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Safe Affordable Necessary Effective

The Creating of an HPV Industry

Key points:

- Human Papillomavirus (HPV) DNA discovered in cervical cancer in 1983-1984
- HPV vaccine patents 1991-1993
- Government becomes partners in HPV vaccine (NCI and Merck) 2006
- NCI and FDA: In effect the business tactics are to "market Gardasil by fear" as Gardasil gets quasi-cancer vaccine status – this misconception is allowed to be perpetuated uncorrected with far reaching consequences. This is supported by in effect "marketing by confusion": via the creation of a not too sensitive, not too specific HPV DNA Test and perpetuated by "confusion" via creating the ASCUS-LSIL Triage Study (ALTS) program to perpetuate the confusion
- Adverse events post Gardasil vaccination rise and higher than any other vaccine tracked on VAERS database
- Gardasil contaminated with recombinant HPV DNA bounded to adjuvant – possible explanation of substantial and diverse adverse events 2011

By Norma Erickson, President

The discovery of human papillomavirus (HPV) DNA in cervical cancer by Dr. Harald zur Hausen – Nobel laureate 2008

1983
Dr. zur Hausen found HPV-16 DNA in human invasive cervical cancer tissues.

> Durst M, Gissmann L, Ikenberg H, zur Hausen H: *A papillomavirus DNA from a cervical carcinoma and its prevalence in cancer biopsy samples from different geographic regions*. *Proc Natl Acad Sci USA* 1983; 80**:**3812-3815.

1984
Dr. zur Hausen found HPV-18 DNA in tissues and cell lines of human cervical cancers.

> Boshart M, Gissmann L, Ikenberg H, Kleinheinz A, Scheurlen W, zur Hausen H: *A new type of papillomavirus DNA, its presence in genital cancer biopsies and in cell lines derived from cervical cancer***.** *EMBO J* 1984, **3:**1151-1157.

The global HPV Business from virus to vaccine

HPV vaccine patents:
(extracted from "Nature Biotechnology" and modified)

The technology underlying L1-VLP based prophylactic vaccines emerged from research conducted at the University of Rochester, the NCI (National Cancer Institute), Georgetown University, and the University of Queensland.

Initially, the National Cancer Institute (NCI) nonexclusively licensed the technology to MedImmune and Merck. MedImmune also acquired worldwide exclusive rights to intellectual property (IP) from Georgetown University and the University of Rochester.

The University of Queensland licensed its patents to CSL, which in turn licensed the technology exclusively to Merck. GSK eventually acquired exclusive rights to MedImmune's entire IP portfolio for HPV vaccine development.

Owing to a first-to-invent system in the United States, patent interference proceedings were triggered at the USPTO when claims overlapped from different patent applications filed by four different groups of inventors. The interference proceedings involved various L1-antigen HPV-related claims. Six two-way patent interferences between the four parties continued for nearly a decade, presumably at significant cost to the institutions or their primary licensees, and were partially resolved in 2005.

Given the uncertainty surrounding the ownership of enabling vaccine technologies and the possibility of mutually blocking exclusive rights (that is, neither firm could be sure its products would not infringe on patent rights held by the other), Merck and GSK cross-licensed their respective IP holdings in 2005 to ensure unfettered access to these technologies.

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As a consequence, they secured their market position in the United States, Europe and other OECD nations such as Canada and Japan. As part of the financial settlement of the patent interference, the nonexclusive licenses awarded by NCI, NIH (National Institutes of Health) to MedImmune and Merck were converted to co-exclusive licenses, thus allowing both GSK and Merck access to this IP.

Merck brought Gardasil to market in the United States in 2006 and Cervarix was introduced in the United Kingdom in June 2008.

Timeline: patents and licensing of HPV L1-VLP–based prophylactic vaccines

July 19, 1991
Frazer *et al*. (Queensland University) filed an international patent application in Australia. It is about expression of the human papillomavirus L1 and L2 proteins together, but not L1 alone for HPV protection.

June 25, 1992
Schlegel *et al*. (Georgetown University) filed a patent application in the US. It is about HPV L1 expression in mammalian cells led to an L1 protein in cells that was recognized by monoclonal antibodies that bind conformational epitopes. No VLPs (virus like particles) were produced in this study.

September 3, 1992
Schiller and Lowy *et al*. (NCI/NIH) filed a patent application in the US. It is about L1 protein from bovine papillomavirus type 1 self-assembled into morphologically correct VLPs that induced high levels of neutralizing antibodies in immunized animals.

March 9, 1993
Rose *et al*. (Rochester University) filed a patent application in the US. It is about L1 protein from HPV 11 self-assembled into VLPs, later shown to induce neutralizing antibodies.

February 1995
University of Queensland's commercial arm UniQuest licensed HPV vaccine technology to CSL (Melbourne).

October 5, 1995
MedImmune acquired exclusive license to HPV vaccine technology from the University of Rochester.

1995
Merck licensed HPV vaccine technology from CSL.

June 26, 1996
MedImmune in-licensed key HPV IP from the German Cancer Research Center.

January 7, 1997
NCI non-exclusively licensed HPV vaccine technology to MedImmune.

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June 24, 1997
The U.S. Patent and Trademark Office (USPTO) declared initial interference.

December 1997
NCI nonexclusively licensed HPV vaccine technology to Merck.

December 11, 1997
MedImmune and SmithKline Beecham formed worldwide HPV vaccine alliance.

January 16, 1998
MedImmune finalized a vaccine agreement with SmithKline Beecham.

October 24, 2001
USPTO declared patent interference 104,771 between Rose and Lowy
USPTO declared patent interference 104,772 between Rose and Schlegel
USPTO declared patent interference 104,773 between Rose and Frazer
USPTO declared patent interference 104,774 between Lowy and Schlegel
USPTO declared patent interference 104,775 between Lowy and Frazer
USPTO declared patent interference 104,776 between Schlegel and Frazer

February 2005
Merck and GSK entered cross-license agreement for HPV patents.

May 2005
NCI's nonexclusive license converted to co-exclusive licenses to Merck and GSK.

September 20, 2005
USPTO Board of Interference announced decision and awarded priority to Schlegel *et al*.

December 29, 2005
Frazer *et al*. appealed USPTO decision, case docketed in Court of Appeals for the Federal Circuit.

August 20, 2007
Court of Appeals for the Federal Circuit reversed USPTO decision and awarded priority to Frazer *et al*.

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Celebrating NCI's HPV vaccine business success

Quotations from the NIH Record February 23, 2007

Bridging the Licensing Gap By Sarah Schmelling

***"NIH Record* celebrated the pivotal role of government researchers in developing Merck's Gardasil product."**

"Science meet Industry, Industry meet Science. This pairing—of NIH- and FDA-developed technologies and the companies interested in licensing them—would seem to be a perfect match."

"NIH's Office of Technology Transfer (OTT) was created by NIH in 1989 to evaluate, protect, license and manage both NIH and FDA discoveries, inventions and other intellectual property."

"One of the most recent products to reach the market is Merck-produced Gardasil, the human papillomavirus vaccine used to protect against cervical cancer. The underlying technology for the vaccine originated at NCI."

NCI and FDA: Business tactics to market Gardasil

Marketing by Fear: Government and Pharma join hands to give Gardasil a quasi-cancer vaccine status

As reported in the February 23, 2007 celebration, the NCI and the FDA are business partners of the drug companies in the HPV vaccine business. Some NCI scientists have openly stated that they worked in both agencies to monitor the vaccine clinical trials, HPV test development, and secure FDA approvals.

As we know now, all patent applications filed for the inventions of the HPV vaccine technology are about methodologies used to produce the capsid L1 and L2 proteins for eliciting antibodies for the protection against type-specific HPV infections. There are no claims of using HPV L1 or L2 protein as a vaccine to prevent cancer.

The NCI and FDA knew or should have known that in the practice of medicine, vaccines are used for the prevention of infectious disease. *To use vaccination to control a virus which may lead to cancer development in order to reduce cancer prevalence in a population is a theoretical possibility, and only a possibility. It is still a concept that needs to be proven; then proven to be safe and effective.*

There has never been a single vaccine that is known to be effective for cancer prevention. But, the vaccine developer and manufacturer also know that if an HPV vaccine can be marketed for cervical cancer prevention with the endorsement of the government agencies (NCI, FDA and CDC) and the medical establishment, then consumers would be willing to pay high price for it. After all, they are all

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conditioned to be concerned about “cancer”, a life-threatening disease with no known effective treatment.

Although not an inventor of HPV VLPs as the antigen for eliciting genotype-specific antibodies in animals, Dr. Mark Schiffman (executive at the NCI) openly offered to take on the task of marketing the HPV vaccines as a cancer vaccine in 2001.

In an article, titled ***Vaccines: The Next Step to Cervical Cancer Prevention***, *Journal of the National Cancer Institute*, Mark Schiffman, MD, National Cancer Institute Division of Cancer Epidemiology and Genetics responded to this question:

“Once we know how to use information from human papillomavirus tests to effectively test and treat women for cervical abnormalities, what is next?”

“Vaccines,” said Mark Schiffman, M.D., of the National Cancer Institute’s Division of Cancer Epidemiology and Genetics. “[Cervical cancer] should be a vaccine-preventable cancer.”

Remember at this time, the technology to make HPV vaccines was not useable due to multiple patent interference declarations. Dr. Schiffman was offering to take on the task of marketing a vaccine that could not yet be produced for fear of patent interference claims from multiple sources.

The term “cancer vaccine” has not been defined in medical science, let alone for medical practice.

To approve Gardasil as a “cancer vaccine” without officially classifying it as a vaccine against cervical cancer, ***the FDA took a creative step.*** It assigned the Gardasil application for pre-marketing approval (PMA) review to the Vaccines and Related Biological Products Advisory Committee (VRBPAC), who then allowed Merck to use a series of histologic changes **or cervical cancer** “*- with virology to determine the associated HPV type- as the primary endpoint in the evaluation of a vaccine to prevent cervical cancer”.*

Specifically, on public record, the VRBPAC committee in November 2001 and in May 2006 officially allowed the vaccine manufacturer, Merck & Co., Inc., to use “*CIN 2/3, AIS, or cervical cancer; i.e. CIN 2/3 or worse by histology- with virology to determine the associated HPV type- as the primary endpoint in the evaluation of a vaccine to prevent cervical cancer.”*

In this landmark decision, the words “*with virology*” are merely a token; a dispensable attachment to the endpoint to justify the assignment of the review task to the VRBPAC committee.

After all, by definition a vaccine is for prevention of an infectious disease caused by a microbe or a virus. Cervical cancer is a disease, but not infectious. HPV is a virus, not a disease. There are well over 100 genotypes of HPV, many of which are associated with cervical cancer.

But in the clinical trials, the HPV found in the trial subjects was never genotyped by an FDA-approved method or a reliable DNA sequencing genotyping. The real primary endpoint was “*CIN 2/3, AIS, or cervical cancer.”* Since cervical cancer takes several decades to develop, there was not a single case of cancer included in the clinical trial data published. Therefore, in reality the only endpoint adopted for efficacy evaluation was “CIN 2/3, AIS” in the materials submitted to the FDA for approval.

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Nevertheless, despite the fact that Gardasil met neither of the two qualifying criteria for FDA fast-track designation, CBER (the Center for Biologics Evaluation and Research) granted the designation anyway in 2002. Merck's development program for the HPV quadrivalent vaccine for 'prevention of cervical cancer' was officially on the fast-track. In short a vaccine was created to treat something that was already being treated effectively (pap smears) and at a fraction of the cost, but worse it was created based on dishonest research produced in effect in collusion with the very agency designed to protect consumers from such an outcome.

Based on the published clinical trial materials listed in the FUTURE I and FUTURE II studies, the efficacy percentages on CIN2/3 lesions were all associated with a [95%CI;<0-] number, which means the efficacy of Gardasil in preventing CIN2/3 lesions expressed in percentage compared to placebo is not statistically significant with high confidence.

In one series, there were more high-grade precancerous CIN3 lesions in the vaccinated women than in the women receiving placebo (FUTURE I, Table 3), with a minus 9% efficacy for "cancer prevention." Yet despite this the process to both approve and distribute globally rolled on with ferocious energy.

The key relevant data are extracted and re-printed at follows.

FUTURE I Study Group. *Quadrivalent vaccine against human papillomavirus to prevent anogenital diseases.* N Engl J Med. 2007 May 10;356(19):1928-43.

FUTURE II Study Group. *Quadrivalent vaccine against human papillomavirus to prevent high-grade cervical lesions*. N Engl J Med. 2007 May 10;356(19):1915-27.

FUTURE I Clinical Trial Data

Table 3

Cervical Lesions with any HPV type According to grade of lesion

	Total	Vac	Plac	% Efficacy (95%CI)
CIN grade 1	2713	277	363	25(12-36)
CIN grade 2	2723	102	116	13(<0-34)
CIN grade 3	2723	79	72	-9(<0-22)
AIS	2723	1	6	83(<0-100)

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FUTURE II Clinical Trial Data

Table 3

Cervical Lesions with any HPV type According to grade of lesion

	Total	Vac	Plac	% Efficacy (95%CI)
CIN grade 2	6087	149	192	22(3-38)
CIN grade 3	6087	127	161	21(<0-38)
AIS	6087	5	83	7(<0-84)

In fact, the above data are even less reliable than what they are claimed to be in these tables for evaluating the efficacy of Gardasil as a cancer vaccine because the NCI scientists knew and even openly admitted in their published scientific articles that:

"*.. CIN2 is not a true biologic entity but an equivocal diagnosis of precancer, representing an admixture of HPV infection and precancer. The existence of CIN2 biopsy results as a clinical entity may be the consequence of the inaccuracies of colposcopy and colposcopically directed biosy….. That CIN2 is the least reproducible of all histopathologic diagnoses may in part reflect sample error, ie, the biopsy procedure could make a CIN 1 of HPV infection appear worse by sampling the lesional area diagonally..*"

Castle PE, Stoler MH, Solomon D, Schiffman M. The relationship of community biopsy-diagnosed cervical intraepithelial neoplasia grade 2 to the quality control pathology-reviewed diagnoses: an ALTS report. Am J Clin Pathol. 2007;127:805-815.

"… there is an increasing recognition that CIN 2 is an equivocal diagnosis of precancer, an admixture of HPV infections by both carcinogenic and noncarcinogenic HPV and misclassified CIN 3 (10). Approximately 25%–50% of CIN 2 will regress within a year or 2 years (11, 12). Although CIN 3 is a better surrogate for invasive potential, it is increasingly clear that it too is heterogeneous (44). Only a third of CIN 3/carcinoma in situ diagnosed in women with a median age in the late 30s invaded over 30 years (5)..."

Castle PE, Schiffman M, Wheeler CM, Wentzensen N, Gravitt PE. *Impact of improved classification on the association of human papillomavirus with cervical precancer*. Am J Epidemiol. 2010 Jan 15;171(2):155-63.

In conclusion, the NCI/FDA/Merck partnership knew or should have known by now that the surrogate endpoint "CIN2/3, AIS" selected is not a valid endpoint for evaluation of the efficacy of Gardasil as a cancer vaccine to prevent cervical cancer.

The statistical data did not even support the efficacy of Gardasil in preventing these poorly defined and potentially self-regressing lesions.

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In short, the business success of marketing Gardasil is entirely based on misleading promotion of Gardasil as a vaccine to prevent cervical cancer by the vaccine manufacturer endorsed and advanced by NCI, FDA and CDC, the very people charged with not allowing this form of blatant dishonesty to occur.

Had Gardasil been reviewed by the FDA's Oncologic Drugs Advisory Committee, the committee members probably would have decided that the risks Gardasil outweigh its benefits as they rejected the two drugs for prevention of prostate cancer in November 2010.
http://www.prlog.org/11343207-cervical-cancer-vs-prostate-cancer-is-the-fda-practicing-sexual-discrimination.html

Marketing by Confusion: The benefits from creating a not too sensitive, not too specific HPV DNA test

Scientifically speaking, Gardasil is qualified as a genotype-specific vaccine to prevent HPV-16 and HPV-18 infections with almost 100% efficacy as claimed, a**nd is proven to be ineffective for clearing vaccine-relevant HPV genotypes which are already present in the subjects being vaccinated.**

If an analytically sensitive and reliable HPV test which is available, but not used to pre-test the sexually active young women before vaccination, and disqualify those already infected with HPV-16 or HPV-18 as candidates to be vaccinated, the sales volume of Gardasil would likely be reduced.

If such a reliable test is applied for post-vaccination monitoring, it may reveal the truth that **the lack of a pre-vaccination screening for an already existent vaccine-relevant HPV infection by HPV-16, -18, -31 and -45, may lead to a post-vaccination increase in precancerous and cancerous lesions due to exacerbation or progression of a persistent vaccine-relevant HPV infection. In short the vaccine may in effect make matters worse not better – defeating its stated objectives.**

It would appear the NCI and FDA do not want to face either scenario. As a result, the NCI and FDA decided not to recommend or approve an analytically sensitive and specific reliable genotyping test for HPV to be used in clinical practice. The question is why and the answer is perhaps obvious!

In particular, Dr. Schiffman of the NCI knew that the polymerase chain reaction (PCR) method is the most sensitive in detection of HPV DNA, as demonstrated in an article he published in 1991, listed below.

Schiffman MH, Bauer HM, Lorincz AT, Manos MM, Byrne JC, Glass AG, Cadell DM, Howley PM. *Comparison of Southern blot hybridization and polymerase chain reaction methods for the detection of human papillomavirus DNA.* J Clin Microbiol. 1991 Mar;29(3):573-7.

The CDC, a sister agency of the NCI and FDA, also published an article, concluding that the most sensitive and reliable method for HPV test is PCR/DNA sequencing, in 2000, listed below.

Vernon SD, Unger ER, Williams D. *Comparison of human papillomavirus detection and typing by cycle sequencing, line blotting, and hybrid capture*. *J Clin Microbiol.* 2000; 38:651-655.

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Both the FDA (2009) and the NCI (2010) openly stated that the most reliable genotyping is by PCR/DNA sequencing in two more recent official publications, listed below.

http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM181511.pdf

https://www.fbo.gov/index?s=opportunity&mode=form&id=da396b97ad6eb7ec4f7d511f85d9e325&tab=core&_cview=0

However, for monitoring the efficacy and safety of HPV vaccination the NCI still insists on using a Digene Corporation's HC2 hybridization method based on a more than 20-year old, analytically inaccurate and unreliable technology developed before PCR was introduced into clinical laboratories. Extraordinary! As a consequence, the most expensive vaccine ever made, does not work, is not warranted, has been rushed to market and has avoided scrutiny and exposure because the powers that be refuse to use a test that they acknowledge is the most appropriate!

Dr. Schiffman, the senior investigator in charge of the HPV project, has co-authored 34 articles with Dr. A. Lorincz, the scientific vice president of Digene Corporation, the manufacturer of the only FDA-approved HPV test kit, to promote this insensitive and unreliable "genotyping" HPV assay. Would a reasonable person consider this a potential conflict of interest?

The titles of these 34 articles are:

1.
Right-sided ectocervical lesions may be associated with false-negative cytology among women with histologic cervical intraepithelial neoplasia 2 or 3.
Jeronimo J, Castle PE, Herrero R, Sherman ME, Bratti MC, Hildesheim A, Alfaro M, Morales J, Hutchinson ML, Burk RD, Lorincz A, Wacholder S, Rodríguez AC, Schiffman M.
J Low Genit Tract Dis. 2003 Jul;7(3):175-83.PMID: 17051065 [PubMed]Related citations

2.
Cervical HPV DNA detection as a predictor of a recurrent SIL diagnosis among untreated women.
Castle PE, Zemlo TR, Burk RD, Scott DR, Sherman ME, Lorincz AT, Kurman RJ, Glass AG, Rush BB, Liaw KL, Schiffman M.
J Low Genit Tract Dis. 2001 Jul;5(3):138-43.PMID: 17050958 [PubMed]Related citations

3.
The elevated 10-year risk of cervical precancer and cancer in women with human papillomavirus (HPV) type 16 or 18 and the possible utility of type-specific HPV testing in clinical practice.
Khan MJ, Castle PE, Lorincz AT, Wacholder S, Sherman M, Scott DR, Rush BB, Glass AG, Schiffman M.
J Natl Cancer Inst. 2005 Jul 20;97(14):1072-9.PMID: 16030305 [PubMed - indexed for MEDLINE]**Free Article**Related citations

4.
Semiquantitative human papillomavirus type 16 viral load and the prospective risk of cervical precancer and cancer.
Castle PE, Schiffman M, Scott DR, Sherman ME, Glass AG, Rush BB, Schussler JE, Wacholder S, Lorincz AT.

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Cancer Epidemiol Biomarkers Prev. 2005 May;14(5):1311-4.PMID: 15894692 [PubMed - indexed for MEDLINE]**Free Article**Related citations

5.
Comparison between prototype hybrid capture 3 and hybrid capture 2 human papillomavirus DNA assays for detection of high-grade cervical intraepithelial neoplasia and cancer.
Castle PE, Lorincz AT, Scott DR, Sherman ME, Glass AG, Rush BB, Wacholder S, Burk RD, Manos MM, Schussler JE, Macomber P, Schiffman M.
J Clin Microbiol. 2003 Sep;41(9):4022-30.PMID: 12958220 [PubMed - indexed for MEDLINE]**Free PMC Article**Free textRelated citations

6.
A comparison between real-time polymerase chain reaction and hybrid capture 2 for human papillomavirus DNA quantitation.
Gravitt PE, Burk RD, Lorincz A, Herrero R, Hildesheim A, Sherman ME, Bratti MC, Rodriguez AC, Helzlsouer KJ, Schiffman M.
Cancer Epidemiol Biomarkers Prev. 2003 Jun;12(6):477-84.PMID: 12814990 [PubMed - indexed for MEDLINE]**Free Article**Related citations

7.
Baseline cytology, human papillomavirus testing, and risk for cervical neoplasia: a 10-year cohort analysis.
Sherman ME, Lorincz AT, Scott DR, Wacholder S, Castle PE, Glass AG, Mielzynska-Lohnas I, Rush BB, Schiffman M.
J Natl Cancer Inst. 2003 Jan 1;95(1):46-52.PMID: 12509400 [PubMed - indexed for MEDLINE]**Free Article**Related citations

8.
Restricted cross-reactivity of hybrid capture 2 with nononcogenic human papillomavirus types.
Castle PE, Schiffman M, Burk RD, Wacholder S, Hildesheim A, Herrero R, Bratti MC, Sherman ME, Lorincz A.
Cancer Epidemiol Biomarkers Prev. 2002 Nov;11(11):1394-9.PMID: 12433717 [PubMed - indexed for MEDLINE]**Free Article**Related citations

9.
Absolute risk of a subsequent abnormal pap among oncogenic human papillomavirus DNA-positive, cytologically negative women.
Castle PE, Wacholder S, Sherman ME, Lorincz AT, Glass AG, Scott DR, Rush BB, Demuth F, Schiffman M.
Cancer. 2002 Nov 15;95(10):2145-51.PMID: 12412168 [PubMed - indexed for MEDLINE]**Free Article**Related citations

10.
A prospective study of high-grade cervical neoplasia risk among human papillomavirus-infected women.
Castle PE, Wacholder S, Lorincz AT, Scott DR, Sherman ME, Glass AG, Rush BB, Schussler JE, Schiffman M.

J Natl Cancer Inst. 2002 Sep 18;94(18):1406-14.PMID: 12237286 [PubMed - indexed for MEDLINE]**Free Article**Related citations

11.
Comparisons of HPV DNA detection by MY09/11 PCR methods.
Castle PE, Schiffman M, Gravitt PE, Kendall H, Fishman S, Dong H, Hildesheim A, Herrero R, Bratti MC, Sherman ME, Lorincz A, Schussler JE, Burk RD.
J Med Virol. 2002 Nov;68(3):417-23.PMID: 12226831 [PubMed - indexed for MEDLINE]Related citations

12.
Viral load of human papillomavirus and risk of CIN3 or cervical cancer.
Lorincz AT, Castle PE, Sherman ME, Scott DR, Glass AG, Wacholder S, Rush BB, Gravitt PE, Schussler JE, Schiffman M.
Lancet. 2002 Jul 20;360(9328):228-9.PMID: 12133661 [PubMed - indexed for MEDLINE]Related citations

13.
Can cervicography be improved? An evaluation with arbitrated cervicography interpretations.
Schneider DL, Burke L, Wright TC, Spitzer M, Chatterjee N, Wacholder S, Herrero R, Bratti MC, Greenberg MD, Hildesheim A, Sherman ME, Morales J, Hutchinson ML, Alfaro M, Lörincz A, Schiffman M.
Am J Obstet Gynecol. 2002 Jul;187(1):15-23.PMID: 12114883 [PubMed - indexed for MEDLINE]Related citations

14.
Results of human papillomavirus DNA testing with the hybrid capture 2 assay are reproducible.
Castle PE, Lorincz AT, Mielzynska-Lohnas I, Scott DR, Glass AG, Sherman ME, Schussler JE, Schiffman M.
J Clin Microbiol. 2002 Mar;40(3):1088-90.PMID: 11880448 [PubMed - indexed for MEDLINE]**Free PMC Article**Free textRelated citations

15.
Human leukocyte antigen class I and II alleles and risk of cervical neoplasia: results from a population-based study in Costa Rica.
Wang SS, Wheeler CM, Hildesheim A, Schiffman M, Herrero R, Bratti MC, Sherman ME, Alfaro M, Hutchinson ML, Morales J, Lorincz A, Burk RD, Carrington M, Erlich HA, Apple RJ.
J Infect Dis. 2001 Nov 15;184(10):1310-4. Epub 2001 Oct 29.PMID: 11679920 [PubMed - indexed for MEDLINE]Related citations

16.
HPV co-factors related to the development of cervical cancer: results from a population-based study in Costa Rica.
Hildesheim A, Herrero R, Castle PE, Wacholder S, Bratti MC, Sherman ME, Lorincz AT, Burk RD, Morales J, Rodriguez AC, Helgesen K, Alfaro M, Hutchinson M, Balmaceda I, Greenberg M, Schiffman

M. Br J Cancer. 2001 May 4;84(9):1219-26.PMID: 11336474 [PubMed - indexed for MEDLINE] **Free PMC Article** Free textRelated citations

17.
HPV DNA testing in cervical cancer screening: results from women in a high-risk province of Costa Rica.
Schiffman M, Herrero R, Hildesheim A, Sherman ME, Bratti M, Wacholder S, Alfaro M, Hutchinson M, Morales J, Greenberg MD, Lorincz AT.
JAMA. 2000 Jan 5;283(1):87-93.PMID: 10632285 [PubMed - indexed for MEDLINE]**Free Article**Related citations

18.
Utility of liquid-based cytology for cervical carcinoma screening: results of a population-based study conducted in a region of Costa Rica with a high incidence of cervical carcinoma.
Hutchinson ML, Zahniser DJ, Sherman ME, Herrero R, Alfaro M, Bratti MC, Hildesheim A, Lorincz AT, Greenberg MD, Morales J, Schiffman M.
Cancer. 1999 Apr 25;87(2):48-55.PMID: 10227593 [PubMed - indexed for MEDLINE]**Free Article**Related citations

19.
Cervicography screening for cervical cancer among 8460 women in a high-risk population.
Schneider DL, Herrero R, Bratti C, Greenberg MD, Hildesheim A, Sherman ME, Morales J, Hutchinson ML, Sedlacek TV, Lorincz A, Mango L, Wacholder S, Alfaro M, Schiffman M.
Am J Obstet Gynecol. 1999 Feb;180(2 Pt 1):290-8.PMID: 9988789 [PubMed - indexed for MEDLINE]Related citations

20.
Human leukocyte antigen class I/II alleles and development of human papillomavirus-related cervical neoplasia: results from a case-control study conducted in the United States.
Hildesheim A, Schiffman M, Scott DR, Marti D, Kissner T, Sherman ME, Glass AG, Manos MM, Lorincz AT, Kurman RJ, Buckland J, Rush BB, Carrington M.
Cancer Epidemiol Biomarkers Prev. 1998 Nov;7(11):1035-41.PMID: 9829713 [PubMed - indexed for MEDLINE]**Free Article**Related citations

21.
Performance of a semiautomated Papanicolaou smear screening system: results of a population-based study conducted in Guanacaste, Costa Rica.
Sherman ME, Schiffman M, Herrero R, Kelly D, Bratti C, Mango LJ, Alfaro M, Hutchinson ML, Mena F, Hildesheim A, Morales J, Greenberg MD, Balmaceda I, Lorincz AT.
Cancer. 1998 Oct 25;84(5):273-80.PMID: 9801201 [PubMed - indexed for MEDLINE]**Free Article**Related citations

22.
Comparison of PCR- and hybrid capture-based human papillomavirus detection systems using multiple cervical specimen collection strategies.

Peyton CL, Schiffman M, Lörincz AT, Hunt WC, Mielzynska I, Bratti C, Eaton S, Hildesheim A, Morera LA, Rodriguez AC, Herrero R, Sherman ME, Wheeler CM.
J Clin Microbiol. 1998 Nov;36(11):3248-54. Erratum in: J Clin Microbiol 1999 Feb;37(2):478. PMID: 9774574 [PubMed - indexed for MEDLINE]**Free PMC Article**Free textRelated citations

23.
Immune activation in cervical neoplasia: cross-sectional association between plasma soluble interleukin 2 receptor levels and disease.
Hildesheim A, Schiffman MH, Tsukui T, Swanson CA, Lucci J 3rd, Scott DR, Glass AG, Rush BB, Lorincz AT, Corrigan A, Burk RD, Helgesen K, Houghten RA, Sherman ME, Kurman RJ, Berzofsky JA, Kramer TR.
Cancer Epidemiol Biomarkers Prev. 1997 Oct;6(10):807-13.PMID: 9332763 [PubMed - indexed for MEDLINE]**Free Article**Related citations

24.
Comparison of the hybrid capture tube test and PCR for detection of human papillomavirus DNA in cervical specimens.
Cope JU, Hildesheim A, Schiffman MH, Manos MM, Lörincz AT, Burk RD, Glass AG, Greer C, Buckland J, Helgesen K, Scott DR, Sherman ME, Kurman RJ, Liaw KL.
J Clin Microbiol. 1997 Sep;35(9):2262-5.PMID: 9276398 [PubMed - indexed for MEDLINE]**Free PMC Article**Free textRelated citations

25.
Evaluation of PAPNET testing as an ancillary tool to clarify the status of the "atypical" cervical smear.
Sherman ME, Schiffman MH, Mango LJ, Kelly D, Acosta D, Cason Z, Elgert P, Zaleski S, Scott DR, Kurman RJ, Stoler M, Lorincz AT.
Mod Pathol. 1997 Jun;10(6):564-71.PMID: 9195573 [PubMed - indexed for MEDLINE]Related citations

26.
Cervical specimens collected in liquid buffer are suitable for both cytologic screening and ancillary human papillomavirus testing.
Sherman ME, Schiffman MH, Lorincz AT, Herrero R, Hutchinson ML, Bratti C, Zahniser D, Morales J, Hildesheim A, Helgesen K, Kelly D, Alfaro M, Mena F, Balmaceda I, Mango L, Greenberg M.
Cancer. 1997 Apr 25;81(2):89-97.PMID: 9126136 [PubMed - indexed for MEDLINE]**Free Article**Related citations

27.
Epidemiologic determinants of seroreactivity to human papillomavirus (HPV) type 16 virus-like particles in cervical HPV-16 DNA-positive and-negative women.
Wideroff L, Schiffman MH, Hoover R, Tarone RE, Nonnenmacher B, Hubbert N, Kirnbauer R, Greer CE, Lorincz AT, Manos MM, Glass AG, Scott DR, Sherman ME, Buckland J, Lowy D, Schiller J.
J Infect Dis. 1996 Nov;174(5):937-43.PMID: 8896493 [PubMed - indexed for MEDLINE]Related citations

28.
Interleukin 2 production in vitro by peripheral lymphocytes in response to human papillomavirus-derived peptides: correlation with cervical pathology.

Tsukui T, Hildesheim A, Schiffman MH, Lucci J 3rd, Contois D, Lawler P, Rush BB, Lorincz AT, Corrigan A, Burk RD, Qu W, Marshall MA, Mann D, Carrington M, Clerici M, Shearer GM, Carbone DP, Scott DR, Houghten RA, Berzofsky JA. Cancer Res. 1996 Sep 1;56(17):3967-74.PMID: 8752165 [PubMed - indexed for MEDLINE]**Free Article**Related citations

29.
Evaluation of seroreactivity to human papillomavirus type 16 virus-like particles in an incident case-control study of cervical neoplasia.
Wideroff L, Schiffman MH, Nonnenmacher B, Hubbert N, Kirnbauer R, Greer CE, Lowy D, Lorincz AT, Manos MM, Glass AG, et al. J Infect Dis. 1995 Dec;172(6):1425-30.PMID: 7594698 [PubMed - indexed for MEDLINE]Related citations

30.
Human papillomavirus testing by hybrid capture appears to be useful in triaging women with a cytologic diagnosis of atypical squamous cells of undetermined significance.
Cox JT, Lorincz AT, Schiffman MH, Sherman ME, Cullen A, Kurman RJ.
Am J Obstet Gynecol. 1995 Mar;172(3):946-54.PMID: 7892889 [PubMed - indexed for MEDLINE]Related citations

31.
Toward objective quality assurance in cervical cytopathology. Correlation of cytopathologic diagnoses with detection of high-risk human papillomavirus types.
Sherman ME, Schiffman MH, Lorincz AT, Manos MM, Scott DR, Kuman RJ, Kiviat NB, Stoler M, Glass AG, Rush BB. Am J Clin Pathol. 1994 Aug;102(2):182-7.PMID: 8042586 [PubMed - indexed for MEDLINE]Related citations

32.
Comparison of Southern blot hybridization and polymerase chain reaction methods for the detection of human papillomavirus DNA.
Schiffman MH, Bauer HM, Lorincz AT, Manos MM, Byrne JC, Glass AG, Cadell DM, Howley PM.
J Clin Microbiol. 1991 Mar;29(3):573-7.PMID: 1645370 [PubMed - indexed for MEDLINE]**Free PMC Article**Free textRelated citations

33.
Temporal associations of human papillomavirus infection with cervical cytologic abnormalities.
Lorincz AT, Schiffman MH, Jaffurs WJ, Marlow J, Quinn AP, Temple GF. Am J Obstet Gynecol. 1990 Mar;162(3):645-51.PMID: 2156423 [PubMed - indexed for MEDLINE]Related citations

34.
Analysis of individual human papillomavirus types in cervical neoplasia: a possible role for type 18 in rapid progression.
Kurman RJ, Schiffman MH, Lancaster WD, Reid R, Jenson AB, Temple GF, Lorincz AT.
Am J Obstet Gynecol. 1988 Aug;159(2):293-6.PMID: 2841858 [PubMed - indexed for MEDLINE]

On one hand, Dr. Schiffman and his colleagues at the NCI claim this HPV DNA test has been clinically validated with histological CIN2 and CIN3 lesions. Clinically validated means a scientific determination has been made proving the test is accurate in determining the presence of, or

predicting the risk for, a health condition or phenotype, including determination of sensitivity, specificity and positive and negative predictive values.

On the other hand, he and his colleagues openly stated that CIN2 lesions are often reversible, "not a true biologic entity," and that CIN3 lesions are highly heterogeneous, histologic diagnoses subject to bias of human observation of cellular morphological changes. In other words, it would be nearly impossible to clinically validate observance of a CIN 2/3.

The contrast of these two positions would be laughable were it not for the fact that whilst Gardasil revenues climbed ever higher (circa $4-5b) hundreds of thousands of girls have been adversely impacted and for no good reason.

The latter NCI conclusion refutes their assertion that analytically validated sensitive and specific methods for HPV detection by PCR and genotyping by DNA sequencing must be clinically re-validated by a CIN2/3 histology.

Dr. Schiffman should have known that any increase in sensitivity of CIN2/3 detection by the Digene HPV test is at the expense of specificity, causing unnecessary colposcopic biopsies on women.

As early as in 2003, his frequent co-author, Dr. Lorincz of Digene Corporation jointly wrote the following conclusion in a Mexico study:

"Both HPV assays detected more cases of CIN2/3 or CC than Pap cytology alone. However, the HPV assays increased the number of colposcopy referrals."

Salmerón J, Lazcano-Ponce E, Lorincz A, Hernández M, Hernández P, Leyva A, Uribe M, Manzanares H, Antunez A, Carmona E, Ronnett BM, Sherman ME, Bishai D, Ferris D, Flores Y, Yunes E, Shah KV. *Comparison of HPV-based assays with Papanicolaou smears for cervical cancer screening in Morelos State, Mexico*. Cancer Causes Control. 2003 Aug;14(6):505-12.

Insisting that molecular HPV DNA-based virology testing (a physical science) be validated by clinical observation (an art of medical practice) as a tool for predicting a precancerous histology (an art in medical practice) deprives the consumers of a scientifically reliable HPV genotyping method for safe and effective vaccination and for development of a paradigm for better health care management.

The only benefit in creating such confusion is to ensure a free-hand marketing of HPV vaccines without an objective scientific tool for monitoring. In the absence of a reliable HPV genotyping method for monitoring, all patients found to have a post-vaccination abnormal Pap cytology result can be easily, casually and arbitrarily labeled as the consequence of persistent infections caused by other "carcinogenic" HPV genotypes not targeted by the vaccine, and thus immediately referred to colposcopic biopsies. In this way the truth would remain unknown forever.

By Norma Erickson, President

NCI Chronological Events:

1988
The passage of the Clinical Laboratory Improvement Amendments of 1988 (CLIA) by the U.S. Congress was conceived predominantly as a response to perceived and documented problems in the Pap smear cytology testing, a well known, long-debated imperfection of a highly successful cervical cancer prevention technology practiced in the U.S. since its inception in the 1940's. This timing coincided with the NCI scheme to introduce a virology-based agenda to replace the historical traditional Pap smear cytology as the corner stone for cervical cancer prevention.

As Congress was preparing for passage of this law, the NCI was busy in organizing a National Cancer Institute workshop to introduce "the 1988 Bethesda System for reporting cervical/vaginal cytologic diagnoses: developed and approved at the National Cancer Institute workshop in Bethesda, MD, December 12–13, 1988".

In this national document, a new category of cellular changes "associated with HPV" is recommended as an official cytological diagnosis.

Diane Solomon. *The 1988 Bethesda system for reporting cervical/vaginal cytological diagnoses-NCI Work Shop*. JAMA 1989; 262:931-934.

1988
Dr. Attila Lorincz of Life Technologies (now with Digene Corp), Gaithersburg, Md and Dr. Mark Schiffman published HPV DNA tests as an adjunct to the Pap smear.

> Kurman RJ, Schiffman MH, Lancaster WD, Reid R, Jenson AB, Temple GF, Lorincz AT. *Analysis of individual human papillomavirus types in cervical neoplasia: a possible role for type 18 in rapid progression*. Am J Obstet Gynecol. 1988 Aug;159(2):293-6.

1989
Life Technologies, Gaithersburg, Md received FDA approval for its VIRAPAP test for HPV DNA in clinical specimens, using radioactive probe hybridization, performed as an adjunct to the Pap smear.

1991
Dr. Attila Lorincz filed a patent application for "Non-radioactive hybridization assay and kit" for HPV DNA test, and later became Chief Scientific Officer, Senior Vice President of Digene Corporation, Gaithersburg, Md to replace the former Life Technologies, introducing the non-radioactive Digene hybrid capture (HC) test to replace VIRAPAP test for HPV DNA.

1996
Cytyc Corp. 10-K405 · For 12/31/96 · EX-13.1 stated that The National Cancer Institute's six-year, multicenter Triage Study uses the ThinPrep Pap Test in conjunction with HPV DNA typing to assess triage strategies.

Through NCI and the FDA, making health care policies for the consumers, Cytyc Corp. and Digene Corp. have monopolized the virology-based cervical cancer program. Dr. Lorincz, the scientific V.P. of Digene Corp. and Dr. M. Schiffman of the NCI co-authored 34 scientific papers to promote the Digene

By Norma Erickson, President

HPV assay as the only FDA-approved HPV test in the US. **It makes one wonder if Hippocrates and Hypocrisy got confused along the way.**

BOXBOROUGH, Mass., Oct. 4, 1996 -- Cytyc Corporation (Nasdaq: CYTC) announced today that it has submitted a Premarket Approval Application (PMA) supplement to the U.S. Food and Drug Administration (FDA) to allow patients with inconclusive or borderline diagnoses of cancerous cells to be tested for human papillomavirus (HPV) directly from the single cervical sample collected to prepare Cytyc's ThinPrep(R) Pap Test.

The clinical study supporting Cytyc's PMA supplement demonstrated that the collection method for the ThinPrep Pap Test was equivalent to the collection method for Digene Corporation's Hybrid Capture Assay for HPV. Digene's Hybrid Capture Assay is the only FDA approved test for HPV.

2000
In support of FDA approval of the HPV test of Digene Corporation, Dr. Mark Schiffman of the NCI attended the FDA Microbiology Devices Advisory Panel Meeting held on December 8, 2000, in support of the Digene HPV test application presented by Dr. A. Lorincz, and stated that he was disturbed at the implication that there were no U.S. studies. He said that there was complete protection for the first 2½ years following a double negative Pap test/HPV assay.

However, when questioned, he admitted that they had not biopsied the double negative women, so there was no histological confirmation for these cases.
http://www.fda.gov/ohrms/dockets/ac/00/minutes/3675m1.pdf

2002
While the NCI was promoting the formation of a huge conglomerate under its total control, combining Cytyc Corporation and Digene Corporation, the FTC blocked the $283 million merger.
http://www.nytimes.com/2002/06/25/business/company-news-ftc-challenges-cytyc-s-purchase-of-digene.html

2002
FDA considered an application for expanded use of Digene's HC2 HPV test.

At the open session microbiology devices panel meeting, March 8, 2002, the device's modified indications were proposed "***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***."
http://www.fda.gov/ohrms/dockets/ac/02/minutes/3846m2.pdf

2003
In an approval letter dated March 31, 2003, the FDA granted Digene Hybrid Capture HC2 High-Risk HPV DNA Test 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."***

Medical consumers need to be aware ASCUS means 'atypical squamous (flat) cells of undetermined significance. **They should also know that 90-95% of all ASCUS results on Pap cytology are benign.**

By Norma Erickson, President

http://www.accessdata.fda.gov/cdrh_docs/pdf/p890064s009a.pdf

This new language is significant. The original proposed indication of use for the test was that a negative result indicates "the absence high-grade cervical disease or cancer". It was a reasonable microbiology panel review which concluded that patients have no risk of high-grade cervical disease or cancer if there is no high-risk HPV infection. Therefore, an annual Pap test screen may not be necessary.

The new language approved is quite different because it says "to determine the need for referral to colposcopy". It not only means a negative result is of no concern, but it also means that a positive HPV test result will determine the need for referring the patient with an ASCUS Pap smear result to colposcopy.
In medical science, the fact that a negative high-risk HPV test result indicates the absence of cervical pre-cancer or cancer does not necessarily mean that a positive high-risk HPV test result will be associated with a high incidence of cervical pre-cancer or cancer.

Since colposcopy in gynecologic practice usually means colposcopic biopsy, an invasive traumatic procedure for cancer diagnostic workup, with this manipulation of language, the Digene HPV test is marketed as a cancer-screening test approved by the FDA for prevention of cervical cancer and for post-licensure monitoring of the HPV vaccination.

As a consequence, more than 95% of the patients referred to colposcopic cancer workup based on the combined Digene HC2 and Pap cytology tests are excessive and unnecessary.

Stout NK, Goldhaber-Fiebert JD, Ortendahl JD, Goldie SJ. Trade-offs in cervical cancer prevention: balancing benefits and risks. Arch Intern Med. 2008; 168: 1881-1889.

In a more recent report, Digene HC2 test only had a 3.2% positive predictive value in detecting CIN2/3 lesions among ASCUS cases.

Zhao C, Zhao S, Heider A, Austin RM. Significance of high-risk human papillomavirus DNA detection in women 50 years and older with squamous cell papanicolaou test abnormalities. Arch Pathol Lab Med. 2010 Aug;134(8):1130-5.

2005
The NCI has been very concerned about the introduction of other more reliable HPV genotyping methods into clinical laboratory practice this can only be because such methods eventually will demonstrate the lack of efficacy of Gardasil as a cancer vaccine.

The following incident is enlightening, as reported in CAP TODAY, a publication of the College of American Pathologists.

In mid-March 2005, concerned about the clinical laboratories developing a more accurate test than the Digene assay, Dr. Schiffman called CAP (College of American Pathologists) TODAY's editor to voice a troubling concern: that laboratories are failing to clinically validate their HPV tests. He was questioning why they are not simply using the Digene HPV test.

By Norma Erickson, President

http://www.cap.org/apps/cap.portal?_nfpb=true&cntvwrPtlt_actionOverride=%2Fportlets%2FcontentViewer%2Fshow&_windowLabel=cntvwrPtlt&cntvwrPtlt%7BactionForm.contentReference%7D=cap_today%2Fcover_stories%2F0905HPVa.html&_state=maximized&_pageLabel=cntvwr

However, according to The CAP Human Papillomavirus (High-Risk) Survey for Cytopathology and Other Laboratories (CHPV), user-developed (homebrew) assays generated the highest concordance rate (100 percent). Specifically, a better performance rate than the NCI-promoted and FDA-approved Digene HC2 HPV test, as summarized in the following report.

http://www.cap.org/apps/cap.portal?_nfpb=true&cntvwrPtlt_actionOverride=%2Fportlets%2FcontentViewer%2Fshow&_windowLabel=cntvwrPtlt&cntvwrPtlt%7BactionForm.contentReference%7D=cap_today%2F0509%2F0509NGC_b_HPV_testing.html&_state=maximized&_pageLabel=cntvwr

2007
Dr. Schiffman was concerned because Digene Corporation was on the way to be sold to a Dutch company for $1.6 billion in June 2007, a more than 5 times gain in value since 2002 when the FTC blocked its sales, thanks to the NCI/FDA promotion. http://www.marketsense.org/entry/dutch-qiagen-acquires-digene-for-16-billion/

2009
The need for reliable HPV detection and genotyping methods for pre- and post-prophylactic vaccine intervention analyses is recognized by a group of medical scientists, who recommended using a test that is not approved by the FDA.

Dobec M, Bannwart F, Kaeppeli F, Cassinotti P. Automation of the linear array HPV genotyping test and its application for routine typing of human papillomaviruses in cervical specimens of women without cytological abnormalities in Switzerland. J Clin Virol. 2009 May;45(1):23-7.

2010
NCI wants to make its virology-based agenda of using mass vaccination of young women, the Digene HC2 HPV test for cancer screening and colposcopic biopsy to prevent cervical cancer a national health policy of the future in the following articles and comments.

Schiffman M, Wentzensen N. *From human papillomavirus to cervical cancer. Obstet Gynecol.* 2010 Jul;116(1):177-85. Comment in: Obstet Gynecol. 2010 Nov;116(5):1221; author reply 221-2.

It is recognized now that a reliable HPV genotyping test is needed for monitoring the HPV-vaccinated population in the United States.

Huh W, Einstein MH, Herzog TJ, Franco EL. *What is the role of HPV typing in the United States now and in the next five years in a vaccinated population?* Gynecol Oncol. 2010 Jun;117(3):481-5.

The NCI group still insists on using the old Digene HC2 HPV test as the standard for the next generation of HPV DNA tests.

By Norma Erickson, President

Kinney W, Stoler MH, Castle PE. *Special commentary: patient safety and the next generation of HPV DNA tests*. Am J Clin Pathol. 2010;134:193-199. Comment in: Am J Clin Pathol 2011; 135:481-483.

Perpetuating the Confusion: Creating the ASCUS-LSIL Triage Study (ALTS) Program

Historically, attempts at accurate cellular classification of cervical cancers began long before Papanicolaou's publications. Such efforts were based on subjective human observations and the controversies around these efforts have been well summarized in the following article.

Clarke AE, Casper MJ. *From simple technology to complex arena: classification of Pap smears, 1917-90.* Med Anthropol Q. 1996 Dec;10(4):601-23.

As the authors in the above article cited, ***"Despite our desperate, eternal attempt to separate, contain, and mend, categories always leak."***

In real life, the Pap cytology test results are bound to generate a gray-zone cellular category because as a benign inflammatory process progresses to a precancerous and then in rare cases to a cancerous stage in a continuum of events leading to malignancy. There is no clear morphologic demarcation which can be used to separate the reversible precancerous cells from those having reached the point of no-return to malignancy.

The NCI exploits this inherent imperfection of the Pap cytotechnology to promote its virology-based cervical cancer prevention program by instituting a reporting system called the Bethesda system, for the first time in 1988, with creation of an "ASCUS/LSIL" class. The imperfection of the latter system is illustrated by its various modifications in a short period of time since its inception.

In an online publication, the NCI stated the following:

"Bethesda 2001 updates the earlier Bethesda System, first published in 1989 and revised in 1991. The 2001 version reflects the most current knowledge about the biology of Pap test abnormalities and addresses new screening technologies that appeared in the past decade.

New term (ASC-H) to denote atypical cells at higher-risk of association with precancer: The older Bethesda System grouped all cells considered equivocal -- atypical but not clearly precancerous -- into one category known as atypical squamous cells of undetermined significance or ASCUS. Bethesda 2001 adds a new category for atypical cells at higher risk of association with precancer: "atypical squamous cells - cannot exclude a high-grade lesion" or "ASC-H."

The Bethesda reporting system created a basket for the gray-zone Pap cytology cases which traditionally need repeated cytology follow up. Now these cases are for triage by the Digene HPV DNA assay to colposcopic biopsies.

By Norma Erickson, President

The NCI formed an ASCUS-LSIL Triage Study (ALTS) just for that promotion, a "hypothesis" arm for marketing an HPV vaccine when the vaccine is shown to be ineffective for prevention of cervical precancerous lesions. Two representative articles related to this subject are listed as follows.

Stoler MH, Schiffman M; Atypical Squamous Cells of Undetermined Significance-Low-grade Squamous Intraepithelial Lesion Triage Study (ALTS) Group. *Interobserver reproducibility of cervical cytologic and histologic interpretations: realistic estimates from the ASCUS-LSIL Triage Study.* JAMA. 2001 Mar 21;285(11):1500-5.

Schiffman M, Solomon D. *Findings to date from the ASCUS-LSIL Triage Study (ALTS). Arch Pathol Lab Med.* 2003 Aug;127(8):946-9.
In an NCI online publication titled "ASCUS/LSIL Triage Study (ALTS) Findings: Questions and Answers" it stated:

HPV Triage: Women in this arm were managed based on results of the Pap test plus a test for the human papillomavirus (HPV), which is the cause of most cervical cancers. If their Pap test showed more severe abnormalities or if their cervical cells contained DNA from certain HPV types associated with cancer, they had colposcopy. The HPV Triage arm tested the hypothesis that HPV testing is effective at determining which women with ASCUS need colposcopy.

Confusing consensus guidelines based on these CIN triage directives have sent numerous women to unnecessary cervical colposcopic biopsies and effectively cover up any potential precancerous or cancerous lesions caused by vaccine-relevant HPV genotypes after HPV vaccinations.

By Norma Erickson, President

Conclusion

In short a vaccine called Gardasil has been created to address a cancer – when it is known that vaccines are for viruses and have never been proven to work in the case of cancer.

Gardasil's widespread distribution has been made possible by virtue of research that uses outdated and insensitive technology – with the regulator (FDA) and NCI in effect 'in bed" with both the vaccine manufacturer and the organization that undertakes research testing.

So called independent researchers and experts are conflicted and worse actively seek to deflect better testing options – despite considerable evidence that what is presently used does not work.

Now we have irrefutable evidence that the vaccine contains harmful contaminants (recombinant HPV DNA) that is tightly bound to the adjuvant Aluminium Hydroxyphosphate (itself widely regarded as dangerous to humans) and where the combination of the two is understood to be particularly dangerous and impactful on the immune system. Explaining the extraordinary numbers of reported adverse events post Gardasil vaccination.

Meanwhile over 40 million doses (perhaps more than 50 million)) of Gardasil have been distributed globally at a cost of USD$120 per dose and following this, tens of thousands of young women have faced extreme adverse reactions due to Gardasil with over 90 associated deaths (this from a reporting system widely regarded as perhaps reporting between 1 and 10% of actual adverse events). Is anyone seeing the links?

Gardasil serves no good purpose, in fact quite the opposite. It needs to be withdrawn from the market immediately and those impacted by it, need to have proper follow-up and assistance provided to them. An independent and transparent inquiry needs to understand how this occurred, why, who was responsible and ensure that appropriate redress is sought and penalties imposed. Finally, the many and manifest conflicts of interest that exist between pharmaceutical companies, regulators and so called independent experts needs to be revealed and repaired so that never again can monetary or ego driven greed outweigh the health of so many young women and men worldwide.

By Norma Erickson, President