

Joint Committee on Vaccination and Immunisation

Biennial Report 2007-2008





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Contents

- 1 Chairman's foreword
- 2 Background
- 3 Members of the committee
- 3 Responsibilities and obligations
- 3 Terms of appointment
- 4 Declarations of interest
- 5 Focus of this report
- 5 The addition of human papillomavirus vaccine to the routine immunisation programme
- 9 Pneumococcal vaccine
- 11 Tuberculosis and BCG
- 14 Rotavirus
- 16 Haemophilus influenzae type b vaccine
- 18 Influenza
- 20 The future
- 20 Varicella/herpes zoster
- 20 Hepatitis B
- 21 Meningococcal vaccines
- 22 Pneumococcal vaccines
- 23 Horizon scanning and new vaccines
- 24 Appendix A: Declaration of members' interests 2007
- 28 Appendix B: Declaration of members' interests 2008



Chairman's foreword

This report describes the work undertaken by the Joint Committee on Vaccination and Immunisation (JCVI) during 2007 and 2008. The committee provides advice to ministers on the national vaccination programme. During these two years, we have been particularly concerned with monitoring the effects of the existing vaccine programme and, where necessary, making modifications. In addition, the committee has provided advice, with other advisory groups, on preparedness for pandemic influenza. This is a particularly difficult area since the precise configuration of the virus cannot be known until the pandemic begins. Finally and most recently, the committee provided advice that formed the basis for the introduction of human papillomavirus vaccine for young girls. This is only the second vaccine available (the first was hepatitis B vaccine) with the promise of preventing cancer.

The members of the committee and of the sub-groups provide their expertise and time free of charge to ensure that the UK benefits from the best possible advice. I thank them all.

I hope you find the report interesting and useful.

Professor Andrew Hall Chairman, JCVI

Background

The Joint Committee on Vaccination and Immunisation (JCVI) is an independent expert advisory committee first set up in 1963. Its key role is:

11 To advise the Secretaries of State for Health, Scotland, Wales and Northern Ireland on matters relating to communicable diseases, preventable and potentially preventable through immunisation.**11** This report sets out the priorities and important activities of JCVI in 2007 and 2008. As key adviser to health departments on immunisation, the committee plays an important role in continually improving the UK's immunisation programme and ensuring that it contributes positively to safeguarding the nation's health.

Members of the committee

Responsibilities and obligations

The committee has a responsibility to provide high quality and considered advice and recommendations to the UK health ministers on matters set out in the terms of reference www.advisorybodies.doh.gov. uk/jcvi/index.htm. This includes giving advice and making recommendations on routine issues and on any specific or special matters that ministers may from time to time request. In formulating any advice and recommendations, the committee must take into account the need for and the impact of vaccines, the quality of vaccines and the strategies needed to ensure that the greatest benefit to the public health can be obtained from the most appropriate use of vaccines. The committee does not have an executive function.

Members of the committee play a critical role in ensuring its standing as an internationally recognised leading body in the field of immunisation. They are people who are committed to the continuing development and improvement of public health policy on immunisation and bring relevant experience to the committee from many different fields and practice areas.

Terms of appointment

Appointments to the JCVI are the prerogative of the Secretaries of State and are normally of four years duration. Appointments may, however, be terminated in the event of unsatisfactory attendance at meetings or conduct which renders the member unfit to remain in office, or at the discretion of the Secretaries of State. The chair and members of JCVI will:

- be committed to the continued development and improvement of this important area of public health
- bring relevant experience to the committee
- contribute to the provision of high quality and considered advice to UK ministers of health
- be expected to make a full and considered contribution to the work of the committee and to contribute fully to the debate and to the decision-making processes of the committee
- provide expert guidance when an issue which falls within their particular area of expertise is under discussion
- contribute to the debate in the capacity of a well-informed health professional where the issue does not fall within their expertise
- take into account the need for and impact of vaccines, the quality of vaccines and their safety and advise strategies to ensure that the greatest benefit can be obtained from the most appropriate use of vaccines
- recommend the best public health advice to ministers
- be prepared, as requested by the secretariat, to occasionally provide expert advice on relevant issues outside of committee meetings
- be prepared, as requested by the secretariat, to occasionally attend and contribute to the deliberations of one or more of the subgroups of JCVI which report to the main committee.

A full list of the committee members can be found at Appendix A.

Declarations of interest

Members are required to declare relevant interests at committee meetings. They must state whether the interests are personal or non-personal and whether they are specific or non-specific to the matter or product under consideration. Interests are considered relevant if they occurred within the last 12 months for new and existing members.

(a) An existing member must declare a personal specific interest if they have in the last year worked on the matter or product under consideration and have received personal payment for that work, in any form, from the industry.

(b) An existing member must declare a personal non-specific interest if they have in the last year a current personal interest in the company concerned which does not relate specifically to the matter or product under discussion.

(c) An existing member must declare a non-personal specific interest if they are aware that in the last year the department for which they are responsible has received payment for work on the matter or product but the member has not personally received payment in any form from the industry for the work done.

(d) A member must declare a non-personal non-specific interest if they are aware that in the last year the department for which they are responsible has received payment from the company concerned which does not relate specifically to the matter or product under discussion.

Declaration of interests at meetings

Members of the committee are required to declare relevant interests at committee meetings. They must state whether the interests are personal or non-personal and whether they are specific or non-specific to the matter or product under consideration.

A member who is in any doubt as to whether they have an interest that should be declared, or whether they should take part in the proceedings, should ask the chairman for guidance.

JCVI sub-groups provide advice to the main JCVI. JCVI sub-group members are required to declare their interests. In general, a JCVI sub-group member with a current personal specific interest should not be invited to participate. However, in exceptional circumstances where they have particular expertise they could be invited to attend the meeting but may not take part in any decisions about advice to the main JCVI subject to their own declaration of interests. All other members of a JCVI sub-group can participate in the discussion and the decision-making. The chair of a JCVI sub-group should not have personal specific interests in any item under discussion.

Further details may be found at **www.advisorybodies.doh.gov.uk/jcvi**

A full list of members' interests can be found in Appendix B of this report.

The remainder of this report will focus on the work of JCVI in the last two years with a particular emphasis on the introduction of the human papillomavirus vaccine.

Focus of this report

The addition of human papillomavirus vaccine to the routine immunisation programme

HPV, cervical cancer and genital warts

HPV is a virus that infects the deepest layer of the skin or genital surfaces (epithelium). There are approximately 100 types of HPV, of which about 40 infect the genital area. HPV is the most common viral sexually transmitted infection and it is estimated that at least half of all sexually active women acquire genital HPV in their lifetimes. Infection is most likely to occur in the late teens and early twenties (Figure 1).



Figure 1. Prevalence of high-risk HPV according to age quinquennia. The graph shows that HPV infection is greater in 20- to 29-year-olds and decreases rapidly after age 30. (Source: Kitchener *et al.*, 2006).

JCVI Biennial Report

Genital HPVs are classified as either:

- 'high-risk' or oncogenic types which cause cervical cancer and the early changes in the cervix associated with cervical cancer, or
- 'low-risk' types, which lead to the development of benign genital warts.

Although the majority of high-risk HPV infections are transient and cause no clinical problems, persistent infection by a high-risk HPV type is by far the most important causal factor for the development of cervical pre-cancerous and cancerous lesions. Persistent infection by high-risk HPV types is detectable in more than 99% of cervical cancers. HPV infections also cause genital warts, other rarer anogenital cancers, and cancers of the head and neck. Routine cervical screening has prevented many deaths and invasive cancers by detecting and preventing cervical changes at an early stage. However, in the UK there were still 949 deaths from cervical cancer in 2006.

JCVI considered the benefits of vaccines that provide protection against HPV infection. Both HPV vaccines – Cervarix[®] and Gardasil[®] – are over 99% effective in preventing infection by HPV types 16 and 18 that cause over 70% of all cervical cancers in the UK. In modelling the impact of HPV vaccination on cervical cancer, it was estimated that up to 400 lives would be saved each year.

The Gardasil[®] vaccine also protects against HPV types 6 and 11 and is over 99% effective in preventing genital warts caused by these HPV types. Around 90% of all genital warts are caused by HPV types 6 and 11.

In recommending that the HPV vaccine should be introduced, the committee had to consider a number of issues shown in Table 1.

Area considered	Detail		
Epidemiology of HPV infection	The amount and severity of disease resulting from HPV infection		
Vaccines	How effective are the HPV vaccines? How long do the vaccines last? How safe are the HPV vaccines?		
The potential impact of the HPV vaccines	The expected health benefits of introducing an HPV vaccination programme		
Who should receive the vaccine	Whether the programme would be cost effective if only girls were vaccinated, or both girls and boys, and at what age		
What parents, girls and boys thought	The attitudes of parents, girls and boys to the vaccination		
Implementation	At what age the vaccine should be delivered and how could this be achieved?		

Table 1. Issues considered by JCVI before recommending the introduction of the HPV vaccine.

Vaccine composition, efficacy, and safety

The committee considered whether either of the two licensed vaccines, Cervarix[®] or Gardasil[®], should be recommended in preference over the other.

Cervarix[®] protects against the two HPV types (16 and 18 – bivalent vaccine) that cause more than 70% of all cervical cancer and Gardasil[®] protects against four HPV types (6, 11, 16 and 18 – quadrivalent vaccine). HPV types 6 and 11 cause genital warts.

JCVI considered the evidence on how safe and effective the HPV vaccines were, based on clinical trial data and post-marketing surveillance reports. The committee concluded that both vaccines have a good safety record, and they are highly effective in protecting against the precursors of cervical cancer. Individuals who received the vaccines have been followed for at least seven years in clinical trials so far, and antibodies remain at a high level and appear not to decline. Based on these high levels, the opinion of the committee was that the duration of immunity is expected to be at least ten years.

Modelling the effects of introducing the HPV vaccine

For JCVI to recommend HPV vaccination, the effects of the programme had to be modelled to determine how the rates of HPV infection and cervical cancer would change. To inform the model, data such as the natural history of HPV disease in the UK, sexual transmission of HPV and sexual behaviour were taken into account. These data were then applied to the cost-effective modelling to determine up to what age and which gender/s would benefit from HPV vaccination.

Considering parents' attitudes

JCVI was presented with date from attitudinal surveys, where parents, girls and boys were asked about their knowledge of the HPV vaccine and parents asked about their thoughts on the age groups considered for vaccination. When considering at what age to recommend the routine HPV vaccination programme, JCVI took the parents' attitudes into account. Results from attitudinal work had shown that parents were unhappy for primary school age children to be offered the vaccine but more comfortable with the notion of the vaccine being offered to girls aged 11 to 12 years in secondary school.

JCVI recommendation

Based on all the available evidence the committee confirmed that a universal HPV vaccination programme for girls aged 12 to 13 years would be cost effective. In addition to this, the committee was also able to recommend a catch-up vaccination of girls aged 13 and up to 18 years. It was suggested that both the routine and the catch-up programme would be delivered most efficiently through schools.

The committee considered whether either of the two licensed vaccines – Cervarix[®] or Gardasil[®] – should be recommended in preference to the other. It recommended that the choice of vaccine to be purchased would be primarily determined by the cost effectiveness evaluation. This evaluation would be highly dependent on the cost of the vaccines. If the vaccines were offered at similar prices, then the committee recommended choosing Gardasil[®], which would prevent genital warts as well as cervical cancer. Any differential between the prices offered would need to compensate for the lack of protection against warts.

So that the work of the committee can be widely available and understood, a detailed description can be found in the JCVI statement on HPV vaccines at: www.advisorybodies.doh.gov.uk/jcvi/ statements.htm

Action from the Department of Health

Ministers accepted the advice from JCVI. The Department of Health (DH) started an EU procurement process and Cervarix[®] was chosen for the immunisation programme. The routine vaccination programme for girls aged 12 to 13 was implemented by the DH, the Scottish Government, Northern Ireland and the Welsh Assembly from September 2008. In addition to the routine programme, a three-year catch-up programme started in September 2008 in England, Wales and Scotland.

Pneumococcal vaccine

Context

In September 2006, pneumococcal conjugate vaccine (PCV) was added to the national immunisation programme along with a catch-up programme for children up to two years of age following careful consideration and advice from JCVI. The vaccine protects against the seven strains of *Streptococcus pneumoniae* that were most common prior to the introduction of the vaccine.

Impact of the vaccination programme

Review of the surveillance data of pneumococcal infections caused by both vaccine-preventable strains and non-vaccine-preventable strains was an integral part of the work of JCVI. The committee continues to monitor the surveillance of pneumococcal serotypes.

Effect of vaccination on the serotypes targeted by the vaccine

The committee was encouraged by the impact of the vaccination programme. Disease surveillance shows that within the first 30 months of the programme in England and Wales there has been a major reduction of invasive pneumococcal disease (IPD) in vaccinated children caused by the seven strains of bacteria against which the vaccine protects. There has been a 90% reduction in IPD in children under two years of age (Figure 2) and a 67% drop in IPD in two- to four-year-olds in 2007/8.



Figure 2. Total number of reports of invasive pneumococcal disease due to any of the seven serotypes in Prevenar[®]. Children aged under two in England and Wales by epidemiological year: July-June (2003 to Feb 2008). (Source: Health Protection Agency, Centre for Infections)

Has the vaccination programme resulted in new serotypes emerging ('serotype replacement')?

The committee was concerned about the potential for serotype replacement. Early indications suggest that the serotypes not covered by the vaccine are increasing. Currently, it is not clear whether this demonstrates serotype replacement as the serotypes not covered by the vaccine were already increasing prior to the introduction of Prevenar[®].

Has childhood immunisation conferred benefits on adults?

In the USA, which has used the Prevenar[®] vaccine since 2000, there was a significant decline in IPD in older individuals who were not vaccinated, pointing towards a more widespread population effect ('herd immunity'). Data from the UK suggests that the level of herd protection seen in the USA (a reported fall of IPD by 62% in individuals aged five and over who were not vaccinated) is not currently being seen here. It has been estimated that a more modest reduction of around 35% is likely.

For the latest information on the incidence of IPD following the introduction of PCV please visit the HPA website at **www.hpa.org.uk**

Tuberculosis and BCG

Context

In its report for 2005/6, www.advisorybodies.doh.gov.uk/jcvi/ annualreports.htm, JCVI recommended that the BCG schools programme should cease at the end of the school year (2005) and be replaced by a targeted programme.

Tuberculosis (TB) is a disease that mainly affects the lungs, with potentially serious consequences. Globally, it kills more than two million people per year. Virtually all these deaths are confined to developing nations, or specific risk groups, with close connections to these countries.

In the UK, TB has been on the decline (see Figure 3) and is now usually only

found in certain risk groups, rather than in the general population. This is significantly different from when the universal immunisation was originally introduced more than 50 years ago. Then TB was found in people across all sections of society.

A total of 8417 cases of tuberculosis was reported in the UK in 2007. This represents a 0.9% decrease compared to 2006. As in previous years, London accounted for the highest proportion of cases (39%, 3265 out of 8417) and had the highest rate in the population (43.2 per 100,000 population compared to the UK rate of 13.8 cases per 100,000 population).



Figure 3. How the incidence of TB has progressively decreased since 1950, when BCG vaccination was introduced. (Source: Health Protection Agency, Centre for Infections)



Figure 4. The number of TB cases reported by UK region/country 2002-2007. The rate of cases in London has been significantly higher than in other parts of the country for a number of years. (Source: Health Protection Agency, Centre for Infections)

The risk to the general population is now extremely low. In 2005, the committee advised that offering the vaccination to all children was no longer appropriate. However, the committee was mindful that some children in the population were at greater risk from TB. In order to ensure their protection, it recommended the targeting of specific at-risk groups.

Following the recommendation, the BCG programme was replaced with a new policy of targeting at-risk groups, see: www.dh.gov.uk/en/ Publicationsandstatistics/ Lettersandcirculars/Professionalletters/ Chiefmedicalofficerletters/DH_4114993

Reviewing the policy change

Following the publication of further epidemiological data in November 2006 (**www.hpa.org.uk**), the committee reviewed its advice on BCG vaccination.

The committee has re-iterated its advice that the targeted BCG vaccination programme announced in 2005 remains the most effective vaccination strategy for the UK.

The data shows that the disease remains most prevalent in certain groups within the population and in certain parts of the country (see Figure 4). Rates of TB in other groups remain low and stable.



Figure 5. TB rates among different ethnic groups. Rates in Black African groups and in Indian, Pakistan and Bangladeshi groups remained higher than other groups in both UK and non-UK born individuals. (Source: Health Protection Agency, Centre for Infections)

The committee maintains that the most effective vaccination strategy is targeting the BCG programme to achieve high rates of coverage in particular ethnic groups with strong familial links to countries with high rates of disease (see Figure 5) and in parts of the country where TB rates are highest. So that the work of the committee can be widely available and understood, a detailed description can be found in the JCVI statement on BCG vaccination at: www.advisorybodies.doh.gov.uk/jcvi/ bcg-jcvi-statement_updateAug2007.pdf The policy to move away from a universal to targeted immunisation of TB risk groups will continue to be a focus for the committee. This will require careful monitoring, both in terms of the effect on the incidence of TB in the general population, and in the definition and extent of take-up by the identified risk groups.

Rotavirus

Context

Rotavirus infection is the most common cause of gastroenteritis (inflammation of the intestines) in children under five years of age worldwide. Gastroenteritis caused by rotavirus leads to severe diarrhoea, vomiting, stomach cramps, dehydration and mild fever, and usually lasts from three to eight days. In developing countries, severe diarrhoea can lead to deaths; in the UK, deaths from rotavirus infection are extremely rare although the number of children hospitalised is substantial. Infection by rotavirus usually leads to an individual developing immunity.

Burden of disease

In England and Wales, it has been estimated that there are around 130,000 cases of rotavirus-induced gastroenteritis each year in children under five years and approximately 12,700 children under the age of five are hospitalised annually with acute gastroenteritis caused by rotavirus. Adults can be infected by rotavirus but the main burden of disease is in children (Figure 6).

Rotavirus infection is estimated to account for around 50% of all intestinal infectious diseases in children under one year of age.



Figure 6. The age distribution of rotavirus infections reported in England and Wales, 2005 (n = 13,549). (Source: Rotavirus LabBase, HPA's website).

A considerable amount of the responsibility in looking after children infected by rotavirus falls on families and to a lesser extent, primary care.

Are the vaccines that prevent rotavirus infection safe and effective?

The committee considered if the currently licensed vaccines are safe and effective at preventing rotavirus infection.

In the past, there have been safety concerns with RotaShield[®] – a rotavirus vaccine that is now no longer available. RotaShield[®] was withdrawn from use in the United States because there was an increased risk of an adverse event called intussusception. This condition occurs when part of the intestine folds into a neighbouring portion. There were also concerns raised about Kawasaki disease following rotavirus vaccination. Kawasaki disease causes a prolonged fever that is associated with damage to the heart and blood vessels.

There are two licensed rotavirus vaccines in the UK – Rotarix[®] (manufactured by GlaxoSmithKline) and RotaTeq[®] (manufactured by Sanofi Pasteur MSD).

The committee looked at evidence on adverse reactions from clinical trials and post-marketing surveillance. The committee concluded that there was no association between either of the two rotavirus-vaccines and the development of intussusception or Kawasaki disease.

The committee therefore concluded that both rotavirus vaccines are safe and effective at preventing severe disease. They may not be equally efficacious, based on current evidence, in preventing milder disease.

Cost effectiveness of the vaccines

The committee examined work carried out on the cost-effectiveness of rotavirus vaccines. This work considered the cost of introducing rotavirus vaccines against the potential benefits of preventing rotavirus illness to the NHS and social care. However, the cost-effectiveness analysis showed that, based on current vaccine prices, the costs of universal vaccination of young children significantly exceeded the commonly accepted threshold for cost-effective healthcare interventions for the NHS.

JCVI recommendation

The committee concluded that rotavirus vaccines were highly effective and would reduce the incidence of diarrhoea in the population and in particular in young children. No particular risk-groups were identified as a priority for immunisation. Although immunocompromised children may be at increased risk from natural infection, as both rotavirus vaccines are live, such children should not receive the vaccine.

The committee did not recommend the introduction of rotavirus vaccines. At the current prices, they do not represent a cost-effective health intervention. The situation may change if the prices of the vaccines changed.

The committee has published a full statement on rotavirus vaccines that can be found at: **www.advisorybodies.doh.gov. uk/jcvi/statements.htm**

Haemophilus influenzae type b vaccine

Context

Haemophilus influenzae type b (Hib) is a serious bacterial infection that can cause meningitis and septicaemia, and can be fatal, especially in young children.

The Hib vaccination programme has been a public health success. The introduction of the vaccine in 1992 resulted in a marked reduction in Hib disease in children, particularly in cases and deaths from Hib meningitis. Following a Hib booster campaign in 2003 for children under four years of age and the introduction of a routine Hib booster at 12 months of age in 2006, the committee monitored Hib disease surveillance data during 2006 and 2007 to ensure that protection against Hib disease was being maintained throughout early childhood.





In February 2007, the committee considered the incidence of Hib disease in children aged three to four years. These children were too young to have had a booster as part of the 2003 Hib catch-up campaign and too old to have received the new Hib/MenC booster vaccine at 12 months of age. More Hib disease was occurring in the three to four year age group than was expected. Following the Hib catch-up campaign in 2003, the number of cases in the age groups targeted had fallen but there had not been a matching decline in those not targeted in the catch-up, as had been seen previously.

The committee considered the cost effectiveness of adding a booster dose of Hib vaccine to the pre-school booster. It was estimated that 50 cases of Hib disease and two deaths could be prevented, but the cost of the programme was very high – above the threshold of about £30,000 per QALY. Despite the cost effectiveness being unfavourable, the committee recommended that Hib booster dose should be given at the time of the pre-school booster to improve Hib protection in children too old to routinely receive the Hib/MenC booster and to protect them further through childhood, in line with the protection already offered to older and younger children. The DH and Scottish ministers accepted this advice on the basis of equity with those who had been eligible for the Hib catch-up campaign.

In July 2007, the four UK health departments initiated a Hib catch-up campaign for children born between 13 March 2003 and 3 September 2005. The Hib booster was offered as part of the pre-school vaccination whenever possible. Following the success of the catch-up programme in 2002/03 the committee expected the new campaign to be effective in reducing the rate of Hib disease in these children.

Influenza

Seasonal influenza

Monitoring the annual influenza immunisation programme is an ongoing priority for the committee. The population at large tends to consider 'flu' to be more of a discomfort than a life-threatening condition. However, it can be a serious disease, particularly in high-risk groups such as older people, with potentially fatal consequences. The most common complications of influenza are bronchitis and bacterial pneumonia. These illnesses may require treatment in hospital and can be life threatening, especially in older people and for example, asthmatics.

In those recent winters when the incidence has been low, 3000-4000 deaths have been attributed to influenza. Severe epidemics were last recorded in 1975 and 1989/90 resulting in around 29,000 and 23,000 deaths respectively.

Successes and challenges for the future

The largest at-risk group is people aged 65 years and over. Encouraging this group to seek vaccination continues to be a priority.

In 2003, the World Health Organization urged member states with influenza vaccination programmes to increase vaccination coverage of all people at high risk and to aim to achieve vaccination coverage levels of elderly people of at least 50% by 2006 and 75% by 2010.

The committee was pleased to see that the take-up in England, Scotland, and Northern Ireland has consistently exceeded 70% in recent years and continues to be close to or over 75% (see Table 2 and Figure 8).

	England	Scotland	Wales	Northern Ireland
	%	%	%	%
2000/01	65	65	39	68
2001/02	68	65	59	72
2002/03	68	69	54*	72
2003/04	71	73	63	73
2004/05	72	72	63	73
2005/06	75	78	68	81
2006/07	74	75	n/a†	75
2007/08	74	74	64	76

Table 2. Flu vaccine uptake percentage in the four UK countries 2000-2008. (Source: ImmForm www.immform.dh.gov.uk or www.immform.dh.nhs.uk)

* Some GP practices experienced problems in collating and reporting data

[†] Uptake figures for these years will be obtained via an automated extraction from GP systems and will be available in autumn 2008.



Figure 8. Flu vaccine up-take in England since 2000. (Source: ImmForm www.immform.dh.gov.uk or www.immform.dh.nhs.uk)

The committee remains concerned by the low levels of uptake in the under-65 clinical risk groups, carers and healthcare workers. The committee is encouraged by the continuing rise in uptake for those aged less than 65 years in clinical risk groups but the levels are still a great deal lower than for the over-65 years age group.

The committee hopes to see significant improvement in the very low levels of uptake among healthcare workers. Influenza can cause significant disruption to health services. Therefore, healthcare workers form an important at-risk group. It has proved an ongoing challenge to convince this group to participate in the vaccination programme. Although there has been an increase in uptake from 16% in 2004/05 to 18.6% in 2005/06, the committee was disappointed to see that this had slipped to 13.4% in 2007/08. The committee advises that this is still a cause for concern and would like to see increasing uptake in healthcare workers.

Pandemic influenza

JCVI was kept informed of the UK Health Departments plans to procure pandemic influenza vaccines and provided advice on a draft national plan for delivering vaccination in the event of a pandemic. The committee also considered the benefits of offering pre-pandemic flu vaccine to the UK population before the start of influenza activity. The benefits included preventing clinical cases and deaths in those most at risk, in the first wave of the pandemic as well as potentially slowing the transmission of the virus if school-children were vaccinated along with clinical risk groups. The committee supported the strategy of pre-pandemic vaccination.

The future

JCVI will be considering a number of vaccines for possible introduction to the national programme in the next few years. An important part of the committee's work is provision of advice on how vaccines already available or in development may benefit the UK programme. It is likely that this will include:

- varicella/herpes zoster
- hepatitis B
- meningococcal vaccines
- pneumococcal vaccines

Varicella/herpes zoster

For the majority of people, varicella (chickenpox) is not a serious condition but in some people it can cause severe complications especially in pregnant women (and their fetuses) and in immunosupressed individuals. Some individuals who develop herpes zoster (shingles) can develop a condition called post herpetic neuralgia. This condition leaves infected individuals in extreme pain that can last several years.

Current recommendations

The current recommendation for varicella vaccination is to protect those who are at most risk of serious illness from exposure to the virus. This is done by immunising other individuals who are in regular or close contact with those at risk and who cannot receive the live vaccine because they are likely to be severely immunocompromised. Since 2003, this recommendation includes vaccinating healthcare workers who are not immune to chickenpox, who, as well as protecting their patients, will themselves derive personal benefit. Varicella vaccine is also recommended for healthy individuals who are not immune to chickenpox and have close contact with immunocompromised patients.

Reviewing current advice

JCVI has been reviewing the current recommendations and looking at the benefits of introducing routine varicella vaccination for infants to protect them from chickenpox and herpes zoster vaccine to boost immunity to shingles in older adults. The committee is taking into account any impact that vaccination will have on older unvaccinated age groups, and the most effective vaccination schedule. The committee will continue to review the evidence in 2009 before making any specific recommendation.

Hepatitis B

Context

Hepatitis B is an infection of the liver caused by the hepatitis B virus (HBV). Many new infections with hepatitis B are sub-clinical or may present as a flu-like illness. Jaundice occurs in about 10% of younger children and in 30 to 50% of adults. Acute infection may occasionally lead to fulminant hepatic necrosis, which is often fatal. Hepatitis B infection can be detected by the presence of serological markers, for example, hepatitis B surface antigen (HBsAg). In most individuals, infection will resolve and HBsAg disappears from the serum, but the virus may persist in some patients who become chronically infected. Around a quarter of individuals with chronic HBV infection worldwide have progressive liver disease, leading to cirrhosis in some patients and also to liver cancer.

Current recommendations

Currently hepatitis B vaccine is recommended for individuals who are most at risk from contracting HepB; this includes:

- injecting drug users
- individuals who change sexual partners frequently
- close family contacts of a person with chronic hepatitis B infection
- families adopting children from countries with a high or intermediate prevalence of hepatitis B
- foster carers
- individuals receiving regular blood or blood products, and their carers
- patients with chronic renal failure
- patients with chronic liver disease
- inmates of custodial institutions
- individuals in residential accommodation for those with learning difficulties
- people travelling to or going to reside in areas of high or intermediate prevalence, and
- individuals at occupational risk.

Review of current recommendations

The committee commissioned the HPA to provide a cost-effectiveness analysis of options for the introduction of hepatitis B vaccination. This included routine infant immunisation, routine adolescent immunisation or a selective infant immunisation programme. The committee will consider this analysis and make a recommendation after the analysis has been independently peer reviewed.

Meningococcal vaccines

Meningococcal bacteria are the most common cause of bacterial meningitis and they also cause septicaemia. Meningitis is an inflammation of the meninges (tissue that surrounds and protects the brain and spinal cord). Meningococcal bacteria are divided into distinct serogroups, according to their polysaccharide outer capsule. The most common serogroups that cause disease worldwide are groups B, C, A, Y and W135. In the UK, since the successful introduction of the meningococcal serogroup C conjugate (MenC) vaccine in November 1999 around 90% of all bacterial meningitis cases are caused by serogroup B (Figure 9).



Figure 9. Laboratory reports of meningococcal disease in England and Wales 1997-2008. (Source: HPA North West, Manchester Laboratory).

The committee was informed about the development of MenB vaccines and is encouraged by their progress. From 2009, the committee will start to gather evidence to inform the cost-effectiveness modelling that forms an essential component of any recommendation.

From 2009, the committee will also be considering conjugate vaccines that protect against serotypes A, C, W135, and Y for travel indications. Vaccines based on capsular polysaccharide against serogroups A, C, Y, and W135 are already available but do not provide adequate protection in children under two years of age. Young infants from three months of age can respond to the A component but not to the Y, W135 and C components, but immunity is short-lived. The committee will look carefully at the evidence that conjugate vaccines provide protection in young infants before making any recommendations.

Pneumococcal vaccines

Vaccines are being developed that give broader protection against pneumococcal strains with either ten or 13 strains targeted. The committee will be considering the benefits of introducing either of these vaccines and in particular, the impact that they may have on the strains that cause disease for which Prevenar[®] provides no protection.

Horizon scanning and new vaccines

As part of the committee's regular horizon scanning activity, it considers reports of any new vaccines that may be in the early stages of development.

A vaccine against Group B *Streptococcus* (GBS), the most common cause of life-threatening infections in newborn babies in this country is also under development. GBS can also cause serious illness and death in pregnant women, older people and people with weakened immune systems (such as cancer patients). Despite the clear need for a safe and effective GBS vaccine, the principal difficulty in developing GBS vaccines is the existence of several serotypes across the world and that one vaccine cannot protect against them all. Vaccines are in early clinical trials in the United States. Cytomegalovirus (CMV) is the most common cause of congenital infection in developed countries and also affects transplant patients, patients with AIDS, the elderly and those in intensive care. Around three in every 1000 babies born in the UK have cytomegalovirus infections. It has been estimated that in the UK congenital CMV infection may account for 15% of sensori-neural hearing loss and 7% of cerebral palsy.

Vaccines against the infection are under trial in the United States, and initial results are encouraging. Vaccines in the early stages of development include those for healthcare associated infections such as MRSA and *Clostridium difficile*. These vaccines are likely to be at least five to ten years in development.

The committee will continue to monitor and keep under review the progress of all these and any other relevant vaccine trials.

Appendix A Declaration of members' interests 2007

Chairman Professor Andrew Hall

MB BS, MSc, PhD, FRCP, FFPH, FMedSci London School of Hygiene and Tropical Medicine

Personal interests

None

Non-personal interests None

Professor Alan Emond

MA, MD, FRCP, FRCPHCH Professor of Community Child Health at the University of Bristol. Director of the Centre for Child and Adolescent Health, Bristol

Personal interests

None

Non-personal interests None

Professor David Goldblatt

Professor of Vaccinology and Immunology, Director of Clinical Research and Development, Head, Immunobiology Unit, Consultant Paediatric Immunologist, Institute of Child Health and Great Ormond Street Hospital for Children NHS Trust

Personal interests

- **Consultancies** Occasional consultancies for Wyeth, Sanofi Pasteur and ACE Biosciences
- Fee-paid work None
- Shareholdings
 None
- Other None

Non-personal interests

- Fellowships None
- Industrial support Research grant from GSK and Wyeth. Contract research for Chiron. Sanofi Pasteur and Merk.
- Other None

Professor Paul Griffiths

BSc, MD DSc, FRCPath Virologist; Professor of Virology, Royal Free and University College Medical School

Personal interests

- Consultancies None
- Fee-paid work

International Herpes Management Forum (member of scientific board). Usually concerns antiviral agents, but in 2007 I co-edited a monograph concerned with VZV vaccines. Wellcome Trust (member of basic immunology and infectious disease panel).

Shareholdings None

• Other

Work in my Department has led to the submission of a patent application in the name of the Medical school concerning the diagnosis of cytomegalovirus infection by means of polymerase chain reaction which began generating royalty payments in 2006.

Non-personal interests

- Fellowships None
- Industrial support

AiCuris (antiviral drug) Novartis (antiviral drug) In 2006, Sanofi-Pasteur began providing vaccine and matching placebo for an investigator-led randomised controlled trial of cytomegalovirus vaccine in allograft candidates funded by a grant from the National Institutes of Health.

• Other

Work in my Department has led to the submission of a patent application in the name of the Medical School concerning the possible prevention of cytomegalovirus infection by means of vaccine.

Professor Simon Kroll

MA, FRCP, FRCPCH, FMedSci Paediatric Infectious Disease Physician; Professor of Paediatrics and Molecular Infectious Diseases, Imperial College School of Medicine

Personal interests

- Consultancies None
- Fee-paid work None
- Shareholdings None

• Other

I have received a grant (to cover travel/ accommodation/registration) from Wyeth Vaccines to attend the 2007 open medical scientific meeting of the European Society for Paediatric infectious Diseases.

Non-personal interests

• Fellowships

Fellow of the Academy of Medical Sciences Fellow of the Royal College of Paediatrics and Child Health Fellow of the Royal College of Physicians.

• Industrial support

Research in my laboratory is funded by Sanofi Pasteur and by the Health Protection Agency.

• Other

I am chairman of the medical/scientific advisory panel of the Meningitis Trust, and a member of the scientific advisory committee of the Lister Institute.

Mrs Vivienne Parry

BSc (Hons) Writer and broadcaster

Personal interests None

Non-personal interests None

Dr Richard Roberts

MB BS, BSc, DCH, MPH, FFPH, MEPHM Consultant in Communicable Disease Control, Vaccine Preventable Disease Programme, National Public Health Service for Wales

Personal interests

None

Non-personal interests None

Professor Brent Taylor

PhD, MB ChB, FRCP, FRACP, FRCPCH Community Child Health/Community Paediatrician; Professor of Community Child Health, Royal Free and University College Medical School

Personal interests

None

Non-personal interests None

Dr Christopher Verity

MA, FRCP, FRCPCH, DCH, DRCOG Consultant Paediatrician and Neurologist, Addenbrook's Hospital, Cambridge

Personal interests None

Non-personal interests None

Dr Paul Jackson

MB BAO, MRCP, MD, FRCP, FRCPCH, FRCPI Consultant Paediatrician, Belvoir Ward, Royal Belfast Hospital for Sick Children, Falls Road, Belfast

Personal interests

- Consultancies None
- Fee-paid work None
- Shareholdings None

• Other

WYETH: sponsored me to go the European Society for Paediatric Infectious Disease meetings 2006 and 2007

Non-personal interests None

Dr Ahmed Syed

MB ChB, MRCP, MFPHM Consultant in Public Health Medicine and Immunisation Coordinator, Greater Glasgow NHS Board, Dalian House, Glasgow

Personal interests

None

Non-personal interests

- Fellowships None
- Industrial support
 Received research grants from GSK and Aventis
 Pasteur over four years ago but no current
 involvements.
- Other None

Professor Jonathan Friedland

MA, PhD, FRCP, FRCPE Department of Infectious Diseases, Imperial College, Hammersmith Hospital, London

Personal interests None

Non-personal interests

- Fellowships None
- Industrial support None
- Other

Merk Sharp & Dhome – Sponsorship for Infectious Diseases Short Course 2007

Ms Anne McGowan

BSc (Hons), RGN, RM, HV, PGCE, MPH Nurse Immunisation Coordinator, Gwent Healthcare NHS Trust, Wales.

Personal interests

None

Non-personal interests

- Fellowships None
- Industrial support None
- Other

Sponsorship from WYETH for Welsh Vaccination and Immunisation conference (March 2007)

Dr Raymond Borrow PhD

Head of Vaccine Evaluation Department, Manchester Medical Microbiology Partnership, Manchester

Personal interests

None

Non-personal interests

Consultancies (monies paid into Trust training fund) Occasional member of expert panels for Baxter

Bioscience; GSK; Novartis; Sanofi Pasteur; Wyeth.

• Other

On medical-scientific advisory panel for the Meningitis Trust and Meningitis Research Foundation.

Mrs Pauline MacDonald

ARRC, BSc (Hons) Nurse Consultant in Communicable Diseases, Dudley Primary Care Trust

Personal interests

None

Non-personal interests

Fellowships None **Industrial support** None

Other

Sales representatives of various companies are invited to have 'stands' at departmental educational sessions. They are charged for these stands and monies help off-set venue and hospitality costs.

Dr Claire Cameron

BSc (Hons), PhD, MSc Epidemiologist (Immunisation)

Personal interests None

Non-personal interests

- Fellowships None
- **Industrial support** Research grant from Schering (to support a study on HCV testing of IDUs in Glasgow general practices, 2007. The funds are for GP payments)
- Other None

Professor David Hill

MD, DTM&H Honorary Professor, London School of Hygiene and Tropical Medicine

Personal interests

- Consultancies None
- Fee-paid work None
- Shareholdings None
- Other Received an honorarium for speaking at MASTA conference, November, 2006

Non-personal interests

None

Ex-officio

Dr Stephen Inglis

BSc, PhD Director of the National Institute for Biological Standards and Control

Personal interests None

Non-personal interests

NIBSC'S role is to assure the quality of biological medicines through a mixture of product testing, development of tests and reference materials, and applied research. In carrying out its role, the institute interacts with a wide range of product developers and manufacturers. In some instances, NIBSC charges commercial organisations for its products and services, in line with guidance issued from HM Treasury ('Fees & charges guide' and 'Selling into wider markets').

Fellowships None

Industrial support

Contracts active within last two years: Alba; Amison Pharma; Angel Biotechnology; Artus Biotech; Baxter; Bayer; BBT Biotech; BD Pharmingen; Berna Biotech; Bharat; Biocon Ltd; Biofact; BioFarm Biolegend inc; Bioneedle Technologies; BPL; CADILA; Cambridge Biostability; Celsus Labs; Chiron; Chiron Behring; CSL Ltd; Dilafor; eBioscience; Emcure Pharmaceuticals; Endell Veterinary Group; GeneMedix; Glycart; Glycoform Ltd; Grifols; GSK; GTC Biotherapeutics; Immunobiology plc; ISEAO; Julphar; Kamada; LGC; Miltenyi Biotec; Momenta; Novartis Novocastra; Octapharma; Pfizer; Philogen; Plasso; Powdermed; Rhinopharma Ltd; Roche; Sanofi; Santa Cruz; Serono; Serum Institute India; Solstice; Stago; Tepnel; West Pharma; Vectura; Wockhardt Ltd; Wyeth.

Other None

Dr Desmond Walsh

Programme Manager, Infections and Immunity Board (Medical Research Council)

Personal interests None

Non-personal interests None

Appendix B Declaration of members' interests 2008

Chairman Professor Andrew Hall

MB BS, MSc, PhD, FRCP, FFPH, FMedSci London School of Hygiene and Tropical Medicine

Personal interests (specific) None

Personal interests (non specific)

Consultancies

Non-executive Director, Health Protection Agency Programme for Appropriate Technology in Health (charity) - Meningitis Vaccine Project Data Safety and Monitoring Board Note: None of these relate to the pharmaceutical industry but do represent paid work.

- Fee-paid work None
- Shareholdings None
 - Other Product development group, aerosol measles vaccine, World Health Organization

Non-personal interests (specific) None

Non-personal interests (non specific) None

Professor Alan Emond

MA, MD, FRCP, FRCPHCH Professor of Community Child Health at the University of Bristol. Director of the Centre for Child and Adolescent Health, Bristol

Personal interests (specific) None

Personal interests (non specific) None

Non-personal interests (specific) None

Non-personal interests (non specific) None

Professor Simon Kroll

MA, FRCP, FRCPCH, FMedSci Paediatric Infectious Disease Physician; Professor of Paediatrics and Molecular Infectious Diseases, Imperial College School of Medicine

Personal interests (specific) None

Personal interests (non specific)

- Consultancies None
- Fee-paid work None
- Shareholdings None
- Other

I have received grants (to cover travel/ accommodation/registration) from Wyeth Vaccines and from Merck to attend the 2007 open medical scientific meetings of the European Society for Paediatric Infectious Diseases, and the 6th International Symposium on Pneumococci & Pneumococcal diseases.

Non-personal interests (specific) None

Non-personal interests (non specific)

Consultancies

Fellow of the Academy of Medical Sciences Fellow of the Royal College of Paediatrics and Child Health

- Fellow of the Royal College of Physicians
- **Industrial support** Research in my laboratory is funded by Sanofi Pasteur, by Baxter and by the Health Protection Agency.
- Other None

Professor Paul Griffiths

BSc, MD DSc, FRCPath Virologist; Professor of Virology, Royal Free and University College Medical School

Personal interests (specific)

- Consultancies
 None
- Fee-paid work

International Herpes Management Forum (member of scientific board). Usually concerns antiviral agents, but in 2007 I co-edited a monograph concerned with VZV vaccines. Occasional consultancy for Merck (vaccines against cytomegalovirus).

- Shareholdings None
- Other None

Personal interests (non specific)

• Consultancies None

> Fee-paid work Wellcome Trust (member of basic immunology and infectious disease panel). Higher Education Funding Council for England (member RAE 2008 panel 3). Occasional consultancies for GSK, Viropharma, Chimerix, Roche, Novartis, AiCuris (antiviral drugs against herpesviruses).

- Shareholdings
 None
- 1001
- Other

Work in my Department has led to the submission of a patent application in the name of the Medical School concerning the diagnosis of cytomegalovirus infection by means of polymerase chain reaction, which began generating royalty payments in 2006.

Non-personal interests (specific)

• Fellowships None

• Industrial support

In 2006, Sanofi-Pasteur began providing vaccine and matching placebo for an investigator-led randomised controlled trial of cytomegalovirus vaccine in allograft candidates funded by a grant from the National Institutes of Health.

• Other

Member of scientific advisory board for Alphavax (vaccines against cytomegalovirus)

Non-personal interests (non specific)

- Fellowships None
- Industrial support AiCuris (antiviral drug) Novartis (antiviral drug)
- Other

Work in my Department has led to the submission of a patent application in the name of the Medical School concerning the possible prevention of cytomegalovirus infection by means of vaccine.

Dr Raymond Borrow PhD

Head of Vaccine Evaluation Department, Manchester Medical Microbiology Partnership, Manchester

Personal interests (specific) None

Personal interests (non specific)

Consultancies

Consultancies (monies paid into Trust training fund): Occasional member of expert panels for Baxter Bioscience; GSK; Novartis; Sanofi Pasteur; Wyeth.

Other: On medical-scientific advisory panel for the Meningitis Trust and Meningitis Research Foundation.

• Fee-paid work

Travel paid for to attend scientific meetings by GSK, Sanofi Pasteur, Novartis and Wyeth.

- Shareholdings None
- Other None

Non-personal interests (specific)

• Fellowships None

Industrial support

Immunoassays for HPV: Merck Immunoassays for Neisseria meningitidis: Wyeth, Emergent BioSolutions, Novartis, Baxter Biosciences, Sanofi Pasteur MSD, GSK, Merck.

• Other

Programme for Appropriate Technology in Health (PATH): Immunoassays for *Neisseria meningitidis*.

Non-personal interests (non specific)

- Fellowships None
- Industrial support Alexion Pharmaceuticals
- Other None

Dr Christopher Verity

MA, FRCP, FRCPCH, DCH, DRCOG Consultant Paediatrician and Neurologist, Addenbrook's Hospital, Cambridge

Personal interests

None

Non-personal interests None

Dr Anthony Harnden

MB ChB, MSc, FRCGP, FRCPCH, DCH University Lecturer and Principal in General Practice, Oxford University and Morland House Surgery, Wheatley, Oxfordshire

Personal interests

None

Non-personal interests (specific)

- Fellowships None
- Industrial support None
- **Other** Wife sold her 169 shares in GSK on 26 March 2008 (total value £1780).

Non-personal interests (non specific) None

Professor Brent Taylor

PhD, MB ChB, FRCP, FRACP, FRCPCH Community Child Health/Community Paediatrician; Professor of Community Child Health, Royal Free and University College Medical School

Personal interests None

Non-personal interests (specific) None

Non-personal interests (non specific)

- Fellowships None
- Industrial support

Educational Grant from GSK to support research assistant involved with study to investigate incidence and associations of intussusception in infants.

• Other None

Dr Paul Jackson

MB BAO, MRCP, MD, FRCP, FRCPCH, FRCPI Consultant Paediatrician, Belvoir Ward, Royal Belfast Hospital for Sick Children, Falls Road, Belfast

Personal interests (specific) None

Personal interests (non specific)

- Consultancies None
- Fee-paid work None

- Shareholdings None
- Other Wyeth sponsorship to attend European Society for Paediatric Infectious Diseases.

Non-personal interests None

Mrs Vivienne Parry

BSc (Hons) Writer and broadcaster

Personal interests None

Non-personal interests None

Dr Ahmed Syed

MB ChB, MRCP, MFPHM Consultant in Public Health Medicine and Immunisation Coordinator, Greater Glasgow NHS Board, Dalian House, Glasgow

Personal interests

None

Non-personal interests (specific) None

Non-personal interests (non specific)

• Fellowships

Industrial support: occasional support from Wyeth, GSK and Aventis Pasteur MSD to the department for organising educational meetings.

• Industrial support None

• Other

On the editorial board of a newsletter/journal Vaccine in practice published by Hayward Medical Communications. Haywood Medical Communications is funded by Wyeth. Annual honorarium (£200 per annum) donated to the Department.

Ms Anne McGowan

BSc (Hons), RGN, RM, HV, PGCE, MPH Nurse Immunisation Coordinator, Gwent Healthcare NHS Trust, Wales.

Personal interests None

Non-personal interests None

Mrs Pauline MacDonald

ARRC, BSc (Hons) Nurse Consultant in Communicable Diseases, Dudley Primary Care Trust

Personal interests (specific)

- Consultancies None
- Fee-paid work None
- Shareholdings
 None
 - **Other** Bursary and travel expenses in April 2008 (GSK) and May 2008 (Sanofi Pasteur MSD) for lecturing specific to HPV vaccine.

Personal interests (non specific) None

Non-personal interests (specific) None

Non-personal interests (non specific)

- Fellowships None
- Industrial support None
- Other

Financial support for immunisation study days at the PCT (Sanofi Pasteur MSD)

Dr Richard Roberts

MB BS, BSc, DCH, MPH, FFPH, MEPHM Consultant in Communicable Disease Control, Vaccine Preventable Disease Programme, National Public Health Service, Wales

Personal interests

None

Non-personal interests None

Professor Jonathan Friedland

MA, PhD, FRCP, FRCPE Department of Infectious Diseases, Imperial College, Hammersmith Hospital, London

Personal interests None

Non-personal interests None

Ex-officio

Dr Stephen Inglis

BSc, PhD Director of the National Institute for Biological Standards and Control

Personal interests

None

Non-personal interests (specific)

• General statement

NIBSC's role is to assure the quality of biological medicines through a mixture of product testing, development of tests and reference materials, and applied research. In carrying out its role, the institute interacts with a wide range of product developers and manufacturers. In some instances, NIBSC charges commercial organisations for its products and services, in line with guidance issued from HM Treasury 'Fees & charges guide' and 'Selling into wider markets'.

Fellowships

None

• Industrial support

Pandemic influenza vaccines (Novartis, Sanofi-Pasteur) HPV vaccines (GSK, Sanofi-Pasteur) Rotavirus (GSK, Sanofi-Pasteur)

• Other None

Non-personal interests (non specific)

• Fellowships None

• Industrial support

Contracts active within last two years: Alba; Angel Biotechnology; Baxter; Bayer; BBT Biotech; BD Pharmingen; Bharat; Biocon Ltd; Biofact; BioFarma; Biolegend Inc; BPL; CADILA; Celsus Labs; Chiron; CSL Ltd; CRT; Dilafor; eBioscience; Endell Veterinary Group; GeneMedix; Glycart; Grifols; GSK; GTC Biotherapeutics; Immunobiology plc; ISEAO; Julphar; LGC; Miltenyi Biotec; Novartis; Novocastra; Octapharma; Paion; Pfizer; Pharmaceutical Scientist Inc; Plasso; Powdermed; Roche; Sanofi Pasteur; Santa Cruz; Serono; Serum Institute of India; Siemens; Solstice; Stabilitech; Stago; Tepnel; West Pharma; Vectura; Wockhardt Ltd; Wyeth

• Other None

Professor David Hill

MD, DTM&H Honorary Professor, London School of Hygiene and Tropical Medicine

Personal interests

None

Non-personal interests None



