(Updated 27 February 2015)

Table 3: Recommendations* for Interrupted or Delayed Routine Immunization - Summary of WHO Position Papers

Antigen		Age of 1st Dose	Doses in Primary Series (min interval between doses)**	Interrupted primary series***	Doses for those who start vaccination late		Booster				
					If \leq 12 months of age	If > 12 months of age					
Recommendations for all immunization programmes											
BCG ¹		As soon as possible after birth	1 dose	NA	1 dose	Not recommended	Not recommended				
Hepatitis B ²		As soon as possible after birth (<24h)	Birth dose <24 hrs plus 2-3 doses with DTP (4 weeks)	Resume without repeating previous dose	3 doses	3 doses	Not recommended				
Polio ³	OPV + IPV	6 weeks (see footnote for birth dose)	4 doses (IPV dose to be given with OPV dose from 14 weeks of age) (4 weeks)	Resume without repeating previous dose	4 doses (IPV to be given with 1st dose of OPV)	4 doses (IPV to be given with 1st dose of OPV)	Not recommended				
	IPV / OPV Sequential	8 weeks (IPV 1st)	1-2 doses IPV and 2 doses OPV (4 weeks)	Resume without repeating previous dose	1-2 doses IPV and 2 doses OPV	1-2 doses IPV and 2 doses OPV	Not recommended				
	IPV	8 weeks	3 doses (4 weeks)	Resume without repeating previous dose	3 doses	3 doses	If the primary series begins < 2 months of age, booster to be given at least 6 months after the last dose				
DTP ⁴		6 weeks (min)	3 doses (4 weeks)	Resume without repeating previous dose	3 doses	3 doses with interval of 2 months between 1st & 2nd dose, and 6-12 months between 2nd & 3rd dose (if > 6 yrs use only aP containing vaccine; if > 7 yrs of age use Td containing vaccine)	DTP booster at 1-6 yrs of age (preferable in 2nd yr of life); Use DTaP if > 6 yrs and dTap if > 7 yrs) Td booster in adolescence, and another in adulthood or pregnancy (for total of 6 doses if primary series started in childhood).				
Haemophilus influenzae type b ⁵	Option 1 Option 2	6 weeks (min)	3 doses (4 weeks) 2-3 doses (8 weeks if 2 doses; 4 weeks if 3 doses)	Resume without repeating previous dose	3 doses 2-3 doses	1 dose >5 yrs not recommended if healthy	None At least 6 months (min) after last dose				
Pneumococcal (Conjugate) ⁶		6 weeks (min)	3 doses with DTP (4 weeks) or 2 doses (8 weeks)	Resume without repeating previous dose	2-3 doses	1-2 yrs: 2 doses 2-5 yrs at high-risk: 2 doses	Booster at 9-15 months if following 2 dose schedule Another booster if HIV+ or preterm neonate				
Rotavirus ⁷	Rotarix	6 weeks (min)	2 doses with DTP (4 weeks)	Resume without repeating previous dose	2 doses	> 24 months limited benefits	Not recommended				
	Rota Teq	6 weeks (min)	3 doses with DTP (4 weeks)	Resume without repeating previous dose	3 doses	> 24 months limited benefits	Not recommended				
Measles 8		9 or 12 months (6 months min, see footnote)	2 doses (4 weeks)	Resume without repeating previous dose	2 doses	2 doses	Not recommended				
Rubella ⁹		9 or 12 months	1 dose with measles containing vaccine	NA	1 dose	1 dose	Not recommended				
HPV 10		As soon as possible from 9 years of age (females)	2 doses (5 months)	If 1st dose given before 15 years of age resume without repeating previous dose	NA	Girls: 9-13 years 2 doses (see footnote)	Not recommended				

* For some antigens the WHO position paper does not provide a recommendation on interrupted or delayed schedules at this present time. When the position paper is next revised this will be included. In the meantime, some of the recommendations are based on expert opinion. ** See Table 2: Summary of WHO Position Papers - Recommended Routine Immunizations for Children for full details (www.who.int/immunization/documents/positionpapers/).

*** Same interval as primary series unless otherwise specified.

Table 3: Recommendations* for Interrupted or Delayed Routine Immunization Summary of WHO Position Papers (Updated 27 February 2015)

Antigen		Are of 1st Dece	Doses in Primary	Interrupted	Doses for those who start vaccination late		Deceter Dece				
	Antigen	Age of 1st Dose	Series (min interval between doses)**	primary series***	If \leq 12 months of age	If > 12 months of age	Booster Dose				
Recommendations for certain regions											
Japanese Encephalitis ¹¹	Inactivated Vero cell- derived vaccine	6 months	2 (4 weeks) generally	Resume without repeating previous dose	2 doses (generally)	2 doses (generally)					
	Live attentuated Live recombinant vaccine	8 months 9 months	1 1	NA NA	1 dose 1 dose	1 dose 1 dose	Not recommended				
Yellow Fever ¹²		9-12 months	1 dose with measles containing vaccine	NA	1 dose	1 dose	Not recommended				
Tick-Borne Encephalitis 13	FSME-Immun & Encepur	≥ 1 yr	3 doses (1st to 2nd 1-3 mos; 2nd to 3rd 12 mos)	Resume without repeating previous dose	3 doses	3 doses	At least 1 booster				
	TBE_Moscow & EnceVir	≥3 yr	3 doses (1st to 2nd 1-7 mos; 2nd to 3rd 12 mos)	Resume without repeating previous dose	3 doses	3 doses	Every 3 years				
Recommend	ations for some high-ri	sk populations									
Typhoid ¹⁴	Vi PS	2 years (min)	1 dose	NA If interruption between	Not recommended	1 dose	Every 3 years				
	Ty21a	Capsules 5 years (min) (see footnote)	3-4 doses (1 day) (see footnote)	doses is < 21 days resume without repeating previous dose; If > 21 days restart primary series	Not recommended	> 5 yrs: 3-4 doses	Every 3-7 years				
Cholera ¹⁵	Dukoral (WC-rBS)	2 years (min)	2-5 yrs: 3 doses	If interval since last	Not recommended	2-5 yrs: 3 doses	2-5 yrs: every 6 months. If booster is delayed > 6 months the primary series must be repeated.				
			≥ 6 yrs: 2 doses (≥ 7 days)	dose ≥ 6 weeks restart primary series		> 6 yrs: 2 doses	 >6 yrs: every 2 years. If booster is delayed > 2 yrs the primary series must be repeated. 				
	Shanchol and mORCVAX	1 year (min)	2 doses (2 weeks)	Resume without repeating previous dose	Not recommended	2 doses	After 2 years				
Meningococcal 16	MenA conjugate (5µg)	9-18 months	1	NA	2 doses if < 9 months with 8 week interval	1 dose of 5µg up to 24 months	Not recommended				
	MenC conjugate	2-11 months	2 (8 weeks min)	Resume without repeating previous dose	2 doses	1 dose	2-11 months of age after 1 year				
		>12 months	1	NA							
	Quadrivalent conjugate	9-23 months	2 (12 weeks min)	Resume without repeating previous dose	2 doses	1 dose					
		≥ 2 years	1	NA							
Hepatitis A ¹⁷		1 year (min)	At least 1 dose		Not recommended	At least 1 dose	Not recommended				
Rabies ¹⁸		As required	3 doses (1st to 2nd 7 days; 2nd to 3rd 14-21 days)	Resume without repeating previous dose; Interval between last two doses should be 14 days minimum	3 doses	3 doses	Only if occupation puts a frequent or continual risk of exposure				
Recommendations for immunization programmes with certain characteristics											
Mumps ¹⁹		12-18 months	2 doses with measles containing vaccine (4 weeks)	Resume without repeating previous dose	Not recommended	2 doses	Not recommended				
Seasonal influenza (inactivated tri- and qudri-valent) ²⁰		6 months (min)	< 9 yrs: 2 doses (4 weeks) ≥ 9 yrs: 1 dose	Resume without repeating previous dose	2 doses	< 9 yrs: 2 doses ≥ 9 yrs: 1 dose	Revaccinate annually 1 dose only				
Varicella ²¹		12-18 months	1-2 (4 weeks – 3 months, depending on manufacturer)	Resume without repeating previous dose	Not recommended	1-2 doses					

Summary Table 3 - Notes

- The attached table summarizes the WHO recommendations for interrupted or delayed routine vaccination. Its purpose is to assist national decision-makers and programme managers to develop appropriate policy guidance in relation to their national immunization schedule.
- This table is designed to be used together with two other summary tables Table 1: Summary of WHO Position Papers Recommendations for Routine Immunization; and Table 2: Summary of WHO Position Papers Recommended Routine Immunization for Children.
- Vaccines can generally be co-administered (i.e. more than one vaccine given at different sites during the same visit). Recommendations that explicitly endorse co-administration are indicated in the footnotes. Lack of an explicit co-administration recommendation is often due to a lack of evidence and does not necessarily imply that the vaccine cannot be co-administered. Exceptions to co-administration are stated.
- Refer to http://www.who.int/immunization/positionpapers/ for the most recent version of this table (and Tables 1 and 2) and position papers.

¹BCG

- Position paper reference: <u>Weekly Epid. Record (2004, 79: 27-38)</u> [pdf 468kb]
- Expert opinion indicates that vaccination of children older than 12 months of age is usually of limited benefit (although it is not harmful or contraindicated).
- BCG vaccination of adolescents and adults has shown variation in protective efficacy with geographical region, possibly as a consequence of differences in previous exposure to environmental mycobacteria. See position paper for details.
- Infants who are HIV positive or unknown HIV status with symptoms consistent with HIV should not be vaccinated. Reference: <u>Weekly Epid. Record (2007, 82: 193-196)</u> [pdf 167kb]

² Hepatitis B

- Position paper reference: Weekly Epid. Record (2009, 84: 405-420) [pdf 830kb]
- In general, the dose for infants and children (aged < 15 years) is half the recommended adult dose.
- Co-administration of HepB vaccine does not interfere with the immune response to any other vaccine and vice versa.
- Data on immunogenicity suggest that in any age group, interruption of the vaccination schedule does not require restarting the vaccine series. If the primary series is interrupted after the first dose, the second dose should be administered as soon as possible and the second and third doses separated by a minimum interval of 4 weeks; if only the third dose is delayed, it should be administered as soon as possible.

³ Polio

Position paper reference: <u>Weekly Epid. Record (2014, 89: 73-92)</u> [pdf 836kb]

OPV plus IPV

- WHO no longer recommends an OPV-only vaccination schedule. For all countries currently using OPV only, at least 1 dose of IPV should be added to the schedule.
- In polio-endemic countries and in countries at high risk for importation and subsequent spread, WHO recommends an OPV birth dose (a zero dose) followed by a primary series of 3 OPV and at least 1 IPV doses.
- The birth dose of OPV should be administered at birth, or as soon as possible after birth, to maximize the seroconversion rates with subsequent doses and to induce mucosal protection.

- The primary series consisting of 3 OPV doses plus 1 IPV dose can be initiated from the age of 6 weeks with a minimum interval of 4 weeks between the OPV doses. If 1 dose of IPV is used, it should be given from 14 weeks of age (when maternal antibodies have diminished and immunogenicity is significantly higher) and can be co-administered with an OPV dose.
- The primary series can administered according to the regular schedules of national immunization programmes, for example at 6, 10, and 14 weeks (OPV1, OPV2, OPV3+IPV), or at 2, 4, and 6 months (OPV1, OPV2+IPV, OPV3 or OPV1, OPV2, OPV3+IPV). Both OPV and IPV may be coadministered with other infant vaccines.
- For infants starting the routine immunization schedule late (age > 3 months) the IPV dose should be administered at the first immunization contact.
- As an alternative to the intramuscular injection of a full IPV dose, countries can consider using a 1/5 fractional doses via the intradermal route, but the programmatic cost and logistical implications of this option should be considered.
- There is no demonstrated benefit from booster doses of OPV after completion of the recommended primary series of 3 OPV doses and at least 1 IPV dose.
- The implementation of the new schedule (3 OPV doses + 1 IPV dose) does not replace the need for supplemental immunization activities (SIAs). Those countries with insufficient routine immunization coverage that rely on SIAs to increase population immunity should continue to do so until routine immunization improves.

Sequential IPV-OPV schedule

- In countries with high immunization coverage (e.g. 90%–95%) and low importation risk (neighbouring countries and connections with similarly high immunization coverage) an IPV– OPV sequential schedule can be used when VAPP is a significant concern.
- The initial administration of 1 or 2 doses of IPV should be followed by ≥2 doses of OPV to ensure both sufficient levels of protection in the intestinal mucosa and a decrease in the burden of VAPP.
- For sequential IPV–OPV schedules, WHO recommends that IPV be given at 2 months of age (e.g. a 3-dose IPV-OPV-OPV schedule) or at 2 months and 3–4 months of age (e.g. a 4-dose IPV-IPV-OPV-OPV schedule) followed by at least 2 doses of OPV. Each of the doses in the primary series should be separated by 4–8 weeks depending on the risk of exposure to poliovirus in early childhood.

IPV-only schedule

- An IPV-only schedule may be considered in countries with both sustained high immunization coverage and the lowest risk of both WPV importation and transmission.
- A primary series of 3 doses of IPV should be administered beginning at 2 months of age.
- If the primary series begins earlier (e.g. with a 6, 10 and 14-week schedule) then a booster dose should be given after an interval of ≥6 months (for a 4-dose schedule).

⁴ DTP (Diphtheria, Tetanus and Pertussis)

- Position paper reference: Diphtheria <u>Weekly Epid. Record (2006, 81: 24-32)</u> [pdf 214kb]; Tetanus - <u>Weekly Epid. Record (2006, 81: 198-208)</u> [pdf 229kb]; Pertussis - <u>Weekly Epid.</u> <u>Record (2010, 85: 385-400)</u> [pdf 320kb]
- WHO recommends that the primary series of 3 doses should be given in infancy (aged < 1 year). The exact timing of the booster should be flexible to take account of the most appropriate health service contacts in different countries. Ideally a DTP booster should be provided at 1-6 years of age. A Td booster should be provided in adolescence, and another in adulthood to further assure life-long protection against tetanus (a total of 6 doses when DTP primary series is given in infancy).

- Delayed or interrupted DTP series For children 1-7 years or older who have not previously been immunized should receive three doses of wP or aP vaccine, with an interval of 2 months between the first and second dose and an interval of 6-12 months between the second and third. Children whose vaccination series has been interrupted should have their series resumed, without repeating previous doses. For unvaccinated individuals 7 years of age and older, Td combination vaccine can be administered, 2 doses 1-2 months apart and a third dose after 6-12 months can be used with subsequent boosters at least 1 year apart for a total of 5 appropriately spaced doses to obtain same long term protection. See position paper for details of interrupted immunization schedules.
- For previously non-immunized adolescents and adults, the recommended tetanus schedule is 2 doses administered at least 4 weeks apart followed by a third dose administered at least 6 months after the second dose, and subsequent boosters at least 1 year apart. Those who receive their first tetanus vaccine doses as adolescents or adults require a total of only 5 appropriately spaced doses to obtain long-term protection. See position paper for details.

⁵ *Haemophilus influenzae* type b (Hib)

- Position paper reference: <u>Weekly Epid. Record (2013, 88: 413-428)</u> [pdf 209kb]
- The use of Hib vaccines should be part of a comprehensive strategy to control pneumonia including exclusive breastfeeding for six months, hand washing with soap, improved water supply and sanitation, reduction of household air pollution, and improved case management at community and health facility levels.
- WHO recommends that any one of the following Hib immunization schedules may be followed: 3 primary doses without a booster (3p); 2 primary doses plus a booster (2p+1); and 3 primary doses with a booster (3p+1).
- Because serious Hib disease occurs most commonly in children aged between 4 months and 18 months, immunization should start from 6 weeks of age, or as early as possible thereafter.
- The number of primary doses should be set after consideration of the local epidemiology, vaccine presentation (Hib conjugate monovalent vaccine versus Hib conjugate vaccine in combination with other antigens) and how this fits into the overall routine immunization schedule.
- In countries where the peak burden of severe Hib disease occurs in young infants, providing 3 doses of vaccine early in life may confer a greater benefit.
- In some settings (e.g. where the greatest disease morbidity and mortality occur later, or where rate reductions of disease are not fully sustained after the routine use of Hib vaccine), it might be advantageous to give a booster dose by following either a 2p+1 or 3p+1 schedule.
- The interval between doses should be at least 4 weeks if 3 primary doses are given, and at least 8 weeks if 2 primary doses are given. Booster doses should be administered at least six months after completion of the primary series.
- If the vaccination course has been interrupted, the schedule should be resumed without repeating the previous dose. Children who start vaccination late, but are aged under 12 months, should complete the vaccination schedule (e.g. have 3 primary doses or 2 primary doses plus a booster).
- When a first dose is given to a child older than 12 months of age, only one dose is recommended.
- Hib vaccine is not required for healthy children after 5 years of age.
- The Hib conjugate vaccine is contraindicated in people with known allergies to any component of the vaccine. There are no other known contraindications or precautions.

⁶ Pneumococcal (Conjugate)

Position paper reference: <u>Weekly Epid. Record (2012, 87: 129-143)</u> [pdf 1.04 Mb]

- Pneumococcal conjugate vaccines (PCVs) are considered safe in all target groups for vaccination, also in immunocompromised individuals. The vaccines are not currently licensed for use in age groups that include women of childbearing age. Although theoretically highly unlikely to be harmful, there is no information on the safety of PCV10 and PCV13 during pregnancy.
- Except for very rare anaphylactic reactions that may follow the administration of any medicine, there are no contraindications to the use of these vaccines. However, it is advisable to defer vaccination until after an acute infection with temperature >39 °C.
- When injected at different sites, PCVs can be administered concurrently with any other vaccines in infant immunization programmes.
- When primary immunization is initiated with one of these vaccines, it is recommended that remaining doses are administered with the same product. Interchangeability between PCV10 and PCV13 has not yet been documented. However, if it is not possible to complete the series with the same type of vaccine, the other PCV product should be used.
- For infants, 3 primary doses (the 3p+0 schedule) or, as an alternative, 2 primary doses plus a booster (the 2p+1 schedule).
- In choosing between the 3p+0 and 2p+1 schedules, countries should consider locally relevant factors including the epidemiology of pneumococcal disease, the likely coverage, and the timeliness of the vaccine doses.
- If disease incidence peaks in young infants (<32 weeks of age), a 2p+1 schedule might not offer optimal individual protection for certain serotypes (e.g. 6B, 23F) compared to a 3p+0 schedule, particularly in the absence of herd protection.
- In contrast, higher antibody levels are induced by the third (booster) dose in a 2p+1 schedule compared to the third dose in a 3p+0 schedule. This may be important for duration of protection or effectiveness against some serotypes.
- If the 3p+0 schedule is used, vaccination can be initiated as early as 6 weeks of age with an interval between doses of 4–8 weeks, depending on programmatic convenience.
- If the 2p+1 schedule is selected, the 2 primary doses should ideally be completed by six months of age, starting as early as 6 weeks of age with a minimum interval of 8 weeks or more between the two doses (for infants aged ≥7 months a minimum interval of 4 weeks between doses is possible). One booster dose should be given between 9–15 months of age.
- Previously unvaccinated or incompletely vaccinated children (including those who had laboratory confirmed invasive pneumococcal disease) should be vaccinated using the recommended ageappropriate regimens. Interrupted schedules should be resumed without repeating the previous dose.
- HIV-positive infants and pre-term neonates who have received their 3 primary vaccine doses before reaching 12 months of age may benefit from a booster dose in the second year of life.
- Catch-up vaccination as part of introduction will accelerate herd protection and therefore the PCV impact on disease and carriage. Maximized protection at the time of introduction of PCV10 or PCV13 can be achieved by providing 2 catch-up dose(s) at an interval of at least 8 weeks to unvaccinated children aged 12–24 months and to children aged 2–5 years who are at high risk of pneumococcal infection.
- Further data are needed from different epidemiological settings on the impact of large-scale PCV vaccination of individuals >50 years of age in order to establish the relative priority of immunization programmes in that age group. However, given the documented effects of herd protection in adult age groups following routine infant immunization with PCV7, higher priority should normally be given to introducing and maintaining high coverage of infants with PCVs.
- The use of pneumococcal vaccine should be seen as complementary to the use of other pneumonia control measures, such as appropriate case management, promotion of exclusive breastfeeding for first 6 months of life, and the reduction of known risk factors, such as indoor pollutants and tobacco smoke.

- For polysaccharide pneumococcal vaccine see position paper: <u>Weekly Epid. Record (2008, 83:</u> <u>373-384</u>) [pdf 308kb]
- In resource-limited settings where there are many competing health priorities, evidence does not support routine immunization of the elderly and high-risk populations with PPV23. Also, because of the low level of evidence for benefit, routine PPV23 vaccination of HIV-infected adults is not recommended in such settings. In countries that do not routinely administer PPV23 to high-risk populations, data are insufficient to recommend introducing this vaccine to reduce the morbidity and mortality associated with influenza.

⁷ Rotavirus

- Position paper reference: Weekly Epid. Record (2013, 88: 49-64) [pdf 950kb]
- Recommended to be included in all national immunization programmes.
- Early immunization is favoured with the first dose of rotavirus vaccine to be administered from 6 weeks of age, however, in order to benefit those who may come late infants can receive doses without age restriction. Because of the typical age distribution of rotavirus gastroenteritis (RVGE), rotavirus vaccination of children >24 months of age is not recommended.
- Rotarix is administered orally in a 2-dose schedule at the time of DTP1/penta and DTP2/penta with an interval of at least 4 weeks between doses.
- RotaTeq vaccine is administered orally in a 3-dose schedule at the time of DTP1/penta, DTP2, and DTP3 contacts, with an interval of at least 4 weeks between doses.
- Rotavirus vaccinations can be administered simultaneously with other vaccines in the infant immunization programme.
- Apart from a low risk of intussusception (about 1-2 per 100 000 infants vaccinated) the current rotavirus vaccines are considered safe and well tolerated.
- Severe allergic reaction (e.g. anaphylaxis) after a previous dose, and severe immunodeficiency including severe combined immunodeficiency, are contraindications for rotavirus vaccination.
- Precautions are necessary if there is a history of intussusception or intestinal malformations, chronic gastrointestinal disease, and severe acute illness. Vaccination should be postponed in case of ongoing acute gastroenteritis or fever with moderate to severe illness.
- The use of rotavirus vaccines should be part of a comprehensive strategy to control diarrhoeal diseases with the scaling up of both prevention (exclusive breastfeeding for 6 months, vitamin A supplementation, safe drinking water, hygiene/handwashing with soap, and sanitation) and treatment (low-osmolarity ORS, zinc and continued feeding).

⁸ Measles

- Position paper reference: <u>Weekly Epid. Record (2009, 84: 349-360)</u> [pdf 724kb]
- Reaching all children with two doses of measles containing vaccine (MCV) should be the standard for all national immunization programmes.
- Delivery of the second dose (MCV2) may occur either at a scheduled age through routine services or periodically through mass campaigns, depending on which strategy achieves the higher coverage. A MCV2 dose may be added to the routine immunization schedule in countries that have achieved > 80% coverage of measles first dose (MCV1) at the national level for 3 consecutive years as determined by the most accurate means available (e.g. survey or WHO/ UNICEF estimates). In general, countries that do not meet this criterion should prioritize improving MCV1 coverage and conducting high-quality follow-up SIAs, rather than adding MCV2 to their routine schedule.
- In countries with ongoing transmission in which the risk of measles mortality remains high, MCV1 should be given at age 9 months. MCV2 should be given between 12-18 months, as providing MCV2 in the 2nd year of life reduces the rate of accumulation of susceptible children

and the risk of an outbreak.

- In countries with low rates of measles transmission (that is, those that are near elimination) and where there is a low risk of measles infection among infants, the first dose may be administered at age 12 months to take advantage of the higher seroconversion rates achieved at this age (>90% seroconversion). In these countries the optimal age for delivering a routine 2nd dose of measles is based on programmatic considerations that achieve the highest coverage and hence the highest population immunity. Administration of the second dose at age 15-18 months ensures early protection of the individual, slows accumulation of susceptible young children and may correspond with other routine immunizations (for example, DTP booster). If first dose coverage is high (>90%) and school enrolment is high (>95%), giving the second dose at school entry may be an effective strategy for achieving high coverage and preventing outbreaks in schools.
- Combined vaccines (Measles and Rubella or Measles, Mumps and Rubella) may not be optimal for use in countries where vaccine coverage for measles vaccine of at least 80% cannot be achieved or maintained.
- In areas where there is a high incidence of both HIV infection and measles, MCV1 may be offered as early as age 6 months. Two additional doses of measles vaccine should be administered to these children according to the national immunization schedule.
- As a general rule, live vaccines should be given either simultaneously, or at intervals of 4 weeks. An exception to this rule is OPV, which can be given at any time before or after measles vaccination, without interference in the response to either vaccine.
- Available data suggest that vaccines against measles, yellow fever, and Japanese encephalitis
 may be administered at the same time at different injection sites. Interference may occur
 between MMR and yellow fever vaccines if they are simultaneously administered to children <
 2 years of age.

⁹ Rubella

- Position paper reference: Weekly Epid. Record (2011, 86: 301-316) [pdf 413kb]
- All countries that have not yet introduced rubella vaccine, and are providing 2 doses of measles vaccine using routine immunization, or SIAs, or both, should consider including rubella containing vaccines (RCVs) in their immunization programme. Countries planning gto introduce RCVs should review the epidemiology of rubella, including the susceptibility profile of the population; assess the burden of CRS; and establish rubella and CRS prevention as a public health priority.
- Because rubella is not as highly infectious as measles and because the effectiveness of 1 dose
 of an RCV is > 95% even at 9 months of age, only 1 dose of rubella vaccine is required to
 achieve rubella elimination if high coverage is achieved. However, when combined with measles
 vaccination, it may be easier to implement a second dose of RCV's using the same combined MR
 vaccine or MMR vaccine for both doses.
- RCV's can be administered concurrently with inactivated vaccines. As a general rule, live vaccines should be given either simultaneously with RCV's, or at least 4 weeks apart. An exception to this is oral polio vaccine, which can be given at any time before or after RCV's without interfering in the response to either vaccine.
- Interference may occur between MMR and yellow fever vaccines if they are simultaneously administered to children < 2 years of age.
- Because of a theoretical, but never demonstrated, teratogenic risk rubella vaccination in pregnant women should be avoided in principle, and those planning a pregnancy are advised to avoid pregnancy for 1 month following vaccination.
- Administration of blood or blood products before or shortly after vaccination may interfere with vaccine efficacy. If using only rubella vaccines persons who received blood products should wait

at least 3 months before vaccination and, if possible, blood products should be avoided for up to 2 weeks post-vaccination. Vaccinated persons are not eligible to donate blood for 1 month after vaccination.

¹⁰ Human Papillomavirus (HPV)

- Position paper reference : <u>Weekly Epid. Record (2014, 89:465-492)</u> [pdf 939kb]
- Recommended target population for the prevention of cervical cancer: females aged 9–13 years, prior to becoming sexually active.
- A 2-dose schedule with an interval of 6 months between doses is recommended for females younger than 15 years. Those females who are ≥15 years at the time of the second dose are also adequately protected by 2 doses.
- There is no maximum recommended interval between doses. However, an interval no greater than 12-15 months is suggested in order to complete the schedule promptly and before becoming sexually active.
- If the interval between doses is shorter than 5 months, then a third dose should be given at least 6 months after the first dose.
- A 3-dose schedule (0, 1–2, 6 months) is recommended for females aged 15 years and older, and for those know to be immunocompromised and/or HIV-infected (regardless of whether they are receiving antiretroviral therapy). It is not necessary to screen for HPV infection or HIV infection prior to HPV vaccination.
- These schedule recommendations apply to both the bivalent and quadrivalent vaccines.
- Both HPV vaccines can be co-administered with other live and non-live vaccines using separate syringes and different injection sites.
- Data on the safety of HPV vaccination in pregnancy are limited, and HPV vaccination of pregnant women should be avoided.
- HPV vaccines should be introduced as part of a coordinated strategy to prevent cervical cancer.
- HPV vaccination of males is not recommended as a priority, especially in resource-constrained settings, as the available evidence indicates that the first priority should be for cervical cancer reduction by timely vaccination of young females and high coverage with each dose.

¹¹ Japanese Encephalitis (JE)

- Position paper reference : Weekly Epid. Record (2015, 90: 69-88) [pdf 950 kb].
- JE vaccination should be integrated into national immunization schedules in all areas where JE is recognized as a public health priority.
- The most effective immunization strategy in JE endemic settings is a one-time campaign in the primary target population, as defined by local epidemiology (typically children aged <15 years), followed by incorporation of JE vaccine into the routine childhood immunization programme.
- The following vaccine dosing schedules and age of administration are recommended. The need for a booster dose in endemic settings has not been clearly established for any of the vaccines listed below:
 - Inactivated Vero cell-derived vaccine: Primary series according to manufacturer's recommendations (these vary by product), generally 2 doses at 4-week intervals starting the primary series at ≥6 months of age in endemic settings
 - Live attenuated vaccine: Single dose administered at ≥ 8 months of age
 - Live recombinant vaccine: Single dose administered at \geq 9 months of age
- Preferably, inactivated mouse brain-derived vaccines should be replaced by the newer generation

JE vaccines discussed in this position paper. Inactivated mouse brain-derived vaccines may continue to play a role in combatting JE in some countries, but overall these products have a less favourable safety profile due to their increased reactogenicity compared to newer JE vaccines. Other disadvantages include the variability of manufacturing, the cost, the higher number of doses required and the need for boosters.

- Despite a lack of comprehensive immunogenicity/effectiveness and safety data for all possible combinations of JE and other routine vaccines, co-administration for programmatic reasons seems acceptable, even in the context of mass campaigns.
- Inactivated JE vaccine can be used in immunocompromised persons including HIV-infected individuals, but the immune response may be lower than in fully immunocompetent persons. Inactivated Vero cell-derived vaccines should be used preferentially over live attenuated or live recombinant vaccines in immunocompromised persons. HIV testing is not a prerequisite for vaccination.
- If the JE risk is sufficient to warrant vaccination of pregnant women, inactivated Vero cellderived vaccines should be used preferentially over live attenuated or live recombinant vaccines based on the general precautionary principle against using live vaccines in pregnant women especially if alternative types of vaccines are available. Pregnancy testing is not a prerequisite for JE vaccination. Inadvertent administration of live attenuated or live recombinant JE vaccine to a pregnant woman is not an indication for termination of the pregnancy.

¹² Yellow Fever

- Position paper reference: Weekly Epid. Record (2013, 88: 269-284) [pdf 1.24mb]
- WHO recommends that all endemic countries should introduce YF vaccine into their routine immunization programmes.
- A single dose of YF vaccine is sufficient to confer sustained life-long protective immunity against YF disease; a booster dose is not necessary.
- It is recommended that YF vaccine be given to children at age 9-12 months at the same time as the measles vaccine.
- The vaccine is contraindicated in children aged <6 months and is not recommended for those aged 6-8 months, except during epidemics when the risk of infection with the YF virus is very high. Other contraindications for YF vaccination are severe hyper-sensitivity to egg antigens and severe immunodeficiency.
- Preventive mass vaccination campaigns are recommended for inhabitants of areas at risk of YF where there is low vaccination coverage. Vaccination should be provided to everyone aged ≥ 9 months, in any area with reported cases. Noting that YF is a live vaccine, a risk-benefit assessment should be undertaken for all pregnant and lactating women.
- Vaccine should be offered to all unvaccinated travelers aged ≥ 9 months, travelling to and from at-risk areas, unless they belong to the group of individuals for whom YF vaccination is contraindicated.
- YF vaccine may be administered simultaneously with other vaccines.

¹³ Tick-Borne Encephalitis (TBE)

- Position paper reference: Weekly Epid. Record (2011, 86: 241-256) [pdf 318kb]
- Since the incidence of tick-borne encephalitis may vary considerably between and even within geographical regions, public immunization strategies should be based on risk assessments conducted at country, regional or district level, and they should be appropriate to the local endemic situation. Therefore, establishing case reporting of the disease is essential before deciding on the most appropriate preventive measures to be taken.
- In areas where the disease is highly endemic (that is, where the average prevaccination

incidence of clinical disease is \geq 5 cases/100 000 population per year), implying that there is a high individual risk of infection, WHO recommends that vaccination be offered to all age groups, including children.

- Because the disease tends to be more serious in individuals aged >50–60 years this age group constitutes an important target for immunization.
- Where the prevaccination incidence of the disease is moderate or low (that is, the annual average during a 5-year period is <5/100 000) or is limited to particular geographical locations or certain outdoor activities, immunization should target individuals in the most severely affected cohorts.
- People travelling from non-endemic areas to endemic areas should be offered vaccination if their visits will include extensive outdoor activities.
- Vaccination against the disease requires a primary series of 3 doses; those who will continue to be at risk should probably have ≥1 booster doses.
- Within the considerable range of acceptable dose intervals, the relevant national authorities should select the most rational primary schedule for their national, regional or district immunization programmes.
- For the vaccines manufactured in Austria and Germany (FSME-Immun and Encepur) that can be given starting from > 1year of age an interval of 1–3 months is recommended between the first 2 doses, and 5–12 months between the second and third doses. When rapid protection is required, for example for people who will be travelling to endemic areas, the interval between the first 2 doses may be reduced to 1–2 weeks.
- With the vaccines manufactured in the Russian Federation (TBE-Moscow and EnceVir) the recommended intervals are 1–7 months between the first 2 doses, and 12 months between the second and third doses. Booster doses are recommended every 3 years for those at continued risk of exposure.
- The currently recommended booster interval should be maintained until more data have been obtained on the duration of protection induced by the Russian vaccines.
- Regardless of the duration of the delay, interrupted schedules should be resumed without repeating previous doses.

¹⁴ Typhoid

- Position paper reference: Weekly Epid. Record (2008, 83: 49-59) [pdf 297kb]
- Recommended for school-age and/or preschool-age children in areas where typhoid fever in these age groups is shown to be a significant public health problem, particularly where antibiotic-resistant S. Typhi is prevalent.
- Vaccine option- Vi polysaccharide typhoid vaccine requires one parenterally administered dose which maybe given after the age of 2 years; the liquid form of Ty21a live oral vaccine (for use in individuals from the age of 2 years) is no longer available; the capsule form of Ty21a (for use in individuals from the age of 5 years) requires 3 or 4 orally administered doses. See position paper for further details.
- If the schedule for Ty21a is interrupted by an interval longer than 21 days, expert opinion indicates that the series should be restarted from the beginning. If the interruption is less than 21 days, resume vaccination without repeating the previous dose.
- Booster- In most endemic settings, a booster dose of the concerned vaccine 3 to 7 years after the primary immunization seems appropriate.

¹⁵ Cholera

- Position paper reference: <u>Weekly Epid. Record (2010, 85, 117-128)</u> [pdf 283kb]
- In cholera-endemic countries, vaccinating the entire population is not warranted. Rather,

vaccination should be targeted at high-risk areas and population groups. The primary targets for cholera vaccination in many endemic areas are preschool-aged and school aged children. Other groups that are especially vulnerable to severe disease and for which the vaccines are not contraindicated may also be targeted, such as pregnant women and HIV-infected individuals. Consider vaccinating older age groups if funding is available.

- Two types of oral cholera vaccines are available: (i) Dukoral (WC-rBS) and (ii) Sanchol and mORCVAX. The live attenuated single-dose vaccine (CVD 103-HgR) is no longer produced. The injectable vaccine is still manufactured in a few countries but its use is not recommended mainly because of its limited efficacy and short duration of protection.
- <u>Dukoral</u> is not licensed for children < 2 years. Children aged 2-5 years should receive 3 doses
 >7 days apart (but not more than 6 weeks). Intake of food and drink should be avoided for 1 hour before and after vaccination. If the interval between doses is delayed >6 weeks, primary vaccination should be restarted. One booster dose is recommended every 6 months, and if the interval between primary immunization, and the booster is >6 months, primary immunization must be restarted.
- Adults and children > 6 years should receive 2 doses of Dukoral > 7 days apart (but not more than 6 weeks). Intake of food and drink should be avoided for 1 hour before and after vaccination. If the interval between doses is delayed >6 weeks, primary vaccination should be restarted. A booster dose every 2 years is recommended. If the interval between the primary series and booster immunization is > 2 years, primary immunization must be repeated.
- <u>Shanchol and mORCVAX</u>: two liquid doses orally 14 days apart for individuals > 1 year. A booster dose is recommended after 2 years.

¹⁶ Meningococcal

- Position paper reference: <u>Weekly Epid. Record (2011, 86: 521-540)</u> [pdf 1.1Mb] and Update for MenA conjugate <u>Weekly Epid Record (2015, 90: 57-68)</u> [pdf 852KB]
- Conjugate vaccines are preferred over polysaccharide vaccines due to their potential for herd protection and their increased immunogenicity, particularly in children <2 years of age.
- Both conjugate and polysaccharide vaccines are efficacious and safe when used in pregnant women.
- MenA conjugate vaccine (5µg) a 1-dose schedule is recommended at 9-18 months of age based on local programmatic and epidemiologic considerations. The vaccine should be administered by deep intramuscular injection, preferably in the anterolateral aspect of the thigh. There is no reason to expect interference when co-administered with other vaccines. The need for a booster dose has not been established.
- If in a specific context there is a compelling reason to vaccinate infants younger than 9 months, a 2-dose schedule should be used starting at 3 months of age, with an interval of at least 8 weeks between doses.
- For monovalent MenC conjugate vaccine one single intramuscular dose is recommended for children aged >12 months, teenagers and adults. Children 2-11 months require 2 doses administered at an interval of a least 2 months and a booster about 1 year after. If the primary series is interrupted, vaccination should be resumed without repeating the previous dose.
- Quadrivalent conjugate vaccines (A,C,W135,Y-D and A,C,W135,Y-CRM) should be administered as one single intramuscular dose to individuals > 2 years. A,C,W135,Y-D is also licensed for children 9-23 months of age, and given as a 2-dose series, 3 months apart beginning at age 9 months. If the primary series is interrupted, vaccination should be resumed without repeating the previous dose.
- Meningococcal polysaccharide vaccines are less, or not, immunogenic in children under 2 years of age.
- Meningococcal polysaccharide vaccines can be used for those > 2 years of age to control

outbreaks in countries where limited economic resources or insufficient supply restrict the use of meningococcal conjugate vaccines. Polysaccharide vaccines should be administered to individuals > 2 years old as one single dose. One booster 3-5 years after the primary dose may be given to persons considered to be a continued high risk of exposure, including some health workers. See position paper for details.

¹⁷ Hepatitis A

- Position paper reference: Weekly Epid. Record (2012, 87: 261-276) [pdf 1.24 Mb]
- Hepatitis A vaccination is recommended for inclusion in the national immunization schedule for children ≥ 1 year if indicated on the basis of incidence of acute hepatitis A, change in the endemicity from high to intermediate, and consideration of cost-effectiveness.
- In highly endemic countries almost all persons are asymptomatically infected with HAV in childhood, which effectively prevents clinical hepatitis A in adolescents and adults. In these countries, large-scale vaccination programmes are <u>not</u> recommended.
- Countries with improving socioeconomic status may rapidly move from high to intermediate endemicity. In these countries, a relatively large proportion of the adult population is susceptible to HAV and large-scale hepatitis A vaccination is likely to be cost-effective and therefore is encouraged.
- For individual health benefit targeted vaccination of high-risk groups should be considered in low and very low endemicity settings. Those at increased risk of hepatitis A include travelers to areas of intermediate or high endemicity, those requiring life-long treatment with blood products, men who have sex with men, workers in contact with non-human primates, and injection drug users. In addition, patients with chronic liver disease are at increased risk for fulminant hepatitis A and should be vaccinated.
- Inactivated HAV vaccine is licensed for intramuscular administration in a 2-dose schedule with
 the first dose given at the age of 1 year or older. The interval between the first and second
 dose is flexible (from 6 months up to 4-5 years) but is usually 6-18 months. Countries may
 consider a 1-dose schedule as this option seems comparable in terms of effectiveness, and is
 less expensive and easier to implement. However, in individuals at substantial risk of contracting
 hepatitis A and in immunocompromised individuals, a 2-dose schedule is preferred. Inactivated
 HAV vaccines produced by different manufacturers, including combined hepatitis A vaccines,
 are interchangeable. Apart from severe allergic reaction to the previous dose, there is no
 contraindication to their use. These vaccines can be co-administered simultaneously with other
 routine childhood vaccines, and should be considered for use in pregnant women at definite risk
 of HAV infection.
- Live attenuated HAV vaccine is administered as a single subcutaneous dose to those ≥ 1 year of age. Severe allergy to components included in the live attenuated hepatitis A vaccine is a contraindication to their use. As a rule, live vaccines should not be used in pregnancy or in severely immunocompromised patients. There is no information available on co-administration of live attenuated hepatitis A vaccines with other routinely used vaccines.
- Vaccination against hepatitis A should be part of a comprehensive plan for the prevention and control of viral hepatitis, including measures to improve hygiene and sanitation and measures for outbreak control.

¹⁸ Rabies

- Position paper reference: <u>Weekly Epid. Record (2010, 85: 309-320)</u> [pdf 370]
- Production and use of nerve-tissue rabies vaccines should be discontinued and replaced with cell-culture-based vaccines (CCVs).
- Recommended for anyone who will be at continual, frequent or increased risk of exposure to the rabies virus, either as a result of their residence or occupation. Travellers with extensive outdoor exposure in rural high-risk areas where immediate access to appropriate medical care

may be limited should also be vaccinated regardless of the duration of stay. Where canine rabies is a public health problem, WHO encourages studies on the feasibility, cost-effectiveness, and long-term impact of incorporating rabies vaccination into the immunization programme for infants and children.

- The series is given by intramuscular or intradermal injection at 0, 7, and 21 or 28 days.
- Intramuscular administration: For adults and children aged ≥2 years, the vaccine should always be administered in the deltoid area of the arm; for children aged < 2 years, the anterolateral area of the thigh is recommended. Rabies vaccine should not be administered in the gluteal area, as the induction of an adequate immune response may be less reliable.
- Booster doses of rabies vaccines are not required for individuals living in or travelling to high-risk areas who have received a complete primary series of pre-exposure or post-exposure prophylaxis with a cell-culture-based rabies vaccine (CCV).
- Periodic booster injections are recommended only for people whose occupation puts them at continual or frequent risk of exposure. If available, antibody monitoring is preferred to the administration of routine boosters.
- Because vaccine-induced immunity persists in most cases for years, a booster is recommended only if rabies-virus neutralizing antibody titres fall to <0.5 IU/ml.
- Antibody testing should be done every 6 months for people at risk of laboratory exposure to high
 concentrations of live rabies virus, and every 2 years for professionals who are not at continual
 risk of exposure through their activities, such as certain categories of veterinarians and animal
 health officers.

¹⁹ Mumps

- Position paper reference: Weekly Epid. Record (2007, 82: 49-60) [pdf 311kb]
- Recommended for use in high performing immunization programs with the capacity to maintain coverage over 80% and where mumps reduction is a public health priority.
- If implemented, a combination vaccine of measles, mumps and rubella is recommended.
- As a general rule, live vaccines should be given either simultaneously, or at intervals of 4 weeks.
- Interference may occur between MMR and yellow fever vaccines if they are simultaneously administered to children < 2 years of age.

²⁰ Seasonal Influenza (Inactivated Vaccine)

- Position paper reference: Weekly Epid. Record (2012, 87: 461-476) [pdf 1.9 Mb]
- For countries considering the initiation or expansion of programmes for seasonal influenza vaccination, WHO recommends that pregnant women should have the highest priority. Children aged < 6 months are not eligible to receive currently licensed influenza vaccines and should be protected against influenza through vaccination of their mothers during pregnancy and through ensuring vaccination of close contacts.
- Additional risk groups to be considered are children aged 6-59 months, elderly persons ≥ 65 years of age, individuals with specific chronic medical conditions, and health-care workers. Countries with existing influenza vaccination programmes targeting any of these additional groups should continue to do so and should incorporate immunization of pregnant women into such programmes.
- A single dose is appropriate for those ≥ 9 years of age, including pregnant women. Inactivated influenza vaccine is safe to give throughout pregnancy.
- Children aged 6-59 months should receive 2 doses at least 4 weeks apart. Children aged 6-35 months should receive a pediatric dosage.
- Annual vaccination (or re-vaccination, if the vaccine strains are identical) is recommended. Previously vaccinated children 6-59 months require only one-dose.

²¹ Varicella

- Position paper reference: Weekly Epid. Record (2014, 89: 265-288) [pdf 889kb]
- Countries where varicella is an important public health burden could consider introducing varicella vaccination in the routine childhood immunization programme. However, resources should be sufficient to ensure reaching and sustaining vaccine coverage ≥ 80%. Decisionmaking on childhood varicella vaccination should also include consideration of the possible impact on herpes zoster.
- Depending on the goal of the vaccination programme, 1-2 doses should be given with the first dose administered at 12-18 months of age. The minimum interval between doses should be as recommended by the manufacturer, ranging from 4 weeks to 3 months.
- Countries with a high average age (≥ 15 years) of acquisition of infection could consider alternative vaccination strategies such as vaccination of adolescents and adults without evidence of varicella immunity. This strategy requires a 2-dose schedule.
- Varicella vaccination is contraindicated during pregnancy and pregnancy should be delayed for 4 weeks after vaccination. Termination of pregnancy is not indicated if vaccination was carried out inadvertently during pregnancy.
- Varicella vaccine can be administered concomitantly with other vaccines. Unless given together
 with other live viral vaccines (measles, MR, MMR), it should be administered at a minimum
 interval of 28 days.
- Countries should consider vaccination of potentially susceptible health-care workers (i.e. unvaccinated and with no history of varicella) with 2 doses of varicella vaccine.