CALIFORNIA
HEALTH BENEFITS REVIEW PROGRAM

June 13, 2007

The Honorable Mervyn Dymally
Chair, California Assembly Committee on Health
State Capitol, Room 6005
10th and L Streets
Sacramento, CA 95814

The Honorable Sheila Kuehl
Chair, California Senate Committee on Health
State Capitol, Room 5108
10th and L Streets
Sacramento, CA 95814

Dear Assemblymember Dymally and Senator Kuehl:

Pursuant to the provisions of Senate Bill 1704 (2006), as chaptered in Section 127600, et seq. of the California Health and Safety Code, the California Health Benefits Review Program (CHBRP) submitted the *Analysis of Assembly Bill 1429 (Evans), Human Papillomavirus Vaccination*, on April 17, 2007. This report may be found on-line at www.chbrp.org/documents/ab_1429_final_leg.pdf

Staff of the Senate Committee on Health have requested that CHBRP provide clarification on how the results of recently published studies affect the conclusions of the CHBRP report on AB 1429, specifically with respect to the level of protection afforded by the vaccine. This letter is in response to that request.

After the submission of the CHBRP analysis of AB 1429, two studies addressing the performance of the human papillomavirus (HPV) vaccine were published in the May 10, 2007 issue of the *New England Journal of Medicine* and have been discussed in the press. The recently published studies refer to the results of a single clinical trial called Females United to Unilaterally Reduce Endo/Ectocervical Disease (FUTURE). The trial is designed to test the efficacy and duration of protection for Gardasil, the only vaccine currently approved by the federal Food and Drug Administration and available in the market. Gardasil is a quadrivalent vaccine that that targets the four HPV strains (types 6, 11, 16, and 18) that cause 70% of cervical cancers and 90% of genital warts.

One of the published studies, FUTURE I, addressed the level of protection the vaccine offered against genital lesions (i.e., genital warts and lesions that can lead to cervical cancer). The other study, FUTURE II, focused on the vaccine's ability to protect against high-grade cervical lesions that can lead to cervical cancer. We focus on the FUTURE II study in this letter per the intent of AB 1429, namely to reduce cervical cancer incidence. Preliminary results of FUTURE II were available in non-peer-reviewed reports and were discussed in CHBRP's *Analysis of Assembly Bill 1429* (page 19 of the report). Thus, the recent release of the FUTURE II data does not affect the fundamental conclusions of the report because CHBRP incorporated these data into its evaluation. However, there may be some confusion caused by the various percentages describing the level of protection afforded by the vaccine that have been cited in the studies and in the media. The reason the percentages vary is that the level of protection afforded by the vaccine

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varies *depending on the population using the vaccine and what HPV types are included in the data analysis*. This is discussed here and further illustrated in the attached Table 1.

- When used in a population of persons who have *no known prior exposure* to HPV[1] and who complete the vaccination series as directed, the vaccine reduced, by 98%, precancerous cervical lesions *caused by HPV types targeted by the vaccine.*

- However, some precancerous cervical lesions may also be caused by HPV types *not* targeted by the vaccine. When these lesions are also included in the data analysis, the overall reduction afforded by the vaccine is 27%.[2]

- These levels of protection, discussed above—98% for lesions caused by HPV types targeted by the vaccine and 27% when including lesions from all HPV types—are what one would expect if the vaccine is used among junior-high-school-aged girls participating in a community vaccination program, for example.

- The *general population* would also include late-teenage and adult women, some with prior exposures to HPV and some with incomplete vaccination regimens. The vaccine is less protective for such persons, and when these individuals are included in the data analysis, the protection afforded by the vaccine is reduced to 44% for precancerous cervical lesions *caused by HPV types targeted by the vaccine.* The protection afforded by the vaccine is further reduced—to 17%—when *all types of HPV* are included in the data analysis for the general population.

In summary, data in the recently published studies were available to CHBRP and are reflected in the AB 1429 report. These data do not change the medical effectiveness conclusions of the CHBRP report. We hope that this letter and accompanying table clarify any points of potential confusion.

Please feel free to contact me if you have any further questions.

Sincerely,

Susan Philip
Director, CHBRP
Division of Health Affairs
University of California Office of the President

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[1] This population had no prior exposure to the HPV types 16 and 18 that cause 70% of all cervical cancers.

[2] This population also had no prior exposure to the HPV types 16 and 18. This population included some persons who, although having received at least one of the three doses, may not have completed the full vaccination series. Note that the article on the FUTURE II study does not specify why the rate of reduction afforded by the vaccine drops to 27% from 98% when the analysis of the data includes the other HPV types. Based on personal communication with the Chair of the FUTURE II Study Group, (Laura Koutsky, June 12, 2007) the decrease is attributable to the difference in population characteristics (e.g. whether they had completed the full vaccination series).

cc: Assemblymember Noreen Evans, Bill Author, Assembly Bill 1429
Assemblymember Fabian Nunez, Speaker of the Assembly
Senator Don Perata, President Pro Tem of the Senate
Assemblymember Alan Nakanishi, Vice Chair, Assembly Committee on Health
Assemblymember Joe Coto, Chair, Assembly Committee on Insurance
Assemblymember John Benoit, Vice Chair, Assembly Committee on Insurance
Assemblymember Mark Leno, Chair, Assembly Committee on Appropriations
Assemblymember Mimi Walters, Vice Chair, Assembly Committee on Appropriations
Senator Samuel Aanestad, Vice Chair, Senate Committee on Health
Senator Michael Machado, Chair Senate Committee on Banking, Finance, and Insurance
Senator George Runner, Vice Chair, Senate Committee on Banking, Finance, and Insurance
Senator Tom Torlakson, Chair, Senate Committee on Appropriations
Senator Dave Cox, Vice Chair, Senate Committee on Appropriations
Anthony Matthews, Legislative Director, Office of Assemblymember Noreen Evans
Teri Boughton, Chief Consultant, Assembly Committee on Health
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John Gilman, Consultant, Assembly Committee on Health
Deborah Kelch, Consultant, Assembly Committee on Health
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Erin Ryan, Principal Consultant, Senate Committee on Banking, Finance and Insurance
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Geoff Long, Principal Consultant, Assembly Committee on Appropriations
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Elizabeth Hill, Legislative Analyst, California Legislative Analyst's Office
Steve Poizner, Insurance Commissioner, California Department of Insurance
Cindy Ehnes, Director, California Department of Managed Health Care (DMHC)
Jennifer Kent, Deputy Legislative Director, Office of Governor Schwarzenegger
David Link, Legislative Director, California Department of Insurance
Sherrie Lowenstein, Senior Supervising Counsel/Legislative Coordinator, California DMHC
Robert Dynes, President, University of California, Office of the President (UCOP)
Bruce Darling, Executive Vice President, University Affairs, UCOP
Steve Arditti, Assistant Vice President and Director, State Governmental Relations, UCOP
Jeff Hall, Legislative Director, Division of Health Affairs, UCOP
Paul Schwartz, Communications Director, Strategic Communications, University Affairs, UCOP
Susan Dentzer, News Hour Health Correspondent and CHBRP National Advisory Council Chair
W. Rory Hume, Provost, Executive Vice President, Academic and Health Affairs, UCOP
Cathryn Nation, Executive Director, Academic Health Sciences, Health Affairs, UCOP

ATTACHMENT

Table 1. Reduction in precancerous cervical lesions afforded by the quadrivalent HPV vaccine by the population receiving the vaccine

Population receiving the vaccine	Reduction of precancerous cervical lesions	Comment
Persons with no known prior exposure to HPV types 16 and 18 and who completed vaccination as directed. [1]	**98%** (95%CI[2]: 86-100%) reduction for lesions *due to HPV types* ***targeted*** *by the vaccine*	The vaccine is highly protective in this population against lesions caused by HPV types that are targeted by the vaccine. It does not protect against lesions caused by HPV types not targeted by the vaccine.
Persons with no known prior exposure to HPV types 16 and 18.[3]	**27%** (95%CI[2]: 4-44%) reduction for lesions *due to all HPV types, including types* ***not targeted*** *by the vaccine*	This is the level of protection one would expect against lesions caused by all HPV types, including types not targeted by the vaccine. This is the level of protection one would expect, for example, in a group of junior-high-school-aged girls participating in a community vaccination program.
General population, including persons who have prior HPV exposure and persons who did not complete the vaccination as directed.	**44%** (95%CI[2]: 26-58%) reduction for lesions caused by *HPV types* ***targeted*** *by the vaccine*	This is the level of protection one would expect in a group from the general population.
General population, including persons who have prior HPV exposure and persons who did not complete the vaccination as directed.	**17%** (95%CI[2]: 1-31%) reduction for lesions caused by *all types of HPV, including types* ***not targeted*** *by the vaccine*	This is the level of protection one would expect in a group from the general population.

Source: The Future II Study Group. Quadrivalent vaccine against human papilloma virus to prevent high-grade cervical lesions. *New England Journal of Medicine 2007; 356:1915-27.*

Notes:

[1] HPV types 16 and 18 cause 70% of all cervical cancers.

[2] The 95% confidence interval (95%CI) reflects statistical uncertainty in measurements, and represents a likely range for the true value of the measurement. In the example of the first row, a 98% reduction in precancerous cervical lesions due to the vaccine was observed. However, the true value of the reduction may be as low as 86% or as high as 100%, as indicated by the 95% CI.

[3] This population included some persons who may not have completed the full vaccination series, although all had received at least one of the three doses.