JOINT COMMITTEE ON VACCINATION AND IMMUNISATION

Minute of the meeting held on Wednesday 8 June 2011
10.30am – 4.00pm
Skipton House, 80 London Road
London, SE1 6NX

Members

Professor Andrew Hall (Chair)
Dr Syed Ahmed
Dr Peter Baxter
Professor Ray Borrow
Professor Judith Breuer
Professor Alan Emond
Professor Jonathan Friedland
Dr Jennifer Harries
Professor Matt Keeling
Dr Gabrielle Laing
Mrs Anne McGowan
Professor Claire-Anne Siegrist
Dr Andrew Riordan
Dr Richard Roberts
Dr Patricia Moore

Invited observers and presenters

Dr Stephen Inglis (NIBSC)
Dr Mary Ramsay (HPA)
Ms Joanne White (HPA)
Mr Nick Andrews (HPA)
Dr Claire Cameron (Health Protection Scotland)
Lt Col Peter Hennessey (MoD)
Lt Col Ashley Croft (MoD)
Dr Darina O'Flanagan (Republic of Ireland)
Professor John Edmunds (LSHTM / HPA)

DH

Professor David Salisbury CB
Dr Dorian Kennedy
Dr Tom Barlow
Dr Stephen Robinson (minute)
Mr Andrew Earnshaw (minute)
Mr Conall Watson
Mr John Henderson
Dr Peter Grove
Mr Guy Walker
Mr Damien Bishop

Devolved administrations

Dr Andrew Riley (Scottish Government)
Dr Elizabeth Reaney (DHSSPSNI)
Dr Sara Hayes (Welsh Assembly)
Mr David Vardy (Welsh Assembly)

MHRA

Dr Phil Bryan
Dr Bridget King
Miss Catherine King

I. Welcome and Horizon Scanning

1. The Chair welcomed members and representatives of the devolved administrations and the MHRA. Apologies had been received from Dr Anthony Harnden, Mr Daniel Jackson and Mrs Pauline MacDonald.

2. The committee reviewed evidence gathered from a horizon scan of vaccines in development conducted during March and April 2011. As much of the information submitted was commercially confidential, the session was held without observers. The committee welcomed the information and considered it extremely informative and helpful in considerations about future JCVI work. It was noted that the horizon scan is unlikely to be complete, for example, smaller biotechnology companies may be unaware of the process or decide not to provide information. Members agreed to inform the committee about any promising new products when possible. Furthermore, whilst the horizon scan investigated when vaccines in development might be authorised, this could not be considered as an indication of when they might be introduced as that would depend on a number of factors including assessment of cost effectiveness, supply, scheduling considerations and contractual agreements in place for the new but also existing vaccines.

3. It was noted that new broader spectrum HPV vaccines are in development and it would be important to begin to gather information on the epidemiology of the additional HPV strains to inform future cost-effectiveness studies. The committee also considered some comparative data on the immunogenicity of a HPV vaccine when administered in two-dose and three-dose schedules and asked that data be requested from the manufacturers to support a future discussion. It was noted that DH had issued a tender for a new contract for HPV and that the contract criteria were based on the current market authorisation for these vaccines. Therefore the contract adjudication and award would be based on the market authorised use of these vaccines only. It was unlikely that any approach to manufacturers for data could be made until the new contract had been awarded.

   Action: secretariat to write to GSK and Sanofi Pasteur MSD/Merck to request data to allow consideration of two-dose schedules for HPV vaccines.

   Action: secretariat to discuss future cost-effectiveness analyses of HPV vaccination with the HPA modelling team.

4. The committee noted that a call for evidence on seasonal influenza vaccines had closed on 1 June 2011 and that the JCVI influenza sub-committee would be considering the evidence submitted at a meeting in September 2011.

II. Welcome

5. The chair welcomed observers, explaining that the committee had a private session to review commercially sensitive data that had been submitted in confidence as part of horizon scanning. Mr Andy Earnshaw was introduced as a new member of the Secretariat.

III. Minute of the previous meeting

6. The committee agreed that the minute of the meeting of 2 February 2011 was an accurate record following:
(i) a change to paragraph 43 to read "*Following consideration of the epidemiological data on the impact of vaccination programmes on pneumococcal disease in England and Wales and the sub-committee's advice, the committee's advice was that PCV13 should be the vaccine of choice for the UK*".
(ii) a changes to paragraph 48 to read "*The committee would consider the use of PCV13 and PPV23 in clinical risk groups once this analysis had been completed*".

IV. Matters arising

7. The action points recorded in the 2 February 2011 meeting minute were reviewed. The Chair noted that:

- a response to observations of low childhood vaccination coverage reported by Haringey Teaching PCT had been received from London SHA for discussion under item 13;
- draft best practice guidance on at-risk infant Hepatitis B vaccination had been circulated to the committee for comment and the final guidance had been published;
- the HPA had yet to assess the feasibility of a sub-analysis of the relative risk of influenza in specific medical conditions, such as specific neurological conditions;
- the HPA had conducted a pilot study of hospital influenza surveillance during winter 2010/11 and intended to establish a larger study for the 2011/12 winter;
- the chair had written to the SPI chair to request a review of the data needed for, and the limitations of, influenza modelling. SPI had discussed the issue and a response was anticipated;
- the HPA was on course to complete a study on the impact and cost-effectiveness of the seasonal influenza programme and possible extensions to it. The JCVI influenza sub-committee supplemented with additional experts in health economics and infectious disease mathematical modelling would meet in September to peer review the completed analysis before consideration by JCVI at its October 2011 meeting. An update on progress of the study would be considered under item 12;

- the influenza chapter of the Green Book had been revised and published on 25 May 2011;
- the committee had issued a statement on its advice on discontinuing the routine adult pneumococcal vaccination programme for those aged 65 years and older and that would be discussed further under item 6;
- the HPA had completed a study on the relative risks of pneumococcal disease in clinical risk groups that would be discussed under item 6;
- the HPA had undertaken an analysis of different options for changes to the vaccination schedule to explore the possible introduction of hepatitis B-containing vaccines that would be discussed under item 8;
- no source for GRADE training in the UK had been identified. It was suggested that a member of secretariat be GRADE trained to then be able to train others. It was agreed that the GRADE system be piloted by the soon to be formed sub-committee on adolescent vaccinations examining the question: would immunising adolescents against pertussis provide effective protection from pertussis infection in neonates?;
- a response on the DH value-based pricing consultation had been submitted;
- the chair had written to the Secretary of State for Health in response to proposals set out in the public health white paper and associated consultations.

8. The chair noted that the listening exercise on NHS modernisation had led to a shift in schedules, and no further significant developments towards the reconstitution of the committee had been made.

9. The chair noted that a work plan for the sub-committee on adolescent vaccinations had been agreed with the sub-committee chair and that suggested members of the sub-committee had been invited to join. A call for evidence would be issued over the summer with a first meeting planned for November 2011.

10. The chair noted a marked increase recently in the incidence of measles in the UK and continental Europe. The committee was informed by HPA that over 400 cases had been reported up to end May 2011 in England; more than the total number of cases reported in 2010 but smaller than earlier years of the previous decade. However, cases were now of a broader age range with the 10-25 year old age group most affected. Most cases were associated with travel, particularly to France. The highest incidence was in London and the south east. Notably four healthcare workers were amongst the cases. The committee concluded that with the current number of cases, and epidemiological trends, the situation did not warrant changes to the vaccination programme. However, it was important that GPs continue to provide catch up MMR vaccinations of under immunised children and adolescents and that the importance of MMR vaccination of healthcare workers is emphasised.

11. The chair noted that reports from epidemiological studies in Sweden and Finland had indicated an increased risk of narcolepsy in children/adolescents vaccinated with the monovalent influenza A H1N1v vaccine (Pandemrix®) compared with those unvaccinated. The committee was informed by MHRA that the European Medicines

Agency (EMA) Committee for Medicinal Products for Human Use had recommended product information be amended to advise prescribers to take into account these preliminary results. It was noted that this was an interim measure pending the outcome of further consideration by EMA expected in July 2011. An HPA study was underway to investigate the vaccination history of cases of narcolepsy referred to UK sleep centres.

V. Assessment of the cost effectiveness analysis of a rotavirus vaccination programme

12. The chair explained that in 2009, JCVI had advised that '*Rotavirus vaccines would reduce the incidence of gastroenteritis in the population. However, at the vaccine prices considered they do not meet the current economic criteria for the introduction of a new vaccine. Introduction of rotavirus vaccines would only become cost-effective if the vaccine prices are much less than those at which they are currently being offered.*' The recommendation had been based on an earlier cost effectiveness study using a static cohort model. Following the recommendation, new data on herd-immunity effects had become available. HPA had constructed a transmission-dynamic model and a new cost effectiveness study had been undertaken taking into account indirect effects of rotavirus vaccination. The study had been independently peer-reviewed. Following peer review, the authors had noted that the model had not taken into account possible vaccine failure from multiple doses of vaccine. A revision to the model was made and the revised model had also been independently peer-reviewed.

13. The committee considered the new study and peer review comments. It concluded that these generally indicated that the model was well constructed, the results were robust and the health economic methodology and criteria were in line with the approach taken by the National Institute of Health and Clinical Excellence. It was noted that one peer reviewer had suggested that given that high levels of vaccine coverage could be expected, modelling suggested that following the introduction of a vaccination programme, years of low disease could potentially be followed by an epidemic that might be of similar magnitude to pre-vaccination epidemics. The committee noted that although possible, data from countries that had introduced rotavirus vaccines had not seen this effect to date.

14. The committee noted that costs associated with a potential increased risk of intussusception had not been taken into account in the model.

15. On the basis of the study, the committee concluded that the findings of the new study supported its original statement that *Rotavirus vaccines would reduce the incidence of gastroenteritis in the population. However, at the vaccine prices considered* (£35 per dose for Rotarix® and £25 per dose for RotaTeq®) *they do not meet the current economic criteria for the introduction of a new vaccine*.

Introduction of rotavirus vaccines would only become cost-effective if the vaccine prices are much less than those at which they are currently being offered.

VI. Pneumococcal vaccination

Routine vaccination programme for those aged 65 years and older

16. The chair explained that DH had sought views from interested parties on JCVI's advice to discontinue the routine pneumococcal vaccination programme for those aged 65 years and older using the 23-valent pneumococcal polysaccharide vaccine (PPV23). The JCVI pneumococcal sub-committee had considered the five submissions received, including a substantial submission from the manufacturer of PPV23. New unpublished epidemiological analyses from the HPA and others had also been considered.

17. The sub-committee chair summarised the sub-committee's consideration of the submissions. The sub-committee had considered that the submission from the manufacturer of PPV23 provided a selective interpretation of evidence and it did not provide any new persuasive evidence that suggested the sub-committee should alter its conclusions about the effectiveness of PPV23 in the UK vaccination programme. The sub-committee had agreed with a request in a submission from the British Medical Association that detailed clinical guidance would be required to inform use of PPV23 in clinical risk groups aged 65 years and older. The other submissions had provided little substantially new or no new evidence.

18. The sub-committee had also considered new extended analyses by the HPA of the effectiveness of PPV23 and the impact of the vaccination programme. Health Protection Scotland (HPS) and Dr Trotter (University of Bristol) had also provided analyses on the impact of the vaccination programme. HPA had also completed a study on the relative risks of invasive pneumococcal disease (IPD) in clinical risk groups. Analyses continued to show that at the population level there had been no observable overall impact of PPV23 on the incidence of IPD in the England, Wales and Scotland since the introduction of the routine pneumococcal vaccination programme for older adults. An analysis of vaccine effectiveness using epidemiological data from England and Wales again suggested that the effectiveness of PPV23 is moderate and relatively short lived, although it may not wane as rapidly as had been suggested by the original analysis. The further analysis also suggested that PPV23 may be less effective in clinical risk groups, particularly those who are immunocompromised. Revaccination was not advisable because of evidence of increased reactogenicity and a lack of evidence on the effectiveness of repeat doses of PPV23.

19. The sub-committee chair explained that the sub-committee had not been able to come to a consensus on advice to JCVI on the vaccination programme.

20. The committee considered the sub-committee's views, the submissions and the new analyses. The committee agreed that the submission from the manufacturer of PPV23 provided no new persuasive evidence that suggested the committee should change its advice. It noted that there remains no evidence from UK studies of a direct impact of PPV23 on IPD in the population aged 65 years and over. Whilst there may be a number of confounding factors that may explain a lack of observable impact, it was notable that indirect protection of this age group arising from the introduction of the pneumococcal conjugate vaccine (PCV) into the childhood vaccination programme could be detected clearly in analyses of English and Welsh data and Scottish data. One possible source of confounding was the staggered introduction of the vaccination programme over several years in England and Wales. However, it was notable that no sustained impact on IPD had been observed in the analysis of data from Scotland where the vaccination programme for people aged 65 years and older had not had a staggered introduction.

21. The committee noted that the new analysis by the HPA of the effectiveness of PPV23 based on a substantially larger dataset of English and Welsh data provided more confidence in the findings and provided an explanation for the lack of observable impact at the population level from the use of PPV23. It showed that effectiveness against IPD is of relatively short duration and may shorten with increasing age. Nevertheless, the analysis showed that the vaccine is moderately effective against IPD for at least two years in the population aged 65 years and older taken as a whole, although this then wanes rapidly and it may have no effectiveness beyond five years. However, in the population without clinical risk factors aged 65 to 74 years, effectiveness may be maintained for five years. Whilst this study looked at the effectiveness of the vaccine against IPD, there is a lack of clear evidence that PPV23 is effective against pneumococcal pneumonia in older people.

22. The committee noted that experience from the seasonal influenza vaccination programme suggested that implementation of universal aged-based programmes may result in higher vaccination coverage than risk group-based programmes with about 25 percentage points difference in coverage of influenza vaccination of those aged 65 years and older compared with those in clinical risk groups aged under 65 years. It may be more difficult for GP practices to identify all those with clinical risk factors for pneumococcal disease compared with those of a defined age. Currently the age of routine PPV23 vaccination is aligned with seasonal influenza vaccination. There are few data that would allow a different optimal age range of PPV23 to be defined with confidence. Thus, given these factors, a risk group-based programme or a different age-based programme are likely to be problematic to implement, and may lead to sub-optimal coverage and may incur greater opportunity costs compared with the existing programme.

23. The committee considered the findings of a study that compared the cost effectiveness of risk group-based and universal age-based vaccination

programmes[1]. This study had been based on a systematic review and meta-analysis of the data on PPV23 effectiveness. PPV23 protection against IPD and mortality had been assumed, although evidence for the latter is poor. In this study the assumptions made about the effectiveness and duration of protection were consistent with the findings of the new HPA analyses. It suggested that routine vaccination of those aged 65 years and older was more cost effective than only vaccinating clinical risk groups aged 65 years and older, although both programmes could be considered cost effective. This was not because the vaccine was highly effective at preventing disease and death but because the vaccine was relatively inexpensive and that, provided it was administered at the same time as seasonal influenza vaccine, the programme was relatively inexpensive to implement. Whilst the impact of herd protection caused by the introduction of PCV7 and now PCV13 into the childhood vaccination programme could influence the cost effectiveness of use of PPV23, it was difficult to predict what that influence might be due to the uncertain nature of pneumococcal serotype replacement.

24. Overall, the committee considered that the submission provided by the manufacturer of PPV23 had used evidence selectively and had failed to explain the lack of observable impact on IPD in the UK. In addition, the data that had been provided on the immunogenicity of PPV23 could not be used to predict clinical outcome due to a lack of an established correlate of protection. The evidence provided by the manufacturer of PPV23 had not materially influenced nor informed the committee's thinking. The four other submissions had added little or no new evidence.

25. The committee concluded that uncertainty remains on the effectiveness of PPV23 against IPD in those aged 65 years and older, and particularly on pneumococcal pneumonia and mortality, and the lack of reliable data in these areas makes evidence-based decisions more challenging. However, new analyses from the HPA on the effectiveness of PPV23 based on the UK experience of the vaccine suggested that it provides at least some short-term individual protection against IPD in older age groups, although protection may be less and wane faster with age and for some clinical risk groups. In addition, the new data are consistent with assumptions made in a study that suggests the current programme is cost effective and is likely to be more cost effective than a risk group-based programme.

26. Therefore, given that PPV23 is likely to provide some, albeit short term, protection against IPD to those aged 65 years and older (particularly the younger cohorts), that the universal routine vaccination of all those aged 65 years and older is likely to be cost effective and that other alternative programmes may be more difficult to implement, be less effective and likely to be less cost effective, the majority of the committee agreed that the existing programme should continue. However, it would continue to be important to keep the epidemiology of pneumococcal disease and the vaccination programme under review, particularly in light of the herd protection

[1] Melegaro and Edmunds (2004) The 23-valent pneumococcal polysaccharide vaccine. Part II. A cost-effectiveness analysis for invasive disease in the elderly in England and Wales. *European J. Epidemiol.* 19, 365-375.

arising from the introduction of PCV13 into the childhood vaccination programme and the possible wider use of PCV13 in adults. In addition, better data and studies are required on the impact and effectiveness of PPV23 on pneumococcal pneumonia and mortality.

27. The committee encouraged the HPA to publish the new studies as quickly as possible.

Action: committee and sub-committee to issue a new statement on the pneumococcal vaccination programme for adults aged 65 years and older.

28. The committee was informed about a letter to the chair from the UK Vaccine Industry Group that had suggested early engagement of industry in assessments of the effectiveness of existing vaccination programmes similar to the calls for evidence that had been recently introduced at the start of assessments of potential new vaccination programmes. The committee agreed that such engagement with industry and other interested parties to gather evidence to support considerations on the effectiveness of, or major changes to, existing programmes would be beneficial.

Wider use of PCV in clinical risk groups

29. At its previous meeting, the committee had noted the potentially substantial costs of use of PCV13 in clinical risk groups. It was considered that advice on wider use of PCV13 should be supported by evidence of anticipated clinical outcome and cost effectiveness.

30. The committee considered an unpublished analysis produced by HPA to assess the risk of developing invasive pneumococcal disease in clinical groups at risk of pneumococcal disease, noting that this might support development of a meaningful cost effectiveness study. It was explained that the HPA modelling team had begun to develop such an analysis. However, given limited data in some areas some assumptions would need to be based on expert judgement and that the committee might be consulted as the study progresses. An approach to the manufacturers for further data would also be made.

Action: secretariat to request further data from the manufacturers of PCV10 and PCV13 following consultation with the HPA modelling team.

VII. Report from the meningococcal sub-committee

31. The meningococcal sub-committee chair summarised discussions of the meningococcal sub-committee. He explained that with respect to meningococcal B the sub-committee had considered: the impact of meningococcal serogroup B disease in the UK; the efficacy and safety of candidate meningococcal serogroup B vaccines; and a provisional cost-effectiveness analysis conducted by the University

of Bristol as well as a cost-effectiveness analysis from a manufacturer. He explained that serogroup B now accounts for the majority (94%) of invasive meningococcal disease in children aged under five years.

32. The committee noted that submissions of evidence had been received from Pfizer and Novartis on their candidate vaccines and that the sub-committee has asked for more information from both manufacturers. With respect to one vaccine, the sub-committee had noted that data showed that it was immunogenic in children and infants but was associated with an increased frequency of fever in infants. The committee suggested that attitudinal research into parent's perception of fever and acceptance of fever following meningococcal vaccination could be very useful.

    Action: secretariat to establish if research has been conducted into parent's perception and acceptance of fever following vaccination and the feasibility of additional attitudinal research if required.

33. The committee noted that the results of a carriage study in adolescents were awaited to inform an updated cost-effectiveness analysis for meningococcal serogroup B vaccines. The committee suggested that the sub-committee should consider if there is an impact on meningococcal serogroup C titres when meningococcal serogroup C and B vaccines are administered concomitantly.

    Action: Secretariat to ask the manufacturer for data on serogroup C-specific SBA titres for infants given meningococcal serogroup C and B vaccines concomitantly.

34. The meningococcal sub-committee chair explained that the sub-committee had also considered: the impact of meningococcal serogroup A, C, W135 and Y disease in the UK; the efficacy and safety of meningococcal C and ACWY vaccines; and a cost-effectiveness analysis supplied by a manufacturer.

35. The committee noted that since the successful introduction of the meningococcal serogroup C vaccination programme meningococcal serogroup C disease remains at very low levels. However, evidence suggests that in children under six years of age vaccinated with the meningococcal serogroup C vaccine in infancy, antibody titres wane rapidly such that only ten per cent have protective antibody levels by early adolescence. In contrast, around fifty per cent of children immunised when over six years of age have protective levels of antibody by early adolescence.

36. The committee noted that disease caused by other serogroups is relatively low. The majority of serogroup Y cases are in people aged 45 years and over, often with co-morbidities, with a small number of cases in teenagers. The committee agreed that since there may be appreciable carriage of meningococcal serogroup Y in adolescents but relatively low level of disease, that a meningococcal serogroup Y-containing vaccine should not be introduced until there is further evidence of how this may affect carriage and disease. Data to inform this consideration would come

from a carriage study being conducted for serogroup B disease that was also looking at the effects of a ACWY conjugate vaccine.

37. The committee noted that clinical trial data shows that a single dose of meningococcal C vaccines (NeisvacC® or Menjugate®) provided sufficient immunity in infancy until the booster dose of Hib/MenC at 12 months of age. Given this evidence and the advice from the sub-committee that a dose of meningococcal C should be considered in adolescence to maintain individual and herd protection, the committee advised that a cost-neutral approach could be to remove a dose from the infant schedule and replace it with an adolescent dose of meningococcal C vaccine. JCVI asked that its adolescent sub-committee look at options for the timing of an adolescent dose of meningococcal C vaccine.

Action: committee and sub-committee to consider the timing of an adolescent dose of meningococcal C vaccine.

VIII. Assessment of the possible options for the introduction of Hepatitis B containing vaccines

38. The committee considered an analysis to assess the possible inclusion of a hepatitis B-containing combination vaccine into the routine childhood immunisation schedule. It had been shown previously that universal immunisation with a single hepatitis B vaccine would not be cost-effective but inclusion of hepatitis B-containing combination vaccine may be as long as the total cost of the new schedule did not appreciably increase. The committee noted that the procurement timelines for vaccines means that any potential changes could only be implemented in two or more years' time.

39. The immunological and practical advantages and disadvantages of five schedules involving use of Infanrix-Hexa™, Infanrix-Penta™, Menitorix™, MenC-CRM conjugate vaccines and NeisVac-C™ set out below were considered.

Schedule	2 months	3 months	4 months
1a	Infanrix-Hexa	Infanrix-Hexa	Infanrix-Hexa
		NeisVac-C	NeisVac-C
	PCV13		PCV13
1b	Infanrix-Hexa	Infanrix-Hexa	Infanrix-Hexa
		Menitorix	Menitorix
	PCV13		PCV13
1c	Infanrix-Hexa	Infanrix-Hexa	Infanrix-Hexa
		MenC-CRM	MenC-CRM
	PCV13		PCV13
2a	Infanrix-Penta	Infanrix-Penta	Infanrix-Penta
		Menitorix	Menitorix
	PCV13		PCV13
2b	Infanrix-Hexa	Infanrix-Penta	Infanrix-Penta
		Menitorix	Menitorix

	PCV13		PCV13

40. The committee noted that none of the schedules presented an ideal option. Specific immunogenicity data are lacking on all options and, for some, reactogenicity data may be needed (e.g. 1b to assess the effect of a double dose of Hib). In addition, for many options, the provision of vaccine would be from only one supplier (e.g. 1b, 2a, 2b), carrying a risk to the programme if supply problems arose. For some schedules current supply of vaccine is insufficient (e.g. 1a in relation to NeisVac-C). Furthermore, the impact of removing one dose of MenC needed to be considered. Whilst the most immunologically preferred option appeared to be a variation of schedule 2b that allowed a MenC dose to be dropped at four months of age by replacing Infanrix-penta and Menitorix with Infanrix-hexa, the use of similar vaccines could lead to confusion amongst immunisers leading to vaccines given at the wrong time. However, it might be possible to explore with manufacturers whether packaging options could be developed to mitigate this risk.

41. The committee also noted that a combined DTaP/IPV/Hib/HepB vaccine from Sanofi Pasteur / Merck was undergoing clinical trials and may provide an alternative option in the future.

42. It was concluded that consideration need to be given to options that include the removal of a dose of MenC and these should be costed to assess whether a change in schedule might be cost effective. Clinical trials to support evaluation of options should be considered especially noting that a trial to examine the immunogenicity of the current schedule following inclusion of PCV13 had not been undertaken.

Action: HPA to consider options and what research might be possible.

IX. Revised rabies Green Book chapter

43. The committee was provided with a draft version of the Rabies Green Book chapter. It noted that the chapter had been extensively revised following advice in October 2010. The committee was informed of the substantial changes made and the ongoing work to establish how serology testing might be implemented. Additional typographical changes to the chapter were suggested. Following those minor changes, the committee was content for the chapter to be published.

X. Study to address recommendation 22 of the Hine Review

44. The committee considered a study produced by the Health Protection Analytical Team (HPAT) at the Department of Health in response to a recommendation of the independent review by Dame Deirdre Hine of the UK response to the 2009 influenza

pandemic[2]. The review had suggested that Ministers should see a range of options when deciding on levels of coverage of pandemic-specific vaccine and had recommended that: "*The Joint Committee on Vaccination and Immunisation should be asked to advise on vaccination strategies across a range of scenarios, including severe and less severe pandemic viruses. This advice should incorporate the views of behavioural scientists and economic analysis, and be published in the revised National Framework no later than March 2011*."

45. It was explained that the study had examined the coverage of pandemic-specific vaccine required to essentially stop any late wave of pandemic influenza infections (i.e. reduce it to seasonal influenza sized outbreaks), in relation to a number of highly uncertain variables. The health and cost implications in terms of lives saved or lost from achieving vaccination coverage levels different to that required to essentially stop any late wave had been considered. The aim of the study was to provide a basis for the production of an updated analysis at the time of a future pandemic based on the circumstances and knowledge available at the time (including behavioural research) that could be used to inform decision making. The JCVI influenza sub-committee had considered the analytical approach proposed by HPAT at its meeting in December 2010 and had considered it to be reasonable. Suggestions made by the sub-committee had been addressed in the analysis.

46. The committee noted that the study showed very clearly that the impact of pandemic-specific vaccination is strongly influenced by the timing of vaccination in relation to the timing of late waves of infection. It is unlikely that a pandemic-specific vaccine could be produced and supplied in sufficient quantities quickly enough for a strategy of vaccinating school children to be effective at stopping large-scale transmission. This may especially be the case with epidemics of highly transmissible pandemic influenza viruses that may be of shorter duration, although it is possible other countermeasures might be introduced such as school closures and use of antivirals to slow such epidemics. Instead, it is most likely that pandemic-specific vaccine would only become available in sufficient quantities late in, or even after, an influenza pandemic. Targeting vaccination to those at highest risk from infection would be the most effective strategy if vaccine became available late in a pandemic.

47. The committee noted that if immunity following pandemic-specific influenza vaccination continued past the pandemic then, should the pandemic strain then circulate as a seasonal influenza strain, vaccinated groups could have some continuing immunity. This immunity might also be boosted by trivalent seasonal influenza vaccination as had been shown in a recent study[3]. Therefore, there may

[2] Dame Dierdre Hine (2010) The 2009 influenza pandemic. An independent review of the UK response to the 2009 influenza pandemic http://www.cabinetoffice.gov.uk/media/416533/the2009influenzapandemic-review.pdf

[3] Pebody *et al.* (2011) Effectiveness of seasonal 2010/11 and pandemic influenza A(H1N1)2009 vaccines in preventing influenza infection in the United Kingdom: mid-season analysis 2010/11. *Euro Surveill.* 16(6). pii: 19791.

be some continuing, albeit uncertain, benefit from pandemic-specific vaccination following a pandemic.

48. The committee was content with the study and concluded that it would provide a useful and informative basis for the production of an updated analysis in the event of a future pandemic.

49. A question was posed in discussion about the appropriate quantities of pandemic-specific vaccine to consider in relation to Advanced Purchase Agreements (APAs). The committee suggested that as vaccine would arrive late in, or after, a pandemic, coverage of the entire population would not be appropriate. However, since it is generally easier to scale down rather than scale up production of vaccine, and that higher volumes of production may increase the speed of supply, a low initial coverage in APAs would carry a risk that insufficient vaccine might be available when it is needed. One pragmatic option might be to consider quantities of vaccine in APAs to ensure coverage of clinical risk groups, so that those most at risk might be protected, and also of school children to prevent the potential for transmission giving rise to a later wave of infections.

XI. Consultation on the UK pandemic influenza preparedness strategy

50. The chair explained that a consultation on the revised UK Influenza Pandemic Preparedness Strategy had been issued and that JCVI might wish to comment.

51. The committee had no specific comments and the chair agreed to respond to the consultation to indicate that the committee was content with the sections relating to immunisation and the role that the committee is proposed to have in responding to an influenza pandemic.

Action: secretariat to draft a letter for the chair to respond to the consultation.

XII. Short report on progress of the seasonal influenza vaccination programme study

52. The chair explained that the HPA had been asked to evaluate the impact and cost-effectiveness of the seasonal influenza vaccination programme and possible extensions to the current programme.

53. The committee was provided with an update on the progress of the study work. The study was on track for completion by the end of August 2011 to be peer-reviewed in September 2011 by the JCVI influenza sub-committee together with additional invited experts.

54. Scottish officials offered to provide Scottish data to inform the study.

XIIa. Use of egg-free seasonal influenza vaccine for children with severe egg allergy

55. In an addition to the agenda, the committee was asked to consider the possible use of an ovalbumin-free seasonal influenza vaccine (Preflucel®) in children with severe egg allergy, outside of its market authorisation.

56. The committee noted that this vaccine would be the only ovalbumin-free vaccine available in the 2011/12 influenza season. However, as there are no data on the immunogenicity or safety of this product in children and given that alternative low ovalbumin-content vaccines are available and authorised for use in children, the committee advised against use of Preflucel® in children with severe egg allergy. Instead, current advice given in the influenza chapter of the Green Book on the use of low ovalbumin-content seasonal influenza vaccines for those with egg allergy should be followed.

XIII. Coverage of childhood vaccines

57. At the JCVI meeting in February 2011, low coverage of routine childhood vaccines reported by Haringay PCT had been noted. In response, a paper had been provided by NHS London outlining what steps had been taken to improve immunisation coverage across London in addition to providing an explanation of Haringay PCT's immunisation rates. The committee were encouraged by improvements in London to increase coverage and hoped that would continue. It noted that provisional data for the fourth quarter of 2010/11 had shown significant increases in coverage in Haringay PCT compared with the first three quarters of 2010/11.

58. Routine childhood vaccine coverage rates for the quarter October to December 2010 were summarised for England, Scotland, Wales and Northern Ireland:

England	http://www.hpa.org.uk/hpr/archives/2011/hpr1211.pdf
Scotland	http://www.isdscotlandarchive.scot.nhs.uk/isd/servlet/FileBuffer?namedFile=child_imms_LatestRates_Quarter410.xls&pContentDispositionType=attachment
Wales	http://www2.nphs.wales.nhs.uk:8080/VaccinationsImmunisationProgsDocs.nsf/3dc04669c9e1eaa880257062003b246b/d9ca72ca29af977a8025783a004b5dfb/$FILE/Cov10q4%20(report97).pdf
Northern Ireland	http://www.publichealth.hscni.net/directorate-public-health/health-protection/vaccination-coverage

XIV. Papers for comment

59. The committee was provided with two letters for comment.

60. First, a letter sent to the chair asking the committee to consider information relating to the safety of thiomersal in vaccines. The committee did not consider that data showed any correlation between the use of thiomersal in vaccines and an increase in food allergies such that an increase in emergency adrenaline injectors was required. Moreover, the committee noted that analyses of prescription data provided by the correspondent and extended by the secretariat to 2010 on adrenaline auto-injectors showed that paediatric use runs parallel to adult use and that this is inconsistent with the hypothesis presented by the correspondent. In addition, it was noted that prescribing of injectors had changed over time with individuals now often having multiple pens provided at any one time. Therefore, the quantity of injector prescriptions could not be correlated to the number of people prescribed adrenaline injectors over time.

61. The committee also noted the reference made by the correspondent to the precautionary principle of Article 174(2) EC and JCVI. However, the Article is directed at decision makers. JCVI provides advice to decision makers (Ministers) and may provide advice in relation to possible precautionary measures where there is a possible threat to health. However, it is does not make decisions about what action is taken, such decisions are taken by Ministers.

62. The committee reiterated its position that other than a risk of localised hypersensitivity reactions, the levels of thiomersal in vaccines are not associated with any harm, including in children, pregnant women and their offspring.

63. Second, the committee received a letter on potential risks to health from climate change that had asked for JCVI's views on the short, medium and long term impacts of climate change on considerations about immunisation and what adaptation measures may be needed to minimise possible impacts.

64. The committee noted that climate change may increase the risk of arthropod-borne infections, including the potential introduction of tick-borne encephalitis. In addition, it noted that the seasonality of diseases such as RSV and influenza may be altered or ablated.

Action: secretariat to draft a response for comment by the committee.

65. The committee was also informed about a consultation of a London TB plan by London Health Programme for NHS London[4]. The consultation document implied

[4] London Health Programmes London TB plan. http://www.londonhp.nhs.uk/wp-content/uploads/2011/03/LONDON-TB-PLAN-exec-summary.pdf

that the current BCG vaccination strategy may be inappropriate and suggested that a universal London wide strategy be applied. Members noted that the proposals had not been discussed with JCVI, NHS London immunisation coordinators nor DH immunisation branch. The chair suggested that he write to the London Health Programme to ask for evidence that the current BCG vaccination strategy was inappropriate and to inform it of the advice JCVI had recently given to the Mayor of London on BCG vaccination in London.

Action: secretariat to draft a letter for the chair to the London Health Programme.

XV. Dates of future meetings

Wednesday 5 October 2011
Wednesday 1 Feb 2012
Wednesday 13 June 2012
Wednesday 3 October 2012

The JCVI agenda and meeting papers are published on the meetings area of the JCVI website http://www.dh.gov.uk/ab/jcvi/index.htm

Annex 1

Declarations of interest

Agenda Item V
The following members declared interests in companies that manufacture rotavirus vaccines (GSK and Sanofi-Pasteur MSD):

Member	Interests	Action
Ray Borrow	Non-personal, non-specific GSK and Sanofi-Pasteur MSD	The member was allowed to participate in the discussion and decision
Judith Breuer	Non-personal, non-specific Sanofi-Pasteur MSD	The member was allowed to participate in the discussion and decision
Anne McGowan	Non-personal, non-specific GSK and Sanofi-Pasteur MSD	The member was allowed to participate in the discussion and decision
Richard Roberts	Non-personal, non-specific GSK and Sanofi-Pasteur MSD	The member was allowed to participate in the discussion and decision
Claire-Anne Siegrist	Non-personal, non-specific Sanofi-Pasteur MSD	The member was allowed to participate in the discussion and decision

Agenda Item VI
The following members declared interests in companies that manufacture pneumococcal vaccines (GSK, Pfizer and Sanofi-Pasteur MSD):

Member	Interests	Action
Ray Borrow	Non-personal, specific GSK, Pfizer and Sanofi-Pasteur MSD	The member was allowed to participate in the discussion but not in the decision
Judith Breuer	Non-personal, non-specific Sanofi-Pasteur MSD	The member was allowed to participate in the discussion and decision
John Friedland	Non-personal, non-specific Pfizer	The member was allowed to participate in the discussion and decision
Anne McGowan	Non-personal, non-specific GSK, Pfizer and Sanofi-Pasteur MSD	The member was allowed to participate in the discussion and decision
Richard Roberts	Non-personal, non-specific GSK, Pfizer and Sanofi-Pasteur MSD	The member was allowed to participate in the discussion and decision
Claire-Anne Siegrist	Non-personal, non-specific Sanofi-Pasteur MSD	The member was allowed to participate in the discussion and decision

Agenda Item VII
The following members declared interests in companies that manufacture meningococcal vaccines (Baxter, GSK, Novartis and Pfizer):

Member	Interests	Action
Ray Borrow	Non-personal, specific Baxter, GSK, Novartis and Pfizer	The member was allowed to participate in the discussion but **not in the decision**
John Friedland	Non-personal, non-specific Pfizer	The member was allowed to participate in the discussion and decision
Anne McGowan	Non-personal, non-specific GSK and Pfizer	The member was allowed to participate in the discussion and decision
Richard Roberts	Non-personal, non-specific GSK and Pfizer	The member was allowed to participate in the discussion and decision

Agenda Item VIII
The following members declared interests in companies that manufacture hepatitis B vaccines (Novartis and Sanofi-Pasteur MSD):

Member	Interests	Action
Ray Borrow	Non-personal, non-specific Novartis and Sanofi-Pasteur MSD	The member was allowed to participate in the discussion and decision
Judith Breuer	Non-personal, non-specific Sanofi-Pasteur MSD	The member was allowed to participate in the discussion and decision
Anne McGowan	Non-personal, non-specific Sanofi-Pasteur MSD	The member was allowed to participate in the discussion and decision
Richard Roberts	Non-personal, non-specific Sanofi-Pasteur MSD	The member was allowed to participate in the discussion and decision
Claire-Anne Siegrist	Non-personal, non-specific Sanofi-Pasteur MSD	The member was allowed to participate in the discussion and decision

Agenda Item IX
The following members declared interests in companies that manufacture rabies vaccines (GSK and Sanofi-Pasteur MSD):

Member	Action	Interest
Ray Borrow	Non-personal, non-specific GSK and Sanofi-Pasteur MSD	The member was allowed to participate in the discussion and decision
Judith Breuer	Non-personal, non-specific Sanofi-Pasteur MSD	The member was allowed to participate in the discussion and decision
Anne McGowan	Non-personal, non-specific GSK and Sanofi-Pasteur MSD	The member was allowed to participate in the discussion and decision
Richard Roberts	Non-personal, non-specific GSK and Sanofi-Pasteur MSD	The member was allowed to participate in the discussion and decision
Claire-Anne Siegrist	Non-personal, non-specific Sanofi-Pasteur MSD	The member was allowed to participate in the discussion and decision

Agenda Item X, XI and XII
The following members declared interests in companies that manufacture seasonal and pandemic influenza vaccines (Abbott, Baxter, Crucell, GSK, MASTA, Novartis, Pfizer, Sanofi-Pasteur MSD):

Member	Action	Interest
Ray Borrow	Non-personal, non-specific Baxter, GSK, Novartis, Pfizer and Sanofi-Pasteur,	The member was allowed to participate in the discussion and decision
Judith Breuer	Non-personal, non-specific Sanofi-Pasteur MSD	The member was allowed to participate in the discussion and decision
John Friedland	Non-personal, non-specific Pfizer	The member was allowed to participate in the discussion and decision
Anne McGowan	Non-personal, non-specific Crucell, GSK, Pfizer, and Sanofi-Pasteur MSD	The member was allowed to participate in the discussion and decision
Richard Roberts	Non-personal, non-specific Crucell, GSK, Pfizer, and Sanofi-Pasteur MSD	The member was allowed to participate in the discussion and decision
Claire-Anne Siegrist	Non-personal, non-specific Sanofi-Pasteur MSD	The member was allowed to participate in the discussion and decision

Agenda Item XIV
The following members declared interests in Novartis and Sanofi-Pasteur MSD:

Member	Action	Interest
Ray Borrow	Non-personal, non-specific Novartis and Sanofi-Pasteur MSD	The member was allowed to participate in the discussion and decision
Judith Breuer	Non-personal, non-specific Sanofi-Pasteur MSD	The member was allowed to participate in the discussion and decision
Anne McGowan	Non-personal, non-specific Sanofi-Pasteur MSD	The member was allowed to participate in the discussion and decision
Richard Roberts	Non-personal, non-specific Sanofi-Pasteur MSD	The member was allowed to participate in the discussion and decision
Claire-Anne Siegrist	Non-personal, non-specific Sanofi-Pasteur MSD	The member was allowed to participate in the discussion and decision

Annex 2

Evidence considered by the committee.

Agenda item 1:
- Horizon scanning for vaccine developments 2011 paper (commercial information withheld)

Agenda item 3:
- Minute of JCVI meeting 2 February 2011

Agenda item 5:

- Cover note on rotavirus vaccination and the new cost-effectiveness model
- Peer review comments, responses from authors and first version of the revised cost-effectiveness analysis
- Peer review comments and second and final version of the revised cost-effectiveness analysis
- JCVI statement on rotavirus vaccination (2009)
- Jit M and Edmunds WJ (2007) Evaluating rotavirus vaccination in England and Wales. Part II. The potential cost-effectiveness of vaccination. *Vaccine* **25**(20): 3971-9

Agenda item 6:
- JCVI statement on discontinuation of PPV programme for 65s+ (2011)
- Sanofi Pasteur MSD response to JCVI advice
- Sanofi Pasteur MSD response - Fedson D1, Nicolas Spony L, Klemets P, *et al*, 23-valent pneumococcal polysaccharide vaccination for adults: new perspectives for Europe (pre-publication)
- Sanofi Pasteur MSD response - Musher D, Manoff S, McFetridge R *et al*. Antibody Persistence 10 Years after 1st and 2nd Doses of 23-Valent Pneumococcal Polysaccharide Vaccine, and Immunogenicity and Safety of 2nd and 3rd Doses in Older Adults (pre-publication)
- Sanofi Pasteur MSD response - Lazarus R, Clutterbuck E, Yu LM *et al*. Pneumococcal conjugate and plain polysaccharide vaccines have divergent effects on antigen-specific B-cells (pre-publication)
- Sanofi Pasteur MSD response - Lazarus R, Clutterbuck E, Yu LM *et al.* (2011) A randomized study comparing combined pneumococcal conjugate and polysaccharide vaccination schedules in adults. *Clin Infect Dis* **52**(6): 736-42
- British Medical Association response to JCVI advice
- Diabetes UK response to JCVI advice
- Meningitis Trust response to JCVI advice
- Trotter. Analysis of Hospital Episode Statistics for pneumococcal-related disease codes, 2002 – 2009. Pre-publication
- Health Protection Agency. Estimation of the Impact of Pneumococcal 23v Vaccine in the Elderly Statistical Analysis Report. (pre-publication)
- Scottish Pneumococcal Invasive Disease Enhanced Reporting (SPIDER). (pre-publication)
- Health Protection Agency. Estimation of 23v PPV vaccine effectiveness using the indirect cohort method in England and Wales. (pre-publication)

- Health Protection Agency. Estimation of 23v PPV vaccine effectiveness using the indirect cohort method in England and Wales. The effect of underlying clinical conditions on the risk of developing invasive pneumococcal disease: a cohort study among hospitalised patients in England. (pre-publication)
- JCVI pneumococcal sub-committee note of considerations

Agenda item 7:
- Cover note on the meningococcal sub-committee
- Minute of the meningococcal sub-committee 18 Feb 2011

Agenda item 8:
- Ladhani S, Borrow R, Ramsay M. Potential Infant Immunisation Schedules To Accommodate The Introduction Of Combination Vaccine Containing Hepatitis B In The United Kingdom. (pre-publication)

Agenda item 9:
- Revised rabies Green Book chapter (pre-publication)

Agenda item 10:
- Cover note on addressing recommendation 22 of the Hine Review of the 2009 Influenza Pandemic
- Extract of the Independent review of the UK response to the 2009 influenza pandemic
- Extract of the JCVI influenza sub-committee minute of its meeting on 1 December 2010
- Implications of Pandemic-specific Vaccine Coverage Levels, When Considered at the Early Stages of an Influenza Pandemic. Department of Health, Health Protection Analytical Team (commercial in confidence)

Agenda item 11:
- Cover note on the UK Influenza Pandemic Preparedness Strategy 2011 consultation
- UK Influenza Pandemic Preparedness Strategy 2011- Strategy for consultation

Agenda item 12:
- Modelling the cost-effectiveness of changes to the seasonal influenza vaccination programme - Progress report for JCVI June 2011 Meeting

Agenda item 12a:
- Cover note on the use of egg-free seasonal influenza vaccine for children with severe egg allergy

Agenda item 13:
- Improving Childhood Immunisation Uptake in the Capital – A Case Study, NHS London
- Quarterly vaccination coverage statistics for children aged up to five years in the UK (COVER programme): October–December 2010
- Percentage of children immunised by their 1st birthday (England), by Government Office Region and PCT coverage, Q3 2010 (October to December)
- Primary Immunisation Uptake Rates by 12 months old (Scotland), Q4 2010 (October to December)
- Vaccine Uptake in Children in Wales October to December 2010 Q4 2010 (October to December)

- Vaccination Coverage Statistics for Children in Northern Ireland: Completed Primary Immunisations by 12 months, Q3 2010 (October to December)

Agenda item 14:

- Letter to scientific advisory committees on the health effects of climate change
- Cover note on the use of thiomersal in vaccines
- Letter to the committee on the use of thiomersal in vaccines
- EMEA (1998) Safety working party assessment of the toxicity of thiomersal in relation to its use in medicinal products (CPMP/SWP/1898/1988)
- EMEA (1999) CHMP position paper on thiomersal. Implementation of the warning statement relating to sensitisation (CPMP/2612/99)
- EMEA (2007) CHMP position paper on thiomersal. Implementation of the warning statement relating to sensitisation (EMEA/CHMP/VWP/19541/2007)
- Gupta R, Sheikh A, Strachan DP et al. (2007) Time trends in allergic disorders in the UK. Thorax 62(1): 91-6
- Graph constructed by the correspondent from prescription cost analysis showing all adrenaline prescriptions from 1991 to 2005
- Additional information from prescription costs analysis