RESPONSES TO REVIEWERS

Response to Reviewer #1:
The authors updated current situation of HPV vaccination simply, although there are no enough new knowledge provided by this review, this review summarized the current situation of HPV vaccine systematically. I have the following comments.

1. Title is not consistent with content, e.g. "Vaccine Development and Rationale" section had not told the readers the content of vaccine development and rationale.
   Response : Discussion of rationale is detailed within the introduction and information added into the section "Vaccine Development and Rationale" see pages 5-6

2. Can you tell the readers why scientists developed bivalent, quadrivalent and 9vHPV vaccine?
   Response: Please see information added in "Vaccine Development and Rationale" and "Vaccine Approval" sections with discussion of differential prevalence of HPV types and need for tailoring vaccines based on these findings. Page 6; 8-9

3. It is better if the authors could summarized the worldwide HPV genotype distribution, and then discussed the possible contradiction between current HPV vaccines and the real distribution of HPV genotype.

   Response: Unfortunately there is only limited data about the worldwide prevalence for HPV genotypes. The information available in specific countries is found within discussion section in both "Vaccine Development" and "Vaccine Approval section". Pg 6; 8-9

4. Efficacy section: "Many subtypes exist of both oncogenic (high risk) and genital wart causing (low risk) HPV", please ensure the validity of terminology, genotype? Subgenotype? Type? Subtype?

   Response: Terminology changed throughout manuscript for consistency "genotype".

5. Citations are not sufficient, for example, no citation for "Worldwide, cervical cancer is the fourth most frequent cancer in women affecting almost 500,000 women each year and is the most common cause of cancer death among women in developing countries. ", beginning of the

introduction. No citation for "The median time from HPV infection to seroconversion is approximately 8-12 months, however because HPV infection is restricted to the intraepithelial layer of the mucosa it does not induce a strong immune response." Discussion section. No citation for " Many subtypes exist of both oncogenic (high risk) and genital wart causing (low risk) HPV. Partial cross-protection against non-vaccine oncogenic HPV types has been reported, however the clinical relevance is undetermined."

Response: All citations have been addressed in the revised version.

RESPONSE TO REVIEWER #2

The article is well written, interesting and it provides a complete revision about HPV vaccination worldwide. Please address minor points that I listed in the "word" document attached, in track changes/commments modality.

Edits from Giovanni:

COMMENT #1 Reference provided for introduction. (ref#1)

COMMENT #2 Clarification of ALL new cancers made within introduction section. See page 4 (para 2&3)

COMMENT # 3 Citation added (ref#3)

Deleted "nine" Number 9 added.

COMMENT #4 Vaccine approval timing added to document page 9 last paragraph

COMMENT #5 Vaccine approval in immunocompromised info added. See page 13 last paragraph

COMMENT # 6 Vaccine acceptability change. Page 15 , first paragraph

REFERENCES FORMATED PROPERLY

TABLES: All changed to address order based on date of article publication and added reference number to each article