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Expert Consultation**Third Wave's Invader Test Well-Positioned****Expecting Rapid Approval and Strong****Summary**

- In vitro diagnostics for human papillomavirus (HPV) are becoming a standard part of the screening regimen for cervical cancer.
- According to Gary Gamerman and Christina Chew from Seraphim Life Sciences, **Third Wave's Invader HPV test is well-positioned to out-compete Qiagen's Hybrid Capture test.**
- Seraphim expects FDA approval of Invader without delay, followed by successful capture of significant HPV diagnostic market share.
- **In spite of successful vaccine programs led by Merck's Gardasil, the market for HPV diagnostics will continue to grow.**

Speaking for Reuters Insight Partners, Gary Gamerman and Christina Chew gave an overview of the science and medicine of HPV infection, focusing on vaccines and diagnostics. Of 30 HPV types that infect the epithelium of the lower anogenital tracts of men and women, 13 have been associated with increased risk of cervical and other cancers. HPV infection is necessary but not sufficient for development of most cervical cancers.

Pap testing results in qualitative assessment of cancer risk. Currently, in vitro diagnostics for HPV are used in concert with pap testing to increase specificity of the testing in women over 30. In younger women, transient HPV infections are common enough to make use of the in vitro diagnostics impractical. Figure 1 diagrams current treatment guidelines in the U.S. for women over 30.

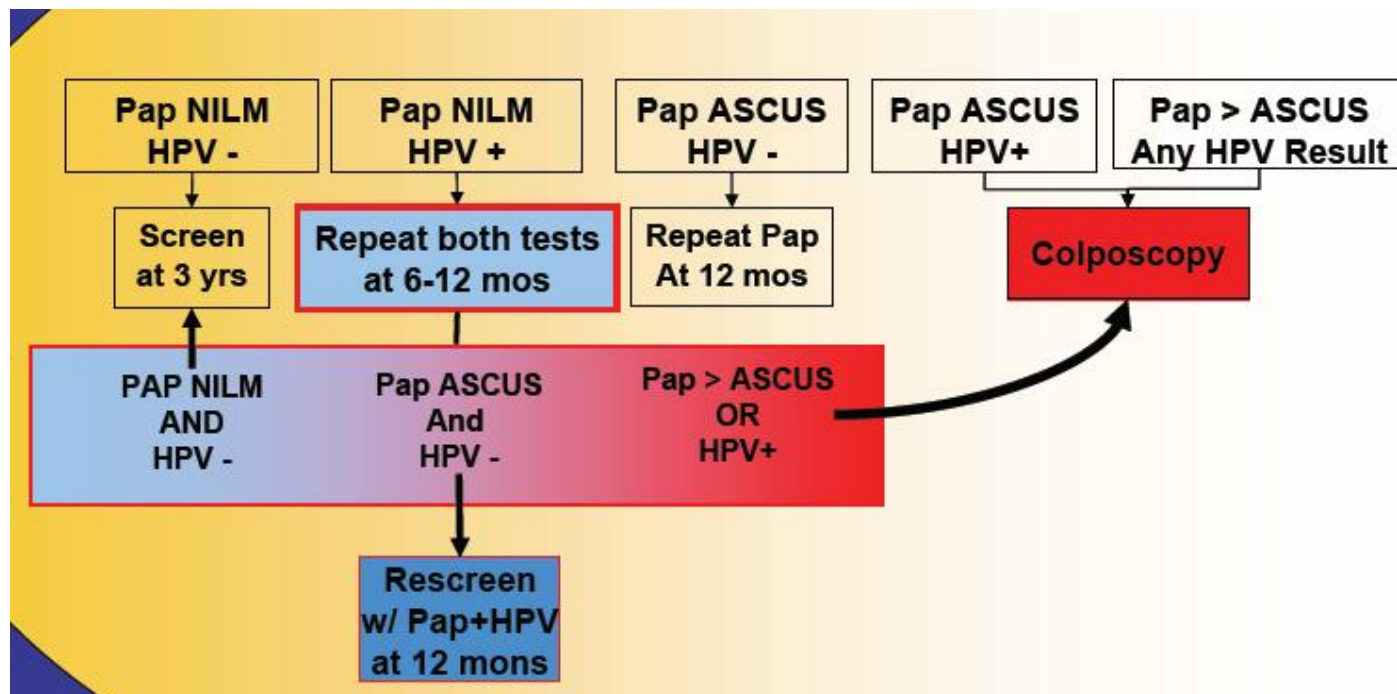
Companies Mentioned

Bold Ticker/company name indicates the company is in our work database

Third Wave Technologies (TWTI)
Qiagen (QGEN)
Gen-Probe (GPRO)
Merck (MRK)
GlaxoSmithKline (GSK)

***Gary Gamerman** is President of Seraphim Life Sciences. Mr. Gamerman was an FDA/CBER reviewer and an attorney in the FDA /Life Sciences practices of two international law firms. **Christina Chew**, a molecular biologist, is senior consultant at Seraphim. She has extensive experience with product development and marketing, including experience with the Hybrid Capture test at Digene.*

Figure 1: Screening Algorithm for Adjunctive HPV DNA Testing in Women Age 30+



Source: Seraphim Life Sciences Consulting

HPV Diagnostics

Several HPV diagnostics are being developed (Figure 2). Some of these are available without commercial backing and without FDA approval. The market is dominated today by the FDA-approved Hybrid Capture test that came to Qiagen via its Digene acquisition. The next approved product is likely to be Third Wave's Invader testing platform.

Seraphim believes that the Invader test will be approved without FDA delay after a six-month review. Advantages of Invader over Qiagen's Hybrid Capture include:

- Specificity for high-risk HPV types.
- Easier to use, with automation expected next year.
- Positive control allows differentiation between negative result vs. lack of sample.
- Poor customer satisfaction with Hybrid Capture and disarray of Qiagen and Digene sales force provides an opportunity to Third Wave to capture significant market share at product launch.

The E6/E7 tests are not likely to have a significant impact on the primary HPV testing market. Seraphim sees these the primary use of these tests as reflex (confirming) tests for patients who score positive on primary screening. Other tests based on PCR and in-situ hybridization (ISH) are laborious, not FDA approved, and not likely to displace the Hybrid Capture and Invader tests.

Figure 2: HPV Screening Technologies

Technology	Company
Hybrid Capture[®] 2	Qiagen (Digene)
Invader[®]	Third Wave Technologies
E6/E7	GenProbe; bioMérieux
PCR/Other	SeeGene, MDL, Homebrew,...
ISH (and "molecular Pap")	Ventana, Dako, Enzo, BD...

Source: Seraphim Life Sciences Consulting

HPV Diagnostic Market Expanding

Seraphim does not believe that Gardasil (Merck), which is already approved, and GlaxoSmithKline's Cervarix (approved in Europe, pending approval in the U.S.) vaccines will lessen the need for HPV diagnostic testing (Figure 3), as the two vaccines will not prevent infection with all HPV strains. In addition, the length and degree of immunity is not known. Seraphim expects HPV testing to become more commonplace, especially as tests are automated and costs decrease. Seraphim also points to potential use of HPV testing (and vaccination) in certain at-risk male populations.

Figure 3: Gardasil and Other HPV Vaccines Will Not Alleviate the Need for HPV Testing

- **Current HPV vaccines only contain HPV-16 and 18 strains and do not offer protection against other types of oncogenic HPV strains**
- **Women who have been infected with HPV prior to vaccination will need to continue being screened**
- **It's unknown how long HPV vaccines will offer protection**
- **It will take 20 years to have the initial impact of the prophylactic vaccine**
- **It will take another 30 years for full impact of the vaccines on Pap/HPV testing**

Source: Seraphim Life Sciences Consulting