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Briefing for the Public Petitions Committee

Petition Number: PE01574

Main Petitioner: Freda Birrell on behalf of UK Association of HPV Vaccine Injured Daughters (AHVID)

Subject: HPV Vaccine Safety

Calls on the Parliament to urge the Scottish Government to convene a roundtable discussion on the safety of HPV vaccines with medical/scientific professionals from both sides of the debate.

HPV infection

Human Papilloma Virus (HPV) is the name for a group of viruses that affect the skin and moist membranes lining the body, such as the cervix, anus, mouth and throat. Some types of HPV can increase the risk of developing cervical cancer. Infection with HPV is the main risk factor and major cause of the main types of cervical cancer – squamous cell cancer and adenocarcinoma. There is also evidence linking HPV with cancers of the vulva and vagina as well as with cancers of the anus[1], mouth/throat (oropharyngeal cancer), and penis in men

There are over 100 different types of HPV. HPV is common but only a small proportion of infections with certain HPV types can persist and progress to cancer. Some types are referred to as the "wart virus" or "genital wart virus" because they cause genital warts. For most sexually active people, the HPV virus causes no harm and goes away on its own, with HPV infections usually clearing up without any intervention within a few months.

At least fifteen types of HPV are considered high risk for cancer of the cervix including types 16 and 18. These two types cause about 70% of cancers of the cervix. If you have persistent infections with high risk types of HPV, you are more at risk of developing cervical cancer.

[1] Though data on anogenital cancers other than cancer of the cervix are limited, there is an increasing body of evidence linking HPV with cancers of the anus, vulva, vagina, and penis.

Morbidity and Mortality

Cervical cancer is the most common cancer in females under 35 in the UK. Overall, about 2% of cancers diagnosed in women are cervical cancers. Around 3,100 women (of all ages) are diagnosed with cervical cancer in the UK each year. The incidence of cervical cancer in females in Scotland decreased by approximately 44% between 1986 and 2012. This may be attributable to the commencement of the cervical screening programme[2].

In 2012, cervical cancer was the 17th most common cause of cancer death among women in the UK, accounting for 1% of all female deaths from cancer. In that year, there were 919 deaths from cervical cancer in the UK, including 112 deaths in Scotland. Cervical cancer mortality rates for females of all ages in Scotland decreased from 8.6 per 100,000 in 1981 to 3.3 per 100,000 in 2013.

Vaccination programme in Scotland

There are now vaccines to prevent HPV infection. All girls aged 12 or 13 in the UK are routinely offered the HPV vaccine at school. By the end of the 2013/14 school year, 81.4% of girls in S2 had completed their course of three HPV immunisations. These vaccines protect against the strains of HPV that are most likely to cause cervical cancer, but not against all strains. Cervical screening (the Pap test) is still needed for women who have been vaccinated, to help prevent the 30% of cervical cancers not targeted by the HPV vaccine.

In September 2008, the HPV vaccination was introduced into the Scottish childhood immunisation programme. The initial vaccine used, Cervarix, protected against infection by HPV types 16 and 18 and was administered routinely to 12-13 year old girls through a school-based programme. For a limited period (until August 2011), it was also offered to older teenage girls who were under 18. By protecting girls from HPV 16 and 18 this immunisation programme aimed to reduce cervical cancer.

Cervarix was used for immunisation from 2008-2012. Following a planned review on which HPV vaccine offered the best overall package; Cervarix was replaced in September 2012 by another vaccine, Gardasil. Gardasil is a quadrivalent vaccine in that it helps to protect against 4 types of HPV. In girls and young women (ages 9 to 26), it protects against 2 types of HPV (types 16 and 18) that cause the majority of cervical and vaginal cancer cases (70%), and up to half of the vulval cancer cases. However, unlike Cervarix, in males and females (ages 9 to 26), Gardasil also helps to protect against most anal cancer (80%) and genital warts (types 6 and 11) cases (90%)[3].

[2] The national cervical screening programme was introduced in Scotland in 1988 with the aim of reducing the incidence of invasive cancer of the cervix

[3] Genital Warts - A Comprehensive Review: Preventative Treatments—the Role of the HPV Vaccine –Table 3.

In March 2014 the Joint Committee on Vaccination and Immunisation (JCVI) which advises UK health departments on immunisation, recommended that, based on the latest immunological evidence, the protection achieved from using a two dose vaccination schedule was likely to be the same as a three dose schedule. The schedule in Scotland changed to reflect this from September 2014.

Safety

Role of the MHRA

The Medicines and Healthcare products Regulatory Agency (MHRA) is the government agency responsible for regulating medicines and medical devices in the UK (including Scotland). The MHRA continually review the safety of all medicines and vaccines in the UK and inform healthcare professionals and the public of the latest safety updates.

During the course of the four years that Cervarix was in use in the HPV immunisation programme, the MHRA closely monitored safety, undertaking a safety review of Cervarix at the end of its routine use, in November 2012. They concluded that the balance of its risks and benefits remained clearly positive.

Adverse reactions

There are a number of reported side effects (also known as adverse drug reactions or ADRs) from the Gardasil vaccine. In clinical trials, the most common Gardasil vaccine-related adverse reactions observed (over 1 person in 10) included swelling, redness and pain at the site of the injection and headaches. Other less common side effects such as fever, nausea, painful limbs, itchy red rashes, difficulty breathing, seizures, fainting, Guillain-Barré syndrome, muscle pain and weakness have also been reported during the worldwide use of Gardasil. As these are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure[4].

Potential long term effects

The petitioner believes that the HPV vaccines are having a negative impact on the health of girls vaccinated in the UK and Scotland, resulting in injuries and

[4] The Electronic Medicines Compendium (eMC) website http://www.medicines.org.uk/emc/ contains approved, up to date, easily accessible information about medicines licensed for use in the UK including possible side effects and their frequency.

long term health issues. They state that many girls have become extremely ill after being inoculated and that serious concerns regarding the safety and efficacy of the vaccines have not been addressed by previous Health Ministers and officials. Their response was to advise that these new medical conditions were simply a coincidence, underlying health condition, related to their age or psychosomatic.

The petitioner provides research material which investigates the causes of neurological manifestations in girls following immunization with the HPV vaccine. Frequent symptoms included headaches, general fatigue, coldness of the legs, limb pain and weakness, which were often compatible with the clinical diagnostic criteria for complex regional pain syndrome (CRPS)[5]. Also included is a letter to the editor of the European Journal of Neurology concerning Postural Orthostatic Tachycardia Syndrome (POTS) after vaccination with Gardasil. The author recommends that doctors should be aware of a possible association between vaccination with Gardasil and POTS.

There have also been reports in the press[6] over the years concerning young women who have developed chronic fatigue syndrome (CFS) or whose health has been affected after HPV vaccination. The cause of CFS (otherwise known as ME or myalgic encephalomyelitis) is not known, but it does occur naturally in teenagers, and is more common in girls than boys. The World Health Organization (WHO) Global Advisory Committee on Vaccine Safety (GACVS) regularly reviews the emerging international evidence on safety of HPV vaccination and issued a statement in March 2014 concluding that there was no proven link between the HPV vaccination and autoimmune disease, of which many think CFS/ME is an example[7].

In July 2015, The European Medicines Agency (EMA) began a specific review to clarify the safety profile of HPV. It will determine whether or not the evidence may support a causal association between HPV vaccine and POTS as well as CRPS and whether these should be reflected in the vaccine product information to better inform patients and healthcare professionals. At present, as these syndromes can occur naturally in those being vaccinated, a link with the vaccine has not been proven. The review does not question that the balance of benefits and risks of HPV vaccines are favourable. The final stage of the review procedure is the adoption by the European Commission of a legally binding decision applicable in all EU Member States.

Scottish Government Action

The Scottish Government, as with other UK health departments, takes current expert advice and guidance on immunisation from the MHRA and the JCVI.

[5] CRPS is a chronic pain condition affecting the limbs.

[6] Thousands of teenage girls report feeling seriously ill after routine school cancer vaccination

[7] Chronic fatigue and the HPV vaccine

They carefully consider their advice and recommendations in respect of HPV vaccination before any decision in Scotland is made. When the JCVI revised its existing recommendation to change the HPV vaccination schedule from a 3 to a 2 dose schedule, the Chief Medical Officer provided an update to NHS professionals providing information about the changes to the programme. The letter includes links providing guidance about HPV and immunisation procedures from The Green Book which details information for public health professionals on immunisation from the UK government.

Scottish Parliament Action

The Scottish Parliament has previously considered petition PE1477 which called on the Scottish Government to extend the HPV immunisation programme to include boys. SPICe produced a briefing on the subject for the Public Petitions Committee in 2013.

A petition lodged on 7th October 2015 PE01584 calls on the Scottish Parliament to urge the Scottish Government to set up an advisory committee within NHS Scotland to provide advice on immunisation and vaccination policy and to withdraw from seeking advice from the JCVI.

A parliamentary question S4W-26271 in June 2015**,** asked the Scottish Government how many young women per 10,000 HPV vaccinations have required referral for specialist assessment following vaccination. Minister for Public Health responded on the 1 July 2015 as follows:

"The information requested is not held centrally. However, as with all vaccines and medicines the Medicines and Healthcare products Regulatory Agency (MHRA) monitors and provides advice on the safety of the HPV vaccine in the UK. Since the introduction of the HPV vaccine in 2008 it has been used in millions of girls across the UK and around the world, and the MHRA continue to advise that the vaccine has a very good safety profile. The MHRA keeps the HPV vaccine under close and continual review and would take regulatory action if new evidence emerged which called into question the safety of the HPV vaccine or any other vaccine currently in use."

UK Parliament Action

On 7 July 2015, The Countess of Mar posed parliamentary question HL1164 concerning the response by the Medicines and Healthcare products Regulatory Agency to a freedom of information request on 25 June. It asked why only 16.8 per cent of reports of serious adverse events relating to human papilloma virus (HPV) vaccines under the Yellow Card Scheme have been followed up. The question also asked how this compares to the percentage of yellow-card reports followed up for all vaccines; and whether the MHRA now plan to follow up all reported serious adverse events relating to HPV vaccines in order to ascertain recovery rates.

The Lord Prior of Brampton responded: "*A total of 2,624 spontaneous suspected serious adverse reaction reports (ADRs) with human papilloma virus (HPV) vaccines have been reported to the Medicines and Healthcare products Regulatory Agency (MHRA) via the Yellow Card Scheme*[8] *up to 7 July 2015.*

To date more than eight million doses of HPV vaccine have been given in the United Kingdom since 2008, with close to 90% eligible teenagers vaccinated. The vast majority of suspected side effects reported so far relate to those we would expect with most types of vaccine; these are most commonly dizziness, headache, nausea, sore arms, vomiting, general malaise, tiredness, fever, and rashes. These tend to be mild and transient. Many serious reports relate to immediate fainting, which is not necessarily a side effect of the vaccine but a response that any type of needle insertion can provoke in some people.

The following table provides a breakdown of UK suspected spontaneous ADRs received via the Yellow card Scheme in association with all vaccines on the immunisation schedule. The table provides the total number of reports, the total number of serious reports and the number of serious reports followed up.

It should be noted that a Yellow Card report is not proof of a side effect occurring, but a suspicion by the reporter that the vaccine may have been the cause. Yellow Card data cannot be used as a reliable indicator of the frequency of suspected ADRs to vaccines or medicines. The level of ADR reporting may fluctuate between given years due to a variety of reasons such as a medicine being new (reporting rates are generally higher when a product is first introduced), stimulated interest/publicity and variations in exposure to the medicine. Comparisons of ADR reporting rates would be an invalid estimate of relative vaccine safety.

Every reporter to the Yellow Card scheme receives an acknowledgement which asks that any new information relating to the case be reported. Follow up procedures for Yellow Card reports are in place and are designed to ensure that relevant information is sought if this is missing from reports of serious reactions[9] *which could potentially be new signals. While in an ideal world full details would be obtained for every report, given there are over 750,000 reports on the database with around 30,000 new reports each year, it will never be possible to ensure all reports on the database are complete.*

There are a number of difficulties with achieving satisfactory follow up. Time pressure on potential reporters has been identified as one of the reasons for under-reporting adverse reactions through the Yellow Card Scheme.

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[8] The Yellow Card Scheme is the website for reporting adverse drug reactions within the UK which enables the MHRA to monitor the safety of all healthcare products.

[9] The MHRA indicate that serious reactions include those that: are fatal, are life-threatening, are disabling or incapacitating, are congenital abnormalities, involve or prolong hospitalisation, or are medically significant. A severe reaction might not be life-threatening or disabling but can seriously affect an individual patient. For example, headaches are not normally considered serious in nature, but may be very severe.

This issue also applies to requests for follow up information and therefore there is a need to be selective and focussed about the reports for which follow up information is requested.

Vaccine Brand	Total number of reports	No of serious reports	No of serious reports followed up	% of serious reports followed up*
Human Papilloma Virus (HPV)	8,276	2,624	441	17%
Diphtheria,tetanus, pertussis, polio andHaemophilus influenza type b (DTaP/IPV/Hib)	1,382	713	103	14%
Tetanus, diphtheria and polio (Td/IPV)	1,152	671	95	14%
Diphtheria,tetanus, pertussis and polio (DTaP/IPV)	1,326	509	65	12%
Rotavirus (Rotarix)	452	283	70	25%
Pneumococcal disease (PCV)	1,611	882	85	10%
Meningococcal group C disease (Men C)	14,671	4,241	81	2%
Hib/Men C	285	155	23	15%
Measles, mumps and rubella (MMR)	5,492	2,804	88	3%
Pneumococcal disease (PPV)	1,726	985	27	3%
Fluenz/ Fluenz Tetra	877	381	74	19%
Zostavax	646	408	105	26%
Influenza virus	5,745	3807	483	13%

* Percentage provided to the nearest whole number

The HPV vaccine has a very good safety record, and surveillance shows it has contributed to a significant decrease in rates of infection with the two main cancer-causing human papillomaviruses. The UK programme is eventually expected to prevent hundreds of deaths from cervical cancer every year.

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30 September 2015

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