

Joint Committee on Vaccination and Immunisation

Minutes of the meeting held on 6 February 2004

Attending

Professor Michael Langman (Chair)
Professor Alan Emond
Professor David Goldblatt (am only)
Professor Andrew Hall
Professor Simon Kroll
Mrs Vivienne Parry

Dr Richard Roberts
Dr Michael Roworth
Professor Lewis Ritchie
Dr Richard Smithson
Professor Brent Taylor
Dr Christopher Verity

Ex-Officio

Dr Claire Bramley - SCIEH
Professor David Hill - NATHNAC

Dr Stephen Inglis - NIBSC
Professor Angus Nicoll - HPA

Observers

Dr P Kishore – Isle of Man
Dr Angela Williams
Dr Eibhlin Connolly - Eire

Wing Co Andy Green - MOD
Dr A Ambler – Netherlands

Invited to attend

Professor Elizabeth Miller - HPA
Dr Mary Ramsay - HPA

Dr Natasha Crowcroft - HPA
Major Hennesy

Department of Health

Dr David Salisbury (Medical Secretary)
Dr Jane Leese
Dr Dorian Kennedy (Administrative Secretary)
Dr Karen Noakes
Mrs Josie Senior-St Juste
Dr Janet Gibson
Ms Hannah Lewis

Dr Arlene Reynolds
Mrs Pamela Gardiner (Minutes)
Mrs Judith Moreton
Miss Julia Falana
Ms Heather Lambert
Mr Zoltan Bozoky

Medicines and Healthcare products Regulatory Agency

Dr Philip Bryan
Dr Mair Powell

Dr Quareoo

National Assembly of Wales

Dr Mike Simmons

Ms Jenny Thorne

DHSS Northern Ireland

Dr Lorraine Doherty

1. ANNOUNCEMENT AND WELCOME

The Chairman welcomed those attending their first meeting:

Professor Alan Emond, Professor of Child Health at the Centre for Child and Adolescent Health in Bristol; Dr Richard Roberts, Consultant in Communicable Disease Control (CCDC), representing Welsh interests on JCVI; Dr Yvonne Doyle, Director of Public

Health and Medical Director for South East London Strategic Health Authority, was unable to attend this meeting; and Dr David Hill, Director of the National Travel Health Network and Centre (NaTHNaC), an ex-officio member.

Apologies were also received from Professor Paul Griffiths, Professor George Griffin, Professor Keith Cartwright, Dr Barbara Bannister, Mrs Joan Saywer, Professor Jonathan Cohen, and from Dr Elizabeth Stewart of the Scottish Executive.

2. MINUTES OF THE LAST MEETING HELD ON FRIDAY 6 JUNE 2003

The minutes were agreed with the following corrections:

2.1 The minutes were agreed with the following corrections

Paragraph 4.1, penultimate sentence amended to read 'A study in the UK that will be published soon is expected to show that serotype 1 is the prevalent serotype of childhood empyema in the area studied in the UK, the majority of which is caused by pneumococcus'.

Paragraph 4.2(i) change the word 'immunogenicity' to 'immunity'.

Paragraph 4.2(iii) delete the words 'aged 2-3 years' in final sentence and replace it with 'aged 18 months'.

Paragraph 4.3 2nd paragraph after (iv) replace 'Northern Ireland' with 'the Republic of Ireland'.

- paragraph 8.1 : the word 'oopritis' should be amended to read 'oophoritis';

- paragraph 19.2 : the sentence ' This follows evidence that some older children may carry the pertussis bacteria and therefore could infect younger children' should be amended to read 'Some older children could infect younger children'.

3. COVERAGE AND OTHER REPORTS

The coverage reports for the UK were tabled.

At 12 months of age, approximately 90% of UK children are fully up-to-date with their immunisations. Scotland and Northern Ireland are maintaining rates of around 95%. The figures for England are lower due to the uptake rate in London being 82 – 83%.

At 24 months, approximately 93% of UK children are up to date with all vaccinations, with the exception of MMR. At 2 years, 79% of UK children had had one dose of MMR. This was an increase in MMR uptake of 0.9%. By five years of age, 91% of children had had one dose of MMR.

The uptake of all vaccines, including MMR, is consistently higher in Scotland and Northern Ireland, and is lowest in London.

4. PNEUMOCOCCAL IMMUNISATION

The following interests were declared:

Vivienne Parry – Personal - non-specific.

The Chairman ruled that participation in discussion in response to questions was allowed, but none in any decision.

Professor Simon Kroll – Non-personal - non-specific.

The Chairman ruled that full participation was allowable.

4.1 Pneumococcal conjugate vaccine in children-update

Two issues formed the basis of the Committee's discussion.

- i. whether adequate protection could be achieved from giving fewer doses of pneumococcal conjugate vaccine; and
- ii. if there was evidence of a long-term community protective effect from infant immunisation, as suggested by early surveillance data from the USA.

The Committee was provided with provisional USA data for 2002. These showed a further overall reduction in invasive pneumococcal disease rates in children under 2 years. Also in older age groups, notably in the 65 years and over age group where the incidence of invasive disease is high, the 2002 data provided further evidence of associated protection in unimmunised older age groups.

Replacement disease had been seen in children in the US, with an increase in non-vaccine serotype disease in children under 2 years of age. However this was outweighed by the reduction in vaccine preventable disease rates in this age group. This issue needed to be carefully considered in the UK where the incidence of serotype 1 disease (a serotype not covered by Prevenar) is high compared to the US (where serotype 1 disease is rarely seen). A study in the UK that will be published soon is expected to will show that serotype 1 is the prevalent serotype of childhood empyema in the area studied of the UK, the majority of which is caused by pneumococcus. National laboratory reports of invasive pneumococcal disease suggest that there has been an increase in serotype 1 disease.

4.2 Results of the Phase II trials in UK infants and toddlers

Results of the Phase II trials with a 9-valent pneumococcal conjugate vaccine were presented. These trials were undertaken by the National Vaccine Evaluation Consortium (NVEC) to investigate whether the same level of protection could be achieved when pneumococcal conjugate vaccine was given at the same time as the meningitis C conjugate vaccine at 2, 3 and 4 months of age compared with the US primary schedule (2, 4 and 6 months of age). A 2-dose primary immunisation schedule of pneumococcal conjugate vaccine given at 2 and 4 months was also compared to the 3-dose schedule. The trials also investigated potential catch-up immunisation schedules for older children (i.e. how to protect young children who were not offered pneumococcal vaccine in the first few months of life).

The results of the primary and booster phases of the infant studies showed that:

- i. **Primary Immunisation**
2 doses of conjugate vaccine given at 2 and 4 months of age provided a comparable response to that from the 3-dose primary immunisation schedule. 2 doses provided satisfactory primary immunity to all the serotypes in the vaccine as well as priming for memory responses to a booster dose in the second year of life. The primary immune responses were comparable to the antibody levels (geometric mean IgG antibody concentration) seen in the US study, and were not adversely affected by concomitant meningitis C vaccine administration.

ii. **Booster dose**

Responses to a booster dose of pneumococcal conjugate vaccine given at 12 months of age following 2 doses of vaccine at 2 and 4 months of age were similar, or for some serotypes superior, to those observed in similar US and German trials. This improvement in boosting is generally seen for vaccines used in the UK schedule at 2, 3 and 4 months of age.

iii. **Catch-up doses**

The antibody response in children after one dose of the vaccine at 12 months of age, or two doses of the vaccine (12 months followed by 14 months) were similar for 7 of the 9 serotypes covered by the vaccine. Antibody levels (GMCs) to serotypes 6B and 14 (serotypes included in Prevenar) were significantly better in toddlers aged 18 months after 2 doses compared to 1 dose.

The responses to a single dose in children aged 12 months were generally superior, though not markedly so to those achieved in infants aged 2-4 months (2 or 3 dose primary schedule), with the exception of serotypes 6B and 14 where titres were similar.

In conclusion, the immunogenicity data supported the use of a 2-dose primary immunisation schedule, with each dose separated by 2 months, in the first 4 months of life (a period when incidence of pneumococcal disease is high). The data supported a single dose catch up programme for children aged 1 year and over. A 2-dose regime would be required to protect against all serotypes in the 9-valent pneumococcal conjugate vaccine.

4.3 Conjugate pneumococcal vaccine and the routine childhood immunisation schedule

A paper was presented to the Committee, which explored how pneumococcal conjugate vaccine could be incorporated in to the UK schedule, should such a policy be introduced. Since this issue was first discussed in January 2002, a number of factors had changed.

- i. A combined meningitis C - pneumococcal conjugate vaccine is unlikely to be available for some time.
- ii. The introduction of new childhood vaccines to replace whole cell DTP/Hib vaccine for primary immunisation would mean that there would be no experience of using pneumococcal conjugate vaccine with the new vaccines according to the UK schedule. The Hib and MenC responses in particular would also need to be monitored carefully.
- iii. One of the available meningitis C vaccines has been licensed for a 2-dose primary immunisation schedule from 2 months of age. There is now data as discussed above supporting a 2-dose pneumococcal conjugate schedule.
- iv. There is, nonetheless, evidence of a waning immunity with both the Hib conjugate and the Meningitis C vaccine given at 2, 3 and 4 months of age. This could suggest that a similar observation may occur with pneumococcal vaccine given according to the UK schedule.

The Committee **agreed** that the immunogenicity data presented supported a 2-dose course of pneumococcal conjugate vaccine, given at 2 and 4 months of age, for primary immunisation. This would need to be confirmed in studies using new DTP and Hib vaccines, Meningitis C vaccine and the pneumococcal conjugate vaccine.

Concern was expressed by the Committee that there were still a number of practical implications to address. A key question was whether 3 injections given routinely for babies at one visit would be acceptable to parents and to health professionals. In the Republic of Ireland a delay in children receiving their immunisations was seen when 3

injections in one visit was introduced. Appropriate training could influence the attitude of health professionals, which could in turn influence parents.

If it was decided that 3 injections were not to be given at the same time, it may be preferable to follow a 2 dose Meningitis C course. Pneumococcal and Meningitis C conjugate vaccine could be given at separate, sequential visits. This would need to be addressed in future DH funded NVEC trials in UK infants. Given the emerging evidence of waning efficacy of both Hib and Meningitis C vaccines, booster studies to address this issue were also planned. The Committee supported the proposal for new clinical trials.

The Committee concluded that the new data discussed on US surveillance data and UK infant clinical trials was encouraging, but there were still questions to be answered and important decisions to be made on how best to fit pneumococcal vaccine into the immunisation schedule, should such a policy be introduced. The Committee **recommended** that an expert group be set up to examine these issues in detail and report back to JCVI.

4.4 Pneumococcal conjugate vaccine for at risk children

A paper was presented on options for extending the current use of Prevenar amongst children at increased risk of pneumococcal disease. The Committee was asked to consider whether children who had previously had pneumococcal meningitis were at increased risk of further invasive pneumococcal disease. It was agreed that there may be a number of risk factors for pneumococcal infection that may go unrecognised in children (such as asplenia), and that children who had previously had invasive pneumococcal disease may be at risk from the other pneumococcal serotypes that cause disease. The Committee **agreed** that at-risk groups should be extended to include children who had previously had invasive pneumococcal disease, but the wording of the recommendation would be agreed by correspondence. **[Action Needed]**

The Committee were also asked to consider whether the use of Prevenar should be extended to all at-risk children under the age of 5 years. Currently the vaccine is recommended for at risk children under the age of 2 years. The incidence of invasive pneumococcal disease is greatest in children under 2 years of age but is still significant in the 2 - 5 year age group. The Committee **agreed** that the policy on pneumococcal conjugate vaccine should be extended to all at risk children under 5 years of age. This would not replace pneumococcal polysaccharide vaccine, which would still be recommended over the age of 2 years. The Committee asked the pneumococcal subgroup to consider the appropriate vaccination schedule for this group and report back.

5. CHILDHOOD VACCINES

The Committee was alerted to potential changes to the vaccines used in the routine UK childhood immunisation schedule.

The Committee recalled that it had previously agreed that oral polio vaccine (OPV) should be replaced by inactivated polio vaccine (IPV) as soon as progress on the global eradication deemed the risk of importation to have declined significantly. This would reflect the change in the balance of decreasing risk of wild poliovirus importation and the risk of vaccine associated paralytic poliomyelitis with OPV. Progress towards global elimination of polio continues with good results from India but with some problems still in Nigeria. The WHO target date for global interruption of wild poliovirus transmission is 2005, and great efforts are being made to meet this deadline.

The Committee recalled that it had also previously agreed to move from wholecell pertussis vaccines to acellular pertussis vaccines when the efficacy of acellular vaccines

at least matched that of the currently available wholecell vaccine. This was due to the lower rates of adverse reactions reported with acellular pertussis vaccines, particularly in older age groups.

The Committee had also previously agreed with the advice from the CSM to move to thiomersal free vaccines when effective alternatives were available.

The Committee was informed that the Department would implement this advice when supplies of licensed vaccines meeting the requirements were available in the UK. The Committee was informed that when IPV is introduced into the routine childhood immunisation schedule, an emergency stock of OPV would be held for use in case of an outbreak.

The Committee supported the Department of Health taking these plans forward. The Committee **agreed** that a change to new vaccines meeting the above recommendations should be made when adequate stocks of new vaccines are available.

6. IMMUNISATION AGAINST INFECTIOUS DISEASE (THE GREEN BOOK) CHAPTERS

The Committee was invited to consider and agree the revised Green Book chapters on diphtheria, tetanus, pertussis, *haemophilus influenzae type b* (Hib), and polio.

JCVI **agreed** that all children up to the age of 10 needed protection against diphtheria, tetanus, pertussis, polio and Hib disease. Pre-school boosting was still needed for diphtheria, tetanus, polio and pertussis. Children 10 years and over did not currently need protection against pertussis or Hib infection.

JCVI agreed with the need to revise the list of contra-indications to childhood vaccines and the proposed changes.

The Committee was advised that for travel purposes, Td/IPV would be offered for protection against all or any of tetanus diphtheria or polio. No single antigen vaccines would be stocked by the Department. The Committee was advised that the travel population were used to receiving multiple vaccines so this should not pose a significant problem.

On disease specific issues, it was agreed that the only contraindication for acellular pertussis vaccines was an anaphylactic reaction to a previous dose, or to a component of the vaccine. Evidence from other countries had shown that other conditions were not contraindications to pertussis vaccination. They may be reasons for deferral of immunisation, such as an evolving neurological condition, but immunisation should be completed when appropriate.

The Committee agreed that children up to the age of 10 years needed to be protected against Hib disease. This was a change from the current advice of up to 4 years of age. It reflected evidence that the risk of unprotected children aged from 5 to 9 years suffering from Hib disease was about three times greater than for the children in this age group who had been protected.

The Committee also **agreed** to include some text in the Green Book which explains the need to check that Injecting Drug Users (IDUs) are protected against tetanus. This follows cases of tetanus still being reported in IDUs.

The advice about vaccinating women during pregnancy, premature infants, and immuno-compromised individuals had been clarified.

7. DRAFT JCVI ANNUAL REPORT

The Committee had previously agreed that an annual report of its work should be published in order to help promote the work carried out by the Committee. A number of comments had been provided by members on the first draft. Members suggested that a glossary would help clarity, and that a complete chronological list of all papers would be helpful.

Members **agreed** to further revision and editing of the document.

8. INFLUENZA

8.1 Minutes of the JCVI influenza panel meeting held on 10 November 2003 (JCVI(04)08)

The Influenza Panel met at short notice in November to consider whether the existing JCVI advice on flu was still appropriate in light of a number of early cases of flu, including some deaths in children.

The Panel had concluded that the current immunisation policy and advice was appropriate, although uptake of the vaccine in children who were at high-risk from flu needed to be encouraged. The Panel decided that more information was required before any change in policy could be recommended. The Panel agreed to meet again in the spring. In the meantime, this further work would be progressed.

8.2 Adult flu programme

The Committee was updated on the progress of the influenza immunisation programme. The 70% uptake target had been met this year in people aged 65 and over (overall uptake 71%). Although cases of flu had occurred early the peak was lower than average.

8.3 Avian Influenza

The Committee was asked to advise on whether poultry workers should be offered flu vaccine in order to be protected against flu. In discussing the item, the Committee recognised the following problems:

- i. Human flu vaccine is unlikely to provide cross protection against avian flu unless human and avian strains have re-assorted.
- ii. It was not clear what the definition of poultry worker included, and further clarification on this issue was sought.
- iii. It was recognised that vaccination, by protecting against human flu, might reduce the risk of re-assortment of flu viruses (which may occur if a person caught human flu and avian flu at the same time). Advice on the risk of re-assortment was welcomed.
- iv. It may be possible to achieve high vaccine uptake in a one-off focused campaign, rather than a routine campaign.

In light of the unknowns, the Committee asked the Influenza Panel to provide advice on this issue due to its greater depth of understanding of influenza.

9. RABIES SUB GROUP

The JCVI Rabies Sub-Group had recommended a precautionary approach with respect to treating bat bites, recommending that immunoglobulin as well as vaccination be offered to all unprotected individuals. However the Advisory Committee on Dangerous Pathogens suggested that this approach only be followed if the bat bite fell into a 'high risk' category.

The Committee considered the advice of the sub group and the advice of ACDP. The discussion in this area was limited by the lack of strong evidence upon which to base discussions.

Following discussion, the Committee asked for more information on the incidence of bat bites in the UK; the risk factors for bat bites; and the availability of rabies vaccine and immunoglobulin, but did not see a clear basis for dissenting from the advice of its rabies subgroup.

12. MENC VACCINE – MENINGOCOCCAL GROUP C CONJUGATE VACCINES AND RELAPSES OF NEPHROTIC SYNDROME

The Committee was informed that the CSM had considered the issue of Men C conjugate vaccine and relapses of nephrotic syndrome. CSM, in considering the available evidence noted some uncertainties in the evidence and concluded that a warning of a possible adverse effect rather than a contra-indication in nephrotic patients was appropriate.

12.1 NEISVAC – MEN C VACCINE

The Committee's attention was brought to a change in the licence for Neisvac – one of the MenC vaccines used in the routine immunisation programme. Neisvac is now licensed for use in a two-dose regime, given 2 months apart from 2 months of age. However the other MenC vaccines were licensed for a 3-dose schedule.

The Committee considered that to use one vaccine in a two-dose programme whilst others were recommended for three doses could cause confusion in the national programme and might even result in missed necessary doses, so leaving some children poorly protected.

Members agreed to continue to recommend a 3-dose schedule.

13. HEPATITIS B

The Hepatitis B subgroup last met in July last year and needs to meet again, in order to discuss the issue of a universal vaccine. A further sub-group meeting needed to be arranged.

14. NATIONAL EXPERT PANEL ON NEW AND EMERGING INFECTIONS

Members were reminded that this Committee was set up in response to the CMO's Infectious Disease Strategy "Getting Ahead of the Curve". Professor Christopher Bartlett chairs the Panel, and Professor Langman attends in his capacity as Chairman of JCVI.

The Chairs of the various advisory Committees have agreed to propose topics that they believed warrant consideration by the Panel in its first year.

Members were asked to identify any issues which JCVI believe the Panel needs to consider. The Committee accepted that flu and tuberculosis remained critically important.

The Committee asked for a list of the membership of this Panel and it was agreed that this would be circulated to members.

15. HORIZON SCANNING

15.1 HPV vaccines

The Committee was informed about the progress towards human papilloma virus (HPVs) based vaccines to protect against cervical dysplasia (a precursor to cervical cancer) and genital warts. Phase II vaccine trials were showing promising results, and Phase III studies were well underway. An application for licensing of an HPV vaccine could be possible within the next 2 years.

The cost effectiveness of a HPV vaccine would be challenging to assess. It appeared to give good protection against infection, but producing evidence of value in preventing cancer would be extremely difficult due to the long period over which this disease develops. Assessing value also involved parallel consideration of the potential impact of vaccination in the context of the current UK cervical screening programme.

The Committee noted progress in the development of the vaccine; it asked to be kept informed.

15.2 Children's Vaccine Tracking Programme

The Department has started a major new project on vaccine tracking.

The Programme was initiated by recommendations made in the Chief Medical Officers strategy "Getting Ahead of the Curve". The aim is to develop a more fully co-ordinated system within England that will link information about vaccines to individual children's health records.

The general benefits the programme is seeking to deliver are to:

- generally improve the quality of information assessing vaccine value
- enhance electronic links between NHS and DH stakeholders
- strengthen integration and access to relevant information
- develop the accuracy of the information collected
- improve the timing of relevant immunisation information to parents
- reduce wastage and duplication of resources where appropriate

The project is very ambitious, complex and will take a number of years to take forward. However it was recognised as key in the future of UK immunisation.

The Committee welcomed this initiative and agreed to be updated periodically about the progress of this project.

16. HIB UPDATE

Following the recent Hib campaign, the Committee was updated on laboratory confirmed cases of Hib disease for 2003.

For 2003 there were 266 cases compared to 269 in 2002. In the last quarter of 2003 there were 74 cases in total compared to 120 cases in 2002. The rate of disease in the under 4 years (19 cases in 2003 compared to 58 cases in 2002) showed a large

reduction in Hib disease suggesting that the Hib campaign has worked in those immunised but as yet there was no evidence of a herd immunity effect.

17. Q FEVER

The Committee was asked to consider if occupational vaccination against Q fever should be recommended.

The vaccination is currently recommended for occupational use in Australia and has been reported to be 100% effective. However, this report is questionable as other evidence suggests that 12 immunised individuals acquired the disease. The disease is occupationally acquired but the burden of the disease is difficult to assess. The vaccine contains thiomersal.

There were several unknowns, such as who was at risk of Q fever in the UK, the efficacy of the vaccine; and the data concerning the risk of vaccinating individuals previously exposed to Q fever.

The Committee asked for more information particularly about the burden of disease in the UK.

18. ARTICLES FOR INFORMATION

18.1 Varicella Immunisation and Healthcare workers; CMO letter and information leaflet

The Committee's attention was drawn to the varicella CMO letter and information leaflet. This new policy followed the committee's recommendation. The new policy was introduced in December.

18.2 MMR/Autism

The Committee's attention was drawn to the most recent publications on MMR and autism. The Committee saw nothing which altered its current views on the safety of MMR.

18.3 Thiomersal

The Committee's attention was drawn to the most recent publications on thiomersal. The Committee again saw nothing to suggest significant problems which had gone unrecognised.

19. ANY OTHER BUSINESS

The Chairman and Dr Salisbury would be meeting Dr Jeremy Metters to discuss his review of access to the yellow card database. There were matters relating to immunisation which were worthy of particular consideration.

20. DATES OF FUTURE MEETINGS

Friday 4 June 2004

Friday 1 October 2004