Summary of recent issues considered by four national immunisation technical advisory groups (NITAGs) and WHO immunisation-related advisory committees

Prepared by the National Centre for Immunisation Research & Surveillance (NCIRS)

Period of review: 12/10/2017 to 22/01/2017

Contents

Note: Yellow highlights indicate key points for noting that are relevant to ongoing/imminent ATAGI considerations

1 Advisory Committee on Immunization Practices (ACIP), U.S.A.

1.1 ACIP meeting: 21-22 June 2017

- Agenda, presentation slides and video recordings of this meeting, and minutes of June 2017: http://www.cdc.gov/vaccines/acip/meetings/meetings-info.html
- **Full minutes for the June 2017 meeting are pending; therefore this summary has been developed from the presentation slides and video recordings.**

Herpes Zoster Vaccines

- Summary of GRADE of herpes zoster vaccines (HZ/su and ZVL)
  - Details presented in past presentations to ACIP
  - Conclusion: the evidence type for critical outcomes (prevent HZ and PHN; no safety concerns regarding SAEs) is 1
- CDC's economic evaluation of vaccination for prevention of HZ and related complications
  - Societal perspective taken; sponsor models (Merck and GSK, presented at previous meetings) used a healthcare perspective
  - Assumes 100% 2 dose completion in base case
  - ICERs in base case analysis HZ/su vs no vaccination $/QALY – 50–59y: $46,824; 60–69y: $25,683, 70–79y: $11,561, 80–89y: $9,739, 90–99y: $27,310; ≥50y: $30,797
  - ICERs among 60–69y compared with no vaccination: HZ/su: $26,000; ZVL: $55,000
  - Models sensitive to duration of VE, incidence of disease outcomes (HZ and PHN), and cost of HZ/PHN episode
- Policy questions and considerations:
  - Should HZ/su be recommended for vaccination of immunocompetent adults ≥50 years?
    - Working Group (WG) favours this policy; ACIP voted in favour (1 negative vote)
  - Should HZ/su be recommended for individuals previously vaccinated with ZVL?
    - ICER of revaccination post ZVL with HZ/su ranges from $15,000 /QALY (80-89 yrs) to $117,000 /QALY (50-59yrs)
    - Interval not specified in recommendation; guidance will be provided; data will be collected
    - WG favours revaccination; ACIP voted in favour (3 negative votes)
    - Concerns raised include lack of interval specified in recommendation (can be interpreted as a preferential recommendation) and insufficient evidence regarding subsequent vaccination
  - Should preferential recommendation for HZ/su over ZVL be made?
    - Pros: VE is significantly higher with HZ/su than ZVL across all age groups, wanes at a slower rate over first 4 years, expected cases of HZ/PHN averted are greater, more cost-effective
    - Cons: HZ/su is more reactogenic than ZVL; unexpected safety problems may arise; uncertainty regarding effectiveness/duration of protection (recommendation would need to be reversed if effectiveness/duration of protection is less than expected; HZ/su requires 2 doses
    - WG favours favour a preferential recommendation; ACIP voted in favour (8 in favour, 7 against)
    - Concerns include uncertainty around use of an adjuvant that has not been used previously, longer term safety concerns, supply issues, potential to wait for a year before making a recommendation (in order to compare population-level data on effectiveness of both vaccines in the absence of head-to-head trials, and absence of data in ethnic minorities)

Hepatitis Vaccines

- HEPLISAV-B (Manufacturer: Dynavax)
  - Yeast-derived recombinant hepatitis B surface antigen (20mg) conjugated to Toll-like receptor 9 (TLR9) agonist 1018 (3mg) [current HepB vaccines use aluminium conjugate]

- Administered in 2 doses over 1 month [current vaccines given as 3 doses over 6 months]
- Proposed indication: active immunisation against infection caused by all known subtypes of hepatitis B virus in adults ≥18 years of age
- Non-inferior in comparative studies with Engerix-B, with significantly higher seroprotection rates at early time points, at peak, and in all adult age groups
- Safety profile similar to Engerix-B (frequency of any post injection reactions 55.1% vs 57.1%); slightly higher frequency of acute myocardial infarction found (0.17% vs 0.05%) – however further evaluation of this found these events occurred at expected rates in patients with cardiovascular risk, no temporal association with vaccination, and no biologically plausible explanation for the imbalance
- Proposed policy recommendation: HEPLISAV-B may be used for adults ≥18 years in a 2-dose schedule over 1 month

- Hepatitis A Virus (HAV) outbreaks
  - CDC assisted with 5 HAV outbreaks since 1 July 2016 (2 foodborne transmission, 3 person-to-person transmission); >1,600 associated cases with multiple ongoing outbreaks
  - California: 600 cases, 395 hospitalisations, 19 deaths. Majority in San Diego. Concentrated in homeless and infection/non-injection drug users. 64 (20%) and 17 (5%) co-infected with chronic hepatitis C (HCV) and chronic hepatitis B (HBV) infections, respectively.
  - Utah: 45 cases in persons aged 23–69 years (median 40y). 27 (60%) hospitalised. 22 (48.8%) homeless with drug use, additional 9 with drug use and 3 homeless. Co-infection with HBV in 7 (15.6%), HCV in 15 (33.3%) and both HBV/HCV in 6 (13.3%).
  - Michigan: 431 cases, 348 (85.7%) hospitalised, 17 (4.2%) deaths. Greater risk associated with drug use and homelessness.
  - New York: 51 cases in MSM; genotype 1A
  - Recent outbreaks (except NY) have been genotype 1B, whereas previously 1A commonly circulated
  - Outbreaks have led to strained supply of HAV vaccines in USA, manufacturers working to increase supply
  - WG considering whether homelessness should be included as a risk group for HAV vaccination in either a routine or an outbreak setting
- Supply issues: Merck not distributing adult or paediatric formulations of HBV vaccine through the end of 2018; GSK has sufficient supply during this period

Mumps

- Update on mumps epidemiology
  - 4677 cases in 2017 (as of October); highest incidence in 18–22y (median: 21y; IQR: 15–31y); 75% ≥2 MMR doses
  - Of 150 outbreaks, 75 in universities, 48 in community setting (close knit communities or other organised groups e.g. church, workplace), 19 in no-university schools, 8 in households
  - MMR3 used in 35 outbreaks: 24 universities, 9 community and 2 schools
  - Of 9,200 cases, 13.3% had 0 MMR doses, 6.5% had 1 dose, 54.5% had 2 doses, 3.8% had 3 doses, 21.9% were unknown
  - Frequency of mumps complications was substantially lower in these outbreaks than historical pre-vaccine era
- Policy consideration of administration of third dose of MMR to persons at increased risk in outbreaks
  - Low level of evidence (type 4) indicating MMR3 prevents mumps; no evidence supporting MMR3 prevents complications; low level of evidence (type 4) supporting MMR3 boosts antibodies in the short-term and seroconverts most seronegative persons

- Lower attack rates observed in those who received 3 MMR doses compared with 2 doses; VE of MMR3 ranged from 61% to 88% (1 estimate significant – 78%)
- WG interpretation: the benefits of MMR3 outweigh the risk, data demonstrates short-term benefit of MMR3 for persons in outbreak settings
- ACIP voted in favour to recommend **a third dose of MMR to at risk persons in outbreak settings** (published in MMWR, see section 1.2.2)

Vaccine safety: Shoulder injury after vaccination

- Shoulder Injury Related to Vaccine Administration (SIRVA) is thought to result from the unintentional injection of a vaccine into tissues and structures lying underneath the deltoid muscle of the shoulder; evidence of a causal relationship between vaccine administration and deltoid bursitis
- VAERS data on shoulder dysfunction following inactivated influenza vaccine (IIV) examined:
  - 1,006 possible cases identified between July 2010 and June 2016, 93% non-serious, 70% in adults 19–59y, <1% in ≤18y; 229 (23%) interfered with ADLs and/or resulted in absenteeism
  - Contributing factors (of 222 cases): vaccination given too high on arm (177), improper/poor administration technique (35), uneven position between vaccinator and patient (5), other (22)
  - Notable places of vaccination (n=1,006): doctor's office/hospital (319, 32%), pharmacy/store (399, 40%), workplace (121, 12%), health department (50, 5%)

HPV vaccines

- Policy issues regarding HPV vaccines:
  - Wording for target age group changed: currently "vaccination at age 11 or 12 years"; proposed alternative wording "vaccination at age 9 through 12 years"
  - Harmonisation of upper age for male and female vaccination: currently vaccination recommended for females through age 26y and males through age 21y; proposed to change upper age limit for males to 26y for simplification
- Estimates HPV vaccination coverage in adolescents 13–17y in 2016:
  - ≥1 dose: 60.4%, ≥2 doses: 49.2%, ≥3 doses: 37.1%; HPV UTD (up to date as per current recommendation – new measure added): 43.4%
  - Gap in coverage between males and females has reduced over time – currently 9.1% gap in 1 dose coverage
- HPV vaccine impact: decline in 4vHPV type prevalence in females – 71% in 14–19y, 61% in 20–24y

Japanese Encephalitis (JE) vaccines

- Epidemiology JE in US travellers: between 1993–2017, 12 cases in travellers, 56 travel-associated cases
  - Consideration of updating recommendation for travellers travelling <1 month at a future meeting
- Safety of IXIARO (JE-VC)
  - Post-marketing surveillance in US military personnel: among 21,347 recipients of 36,358 doses of JE-VC, no statistically increased rates of AEs compared with recipients of JE-VAX (n=19,441)
  - Data from VAERS from May 2012–April 2016: 119 AEs, 9 serious (8%), 110 non-serious (92%); incidence of AEs 14.8 per 100,000 doses distributed
    - Most occurred when administered concurrently: 8/9 of serious AEs, 80/119 of all AEs
    - Overall, AE rates have not increased since previous analysis; supports good safety profile

Pneumococcal vaccines

- Paediatric nasopharyngeal pneumococcal carriage
  - 4765 children enrolled – 30.4% colonised with *S. pneumoniae*, similar to pre-PCV13 rates
  - Significant reductions compared with pre-PCV13 era in carriage of serotype 19A and 6C (to a lesser extent)

- Low level carriage of 19F, 3, 19A and 6C carriage persists
- No single non-vaccine serotype (NVT) has emerged as a dominant carriage serotype
- IPD generally mirrors carriage with some exceptions

- Preliminary findings of adult (≥65y) pneumococcal colonisation study
  - 3008 enrolled (2984 included), mean age 75.5y, higher proportion of African Americans compared with general population (23.8% vs 8.9%); 47.9% vaccinated with PCV13, 58.2% vaccinated with PPSV
  - Carriage prevalence: 1.8%; vaccine-type carriage prevalence: 0.2% (PCV13 types were 13% of pneumococcus detected). Prevalence similar in vaccinated and non-vaccinated.
- Epidemiology of IPD in USA 2008–2016
  - Significant reductions in overall and PCV13 serotype IPD among children and adults since PCV13 introduction, driven by reductions in types 19A and 7F. Reductions in pneumococcal meningitis incidence:
    - <5y – PCV13 types: –81.9%; non-PCV13 types: 27.1% (NS); all IPD: –34% (NS)
    - ≥65y – PCV13+6C: –76.1%; PPSV11: –5.3 (NS); NVT: –32.4% (NS); all IPD: –43.6%
  - Rates have plateaued in 2014–2016
  - No further reductions in PCV13 serotype IPD in adults ≥65 years since 2014 adult PCV13 recommendations
  - Despite reductions, IPD rates including PCV13 serotypes, remained high in adults with HIV compared to those without HIV
  - No large increases in any non-PCV13 serotype among children or adults, including those living with HIV
- Key policy considerations for 2018:
  - Is PCV13 use among adults ≥65 years old preventing disease?
  - To what extent are the observed benefits driven by adults PCV13 use (direct effects) vs. paediatric PCV13 use (indirect effects)?
  - What benefits would we expect from continued PCV13 use among adults?

Anthrax vaccines

- Review of safety data on Anthrax Vaccine Adsorbed (AVA) from studies and VAERS revealed no unexpected patterns or unusual AEs
- FDA priming schedule was simplified from 5 intramuscular (IM) doses over 18 months to 3 IM doses over 6 months
- Implementation concerns in the event of mass vaccination include: lack of sufficient 5/8" needles to administer AVA subcutaneously (SC); potential errors due to having two vaccines for post-exposure prophylaxis with different routes of administration; AEs higher via SC route administration and IM more efficient, however antibody titres are significantly higher at 4 weeks for SC vs IM

1.2 Newly published or updated recommendations

1.2.1 Prevention of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices

- Published MMWR 12 January 2018 – https://www.cdc.gov/mmwr/volumes/67/rr/rr6701a1.htm
- The following recommendations are new or updated:
  - universal HBV vaccination within 24 hours of birth for medically stable infants weighing ≥2,000 grams
  - testing HBsAg-positive pregnant women for hepatitis B virus deoxyribonucleic acid (HBV DNA);

- postvaccination serologic testing for infants whose mother's HBsAg status remains unknown indefinitely (e.g., when a parent or person with lawful custody surrenders an infant confidentially shortly after birth);
- single-dose revaccination for infants born to HBsAg-positive women not responding to the initial vaccine series;
- vaccination for persons with chronic liver disease (including, but not limited to, those with HCV infection, cirrhosis, fatty liver disease, alcoholic liver disease, autoimmune hepatitis, and an alanine aminotransferase [ALT] or aspartate aminotransferase [AST] level greater than twice the upper limit of normal); and
- removal of permissive language for delaying the birth dose until after hospital discharge.

1.2.2 Recommendations of the Advisory Committee on Immunization Practices for Use of a Third Dose of Mumps Virus-Containing Vaccine in Persons at Increased Risk for Mumps During an Outbreak

- Published MMWR 12 January 2018 - https://www.cdc.gov/mmwr/volumes/67/wr/mm6701a7.htm
- New recommendation: Persons previously vaccinated with 2 doses of a mumps virus–containing vaccine who are identified by public health authorities as being part of a group or population at increased risk for acquiring mumps because of an outbreak should receive a third dose of a mumps virus–containing vaccine to improve protection against mumps disease and related complications.
- Rationale for recommendation:
  - current routine recommendation for 2 doses of MMR vaccine appears to be sufficient for mumps control in the general population, but insufficient for preventing mumps outbreaks in prolonged, close-contact settings
  - Waning of vaccine-induced immunity with time after receipt of the second vaccine dose in high intensity exposure settings typical of outbreaks
  - A third dose of MMR vaccine has at least a short-term benefit for persons in outbreak setting
- No additional dose is recommended for persons in outbreak settings who have already received ≥3 doses of a mumps virus–containing vaccine (due to absence of evidence on the benefit of additional doses)

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2 Immunisation Advisory Centre (IMAC), New Zealand

2.1 PTAC Considerations

- Meeting held on 10th & 11th August 2017 – https://www.pharmac.govt.nz/assets/ptac-minutes-2017-9.pdf
- No vaccine-specific considerations; however the following was noted in relation to the nephrology subcommittee's considerations on immunisations in patients with renal disease:
  - Widening access to HBV, pneumococcal and zoster vaccines referred to Immunisation Sub-committee, for consideration at November 2017 PTAC meeting
  - The use of HPV vaccine in patients with CKD 5 or on dialysis is required, as well as use of HPV vaccine in patients pre/post transplantation who are over 26 years old
- A meeting was held on 9th & 10th November 2017 – no minutes available yet, agenda not published

2.2 Other updates

- Antigen literature review for the NZ National Immunisation Schedule, 2017: Rotavirus
  - Published by IMAC August 2017, part of a series of antigen literature reviews commissioned by the Ministry of Health – http://www.immune.org.nz/sites/default/files/publications/AgRev2017_Rotavirus_final.pdf

- Main objective is to provide information around the use of vaccines and to help inform decisions relevant to immunisation programs in NZ. This review summarises selected literature published from January 2013 to August 2017 around the use of rotavirus vaccines in high income countries

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3 Joint Committee on Vaccination and Immunisation (JCVI), UK Department of Health

3.1 JCVI meeting: 4th October 2017

Agenda / draft minutes:

https://www.gov.uk/government/groups/joint-committee-on-vaccination-and-immunisation#minutes

This summary was based on the draft minutes only

Pneumococcal vaccination

- Updated on epidemiology of IPD:
  - Overall 37% reduction in IPD incidence since introduction of PCV7; further 7% reduction since introduction of PCV13
  - PCV13 serotypes account for 19% of IPD cases overall, mostly in adults aged >15 years (96%); these were mostly serotypes 3 (49%) and 19A (29%)
  - PCV13 type IPD rare in children; 10% of cases are <2 years; serotypes 3 and 19A responsible for almost all these cases
  - CFR has reduced from pre-PCV era
- Immunogenicity of PCV13 in a 1+1 schedule in UK infants
  - immunogenicity of a 1+1 schedule was equivalent to, or superior to, a 2+1 schedule for 9 of the 13 serotypes in PCV13
  - almost all infants in both the 1+1 and 2+1 schedules had IgG above the protective titre of 0.35µl/ml, for all serotypes except serotype 3, for which fewer vaccinated infants reached protective thresholds in both schedules
  - geometric mean concentrations (GMCs) following the primary series were higher in the 2+1 schedule; both GMCs and proportion of infants protected against serotype 19A were similar between the two schedules
- Findings of the Pneumococcal Carriage Study undertaken in 2015/16:
  - between 2012/13 and 2015/16 there had been an overall significant increase in the non-vaccine type case:carrier ratio from 10.9 to 16.8 cases/100,000 carriers
  - carriage of serotype 6C had significantly reduced between 2012/13 and 2015/16, consistent with cross protection from the 6A component of PCV13
  - although overall carriage prevalence was similar between surveys, there had also been a small overall rise in carriage of non-PCV13 serotypes (consistent with an increased force of infection)
  - low levels of serotypes 3 and 19A remained in circulation in the population
- Modelling of the impact of changing to a PCV13 1+1 schedule (compared with current 2+1 schedule)
  - despite more aggressive serotype replacement than initially predicted, if the increased force of infection and case-carrier ratio persisted, then there would still be a long-term reduction in overall IPD cases compared with the pre-PCV7 era; the model also predicted that the increase in non-vaccine types would plateau in about 2 years
  - moving to a 1+1 schedule might increase IPD cases in infants because of loss of direct protection and in older adults because of a reduction in herd immunity as a result of less protection against

carriage in infants after a single dose; any excess cases in infants or the older age groups would be very small

- JCVI agreed that given the success of the PCV13 program in producing large and sustained decreases in PCV13 serotype disease, a move to a 1+1 schedule was appropriate for the UK population. The revised schedule will have doses at 3 and 12 months of age.

HPV vaccination for adolescent boys

- The PHE model on cost-effectiveness of HPV vaccination in boys was reviewed: cost-effectiveness was improved in this model but still not cost-effective at the current list price. It was noted that the price paid in the UK program may be lower; however such a program would only be cost-effective at a price at or around zero.
- The model indicated that the main benefit of boys' vaccination was due to additional herd protection provided to girls (approximately half). Of the remaining additional benefit i.e. that in males, just under half was accounted for by the prevention of disease in MSM.
- Changes to the model were suggested, and it was agreed that the modelling work required final checks, peer review and additional scenarios and sensitivity analyses explored. Other issues relating to consideration of this policy were also outstanding (including equality analysis and rules regarding economic analysis). JCVI deferred finalising its recommendation on boys' vaccination.

Influenza

- JCVI noted reports of an intense A/H3N2 influenza season in the southern hemisphere, and that the A/H3N2 subclade C3.21a circulating was the same as that which circulated in the UK the previous winter.
- JCVI noted that the WHO had recently met to determine the vaccine composition for the next season; A/H3N2 component had been changed, though the new vaccine strain had a very similar antigenic profile to the previous strain.
- At the time of the meeting, the influenza activity in the UK was low and there was good matching between the vaccine and circulating strains.
- Review of the 2016/17 season:
  - Vaccine uptake was high in ≥65 year olds (70.5%)
  - Reduced VE observed in the elderly
  - VE against A/H3N2 significant in 18–64y but non-significant in ≥65y
- Excess all-cause mortality estimates over the previous six seasons were higher in both the 65-74y age group and ≥75 years age groups during A/H3N2 seasons compared to A/H1N1pdm09 seasons. Influenza attributable mortality rate was higher in the ≥75y age group (~7 times greater 65–74y olds).
- Pooled analysis of data since 2005/06 showed significant VE in the 65–74y age group for all influenza, A/H1N1pdm09 and B and evidence of protection against A/H3N2. In ≥75y, pooled estimates of VE across all seasons were non-significant against all influenza virus types.
- An adjuvanted inactivated influenza vaccine (aTIV) has been licensed in the UK for use in the elderly and available for the 2018/19 season. Cost-effectiveness analysis undertaken by PHE and the manufacturer both indicated a program with this vaccine for people aged ≥65y would be cost-effective at the list price of the vaccine. Additional analysis showed it was cost-effective in both the 65–74y and ≥75y age groups.
- JCVI agreed that if a change in approach were to be considered, switching vaccination of the ≥75y age group to aTIV would be the first priority, given poor VE observed with regular TIV.
- A high dose vaccine is unlikely to be licensed in the UK for the foreseeable future.

Varicella

- Sub-committee had begun considerations on a new, non-live HZ vaccine.
- Updated modelling and factors relevant to programmatic use of this vaccine to be considered in 2018.

3.2 Newly published or updated statement/recommendations

There have been no newly published or updated statements or recommendations since the previous update.

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4 National Advisory Committee on Immunization (NACI), Canada

A meeting was conducted on 27–28 September 2017 in Ottawa, Ontario; however, the summary of discussions has not been released. The latest available summary was for their October 2016 meeting, which is available at https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/immunization/national-advisory-committee-on-immunization-naci.html.

4.1 Newly published or updated statement/recommendations

There have been no newly published or updated statements or recommendations since the previous update.

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5 Immunisation updates from the World Health Organization (WHO)

5.1 Strategic Advisory Group of Experts (SAGE) on Immunization, WHO

- Agenda, meeting background documents and presentations:
  http://www.who.int/immunization/sage/meetings/2017/october/en/
  Summary report:
  http://www.who.int/immunization/policy/sage/SAGE_oct_2017_meeting_summary.pdf?ua=1
  Full report: http://apps.who.int/iris/bitstream/10665/259533/1/WER9248.pdf?ua=1
- Polio eradication
  - As of 17 October 2017, there had been 6 cases due to wild-type poliovirus (WPV) during the previous 6 months, compared with 13 cases during the comparable period in 2013.
  - Six post-switch circulating vaccine derived polio virus type 2 (cVDPV2) outbreaks occurred in 4 countries. SAGE reiterated its previous recommendation prioritising stopping cVDPV2 outbreaks over WPV elimination.
  - The IPV supply situation is expected to improve in 2018; all countries are expected to have access to IPV for their routine immunisation programs from the end of Q1 2018.
  - SAGE recommended that countries with delayed introduction of IPV or had a vaccine stock-out should provide one full dose or 2 fractional IPV dose (fIPV) to all children who were missed as soon as supply becomes available.
- Typhoid vaccine
  - SAGE recommended introduction of typhoid conjugate vaccine (TCV) for infants and children over 6 months of age as a single dose in typhoid endemic countries, with catch-up wherever feasible and prioritising the youngest age group (up to 15 years of age). Data will be needed on co-administration of TCV with other routine childhood vaccines.
- Pneumococcal conjugate vaccine (PCV)

- Scheduling: SAGE recommended administration of PCV in a either 2+1 (4 weeks minimum and 8 weeks maximum interval between doses in primary series, booster at 9–18 months after) or 3+0 schedule starting as early as 6 weeks of age.
- Product choice: PCV13 may have additional benefit where disease attributable to 19A or 6C is significant.
- Catch up vaccination: Modelled data indicate that catch-up in those <5y will accelerate PCV impact on disease burden regardless of transmission intensity. However, the efficiency of catch-up (cases prevented per dose delivered) varies by age strata and transmission intensity
- Surveillance and research priorities to guide future policy revisions include:
  - Sentinel and population-based surveillance for pneumococcal disease and carriage, ideally indefinitely but no shorter than 5 years following full PCV introduction
  - Establishment of serotype-specific immune correlates of protection
  - Assessment of duration of protection
  - Further assessment of dosing schedules and outbreak epidemiology, especially epidemics of serotype 1 disease
  - PCV impact on antimicrobial resistance and on antibiotic use
  - A systematic analysis of 1 vs 2 dose catch up schedules

- Rabies vaccine
  - Current WHO recommendations for pre-exposure prophylaxis (PrEP, using vaccine only) and post-exposure prophylaxis (PEP, using vaccine or together with rabies immunoglobulin [RIG]) have proven difficult to implement, due to high cost, low demand, uncertain supply, variable quality and short-shelf-life of RIG.
  - Accelerated PrEP regimens: either a 2-site (0.1 mL per site) ID regimen, or a 1-site (1 vial per site) IM regimen on day 0 and 7.
  - PEP regimens: (i) 2-site (0.1 mL per site) ID on day 0, 3, and 7; (ii) 1-site (1 vial per site) IM regimen on day 0, 3, and 7; (iii) 2 sites IM on day 0 and 1 and 1 site IM on day 7 and 21.
  - Immunocompromised individuals need different regimens of PrEP/PEP, however it is not contraindicated.
  - PrEP is indicated for: 1) individuals exposed to rabies by occupation, place of residence or travel; 2) a subpopulation when bite incidence is high and local epidemiology makes it a cost-effective intervention.
- BCG vaccine
  - Current recommendation of universal birth dose in high incidence tuberculosis (TB) settings reaffirmed; expanded to include high burden leprosy settings regardless of TB incidence.
  - Countries with a low incidence of TB and leprosy may choose to selectively vaccinate neonates in groups at high risk.
- Measles and rubella elimination
  - SAGE recommended that countries should strengthen their routine program to achieve and maintain 95% vaccination coverage for MCV1 and MCV2, and identify immunity gaps.
  - Immunity gaps in school-age children are important because of high contact rates after school entry. Countries should put in place school entry checks for vaccination.
  - Given the paucity of evidence, SAGE concluded that there is insufficient evidence to recommend MCV for infants aged less than 6 months.
  - SAGE concluded that the available evidence does not support additional dose of measles vaccine HIV-infected individuals following HAART.
  - Research gaps: transmission drivers, blunting and maternal immunity in infants aged < 6 months, the impact of vaccination < 6 months of age on subsequent MCV doses, head-to-head comparison of measles vaccine strains.

5.1.1 WHO position papers

There have been no new WHO position papers published since the previous update.

5.2 Meeting of the Global Advisory Committee on Vaccine Safety (GACVS)

- 6–7 December 2017, Geneva, Switzerland. Full meeting report available at: http://apps.who.int/iris/bitstream/10665/259874/1/WER9303.pdf
- The pilot implementation plans for the RTS,S malaria vaccines in Kenya, Malawi and Ghana have continued to develop since the GACVS meeting in June 2017. Pilot introduction is anticipated to start in mid- to late-2018.
- A systematic review was conducted to update a 2012 Cochrane review regarding efficacy and safety of rotavirus (RV) vaccines. Available evidence from RCTs showed that there was no difference in incidence of serious adverse events in the use of RV1, RV5, Rotasiil®, or Rotavac® compared with placebo, up to 2 years after vaccination. There was conflicting evidence from different sources as to whether RV1 or RV5 was associated with an increased risk of intussusception. Full report available at: http://www.cochrane.org/CD008521/INFECTN_vaccines-for-preventing-rotavirus-diarrhoea-vaccines-in-use
- GAVCS reviewed experiences with Dengvaxia in Asian and Latin American countries in detail. The vaccine is safe and efficacious in individuals who have had a primary infection with wild dengue preceding immunization, thus preventing a “second” and therefore more severe episode of dengue. The new data indicate that the increased risk of hospitalization (and severe disease) from dengue affects vaccinated subjects who are naïve to wild dengue infection prior to vaccination. Notable is that the clinical data presented by Sanofi Pasteur also showed that, even among seronegative population, the number that would experience untoward severe dengue is likely to be <1%, and that with proper clinical care, more serious consequences can be prevented in most instances. GACVS recommends that Dengvaxia should not be administered to individuals who have not been previously infected with wild dengue virus. Data by number of doses received by seronegative subjects is currently unavailable.
- Tools to assist healthcare personnel in the assessment of causality of an AE and use of a vaccine have been developed; the methodology and interrater reliability was presented to GAVCS.
- A draft manual for program managers to prevent, identify and response to stress related events associated with immunisation was presented. A new term “Immunisation Triggered Stress Response” was proposed to incorporate all events that manifest just prior to, during or after immunisation. The manual is to be circulated to stakeholders for consultation. Training materials are to be developed.
- As part of developing a roadmap for improving maternal, neonatal and child health programmes and assessments of vaccine safety in pregnancy, a WHO interdepartmental task force will be established to address harmonization of coding and data systems. The task force will establish a common platform to assess pregnancy related outcomes for any intervention delivered to women during pregnancy.

5.3 Meeting of the Immunization and Vaccine-related Implementation Research Advisory Committee (IVIR-AC)

- 20–22 September 2017. Summary and conclusions available at: http://apps.who.int/iris/bitstream/10665/259800/1/WER9301.pdf?ua=1
- Impact of rotavirus (RV) vaccines: presentation by London School of Hygiene & Tropical Medicine on the global evidence around age distribution of RV disease and waning efficacy of RV vaccines in children <5y. This will inform forthcoming analyses assessing the risks and benefits of alternative RV vaccination schedules in different settings.
- Global research agenda of HPV vaccines: The overall project approach, methods and implementation plan of the “One-Dose Consortium” for human papillomavirus (HPV) vaccine, funded by the Bill &

Melinda Gates Foundation, was presented to the Committee by PATH's Center for Vaccine Innovation and Access. Recommendations were made regarding considerations for modelling and implementation issues.

- Rabies vaccination: A global business plan is being developed for the programmatic implementation of the global framework developed in 2015 to reach zero human deaths from dog-transmitted rabies by 2030. Modelling is being undertaken to estimate needs, resources and socioeconomic benefits.
- Typhoid vaccination: Modelling is being undertaken to assess vaccine impact and cost-effectiveness of typhoid vaccination to inform vaccination recommendations. Scenarios include different schedules, with/without catch-up campaigns, and different economic perspectives.
- Costing of malaria RTS,S vaccine: Estimating the cost of delivering the vaccine schedule, and in particular the fourth dose, will be important for informing subsequent questions on implementation and cost-effectiveness. The Malaria Vaccine Introduction Cost Tool (MVICT), developed and designed by PATH consultants, was presented to IVIR-AC for review. This tool captures incremental costs associated with the delivery of all doses, and is capable of calculating the specific costs of the fourth dose.
- An introduction of the Child Health and Mortality Prevention Surveillance network (CHAMPS) was presented to the Committee with a view to discussing the potential use for defining priorities for the development of vaccines and vaccine impact evaluations.

5.4 Global Immunization News

Available here: http://www.who.int/immunization/gin/en/

- Publication on Japanese Encephalitis surveillance and immunisation in WPRO - https://www.cdc.gov/mmwr/volumes/66/wr/mm6622a3.htm

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6 Other items

6.1 Updates from TGA

- New/updated registrations for vaccines:
  - Influvac Tetra: registered 2 November 2017
  - Fluzone High-Dose: registered 21 December 2017
- No recent media releases related to vaccinations.

6.2 Northern Hemisphere 2017/18 influenza season update

- USA (update as of the week ending 20th January 2018, available at: https://www.cdc.gov/flu/weekly/summary.htm)
  - 39 states plus New York City and Puerto Rico reporting high influenza activity, 5 states & the District of Columbia reporting moderate activity, 3 states reporting low activity and 3 states reporting minimal activity.
  - 11,965 laboratory-confirmed influenza-associated hospitalisations have been reported (rate: 41.9 per 100,000). Hospitalisation rates per 100,000 by age group – 0–4y: 27; 5–17y: 6.9; 18–49y: 13.4; 50–64y: 44.2; ≥65y: 183.1.
  - The proportion of deaths attributable to pneumonia and influenza increased sharply to 9.1% the week ending 6/1/2018 (above the 7.2% epidemic threshold). A total of 37 paediatric influenza-associated deaths have been reported since the start of the season.
  - A/H3 is the most frequently reported influenza subtype. Proportions of influenza type and subtype among 19,869 specimens from public health laboratories – A/H3: 77.4%; A/H1 7.7%; A not subtyped: 1.5%; B/Vic: 0.9%; B/Yam: 8.8%; B lineage not performed: 3.7%.

- The majority of viruses were characterised antigenically and genetically as being similar to the cell-grown reference viruses representing the 2017–18 influenza vaccine viruses.

- Canada (update as of the week ending 20th January 2018, available at: https://www.canada.ca/en/public-health/services/diseases/flu-influenza/influenza-surveillance/weekly-influenza-reports.html)
  - Among 53 regions, 11 reported widespread activity and 23 reported localised activity.
  - Influenza A comprised ~67% of all laboratory-confirmed influenza detections. Proportions of influenza type and subtype among 24,607 specimens: A not subtyped: 37.5%; A/H3: 28.0%; A/H1: 1.6%; B: 33.0%. Of type A that were subtyped, 94% were A/H3.
  - Detection rates of type A have been stable in the past 2 weeks, indicating type A may have peaked in the first week of January.
  - Influenza activity increased slightly in the most recent week, mainly driven by influenza B (type B detection rates are higher than has been observed over the past 7 seasons).
  - Age distribution of lab-confirmed influenza cases: 0–4y: 7%; 5–19y: 9%; 20–44y: 15%; 45–64y: 19%; ≥65y: 50%. Of A/H3 cases, 53% were ≥65y. Type B cases were more evenly distributed, but the majority were still ≥65y (46%).
  - Overall this season, 2,643 influenza-associated hospitalisations have been reported, 80% were due to type A. 1,814 (69%) were in ≥65y. Other age groups: 0–4y: 158 (6%); 5–19y: 92 (3%); 20–44y: 166 (6%); 45–64y: 413 (16%)
  - 241 ICU admissions and 110 deaths have been reported overall.
  - Among paediatric cases: 354 hospitalisations (of which 71% were type A), 58 ICU admissions and <5 deaths have been reported.
  - Most viruses were antigenically similar to the cell-culture propagated reference strains recommended by WHO.
- UK (update as of the week ending 21st January 2018, available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/676759/Weekly_national_influenza_report_week_04_2018.pdf)
  - Weekly GP consultation rate in the week of the report was 54.1 per 100,000, above the medium intensity threshold of 24.2 per 100,000 for this season. GP consultations decreased in adults but increased in 5–14 year olds.
  - Overall since the start of the season, 6,557 hospitalised confirmed influenza admissions have been reported via the sentinel scheme – A/H1: 261 (7.4%); A/H3: 615 (17.4%); A not subtyped: 914 (25.8%); B: 1,767 (49.4%).
  - Overall since the start of the season, 1,283 influenza-attributable ICU/HDU (high dependency unit) admissions have been reported – A/H1: 83 (6.5%); A/H3: 165 (12.9%); A not subtyped: 413 (32.2%); B: 622 (48.5%). 155 confirmed deaths have been reported through the same surveillance system.
  - By age group, statistically significant excess mortality was seen in the ≥65 year olds.
  - Influenza A and B are co-circulating. Based on 814 specimens received through the sentinel swabbing schemes in England and Devolved Administrations, 279 were A/H3 (34.3%), 44 A/H1 (5.4%), 39 A unknown type (4.8%), and 452 type B (55.5%).

7 Upcoming meetings and agendas

ACIP, USA (http://www.cdc.gov/vaccines/acip/meetings/upcoming-dates.html)

- 21-22 February 2018
- 20-21 June 2018

PTAC, New Zealand (https://www.pharmac.govt.nz/about/committees/ptac/)

- 8-9 February 2018
- 3-4 May 2018

JCVI, UK (https://www.gov.uk/government/policy-advisory-groups/joint-committee-on-vaccination-and-immunisation)

- Future meeting dates pending, but usually the 1st Wednesday of February, June and October

NACI, Canada (http://www.phac-aspc.gc.ca/naci-ccni/meetings-reunions-eng.php)

- 7-8 February 2018
- 6-7 June 2018

SAGE WHO (http://www.who.int/immunization/sage/future_meetings/en/)

- 17-19 April 2018
- 23-25 October 2018
