



STATE OF NEW YORK DEPARTMENT OF HEALTH

Wadsworth Center

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August 25, 2009

Dear Laboratory Director:

This is the summary and evaluation of the graded New York State Proficiency Test for human papilloma virus (HPV) determination. Five vials (HPV016 – HPV020) containing cervical cells in PreservCyt® medium were sent out to every participating laboratory on July 14, 2009, and the due date for the test result was August 3, 2009. A correct answer (one vial) received 20 points, and an incorrect one zero points. Passing the test required a sum of 80 points (80 percent) for the entire test event. Answers could be provided in two categories, positive (pos), negative (neg), or indeterminate (ind) for high risk HPV, and/or for those laboratories performing genotyping, the genotype(s) present.

Results

In this mailing, 64 test sets were sent out, and valid answers were received from 62 laboratories by the due date. Fifty-one laboratories (82 %) used the Hybrid Capture® method, six (10 %) Cervista® (Invader technology), four (6 %) polymerase chain reaction, and one (2 %) in situ hybridization. The results are shown in Table 1. Regardless of the methods used, the consensus was in general excellent. Among the 255 responses obtained by the Hybrid Capture® method, there was a single discrepancy, a positive result instead of a negative, thus suggesting that this result represents an error. The results of the polymerase chain reaction (PCR) method were the least consistent since among the sum of 20 diagnoses 3 (15 %) were discrepant. One was positive when all other results were negative, suggesting a possible contamination. The other two were indeterminate for a positive sample, raising the question of the analytical sensitivity of these homebrew assays. The labs that reported these results should carefully reevaluate the performance of their assays. Finally, all responses by the Cervista and by the in situ hybridization methods were in complete agreement with the overall consensus.

Table 1. Results obtained using Hybrid Capture®, PCR or Cervista methods:

| | HPV016 | HPV017 | HPV018 | HPV019 | HPV020 |
|-----------------------|------------|------------|------------|------------|------------|
| Hybrid Capture | | | | | |
| Total | 51 | 51 | 51 | 51 | 51 |
| Negative | 51 | 0 | 0 | 0 | 50 |
| Positive | 0 | 51 | 51 | 51 | 1 |
| Indeterminate | 0 | 0 | 0 | 0 | 0 |
| | | | | | |
| % Negative | 100.0% | 0.0% | 0.0% | 0.0% | 98.0% |
| % Positive | 0.0% | 100.0% | 100.0% | 100.0% | 2.0% |
| % Indeterminate | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% |
| | | | | | |
| Consensus | NEG | POS | POS | POS | NEG |

| | | | | | |
|------------------|------------|------------|------------|------------|------------|
| PCR | | | | | |
| | <i>POS</i> | POS | POS | <i>IND</i> | NEG |
| | NEG | <i>IND</i> | POS | POS | NEG |
| | NEG | POS | POS | POS | NEG |
| | NEG | POS | POS | POS | NEG |
| | | | | | |
| % Negative | 75.0% | 0.0% | 0.0% | 0.0% | 100.0% |
| % Positive | 25.0% | 75.0% | 100.0% | 75.0% | 0.0% |
| % Indeterminate | 0.0% | 25.0% | 0.0% | 25.0% | 0.0% |
| | | | | | |
| Consensus | NEG | POS | POS | POS | NEG |
| | | | | | |
| Cervista | | | | | |
| Total | 6 | 6 | 6 | 6 | 6 |
| Negative | 6 | 0 | 0 | 0 | 6 |
| Positive | 0 | 6 | 6 | 6 | 0 |
| Indeterminate | 0 | 0 | 0 | 0 | 0 |
| | | | | | |
| % Negative | 100.0% | 0.0% | 0.0% | 0.0% | 100.0% |
| % Positive | 0.0% | 100.0% | 100.0% | 100.0% | 0.0% |
| % Indeterminate | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% |
| | | | | | |
| Consensus | NEG | POS | POS | POS | NEG |
| | | | | | |
| Ventana | | | | | |
| | NEG | POS | POS | POS | NEG |

Genotyping

Laboratories that do determine HPV genotypes were also asked to submit those results (“genotyping”). The methods used for genotyping were diverse, and since the number of laboratories doing it was small, the genotyping results were evaluated only but not graded. In other words, no penalties were imposed because of potential errors in genotyping. Table 2 summarizes the genotyping results.

Table 2. Genotyping results, 8 laboratories:

| HPV016 | HPV017 | HPV018 | HPV019 | HPV020 | Method |
|--------|------------------------------------|--------------------------------|----------------------------|--------|--------|
| NA | 6/11, 16,18/45, 31/35 | 16,18, 45 | 6/11, 16,18/45 | 6/11 | PCR |
| NA | 16, 45, 51/59 | 16,18,31,51/59 | 16,18,39/56,51/59 | NA | PCR |
| NA | 16, 31, 45, 51, 52, 58, 59 | 16, 18, 45, 51 | 16, 18, 45, 51, 52, 59 | NA | PCR |
| NA | 16, 18, 39, 45, 51, 52, 56, 58, 59 | 16, 18, 35, 45, 51, 52, 58, 59 | 16, 18, 35, 45, 51, 58, 59 | NA | PCR |
| UNK | 53, 83, 45, 58, 61, 6 | 18 | (weak signal) | 6 | RFL |
| NA | 45, 52, 83 | 18 | 16, 68 | NA | RFL |
| NA | 16 | 16, 18 | 16, 18 | NA | INV |
| NA | 16 | 18 | 16, 18 | NA | INV |

NA = not applicable, UNK = unknown, INV = Cervista, RFL = PCR followed by restriction fragment length polymorphism determination

Low risk types

It should be noted that only the determination of high risk types of HPV has clinical implications. Testing for low risk types has little clinical value.

Persistence of HPV infections

The persistence of infections with high risk HPVs seems to be important for the development of precancerous or cancerous cervical lesions. However, according to some observations, HPV genotype-specific persistence was no more related to risk of precancer than was repeatedly testing positive for any high risk HPV type (Castle, 2008). If this conclusion will be confirmed, then the exact determination of the genotype in cases of HPV infections will somewhat lose from its importance.

Conclusion

Overall, the results are encouraging, and constitute proof that the laboratories in New York State perform high quality HPV tests.

Tentative schedule for the last New York State HPV proficiency test in 2009:

| Mail-out Date | Due Date |
|----------------------|------------------|
| October 19, 2009 | November 9, 2009 |

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Reference:

Castle PE: Is monitoring of human papilloma virus infection for viral persistence ready for use in cervical cancer screening? Am J Epidemiol 2008; 168: 138 - 144