- Single and multiplex samples available
- Reference **Table 1**

MICROBIX

Microbix's HPV Controls and Samples

Product	REDx™	PROCEEDx™
HPV16 Positive	RED-62-16	VP-62-16
HPV18 Positive	RED-62-18	VP-62-18
HPV31 Positive		VP-62-31
HPV33 Positive		VP-62-33
HPV39 Positive		VP-62-39
HPV45 Positive	RED-62-45	VP-62-45
HPV51 Positive		VP-62-51
HPV52 Positive		VP-62-52
HPV66 Positive		VP-62-66
HPV67 Positive (high-risk negative)		VP-62-67
STI Negative	RED-99-M1	VP-99-M1
HPV16/18/45 Positive		VP-62-M1
HPV39/51/52 Positive		VP-62-M2
HPV31/33/66 Positive		Coming Soon

Table 1: HPV Product Catalogue Numbers

Product Line Descriptions

RED™ controls

REDx™ products are unassayed controls used for evaluating laboratory testing performance, procedures and workflow

PROCEED™

PROCEEDx™ products are used for assay verification/validation, training, and R&D purposes. Products are for RESEARCH USE ONLY!

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3. CAP. (2014). (rep.). CAP Accreditation Program - Microbiology Checklist. College of American Pathologists. Retrieved October 7, 2021, from https://webapps.cap.org/apps/docs/education/OnlineCourseContent/2014/TLTM/MIC04212014.PDF.
4. Cuschieri, K., Schuurman, R., & Coughlan, S. (2019). Ensuring quality in cervical screening programmes based on molecular human papillomavirus testing. Cytopathology, 30(3), 273–280. https://doi.org/10.1111/cyt.12679