



A new external quality assessment scheme for molecular detection of human papillomaviruses



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Introduction

Human Papillomavirus (HPV) is a DNA virus that belongs to the family *Papillomaviridae*. There are over 100 genotypes of HPV, of these over 25 can cause genital infections. HPV has been linked to cervical cancer since 1976¹ and declared a human carcinogen by the WHO in 1995². Genital HPV infection is divided into 2 categories: high-risk (oncogenic, cancer-associated) and low-risk (non-oncogenic).

HPV vaccination will be introduced in the UK in September 2008. EU guidelines state that screening will be essential for monitoring the impact of the vaccine and recommend that national authorities continue to improve the quality of their screening programmes³. An external quality assessment (EQA) scheme for HPV DNA testing was developed by the Royal Infirmary of Edinburgh⁴. In collaboration with United Kingdom National External Quality Assessment Service (UK NEQAS), three pilot distributions were dispatched in July 2007, January 2008, and June 2008 each consisting of four cervical specimens in liquid based cytology fluid.

Aim

To analyse the performance of clinical laboratories participating in the pilot scheme for the molecular detection of papillomaviruses, and to assess its value and utility, in order to establish a robust EQA scheme.

Methods

- ❖ From 2007 to 2008, 12 cervical specimens in PreservCyt have been distributed.
- ❖ 8 were positive for high risk HPV genotypes, 4 were negative for high risk HPV genotypes.
- ❖ Results reported by participants for these specimens were analysed to determine concordance between genotypes detected.

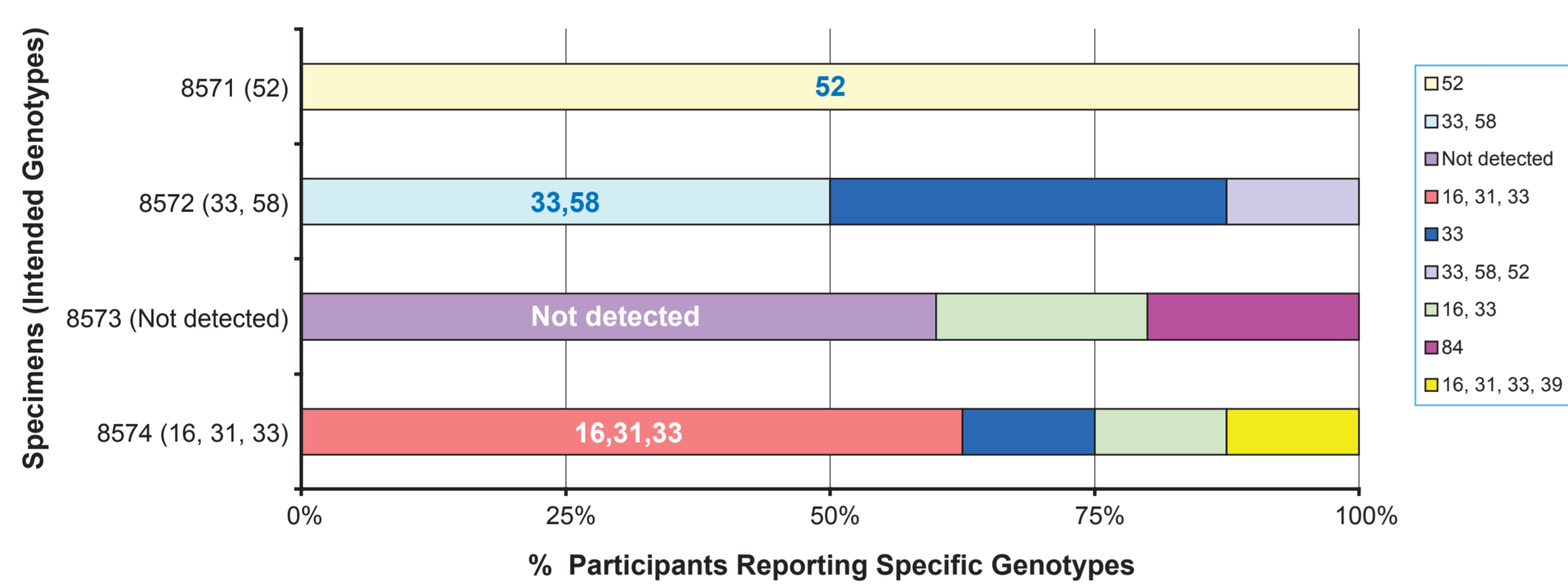
Results

Pre-pilot distribution (July 2007)

The four specimens, sent to 14 laboratories, included two single HPV high risk (HR)-positive specimens, one pooled HPV HR-positive specimen and one pooled HPV HR-negative specimen.

- ❖ 13 responses were received (93%).
- ❖ Performance was good with three out of four specimens showing 92% agreement.
- ❖ Genotyping gave 100% concordance for one specimen containing a single genotype with a variety of typing methods, while differences in genotypes were reported for the remaining specimens (figure 1).

Figure 1. Genotype Combinations Reported for Molecular Detection of Papillomaviruses: Pre-Pilot Distribution July 2007.



First pilot distribution (January 2008)

Four specimens were sent to 59 participants consisting of: one pooled HPV HR-positive specimen, one single HPV HR-positive specimen, one HPV HR-negative specimen and one HPV HR-negative specimen spiked with MRC5 cells.

- ❖ 51 responses were received (86%).
- ❖ Performance was good with 97% of participants reporting correctly on whether or not they detected HR genotypes.
- ❖ However, a wide variety of genotyping results were reported by participants (figure 2) and different combinations of genotypes were not associated with any particular method (data not shown).

Figure 2a. Genotypes Reported for Molecular Detection of Papillomaviruses: Pilot Distribution January 2008.

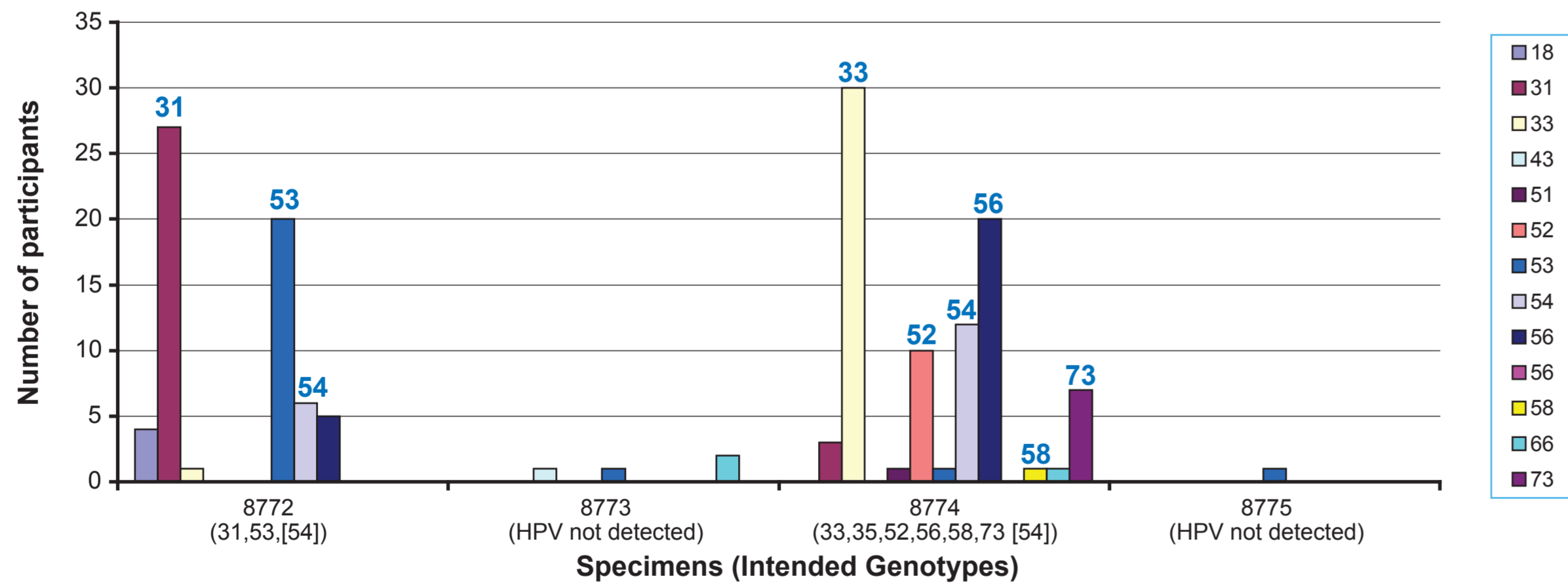
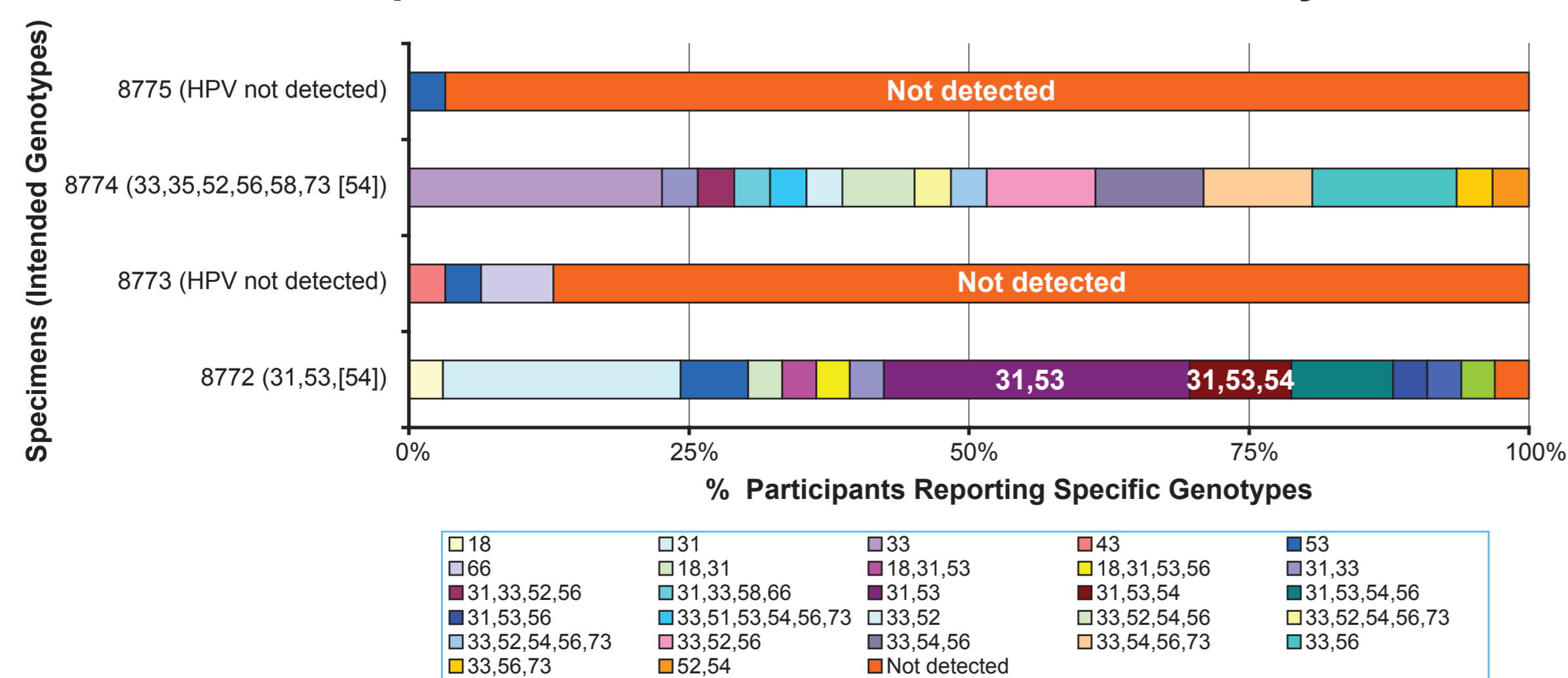


Figure 2b. Genotype Combinations Reported for Molecular Detection of Papillomaviruses: Pilot Distribution January 2008.



Second pilot distribution (June 2008)

Four specimens were sent to 55 participants consisting of: one pooled HPV HR-positive specimen, two single HPV HR-positive specimens, and one pooled HPV HR-negative specimen.

- ❖ 42 responses were received (76%).
- ❖ Performance was good with 92 to 97% of participants reporting correctly on whether or not they detected HR genotypes.
- ❖ Genotyping gave 96% concordance for two specimens containing single HR-genotypes with a variety of typing methods, although other genotypes were also reported as being present in these specimens (figure 3).
- ❖ A wide variety of genotyping results were reported by participants for the remaining specimens (figure 3) and different combinations of genotypes were not associated with any particular method (data not shown).

Figure 3a. Genotypes Reported for Molecular Detection of Papillomaviruses: Pilot Distribution June 2008.

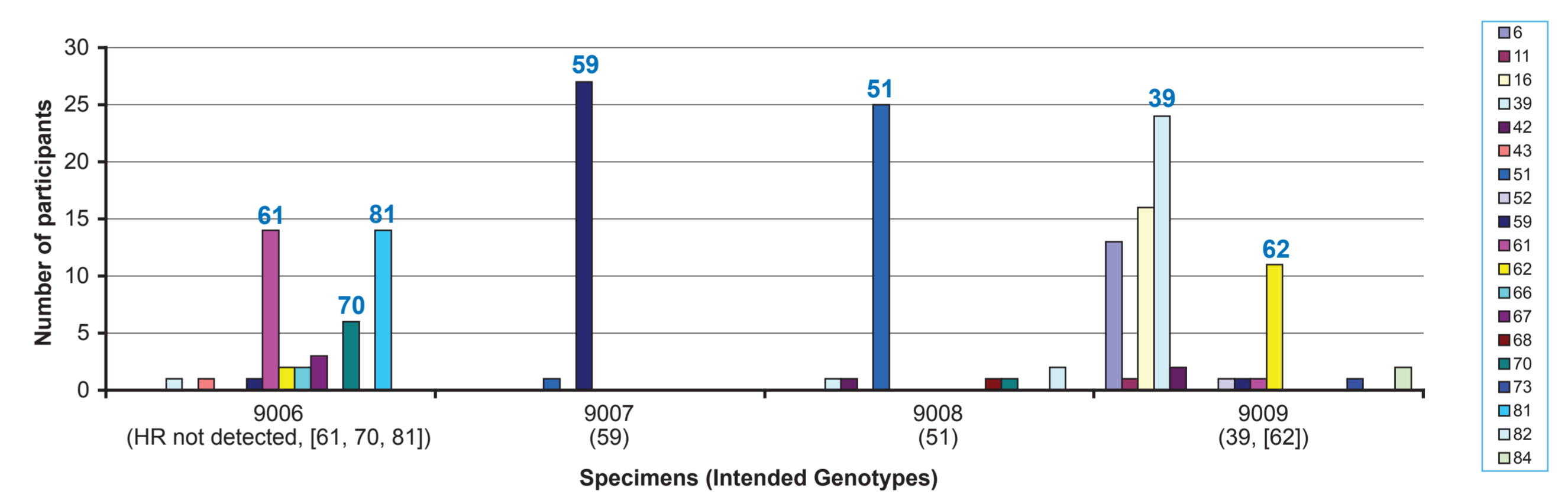
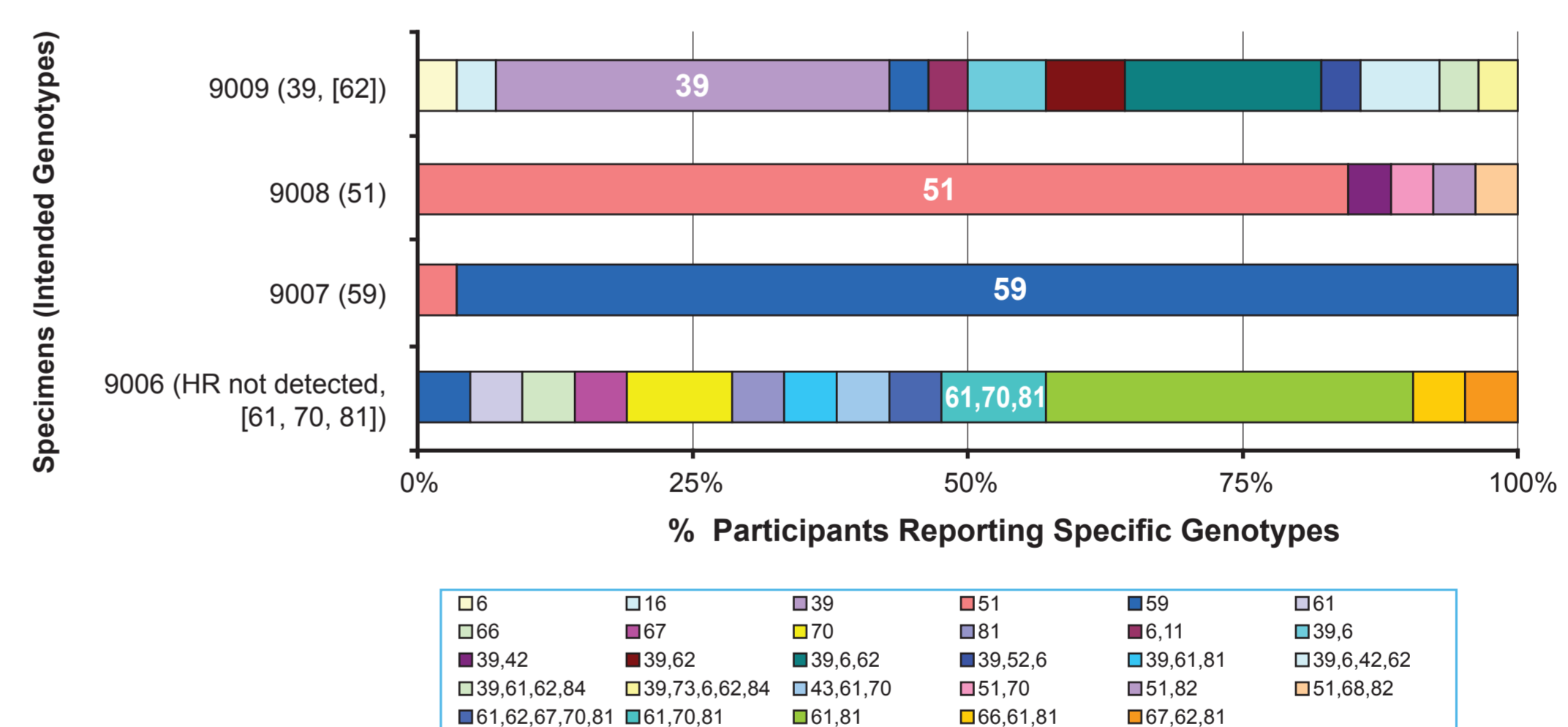


Figure 3b. Genotype Combinations Reported for Molecular Detection of Papillomaviruses: Pilot Distribution June 2008.



Discussion

- ❖ Feedback suggests that the specimens and scheme were relevant to the clinical needs of participants.
- ❖ Specimens distributed to participants were stable and homogeneous.
- ❖ The variety of genotyping results seen, using different methods and between laboratories using the same method, demonstrates the need for an EQA scheme.
- ❖ A third pilot distribution is planned for January 2009.
- ❖ The EQA scheme for the detection of HPV DNA will be available in 2009 and will consist of four specimens distributed three times a year.
- ❖ Robust external quality assessment of Human Papillomavirus molecular screening programmes will be essential for monitoring the impact of the vaccine.

References

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