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Steven I. Gutman, M.D., M.B.A.
Director
Office of *In Vitro* Diagnostic Device Evaluation and Safety
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Boulevard
Rockville, MD 20850 Tel. 301 594-3084

FedEx Overnight: 8582 4858 4530

Re: Seeking guidance to submission of a 510(k) for human papillomavirus (HPV) polymerase chain reaction (PCR) reagents

Dear Dr. Gutman:

We have completed a comparative study between the FDA-approved Digene Hybrid Capture 2 (HC2) High-Risk HPV DNA Test and the research-oriented methodology of using Nested PCR/Genotyping by DNA Sequencing of HPV DNA on 513 liquid-based cervicovaginal clinical specimens. The results are summarized in the enclosed manuscript titled "Human Papillomavirus Genotyping by DNA Sequencing-The Gold Standard HPV Test for Patient Care" which is under review for publication in a medical journal.

The classic molecular biological approach to identify HPV DNA in clinical materials, as outlined in the Materials and Methods section of the above-referenced manuscript, is to first use a PCR-based technique to amplify a target segment of the HPV genomic DNA released from the cells in the clinical sample by proteinase K digestion. A positive 150 bp nested PCR product with the consensus general primer pair GP5+/GP6+ constitutes presumptive evidence for the presence of HPV DNA in the sample. The final confirmation of the HPV DNA and its genotyping are carried out by direct automated DNA sequencing of the hypervariable segment in the nested PCR product via the on-line BLAST analysis, using the database stored in the GenBank for algorithmic sequence alignments. This is a scientifically straightforward approach, but is still not readily implemented by most clinical laboratories.

Now, we want to explore the feasibility of providing the key reagents needed for PCR amplification of HPV genomic DNA and the method of their proper usage commercially to transfer this research tool to the clinical laboratories which desire to set up their own facility for

detection of HPV DNA in clinical cervicovaginal samples. The reagents would include washing buffer for the fixed cells, proteinase K solution for the cell digestion, ready-to-use DNA polymerase mix in individual 0.2 ml PCR tubes, the MY09/MY11 primers in correct concentrations, the GP5+/GP6+ primers in correct concentrations, the β-globin primers in correction concentrations, and the standard plasmid HPV DNA purchased from the American Type Culture Collection (ATCC) as positive control. The clinical laboratories may set up their own DNA sequencing facility to perform the final HPV genotyping or send the samples proven positive for HPV nested PCR to a reference laboratory for final genotyping by DNA sequencing.

I am writing to seek your advice if submitting a 510(k) application is the correct approach since our device appears to be substantially equivalent to the Digene Hybrid Capture 2 (HC2) High-Risk HPV DNA Test. If so, what would be the steps that we should take to properly submit an application for your review.

I thank you for your guidance and look forward to receiving your reply.

Sincerely yours,

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Encl. Manuscript titled "Human Papillomavirus Genotyping by DNA Sequencing-The Gold Standard HPV Test for Patient Care"