Supporting documentation for pathology laboratories on handling HPV positivity rates

Purpose

To assist pathology laboratories with the quality assessment process for handling the HPV positivity and unsatisfactory rates under the *National Pathology Accreditation Advisory Council (NPAAC) Requirements for cervical screening (Second edition 2024).*

Background

- The NPAAC Requirements for cervical screening (Second edition 2024) (the Cervical Requirements) came into effect on the 1 February 2025 and replaced the Requirements for Laboratories Reporting Tests for the National Cervical Screening Program (Second Edition 2019). The Cervical Requirements for pathology laboratories relating to the quality assessment process for handling of the HPV positivity and unsatisfactory rates are as follows: Quality management process for handling HPV detection

Pathology laboratories must follow the directions outlined in the Cervical Requirements at **Action 3.02**, **Action 3.05** and **Action 3.06** as detailed below.

- Quality Measures for HPV NAT (applies to all testing settings, including screening, test of cure and self-collected specimens)

> **3.05** The laboratory has procedures to identify, investigate and act when a batch of reagent fails
>
> **3.06** The laboratory notifies the Therapeutic Goods Administration and the National Cervical Screening Program within five business days when a batch of reagent fails, and this failure could impact the quality of testing of other providers

Laboratories **must** notify the NCSP via the Australian Government Department of Health and Aged Care through the NCSROperations@health.gov.au inbox. A notification template that laboratories can complete and submit is provided in **Attachment A.** The template outlines the required information, including the date of reagent batch failure, reagent data (lot numbers and expiry dates) and contact details. The NCSP Clinical Advisory Group will be notified in accordance with the processes under the NCSP Quality Framework (currently under review).

Laboratories **must** also notify the TGA via the medical device Incident Reporting and Investigation Scheme (IRIS) through the following link: Report a medical device adverse event (medical device health professional). All relevant fields within the form must be completed in order for the notification to be accepted.

IRIS is used by the TGA to manage all reports of adverse events or problems associated with medical devices, including in vitro diagnostics. Reports are automatically entered into the publicly searchable Database of Adverse Event Notifications (DAEN). Batch related failures may result in a recall action which would be initiated by the supplier of the product in conjunction with the TGA.

The TGA and NCSP must be notified within five business days when a batch of reagent fails, and this failure could impact the quality of testing of other providers.

Quality Measures for HPV NAT, screening specimens only

> ***3.02*** *The laboratory has processes to review its Human Papillomavirus 16, 18 and non 16 or 18 detection rates at least quarterly and:*
>
> - Monitor the positivity rate and the unsatisfactory rate for clinician-collected and self-collected specimens
> - Benchmark its rates against current rates reported from the National Cancer Screening Register

Unsatisfactory rate

- The benchmark for unsatisfactory rates for clinician-collected specimens is in line with the numerical standard for Indicator 1 (see **Appendix 1: Program Indicators of the 2024 Cervical Requirements**):

  The percentage of clinician collected laboratory specimens that are reported as unsatisfactory for HPV NAT testing should not exceed 0.5%.

- The unsatisfactory rate for self-collected specimens is for monitoring only, as these are largely influenced by factors outside laboratory control.

Positivity rate

- The positivity rates for clinician-collected and self-collected specimens should be monitored separately.
- If a laboratory's HPV detection rate is found to be outside of the 99% confidence interval from the mean national positivity rate, this may be a result of differences in the age distribution, high-risk population, classification of screening status or other unmeasured factors.
- Laboratories should consider the implementation of internal benchmarks using control charts, such as P-charts, for ongoing monitoring of the laboratory-specific positivity rate. The *Requirements for Testing of Microbial Nucleic Acids*[1] also provides additional advice on operational validation and ongoing monitoring of assays.
- The NCSR will use the routinely submitted data to produce a periodic age stratified data set (including mean and 99% confidence interval), compiled from data from all screening HPV testing throughout Australia.
- If a laboratory's overall HPV positivity rate in screening tests for a particular collection method is not within the 99% confidence interval, the laboratory can investigate the cause as follows:
  - The laboratory should compare its HPV positivity rates for the younger

[1] *Requirements for Medical Testing of Microbial Nucleic Acids (Second Edition 2013)*

vaccine-eligible age cohort (born post-June 30, 1980) and older age cohorts (born pre-June 30,1980) with the most recently available NCSR age-specific rate as described in **Attachment B.**

- If the HPV positivity rate is **within** the 99% confidence interval for the age cohorts, the investigation does not need to proceed.
- If the HPV positivity rate is **not within** the 99% confidence interval for one or more of the age cohorts, laboratories should investigate the device-specific ranges. Device-specific ranges are available by contacting the NCSR through the NCSRreporting@health.telstra.com inbox.
- If the HPV positivity rate is **not within** the device-and assay-specific 99% confidence interval, laboratories should continue the investigation to determine the likely cause of the variance and ensure there has been no failure in quality.

- Monitoring of HPV positivity and investigation, if required, must occur at least quarterly and the results or outcomes of any investigation recorded.

Attachment A

Reagent Batch Failure Notification Form – NCSP Notification

Name and address of pathology laboratory	
Pathology laboratory contact details including responsible Pathologist (phone number and email)	
Date of reported reagent batch failure	
HPV test type (manufacturer and device)	
Reagent batch Lot numbers and expiry date Please list all Lot numbers and expiry dates for any reagents used as part of this batch of tests under the general process categories listed below. Where a reagent is used at multiple steps in the process please repeat under each category.	
1. Control kit	
2. Cellular (LBC) extraction kit	

3. Nucleic acid extraction kit	
4. Amplification kit	
5. Detection kit	
6. Wash buffer	

Attachment B

Comparison of the batch HPV positivity rate to the national reference range

The National Cancer Screening Register (NCSR) will produce overall and stratified national HPV positivity rates which will allow laboratories to assess their own positivity rates against the national average. These rates will be available for both clinician-collected and self-collected specimens.

The national report will include an acceptable reference range above and below the average. An acceptable HPV positivity rate is a rate that falls within this reference range.

As the number of tests included in a batch can affect the width of the reference range, a funnel plot and a table of values will be produced which provides the reference range for each batch volume.

The laboratory can refer to the number of tests in their batch and the observed HPV positivity rate, and identify if this falls outside of the funnel plot reference range. An example funnel plot is provided below in Figure 1.

The most recently available national averages should be used for comparisons. Rates for clinician-collected specimens should be assessed separately from self-collected specimens.

Where to find the national average, funnel plots and tables

The national average and associated tables and funnel plots are made available from the NCSR website at www.ncsr.gov.au.

The overall and stratified national HPV positivity rates, funnel plots and table of reference values as an excel file. Instructions for use will also be available on the website.

How to contact the National Cancer Screening Register regarding the national reference range

Pathology laboratories may email the NCSRreporting@health.telstra.com if there are any issues with accessing the national HPV positivity reference range.

When will the national average be available?

The national average will be calculated monthly and pathology laboratories should use the latest published figure and associated funnel plots for comparison.

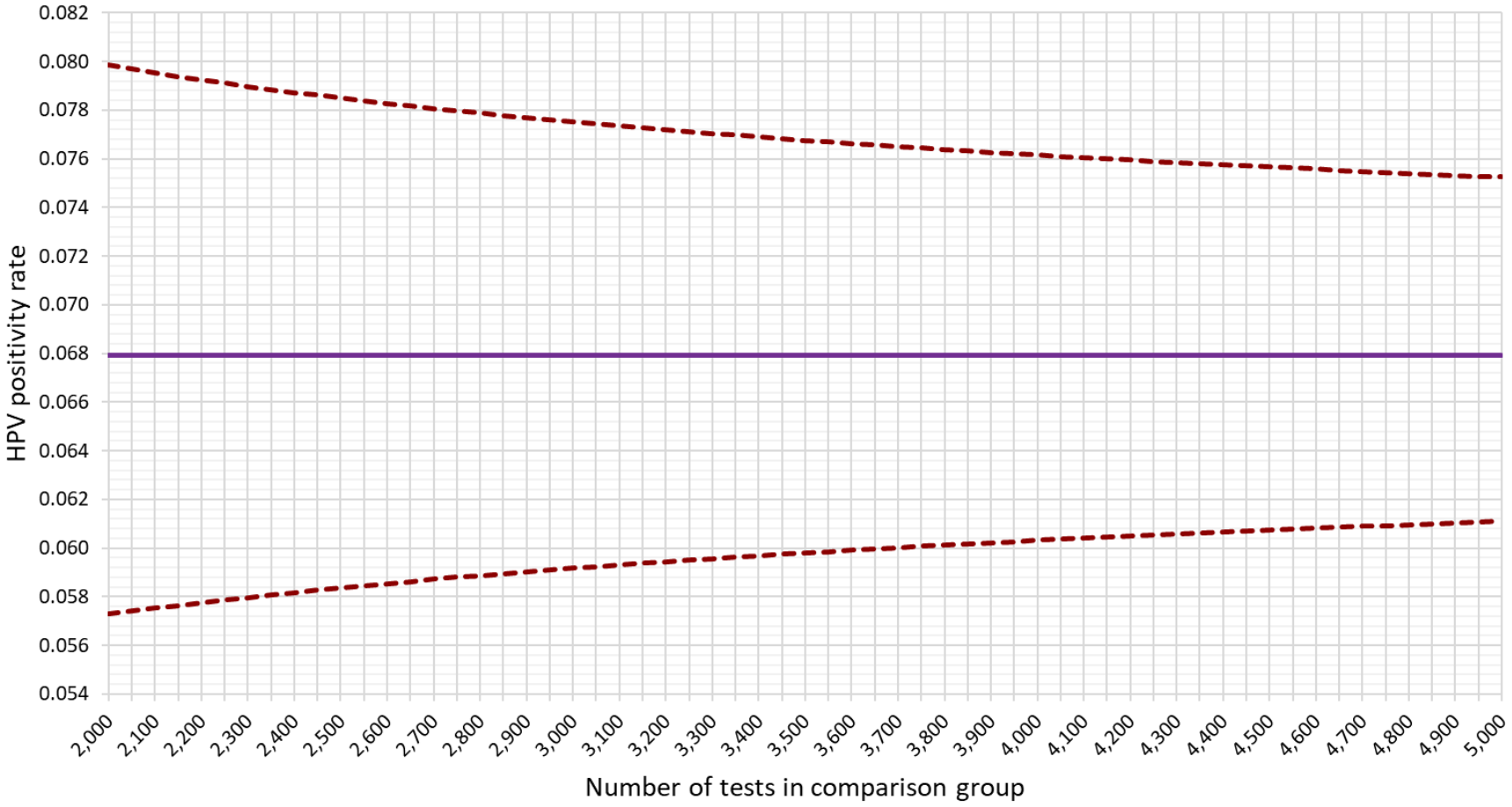

Figure 1: Sample Funnel Plot, National HPV Detection Rate for clinician-collected samples = 0.068 (6.8%)