

To: Mr. Matt Whitman

File: STN 125259/0 CERVARIX

RE: Pregnancy Outcomes and MPL AEs

Date: July 26, 2007

APPROVED

By: [Redacted] Date: [Redacted]

1. We note that data are presented regarding the outcomes of pregnancies in studies submitted in support of the license application for Cervarix® (Summary of Clinical Safety, Table 58, Page 174). We request that you provide information regarding all diagnoses of congenital anomalies. Specifically, please indicate the treatment group and provide narratives (including family history, medical history, dates of vaccination, time to conception and time to event, and concomitant medications). Please also provide International Event forms for subjects who had children diagnosed with congenital anomalies and/or still birth and/or intra-uterine death. If narratives are provided in the BLA, please indicate the location within the BLA.
2. For HPV-009, congenital anomalies and/or still births and/or intra-uterine deaths have been reported to the IND. Please submit all information regarding congenital anomalies and/or still births and/or intra-uterine deaths that occurred in HPV-009 to the BLA.

Please refer to your July 20, 2007 email to Ms. Helen Gemignani which contained the document entitled: *Preliminary Safety evaluation: Adverse events reported in vaccines developed by GSK Biologicals formulated with GSK's proprietary adjuvant systems containing MPL*. This document was also submitted to your IND [Redacted]. We have the following comments:

3. Please provide clinical narratives and International Event forms for the following subjects:
 - a) In Table 4 (Page 6), subjects identified as having arthritis rheumatoid, lupus erythematosus syndrome, colitis ulcerative and colitis ulcerative aggravated, erythema nodosum, and uveitis.
 - b) In Table 7 (Page 8), subjects identified as having sarcoidosis, multiple sclerosis-like syndrome, myasthenia gravis like syndrome, anti-nuclear antibody positivity, arthritis rheumatoid, colitis ulcerative and colitis ulcerative aggravated, hyperthyroidism, hypothyroidism, thyroid disorder, thyroiditis, thrombocytopenia, erythema nodosum, and uveitis.
 - c) In Table 8 (Page 9), subjects listed as having multiple sclerosis, Crohn's disease, myasthenia gravis or multiple sclerosis, thyroiditis Hashimoto's or Quervain, thrombocytopenia, and hemolytic anemia.

CBER acknowledges that the report submitted on July 20, 2007 contains a preliminary safety evaluation of your proprietary adjuvant systems containing MPL. You will submit a detailed meta-analysis plan and datasets for the analysis as CBER requested in the teleconference on July 18, 2007. Please acknowledge.