Joint Committee on Vaccination and Immunisation

Minutes of the meeting held on 6 June 2003

Attending:
Professor Michael Langman (Chair)
Professor Keith Cartwright
Professor Jonathan Cohen
Professor Paul Griffiths
Dr David Goldblatt
Professor Andrew Hall
Professor Simon Kroll
Mrs Vivienne Parry
Dr Michael Rowarth
Professor Lewis Ritchie
Mrs Joan Sawyer
Dr Richard Smithson
Professor Brent Taylor
Dr Christopher Verity

Ex-officio
Dr Syed Ahmed SCIEH
Dr Steven Inglis NIBSC

Observers
Lt Col Eadon
Dr P Kishore
Dr A Williams

Invited to attend
Dr John Emonds (HPA)
Dr A Ambler (Netherlands)
Dr Cressida Auckland (HPA)
Dr Natasha Crowcroft (HPA)

Department of Health
Dr David Salisbury (Medical Secretary)
Dr Graham Bickler
Dr Hugh Nicholas
Dr Dorian Kennedy (Administrative Secretary)
Dr Arlene Reynolds
Dr Karen Noakes
Mrs Debby Webb
Mr Richard Griffiths (Minutes)
Mrs Pamela Gardiner
Miss Julia Falana
Mrs Josie Senior-St Juste
Ms June Boggis
Ms Jo Yarwood

Medicines and Healthcare products Regulatory Agency
Dr Phillip Bryan
Dr Theresa Pepper

Scottish Executive
Dr Elizabeth Stewart

National Assembly of Wales
Dr Mike Simmons
Jenny Thorne

DHSS Northern Ireland
Dr Lorraine Doherty

Apologies:
Professor Emond
Dr C Bramley
Professor A Nicoll
Professor Brian Duerden

1. **ANNOUNCEMENTS AND WELCOME**

   The Chairmen welcomed everyone to the meeting.

   The Chairman welcomed Dr Bickler to the meeting. Dr Bickler had replaced Dr O'Mahony as Head of the Communicable Disease Branch at the Department of Health.

   Members were reminded to declare any interests

2. **MINUTES OF THE MEETING HELD ON 7 FEBRUARY**

   The following were agreed, and the minutes would be amended accordingly:
   - Dr Verity confirmed that he had sent his apologies to this meeting.
   - Paragraph 6 – The non-personal/non-specific interest of the Chairman was in Aventis Pasteur
   - Paragraph 9.2 – The final sentence should read "An OPV to IPV switch needs lead-in time for manufacturers".

3. **MATTERS ARISING**

   Membership

   Professor Emond had recently been appointed to the Committee. He is currently Professor of Child Health at the University of Bristol.

   Interviews would be held in July for a member to represent Welsh interests on the Committee. It was anticipated that an appointment would be made in time for the next meeting. The Secretariat would be considering other vacancies on the Committee.

   Members of the Committee were advised that Appraisal Reports would be needed for those people who would complete their first term of appointment next year. The Secretariat would contact those members concerned. Any member who did not wish to be appointed for a second term was asked to let the Secretariat know.

   3.2 Annual Report

   It had been agreed previously that the Committee would produce an Annual Report. The Secretariat had already started work on this and it was hoped to have an initial draft for consideration at the next meeting.

3.3 Hib Sub-Group

It had previously been agreed that the Hib sub-Group would need to reconvene to examine the evidence regarding the potential benefit of adding a fourth dose of Hib vaccine to the routine childhood immunisation schedule. The Sub-Group would meet after an initial assessment of the impact of the current catch-up campaign could be made, and other data from the UK and abroad was available.

3.4 Cabinet Office Group on Imported Infection

The Cabinet Office Group was continuing to meet, but there was no report or conclusions as yet.

4. COVERAGE

The Committee received an update on childhood immunisation rates in England, Scotland, Wales and Northern Ireland. Overall uptake was generally stable, but with a slow decline in MMR in some areas.

It was noted however that the mobility of the population in large cities presents difficulties in securing accurate vaccine uptake data. Current data systems are not good for exchanging data when people move, which can result in them being recorded as living in their previous and present location. As part of a recent DH initiative, some areas had demonstrated that the accuracy of data collection could be improved through cleaning up the data systems.

During the discussion it was noted that a recent study published by the ESRC had shown that [to be provided]. Other work by the Department of Health has shown that vaccine uptake falls each time there is significant publicity in the media about MMR. This may reflect parents delaying having their child immunised rather than simply not having the vaccine at all.

The recent outbreak of measles in South London has shown that declining vaccine uptake did not only affect the children who had not received MMR. Some of the children who contracted measles in the South London outbreak were too young to be immunised, demonstrating that unimmunised children put other children at increased risk of infection.

The Committee was advised that a meeting would shortly be arranged for Immunisation co-ordinators in the 20 health authorities, which had the lowest uptake levels, recorded for MMR.

5. THIOMERSAL

5.1 **Statement from the Committee on Safety of Medicines on Thiomersal in vaccines**.

The Committee was informed that the Committee on Safety of Medicines (CSM) had recently considered further evidence that supports the safety of thiomersal (which contains ethylmercury) in vaccines. A statement by the CSM had been published and is available at medicines.mhra.gov.uk/whatsnew/thiomersalstatement_210203.pdf)

There had been two independently conducted UK epidemiological studies that investigated the safety of thiomersal-containing vaccines for infants. These

studies showed no evidence of adverse developmental effects from levels of thiomersal at the amounts used in existing UK vaccines. A further study had shown that ethylymercury is rapidly excreted from the body following administration of thiomersal-containing vaccines, and provides good evidence that it does not accumulate in the body.

5.2 **Thiomersal in Childhood Vaccines, Neurodevelopment Disorders and Heart Diseases in the United States.**
Geier MR and Geier DA. *Journal of American Physicians Surgeons* 2003;8:6-11.

The paper was accompanied by an independent expert critique. This highlighted that it was difficult to work out from the paper what methods had been employed, what data was used and what the results really meant.

The study relied on analysis of a US system through which parents and health care workers can report adverse events, which they believe to be linked to a vaccine. These adverse events are suspected rather than confirmed events. Overall the paper was considered to be very poor. The JCVI concluded that it agrees with the CSM Statement on the issue, which supported unequivocally the safety of current UK vaccines containing mercurial preservatives.

The Committee also considered a different publication by Geier and Geier (International Pediatrics 2003; 18(2): 108 – 113) which used similar methods to look at MMR and autism. This paper shared many of the weaknesses of the paper above.

A major problem was that the paper compared children who had received MMR vaccine against a ‘control group’ who had received DTP vaccines. But these vaccines are usually given to children at different ages: DTP is usually given in the first four to six months of life, whereas MMR is usually given at over 12 months of age. The Committee thought it obvious that more suspected neurological disorders would be reported after MMR than the control group simply because children are older when they receive MMR and it is extremely difficult if not impossible to reliably diagnose a range of neurological disorders in the first six months of life. The Committee also noted that a diagnosis of mental retardation or autism cannot be diagnosed within one month – which was one of the criteria of the study.

The paper was considered to be seriously flawed. It did not alter the Committee’s opinion regarding the safety of the MMR vaccine.

6. PNEUMOCOCCAL

6.1 Pneumococcal conjugate vaccine infant clinical trials

The Committee was updated on progress of the ongoing pneumococcal vaccine clinical trials to examine the immunogenicity of a 9-valent pneumococcal conjugate vaccine in infants. This vaccine protects against the 9 strains of pneumococci that are responsible for the majority of pneumococcal infections in children in the UK.

The trials include examining the number of doses required to provide an appropriate level of protection. The committee will be kept informed of the results of the studies as they become available.

6.2 Pneumococcal conjugate vaccine in adults

A study looking at the effectiveness of the 7-valent conjugate pneumococcal vaccine in elderly people is due to start. The Committee would be updated on its progress.

6.3 **Pneumococcal conjugate vaccine – cost effectiveness**

An economic evaluation had been performed by the HPA to provide information to the Committee about the cost effectiveness of pneumococcal vaccination in young children.

The Committee considered that more information and underlying evidence was needed issues to gain a better understanding of the potential impact of offering children pneumococcal vaccine. The Committee accepted that the model had tried to compensate for many of the uncertainties in the data. However, the Committee also recognised that the outcome of the model was considerably influenced by the assumptions within it, and the imprecision of the epidemiology of pneumococcal disease. This is particularly the case for the burden of pneumonia caused by pneumococci that are vaccine preventable.

The Committee concluded that the presently available evidence suggested that the cost-benefit of a pneumococcal conjugate programme was probably unjustifiable. However that conclusion could change if:

i. the price of the vaccine was considerably cheaper;
ii. adequate protection could be achieved from few doses;
iii. the burden of disease from which protection could be obtained was shown to be significantly higher than estimated;
iv. the "herd immunity" effect, suggested by early data from the US, were confirmed; and
v. there was a significant protection against antibiotic resistant strains, as well as reducing antibiotic use.</< p>

Furthermore the Committee also noted that serotype replacement (in which the strains pneumococci that this vaccine protects against are replaced by other strains against which the vaccine does not protect) would undermine the benefits of this vaccine if this replacement was shown to occur.

7. **DIPHTHERIA VACCINE SUPPLIES**

Low dose diphtheria (d) vaccine for adults had been provided over a number of years to protect adults against this disease. The Committee was informed that the Department was having increasing difficulty in getting supplies of single low dose diphtheria vaccine. The Committee agreed that the combined tetanus and low dose diphtheria (Td) vaccine should be offered as a replacement to single low dose diphtheria vaccine for adults whenever low dose diphtheria was required. Further consideration needed to be given to laboratory workers who need repeat doses and may have reactions to repeat exposure to tetanus toxoid.

8. **MMR**

The following interests were declared:

Professor Langman – Non personal/Non- Specific in Aventis Pasteur [MSD]

Professor Cohen – Personal Non-Specific in Aventis Pasteur

Non-personal and non-specific interests did not debar from taking a full part but the Chairman ruled that a personal interest precluded any part in the decision-making but did not preclude participation in prior discussion.

8.1 **Mumps outbreak in Sheffield**

Between 1 January 2003 and 28 April 2003 there had been 175 suspected and confirmed cases of mumps in Sheffield. Over 100 cases were amongst students at the University of Sheffield, with some cases also reported at Sheffield Hallam University. The rate of complications and hospitalisation rate was about 10%, with 3 cases of meningitis, 2 of pancreatitis, one of oophoritis and pancreatitis, and one of orchitis. All cases were between 18 and 25 years (born 1977 to 1985). In light of the large numbers or cases and the high rate of complications, it was decided to offer MMR to students in this age group as anyone born before 1984 would not have been offered MMR previously.

Over a period of two days, about 6000 students were vaccinated with MMR. The lessons learnt from dealing with this outbreak included the fact that e-mail and text messaging proved effective ways of spreading the message; and that many students were often unsure whether they had received MMR or MR as a child.

The Committee noted that the 1996 Edition of "Immunisation Against Infectious Diseases" (the Green Book) stated that students who have not received MR or MMR vaccine should be offered MMR at or before entry to college or university, and noted that the Department of Health had updated the advice in 2001 when advising Immunisation Co-ordinators that students who had either received no or one dose of MMR should be offered another dose of the vaccine. This outbreak of mumps demonstrates the importance of this advice.

The Committee supported the action taken locally together with the HPA in dealing with this outbreak.

8.2 **Shortage of Single Rubella Vaccine**

Women of childbearing age who are not protected against rubella are currently offered a dose of rubella vaccine. However the Department is having increasing difficulty in sourcing this vaccine as manufacturers preferentially switch to MMR production. In light of this, the Committee was asked to advise on the appropriate action to take, in case supplies of rubella vaccine become exhausted. DH is currently inviting tenders to supply rubella vaccine but in the event of a lack of response, an alternative will be needed to protect women against rubella.

The Committee concluded that:

- rubella infection in pregnant women, particularly at the beginning of pregnancy, can have extremely serious consequences on the unborn child;
- the policy of offering MMR vaccine to children, and rubella vaccine to women of childbearing age, has proved very effective in preventing the transmission of rubella and reducing the incidence of Congenital Rubella Syndrome (CRS) in the UK;
- this policy has also reduced the number of terminations of pregnancies associated with rubella infection;
- the policy in the UK is consistent with the WHO recommendation for the elimination of rubella and CRS;

- women of childbearing age who are unprotected against rubella need to be offered a rubella containing vaccine; and
- MMR is an appropriate alternative to single rubella to protect such individuals.

9. **Update of BCG Immunisation Policy**

The BCG Panel had recently met to review the current policy on BCG immunisation. The Panel is considering the options, taking into account the latest evidence. The Panel will continue this consideration.

10. **Hib**

The Hib catch-up campaign had started on 12 May. This followed the recommendation from JCVI that children under the age of four should be offered an additional dose of Hib vaccine to combat the recent increase in Hib disease. In order to ensure effective distribution of vaccine supplies, the Hib vaccine had been allocated to surgeries based on their population data. Information resources such as leaflets, and Factsheets had also been distributed, and a website created (www.immunisation.nhs.uk/hib).

The Committee was also told that raising the profile of the campaign had been carried out through "sign posting" style advertising (i.e. informing parents of the issue and directing them where to find further sources of information) in national, regional and newspapers and parenting magazines.

11. **SARS**

The Committee was provided with a brief update on SARS. One confirmed case of SARS has been reported in the UK. Samples taken from the three remaining probable cases and those categorised as "suspected" were still being analysed. It is possible that this testing will confirm further cases. However these samples are all from people who have recovered. No new cases of SARS have been reported in the UK since 29 April.

Key to the success in controlling SARS has been the high level of international co-operation and exchange of information. While a reliable test to detect SARS had been developed, it may be some time before an effective vaccine to protect against this infection is available. The WHO was organising a Conference on SARS in July this year.

12. **SMALLPOX**

The Committee was updated on the Government’s continuing policy to vaccinate a cohort of key health workers. The programme is underway and the regional response teams are being built up. All symptoms of possible adverse reactions are recorded, and serious events are reported to the MHRA.

13. **POLIO**

The draft minutes of the Meeting of the Working Party for the Laboratory Containment of Poliovirus were provided for information. Progress is being made for the future laboratory containment of wild poliovirus, starting with the identification of laboratories that may hold wild poliovirus or have potentially infected poliovirus materials. The work is progressing satisfactorily.

14. DISEASE SURVEILLANCE DATA

14.1 Paper for information on disease data in 2002 by CDSC

The paper updated the Committee on the incidence of vaccine preventable disease in the UK in 2002. It was noted that the incidence of most vaccine preventable diseases remains constant, except for measles, Hib and rubella for which increases have been recorded.

It was noted that the number of notifications of pertussis was an under estimate because it is very unlikely that all cases are reported.

14.2 Meningococcal Disease Update

The Committee received its regular update on the rates of meningitis C, following the introduction of Meningitis C vaccine in 1999. While cases rapidly increased to a peak of just under 1000 cases of meningitis C per year in 1999, rates of meningitis C continue to fall and are now down to about 70 cases per year. While rates are lowest in the vaccinated age groups, rates are also falling in those age over 25 years old, which suggests that herd immunity may be occurring. It was also noted that the efficacy of this vaccine is over 80% in all age groups.

While the introduction of the Men C vaccine has been a huge success, there is no vaccine to protect against meningitis B. This now accounts for the vast majority of meningitis cases in the UK.

15. HEPATITIS

15.1 The hepatitis B sub-group

A JCVI subgroup had been set up to review the evidence regarding hepatitis B, such as incidence and distribution of the disease in the population; the efficacy of available vaccines; and the potential impact of such vaccines on public health. While the Committee noted the work carried out so far by the sub-group, a further meeting had been scheduled to try to conclude the work of the sub-group.

15.2 EMEA reviews hexavalant vaccines: Hexavac and Infanrix Hexa

The MHRA informed the Committee that the European Agency for the Evaluation of Medicinal Products (EMEA) through its Scientific Committee (Committee for Proprietary Medicinal Products (CPMP)) had reviewed the safety of two vaccines, Hexavac and Infanrix Hexa. This review followed five reports of unexplained deaths in children in Germany and Austria occurring within 24 hours of receiving these vaccines. Neither of these vaccines is used in the UK immunisation programme.

The overall conclusions were that, apart from the temporal association, there was no evidence to link the vaccines to the events and possible alternative explanations existed. Nonetheless, on the basis of the available evidence, a causal relationship could not be established or excluded. CPMP concluded that there was no change in the benefit/risk profile of these vaccines and did not recommend any change to their use. JCVI endorsed this recommendation.

16. MENINGITIS AND TRAVELLERS

Advice was sought from the Committee on the appropriate travel vaccine to protect against meningococcal infection when abroad.

Currently the combined meningococcal polysaccharide A and C vaccine is the recommended vaccine for travellers. The largest epidemics occur across a belt in Africa from Senegal to Ethiopia, and have traditionally been caused by meningococcal A infection. However accurate determination of the strain of meningitis is challenging in parts of Africa.

Meningitis outbreaks have been clearly documented following the annual pilgrimages to Mecca (the Hajj). After s large outbreak of meningococcal A infection in 1977, Saudi authorities required all pilgrims attending the Hajj to be immunised against at least meningitis A.

An outbreak of meningitis W135 among pilgrims in 2000 resulting in cases in many countries, including 45 cases and 8 deaths in the UK. Since then the Department of Health recommends, and the Saudi authorities require, that all pilgrims receive the quadravalent meningococcal ACWY vaccine. Outbreaks of W135 infections have been reported in Burkina Faso in 2001 and 2002, and cases of W135 infection have been reported to the WHO from Benin, Ghana, Mali, Niger and Nigeria.

The Committee considered this evidence and recommended that people in the recognised risk groups intending to visit high risk areas be offered the ACWY vaccine, which gives protection against meningitis strains A, C, W and Y.

The Committee was also asked to advise on whether meningococcal vaccine should still be recommended to people travelling to Bhutan, Brazil, Mongolia and Nepal.

The risk to travellers (apart from the pilgrimages) was considered very low, apart from certain travellers to the African meningitis endemic zones during the dry season (when the risk is greatest), specifically those on longer trips and/or backpacking or working with the local population.

There have been no recent outbreaks or documented cases in travellers to non-African countries. Most European and the American and Canadian authorities have removed all non-African countries from the list of countries where vaccination is recommended for visitors. This change in advice has resulted in no increase in cases among travellers.

In light of this evidence, the Committee recommended that Bhutan, Brazil, Mongolia and Nepal should be removed from the list of countries for which meningitis vaccine is recommended.

17. **National Travel Health Network and Centre**

The Committee was updated about the National Travel Health Network and Centre that has been set up with funding from the Department. Its primary aims are to develop and promulgate guidance on travel health matters for health professionals advising the public travelling abroad; to carry out surveillance of infectious and non-infectious hazards abroad; to administer the yellow fever vaccination centres, and to help train health care professionals on travel health issues.

In light of the remit of the National Travel Health Network and Centre, its Director will be invited to attend JCVI as an ex-officio member.

18. **Articles for information**

The Committee was updated about the Report of the National Audit Office "Procurement of Vaccines by the Department of Health" that was published recently and attracted some media interest.

The Committee was informed that "For the vaccine contracts that we examined, the Department acted properly in awarding these contracts by complying with appropriate EU procurement regulations, encouraging sufficient competition and evaluating tenders fairly. The procurement arrangements for emergency supplies of smallpox vaccine were unusual as the Department chose not to adopt standard competitive procedures for national security reasons, which is allowable under EU regulations."

The recommendations specific to vaccine purchase included looking at ways to make information on the vaccine purchase process available to the public; to develop protocols in relation to procurements addressing specific threats; and to consider the need for a more proactive approach to address the threat of supply shortages of some vaccines.

18.1 **Extract from Hansard about Tetanus**

The Committee was provided with the extract from Hansard from 25 March which recorded the debate in the House of Commons about tetanus and tetanus vaccinations.

18.2 **Autism; Vaccine Link Considered by Mark Benjamin from the Washington politics and Policy Desk**

A Report of a meeting in the US that claims that autism and other brain problems in American children are linked to vaccines.

18.3 **MMR vaccine and idiopathic thrombocytopenic purpura (ITP). C Black et al**

ITP is an autoimmune disease in which platelets are destroyed leading to spontaneous bruising. This research paper confirms pervious evidence that the increased risk of ITP within 6 weeks of MMR vaccination, and that the risk is about 1 in 25000 vaccinations. This is distinctly lower than the risk of 1 in 3000 in children suffering from rubella, and 1 in 6000 for children suffering from measles.

MMR and autistic enterocolitis: Consistent Epidemiological Failure to find an association. E Fombonne and EH Cook.

This paper reviews the epidemiological evidence about MMR and autistic enterocolitis. The reports that all papers that have studies the association between trends in autism and either the introduction of the MMR vaccine or variations in vaccine uptake have failed to demonstrate an association.

18.4 **Bacterial Infections, Immune Overload and MMR vaccine. E Miller et al**

This paper examined whether MMR vaccine increased the risk of hospitalisation with invasive bacterial infection in a three-month period after vaccination. It was carried out to test whether the MMR vaccine somehow overloads the immune system, as has been claimed. If the immune system was overloaded, the body would be less able to fight infections and more cases of bacterial infections would be seen.

The paper found that children are at no greater risk of being hospitalised from invasive bacterial infections after receiving MMR than before. It in fact suggests a protective effect. The paper does not support the concept of "immunological overload"

18.5 **MMR Vaccine. How effective and How Safe. Independent Review from the Consumers' Association**

This paper reviews the evidence for the effectiveness and safety of MMR vaccine. The paper concludes that there is no convincing evidence that MMR vaccine causes, or facilitates the development of, either inflammatory bowel disease or autism. It also finds no good reason to adopt a policy of single use antigen vaccine because it has no sound scientific basis and is likely to result in increased rates of disease, leading to an increase in morbidity, mortality and risk to others through reduced overall vaccine uptake.

18.7 **Pediatric MMR Vaccine safety. Geier and Geier**

A copy of the article by Geier and Geier was provided. This article had been discussed under Item 5.

19. **Any other business**

19.1 **Rabies**

The Advisory Committee on Dangerous Pathogens (ACDP) had recently considered issues relating to rabies. They had a number of questions relating to rabies vaccination, and sought advice from JCVI. It was agreed that a sub-group of experts should be established to examine the issue and report back to the main committee.

19.2 **Pertussis**

Concern was raised about the lack of vaccines licensed for use in children over the age of 7 years. This follows evidence that some older children could infect younger children.

The Committee agreed to continue to monitor the incidence of pertussis infection, and review its advice on pertussis when appropriate.

20. **DATE OF NEXT MEETING**

The next meeting will be on Friday 3 October.