Joint Committee on Vaccination and Immunisation

Minutes of the meeting held on Wednesday 20 June 2007 at 10.30am

Attending

Professor Andrew Hall (Chair)
Professor Brent Taylor
Professor Paul Griffiths
Professor Alan Emond
Ms Anne McGowan
Professor David Goldblatt
Dr Paul Jackson
Professor Jonathan Friedland
Dr Richard Roberts
Professor Simon Kroll
Dr Syed Ahmed
Dr Ray Borrow
Mrs Vivienne Parry
Professor Brent Taylor
Mrs Pauline MacDonald
Dr Anthony Harnden

Ex-Officio
Professor David Hill - NathNac
Dr Steven Inglis - NIBSC
Dr Jim McMenamin - HPS

Observers

Wg CDR Andy Green - MoD
Sq Leader Tania Thomas - MoD
Dr Parameswaram Kishore - Isle of Man

Invited to attend

Professor Elizabeth Miller - HPA
Dr Richard Pebody - HPA
Dr John Edmunds - HPA
Stephen Smith - Connecting for Health

Welsh Assembly Government

Mr Neil Robins

Scottish Executive

Dr Elizabeth Stewart

Department of Health

Professor David Salisbury (Medical Secretary)
Dr Dorian Kennedy
Dr Kevin Perrett
Dr Karen Noakes
1. ANNOUNCEMENTS AND WELCOME

The Chairman welcomed all those present to the meeting. Pauline MacDonald, Anne McGowan and Dr Ray Borrow were welcomed as new members now that they had been officially appointed by the NHS Appointments Commission. Dr Kevin Perrett and Bela Vatsa were introduced to the Committee as the new members of the DH Immunisation Team.

The following members had sent their apologies: Dr Chris Verity and Dr Claire Cameron (who was represented by Dr Jim McMenamin). Dr Lorraine Doherty also sent her apologies.

Members were reminded of the need to ensure their declarations of interest were up-to-date, and to declare their interests relevant to each agenda item.

2. MINUTES OF THE LAST MEETING HELD 14 FEBRUARY 2007

Members agreed the following change:

The declarations of interest for members on agenda items 8, 10 and 11 should be consistent.

With this amendment it was agreed that the final minutes would be placed on the website.

3. MATTERS ARISING

3.1 BCG statement

The Committee was pleased that the BCG statement had been placed on the website. The Committee also noted that the statement needed to be modified to clarify that travellers under 16 years of age who were:

- previously unvaccinated and tuberculin-negative; and

- going to live or work with local people for more than 3 months in a country where the annual incidence of TB is 40/100,000 or greater

were recommended to receive BCG vaccine.

The Committee agreed that the modified statement would be placed on the website.
The Chairman informed JCVI that NEPNEI has expressed concern at the incidence in Drug Resistant TB (XDRTB). It was noted that the issue would be discussed at a future JCVI meeting.

3.2 Tetanus
The Committee was informed that the issues around tetanus policy had been discussed at a meeting of the JCVI chairman, DH officials and the HPA. It was agreed that a document will be prepared for the October meeting of JCVI.

3.3 Hepatitis B
The Committee was reminded of the further work on a targeted hepatitis B vaccination approach in which immunisation is offered to all infants with one or more parents born in a country with a high or intermediate enemicity for hepatitis B, and in areas with higher Hepatitis B incidence. This work was dependent on the availability of data from the Office of National Statistics (ONS) on the likely number of children who fall into this category, and this data had been requested.

It was noted that in some areas, where a significant proportion of infants are recommended the vaccine, that implementation of the vaccination programme may be easier to deliver by targeting all children in that area.

A targeted vaccination approach was recently introduced in the Netherlands, and Sweden are currently in the process of introducing a programme.

3.4 Hib catch up vaccination
Members were reminded that they had recommended at their last meeting that the cohort of children who had not previously been offered a booster dose of Hib vaccine, as part of the 2003 Hib catch-up campaign or at 12 months of age following its introduction in September 2006, should be offered a booster.

The Hib booster will be offered as part of the pre-school immunisation programme by temporarily changing the pre-school booster vaccine to one that contains an additional Hib component. Accordingly, the current pre-school booster will be temporarily changed from DTaP/IPV (Infanrix IPV™) or dTaP/IPV (Repevax™) to DTaP/IPV/Hib (given as Infanrix-IPV+Hib™, or alternatively Pediacel™). Older children who have already received their pre-school booster will be offered Hib-MenC (Menitorix™). Also, during the course of this campaign, the age at which the pre-school immunisation is offered will be reduced - in areas where this is not already the case - to between 3 years 4 months and 3 years 6 months of age, in line with recommended best practice.

This will require that Infanrix-IPV+Hib™ and Pediacel™ are used off label beyond the upper age limit of ‘36 months’ and ‘the fourth birthday’ respectively. In the case of Menitorix™, although there is no upper age limit specified in the SPC, there is no experience of its routine use in older age groups. The Committee noted that Pediacel™ is already currently used off-label in older children, in cases of uncertain or incomplete immunisation. A similar vaccine to Pediacel™ is also frequently used in older children in Canada. Some members asked to review the available safety and efficacy data of these vaccines in older age groups in order to come to a decision as there was a theoretical risk that these vaccines could be more reactogenic in older age groups. Members also noted that booster doses of aP containing vaccines, if they follow primary immunisation with an aP vaccine, had been associated with an increased risk of limb swelling. This is more common in countries where a fifth dose of aP containing vaccine is recommended and is related to an increased number of aP doses rather than older age of vaccination.
The Committee agreed that a small representative group meet next week in a teleconference with the scientific data to support this proposal.

4. JCVI processes

This paper providing draft text that could be placed on the JCVI website, explaining the Committee's functions and decision making process was tabled on the day.

The Committee agreed that members should give comments by e-mail.

5. Pandemic Flu update

Delivery plan for the pandemic flu vaccine

The following members declared interest in Sanofi Pasteur or GSK.

Professor Simon Kroll non-personal, non-specific
Professor Jon Friedland non-personal, non-specific
Dr Syed Ahmed non-specific, non-personal
Dr Ray Borrow non-personal, non-specific
Dr Stephen Inglis non-personal, non-specific
Pauline MacDonald non-personal, non-specific
Dr John Edmunds from the HPA also declared a personal, non-specific interest.

A brief summary was given of what is covered by the draft national plan for delivering vaccination in the event of a pandemic. A national delivery plan is required to support the policy decisions on vaccination outlined in the national framework for responding to an influenza pandemic.

The plan being developed covers the delivery of a specific pandemic vaccine to the entire population and also the delivery of the current limited stockpile of A/H5N1 pre-pandemic vaccine to health care workers.

The plan offers a model for immunising the whole population using a specific pandemic vaccine over several months based on existing primary care delivery systems. The plan concludes that the balance of arguments favors a primary care based model.

Several points were raised by committee members. Vaccine supply security was noted as a potential problem and it was suggested security arrangements would be easier if a mass vaccination centre model was used. It was also noted that prioritisation of specific pandemic vaccine would be needed, particularly in light of the fact that producing sufficient vaccine for the entire population would take several months. Questions were raised about the criteria for prioritisation and the committee asked that planning be strengthened in regard to this issue.

It was confirmed that sleeping contracts are now in place for specific pandemic vaccine supply. It was noted that vaccine availability will occur within a European and wider international context.

Members of the committee raised several questions about the practicalities of delivering population-wide immunisation in the event of a pandemic, and it was agreed that members would be invited to send in comments on the full delivery plan.

Estimating the effect of vaccination against pandemic influenza
An age-structured transmission dynamic model was presented that estimated the number of clinical cases and deaths prevented if vaccination was offered before and after the first wave of influenza activity. The model predicts that if a pandemic flu vaccine prevents infection as well as providing individual protection then the most benefit is achieved if children are vaccinated as a priority. This is because children are known to be efficient spreaders of influenza virus due to high levels of viral secretion and social mixing behavior. If a pandemic flu vaccine only protects against disease, then more benefit is gained by vaccinating those most at risk from influenza such as the clinical risk groups and the elderly.

Predicting the effectiveness of a pre-second wave immunisation programme is difficult because the size of the second wave of influenza is dependent on the number of people still susceptible in the population. This type of information, including the case fatality ratio, would be collected during the first wave. It is likely that the second wave of influenza activity would only be bigger than the first wave if seasonality comes into the equation. If the first wave starts in the UK summer, then a second wave occurring in the winter period could be bigger.

The Committee noted the importance of obtaining information on the immunogenicity of any pandemic flu vaccine on these groups so that the vaccine wasn't prioritised in a group for whom the vaccine wasn't immunogenic.

6. HPV subgroup

The following members declared interest in Sanofi Pasteur or GSK.

Professor Simon Kroll non-personal, non-specific
Professor Jon Friedland non-personal, non-specific
Dr Syed Ahmed non-specific, non-personal
Dr Ray Borrow non-personal, non-specific
Dr Stephen Inglis non-personal, non-specific
Pauline McDonald non-personal, non-specific
Dr John Edmunds (HPA) also declared a personal, non-specific interest

Additional papers were circulated prior to the meeting that summarised the scientific evidence reviewed by the HPV subgroup.

The Chairman read out the executive summary of the HPV subgroup;

- The subgroup’s view was that there is sufficient evidence on the protective effect of HPV vaccines on cervical cancer in the UK to suggest vaccination of girls at 11-12 years of age (in the first year of secondary school) as part of a school-based programme in conjunction with a sexual education programme (through Personal & Social Education-PSE).

The vaccine has been shown to have a good safety record, and be highly effective in protecting against the precursors of cervical cancer. The vaccine has been followed for 5 years in clinical trials so far, and the level of antibodies remained at a high level and appears not to decline. This suggests that the duration of immunity is expected to be long-lasting.

The Committee discussed whether the programme would be more practical for schools if the age was from 12-13 years old because the girls would be established within the school and their records transferred to their new school and up to date. A cross-sectional panel of serum samples from women aged 10-29 years in England suggests that HPV seroprevalence is low up to age 14 and then increases rapidly. Taking into account that it
can take from 6 months to up to a year to seroconvert and that girls will start to become infected just before seroprevalence is seen to rise, 12 to 13 years was considered to be an appropriate age to vaccinate.

- The subgroup considered that a catch-up campaign to include all girls up to the age of 15/16 years would be beneficial.

The main Committee noted this advice and the need for a cost-effectiveness analysis to consider this issue further.

- The subgroup strongly recommended the implementation of procedures to record individual vaccination and other disease surveillance measures to facilitate subsequent assessment of the impact of the vaccination programme.

The Committee agreed with the need for careful recording of vaccination data in order to assist the effective implementation of an HPV vaccination programme, and to assessing the impact of the programme. A detailed surveillance plan will be provided at the next meeting.

- The sub-group agreed that the effectiveness and cost-effectiveness model developed by the HPA needed to be peer reviewed by biologists, mathematical modellers and economists to ensure that the model was robust.

- The main Committee agreed that peer-review of the HPA cost benefit analysis would add rigour to the JCVI decision-making process.

- The subgroup noted that with any introduction of routine HPV vaccination the national cervical screening programme should continue unchanged until further investigation assesses the impact of immunisation on its cost-effectiveness. This may also help to identify HPV related cervical lesions that are not covered in the current HPV vaccines and to evaluate the impact of the vaccination programme. It was suggested that as the vaccinated individuals reach screening age, the frequency of screening might need to be amended.

- Based on the data provided, the subgroup committee felt that further analysis of the benefits of warts prevention was necessary to make an informed decision on the choice of vaccine (bivalent vs. quadrivalent). This was not essential to forming a recommendation on vaccination in general, as the main objectives relate to the prevention of cervical cancer. The sub-group favoured the use of the most cost-effective vaccine against all endpoints, including genital warts.

The Committee agreed with the remaining conclusions of the subgroup and would await the final peer-reviewed analysis before making detailed recommendations. It was noted that this would be the first published analysis that hadn't been funded or carried out by manufacturers of the vaccine.

The Chairman pointed out that there were two recent vaccine safety concerns reported by the media. Firstly, there were 3 reported cases of death in women in the US who were vaccinated with HPV vaccine. However the cause of death in all three cases was due to pre-existing medical conditions (heart conditions and thrombosis) and were not related to HPV vaccine. Secondly, the media reported 30 girls in Australia who had recently been immunised with HPV vaccine and had fainted following the injection but this was not
directly related to the vaccine (because fainting is known to have occurred in similar situations), nor was it an unexpected observation in this age group.

Advice on the choice of HPV vaccine would be based on the cost effectiveness of each vaccine taking into account that one does not protect against genital warts caused by HPV types 6 and 11. The additional benefits of vaccinating against genital warts would be examined as part of the peer reviewed economic analysis.

With high vaccine coverage in girls, the vaccination of boys adds little additional benefit to either the prevention of cervical cancer or genital warts due to the expected benefits of herd immunity. There was not yet any data on the efficacy of this vaccine against cancers also affecting males such as anal, head and neck cancers. When more data becomes available, high risk groups such as gay men would be considered.

A further point was raised about what advice should be offered to girls and women requesting vaccination, who fall outside of these specified age groups including the catch up. The JCVI agreed that their remit was only to advise on the national programme and this was not for them to address but noted this was an issue for DH.

The Committee agreed the following advice;

- HPV vaccines should be introduced routinely for girls aged around 12-13 years, subject to independent peer review of the cost benefit analysis.
- An additional cost-effectiveness analysis to determine the benefits of a catch-up for older girls was required before a recommendation could be made by the main Committee. This would be available for the meeting in October.
- Any new data on HPV vaccines would be kept under review by JCVI

7. Horizon Scanning

A summary paper highlighting new vaccine developments that were relevant to the UK was presented. The vaccines in development were Meningococcal group B, Pseudomonas aeruginosa, Staphylococcus aureus, Clostridium difficile, Cytomegalovirus and Epstein-Barr virus. It was noted that this review did not include progress on the development of vaccines to protect against HIV, Malaria, TB and Hepatitis C which all were of major global interest.

Meningococcal group B

The Health Protection Agency reported on clinical trials that were being conducted by the National Vaccine Evaluation Consortium on candidate Meningococcal group B vaccines. Recombinant vaccines that protect against a broad range of strains are also being developed by Novartis. Phase 1 trials are showing promising results and interim immunogenicity results are expected at the end of 2007. A carriage study in adolescents to assess potential herd immunity from the candidate vaccines is planned.

A Lactamica vaccine being developed by the HPA was also being tested in a phase 1 trial.

Pseudomonas aeruginosa
A vaccine against Pseudomonas aeruginosa for people with cystic fibrosis is currently being developed by Berna Biotech. The vaccine is in phase III trials in Europe and is believed to prevent the progressive destruction of the lungs caused by colonisation.

Staphylococcus aureus and Clostridium difficile

Vaccines to protect against healthcare associated infections are a high priority.

Trials on the S. aureus vaccine developed by Nabi were terminated in 2005 due to disappointing results. Prospects for a S.aureus vaccine include a chloroform inactivated whole S.aureus vaccine being developed by Vaccine Research International, who are currently taking a vaccine into a phase 2 trial.

In February 2006, Acambis plc announced results from a Phase 1 trial of its vaccine against C. difficile. A second phase 1 trial is currently underway in healthy elderly adults with phase 2 trials also scheduled to commence.

Cytomegalovirus

In 1999, the Institute of Medicine ranked a vaccine to prevent cytomegalovirus (CMV) disease at the highest priority on the basis of the economic costs that would be avoided and the years of life and disability that would be saved by a successful vaccine. CMV is a cause of mononucleosis (glandular fever) in healthy individuals and is a well known cause of serious morbidity and sometimes fatal infections in immunocompromised individuals. Congenital CMV infection can lead to deafness and other neurological problems. A clinical trial is being conducted on a candidate vaccine at the Royal Free by Professor Griffiths. Results are expected later in the year and these would be reported back at a future meeting.

Epstein-Barr virus

The Epstein-Barr virus is thought to be responsible for a number of disease in addition to mononucleosis and Burkitt's lymphoma. It has been proposed as a possible cause of Hodgkin's disease and nasopharyngeal carcinoma. Separate lines of research are being carried out to develop vaccines to prevent glandular fever and the possible cancers caused by EBV.

8. Rotavirus

A subgroup consisting of JCVI members, laboratory scientists, clinicians and epidemiologists were asked via correspondence to review published papers on rotavirus disease burden, vaccine efficacy and safety and cost effectiveness. They were asked to comment on the suitability of these vaccines for the routine immunisation programme, including where the two vaccines were interchangeable and whether they could be safely given with the other vaccines already in the programme.

The subgroup considered that:

- The current data on rotavirus disease burden was reasonably robust and consistent with other developed countries.

- Although some groups of children may be at increased risk, overall the group considered that all children are at risk and it would be difficult to determine risk groups.
• The two vaccines (RotaTeq and Rotarix) are comparable in terms of their vaccine efficacy and the impact they would have on burden of disease. They are not interchangeable. It is not known what impact these vaccines would have on genotype replacement.

• There has been no signal of risk from intussusception with these vaccines. There has been a potential signal for Rotateq from the US of an association with Kawasaki disease. Currently there is insufficient evidence to confirm a causal association between RotaTeq and intussusception and Kawasaki's disease. However, in view of the serious nature of these conditions, the diseases will be further evaluated by analysis of spontaneous reporting data and post-marketing surveillance.

The conclusions of the subgroup would be written up in detail and reported at the next meeting, together with additional safety data from post-marketing surveillance.

9. COVERAGE

9.1 & 9.2 Quarterly COVER report for England

The quarterly vaccination coverage statistics for the United Kingdom for the period October to December 2006 were presented to the Committee in paper JCVI(07)40 and JCVI(07)41.

The Committee noted that uptake of the primary vaccinations ranged from 93.7% in England to 98% in Scotland (by aged 24 months). MMR uptake at the same age ranged from 85% (England) to 92.8% (Scotland), with all countries seeing an encouraging increase in MMR uptake over the last couple of years. It is hoped that the increase in MMR uptake will continue in future months.

The overall uptake was encouraging but the Committee expressed its concern at the continuing lower vaccination uptake in London.

9.3 Informatics update

The DH Immunisation Informatics team presented on the background and process leading up to the deployment of the Health Protection Informatics Website and the projects delivered and being developed by the team. These included projects for pandemic preparedness, the influenza surveillance programme, pneumococcal vaccine uptake, seasonal influenza vaccine uptake, and an Immunisation leaflet service as well as developments on the web site itself to enable geographic mapping, role profiling and new web links which have now been incorporated.

Enhancements to the COVER collections to be deployed later this year and the development of a new vaccine supply project to be piloted this year and deployed next year were also outlined.

In addition, the team were participating in a new National Child Health Board that had been set up by the Connecting for Health team to co-ordinate IT standards in child health systems. In conjunction with this an Immunisation subgroup is being set up by the Immunisation team to be chaired by Professor David Salisbury.

9.4 Connecting for Health

A paper was presented by Connecting for Health.
In summary the Information and IT support for child health services is currently provided mainly through a range of standalone IT systems (including Child Health systems and GP systems) in health and social care agencies. These typically cover specific functional needs rather than providing a holistic view. The NPfIT Child Health Programme is exploring potential opportunities to ensure that professionals (and parents and carers) can access an integrated child health record and that system development and deployment plans are aligned with the emerging pattern of service delivery by NHS and other agencies.

The overall aims of the NPfIT Child Health Programme are to ensure that NPfIT work programmes take account of and reflect the requirements of child health and related maternity services which includes consistency across the country in core content, and to establish and provide a definitive source of advice and guidance for NPfIT programmes and suppliers on these requirements.

The principal specific objectives of the NPfIT Child Health programme are to:

1. Define a standard child health record for use by NHS and other agencies and parents and carers to support both the provision of preventive and therapeutic care to the individual and the planning and delivery of services to children across all settings, and a ‘reference specification’ for child health information systems (CHIS) used by child health organisations (usually PCTs).

2. Ensure that requirements and delivery are aligned with a coherent and widely accepted clinical and business model for child health and related maternity services.

3. Develop a business case for investment to deliver a child health record, along with a strategy for delivery of the child health record and for CHIS compliance with the reference specification, including procurement and commercial strategy, technical architecture (including interfacing/ integration), existing systems and planned developments, and business process redesign.

4. Plan, commission and manage delivery (by NHS CFH and others) of the solutions and services.

5. Provide direction and guidance to NHS CFH and other organisations, including NPfIT suppliers, regarding current and planned IT support for child health services, to ensure convergence, compatibility and consistency.

The Committee was informed and supported the programme of work, it was also reminded that consultations are still taking place looking at data quality and matching issues.

10. SEASONAL INFLUENZA VACCINATION

The following members declared interest in Sanofi Pasteur or GSK.

Professor Simon Kroll non-personal, non-specific
Professor Jon Friedland non-personal, non-specific
Dr Syed Ahmed non-specific, non-personal
Dr Ray Borrow non-personal, non-specific
Dr Stephen Inglis non-personal, non-specific
Pauline MacDonald non-personal, non-specific
Dr John Edmunds also declared a personal, non-specific interest

10.1 Flu review progress report
The Committee was updated on the seasonal flu review, which was published on 8 March 2007 alongside a Written Ministerial Statement.

A main conclusion of the Review is the achievements already reached by the programme, its management and the high uptake in England. Year on year increases in vaccine uptake led the NHS to achieve the WHO target of 75% coverage of older people in 2005/06, ahead of 2010 target. Uptake was slightly lower in 2006/07 due to delays in vaccine supply.

The Review contains 14 recommendations for the DH and NHS to consider including the current vaccine supply system and the scope of improving the national programme. DH is continuing to work on the recommendations appropriate, and will keep JCVI updated on developments.

10.2 Immunisation of Poultry workers

An oral update provided about programme which was introduced in December 2006 following expert advice that a theoretical risk existed for circulating human flu virus to genetically re-assort with avian flu virus, thereby producing a new flu virus. 90% of PCTs ran schemes.

The DH estimated a maximum possible of 75,000 poultry workers although recognised that it would be highly unlikely that the NHS would be able to reach all of these through the programme. Data was collected centrally through the DH Health Protection Informatics website and is currently being validated.

The Committee were also informed of the latest Defra assessment of risk of avian influenza for the UK, based on the migration of birds confirming the current risk of avian influenza is low, but not nil. The Department is likely to run the programme again this winter.

10.3 Flu uptake CMO letter

The Committee was pleased that the CMO letter announcing the seasonal flu programme had been sent out in March this year, earlier than ever before. It also noted that vaccination uptake in 2006/07 was 74% in those aged 65 years and over.

10.4 Roles and responsibilities of Flu coordinators

DH gave a summary paper on the roles and responsibilities of Flu Coordinators. The Seasonal Flu Review had highlighted the importance of the Flu coordinators, and suggested that their roles needed to be clarified.

At this years Flu Coordinators Conference, a helpful discussion was held on what resources were needed by PCT Flu co-ordinators. In light of these discussions, DH will work with a group of co-ordinators to develop a 'toolkit' providing information on the various issues upon which PCT co-ordinators want advice and guidance.

10.5 Flu subgroup minutes

The Committee was informed that the minutes of the JCVI flu sub-group had not yet been signed off, and that they would be completed as soon as possible.

11. Health Professionals Survey
DH explained that the survey is conducted in six annual waves of research that have been conducted among health professionals from 1999 to 2005.

The Committee agreed that this was a useful paper and would be helpful data for training purposes for health professionals.

12. Articles for information
The following articles for information were bought to the Committee's attention.

- Annual update on the meningococcal campaign
- Annual vaccine safety report MHRA
- JCVI annual report 2005 and 2006
- Working party for the Laboratory Containment of Poliovirus minutes
- UK Panel for Certification of the Elimination of Poliovirus minutes
- Peer Review of other Committees SAGE recommendations
- Global advisory committee on Vaccines
- Hepatitis B paper
- 2 Hepatitis E vaccine papers

The Committee agreed that the Annual vaccine safety report provided by the MHRA was very good. The JCVI annual report 2005 and 2006 was welcomed and members were asked to send their comments by e-mail to the DH secretariat.

13. AOB
The Committee asked for an update on proposed subgroups. The Pneumococcal subgroup will meet in September 2007 and the Varicella subgroup plan to meet at the end of the year.

14. Dates of future meetings
Wednesday 17 October 2007 confirmed
Wednesday 13 February 2008 confirmed
Wednesday 18 June 2008 tbc
Wednesday 15 October 2008 tbc