MHRA
Regulating Medicines and Medical Devices

MHRA
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[redacted]

R.E. FOI 14/555

12th January 2015

Dear [redacted]

Thank you for your FOI request of 10th December 2014 where you requested Yellow Card data in relation to the Human Papilloma Virus Vaccine. Please find a response to the questions raised in your request below:

- **The actual number of SAE since HPV vaccination was introduced**

We have received a total of 8,055 individual spontaneous suspected Adverse Drug Reaction (ADR) reports in association with the HPV vaccine up to and including 22nd December 2014. As stated in previous correspondence, a suspected individual ADR report is not necessarily proof that a reported symptom/event was a true side effect caused by the vaccine. Of these 8,055 individual ADR reports, 2,537 reports were coded serious on our system.

The seriousness criteria for ADR reporting were determined by a working group of the Council for International Organizations of Medical Sciences (CIOMS) and are defined as 6 possible categories which are explained on the Yellow Card. MHRA asks reporters to select one of the following criteria by ticking the appropriate box on the Yellow Card: (1) patient died due to reaction (2) life threatening (3) resulted in hospitalisation or prolonged inpatient hospitalisation (4) congenital abnormality and (5) involved persistent or significant disability or incapacity or (6) if the reaction was deemed medically significant. In addition to this, seriousness of an individual reaction term has also been defined by the MHRA in our medical dictionary.

Please be aware that one individual ADR report may contain more than one reaction term and therefore the total number of reactions will be greater than the total number of reports. Within the 2,537 serious reports there are a total of 8,703 reported reaction terms.

- **How many of these reported SAE remain unresolved, or undetermined, by each illness type, including the 4 deaths reported?**

When individual suspected ADR reports are submitted to MHRA the reporter states the outcome of the reaction terms as either recovered, recovered with sequelae, not recovered, recovering, not known or fatal. The attached table summarises the outcomes for each reported reaction term within these 2,537 serious reports as stated by the reporter. It is important to note that this table includes all reaction terms within a serious report, even if every

reaction term in a report may not individually be considered as serious.

When additional information is received, a report will be up-versioned to include additional information including the outcome of the reactions if provided. Please note that reaction outcome is not a mandatory field on the Yellow Card form and so this information will not always be provided to us. Not known is the default term if no outcome is stated. Therefore, some events listed as not recovered, recovering or not known at the time of reporting may have subsequently recovered after the initial Yellow Card report was submitted, however additional information has not been received. In relation to the 4 reports with a fatal outcome, there is no indication that the vaccine was the cause of death from the details provided by the reporter. One report related to an existing tumour, one to a concurrent bacterial infection, one was death of a premature baby and one has a fatal outcome due to leukaemia.

- **Please provide the estimated reporting rate (ERR) for SAE for this vaccine since it was introduced**

Over 7.5 million doses of HPV vaccine have been given since 2008 in the UK. This equates to around 34 serious suspected ADRs per 100,000 doses administered.

You have provided a comparison of ADR reporting rates across vaccines and asked why it is acceptable for HPV vaccines to have a higher ADR reporting rate than other vaccines. It is important to bear in mind that ADR reporting rates are influenced by many factors and, as suspected ADRs are not all necessarily proven side effects, such rates should not be used to estimate or compare the incidence of true side effects or relative safety between different vaccines. Comparisons of ADR reporting rates would be an invalid estimate of relative vaccine safety.

- **The eMC Medicine Guide for HPV vaccines states 'some side effects may be serious'. There are over 2000 SAE reported by Yellow Card and yet the patient information leaflet (PIL), for Cervarix, never mentions any serious side effects, neither does the NHS Choices web page (except in the public comments).**

A suspected serious ADR is not necessarily proof that the reported event was a true side effect caused by the vaccine. The possible side effects are listed in the SmPC and PIL, which are part of the licence. The Cervarix SmPC and PIL list anaphylactic reactions as a possible side effect, which are often serious.

- **Please identify which 'old' safety issues are considered to be serious SAE.**

The Cervarix SmPC and PIL list anaphylactic reactions as a possible side effect, which are often serious.

- **Please also explain how the 'benefit risk balance remains positive' when Cancer Research UK tell us that deaths due to cervical cancer have reduced from 8/100,000 to 2/100,000 over the last 40 years, without any help from this vaccine.**

The vaccine is expected to further reduce the number of deaths from cervical cancer. Public Health England are monitoring the effectiveness of the vaccine programme in this respect. This expected benefit outweighs the risks that are known to be associated with the vaccine as described in the SmPC and PIL.

If you are dissatisfied with the handling of your request, you have the right to ask for an internal review. Internal review requests should be submitted within two months of the date of receipt of the response to your original letter.

Please remember to quote the reference number above in any future communications.

If you are not content with the outcome of the internal review, you have the right to apply directly to the Information Commissioner for a decision. The Information Commissioner can be contacted at:
Information Commissioner's Office, Wycliffe House, Water Lane, Wilmslow, Cheshire, SK9 5AF

Yours sincerely,

FOI Team,
Vigilance and Risk Management of Medicines Division.