Sin Hang Lee, MD

1956 MD, Wuhan Medical College, China

1964 Chief resident in pathology, New York Hospital (Papanicolaou's Lab)

1966 Certified, American Board of Pathologist, F.R.C.P.(C)

1966- Practicing diagnostic cancer pathology and clinical microbiology. Patentee of first estrogen-receptor assay for breast cancer (PMA) and a specific *mycoplasma pneumoniae* serologic test (510K), both approved by FDA. Recent publications:

1)Lee SH, Vigliotti VS, Vigliotti JS, Pappu S. Routine human papillomavirus genotyping by DNA sequencing in community hospital laboratories. *Infect Agent Cancer* 2007; 2:11.

2) Lee SH, Vigliotti VS, Pappu S. DNA Sequencing Validation of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* Nucleic Acid Tests. *Am J Clin Pathol.* 2008; 129:852-859.

3) Lee SH, Vigliotti VS, Pappu S. Human papillomavirus (HPV) infection among women in a representative rural and suburban population of the United States. *Inter J Gyn Ob.* 2009; 105: 210-214.

4) Lee SH, Vigliotti VS, Vigliotti JS, Pappu S. Molecular tests for human papillomavirus (HPV), *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in liquid-based Pap cytology specimen . *BMC Women's Health* 2009; 9:8.

5) Lee SH, Vigliotti VS, Vigliotti JS, Pappu S. Validation of human papillomavirus genotyping by signature DNA sequence analysis. *BMC Clin Pathol.* 2009; 9:3.

Pathologist, Milford Hospital, Milford, CT 203 876-4258. Director, Milford Medical Lab.

President, HiFi DNA Tech, LLC, Trumbull, CT - PCR/DNA sequencing in hospitals.

Inappropriate use indication for FDA-approved HPV DNA test promotes unnecessary cervical biopsies in US at ? >$ 10 billion per year

- More than 95% of referrals to colposcopy for diagnostic workup are false positive and/or potentially excessive (*unnecessary*). Screening with combined cytologic and HPV testing, regardless of patient age, leads to the highest number of excessive colposopic referrals. [Stout NK et al. Department of Health Policy and Management, Harvard School of Public Health. 2008]
- The estimated 1992 annual cost of the overused colposcopic biopsy was at $6 billion. The number of colposcopic biopsies increased markedly since. [Lousuebsakul V et al. Is colposcopic biopsy overused among women with a cytological diagnosis of atypical squamous cells of undetermined significance (ASCUS)? J Women's Health (Larchmt). 2003; 12:553-9.]
- Since 2003, more ASCUS diagnoses have been made by pathologists after the HPV DNA test was approved for triage to 4-quadrant cervical biopsies. Now the unnecessary biopsies may cost more than $10 billion in 2009.
- Cost due to psychological and physical trauma to patients not counted.
- Cost for complications, such as excessive bleeding and infections not counted.
- Cost of loss of work days of the patients not counted.

Inappropriate 2003 FDA (PMA) approval of expanded use of HPV test

- At the open session microbiology devices panel meeting, March 8, 2002, the device's modified indications were presented "***for use as a general population screening test in conjunction with the Papanicolaou (Pap) smear for women age 30 and older, as an aid to determining the absence of high-grade cervical disease or cancer.***"

- In the approval letter for Digene Hybrid Capture HC2 High-Risk HPV DNA Test dated March 31, 2003 and signed by OIVD, the test was approved for: ***"1. To screen patients with ASCUS Pap smear results to determine the need for referral to colposcopy. The results of this test are not intended to prevent women from proceeding to colposcopy."***
(Approved by Steven Gutman/Elizabeth Mansfield, over the objections of the FDA review scientists and the Panel members)

? Connected events

- **Digene Corp. DEF 14A SEC Filing under How chief executive officer is compensated: (1) 2001: *for assembling a team for Digene's progress with FDA…in entering into agreements with strategic partners* ; (2) 2004: for *Digene's progress with FDA approvals and his success ..Digene's diagnostic test products for HPV.* [Lobbying]**

- **FDA CDRH OIVD official website April 22, 2003 by Mark A. Del Vecchio, Director, Regulatory and Clinical Affairs, Digene Corporation - How to work with FDA: Important not to surprise the Agency. FDA interaction (*asymmetrical in FDA practice*).**

- **Elizabeth Mansfield: Director of Regulatory Affairs, Affymetrix, Inc. (J Mol Diagn 2005; 7:2-7, accepted Nov 2, 2004; April 11-13, 2005 FDA-sponsored Workshop), June 8, 2004 Bio 2004 Breakout Sessions OIVD/FDA Scientific Reviewer.**

- **Letter dated July 11, 2003 from Affymetrix, Inc. Senior Vice President to Elizabeth Mansfield, PhD, FDA: Developing Multiplex Test Policy.**

What to do to protect public health and cut cost

- Conduct an open session microbiology advisory panel meeting to review the indications of use in the March 31, 2003 approval letter for HPV test.
- Review *in vitro* (*untainted glass is transparent*) devices strictly based on the science governed by the law of physics and mathematical probabilities.
- Avoid pseudoscience, such as using subjective clinical data for validation of *in vitro* tests (the least burdensome provision of the FDAMA of 1997).
- Respond even-handedly to avoid asymmetrical application of medical device law and regulations, or its public perception.
- Confine the role of OIVD to regulate commercial medical devices, not the tests developed under the regulations of CLIA 88' (OIVD cannot keep up with the advance of medical science in this era of information explosion).
- Prohibit managers/policy makers from taking employments or consultation fees from the OIVD-regulated industry for 5 years after they leave FDA.

Supportive documents submitted

1)Lee SH et al. *Infect Agent Cancer* 2007; 2:11.

2) Lee SH et al. *Am J Clin Pathol*. 2008; 129:852-859.

3) Lee SH et al. *Inter J Gyn Ob.* 2009; 105: 210-214.

4)Lee SH et al.. *BMC Women's Health* 2009; 9:8.

5)Lee SH et al.. *BMC Clin Pathol*. 2009; 9:3

6) Stout NK et al. Harvard School of Public Health. Arch Intern Med 2008;168:1881-1889.

7) Lousuebsakul V et al. J Women's Health (Larchmt). 2003; 12:553-9.

8) Open session microbiology devices panel meeting, March 8, 2002.

9) FDA OIVD approval letter March 31, 2003 expanded use of HPV test (Reviewer: E. Mansfield) .

10) Digene Corp. DEF 14A SEC Filing date 9/26/2001 EDGAR Online.

11) Digene Corp. DEF 14A SEC Filing date 9/23/2004 EDGAR Online.

12) FDA OIVD official website April 22, 2003 by Digene's director of regulatory & clinical affairs.

13) Mol Diagn 2005; 7:2-7 (accepted Nov 2, 2004) stated E. Mansfield was with Affymetrix, Inc.

14) April 11-13, 2005 Workshop co-sponsored by FDA: E. Mansfield was listed as Director of Regulatory Affairs, Affymetrix Inc.

15) June 8, 2004 Bio 2004 Breakout Sessions: E. Mansfield was OIVD/FDA Scientific Reviewer.

16) Letter dated July 11, 2003 from Affymetrix, Inc. to Elizabeth Mansfield, PhD, FDA, showing an FDA employee was to be an employee of a manufacturer she was regulating on behalf of FDA.

17) Han J. Harvard J Law Tech. 2007; 20:423-441: OIVD regulates without FDA policy or rules.

18) The New York Times June 25, 2005: Digene's planned sales price $283 million.

19) Washington Post June 4, 2007: Digene Corp. sold to Qiagen NV for $1.6 billion.