



STATE OF NEW YORK DEPARTMENT OF HEALTH

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Commissioner

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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 (HPV011 – HPV015) containing cervical cells in PreservCyt® medium were sent out to every participating laboratory on April 14, 2009, and the due date for the test result was May 5, 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. If your laboratory does genotyping only and does not routinely provide an interpretation of the result, it was acceptable to enter NA (not applicable) in the first category. We will clarify this in the instructions for the next PT event.

Results

In this mailing, 58 test sets were sent out, and valid answers were received from 55 laboratories by the due date. Among the 54 laboratories reporting pos, neg or ind, 49 (91%) used Hybrid Capture®, 2 (4%) PCR, and 3 (6%) Cervista® (Invader technology). One laboratory performed only genotyping and did not provide an interpretation, in accordance with their standard practice. As shown in Table 1, for samples HPV012 - HPV015 there was excellent consensus by Hybrid Capture®. Among the 196 valid answers, only 5 (2.5 %) did not agree with the consensus and were therefore graded as incorrect. In contrast, there were some disagreements between laboratories using one of the other two methods (PCR or Cervista®). However, because of the low number of answers, it is not possible to draw any further conclusions about these methods.

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

	HPV011	HPV012	HPV013	HPV014	HPV015
Hybrid Capture					
Total	49	49	49	49	49
Negative	23	45	0	0	48
Positive	16	2	49	49	0
Indeterminate	10	2	0	0	1
% Negative	46.9%	91.8%	0.0%	0.0%	98.0%
% Positive	32.7%	4.1%	100.0%	100.0%	0.0%
% Indeterminate	20.4%	4.1%	0.0%	0.0%	2.0%
Consensus	NA	NEG	POS	POS	NEG

	HPV011	HPV012	HPV013	HPV014	HPV015
PCR					
	POS	POS	POS	POS	NEG
	NEG	NEG	POS	POS	NEG
Cervista					
	NEG	POS	POS	POS	POS
	NEG	NEG	POS	POS	NEG
	NEG	NEG	POS	POS	NEG

Results for specimen HPV011 are contradictory and therefore upgradeable. Every laboratory will therefore receive 20 points for this specimen. The cause of the variation of results in this sample is not clear. However, one of the genotyping laboratories detected a weak HPV16 signal, suggesting that this sample may have been borderline positive for this genotype.

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. Also, the passing rate was not affected if genotyping results were submitted without qualifying the HPV types as “high risk” or “low risk”. Table 2 summarizes the genotyping results. While it is difficult to draw firm conclusions from the limited number of results submitted and also because of the multitude of genotypes detected in HPV013 and HPV014, it seems that both positive samples contained HPV16 and possibly 18, though there was less consensus about the latter. These results are not unexpected given the fact that the number of types detected varies by individual method.

Table 2. Genotyping results, 8 laboratories:

HPV011	HPV012	HPV013	HPV014	HPV015	Method
NA	NA	16,31,35/68,39/56,51/59	16,18,31,39/56,51/59,52/58,6/11	NA	PCR
NA	6/11	6/11, 16,18/45,31/33/35/39	6/11, 16,31/33/35/39	6/11	PCR
NA	NA	16,18,51,59	16,18,51,58,59	NA	PCR
NA	NA	16	16	NA	PCR
16	53+unk	16,83,6,61	83,58,6,61	unk	RFL
NA	NA	16, 18	16, 18	NA	INV
NA	NA	16	16	NA	INV
NA	NA	16,18	16,18	NA	INV

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

Both genotype-specific and genotype-unspecified viral persistence may be clinically important (Ref. 1).

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 (Ref. 2). Along with the test vials, we sent out an accompanying questionnaire whose answers were requested on a voluntary basis. One question asked, among others, in this questionnaire was whether the laboratory performs HPV

tests for low risk types, and if so, for what reason. According to the replies, one laboratory does it for quality assurance purposes and all the other laboratories do low risk HPV determination only if clinicians request it. So we can conclude that laboratories that perform low risk HPV determination are fully aware of today's clinical standards.

Cervista

In March 2009, Cervista® HPV HR (high risk) and Cervista® HPV 16/18 by Hologic, Inc. gained FDA approval for HPV determinations. It will be interesting to see how the Cervista results compare to the Hybrid Capture results when or if more laboratories start using this method.

Conclusion

Overall, the results are encouraging, and constitute proof that the laboratories in New York State perform high quality HPV tests. Given the low number of results submitted from methods other than Hybrid Capture, it is not possible to determine the reason for the inconsistencies in those results. If and when the number of results increases, we may get a better picture on the degree of inter-laboratory concordance among those methods.

Tentative schedule for future New York State HPV proficiency tests:

Mail-out Date

July 14, 2009
October 19, 2009

Due Date

August 3, 2009
November 9, 2009

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