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 and Surveillance (NCIRS)

Period of review: 14/09/2019 – 16/12/2019

Contents

1 Advisory Committee on Immunization Practices (ACIP), USA

1.1 ACIP meeting: 23-24 October 2019

Agenda and presentation slides of this meeting:

- https://www.cdc.gov/vaccines/acip/meetings/slides-2019-10.html
- Full minutes of the October 2019 meeting are pending. Therefore, this summary has been developed from the presentation slides and video recordings.

Pertussis vaccines

Work Group terms of reference:

- Consider the evidence for a potential policy change to allow either Td or Tdap vaccine to be used in situations where only Td vaccine is currently recommended for:

1) Decennial Td booster in adults
2) Tetanus prophylaxis as needed for wound management
3) Catch-up immunisation schedule

Safety of closely spaced Tdap vaccines in the catch-up immunization schedule

Review published literature on studies that have assessed the safety of closely spaced Tdap compared with closely spaced Td doses

- Study of Tdap versus Td:
  - Study design: double-blind, randomised, controlled clinical trial
  - Study population: 460 adults ≥ 40 years from 3 European countries with no Td vaccine for 20 years or unknown vaccination history
  - Study arms: received the following in a 0-1-6 month schedule: 3 doses of Tdap, 1 dose of Tdap-IPV followed by 2 doses of Td, or 3 doses of Td vaccine (control)
  - Outcomes: immunogenicity and reactogenicity
  - Results: No statistically significant differences in local or general symptoms between groups were observed
- Study of maternal Tdap reactogenicity:
  - Study design: cohort study
  - Study population: 374 pregnant women; 225 non-pregnant women
  - Study sub-population of interest: 8 pregnant women who had more than one Tdap within the past 12 months
  - Comparison groups: none
  - Outcomes: injection site and systemic reactions
  - Results: no severe local or systemic reactions
  - Conclusion: no adverse event of concern but small number of subjects
- Closely spaced Tdap reports in Vaccine Adverse Event Reporting System (VAERS) – Methods (unpublished data)
  - Search VAERS database for U.S. reports of all persons who received more than one dose of Tdap
  - Jan 1, 1990 – June 30th, 2019
  - Review of VAERS reports and any medical records to assess for the length of interval between doses and the adverse event (AE), if any
  - Reports where interval of two Tdap doses ≤12 months included in final analysis
  - Among 34,804 reports of Tdap submitted to VAERS during the search period, 342 involved multiple doses of Tdap
  - In 88 reports interval of two Tdap doses ≤12 months
    - 67 (76.1%) did not describe an AE (vaccination errors)
    - 21 (23.9%) described an AE
  - The most common AEs were injection site reactions in 8 reports
- Vaccine Safety Datalink (VSD) unpublished analysis
  - Retrospective Cohort Study assessing repeated doses of Tdap versus Td – unpublished analysis
  - Data source: unpublished data from VSD retrospective cohort study evaluating repeated Tdap doses
  - Study sub-population of interest (unpublished data): 13,599 non-pregnant adolescents and adults 11-64 years who received Tdap or Td within 12 months of prior Tdap
  - Comparison groups: 11,687 Tdap versus 1,912 Td vaccines given within 12 months of prior Tdap

    - Outcomes: pre-specified local reactions and neurologic adverse events
    - Results: Repeated Tdap was not associated with an increase in any adverse event compared to Td within 12 months of prior Tdap
- Maternal Tdap safety in the VSD – unpublished analysis
    - Data source: unpublished data from VSD retrospective cohort study evaluating maternal Tdap safety
    - Study sub-population of interest (unpublished data): 187 women with multiple Tdap vaccines during the same pregnancy (excluded from larger published study)
    - Comparison group: None
    - Outcomes: acute adverse events (fever, allergy, and local reactions) and adverse birth outcomes (small for gestational age, preterm delivery, and low birth weight)
    - Only 1/187 with acute event following multiple Tdap vaccines in same pregnancy
        - ICD-9 code of limb pain and limb swelling 7 days after vaccination
        - Occurred on the day of delivery
        - Affected limb(s) unspecified
        - Baby born at 39 weeks
    - Birth outcome rates were similar to pregnant women exposed to a single Tdap dose during the same pregnancy
- Summary - unpublished data
    - VAERS: Most reports (76%) of excess doses of Tdap in VAERS did not describe an AE. Among reports with AEs (n=21), local reactions were most commonly reported (n=8)
    - VSD: Among subjects who received a Tdap dose ≤12 months compared to Td, no increased rates of AEs were observed. Among 187 women in the VSD who received multiple Tdap doses in the same pregnancy, one presented with limb pain and limb swelling 7 days after vaccination (unclear if related)
- Conclusions
    - Published data on closely spaced Tdap doses shows no increase in AEs when Tdap or Td was administered as a second or third dose
    - Regimens similar to the current and proposed catch-up schedule did not show differences in reactogenicity
    - Unpublished data of closely spaced Tdap doses shows no unusual or increased reporting of any AE
    - While data on multiple Tdap doses is limited, our review of published and unpublished safety data is reassuring

<u>Tdap and Td: Summary of Work Group considerations and proposed policy options</u>

Work Group assessment: Safety of >1 dose of Tdap for catch-up immunization schedule

- Published studies reassuring
    - Data limited
    - Includes an RCT comparing safety and immunogenicity of Tdap v. Td for catch-up immunization schedule
- Available published and unpublished data on closely-spaced Tdap vaccines
    - No concerning safety signal, including in pregnant women
    - Data sparse on safety of multiple doses of Tdap during a single pregnancy
- Need for continued safety monitoring
- <u>Work Group consensus: Either Td or Tdap can be used for additional doses of the catch-up immunization schedule for persons ≥7 years, both in the general population and for pregnant women</u>

Clarification of CDC guidance: Tdap in persons aged 7–10 years

- Current guidance: Children 7–10 years who receive Tdap inadvertently or for catch-up immunization should receive Tdap again at age 11–12 years
- Questions from health departments, immunization programs, and providers about 10 year-olds who receive Tdap for school entry requirements
- Both Tdap vaccines are now licensed to 10 years of age
- Clarification of guidance in children 7–10 years who receive a dose of Tdap:
    - Children 7–9 years: receive adolescent Tdap at 11–12 years
    - Children aged ≥10 years: Tdap does not need to be repeated
- Similar changes made to inadvertent DTaP administration guidance
- Plan to include changes as "CDC Guidance" in Policy Note
    - Should either Td or Tdap be allowed for use in settings where only Td is currently recommended for the decennial booster, tetanus prophylaxis for wound management, and the catch up immunization schedule?

Work Group interpretation:

- Benefits and Harms
  - Increased flexibility for providers
  - May be some additional benefit for pertussis control
  - Not enough evidence to recommend Tdap preferentially replace Td
  - No substantive safety concerns
  - Benefits outweighs potential harms
- Values, Acceptability and Feasibility
  - Providers value flexibility
  - Evidence of widespread use of Tdap instead of Td
  - Valued by stakeholders; change is acceptable and feasible
- Resource Use
  - Tdap more expensive than Td
  - Economic analyses limited by uncertainty in key parameters
  - Economic impact not a major consideration

Summary: Proposed policy change

Recommendations should be changed to allow either Td or Tdap vaccine to be used in situations where only Td vaccine is currently recommended for:

- Decennial booster
- Tetanus prophylaxis for wound management
- Catch-up immunization schedule, including in pregnant women

Adult Immunization Schedule

2020 Adult Immunization Schedule revisions

- Hepatitis A vaccination
  - Living with HIV as an indication
- HPV vaccination
  - 2 or 3 doses for men through age 26 depending on age at initial vaccination
  - Shared clinical decision-making for persons 27–45 years
- MMR vaccination in HCW
- Pneumococcal vaccination
  - Shared clinical decision-making for immunocompetent persons ≥65 years
- Meningococcal B vaccination
  - Shared clinical decision-making for persons 19–23 years
- Tdap vaccination
  - Tdap may be used any time Td is indicated
- Varicella vaccination
  - Indications for adults with HIV infection

Influenza vaccines

Influenza surveillance update

Recommendation for 2020 Southern Hemisphere influenza vaccine

- It is recommended that the following viruses be used for trivalent influenza vaccines in the 2020 Southern Hemisphere influenza season:
  - A/Brisbane/02/2018 (H1N1)pdm09-like virus
  - A/South Australia/34/2019 (H3N2)-like virus
  - B/Washington/02/2019-like virus (B/Victoria lineage)
- For quadrivalent vaccines containing 2 B components:
  - Above 3, plus B/Phuket/3073/2013-like virus (B/Yamagata lineage)

Summary

- Influenza activity remains low in the US overall
- Numbers are small, but so far, influenza A(H3N2) viruses are predominant in the US overall but this varies by region
  - Too early to tell what viruses will be predominant for the season
- While 2 of the 4 vaccine components were updated for the Southern Hemisphere, the components selected for the 2019–20 Northern Hemisphere vaccine, at this time, look appropriate for our season

High-dose inactivated influenza vaccine update

Sanofi presented Phase III (Study QHD00013) High-Dose Influenza Quadrivalent (QIV-HD) Vaccine Study results in subjects aged 65 years and older

- Summary of safety results
  - While higher percentages for some solicited reactions were observed for QIV-HD, the overall reactogenicity profile was comparable to TIV-HD
  - QIV-HD and TIV-HD study groups showed similar rates of unsolicited events, AEs leading to study discontinuation, serious adverse events (SAEs), fatal SAEs, and AEs of special interest.
  - One related SAE: a subject reporting small fiber neuropathy diagnosed 42 days after QIV-HD vaccination with other concomitant etiologies (vitamin B12 deficiency and recent viral illness)
  - Our (the Sponsor) assessment was unrelated to study vaccine given the other more likely etiologies and symptom improvement with vitamin B12 supplementation
- Overall key study results
- Safety results
  - No safety issues were observed with QIV-HD in adults 65 years of age and older
  - Safety profiles between QIV-HD and TIV-HD were similar
- Immunogenicity results
  - Primary objective met: QIV-HD was non-inferior to TIV-HD by GMTs and seroconversion rates for all 4 strains.
  - Secondary objective met: QIV-HD induced an immune response superior to that induced by the TIV-HD that did not contain the corresponding B strain.
- The study results demonstrated that addition of a second influenza B strain in QIV-HD did not impact the safety or immunogenicity of the other 3 strains in subjects 65 years of age and older

Work Group considerations

Challenges in assessing relative benefits of specific vaccines for older adults

- Large variety of available influenza vaccines
  - 8 are appropriate for this age group by licensed indications
- Growing canon of studies comparing individual vaccine types, but data limited for some relevant comparisons
- Vaccine effectiveness (and relative effectiveness of different vaccines) varies from season to season
  - Cannot be certain that results from one or a few high-quality studies will generalise across all or most influenza seasons

Planned systematic review/meta-analysis – question

- Do the relative benefits and harms of HD-IIV, aIIV and RIV as compared with one another and with other influenza vaccines favour the use of these vaccines over others for persons aged 65 years and older?

Ebola vaccine

Terms of Reference

- Review the available data on the rVSVΔG-ZEBOV-GP vaccine and inform domestic vaccine policy options for ACIP consideration
- Inform recommendations for use of the rVSVΔG-ZEBOV-GP vaccine in pre-exposure vaccination of healthy adults ≥18 years of age at occupational risk for exposure to Ebola virus (species Zaire ebolavirus)

Ebola virus disease

- August 1, 2018, Ministry of Health confirmed an outbreak of Ebola virus disease (EVD) in North Kivu Province in Eastern Democratic Republic of Congo
- Zaire ebolavirus species
- 10th EVD outbreak in DRC, largest to ever have occurred there

Recombinant Vesicular Stomatitis Virus-Based Ebola Virus Vaccine (rVSVΔG-ZEBOV-GP)

- Live-attenuated recombinant vesicular stomatitis virus vaccine
- Initially developed by Public Health Agency Canada and New Link Genetics
- Merck currently holds intellectual rights

Summary slide

- Ebola virus responsible for 64% of EVD outbreaks; >31,000 infected; >12,000 deaths
- US personnel at risk for occupational exposure
  - Laboratory personnel
  - Healthcare personnel at Special Pathogen Treatment Centers
  - Persons responding to EVD outbreaks

Work Group interpretation and next steps

Work Group interpretation of MERCK data

- Encouraging evidence for effectiveness in prevention of EVD when administered in an outbreak setting using a ring-vaccination strategy
- Acceptable safety profile
- Arthritis was an adverse event in a subset of study participants (Europe, U.S.)
- No known immune correlate for protection
- EBOV-GP specific IgG antibodies can persist in vaccinees up to 24 months

Vaccine safety discussion points

- Virus dissemination and replication (skin, joints) can occur and persist for up to 2-3 weeks after vaccination
  - Seeding of rVSV-ZEBOV into joints as demonstrated by detection of rVSV DNA in synovial fluid
  - Replicating rVSV-ZEBOV recovered from skin vesicles (culture)
- Pathophysiology of chimeric rVSV-ZEBOV vaccine may include features attributable to both its VSV and ZEBOV glycoprotein components; may play a role in the development of arthralgia/arthritis

Anticipated next steps

- GRADE and Evidence to Recommendations Framework
- Presentation of policy options
- Vote on policy options, pending vaccine licensure, February 2020
  - Potential for an emergency meeting in the event the vaccine is not licensed by February 2020

Vaccine safety

CDC vaccine safety onitoring systems

- Vaccine Adverse Event Reporting System (VAERS) monitoring: methods
  - Signs, symptoms, and diagnoses coded using Medical Dictionary for Regulatory Activities (MedDRA) terms
  - Clinical review of reports (includes medical records when available):
    - All serious reports
    - Selected conditions of special interest
  - Trends and patterns of reports
  - Reporting rates
  - Empirical Bayesian data mining to detect disproportional reporting for vaccine-adverse event pairings
  - Strengths: rapidly detects safety signals, can detect rare adverse events
  - Limitations: Generally cannot assess causality
- Vaccine Safety Datalink (VSD) methods:
  - Traditional epidemiologic studies descriptive analyses (e.g., background rates, vaccination coverage)
    - Cohort
    - Case-control
    - Self-control
    - Self-control
  - Tree-temporal scan data mining
  - Rapid Cycle Analysis (RCA) for near real-time monitoring
- Rapid Cycle Analysis in VSD
  - Near real-time vaccine safety monitoring (using sequential monitoring techniques)
  - Employs an automated analysis of ICD-coded diagnoses from administrative data
  - Designed to detect statistical signals (values above specified statistical thresholds)
    - When a statistical signal occurs, CDC conducts a series of further evaluations, including traditional epidemiologic methods
    - Chart-confirmation of diagnoses to confirm or exclude cases as true incident cases is a key part of statistical signal assessment
  - Not all statistical signals represent a true increase in risk for an adverse event
- Monitoring a recent vaccine: 9vHPV in VAERS and VSD
  - Summary of VAERS Review of 9vHPV safety:
    - VAERS received 7,244 reports following 9vHPV during the study period, December 1, 2014 − December 31, 2017
    - Most (97%) reports were non-serious
    - ~29 million 9vHPV doses were distributed in the United States

        - No new safety signals or unexpected patterns were observed
        - The safety profile of 9vHPV is consistent with data from pre-licensure trials and post-licensure data on 4vHPV
    - Summary of findings in VSD RCA for 9vHPV:
        - Statistical signals occurred for several adverse events after 9vHPV
            - Syncope and injection site reactions were expected
            - All other signals were further investigated
        - Signals for allergic reaction, pancreatitis and appendicitis were not confirmed after further evaluation (e.g. diagnosis not verified)
    - Summary of VAERS and VSD findings on HPV vaccine
        - No new safety concerns identified in VAERS or VSD RCA
        - Epidemiologic studies in VSD found no increased risks for:
            - autoimmune and neurologic conditions
            - venous thromboembolism
            - mortality
            - pregnancy-related conditions
        - Studies in progress in VSD: POTS, CRPS, CFS
- Conclusions
    - Pre-licensure activities form the foundation of vaccine safety
    - US has a comprehensive robust vaccine safety monitoring system
        - Essential to maintaining public confidence in vaccines
    - Science is not sufficient in maintaining acceptance of vaccines
        - Vaccinate with Confidence: CDC's strategic framework for strengthening vaccine confidence and preventing outbreaks of vaccine preventable diseases in the United States

Orthopoxvirus vaccine

Use of Vaccinia Virus Vaccine in Persons at Risk for Occupational Exposure to Orthopoxviruses: Background

- Poxviridae are a family of DNA viruses that infect a broad range of hosts
- Orthopoxvirus genus includes several species that cause disease in humans
    - Variola virus (causative agent of smallpox)
    - Vaccinia virus (principal source of smallpox vaccine)
    - Monkeypox virus (cause of multiple outbreaks in Africa and imported cases to other countries including the US)
    - Cowpox virus (endemic in Europe)
    - Newly discovered species (Akhmeta virus, Alaskapox virus)

Occupational exposures

- Diagnostic laboratorians directly handle specimens from persons with suspect orthopoxvirus infections
- Research personnel use replication-competent orthopoxviruses in biomedical research
- Healthcare workers in U.S.
    - Administer Vaccinia virus vaccine to (e.g., to military personnel)
    - Would treat patients with smallpox or monkeypox due to accidental or intentional exposures

Vaccinia virus vaccine prevents other orthopoxvirus infections

- Provides cross-protective immunity against other orthopoxviruses
- Facilitated smallpox eradication as main component of smallpox vaccine
- Recommended by ACIP for use in laboratory and healthcare personnel at risk for occupational exposure to orthopoxviruses

Work Group activities

- Review available data about safety and effectiveness of JYNNEOS™, including among persons with atopic dermatitis, immunocompromising conditions and pregnancy.
- Consolidate US recommendations for vaccination of persons who may have occupational exposures to orthopoxviruses.
- Identify areas in need of further research for informing potential future vaccine recommendations to prevent Orthopoxvirus infection

Dengue vaccine

GRADE analysis for Dengvaxia (Dengue vaccine CYD-TDV)

- PICO
  - Population: Persons 9–16 years of age with laboratory-confirmed previous dengue infection and living in endemic areas (Puerto Rico, American Samoa, USVI, Palau and Federated States of Micronesia)
  - Intervention: Routine administration of three doses of CYD-TDV
  - Comparison: No vaccine
  - Outcomes: Symptomatic dengue illness, hospitalisation and severe dengue
- Policy question
  - Should 3 doses of CYD-TDV be administered routinely to persons 9–16 year olds with laboratory-confirmed previous dengue infection and living in endemic areas to prevent virologically confirmed dengue, hospitalisations and severe dengue?
- Evidence retrieval
  - Systematic review of CYD-TDV vaccine trials in Medline, Embase, CINAHL, Cochrane Library and Scopus published between 2009 and 2019
  - Trials of CYD-TDV in 9–16 year olds by serostatus
  - Efforts made to obtain unpublished or other relevant data
  - Clarification of data from vaccine manufacturer
- Summary
  - Studies for vaccine efficacy include both RCTs and case cohort studies
  - For seropositives there is high-quality evidence of benefit for VCD, hospitalisation and severe dengue with no harm
  - Among seronegatives the evidence level is lower and there is a signal of increased risk among those receiving the vaccine

<u>Dengvaxia cost effectiveness in Puerto Rico</u>

- Discussion:
  - To reduce risk of seronegatives, high specificity of serological screening should be a priority in Puerto Rico
  - Lower coverage does not significantly affect the cost-effectiveness of the intervention
  - More recent estimates of costs, particularly the unit cost of screening and vaccination would improve calculations
  - A rough estimate suggests that a catch-up campaign in 10–16 year olds might roughly double the population impact of vaccination during a 10-year time frame

<u>Summary of work group discussion and next steps</u>

- Dengue Vaccine Workgroup considerations summary
  - GRADE analysis – evidence of high quality for CYD-TDV protection and safety among seropositive children 9–16 years
  - Major challenge: identifying a sensitive and specific and cost-effective IgG screening test
  - Puerto Rico immunisation program presentation and discussion
- CYD-TDV cost effectiveness comments/discussion
  - Presentation on validated model vaccinating 9-year olds, dengue antibody prevalences of 50%/30%, vaccine coverage 80%
    - Vaccination beneficial from a public health and individual perspective as long as sero_screening moderately Sp and Se
    - 6% of overall hospitalisations prevented
    - Increasing test Se increases public health impact but higher Sp more important to maximise cost effectiveness
      - 2 hospitalisations in misclassified seronegatives for every 1000 vaccinated persons with Sp at 95% (prevalence 50%)
      - Higher seroprevalence increases cost effectiveness, decreases misclassifications
  - Vaccine unit cost ICER
  - Incremental cost to avert a hospitalised case $1,500 (50% prevalence)
  - Changes in the cost of hospitalisations and serologic screening can affect the ICER significantly
    - Increased hospitalisation costs decrease ICER
    - Increased laboratory tests costs increase ICER

Rabies vaccine

Introduction

- Note: Current rabies vaccine and immune globulin shortages
- The shortages should not impact patient care. Vaccine and RIG available for every patient who needs it. No modification to current practices.

- Vaccine
  - RabAvert (GlaxoSmithKline): available directly from the manufacturer
  - Imovax® (Sanofi Pasteur): Currently unavailable but expected to be available late Oct/early Nov
- RIG
  - Imogam® (Sanofi Pasteur): available directly from manufacturer
  - Kedrab™ (Kedrion Biopharma) and HyperRab® (Grifols): unchanged availability and no difficulties filling gap from Imogam
- GSK divesting rabies vaccine (RabAvert in U.S.) to Bavarian Nordic
    - Vaccine will continue to be manufactured primarily at GSK's Marburg, Germany site until full production is transferred to Bavarian Nordic
    - No immediate impact to vaccine supply

<u>Rabies PrEP schedule and serological monitoring by risk category in healthy non-pregnant persons and special populations</u>

- Current schedule: 3-dose, 3-4 week schedule (0,7, 21 or 28)] and serological monitoring and boosters based on risk category
- Should a 2-dose, 1-week schedule (0,7)] for rabies PrEP be recommended?
  - Recommended routes of administration
  - Special populations
    - High-risk categories: booster/serological monitoring?
    - Immunocompromised: alternate schedules/serological monitoring?
  - All rabies vaccines are FDA approved as 3-dose series for PrEP
- Vaccine potency
    - Modern rabies vaccine highly potent
    - WHO and ACIP recommend ≥2.5 IU potency
    - Potency and immune response correlated up to 2.5IU/IM dose
        - No significant association identified above 2.5IU (or 0.5IU / dose ID)
- Kinetics of rabies vaccine immune response
    - Limited studies beyond neutralising antibody response
- Neutralising antibody as surrogate of protection
    - 0.5 IU/mL rabies neutralising antibodies (RFFIT)
        - Not a measure of protection
        - Measure of adequate response
        - Reliable detection limit
    - Correlation between antibody titer and survival
    - Variability between species
    - Adequate antibody response after primary vaccination and anamnestic response to challenge best surrogates
- Vaccination route
  - ID globally recommended vaccination route since 1980s
      - ACIP recommendation 1984–2008
  - ID found more cost effective in most settings and dose sparing in supply limited settings
  - No licensed single use ID packaging or multi-draw vials for rabies vaccine
  - Injection safety not well studied in setting of rabies ID administration
  - Cost effectiveness (ID versus IM) relational to PrEP or PEP patient volume
- Pre-exposure Prophylaxis (PrEP) schedules
  - 3-dose
      - 0, 7, 21/28
      - 0, 3, 7
  - 2-dose
      - 0, 28
      - 0, 7
  - 1-dose
  - Childhood immunisation schedules (typically 2-dose, 2–3 months apart)
  - Most schedules evaluated by both IM and ID routes
- 2-dose, 1-week schedule
  - 2018: Recommended WHO PrEP schedule (IM or ID)
  - 1 dose vaccine administered <u>IM</u> on days 0 and 7
      - Primary response well documented
      - Infer from existing 3-dose schedule
  - Clinical trials

        - ID
        - N=500
        - 100% adequate response at day 35
        - 2-dose (0,7 days) group had significantly higher GMT at 1 year compared to 3-dose (0,7,28 days)
        - No difference in post-booster response at 1 year
- Duration of immunogenicity - evidence
    - Follow-up typically less than 1 year
    - Longer follow-up
        - Mostly (0, 7, 21/28) schedules
        - Few [0, 28]
    - Primary response titer not effective at predicting duration of immunogenicity
        - Titer at 1 year or post booster significantly associated with titer 2–7 years later
        - Titers >30 IU/mL post 1 year booster associated with adequate response 5–10 years later
- Booster
    - Booster at 1 year associated with long-term immunogenicity
- Booster response
    - Anamnestic response nearly universal to vaccine booster
        - One non-responder reported in study (later diagnosed with B-cell lymphoma)
    - Survival following exposure without booster
        - 2010 liver recipient from rabid donor in Germany
            - Vaccinated >20 years prior, anamnestic response documented
        - Reports of significant titer increases following bat bites among wildlife biologist
        - Reduction in rabies cases in Amazonia region of Peru after mass childhood immunisation campaign
- PrEP failure
    - 1 well-documented PrEP failure reported
        - 1982, Peace Corp volunteer, vaccinated ID with HDCV vaccine in Kenya
            - Bitten by dog ~6 months later
            - Died of rabies 3 months after bite
        - Classically attributed to co-administration of chloroquine during PrEP series
            - Study at time found other groups give ID HDCV abroad at time had lower or undetectable titers compared to those in the US
            - Likely multiple causes
    - Inadequate response to primary vaccination reported in immunocompromised persons
- Special populations – high risk
    - High risk (continuous and frequent) categories
        - High rate of exposure events, high risk of rabies from exposure
        - High titer (>0.5 IU/mL)
        - Booster at 6–12 months after primary vaccination improve likelihood of maintaining adequate titer
    - Moderate risk (Infrequent) category
        - High rate of exposure events, low risk of rabies from exposure
        - Increased risk sporadic and shortly after primary vaccination (e.g. travellers)
        - Routine booster at 6–12 months and routine serological monitoring not critical
        - Adequate anamnestic response expected regardless of titer
        - Serology or booster if risk status changes
- Special populations - immunocompromised
    - Data scarce for any schedule
    - Risk reduction
        - Increased focus on exposure avoidance, appropriate PPE, and prompt health seeking behaviour
    - Serological confirmation of adequate immune response recommended
        - >0.5 IU/mL
- Special populations – pregnant women
    - No safety concerns reported
        - Scarce data
    - Risk reduction
        - Increased focus on exposure avoidance, appropriate PPE and prompt health seeking behaviour

- May consider deferring where risk reduction possible and PEP readily available

Measles

Summary of recent measles activity in the US, 2019

- Highest annual number of importations since measles eliminated
- Highest annual number of measles cases since 1992
  - 75% related to outbreaks in NYC or NYS
  - Driven by delays in or lack of vaccination
- Reasons for increases in measles cases in the US
  - Global increase
  - Importations
  - Pockets of under-vaccination

1.2 Newly published or updated recommendations

Nil

1.3 Newly published or updated recommendations – not yet published

ACIP approved the following recommendations by majority vote at its October 2019 meeting. These recommendations have been adopted by the CDC Director and will become official once published in MMWR. Information available on https://www.cdc.gov/vaccines/acip/recommendations.html

- Either Td or Tdap vaccine can be used in the following situations when previously only Td was recommended (new language italicized):
  - Decennial booster dose: "To ensure continued protection against tetanus and diphtheria, booster doses of *either Td or Tdap* should be administered every 10 years throughout life."
  - Tetanus prophylaxis for wound management: "For non pregnant persons with documentation of previous vaccination with Tdap, *either Td or Tdap* should be used if a tetanus toxoid-containing vaccine is indicated."
  - Catch-up immunization:
    - "Persons aged (7–18 years and ≥19 years) who have never been vaccinated against pertussis, tetanus, or diphtheria should receive a series of three tetanus and diphtheria toxoid-containing vaccines, which includes *at least 1 dose* of Tdap. The preferred schedule is a dose of Tdap, followed by a dose of *either Td or Tdap* at least 4 weeks afterward and another dose of *either Td or Tdap* 6 to 12 months later.
    - Persons aged (7–18 years and ≥19 years) who are not fully immunized against tetanus and diphtheria should receive 1 dose of Tdap (preferably the first) in the catch-up series; if additional tetanus toxoid–containing doses are required, *either Td or Tdap* vaccine can be used."
  - Prevention of neonatal and obstetric tetanus: "If more than one dose of a tetanus-toxoid containing vaccine is needed, either Td or Tdap vaccine can be used for those doses."
- The Recommended Child and Adolescent Immunization Schedule, United States, 2020, for ages 18 years or younger.
- The Recommended Adult Immunization Schedule, United States, 2020, for ages 19 years and older.

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2 Immunisation Advisory Centre (IMAC), New Zealand

2.1 PTAC Considerations

Meeting on 22–23 August 2019 –https://www.pharmac.govt.nz/assets/ptac-minutes-2019-08.pdf

- There were no vaccine-specific considerations at this meeting

2.2 Other updates

Notification: widen access to meningococcal ACWY vaccine for people in close-living situations

- https://pharmac.cwp.govt.nz/news/notification-2019-11-13-acwy-vaccine/
- From 1 December 2019, vaccination will be funded for people aged from 13 to 25 years living in boarding school hostels, tertiary education halls of residence, military barracks or prisons. After the first year, funding will only be available to people entering their first year of living in such institutions

Zostavax catch-up programme extended

- https://www.immune.org.nz/hot-topic/zostavax-catch-programme-extended
- PHARMAC has extended the Zostavax catch-up programme for adults aged 66–80 years inclusively on 1 April 2018. Adults who meet this eligibility criteria now have until 31 December 2020 (the catch-up programme was previously due to end on 31 March 2020) or they turn 81 years of age, whichever occurs first, to receive one funded dose of Zostavax.

Measles in New Zealand

- https://www.immune.org.nz/hot-topic/measles-overseas-and-new-zealand
- In response to the current measles outbreaks, American Samoa, Republic of Marshall Islands, Tokelau and Solomon Islands are requiring travellers to show evidence of measles vaccination at least 2 weeks before entry to these countries. Other Pacific countries such as Samoa and Fiji have not formally implemented travel measures; however, it is recommended travellers to these countries are vaccinated against measles.
- Unvaccinated New Zealanders over the age of 50 can be given MMR if vaccination is required for proof of entry or is necessary for protection in countries currently experiencing measles outbreaks.
- Due to the ongoing measles outbreaks across the Pacific, the Director General of Health has authorised health providers to access MMR vaccine for unimmunised Pacific temporary migrant workers, including those on the RSE scheme. Pacific temporary migrant workers, under normal circumstances, are not eligible for access to publicly funded health care in New Zealand, including access to the MMR vaccine. However, the Ministry of Health has worked with PHARMAC, the Ministry of Foreign Affairs and Trade, and Immigration New Zealand to enable access to one dose of MMR vaccine for workers who are non-residents.

Extended eligibility for funded Boostrix (Tdap) vaccination

- https://www.immune.org.nz/resources/immunz
- PHARMAC has extended eligibility for funded Tdap vaccination to include parents or primary caregivers of infants: who are admitted to a Neonatal Intensive Care Unit (NICU) or Specialist Care Baby Unit (SCBU) for more than 3 days, and whose mother did not receive a maternal Tdap vaccination at least 14 days before the baby's birth

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

3.1 JCVI Meeting: 2 October 2019

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

This summary was based on the draft minutes only.

- HPV programme update
  - Public Health England (PHE) informed the Committee that work had been undertaken to implement a gender-neutral HPV programme from the 2019–20 academic year
- BCG and SCID screening
  - The Committee agreed that it would be necessary to remove the neonatal BCG programme from birth to after Severe Combined Immunodeficiency (SCID) screening results were available
  - Deferring vaccination could however raise challenges in delivery and reduce uptake of the vaccine
- PCV vaccination in older adults
  - Pfizer asked the Committee's advice on pneumococcal conjugate vaccination in older adults
  - There has been an increase in pneumonia admission and increase in PCV13 serotype disease and non-PCV13 vaccine type disease in Nottingham
  - Previously it was agreed that vaccination with PCV13 in older age groups was not cost-effective
  - Pneumococcal polysaccharide vaccines (PPV23) were being used due to a shortage of vials, although pre-filled syringes were more expensive. This raised a question around whether PPV23 remained cost-effective, especially with changes to the circulating serotypes and development of higher-valency pneumococcal conjugate vaccines. PPV23 was likely to remain cost-effective at the higher price
  - The cost-effectiveness of the PPV23 vaccination programme could be reviewed along with other issues, including the potential use of higher valency pneumococcal conjugate vaccines and the cost-effectiveness of PPV23 vaccination strategies
- Department of Health and Social Care Vaccine Strategy
  - The UK has lost its 'measles-free status' with the WHO and this has led to the vaccine strategy being brought forward. There is a shorter-term focus on improving coverage of vaccines, including MMR
- Ebola post-exposure prophylaxis
  - PHE has been asked to advise use of vaccine in pregnant or immunosuppressed individuals, should they require post-exposure prophylaxis
  - There are two vaccines available for use of Ebola post-exposure prophylaxis in Western Europe: vesicular stomatitis vaccine (VSV) (Merck) and a prime-boost with two separate composition (J&J) – neither of which was replication-competent
  - Immunogenicity and safety data from use in pregnant or immunosuppressed individuals were limited for both vaccines
  - It was noted the Merck vaccine was now being used in DRC in pregnant and lactating women
  - Overall, use of vaccine in pregnant women and immunosuppressed individuals would require consideration of the potential risk of Ebola disease compared with the potential for adverse effects from the vaccines

- Pandemic influenza preparedness
  - Since June, the Influenza Sub-committee has been considering potential pandemic-specific influenza vaccines and modelling on the potential impact of vaccination strategies in a range of pandemic scenarios
  - There are promising new technologies, but these would not be available for the next few years
  - Timelines for the availability of these vaccines was approximately 5 to 6 months from the declaration of a pandemic and dependent on a number of factors
  - Currently there are only three pandemic specific vaccines (PSV) available, two inactivated adjuvanted and one live attenuated, for use in a pandemic, and all relied on the use of eggs in their manufacture, no new technologies were available for the next three to five years
  - The Committee agreed that it would be important to have early access to more than one vaccine for a) security of supply and b) because there may be differences in the population you target where different vaccines may be appropriate.
  - The Committee agreed that there should be an appropriate vaccine available for use in children
  - The Committee agreed that the PSV landscape should be reviewed again in three years because new pandemic vaccine technologies might then be available with shorter manufacturing timelines.
- Annual National Immunisation Schedule Evaluation Consortium (NISEC) update
  - IMAP3: is a follow-on from IMAP2 which evaluated the use of 2 different pertussis-containing vaccines in pregnancy and the impact on the response to infant immunisation in the offspring.

IMAP3 was following infants through to 3.5 years of age, to determine if there was any impact of maternal vaccination on pre-school boosters; 75% of the original participants had been retained and the results were expected at the end of October 2019; they would also be looking at the persistence of DTaP vaccines and the impact on pre-school boosters
    - OPTIMUM: this study included 354 women randomised to receive the DTaP-IPV vaccine at three different time points during gestation. The primary outcome measure was antibody concentrations against pertussis toxin (PT) in the cord-blood of term infants at delivery
    - What's the story? : a sero-epidemiology study that aims to evaluate the feasibility and added public health benefit of a UK population based sero-epidemiological programme in 0- to 24-year olds. The consortium aimed to undertake analyses of blood from schedule 3 study participants 5 to 13 months of age, to examine the immunogenicity of the 2 + 1 schedule of 4CMenB against hyperinvasive MenW and clinically relevant MenC strains; and blood was also drawn at 2 years of age to examine the persistence of immunogenicity following the 2+1 4CMenB schedule for: 3 MenB strains, MenW and clinically relevant MenC strains.
    - Shingrix studies are on hold until vaccine was available from the manufacturer.
    - A study is considering alternative DTaP-IPV-Hib-HepB vaccine, Vaxelis, where there is no co-administration data with MenB vaccine
- Seasonal influenza vaccines for 2020–2021
    - Sanofi Pasteur and Seqirus had presented to the Sub-committee the latest evidence for their respective vaccines, high-dose trivalent inactivated influenza vaccine (TIVHD) and adjuvanted trivalent inactivated influenza vaccine (aTIV)/ quadrivalent influenza cell-culture vaccine (QIVc), Flucelvax (Seqirus); all evidence came from the 2017–18 season and mostly concerned its effectiveness compared with quadrivalent influenza egg-culture vaccine (QIVe). Study results were mixed but with some evidence indicating QIVc performed better than QIVe in the 2017–2018 season. The Sub-committee had also looked at data presented by Sanofi Pasteur and Seqirus on the vaccines recommended for the elderly, aTIV and TIV HD. The Sub-Committee concluded that it could not say whether one vaccine was better than the other based on the available evidence.
    - The Committee adjusted its advice for vaccines for the elderly saying that TIV HD and aTIV were preferable, but that QIVc could also be considered. This was because there was more evidence and stronger evidence in support of TIV HD and aTIV (compared with standard inactivated influenza vaccines) than there was for QIVc.
    - The Committee's advice for QIVc in the under 65 at-risk groups had also been adjusted to highlight a slight preference for QIVc because of the issue of egg adaptation (in an egg-adapted AH3N2 season); however, QIVe was still considered a suitable vaccine for this group, and likely to be similar in H1N1/B seasons or in years in which egg-adaptation was not a major H3N2 issue.
    - The manufacturer highlighted in its letter that the quality of the evidence in support for TIV HD was better than that for aTIV, because of the number of randomised control trials conducted. The Committee felt that supporting data from further seasons were needed to distinguish between TIV HD and aTIV
    - The Committee agreed that it would like to see more data from the UK on the performance of the vaccines being used, as currently most of the evidence came from studies in the US and Europe.
    - Overall the Committee agreed that the available evidence supported the position that TIV HD and aTIV were preferable to standard egg-based influenza vaccines for those aged 65 years and over, but the evidence was insufficient to distinguish between the two vaccines on the grounds of their relative vaccine effectiveness
- Tick-borne encephalitis
    - PHE recently found tick borne encephalitis virus (TBEV) in a small number of ticks in England, and that a possible case of TBE had been identified. All cases identified in the UK had previously been travel-related.
    - PHE concluded that there were two different strains in the UK from two separate introductions, potentially from birds and imported animals. However, Lyme disease continued to be the most common tick-borne infection in the UK
    - PHE has undertaken several actions following this case, including: sharing key information locally (Thetford Forest and New Forest) and nationally; the Rare and Imported Pathogens Laboratory (RIPL) were testing cases of unidentified acute encephalitis in these areas for evidence of TBEV exposure, with three samples tested and confirmed negative; and samples sent to RIPL for neuroborreliosis, with a general acute encephalitic presentation, which were negative for Lyme disease were being automatically screened for TBEV, with no evidence of exposure to date
    - It was suggested that PHE expanded the testing of cases to include other meningo-encephalitis presentations rather than just neuroborreliosis

- The Committee noted that WHO recommended that where vaccination was undertaken, older adults should be vaccinated as a priority, as disease was more severe in this age group
- The Committee agreed that this issue should be further reviewed, once more data were available, especially around whether certain occupational groups were at increased risk, and requested that at that time information be provided on the vaccines, their formulation and efficacy

- Update from the Travel Sub-committee
  - Influenza vaccination for travellers: travellers eligible for the vaccine the UK should be encouraged to receive it in the UK each year, especially for those attending 'mass gatherings' such as the Hajj or those travelling on cruise ships; and those intending longer stays in the southern hemisphere could consider vaccination after arrival, where available
  - HPV for male travellers: The increased risk of sexually transmitted diseases (STD) to travellers was well known and these STD risks should be expanded to include HPV. The HPV vaccine is available privately and barrier forms of contraception should also be advised.
  - Japanese encephalitis vaccination: The vaccine is offered as two doses 28 days apart with a booster at 1–2 years. Where there is continued risk of exposure an additional booster dose is recommended at 10 years in those aged 18–64 years. There was no recommendation for a second booster in place for those under 18 or over 64 years of age. The evidence in young children indicated the protection would not extend beyond 10 years, and an additional booster could be considered, where appropriate; and NaTHNaC and HPS had agreed to prepare an update to current guidance
  - Yellow fever and measles vaccine guidance: The Green Book guidance indicates that measles protection may be sup-optimal where the MMR vaccine is given with yellow fever vaccine. The sub-committee considered that where yellow fever and MMR are given together or within one month of each other, an additional dose of yellow fever vaccine should be given at 10 years
- Annual meningococcal update (based on a presentation from the PHE on meningococcal epidemiology in England and vaccine effectiveness estimates)
  - Men B vaccination implemented in 2016, in a 2+1 schedule with a small catch-up in 3- and 4-month old infants; 95–96% received one dose, and more than 90% received the second dose. At two years of age around 88% had received the advised three dose schedule. PHE reported a large reduction in disease within the first 10 months of the programme
  - Using the screening method, vaccine effectiveness for one dose was 24.1%, for two doses was 52.7% and after three doses was 58.9%, the estimate of effectiveness against vaccine preventable MenB IMD was 70.5%
  - After three million doses of 4CMenC, there were no new safety concerns
  - It has been estimated that 277 cases of MenB IMD has been prevented in the first three years of the programme
  - The UK experienced a national MenW outbreak beginning in 2009. MenACWY vaccination started August 2015, with the aim of vaccinating all 13–18-year olds over a 3-year period
  - There was an impact in school leavers (17–18-year olds) within 12 months of the start of the programme, despite 36% vaccine coverage, 2017–2018 was the first year with an overall decline in MenW cases across the population
  - PHE noted that there is a clear impact from the 4CMenB programme
  - PHE noted that an infant programme should have no impact on strains circulating in adolescents (the main carriers of meningococcal bacteria) and as such there should be no charge in the circulating strains attributable to the programme
  - It was noted that an ongoing meningococcal carriage study indicated around a two-third reduction in MenW carriage in Year 12 (England) students, since the last (pre-MenACWY vaccination) study
  - It was noted that the Austrian NITAG had recommended booster doses of 4CMenB for at-risk groups, and PHE agreed that they would prepare a paper for JCVI to consider on this
- Coverage
  - The Committee agreed that action was required to reverse the trends in coverage. There was no evidence that the declining trends were associated with parental confidence and the declines were likely to be associated with delivery of the programme.
  - Action: Representative from England, Wales, Scotland and Northern Ireland to present on their strategies to improve uptake

3.2 Newly published or updated statement/recommendations

3.2.1 JCVI advice on influenza vaccines for 2020–21

- For vaccination of those aged 65 years and over:

- JCVI advises the use of the following vaccines: aTIV or TIV HD
- QIVc is suitable for use in this age group if aTIV or TIV HD are not available
- When considering a preference between TIV HD and aTIV, the available data are few, somewhat inconsistent, are not available over multiple seasons, are at risk of bias, and are limited by the use of non–laboratory-confirmed influenza endpoints. The level of uncertainty in the available evidence is considered too great to allow for a preferential recommendation between TIV HD and aTIV

- For vaccination of those in at-risk adults and children for whom there are contraindications for use of live attenuated egg-cultured intranasal influenza vaccine:
  - Aged 9 to less than 65 years of age in at-risk group, JCVI advises the use of the following vaccines: QIVc or QIVe
  - Aged less than 9 years of age in an at-risk group, JCVI advises the use of QIVe
  - Evidence from recent influenza seasons indicate a clear additional benefit in the use of quadrivalent influenza vaccines in those less than 65 years of age in an at-risk group, compared with trivalent influenza vaccines
  - There is a potential advantage to using cell-culture influenza vaccines compared with egg-based culture influenza vaccines, due to the possible impact of "egg-adaption" on the effectiveness of influenza vaccines, particularly against A(H3N2) strains
  - QIVe can also be considered for use in this group. Both QIVc and QIVe are preferable to standard egg-culture inactivated trivalent vaccines

3.2.2 Updated guidance for Measles – Green Book chapter 21

- Updated 31 October 2019 - https://www.gov.uk/government/publications/measles-the-green-book-chapter-21
- Added revised chapter, including the epidemiology data, viral rash in pregnancy and measles prophylaxis content

3.2.3 Updated guidance for Tetanus – Green Book chapter 30

- Updated 13 November 2019 - https://www.gov.uk/government/publications/tetanus-the-green-book-chapter-30
- Added the revised chapter to include updates on the epidemiology and management of wounds and immunoglobulins.

3.2.4 Updated guidance for Yellow Fever – Green Book chapter 35

- Updated 21 November 2019 - https://www.gov.uk/government/publications/yellow-fever-the-green-book-chapter-35
- Added yellow fever vaccine guidance for those with weakened immune systems, those over 60 years and anyone who has had their thymus removed.

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4 National Advisory Committee on Immunization (NACI), Canada

4.1 NACI Meetings

The most recent meetings were conducted 5-6 June 2019 and 25-26 September 2019 in Ottawa, Ontario; however, the summary of discussions has not yet been released.
https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/immunization/national-advisory-committee-on-immunization-naci.html

4.2 Newly published or updated statement/recommendations

Nil

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5 Immunisation updates from the World Health Organization (WHO)

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

- 8–10 October, 2019 Geneva, Switzerland. Full meeting report available at: https://apps.who.int/iris/bitstream/handle/10665/329962/WER9447-eng-fre.pdf
- Measles and rubella elimination:
  - SAGE confirmed that no changes were required to the current WHO recommendation related to vaccine performance regarding rubella vaccine
  - SAGE recommended a gender-neutral high coverage paediatric vaccination and catch-up strategy to avoid gaps in population immunity
  - SAGE considered the modelling and economic analyses presented and current progress towards measles and rubella elimination goals and concluded: 1) Eradication of measles and rubella will be achieved only with sustained, high, equitable coverage with 2 doses of measles- and rubella-containing vaccine. Countries and regions should focus on making substantial progress toward their elimination goals, 2) Stronger support and more coordinated strategies globally, within regions and across transmission blocks must be developed to complement the work of individual countries, 3) Substantial strengthening of primary health care systems is required to effectively deliver routine vaccination, 4) A monitoring and accountability framework should include new benchmarks to measure progress towards measles and rubella elimination, 5) The development of innovative tools (e.g. microarray patches) should be prioritised to support and improve equity and high coverage.
- Human papillomavirus vaccine:
  - SAGE reaffirmed WHO current recommendations for the use of HPV vaccines
  - SAGE reiterated that all three licensed HPV vaccine have excellent safety profiles and offer comparable immunogenicity, efficacy and effectiveness for the prevention of cervical cancer, which is caused mainly by HPV types 16 and 18
  - There is a current shortage of HPV vaccines that could result in failure to introduce or sustain HPV vaccination programmes in some countries, particularly in those with a high burden of cervical cancer. In the context of a limited supply of HPV vaccine, SAGE recommends the following additional strategies:

    1) All countries should temporarily pause implementation of gender-neutral, older age group (>15 years) and multi-age cohort HPV vaccination strategies until vaccine supply allows equitable access to HPV vaccine by all countries. This will significantly relieve supply constraints in the short term and enable allocation of doses to high-burden countries that are currently planning to introduce or sustain HPV vaccination.

    2) In the context of constrained supply and in consultation with their NITAG, countries should consider alternative strategies to ensure girls receive 2 doses of HPV vaccine before they become sexually active. Based on an analysis of efficiency, cost-effectiveness and disease impact, the following alternative strategies are recommended but will require consideration of country context and programmatic feasibility:
    - Countries could target girls who are 13 or 14 years old in the equivalent school grade for 2-dose vaccination. The success of this approach depends on achieving high 2-dose coverage in this age group, and initiation of sexual activity after 14–15 years. The programme challenges of reaching older girls (e.g. in the setting of school vaccination, school enrolment rates and ability to reach out-of-school girls) and accurate record-keeping through vaccination registers and vaccination cards should be carefully considered. If targeting of this older cohort results in unacceptably low coverage or high drop-out rates for the second dose, it may be necessary to target girls aged 9 or 10 years or in the equivalent lower school grade instead
    - Countries could adopt an extended interval of 3–5 years between the 2 doses, with the first dose being given to younger girls, such as those aged 9 or 10 years or in the equivalent lower school grade, and the second dose to 13–14 year old girls or in the equivalent higher school grade. This strategy constitutes off-label use of the vaccine. Adoption of this approach will require careful consideration of programmatic challenges to achieving high 2-dose coverage, strong communications, accurate record-keeping in vaccination registers and vaccination cards and the assumption of a low risk of exposure to HPV infection between doses 1 and 2. Countries should consider the median age of sexual debut and the availability of tool so track administration of dose 2 (e.g. vaccine registry for reminders) before using such a strategy
    - Any country with a stock-out of HPV vaccine should maintain good records of coverage and ensure that girls who were missed are vaccinated as soon as the vaccine becomes available
  - SAGE welcomed the ongoing and planned trials of single-dose schedule, as they will inform future policy recommendations
  - SAGE welcomed studies of the outcomes of different vaccination schedules, including for special populations such as those with a high prevalence of HIV infection or at risk for HIV acquisition

- Review of the Global Vaccine Action Plan, lessons learned and recommendations:
  - Most objectives were not met, but tangible progress was made in many areas
  - SAGE agreed that GVAP's scope and underlying principles remain relevant, even in changing contexts
  - More emphasis should be placed in the next decade on emerging issues such as migration, accelerating urbanisation, outbreaks and other destabilising factors, increasingly large underserved populations and ensuring the availability and affordability of vaccines
  - SAFE endorsed recommendations for the post-2020 global immunisation strategy, to focus on a country-centred, bottom-up approach, ensuring flexibility, a more appropriate governance model, with greater emphasis on advocacy and communication; effective use of data in planning and assessing actions and their impact; long-term planning, in particular in research, development and delivery of vaccines and innovations; and the importance of monitoring, evaluation and accountability at country and subnational levels
- Immunisation agenda 2030 (IA2030)
  - The seven strategic priorities of the IA2030 framework are: 1) immunisation for primary health care and universal health coverage, 2) commitment and demand, 3) coverage and equity, 4) life-course and integration, 5) outbreaks and emergencies, 6) supply and sustainability and 7) research and innovation
  - These priorities will be achieved on the basis of 4 core principles: people-focused, country-owned, partnership-based and data-enabled
- Ebola virus vaccines:
  - SAGE has made several recommendations on Ebola Virus Disease (EVD) vaccination strategies, such as vaccination of infants and children aged ≥6 months and of pregnant and lactating women and on the adjusted-dose recombinant vesicular stomatitis virus-Zaire Ebola virus vaccine (rVSV-ZEBOV GP vaccine)
  - SAGE will develop a priori defined criteria for implementation of the dose reduction if future vaccine supply is significantly constrained and the outbreak is not contained
  - Licensure of the rVSV-ZEBOV GP vaccine was pending at the time of the SAGE meeting
  - SAGE informed planned use in the DRC of a second investigational EVD vaccine
- Quality and use of data on immunisation and surveillance:
  - The Working Group recommended strengthening of governance, tools and workforce capacity for data management and use, and assessment using continuous quality improvement methods
  - SAGE noted that improvements rather than absolute targets for data quality are important and that the data use defines the quality required
  - SAGE endorsed the following recommendations: 1) Embed monitoring of data quality into global, regional and national monitoring of the surveillance of immunisation and VPDs, 2) Increase the capacity and capability of the workforce for ensuring data quality and use, starting at the level at which data are collected, 3) Improve the accuracy of denominators, 4) Enhance use of all available data for tailored action, including program planning, management and decision-making, 5) Adopt a data-driven continuous quality improvement approach as part of health system strengthening at all levels, 6) Strengthen governance of the pilot-testing and use of new tools for collection and use of immunisation and surveillance data, 7) Improve data-sharing and knowledge management among areas and organisations for greater transparency and efficiency and 8) WHO and UNICEF should strengthen global reporting and data monitoring through a periodic needs assessment and revision process
- Polio eradication:
  - SAGE was informed about the progress in the clinical development of novel oral type-2 polio virus (nOPV2)
  - SAGE recommended the following urgent actions:
    - Conduct high-level advocacy, followed by immediate action, to ensure government and community commitment in Afghanistan and Pakistan to stop the current increase in WPV
    - Revise the standard operating procedures on the scope, quality and timeliness of the monovalent oral type-2 polio virus (mOPV2) response to cVDPV2 outbreaks
    - Secure and uninterrupted supply of mOPV2 by identifying "fill and finished" capacity and by new bulk production
    - If the mOPV2 supply becomes critically low and is not sufficient to control cVDPV2 outbreaks, use a 1-drop mOPV2 strategy
    - Maintain the public health emergency of international concern status of polio
    - Accelerate clinical development of nOPV2 and prioritise its assessment under the WHO EUL procedure

- Develop and use clear communication to educate health workers and the general public about the complex issue of cVDPVs to prevent misunderstanding and negative impacts on immunisation activities
- Review the strategy to prevent paralysis in at-risk populations in regions of cVDPV2 outbreaks by accelerating access to and use of IPV

5.2 Meeting of the Technical Advisory Group (TAG) on Immunisation and Vaccine-Preventable Diseases in the Western Pacific Region (WPRO)

- 18–21 June, 2019 Manila, Philippines. Final meeting report is pending. Therefore, this summary has been developed from the draft meeting report available at https://www.who.int/immunization/sage/meetings/2019/october/4_WPR_TAG28.Draft-Report2019September08_with_Annexes.pdf
- The intention of the meeting of the TAG on Immunisation and Vaccine-Preventable Diseases in the WPRO was to provide practical recommendations for implementing the Global Vaccine Action Plan (GVAP) towards 2020 and also to prepare new visions and strategic direction for immunization and vaccine-preventable disease (VPD) control and elimination in the Western Pacific in the coming decade.
- Three different areas were explored: 1) measles and rubella elimination strategies and poliovirus eradication, 2) regional plans for surveillance, data management and laboratories and laboratory networks for vaccine-preventable disease control and elimination, 3) goals for immunization and VPDs during 2021–2030 for the 37 countries and areas that make up the WPR
- The potential risk for the resurgence of VPDs such as measles, polio, diphtheria and pertussis due to population immunity gaps is a huge concern in the region
- Although the WPR is experiencing an increase in measles transmission during 2018–2019, including the importation of the virus from endemic countries to many WPR Member States, WPR continues to make encouraging progress towards measles and rubella elimination. All Member States except one has introduced a second dose of measles containing vaccine. The overall two-dose MCV coverage is 94% region-wide, but there is still wide variation in coverage among Member States. As of September 2018, the Regional Verification Commission (RVC) for measles and Rubella Elimination verified nine countries and areas as having eliminated measles; and five have eliminated rubella
- The Regional Strategy and Plan of Action for Measles and Rubella Elimination in the Western Pacific describes several operational targets for 2020 including: 1) prevent the resurgence of endemic measles virus; 2) sustain interruption of measles virus in countries that have achieved elimination, and 3) prevent large-scale outbreaks after importation
- The regional 2030 and strategic direction for measles and rubella elimination include: 1) strengthening and enhancing overall immunization systems through measles and rubella elimination strategies, such as school-based immunisation initiatives, injections and immunisation safety, and cold chain capacity building, 2) improving broader public health infrastructure and interventions through measles and rubella elimination strategies, 3) developing and implementing coordinated and synchronised cross-border initiatives to improve immunity among migrant and stateless populations and reduce cross-border importation
- The WPR successfully maintains its polio-free status since 2000. Majority of Member States maintain 90% coverage with three doses of polio vaccines. All countries and areas in the Region have successfully introduced one dose of IPV in their national schedules. WHO/EPI started development of the Regional Strategic Framework for VPDs and Immunisation in the Western Pacific 2021–2030. One of its proposed goals is “no paralysis due to any type of poliovirus in the WPR.”
- WHO (Headquarters and all Regional Offices) is developing the WHO Immunisation Information System (WIISE), which is a collection of applications to collect, manage, analyse and disseminate immunisation and VPD surveillance data reported to WHO worldwide. WHO is developing a Global Comprehensive VPD Surveillance Strategy, which will be finalised by the end of 2019, to support the Immunisation Agenda 2021–2030
- WPRO convened the Seventh Workshop for National Regulatory Authorities for Vaccines and Medicines in the Western pacific in Manila on August 2018

- The 25th Meeting of the TAG on Immunisation and VPD in the Western Pacific recommended developing a guidance document to support countries in the Region to overcome vaccine hesitancy and generate and sustain acceptance and demand. The draft guideline is for the use of EPI staff and partners. WPRO will continue working with relevant stakeholders to finalise the draft for Member State endorsement at the 29th TAG Meeting in 2020
- TAG urged all Member States to continue to introduce new vaccines that are recommended by WHO for inclusion in national immunisation programmes. There are three focus areas 1) patterns of uptake and coverage including, case studies on *Haemophilius influenza* type b (Hib), pneumococcal conjugate and rotavirus vaccines, 2) factors influencing uptake and coverage and 3) a look into the future for new vaccines. Selected new vaccines that are expected to be introduced in the Western Pacific Region during 2021–2030, including typhoid conjugate vaccine, respiratory syncytial virus, dengue and malaria vaccines
- The draft Regional Strategic Framework for Vaccine preventable diseases and immunisation in the Western Pacific, 2021–2030 was discussed. The strategic objectives of the regional framework are to 1) strengthen and expand immunisation systems and programmes; 2) manage health intelligence on vaccine-preventable diseases and immunisation and 3) prepare for and respond to public health emergencies
- The following immunisation partners' role and their work in the region were acknowledged: Asian Development Bank, International Vaccine Institute (IVI, Republic of Korea), National Centre for Global Health and Medicine (NCGM, Japan), National Centre for Immunisation Research and Surveillance (NCIRS, Australia), National Institute of Infectious Diseases (NIID, Japan), PATH, UNICEF and the U.S. Centres for Disease Control and prevention
- The TAG endorsed the draft of Regional Guide for Accelerated Control on Japanese Encephalitis in the Western Pacific, taking into account the inputs provided during the TAG meeting

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

The most recent meeting was conducted 4-5 December 2019 in Geneva, Switzerland but the summary of discussions has not yet been released.

5.4 Global Immunisation News and other items and resources

- Latest news available here: https://www.who.int/immunization/newsroom/en/
- The Regional Verification Commission declared that Bahrain, Iran and Oman achieved elimination status for measles and rubella
- The Sixteenth Annual Meeting on Surveillance, Preparedness and Response to Meningitis Outbreaks in Africa & 6th Meeting of MenAfrinet Partners was held in Cameroon 22–24 October 2019
- Global NITAG Network Meeting in Atlanta, USA 24–25 February 2020

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6 Other items

6.1 Published information on assessment and registration of vaccines in Australia by TGA

New/updated registrations for vaccines:

- Fluad Quad is indicated for the active immunisation against influenza in persons 65 years of age and older

6.2 Global measles outbreaks

- Many countries around the world are experiencing measles outbreaks. As of 5 November 2019, there have been 413,308 confirmed cases reported to WHO through official monthly reporting by 187 Member States in 2019 - https://www.who.int/csr/don/26-november-2019-measles-global_situation/en/

- Samoa – on 16 October 2019, the Samoa Ministry of Health (MoH) declared a measles outbreak with a state of emergency being declared on 15 November 2019. From 1 January through 4 December 2019, a total of 4,217 confirmed and suspected cases including 62 measles associated deaths have been reported, with the majority of cases reported among children under 5 years of age
- On 20 November 2019, Samoan authorities launched a mass vaccination campaign which initially targeted all boys and girls aged 6 months to 19 years and women aged 20 to 35 years (unless pregnant)
- On 2 December 2019, the target age group was expanded to include people aged 6 months to 60 years. As of 1 December 2019, over 77,000 doses of measles-containing-vaccine have been administered through the mass vaccination campaign initiated on 20 November by the Ministry of Health (MoH) - https://www.who.int/csr/don/15-december-2019-measles-pacific-island-countries-and-areas/en/

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7 Upcoming meetings and agendas

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

- 26–27 February 2020
- 24–25 June 2020
- 28–29 October 2020

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

- 20–21 February 2020
- 21–22 May 2020
- 20–21 August 2020
- 12–13 November 2020

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)

- 5–6 February 2020
- 10–11 June 2020
- 23–24 September 2020

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

- 31 March–2 April 2020
- 6–8 October 2020
- 23–25 March 2021
- 5–7 October 2021
- 5–7 April 2022
- 4–6 October 2022

WHO-GACVS (https://www.who.int/vaccine_safety/committee/en/)

- 3–4 June 2020
- 2–3 December 2020
- 2–3 June 2021
- 1–2 December 2021