JOINT COMMITTEE ON VACCINATION AND IMMUNISATION

Minute of the meeting held on 06 February 2019

Wellington House, Waterloo Road, London

Members

Prof Andrew Pollard (Chair)
Prof Anthony Harnden (Deputy Chair)
Prof Som Jeremy Brown
Prof Judith Breuer
Prof Judith Breuer
Prof Simon Kroll
Prof Adam Finn
Prof Rob Read
Prof Anthony Scott
Dr Maggie Wearmouth
Dr Peter Elton
Dr Martin Williams
Prof Maarten Postma

Medical Advisor

Prof Jonathan Van Tam

Co-opted members

Dr Jillian Johnston (NI)

Mrs Anne McGowan (Wales)

Dr Lorna Willocks (Scotland)

Dr Julie Yates (England)

Secretariat

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

Invited speakers

Dr Richard Pebody (PHE)
Dr Shamez Ladhani (PHE)
Dr Christophe Steffen (WHO)
Dr Helen Campbell (PHE)
Dr Alicia Rosello (PHE)
Dr Paul Turner (ICL)

Invited observers from Devolved Administrations

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

Other invited observers

Dr Sandra Anglin (NHS England) Gary Holden (MoD) Christine Cook (NHS England) Joanne Yarwood (PHE) Dr Linda Diggle (Jersey) Dr Sema Mandal (PHE) Dr Jacqui Dunn (IoM) Dr Ian Feavers (NIBSC) Joana Rocha (Guernsey) Dr Caroline Trotter (PHE) Nicola Brink (Guernsey) Julie Nugent (PHE) Alex Hawkins-Drew (Guernsey) Dr Sarah Tarr (PHE) Dr Dipti Patel (NaTHNaC) Dr Jamie Lopez (PHE)

This minute will remain draft until ratified by JCVI at its next meeting

The advice of JCVI is made with reference to the UK immunisation programme and may not necessarily transfer to other epidemiological circumstances

Dr Michael Edelstein (PHE)
Dr Louise Newport (DHSC)
Sarah Hicks (DHSC)

Prof Marion Koopmans (Netherlands)
Toos van den Borne-Oudenaarden

(Netherlands)

Amanda Cohn (US)
Erin Kennedy (US)
Abigail Shefer (US)
Althea House (Canada)
Louise Henaff (WHO)
Christophe Stefen (WHO)

Prof. Gerhard Zielhuis (Netherlands)

David Green (PHE)
Rachel Hornigold (PHE)
Nick Andrews (PHE)
Dr Claire Cameron (HPS)
Dr Richard Roberts (PHW)

Anna Clarke (Eire) Lucy Jessop (Eire)

Dr Hajime KAMIYA (Japan)

Dr Munehisa FUKUSUMI (Japan)

Ms Ikuko DOI (Japan)

Dr. Kees Groeneveld (Netherlands)

Dr. Gwen Soete (Netherlands)

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 Professor Simon Kroll to the meeting, who was the new member for paediatric infectious diseases.
- 4. Apologies were noted from Professor Matt Keeling and Professor Wei Shen Lim.
- 5. The Chair noted that this was the last meeting for Judy Breuer following 10 years' service. The Chair thanked Judy for her work on the Committee and in Chairing the HPV and Varicella sub-committees.
- Dr Lucy Jessop, the co-opted member representing Northern Ireland was leaving her position in Northern Ireland and would be replaced by Jillian Johnson.
- 7. The Chair welcomed representatives from the Netherlands, Japan, the US and Canada, and from the World Health Organisation, who would be observing the meeting.

I. Minute of the October 2018 meeting

8. The Minutes of the October 2018 meeting were agreed.

II. Matters arising

EU EXIT

9. The Committee noted that PHE was undertaking several actions in relation to exit from the European Union to assure continued vaccine supply for the national immunisation programme. The Committee confirmed that it would be available at short notice to consult, where necessary, in the event of any potential disruptions to vaccine supply and the national programme.

Sub-committee Chairs

10. The Committee noted that Professor Simon Kroll had agreed to chair the Travel subcommittee and Professor Adam Finn had agreed to chair the meningococcal subcommittee.

Update from DHSC

- 11. The Committee received an update from the DCMO at DHSC noting that:
 - a response was expected fairly soon on the consultation concerning the recommendations in the CEMIPP report;
 - a policy decision was still awaited concerning the JCVI's advice to move to a one plus one infant schedule for the pneumococcal vaccine as the minister was considering all the evidence and advice put forward;
 - following JCVIs advice the Government had announced extension of the HPV programme to boys;
 - DHSC also confirmed a decision had been made to not have a catch up for older cohorts of boys, but that boys who were eligible would remain so until the age of 18 years.
- 12. The Committee noted the reasons behind the policy for not having a catch up in older cohorts of boys included that:
 - the epidemiological situation was very different now compared with when the programme first started for adolescent girls in 2008, which had included a time limited catch up;
 - the success of 10 years of the girls' programme had established good levels of herd protection which meant that there would be limited additional benefits to be gained from a catch-up programme in boys;
 - the priority was establishing the extension of the routine adolescent programme to adolescent boys and ensuring high uptake in boys whilst maintaining the high uptake in the girls; and
 - under standard economic methodology, a catch up in older boys was

13. The Committee noted that planning by PHE and NHS England was well advanced working towards including boys in the HPV vaccination programme for the academic year 2019/20.

Yellow Fever

14. The Committee noted that, following an incident last year, changes had been made to the Green Book Chapter on yellow fever vaccination to clarify the wording on the contraindication for those with a history of a thymectomy. The Committee noted that, in light of recent deaths associated with the vaccine, the MHRA were planning to convene an expert group to review risk benefit and risk minimisation for yellow fever vaccine. The MHRA was consulting with the JCVI on this issue and welcomed comments and suggestions from members.

NHS Long Term Plan

15. The Committee received an update on the NHS long term plan which included commentary on the national immunisation programme. PHE had worked closely with NHS colleagues in contributing to the plan on the issue of improving uptake and exploring ways and approaches to achieve this. This included looking at GP reimbursement on vaccines and more hands-on coordination at the local level. The Committee noted that immunisation remained a top priority both in the NHS plan and as part of the Secretary of State's policy of focusing on prevention.

III. Rotavirus Epidemiology

- 16. The Committee noted an update from PHE on the impact of the rotavirus vaccination programme in England. The Committee noted that:
 - a rotavirus programme began in 2013 using Rotarix®;
 - the national programme was implemented rapidly;
 - there is a very small risk of intussusception associated with rotavirus vaccination;
 - the longer the first dose was delayed, the risk of intussusception increased, and as such the vaccine was only licensed up to 24 weeks of age;
 - within six months of the programme coverage was 89% by three months of age and 93 % by four months of age;
 - these improved as the programme continued;
 - rotavirus was seasonal, with disease usually seen between January

- the vaccine came in July 2013; and there was an 80-90 percent reduction in laboratory confirmed rotavirus infections in the following season (where only half the first cohort had been vaccinated);
- the reduction in cases was also seen in 1 year olds, 2-4 year olds and 5+ year olds;
- GP and emergency department attendances for rotavirus infection reduced substantially;
- Within one year of the programme hospitalisations for gastroenteritis reduced across all ages;
- over the last five years there had been a dramatic impact on laboratory confirmed rotavirus infections and hospitalisations for allcause gastroenteritis.
- 17. The Committee considered the information provided and commented on strain types, incidental post-vaccination diarrhoea being wrongly attributed to wild-type infection, and impact on adult all-cause gastroenteritis. Overall the Committee commented that the programme had been very successful and gave thanks to those who had been involved in the implementation and monitoring of the programme.

IV. Meningococcal epidemiology

- 18. The Committee noted that during the October 2018 meeting, there had been discussion on the small rise in invasive meningococcal C cases seen in England, and, in particular, the rise in cases in the Yorkshire and Humber region. The vaccination programme had evolved over time, moving from three priming doses, to two priming doses with a booster at 12 months of age, then to a single priming dose with booster doses at 12 months and in adolescence, alongside the addition of MenB vaccine into the childhood schedule. In 2016 the final infant dose was removed from the programme, leaving a dose at 12 months and in adolescence.
- 19. The Committee noted that the Chair had written to the Chief Medical Officer (CMO), noting the lower coverage in older teenage and young adult cohorts, and asking for support for GPs to improve coverage in older cohorts. The Committee noted that the CMO had begun a dialogue with the Chair of the RCGP, who had included a piece on MenACWY on one of her member communications, and further work was planned to support the advice to GPs.
- 20. The Committee noted the latest invasive meningococcal C epidemiology. The most recent epidemiological year had seen lower IMD cases than at the same time the previous year. The reduction was seen across all age groups except those aged 20-24 years, where the number of cases

remained stable. In Yorkshire and Humber, the number of cases was proportionately higher than that seen across the rest of England. There had not been any infant cases in the Yorkshire and Humber region in the epidemiological year to date. There were still a disproportionate number of cases in Yorkshire and Humber, but cases were mainly seen in unvaccinated age groups.

- 21. Uptake data from Yorkshire and Humber indicated as good or better coverage compared with the national average.
- 22. The Committee noted that the increase in cases in the Yorkshire and Humber region appeared to have reduced. PHE currently considered that there was no longer a specific issue regarding invasive meningococcal disease in infants in the region.
- 23. The Committee agreed that the data were reassuring and the ongoing reduction in invasive meningococcal W disease supported the approach of the adolescent ACWY vaccination programme to generate herd protection.

V. Herpes zoster vaccination programme

- 24. The Committee noted an update on the impact of the current routine and catch-up zoster vaccination programme using Zostavax®.
- 25. The Committee noted the published data coming out of clinical trials with Shingrix®, for which there were 4 years of follow-up data.
- 26. It was noted that the Varicella sub-committee had discussed the potential use of Shingrix® in the UK programme and had advised JCVI in February 2018 that Shingrix® should be offered to immunocompromised individuals who were eligible in the current programme but contraindicated for immunisation with Zostavax®.
- 27. It was noted that, at their June 2018 meeting, JCVI agreed that Shingrix® had been shown to be effective and cost-effective and should be considered in the current programme.
- 28. It was noted that, at their January 2019 meeting, the sub-committee had reviewed modelling on cost-effectiveness of Shingrix® by age, incremental on no vaccine programme, which had concluded that the optimal age for immunisation of immunocompetent individuals was 65 years (based on the age of routine vaccination with the highest net monetary benefit) and that Shingrix® would be cost-effective at any age from 50 to 90 years in the immunocompromised.
- 29. It was noted that implementation of a potentially large programme would be dependent on supply of vaccine and supplier capacity, and that certain groups would need to be prioritised; the first priority being those immunocompromised individuals who were eligible under the current programme.

- 30. A working group to consider the definition of 'immunocompromised' and also the implications of commencing a programme with Shingrix®, such as commissioning and procurement issues, was proposed.
- 31. Amongst the immunocompetent, it was proposed by the sub-committee that the routine programme should start at 65 years of age, but it was recognised that there may be more clinical benefit from starting at a lower age. The Committee noted that programmes initially requiring vaccination of a large number of cohorts, such as the existing zoster programme for those aged 70-79 years of age, were complicated to deliver. The Committee agreed that their recommendations should take this into account.

Impact and cost effectiveness modelling

- 32. The Committee noted modelling undertaken by PHE on the impact and cost-effectiveness of a routine zoster vaccination programme using Shingrix®, by age.
- 33. The Committee noted that the modelling was based on:
 - population and mortality from the Office of National Statistics data 2015;
 - EQ-5D population norms were taken from Szende et al. (2014);
 - incidence of community HZ and the proportion of HZ with PHN from Walker et al (unpublished)
 - HZ mortality, hospitalisation rate and costs and proportion of the population immunocompromised from Hobbelen et al. (2016);
 - GP costs per HZ case from Gauthier et al. (2009)
 - QALY loss from a systematic review and random effects model (PHE, unpublished);
 - vaccine coverage from the PHE programme report 2016/17;
 - vaccine efficacy from Shingrix® trial data, modelled for uncertainty, Morrison et al. (2015), Schmader et al. (2002), Cunningham et al. (2016);
 - the model assumed vaccine coverage of 48.3%
 - cost and benefits were discounted at 3.5%
 - vaccine efficacy was dependent on time since vaccination and age at vaccination;
 - the reactivation rate and waning were linear functions of age;
 - no HZ recurrence was included in the modelling; and
 - assumptions of vaccine efficacy in the immunocompromised was taken from a study of vaccine efficacy in recipients of autologous haemopoietic stem cell transplant recipients.
- 34. Results indicated that at the assumed price in the immunocompromised population, Shingrix® vaccination was likely to be more cost-effective than no vaccination for ages 50 to 90. For the immunocompetent population,

vaccination with Shingrix®, at the assumed price, was likely to be the most cost-effective strategy from age 56 to 71. The highest net monetary benefit from a routine programme was seen at age 65 years. Depending on the price per dose, vaccination with Shingrix® could be cost-effective at older ages.

Considerations

- 35. It was felt important that lessons were learnt from the implementation of the Zostavax® programme for those aged 70-79 years. The Committee agreed it would be important to have good quality messaging, that vaccination be offered year-round, and that call/recall be undertaken, particularly as the programme would offer 2 doses of vaccine.
- 36. In the light of the potential to offer immunisation to people under the age of 65 it would be important for them to have appropriate access.
- 37. The Committee noted a lack of published data on the concomitant administration of Shingrix® with the adjuvanted influenza vaccine. The Committee agreed that there was a need for data on concomitant administration of these two adjuvanted vaccines in the target population, and that this should be added to the list of research recommendations.
- 38. The Committee agreed that while modelling indicated that the maximum net monetary benefit was seen at age 65, it also indicated that a greater number of cases would be prevented with vaccination at age 60.
- 39. When the programme changed, it was considered important to ensure that those at greatest risk of disease were vaccinated earlier, and that implementation be undertaken in such a way as to ensure that all individuals in the age range specified would be offered vaccination.

Recommendations

- 40. The Committee recommended that the zoster vaccination programme be changed, with Shingrix® offered routinely at the age of 60 years. The Committee recommended that those aged between 60 and 70 years should also be offered Shingrix®. The Committee recommended a two-dose schedule.
- 41. The Committee advised that the programme should be implemented in stages, starting with vaccination at ages 65 and 70 years. This should continue until vaccine had been offered to all those aged 65 to 70 years of age. Once that group had been offered vaccination, the routine age for vaccination should then move to 60 years of age, with vaccination continuing at 65 years of age, until vaccine had been offered to all those aged 60 to 65 years of age. Vaccination should then be routinely offered at age 60.
- 42. The Committee agreed that those aged 86 or over who had not previously

been offered Zostavax® should also be considered for vaccination with Shingrix®. The Committee noted capacity within the system could be a constraint, and asked PHE to consider this further before implementation in this age group. The Chair proposed that the Committee not discuss further use of Shingrix® in the 70-86 age group (those who would have been offered/would be offered Zostavax® under the existing programme), as more modelling was required to consider the cost-effectiveness of revaccination in this group.

- 43. The Committee further recommended that Shingrix® should be offered to immunocompromised individuals aged 50 and over, and that a PHE working group be formed to consider the definition of immunocompromised for vaccination.
- 44. All the recommendations provided would be subject to procurement of Shingrix® at a cost-effective price.
- 45. It was noted the recommendation of JCVI regarding the vaccine, and age of routine vaccination, constituted a recommendation under the Health Protection (Vaccination) Regulations 2009.

Varicella modelling

- 46. It was noted that the JCVI subcommittee reviewed varicella control options in 2009. At the time the decision was not to proceed with a varicella programme because of the possible impact on zoster as a result of the removal of exogenous boosting.
- 47. It was noted that in 2012 Van Hoek *et al.* had published modelling on the impact on zoster incidence if only Zostavax® was introduced, as well as if children were immunised against varicella. Any programme that included varicella immunisation was predicted to result in an increase in zoster lasting for almost 50 years, but then the incidence would decrease to insignificant levels.
- 48. It was noted that the Van Hoek *et al.* paper (2012) suggested that 'infant vaccination was expected to increase the incidence of zoster in the medium term (up to 30-50 years after vaccination), and this was only partly offset by vaccination of the elderly, as the estimated duration of protection was rather short, and the largest increase in zoster incidence was expected to occur in adults too young to be vaccinated.'
- 49. It was also noted that Ogunjimi *et al.* in a 2013 paper based on observational data, concluded that 'exogenous boosting existed, although not for all persons, nor all situations. Its magnitude was yet to be determined adequately in any study field'.
- 50. It was noted that although the Van Hoek *et al.* model predicted an increase in zoster if varicella immunisation was introduced, the incidence of zoster had been increasing in the USA prior to the introduction of

- 51.JCVI suggested the use of a model in which demographic changes were included and preferred the progressive immunity model. Data on QALYs of children with varicella were needed to inform an estimate of varicella immunisation cost-effectiveness. Discussions were ongoing as to the correct model, and parameters to use, to recognise any exogenous boosting.
- 52. The proposed next steps were to re-run the economic model with new QALY data and discount rates, consider different assumptions on duration of exogenous boosting (20 years to 5 years) and evaluate whether the model reproduced the US trends. It should also take into account a programme from 60 years with Shingrix®.
- 53. It was noted that the subcommittee would like these matters addressed as soon as possible. PHE would coordinate and update the committee at the June 2019 meeting.
- 54. It was noted that it was the last JCVI meeting for Prof Judy Breuer, although she would continue to support the subcommittee. She was thanked for her valuable contribution to the work of JCVI.

VI. NITAG update from WHO

- 55. The Chair outlined that JCVI was one of the first National Immunisation Technical Advisory Groups (NITAGs) and has been sharing knowledge with other NITAGs on specific issues through the Secretariat, and by inviting representatives from the NITAGs of other counties to attend JCVI meetings.
- 56. WHO updated JCVI on work they were undertaking around supporting NITAGs and the Global NITAG Network (GNN).
- 57. WHO currently supported immunisation policy development at three levels: national NITAGs, regional Regional Technical Advisory Groups (RTAG) in all six regions, and global Strategic Advisory Group of Experts on Immunisation (SAGE) providing global recommendations.
- 58. SAGE was established in 1999 as the principal group providing advice to the WHO Director General around global policies and strategies ranging from vaccines and technology research to delivery of immunization and its linkages with other health interventions. It also had a broad view of the ages covered by its recommendations, which was traditionally children, but now encompassed the whole of life.
- 59. SAGE had 15 members, appointed through a public call for nominations and several working groups. A range of topics had been discussed in the last 7 to 8 years including: Vaccine specific issues, reports from various committees, programmatic challenges and the Global Vaccine Action Plan

(GVAP)

- 60. Regarding processes, SAGE uses the GRADE and DECIDE frameworks to draft recommendations. A Working Group prepared a "Yellow Book" of papers for discussion at each full session, which included evidence and grading. Each slot was around two hours for presentations, discussion and decisions.
- 61. The main outputs were the SAGE report following each session (April and October) and vaccine position papers (27 papers published since 1998).
- 62. Moving to NITAGs, WHO has supported them historically to promote ownership of vaccination decisions by each country. WHO encouraged countries to review and report the impact of vaccination programmes on their own populations. This was especially important as programmes had become more complex and more vaccines came to market each year, which impacted on national budgets.
- 63. In 2018 there were around 100 countries with a functional NITAG (meeting the WHO functionality criteria). There were another 34 countries which declared a NITAG but which did not meet the criteria. This compared favourably to 55 reported in 2010. NITAGs have been recognised as important at the highest levels of WHO and the WHO looked to JCVI as a model of how a NITAG should work.
- 64. WHO supported NITAGs in various ways. Globally this included: a NITAG resource centre providing information, training, and guidelines, and the Global NITAG network (GNN) which brought NITAGs together to discuss issues and allow peer-to-peer learning and collaboration. Regional and National work included networks, inviting NITAGs from developing countries to SAGE and RTAG meetings and strengthening training.
- 65. Regarding the NITAG Resource Centre, launched in 2015, it contained a lot of information in an online space to exchange minutes and technical reports and learning.
- 66. The GNN aimed to support NITAGs in producing evidence-informed recommendations by having a global platform for collaboration and cooperation. There was a successful meeting in Ottawa in December 2018 where working issues were identified for the 2019 work plan, including training packages.
- 67. JCVI queried how language barriers were overcome. It was noted that WHO had produced training materials and evaluation tools in English, French, Russian and Spanish. Additionally, regions could prepare local translations and the WHO was reviewing which were the main documents to be translated universally.

VII. Influenza

Mid-season effectiveness

- 68. PHE provided an update on the latest influenza epidemiology and surveillance data from the current season 2018/19.
- 69. So far, the season had been dominated by A(H1N1)pdm09 influenza virus. Primary care influenza indicators showed that activity had been quiet and there had been far fewer outbreaks compared with last season. Impact on secondary care had, however, been high and similar to last season with the burden mainly in young and middle-aged adults. No significant excess all-cause mortality had been observed overall or by age group.
- 70. Genetic typing results of circulating A(H1N1)pdm09 viruses indicated that there has been little change compared with last season viruses and that they were antigenically similar to the current vaccine strain. Genetic characterisation of the A(H3N2) viruses indicated that they belonged to subclade 3C.2a, and within this some belonged to subclade 3C.2a1, which was the same subclade the vaccine strain belonged to.
- 71. Vaccine uptake in the elderly was slowed by the phased delivery of the adjuvanted trivalent vaccine, such that rates were much lower for the first few months of the programme compared with last year. However, by week 51 uptake levels were similar to those achieved the previous year. Uptake levels in risk groups aged under 65 years old were similar, and in young children uptake levels improved, compared with the previous year. The Committee noted that by 2019/20 the childhood programme in England would have rolled out to include all children in primary schools.
- 72. Mid-season vaccine effectiveness (VE) for influenza A and B was estimated to be 43.7% (95%CI 3.9-67.1), and 56.9% (95%CI 19.5-77) for A(H1N1)pdm09, after adjustment. VE estimates for A(H3N2) were non-significant owing to the small numbers of cases. VE estimates in the elderly were 56.9% and 82.6% for flu A and B, and A(H1N1)pdm09 respectively but statistically non-significant owing to the small numbers of cases and controls. In children VE for the live attenuated vaccine was 86.9% (95%CI 3.6-100) for A(H1N1)pdm09. The UK VE mid-season results were also broadly in agreement with results published by Canada.

Timing of programme delivery

- 73. The Committee noted a report by PHE on whether the timing of the delivery of vaccination should be delayed in order to optimise immunity levels with the timing of peak influenza activity. The report highlighted that:
 - there was accumulating evidence that waning influenza vaccine related immunity may contribute to reducing vaccine effectiveness (VE) in some seasons – particularly those dominated by A(H3N2) and in the elderly;

- this picture was complicated by a range of factors potentially associated with a reduction in VE, including the emergence of drift variants less well matched to the season's vaccine virus, immunosenescence and repeat vaccination;
- based on the uptake in the national programme, optimal population protection in terms of reaching maximum coverage levels two weeks after vaccination, was usually achieved from mid-December onwards:
- the timing of the start of circulation of influenza varied each year, with activity often starting to increase from early/mid-December onwards; and
- mathematical modelling work (Hodgson et al) had predicted that more rapid vaccination of school age children provided better indirect population protection in terms of reduction of infection.
- 74. PHE concluded that delaying influenza vaccination posed significant risks of infection before immunization, and that decreasing the period of vaccination would pose huge logistical challenges to a programme that currently delivered 14 million vaccinations during the flu season. PHE advised that the current timing of the programme was not changed and that the focus should be improving uptake in eligible groups particularly children.
- 75. It was noted that the Committee had already sought to address some of the issues concerning poor effectiveness against the AH3N2 virus, including immunosenescence and egg adaption, with recent advice on newly available vaccines. Given the potential operational difficulties with delivering a huge programme in the existing time-period and the variability of when influenza began to circulate, the Committee did not consider that the current evidence was sufficient to recommend any changes to the timing of delivery of the programme.

Sniffle 4

- 76. The Committee received a presentation on the Safety of Nasal InFLuenza Immunisation in children with asthma "the SNIFFLE-4 study". The Committee were reminded that previous SNIFFLE research on egg allergy and influenza vaccination had shown use of LAIV to be safe for use in most egg allergic children.
- 77. Sniffle 2 and 3 cohorts had also been investigated as to whether LAIV exacerbated asthma, showing that it was safe in the majority of asthmatic children with mild to moderate asthma, however severe asthma had not been investigated as study numbers were insufficient. SNIFFLE 4 aimed to address the safety of LAIV in children with recurrent wheezing asthma and severe asthma and on high dose inhaled corticosteroid steroids (ICS).
- 78. The Committee noted that CDC guidelines recommended against using

LAIV in children less than five years old with asthma or an episode of wheezing in the last year, however the UK guidelines allowed the use of LAIV in children with mild to moderate asthma but not those with severe or uncontrolled asthma or with active wheezing.

- 79. The Committee noted that it was likely the Green Book advice was not being followed as the SNIFFLE study had trouble recruiting children with severe asthma who had not already been given LAIV, however, the study was considered adequately powered.
- 80. In conclusion the results of SNIFFLE 4 showed LAIV to be safe in children receiving high dose ICS. The Committee agreed that the Green Book guidance should be updated to reflect that LAIV can safely be given in those on high dose ICS. The Committee noted that the advice concerning active wheezing in the previous 72 hours remained the same. The Committee also agreed that it would be important to check with the MHRA that no new safety signals had been observed with regards to LAIV and severe asthma.

VIII. MHRA annual update

81. The Committee noted the written update from the MHRA. As no representative from the MHRA could attend the meeting, it was agreed that the report be brought to the next meeting for consideration.

IX. Coverage

- 82. JCVI noted brief updates on vaccine coverage from England, Wales, Scotland and Northern Ireland.
- 83. It was noted that in England and Scotland there had been a small decline in childhood coverage this quarter for those under 5 years of age. However, coverage for the non-childhood programmes for MenACWY, HPV, prenatal pertussis and shingles had increased. Scotland, Wales and Northern Ireland noted similar positions to England.
- 84. The Chair recommended that a more detailed discussion on Coverage should be included in the June meeting looking at why some vaccination rates were falling. PHE were also asked to share information with the committee on the monitoring of attitudes towards vaccination.

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.

Dr Fiona Van der Klis

Dr Fiona van der Klis has no registered conflicts of interest

Ms Alison Lawrence

Ms Alison Lawrence has no registered conflicts of interest

Prof Maarten Postma

Professor Postma has received honoraria from SPMSD (health economics) MSD (health economics) and is an advisor to companies on Rotateq and Rotarix vaccines.

Professor Postma works for the University of Groningen which receives grants from SPMSD and GSK for work related to influenza vaccines.

Professor Postma attends advisory boards unrelated to vaccines or vaccine industry

Professor Postma organized a conference which was financially supported by Pfizer relating to Health Economics.

Prof Robert Read

Professor Read receives no payments from the manufacturers of vaccines.

The University of Southampton receives CASE studentship awards from Novartis and GSK.

Prof Anthony Scott

Professor Scott receives no payments from the manufacturers of vaccines.

Professor Scott is Director of the Health Protection Research Unit at the London School of Hygiene and Tropical Medicine. He receives research funding from the National Institute for Health Research, the Medical Research Council, the Wellcome Trust and Gavi, The Vaccine Alliance, and the Bill & Melinda Gates Foundation.

Dr Maggie Wearmouth

Dr Wearmouth has no registered conflicts of interest

Professor Simon Kroll

Professor Kroll received research funding from Meningitis Now, to investigate carriage of meningococci and non-pathogenic Neisseria in infants. The funding period ended in 2018.

He is the Honorary Medical Director of Meningitis Now

Dr Jillian Johnston (co-opted member)

Dr Jillian Johnston has no registered conflicts of interest

Mrs Anne McGowan (co-opted member)

Mrs McGowan receives no payments from the manufacturers of vaccines

Mrs McGowan's employer Public Health Wales develop educational materials with funding from Pfizer, Sanofi Pasteur MSD, Novartis, Astra Zeneca and Wyeth.

Dr Lorna Willocks (co-opted member)

Dr Lorna Willocks has no registered conflicts of interest

Ms Julie Yates (co-opted member)

Ms Julie Yates has no registered conflicts of interest