MEMORANDUM DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration
Center for Biologics Evaluation and Research
Office of Vaccines Research and Review
Division of Viral Products

Date: September 29, 2014

To: The File STN125549

From: Haruhiko Murata, DVP

Through: Keith Peden, DVP
Jerry Weir, DVP
Robin Levis, DVP

Sponsor: Pfizer Inc.

Subject: Review of Human Papillomavirus Vaccine Immunogenicity Assay Used in Support of Original BLA STN125549 (Meningococcal Group B Vaccine)

The Human Papillomavirus (HPV) competitive Luminex Immunoassay (HPV cLIA) is a multiplexed, competitive immunoassay that measures HPV types 6, 11, 16, and 18 specific antibodies to neutralizing epitopes on Virus-Like Particles (VLPs) from a single serum sample. The assay uses ----------
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----------(b)(4)----------

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cLIA was used to assess HPV-specific immune responses in clinical study B1971011 (concomitant administration of MenB vaccine rLP2086 and HPV vaccine Gardasil).

HPV cLIA was originally validated in 2003 and re-qualified in March 2006 as HPV cLIA (b)(4). The re-qualification report (dated 20 March 2006) is included in STN125549. ----------
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The re-qualification results of HPV cLIA (b)(4) are summarized below.

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One page determined to be not releasable: (b)(4)

The following information requests were issued to the Sponsor on 05 August 2014.

Please verify that the HPV immunogenicity assay for the concomitant administration study (B1971011) was version (b)(4) of HPV cLIA rather than version (b)(4).

Sponsor's Response
Pfizer confirms that Version **(b)(4)** *of HPV 6, 11, 16 & 18 Competitive Luminex Immunoassay (HPV-4 cLIA* **(b)(4)***) was used to support HPV testing in the Phase 2 concomitant administration study B1971011.*

Please verify that the only significant difference between HPV cLIA versions (b)(4) and (b)(4) is the ----------(b)(4)----------). If other substantive changes exist between the assay versions, please provide relevant qualification reports that support these changes.

Sponsor's Response
Pfizer confirms that the only significant difference between HPV cLIA versions ----------(b)(4)----------.

Please provide an analysis of any trend in the change in HPV immunogenicity assay results over time for the control samples used in HPV cLIA.

Sponsor's Response
All clinical testing using this assay was performed at ----------(b)(4)----------. The HPV cLIA is a Merck proprietary assay and since Merck is the owner of all trending data, Pfizer requested (b)(4)/Merck to provide the trending charts for all the quality control samples (QCS) since the inception of HPV cLIA version (b)(4). As can be seen from the trending charts, the HPV cLIA version (b)(4) demonstrated stable performance over time since its inception in 2011. (Graphs showing control sample trends between July 2011 and November 2013 were included in the response.)

Please include the period (with dates) in which control samples and samples for the concomitant administration study were assessed.

Sponsor's Response
The HPV cLIA testing for study B1971011 was conducted from 05-November 2013 to 15-November 2013.

Reviewer's Comments:

- HPV immunogenicity in study B1971011 was assessed on behalf of the Sponsor by the contract organization ---(b)(4)------- is the same testing entity that developed the HPV cLIA in conjunction with Merck and used it to generate efficacy data for licensure of Merck's Gardasil HPV vaccine.
- HPV cLIA appears to have undergone two major validation/qualification studies: one in 2003 for version (b)(4), and another in 2006 for version (b)(4). In 2009, a ----------(b)(4)----------; the assay was referred to as version (b)(4) following this change.
- The strategy used for assay qualification of HPV cLIA (b)(4) is very similar to the one used for validation of the original version of cLIA ((b)(4); reviewed in original BLA submission STN125126). The information on HPV cLIA (b)(4) supplied in STN125549 is identical to what was supplied by Merck in approved Gardasil efficacy supplements (STN125126/1297, new indication for males; STN125126/1516, concomitant use of Gardasil with Adacel/Menactra).
- The Sponsor's responses to the information requests are satisfactory. Assay version (b)(4) was used to assess samples in study B1971011 between 05 November 2013 and 15 November 2013. There appears to be no substantive difference between assay versions (b)(4) and (b)(4) other than ----------(b)(4)----------. No discernable adverse trends were noted for the control sample data from July 2011 to November 2013, suggesting that the assay is well-controlled.
- Overall, the data supplied in STN125549 for the qualification of HPV cLIA (b)(4) support its use for assessing HPV immune responses in study B1971011.
- Based on the scope of this review, I recommend approval of BLA STN125549.