JOINT COMMITTEE ON VACCINATION AND IMMUNISATION

Minute of the meeting on 03 October 2018

Skipton House, London Road, London

Members

Professor Andrew Pollard (Chair)
Professor Anthony Harnden (Deputy Chair)
Professor Wei Shen Lim
Professor Jeremy Brown
Alison Lawrence
Prof Adam Finn
Prof Rob Read
Prof Anthony Scott
Dr Maggie Wearmouth
Dr Peter Elton
Dr Martin Williams

Co-opted members

Dr Lucy Jessop (NI)
Anne McGowan (Wales)
Dr Lorna Willocks (Scotland)

Secretariat

Andrew Earnshaw
Ruth Parry
Jonathan Crofts
Chris Lucas
Dr Mary Ramsay
Dr Gayatri Amirthalingam

Medical Advisor

Professor Jonathan Van Tam (DCMO)

Invited Speakers

Dr Richard Pebody (PHE)
Professor David Elliman (NSC)
Dr Shamez Ladhani (PHE)
Dr Jay Lucidarme (PHE)
Dr Marc Baguelin (PHE)
Professor Matthew Snape (NISEC)
Dr Helen Campbell (PHE)

Invited observers from Devolved Administrations

Dr Syed Ahmed (Scotland)
Dr Gillian Armstrong (NI)
Dr Stephen Thomas (Wales)
Dr Marty Coleman (NI)

Other invited observers

Dr Sandra Anglin (NHS England)
Dr Linda Diggle (Jersey)
Jacqui Dunn (IoM)
Dr Dipti Patel (NaTHNaC)
Dr Michael Edelstein (PHE)
Cheryl Cavanagh (DHSC)
Dr Anne Kilgallen (DHSSNI)
Dr Yoon Choi (PHE)
Cheryl Cavanagh (DHSC)
Dr Louise Newport (DHSC)
Professor Daniel Stecher (Argentina)
Dr Vanessa Saliba (PHE)
Ruth Howlett-Shipley (MoD)
Joanne Yarwood (PHE)
Dr Sema Mandal (PHE)
Dr Ian Feavers (NIBSC)
Dr Caroline Trotter (PHE)
Dr Claire Cameron (HPS)
Dr Richard Roberts (HPW)
Dr Tom Irving (DHSC)
Professor Jahit Sacarlal (Mozambique)

Welcome

1. The Chair welcomed all to the meeting. The Chair reminded members and observers that the papers provided for the meeting included information provided in confidence. Attendees were asked not to circulate the papers more widely or discuss the information provided with others outside of the meeting. Attendees were asked not to discuss any considerations of the Committee with others outside of the meeting. Any requests for information should be directed to the Secretariat.

2. The Chair asked members to provide an update about any declarations of interest.

3. The Chair welcomed the following new members to the JCVI: Dr Martin Williams (Healthcare Associated Infections (HCAI)), Professor Jeremy Brown (Geriatrics and Respiratory), and Professor Wei Shen Lim (Respiratory).

4. Apologies were noted from Professor Andrew Riordan, Professor Fiona van der Klis and new member Professor Simon Kroll (Paediatric Infectious Diseases).

5. The Chair noted that this would have been the last meeting for Andrew Riordan following 10 years' service. The Chair thanked Andrew for his work and the secretariat would formally write to Andrew expressing the gratitude of the Committee.

6. The Chair also welcomed Professor Jahit Sacarlal and Professor Daniel Stecher from the Mozambique and Argentinian NITAGs respectively.

I. Minute of the June 2018 meeting

7. The Minutes of the June 2018 meeting were agreed.

II. Matters arising

<u>Letter from Pfizer about pneumococcal schedule advice</u>

8. The Chair introduced the item and noted a letter from Pfizer about the JCVI recommendation to move to a 1+1 schedule for pneumococcal conjugate vaccine (PCV), which raised issues similar to those discussed previously by JCVI.

9. The Committee noted the letter and discussed the question around the legal position of JCVI advice on using a product outside of its license. JCVI had previously provided advice to DHSC on use of products outside of license and as JCVI does not consider legal implications of operational delivery this point was not considered further. It was also noted that the Committee had some concerns on the mathematical model used by Pfizer to support their letter.

<u>Letter from Meningitis Research Foundation (MRF)</u>

10. The letter received from the MRF about Meningococcal vaccine was noted and JCVI would be considering the issues raised as part of the full agenda item on Meningococcal vaccination.

Ongoing Ebola outbreak

11. The Chair advised the Committee that he had been representing JCVI at various discussions about the UK response, and use of vaccine for UK nationals, during the ongoing Ebola outbreak in the Democratic Republic of Congo (DRC).
12. Currently two unlicensed products available, with recombinant vesicular stomatitis virus–Zaire Ebola virus (rVSV-ZEBOV) being used for ring vaccination in DRC and also for those being deployed to support the outbreak. The Committee noted that this vaccine was being monitored closely to provide further assessments of efficacy and safety.

Monkey pox

13. In the UK there had recently been two imported cases from Nigeria and one case in a contact in the UK. JCVI had been involved in discussions around use of the licensed Smallpox vaccine Imvanex (replication deficient modified vaccinia ankara) which provides some protection against Monkey Pox for pre-exposure prophylaxis.
14. Advice had also been sought on post-exposure and there was evidence that post-exposure prophylaxis might prevent infection or reduce severity of disease if administered immediately after exposure with useful effects less likely more than 4 days post-exposure. However, a question remained about whether to complete a course following a first dose post exposure. The Committee advised that front-line healthcare workers were unlikely to be subsequently exposed to this rare disease so a second dose would not be required. However, the course should be completed for those at ongoing risk, e.g. those working with Monkey Pox.

Polio containment

15. The Chair had been copied into correspondence from the WHO committee on Polio containment about sampling. This was not a JCVI matter and would be passed to DHSC to consider.

Pandemic influenza vaccines

16. Discussions had been held on trials for MF59 adjuvanted pandemic influenza vaccine if deployed, with a focus on trials for use in children.

III. Meningococcal epidemiology

17. The Chair summarised the evolution of the meningococcal programme and how the Committee had historically considered the meningococcal programme as a whole. The Committee noted that the current programme covered meningococcal A, B, C, W and Y disease, and no other country in the world had such a comprehensive national programme. The epidemiology was often considered by capsular group, but the programme aimed to consider overall control of meningococcal disease.

18. The JCVI had advised a number of changes to the MenC vaccination programme over the last two decades. The 3-dose infant MenC programme in 1999 moved to 2 infant doses with a 12-13 month booster in 2006. In 2013 a dose was moved from infancy to adolescence to maintain the herd protection from the large MenC catch-up programme undertaken in the late 1990s.The adolescent MenC vaccination was changed to MenACWY in 2015 to provide direct protection to the teenagers and indirect protection for the population following a surge in MenW cases nationally.

19. The JCVI advice to remove the last infant MenC dose was agreed as part of the advice on MenB vaccination. It was agreed by JCVI that a comprehensive package of control for invasive meningococcal disease (IMD), by inclusion of Bexsero® in the national programme, could only be considered with removal of the infant MenC dose. This was in part due to considerations of cost-effectiveness. Following JCVIs advice, the UK now had a MenB programme, as well as a MenC programme.

20. The Committee considered a presentation from PHE on invasive MenC disease in England, noting that:

    - there had been a reduction in MenB disease and an expansion of MenW from 2010;
    - MenB accounted for 57% of IMD cases in the last epidemiological year;
    - MenW accounted for around 25% of IMD cases, and Y was around 9% of IMD cases in the last epidemiological year;
    - there had been a small rise in MenC IMD cases in the last epidemiological year with these accounting for 5% of all cases in 2017/18;
    - the small rise in MenC IMD cases, was seen predominantly in infants and mid to older aged adults;
    - before removal of the infant MenC dose, careful consideration was given to how well MenC disease was likely to continue to be controlled with the assumption that herd protection would remain;
    - this included data from other countries that do not use an infant dose, that suggested disease could be controlled through herd protection under such schedules;
    - of the 15 infant MenC cases seen in England in the most recent epidemiological year, 8 of these were in the Yorkshire and Humber region;
    - of the 64 cases across all age groups in the last epidemiological year, 19 were in Yorkshire and Humber;

- Yorkshire and Humber had been asked to review the local situation;

- the Yorkshire and Humber team reviewed case demographics and outcome, for age, sex, household contacts, clinical risk factors, deprivation, vaccination status and geographical location;

- overall the Yorkshire and Humber team concluded that there were no underlying population based causative factors for the increased incidence of MenC IMD that they had seen, and no region specific genetic strains were responsible;

- they would continue to keep the situation under review and undertake further coverage surveys and work to improve coverage in those who were not receiving vaccination at the appropriate age;

- national coverage in infants with Bexsero® (2 doses) by 12 months of age was 92.5%;

- coverage for MenC vaccine by 12 months was 92.5% and by 24 months of 91.2%;

- MenACWY vaccine uptake is around 80-85% in young people aged14-16 years, 70-80% in those aged 16-18 years and up to 40% in those aged 18-21 years;

- school leavers aged 18 years during 2015-2017 were offered MenACWY vaccine every year through general practice rather than schools, because of the diverse nature of educational settings in this age group and

- those who missed the school-leaver vaccination, and older first-time university entrants (up to their 25th birthday), were also offered MenACWY vaccine on an opportunistic basis through general practice.

21. On the MenB vaccination programme, the Committee noted that:

- in the second year of the programme, there had been an estimated 72% reduction in the number of cases of MenB IMD in infants;

- in the third year of the programme there had been a 60% reduction in the estimated number of cases of MenB IMD in infants;

- the data indicated protection from the two dose infant schedule up until the 12 month booster dose;

- the data indicated that protection lasted at least until at least the end of the second year of life;

- effectiveness estimates for those less than 12 months (2+0), were 64% against all MenB strains, and 82.9% against vaccine preventable strains (based on MATS, not taking into account any cross protection);

- vaccine effectiveness for the 2+1 was estimated at 70% against all MenB strains, and 88% against vaccine preventable strains(based on MATS, not taking into account any cross protection); and

- there were no safety concerns after ~3 million doses had been given.

22. On the MenW vaccination programme, the Committee noted that:

    - there had been a small overall reduction in MenW cases in England for the first time since the beginning of the outbreak;

    - those age cohorts targeted for MenACWY vaccination had seen a marked reduction in MenW IMD;

    - there had been no reduction in MenW IMD cases in infants; and

    - there had been a reduction in MenW IMD in those aged 1-4 years.

23. Overall the Committee noted estimates that the MenB programme had prevented about 250 cases in the last three years, with the MenACWY programme preventing around 50 cases of MenW disease. There had, in contrast, been a small increase in MenC cases.

24. The Committee considered the information provided and questioned whether there was information on adolescent coverage by sub-region of Yorkshire and Humber. The Committee reviewed infant coverage data and noted the value of reviewing the sub-regional adolescent coverage data.

25. The Committee considered a presentation on genomic analysis of those strains isolated in the Yorkshire and Humber region, noting that:

    - the Yorkshire and Humber isolates belonged to lineage 11.1, with several sub-lineages present;

    - the 11.1 lineage was in general circulation in England;

    - there is no evidence of a strain specifically targeting infants in Yorkshire and Humber;

    - this was based on culture from 12 of 20 MenC IMD cases; and

    - evidence indicated that protection from Bexsero® against MenC would not be present until after the 12 month booster dose.

26. The Committee agreed with the conclusions from the Yorkshire and Humber report, and from the national data, that there was no obvious link regarding the strain or the local situation which explained the small regional rise in MenC IMD cases. The Committee considered the situation was most likely to be associated with vaccine coverage of adolescent MenACWY and herd

immunity.

27. Vaccine coverage in younger adolescents with MenACWY through the school-based programme was high. Coverage in older adolescents and young adults who were eligible for the vaccine was lower, including in those who had not chosen to move into higher education.

28. The Committee noted that the focus of the MenC programme was predominantly on generating herd immunity, and agreed that this should remain the focus of the programme, and ways of optimising the programme should be considered. This was particularly important as herd immunity would provide protection for the elderly as well as for infants.

29. The Committee noted that coverage could vary by school or GP practice, and that regional and national data could not provide the granularity required to identify any specific issues. However, the national data did indicate lower coverage in school leavers. The Committee agreed that work could be undertaken to improve coverage in this group, and this should be supported by PHE, DHSC and NHSE.

Conclusions

30. Overall cases of meningococcal disease were low across the population, primarily because of the excellent coverage with meningococcal vaccines in target groups.

31. The Committee considered that the number of MenC cases remained low but there had been a very gradual rise over the last few years, in part due to a larger increase in cases in the Yorkshire and Humberside region of England. Cases of MenC disease were mainly being seen in infants and older adults.

32. The aim of the MenC vaccination programme was to provide direct protection to toddlers, teenagers and young adults and also to provide indirect protection to the wider population by generating herd immunity. The MenACWY vaccination programme focussed on teenagers to generate herd immunity.

33. Vaccine coverage in younger adolescents with MenACWY through the school-based programme was high. Coverage in older adolescents and young adults who are eligible for the vaccine was lower (but had been improving), including those who had not entered higher education. JCVI agreed that optimum control of MenC disease could only be achieved if vaccine coverage in older adolescents and young adults was improved.

34. JCVI therefore advised that GPs should be strongly encouraged and supported to improve coverage in those aged 18 to less than 25 years who are eligible for vaccination. It was anticipated that efforts to improve MenACWY vaccine coverage in this age group would lead to a reduction in cases of MenC and MenW disease across the population. JCVI also advised that further evaluation of coverage at sub-regional levels would be helpful in assessing the situation and that sero-epidemiological studies might also help highlight gaps in population immunity.

IV. Influenza

35. The Committee was reminded that low influenza vaccine effectiveness had been observed in recent years especially in the elderly against the A(H3N2) influenza virus. The Committee had recently advised that adjuvanted (aTIV) and high dose (TIV HD) inactivated influenza vaccines were now preferentially recommended over standard dose non-adjuvanted influenza vaccines for use in those aged 65 years and over. The adjuvanted vaccine would be available for use in the elderly this season (2018/19) and TIV HD was expected to be available in 2019/20.
36. The Committee noted that overall effectiveness against A(H3N2) viruses had been declining in recent years culminating in non-significant effectiveness in all age groups in 2017/18. This was thought to be partly due to the phenomenon of egg adaption altering the antigenic profile of the A(H3N2) egg propagated vaccine virus compared with the wild type reference strain. Other factors thought to be involved were immunosenescence in the elderly and genetic drift of the circulating A(H3N2) wild type strain.
37. Cell based or recombinant influenza vaccines had been developed which do not require isolation and manufacture using eggs and therefore were not affected by the problem of egg adaptation. A JCVI *ad hoc* influenza subcommittee meeting had been convened to look at a quadrivalent cell cultured inactivated vaccine (QIVc) and provide advice on its potential use in 2019/20. QIVc was expected to gain licensure in the coming months and therefore be available for use in the 2019/20 influenza season, The Committee was asked to consider the data on QIVc and the advice of the ad hoc influenza subcommittee.
38. The Committee received a presentation from PHE briefly summarising the 2017/18 season and noting that:
    - 2017/18 had been an intense influenza season with mainly influenza A(H3N2) and B Yamagata in circulation;
    - influenza morbidity and mortality was highest in the elderly and all cause excess mortality was also high in this group and mostly attributed to influenza and similar to the previous season of 2016/17 when A(H3N2) was also dominant;
    - influenza B had also impacted quite highly on morbidity in the elderly as the main B strain in circulation was not included in the trivalent inactivated vaccine predominantly used in this age group;
    - vaccine effectiveness against A(H3N2) across all age groups was very low and not statistically significant; and
    - the cause of the low VE against A(H3N2) was thought to be multifactorial including genetic drift with different subclades circulating, waning immunity, immunosenescence in the elderly and egg adaptation of the A(H3N2) vaccine strain.
39. The Committee noted data were available from a number of studies in the US on the effectiveness of QIVc compared with egg based influenza vaccines during the US 2017/18 influenza season.
40. Using electronic medical records the manufacturer had conducted a retrospective cohort analysis of primary care consultations from a nationally representative data set (age range 4 to >75 years of age). The Committee noted that:
    - the clinical endpoint was influenza like illness within a narrow definition based on more than a 75% likely positive laboratory result;

- after adjustment for demographic variables and comorbidities the overall relative effectiveness (rVE) against influenza like illness for QIVc was 36% (95% CI 26.1,44.9; P<0.001; P value <0.001) when compared with egg grown quadrivalent inactivated vaccine (QIVe) ; and
- age group stratified analysis gave a positive and significant rVE estimate for those aged 18-64 years old but non-significant rVE estimates for those aged 4 to 17 years and 65+ years old.

41. The FDA conducted a retrospective observational study and compared VE for all available influenza vaccines using data from more than 13 million people aged over 65 who were Medicare Fee-for-service beneficiaries. The primary end-point was influenza hospitalization (in-patient and emergency room attendance). The Committee noted:
    - there was no virological case confirmation and it was not possible to distinguish between influenza A subtype and influenza B type infections;
    - results showed that QIVc, was statistically significantly more effective than QIVe (rVE 10.7%,) in reducing hospital visits for influenza encounters; and
    - QIVc also appeared to be statistically significantly more effective than adjuvanted trivalent influenza vaccine and non-inferior to high dose TIV.
42. The Committee noted headline results from an abstract provided by the Kaiser Permanente Northern California (KPNC) Vaccine Study Centre:
    - the study investigated VE against lab confirmed (PCR) influenza consultations in those aged 4 to 64 years;
    - VE for QIVc was compared with egg based inactivated influenza vaccines (ebIIV) the majority of which were trivalent; and
    - rVE for QIVc against influenza A was 8% (95%CI:-10,23) and the absolute VE was 31% (95%CI:18.7,42.6) for QIVc and 20.1 (95%CI:4.5,25.4) for ebIIV.
43. The Committee received a presentation by PHE on an impact and cost effectiveness analysis of QIVc relative to egg based trivalent influenza vaccine (TIVe) and aTIV in the elderly and at risk groups less than 65 years old. The model used the rVE findings of 36% for QIVc from the manufacturer's study and an rVE of 25% for aTIV against TIVe.
44. PHE estimated the willingness to pay of QIVc incremental to that for TIVe. Baseline assumptions for TIVe VE were derived from the systematic review by Belongia et al.,2016. The Committee noted the results which showed that:
    - there was a greater benefit in terms of QALYs gained in vaccinating the at risk groups under 65 years old with QIVc compared with TIVe and therefore a higher willingness to pay price for QIVc than TIVe;
    - there was a greater benefit in terms of QALYs gained in vaccinating those aged 65 years and older with QIVc compared with TIVe and therefore a higher willingness to pay price for QIVc than TIVe;
    - when compared incrementally with the adjuvanted trivalent influenza vaccine, QIVc provided more benefit in terms of QALYs gained; and
    - the difference between QIVc and aTIV in terms of willingness to pay was small and there was greater uncertainty over this difference.

45. The committee noted that the findings of the model were based on relatively sparse but positive VE data for QIVc using the single rVE estimate of 36% for A(H3N2) for all ages from the manufacturers study. At the request of the ad hoc Influenza Subcommittee PHE had also conducted a sensitivity analyses based on the rVE estimates from the FDA study using a rVE for QIVc of 10.7% (instead of 36%) against A(H3N2) and rVE aTIV of 3.3% (instead of 25%) against all strains .
46. In the sensitivity analysis QIVc still provided greater benefit in terms of QALYs gained in vaccinating both at risk groups <65 years and those over 65 years of age compared with TIVe. When compared incrementally with aTIV, QIVc provided more benefit in terms of QALYs gained however, the difference between QIVc and aTIV in terms of willingness to pay remained small and there was greater uncertainty over this difference
47. The Committee agreed that the sensitivity analysis was more realistic in terms of using lower rVE estimates for QIVc. The Committee also noted that the Belongia meta-analysis used for the baseline VE estimates in the model did not include the last three seasons in which there were very low VE estimates for TIVe against A(H3N2) in the elderly. Thus the difference between the VE estimates for TIVe and QIVc/ aTIV might be greater than that modelled, and the cost effectiveness of the two vaccines underestimated.

Conclusions

48. The Committee agreed that for adults under 65 the data were supportive for using QIVc in at risk groups alongside QIVe. QIVc appeared to be at least as good as QIVe and possibly better.
49. The stratified data provided by the manufacturer indicated a significant rVE for QIVc in those aged 18- 64 years old whilst the KPNC indicated a positive but non-significant rVE in a similar age range. The Committee agreed that there were not enough influenza seasons of data to express a preference for QIVc in at risk groups under 65 years of age.
50. The Committee agreed that the data on QIVc in the elderly was less clear cut. Again there were data available from only a small number of observational studies and from only one season. There was a positive and significant rVE for QIVc in the FDA study but not in the in the manufacturer's stratified analysis. There was also no data on effectiveness against lab confirmed influenza. Based on the limited data available QIVc could be considered for use in the elderly. The Committee agreed, however, that there were not enough data accumulated to express a preference for the use of QIVc in the elderly over aTIV or TIV HD.
51. The Committee agreed with the ad hoc influenza subcommittee that diversity in available vaccines was important and cell based vaccines could add resilience to the programme. From a scientific point of view egg adaptation was an important issue and not likely to go away. It was right that the UK should be seeking to make QIVc available for use in the programme and to evaluate such vaccines in the programme.
52. The Committee agreed that QIVc could be recommended for use along with QIVe in risk groups under 65 years old pending licensure and that it was also suitable for use in those over 65 years of age along with TIV HD and aTIV.
53. The Committee also agreed that it would be useful to update the influenza model baseline vaccine effectiveness data with more recent seasons data to take

account of the declining VE against A(H3N2).

V. Tetanus post-exposure prophylaxis

54. The Committee noted that in July 2018, PHE had become aware of a severe shortage of tetanus specific immunoglobulin (TIG) and human normal immunoglobulin (HNIG) products for the management of tetanus prone wounds. In response to this significant shortage, PHE undertook an urgent review to prioritise the use of TIG /HNIG for those susceptible individuals at greatest risk.

55. PHE urgently issued updated recommendations in July 2018 on the use of TIG for the NHS, which had been supported by the Chair of the Committee.

56. The Committee noted the updated guidance and that key changes were:
    - assessment of susceptibly using a combination of age, immunisation status and time since last vaccine dose to inform the need for TIG +/- vaccine;
    - recommending booster doses of vaccine for those individuals likely to mount a rapid and sufficient memory response and thereby restricting use of TIG; and
    - clarification of definitions of tetanus prone and 'high risk' injuries.

57. The Committee agreed that the changes were sensible and endorsed them.

VI. BCG vaccination and SCID screening

58. The Chair introduced the item and outlined that a screening programme for Severe Combined Immunodeficiency (SCID) was being proposed to DHSC, which would allow identification and management of affected infants prior to them presenting with severe illness. This was complicated by the use of BCG vaccine, routinely given to at risk babies in maternity units shortly after birth, which can cause serious complications in infants with SCID. The National Screening Committee had recommended that administration of the BCG vaccine be delayed until SCID screening could be undertaken and had asked the JCVI for views.

59. Professor David Elliman from the NSC briefed the committee, which noted:

    - the NSC had been looking at screening for SCID for a number of years and the most recent economic analysis had concluded that it is likely to be cost effective;
    - the NSC had planned to undertake a pilot evaluation for 18 months to cover two thirds of England;
    - in pilot areas screening for SCID would form part of the routine new-born screening test at five days, with most results expected within 10-12 days;
    - while the NSC awaits official Ministerial approval and notification of funding, the Newborn Bloodspot Screening Programme was starting to plan the implementation;
    - BCG would be routinely given in maternity units, targeted at those at

high risk (those living in high incident areas, or with grandparents/parents who have lived abroad in a high risk country) or infants born in London;

- there was some variability around the country in regards to BCG vaccine delivery and although usually offered in maternity units, vaccination could also be given in the community;
- as a result most babies would receive BCG vaccine before the results of SCID tests were available;
- treating SCID patients for the effects of BCG vaccine as soon as possible resulted in a much better outcome, however, it required treatment and monitoring in addition to multiple therapy for SCID and increases the risk of hepatotoxicity;
- this would be avoidable if the administration of BCG were delayed until SCID screening results were known;
- this is currently the position in the Netherlands, where BCG is given selectively and they are rolling out SCID screening and delaying BCG vaccination;
- those most at risk of SCID may also be at risk of TB (and therefore will need vaccination) due to both diseases affecting certain population groups e.g. those from the Indian subcontinent;
- the NSC had reviewed options, including – 1) continuing with the current arrangements, 2) offer of vaccine in maternity unit with parents given an option to delay until after SCID screening, or 3) routinely defer BCG vaccination to 3-4 weeks of age until after SCID screening, which would be undertaken in the community setting; and
- the NSC were recommending option 3.

60. Discussion followed and the Committee and NSC agreed that infants remaining in hospital for more than 4 weeks, e.g. premature infants, should receive BCG vaccination as soon as their SCID result was known, rather than waiting for vaccination in the community setting.

61. The Committee commented on the incidence of SCID, which was 1 in 40-50,000 and it was estimated that annually 15-17 babies would have SCID. A third of these would be identified from family history, leaving about 12 unidentified at time of BCG vaccination. NSC considered that a significant proportion of those with SCID given BCG vaccine would go on to develop complications. NSC also considered that delaying BCG vaccination would not have an impact on the numbers of TB cases, but this assumed that the delay did not mean infants miss vaccination.

62. The Committee agreed it would be necessary to move the programme from birth to after SCID screening results were available, as vaccination before testing would not be acceptable. However, deferring vaccination would require a change in delivery setting from secondary care to the community, and the Committee raised concerns about the challenges this would present, and the risk of lower uptake levels. This would also potentially expand as further immunodeficiency testing became available. Additional work would be required to plan for delivery of BCG vaccine after discharge from hospital and there was a need to ensure community vaccination was as robust as the

current programme.

VII. CMV: Initiative for cooperation between EMA and European NITAGs."

63. The chair raised the issue of a request from European Medicines Agency to provide some advice from NITAGs around Europe. This was the first time that NITAGs would be involved in a parallel procedure, recognising that some of the key vaccine development and study design questions e.g. population, endpoints, economic viability of the project, cannot be answered in a comprehensive way without multi-stakeholder consultation. The EMA hoped that scientific advice, which is not legally binding, could be a platform for such discussions. EMA also expected that parallel consultations would enable vaccine development plans to generate data addressing the needs of all the stakeholders involved in vaccine authorisation, reimbursement and deployment.

64. The overall aim was that in the future, when they were going through licencing processes, industry are doing so in a way that they can ensure that what they are licencing is going to be useful for Public Health programmes. The way they propose to do this is to make a part of the early advice given to industry about the development of their products, indications of the type of trials that NITAGs may wish to see when making a public health decision. This may also result in better licencing decisions.

65. The vaccine in question was selected by EMA as a trial candidate vaccine as it is a complicated issue and it is not entirely clear how the vaccine might be used and what types of data NITAGs might wish to see in order to help make a decision going forward. The Committee was provided with an early dossier detailing the development programme of this vaccine, which would, when the trials were done, form the licencing opinion and enable JCVI, along with other NITAGs to provide feedback to provide useful information which may help to make a public health decision.

66. There were discussions about which was the most appropriate group to receive the vaccine. It was noted that the company had suggested immunising a particular group of people and to licence the vaccine using data on the prevention of infection. It was agreed that the proposed trial was likely to address this question.

67. The potential size of the study was discussed and the ease with which excluding those who are already immune could be achieved.

68. There was insufficient time to answer all of the questions posed, but it was agreed that the principle of involving NITAGs at an early stage was of value. The Committee would like to confirm that JCVI are advising EMA and not the vaccine developer.

69. The Chair indicated that there will be another meeting with the EMA soon and requested a volunteer from amongst the Members to attend along with the secretariat.

VIII. NISEC annual update

70. The Chair reminded the Committee that the National Immunisation Schedule Evaluation Consortium (NISEC) had taken over from the National Vaccine Evaluation Consortium (NVEC), to provide important studies which would inform vaccine policy in the UK. The Chair invited Professor Matthew Snape from NISEC to present to the Committee.

71. The Committee noted:
    - an overview of the NISEC Steering Committee and Advisory Board;
    - the Advisory Board was informed by information from JCVI, DHSC, PHE and NISEC; and
    - planned or proposed studies included:
        - the impact of concomitant administration of alternative hexavalent vaccines with Bexsero®;
        - a follow-up study (IMAP3) of an observational cohort study (IMAP2) comparing vaccine responses in children born to mothers who received pertussis vaccine in pregnancy;
        - optimal timing of the maternal pertussis vaccination (OptiMUM)
        - two doses of non-live zoster vaccine 12 months apart;
        - immunogenicity of 2+1 Bexsero® schedule against MenW and MenC disease;
        - a sero-epidemiology study.

72. The Committee thanked Professor Snape for his update.

IX. Update from the Travel sub-committee

73. The Chair provided a brief update on the recent meeting of the Travel Sub Committee. The Chair requested members put themselves forward to chair the Subcommittee as the current chair was leaving the JCVI. The Committee noted several suggested changes to the Green Book:
    - clarification over the wording in the typhoid chapter, distinguishing vaccine protection against *Salmonella* Typhi (typhoid) and *Salmonella* Paratyphi (para typhoid) A, B or C;
    - that the injectable and oral typhoid vaccines provided some protection against S. Paratyphi C and B respectively and both protect against typhoid;
    - that data were reviewed on the oral cholera vaccine, including a WHO position paper, in order to consider the issue of when to restart a course;
    - the chapter should be updated to reflect this and in particular the need to revaccinate children;
    - in the UK the cholera vaccine is largely confined for use in aid workers and is not usually required for other travellers;
    - that clarification was also sought over the wording in the Green Book concerning the use of the yellow fever vaccination for those who have had a thymectomy;
    - the vaccine was contraindicated, due to the risk of viscerotropic disease, in those with a dysfunctional thymus such as those with a

thymoma or in those who have had a diseased/dysfunctional thymus removed; and

- that in those who had an incidental thymectomy when the thymus was not diseased/dysfunctional, the evidence was that it was safe to give the vaccine (according to CDC guidance).

74. The Committee agreed in principle to the proposed changes, and asked the secretariat to liaise with Nathnac, PHE and MHRA on the proposed changes to the Yellow Fever chapter.

X. Update from the HCAI working group

75. The Chair updated the Committee on the progress of a new Health Care Associated Infection (HCAI) Working Group. The Working Group would be looking at vaccines identified during the 2018 horizon scanning for *S. aureus, E. coli, C. difficile* and Norovirus and the issues around how the vaccines might be used in the UK.

76. The Working Group recently held a first meeting around the current UK position for *S. aureus, E. coli*, and Norovirus and a follow up meeting would be arranged next year with a focus *on C. difficile* and hopefully presentations from the vaccine manufacturers.

77. There was also discussion on AMR modelling, which is likely to become more pertinent for other vaccines going forward.

XI. Coverage

78. The Committee noted the latest coverage data from the UK. The Committee noted a continuing small decline in coverage across the four countries, although overall coverage rates were still very high.

Prof Andrew Pollard (Chair)

Professor Pollard receives no personal payments from the manufacturers of vaccines

He is Director of the Oxford Vaccine Group in the Department of Paediatrics, University of Oxford and has current research funding from the Bill and Melinda Gates Foundation, the National Institute for Health Research, the European Commission, Medical Research Council, Wellcome Trust, Innovate UK, Meningitis Research Foundation, and the Global Alliance for Vaccines and Immunisation. He chairs the scientific advisory group on vaccines for the European Medicines Agency and is a member of WHO's SAGE.

Other investigators in the Department conduct research funded by vaccine manufacturers and the Department has received unrestricted educational grant funding for a three day course on paediatric infectious disease from Gilead, MSD, GSK and Astra Zeneca.

Prof Anthony Harnden (Deputy Chair)

Professor Harnden has no registered conflicts of interest.

Prof Judith Breuer

Professor Breuer has no registered conflicts of interest

Dr Peter Elton

Dr Peter Elton has no registered conflicts of interest

Prof Adam Finn

Professor Adam Finn receives no personal payments from the manufacturers of vaccines.

Professor Finn undertakes unpaid advisory work for Astellas on a klebsiella-pseudomonas vaccine.

Professor Finn's Department receives funding for consultancy work from VBI vaccines on a developmental Hep B vaccine, and Bionet on a developmental pertussis toxin vaccine.

The University of Bristol conducts research funded by GSK on meningococcal carriage, by Pfizer on pneumococcal carriage and transmission.

Prof Matt Keeling

Professor Matt Keeling has no registered conflicts of interest.

Prof Wei Shen Lim

Professor Wei Shen Lim's Department has funding from Pfizer for work indirectly related to pneumococcal vaccines.

Prof Jeremy Brown
Professor Brown has received payment for consultancy work from ImmunoBio on a novel pneumococcal vaccine. Professor Brown's Department has undertaken work for Novartis on the effects of monoclonal antibodies on vaccine responses.
Dr Martin Williams
Professor Martin Williams has no registered conflicts of interest. Professor Williams holds a contract for work with Public Health England.