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FOREWORD

Congratulations to the Philippine Society for Microbiology and Infectious Diseases (PSMID), AIDS Society of the Philippines (ASP) and the National AIDS and STI Prevention and Control Program (NASPCP) of the Department of Health of Health's National Center for Disease Prevention and Control (DOH-NCDPC), for the development of the Philippine Guidelines on Immunization for Adults Living with Human Immunodeficiency Virus 2010. This endeavor has been truly supported by DOH as the country scales up not only prevention and treatment but the holistic public health approach to combat HIV and AIDS in the country.

Prevention of HIV transmission among the most-at-risk population remains to be the primary focus of DOH ever since the first case of HIV was detected in 1984. In the spirit of achieving Universal Access to HIV Prevention, Treatment, Care and Support to HIV and AIDS, the DOH facilitated for the mechanism of providing various Anti-Retroviral (ARV) drugs to People Living with HIV (PLHIV) through its designated Treatment Hubs that are geographically accessible in the country in 2005. Provision of antiretroviral in these facilities is complemented by adherence counseling, free monitoring of key laboratory investigations, provision of drugs for common opportunistic infections (OI), prevention of ARV drug resistance, and continuing psychosocial supports which are provided not only by DOH Treatment Hubs but also thru its partner care and support non-government and faith-based organizations.

HIV infection is a lifetime diagnosis that is accompanied by various medical, psychosocial and even financial challenges that needs to be addressed. A very important medical condition significantly affecting the productivity and lifestyle of PLHIV is the occurrence of various opportunistic infections that may take place anytime during the HIV disease spectrum. Reduction of co-morbidities as part of the AIDS syndrome will certainly contribute to better quality of life of PLHIV. Thus, we sincerely appreciate the efforts of HIV service providers, writers, planners and funders to this initiative including the Global Fund to Fight AIDS, Tuberculosis and Malaria, for working tirelessly to provide greater access and availability of quality holistic HIV care in the country.

We encourage all specialists, clinicians, medical interns and those in allied health professions to continue supporting the advocacy and programme of DOH on HIV and AIDS.

Mabuhay tayong lahat!!!

ENRIQUE T. ONA, MD, FPCS, FACS
Secretary of Health

PREFACE

Persons living with HIV (PLHIV) have a higher risk of infection compared to healthy, immunocompetent individuals. They may even experience more severe disease following exposure to infections that are preventable with immunization such as pneumonia, influenza or hepatitis B. Thus, immunization is an important core preventive measure in the care of PLHIV for the following reasons: First, immunization will provide clinicians an opportunity to prevent life-threatening vaccine-preventable diseases among PLHIV. Second, with the availability and administration of highly effective combination antiretroviral therapy (cART), PLHIV are likely to be asymptomatic with improved health and well-being. As such, they may engage more in exposure-prone activities related to occupation and travel. Immunization will enhance their chances of protection against these infections. Third, previously contraindicated vaccines can now be given once immunity is restored with the use of cART. Thus, it is the objective of this guideline to provide clinicians with evidence-based recommendations on the appropriate use of immunization in the care of PLHIV.

The HIV Immunization Guidelines Working Committee

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I. GENERAL PRINCIPLES OF IMMUNIZATION IN PERSONS LIVING WITH HIV

Immune responses to vaccine may vary depending on the nature of the vaccine and the individual's immune response. Among PLHIV, the humoral and cellular responses are inversely correlated with a patient's CD4++ T lymphocyte cell count. Malnutrition and concurrent infections and co-morbidities can likewise affect how PLHIV respond to the vaccine. Higher doses or frequent boosters may be required in certain circumstances. With the advent of cART and subsequent restoration of immune response to vaccines, it may be reasonable to even repeat vaccination or delay its administration until immune reconstitution.

Principles in Immunizing PLHIV

1. Asymptomatic PLHIV with CD4+ counts higher than 400-500 cells/mL are generally regarded as sufficiently immunocompetent; whereas those with CD4+ counts between 200 and 400 cells/mL are considered to have limited immunodeficiency. It is generally recommended that the current CD4+ cell count can be used to categorize PLHIV. When safety concerns restrict vaccine use according to the level of immunoreconstitution, it is recommended that the CD4+ cell count should be stably above the threshold for at least three months before proceeding with vaccination.

2. Live vaccines must NOT be given to symptomatic PLHIV or if the CD4+ counts are less than 200 cells/mL. If indicated, reconsider vaccination following immunoreconstitution.

3. In vaccine candidates with CD4+ counts < 200 cells/mL, consideration may be given to delaying immunization until the CD4+ cell count has recovered with cART. Because responses to vaccination can be observed in a substantial proportion of patients with CD4+ counts < 200 cells/mL, the potential benefit of immunization should not be denied to such persons. Therefore, it is generally recommended that vaccination should be given to persons with CD4+ counts less than 200 cells/mL if indicated and safe, and then repeated following immunoreconstitution if required.

4. Considerations about destination and risk behavior apply equally to HIV-positive and HIV-negative travelers. However, the consequences

of not administering an indicated vaccine may be more severe in PLHIV. Modification of the travel itinerary may be required where a vaccine is contraindicated in a PLHIV, if the risk of infection is significant.

5. PLHIV vaccine recipients should be advised that the levels and duration of protection induced by vaccination may be reduced compared to healthy individuals. The importance of additional measures of protection should be emphasized.

6. Household and other close contacts of severely immunocompromised PLHIV should not receive the oral polio and the intranasal influenza vaccines. They can receive the MMR, varicella and yellow fever vaccines.

II. GENERAL PRINCIPLES OF IMMUNIZATION

Immunity refers to the ability of the body to tolerate the presence of material indigenous to the body (self) and to eliminate foreign material (non-self). This ability provides protection from infectious diseases. Immunity is usually indicated by the presence of antibody and is highly specific to a single antigen.

An antigen is a live or inactivated substance (e.g., protein, polysaccharide) capable of producing an immune response while an antibody is a protein molecule (immunoglobulin) produced by B lymphocytes to help eliminate an antigen.

Immunity is acquired through two basic mechanisms:

1. Active immunity
    - Protection produced by a person's own immune system
    - Usually permanent
    - Also produced by vaccination
2. Passive immunity
    - Protection transferred from another person or animal as antibody
    - Transplacental - most important source in infancy
    - Usually temporary

A. Timing and spacing of vaccines

1. Live vaccines can be administered simultaneously in different sites or with an interval of 4 weeks. When multiple vaccines are given at the same time, a separate site should be used. If the vaccines are given in the same limb, they should be given at least 2.5 cm apart.

2. There is no contraindication to the simultaneous administration of any vaccines. Individual vaccines, however, should not be mixed in the same syringe unless they are licensed for mixing by the FDA.

3. Live vaccines should be administered at least 14 days before or 3 months after the administration of antibody-containing blood products, because passively acquired antibodies may interfere with the response to the vaccine.

Timing and spacing of sequential administration of antibody and live vaccines

Product given first	Action
Vaccine	Wait 2 weeks before giving the antibody
Antibody (blood/blood products, immune globulin)	Wait > 3 months before giving the vaccine

- All live vaccines must replicate in order to cause an immune response, so that antibody against a live injected vaccine antigen may interfere with replication.
- If the live vaccine is given first, it is necessary to wait for at least two weeks before giving the antibody.
- If the interval between the vaccine and antibody is less than two weeks, the recipient should be tested for immunity or the vaccine dose should be repeated.
- Inactivated antigens are not substantially affected by circulating antibody, so that they can be administered before, after, or at the same time as the antibody.

4. Spacing of vaccine combinations not given simultaneously

Vaccine combination	Minimum interval
Two live injected	4 weeks
All other	None

5. Interval between doses of the same vaccine
   - Increasing the interval between doses of a multidose vaccine does not diminish the effectiveness of the vaccine.
   - Decreasing the interval between doses of the multidose vaccine may interfere with antibody response and protection.
6. Minimum intervals
   - Vaccine doses should not be given at intervals less than the minimum intervals or earlier than the minimum age.
7. Extended intervals
   - It is not necessary to restart the series of any vaccine due to extended intervals between doses.
8. Number of doses
   - Live attenuated vaccines generally produce lasting immunity with a single dose.
   - Inactivated vaccines require multiple doses and may require periodic boosting to maintain immunity.

B. Adverse events following immunization

1. Adverse event following immunization is any event that follows immunization "believed to be caused by the immunization".
2. Can either be a true vaccine reaction or a coincidental event or due to a human or program error
3. Local
   - Pain, swelling, redness at the site of injection
   - Common with inactivated vaccines
   - Usually mild or self-limited
4. Systemic
   - Fever, malaise, headache
   - Non-specific
   - May be unrelated to the vaccine
5. Allergic
   - Due to the vaccine or vaccine component
   - Rare
   - Risk is minimized by screening

C. General contraindications and precautions to vaccination

- A contraindication is a condition in a vaccine recipient that greatly increases the chance of a serious adverse reaction.
  Example: Administering influenza vaccine to a person with a true anaphylactic allergy to egg could cause serious illness or death to the person.
- A precaution is a condition in a recipient that may increase the chance or severity of an adverse event or may compromise the ability of the vaccine to produce immunity.
  Example: Administering measles vaccine to a person with passive immunity to measles from a blood transfusion

1. In general, vaccines are contraindicated in persons with a history of previous severe adverse reaction or allergy to the vaccine or its components. In addition, persons with acute moderate or severe febrile illness usually should NOT be vaccinated until their symptoms have abated.
2. Inactivated vaccines may be used in pregnancy if there is a significant risk of infection. Live vaccines are contraindicated in pregnancy, although in most cases the theoretical risk to the developing fetus is expected to be low.
3. Permanent contraindications to vaccination
   - Severe allergy to a prior dose of vaccine or to a vaccine component
   - Encephalopathy following pertussis vaccine

Contraindications and precautions to vaccination

Condition	Live vaccine	Inactivated vaccine
• Allergy to vaccine component	C	C
• Encephalopathy	-	C
• Pregnancy	C	V
• Immunosuppression	C	V
• Severe illness	P	P
• Recent blood products	P	V

C-contraindication P-precaution V-vaccinate if indicated

- Immunosuppression
  - Live vaccines can be given after chemotherapy has been discontinued for at least three months.
  - Persons receiving large doses of corticosteroids should not receive live vaccines, i.e., > 20 mg of prednisone per day or > 2 mg/kg per day of prednisone.
  - Vaccines are not contraindicated with steroids given via aerosol or topical route on alternate days, or with short course regimens.
- Recent blood products
  - Varicella and MMR vaccines should be given 14 days prior to the blood product, or delayed until the antibody from the blood product has degraded.
  - If MMR is given sooner than the minimum interval (3-7 months depending on the blood product), the recipient should be tested for immunity or the dose repeated after the appropriate interval.

4. Invalid contraindications to vaccination
   - Mild illness, e.g. low grade fever, upper respiratory tract infection
   - Disease exposure or convalescence
   - Mild diarrhea
   - Antibiotic therapy
   - Pregnancy in the household
   - Breastfeeding
   - Allergies to products in the vaccine
   - Premature birth
   - Family history unrelated to immunosuppression
   - Need for TB skin testing
   - Need for multiple vaccines

5. Screening questions for contraindications and precautions to vaccination
   - Allergies to food or medications?
   - Any problem after the last shot?
   - Any problem with the immune system?
   - Any blood products received in the last year?
   - Are you pregnant or trying to be pregnant?

D. Classification of Vaccines

1. Live attenuated vaccines
   - Attenuated (weakened) form of the " wild" virus or bacteria
   - Must replicate to be effective
   - Immune response similar to that of a natural infection
   - Usually effective with one dose
   - Severe reactions possible
   - Interference from circulating antibody
   - Unstable

   Examples: Viral measles, mumps, rubella, varicella, yellow fever, oral polio, influenza nasal spray, bacterial BCG, oral typhoid
2. Inactivated vaccines
   - Not live and cannot replicate
   - Minimal interference from circulating antibody
   - Generally not as effective as live vaccines
   - Generally require 3-5 doses
   - Immune response mostly humoral
   - Antibody titers decrease over time

   Examples

   Whole cell vaccines

   Viral: influenza, polio, rabies, hepatitis A

   Bacterial: pertussis, typhoid, cholera

   Fractional vaccines

   Subunit: hepatitis B, influenza, acellular pertussis, typhoid Vi

   Toxoid: diphtheria, tetanus

   Pure polysaccharide vaccines
   - Not immunogenic in children < 2 years of age
   - No booster response
   - Antibody with less functional activity
   - Immunogenicity improved by conjugation

   Examples: Conjugate polysaccharide: *H. influenzae* type b, pneumococcal

   Pure polysaccharide: pneumococcal, meningococcal, *H. influenzae* type b

   Recombinant vaccines
   - Genetically engineered

   Examples: Hepatitis B, typhoid (Ty 21a)

E. Handling and Storage

See sections on individual vaccines.

III. Summary of Vaccines in Persons Living with HIV

Table 1. Vaccines that MUST be given to all PLHIV REGARDLESS of CD4+ T CELL COUNT

Vaccine	Dose	Route	Schedule of Immunization	Indications	Adverse reactions
1. Hepatitis B	20 ug/ml vial, administer 2 vials on a 3-dose schedule Alternative regimens: - Accelerated schedule using 4 doses	Intramuscular (IM)	Day 0,1 month and 6 months Alternative regimens: Day 0,1 month, 2 months and 12 months If combined with Hepatitis A, give doses at days 0, 7, and 21 and a booster dose at 1 year	- Patients without evidence of past or present hepatitis B infection - Injecting drug users (IDU) - Homosexual males - Those with multiple sexual partners - Household and other close contacts of HBV-infected persons - Those receiving regular blood and blood products - Patients and staff of hemodialysis units - People sharing unsterile medical and dental equipment, - People providing and receiving acupuncture and tattooing with unsterile devices - Healthcare workers - Travelers to areas of high prevalence	Common: transient soreness, erythema and induration at injection site Uncommon systemic early onset events temporally related to vaccination include: - fatigue, dizziness, syncope, hypotension, arthritis, arthralgia, lymphadenopathy, rash and urticaria - influenza-like symptoms, such as low-grade fever, malaise, headache, myalgia - gastrointestinal upsets, such as abdominal pain, diarrhea, vomiting, nausea and abnormal liver function tests - neurological manifestations include rarely paresthesia and extremely rarely paralysis, neuropathy, and neuritis (including Guillain-Barre syndrome, multiple sclerosis and optic neuritis) - severe skin disorders such as erythema multiforme

Vaccine	Dose	Route	Schedule of Immunization	Indications	Adverse reactions
2. Influenza	0.5 mL Single dose	IM (or by deep subcutaneous injection- SC in case of bleeding disorders)	Annually	- Elderly - Those with underlying conditions e.g., chronic respiratory disease, cardiovascular disease, chronic renal or liver disease, immunodeficiency	Most frequent: soreness at the injection site Rare: fever, malaise, muscle pain, arthralgia (beginning 6-12 hrs after immunization and lasting up to 48 hrs) - allergic reactions may occur most likely due to hypersensitivity to residual egg protein - Guillain-Barre syndrome has been reported but causal relationship with the vaccine has not been established
3. Pneumo-coccal	0.5 ml single dose of the 23 polyvalent polysaccharide vaccine	SC or IM injection, preferably into the deltoid	Indications for revaccination - Those > 65 years who received their first dose > 5 years ago and before they reached age 65 - After 5 to10 years of the first dose in high-risk groups in whom antibody levels are likely to decline - Persons < 65 years old who received the vaccine > 5 years ago and who have the following: Anatomical or functional asplenia, HIV, leukemia, lymphoma, malignancy, multiple myeloma, chronic renal failure or nephrotic syndrome, receiving immunosuppressive therapy, including corticosteroids, received solid organ or bone marrow transplant	- ≥ 65 years - Anatomical or functional asplenia - HIV, leukemia, lymphoma, malignancy, multiple myeloma, - Chronic renal failure or nephrotic syndrome, - Receiving immunosuppressive therapy, including corticosteroids, - Received solid organ or bone marrow transplant	Most frequent: soreness, swelling and redness at injection site; resolves within 48 hrs Rare: fever, malaise and muscle pain Allergic reactions may occur Local reactions reported more frequently following a second dose of PPV-23 than after the first dose, especially if < 3 years interval from the first injection

Table 2. Vaccines that MAY BE GIVEN safely to PLHIV IF INDICATED, REGARDLESS OF CD4++ T CELL COUNT

Vaccine	Dose	Route	Schedule of Immunization	Indications	Adverse reactions
1. Cholera	- Dissolve buffer in 1 glass water. Add 1 vial vaccine. Mix well and drink	Oral vaccine (against cholera and enterotoxigenic *E coli*- ETEC)	2 doses at 10 - 14 days interval If > 6 weeks has elapsed between doses, repeat course Booster after 2 years if continuous protection is required	- For travelers visiting areas with ongoing epidemics/ outbreaks - For long term travelers who drink untreated water, eat poorly cooked or raw seafood in disease endemic areas, in highly endemic areas in unsani-tary conditions without access to medical care - Persons with compromised gastric defense mechanisms (achlorydia, prior ulcer surgery, on antacid treatment) visiting cholera risk areas - For refugees in countries where cholera is known to be present - Aid workers assisting in disaster relief or refugee camps	- Common: upset stomach, nausea, vomiting loss of appetite - Rare: fever, malaise, dizziness, runny nose, cough, dizziness - Very rare: fatigue, joint pains, sweating, sore throat, rash, severe diarrhea, itching, swelling of lymph glands
2. *Haemophilus influenzae* type B	0.5 mL	IM injection (or SC injection in persons with bleeding disorders), preferably in the deltoid	Single dose	- PLHIV who acquire splenic dysfunction, whether or not they were immunized in infancy - PLHIV who have recovered from Hib disease and have risk factors for further disease, those with recurrent pulmonary infections or other risk factors for severe disease	- Fever, restlessness, prolonged crying, loss of appetite, vomiting and diarrhea - Redness and pain at injection site - Potentially fatal: Anaphylaxis

Vaccine	Dose	Route	Schedule of Immunization	Indications	Adverse reactions
3. Hepatitis A	1 mL CD4+ count >300: 2- dose CD4+ count <300: 3-dose	IM route (deltoid)	CD4+ count > 300: 2- dose at either 0 and 6 through 12 months CD4+ count < 300: 3-dose IM route schedule over 6-12 months Alternative dose schedule: 4-dose schedule - days 0, 7, and 21 to 30 followed by a booster dose at month 12 - For travelers to endemic areas, vaccine should be given at least 2 weeks before travel - If combined with hepatitis B vaccine, should be administered at days 0,1 month, and 6 months IM route	- Chronic liver disease - People with occupational risk of infection (e.g. health care workers, some laboratory workers) - Men who have sex with men (MSM) - Injecting drug users - People with clotting factor disorders (e.g. hemophiliacs) - People from non-endemic countries who are traveling to countries with high or intermediate risk of HAV infection	- Common adverse events: injection site reactions such as soreness, induration, redness and swelling - Less common: headache, malaise, fatigue, fever, nausea, & loss of appetite - Rare: serious allergic reactions
4. Human papilloma virus	Quadrivalent vaccine – 3 doses Bivalent HPV vaccine – 3 doses	IM (deltoid)	Quadrivalent vaccine within 6 months at 0, 2, 6 months Bivalent HPV vaccine within 6 months at 0, 1, 6 months Minimum intervals for both vaccines are: 4 weeks between doses 1 and 2 12 weeks between doses 2 and 3	- Before potential exposure to HPV through sexual activity - Females who are sexually active - Sexually active females who have NOT been infected with any of the four HPV vaccine types	- Local reactions: mostly pain and swelling - Fever - Syncope (fainting) may follow any vaccination, especially in adolescents and young adults. Syncope, sometimes associated with falling, has occurred after vaccination with quadrivalent HPV recombinant vaccine. Therefore, vaccinees should be carefully observed for approximately 15 minutes after administration of quadrivalent HPV recombinant vaccine

Vaccine	Dose	Route	Schedule of Immunization	Indications	Adverse reactions
5. Japanese B encephalitis	Three doses	Deep SC route	Days 0, 7–14 and 28 - Last dose should be administered at least 10 days before the commencement of travel to ensure an adequate immune response and access to medical care in the event of delayed adverse reactions. - For those aged >60 years, a 4th dose is recommended 1 month after completion of the initial course. - A booster is recommended after 3 years for those at continued risk.	- People living in endemic areas - Travellers to Southeast Asia and the Far East who will be staying for more than 30 days in endemic areas, especially if travel will include rural areas - Travellers to and residents of areas experiencing epidemic transmission persons with extensive outdoor activities in rural areas - Expatriates whose principal area of residence is an area where JEV is endemic or epidemic	Adverse reactions tend to occur within 48 hours for the first dose but around 96 hours for the second. The hypersensitivity reaction may occur as late as 10 to14 days after the last dose - Common: Tenderness, redness, swelling, and other local effects - Less common: fever, headache, malaise, rash, and other reactions such as chills, dizziness, myalgia, nausea, vomiting, and abdominal pain - Rare: severe hypersensitivity, including angioedema or urticaria
6. Meningo-coccal	Single dose 0.5ml.	Deep SC or IM injection preferably in the deltoid	Boosters are recommended after 5 years for those at continuous risk	- Household contacts of cases of meningococcal infection persons who travel to or reside in countries in which *N. meningitidis* is hyperendemic or epidemic, particularly if contact with the local population will be prolonged - College students living in dormitories; military recruits - Microbiologists who are routinely exposed to isolates of *N. meningitidis*	- Very common: Transient local pain with associated swelling or redness and fever - Common: headache, vomiting, irritability, fatigue and loss of appetite - Rare: serious (neurological) complications or anaphylaxis

Vaccine	Dose	Route	Schedule of Immunization	Indications	Adverse reactions
				- Persons who have terminal complement component deficiencies - Persons who have anatomic or functional asplenia - PLHIV at risk of infection through travel - Travelers who will be living or working with local people in an area of risk; for long stay and rural travelers visiting areas of risk - Backpackers; travelers visiting an area of risk during an outbreak	
7. Polio vaccine-Inactivated	0. 5 mL three doses	IM or SC in persons with bleeding disorders	The first 2 doses are given at a 4-8 week interval and a third dose 6 to 12 months after the second dose. Booster dose is given after 5 and 10 years	- Household members or other household contacts - Nursing personnel in close contact - Unvaccinated or incompletely vaccinated PLHIV who intend to travel to a polio endemic area such as India, Pakistan, Afghanistan and Nigeria. - PLHIV with a history of incomplete vaccination should receive the remaining doses of IPV to complete a five-dose vaccination course, regardless of the interval since the last dose and type of vaccine received previously	- Most common: Injection site reactions

Vaccine	Dose	Route	Schedule of Immunization	Indications	Adverse reactions
8. Rabies	Pre-exposure prophylaxis - 3 doses Post exposure prophylaxis 1 dose each on Days 0, 3, 7, 14, 28 or 30: or 2 doses on Day 0, and 1 IM dose each on Day 7 and Day 21	IM (deltoids) IM	Pre-exposure prophylaxis: Days 0, 7, and 28 Post exposure prophylaxis: 1 dose each on Days 0, 3, 7, 14, 28 or 30 or 2 doses on Day 0, and 1 IM dose each on Day 7 and Day 21 If currently asymptomatic, with CD4+ >400cells/mm, with completed pre-exposure prophylaxis: 1 IM dose on Day 0, and 1 IM dose on Day 3 Serologic testing like rapid focus flourescent inhibition test (RFFIT), if available, should be done between day 14 and 28. If the antibody response is <0.5 IU/ml, a further booster dose of rabies vaccine should be administered	- Health care workers in hospitals that handle dog bites and rabies cases (doctors, nurses, paramedical staff) - Rabies research and diagnostic lab workers - Rabies biologic production workers - Veterinarians and vet students - Animal control and wildlife handlers - Spelunkers and other animal handlers - Field workers (bill collectors, mailmen, delivery men) - Morticians and embalmers	- Soreness, swelling or itching, induration at injection site - Headache, dizziness, nausea, abdominal pain - Rare: neurologic reactions reported, resolved spontaneously
9. Td/Tdap	Td 0.5 mL	IM	- 2 doses of Td at 4 to 8 weeks apart followed by 3rd dose, tetanus diphtheria pertussis (Tdap) to be given 6 to 12 months later	Adults who have NOT been immunized previously or have an uncertain vaccination history	- Local: Pain at the injection site - Systemic: Headache, generalized body aches, tiredness, fever

Vaccine	Dose	Route	Schedule of Immunization	Indications	Adverse reactions
			- Booster every 10 years with Tdap - Partially immunized pregnant women should complete the 3 series. In pregnancy 3rd dose given at least two weeks before delivery - Adults who have received a full primary course (3 doses) as infants and a booster at pre-school age (total of 4 doses) require a single booster dose. - Persons who have received five vaccine doses require a booster dose at 10-yearly intervals if with increased risk of exposure or if they are due to travel to remote areas where they may not be able to receive tetanus immunoglobulin (TIG) in the event of a tetanus-prone injury	Pertussis For individuals at high risk of infection (for example those exposed in the household or in high-risk occupations), a single dose of a pertussis-containing vaccine (Tdap) could be considered.	- Rare: severe systemic reactions such as generalized urticaria, anaphylaxis or neurological complications
10. Typhoid Vi polysaccha-ride (Paren-teral)	25 mcg (0.5 ml) - Single dose	IM (preferably in the deltoid) or SC in persons with bleeding disorders)	- At least 2 weeks before expected exposure - Booster recommended every 3 years in those who remain at risk. Interval might be reduced to 2 years if the CD4+ count is < 200 cells/mL	- Those with significant risk of exposure to S. typhi (i.e. local outbreaks, travel to high risk areas) - Those who will have close contact with a documented S. typhi carrier - Laboratory workers exposed to *S. typhi*	- Mild reactions: Fever, headache, redness or swelling at the site of the injection - Very rare: severe allergic reactions

Table 3. Vaccines that CAN BE GIVEN SAFELY to PLHIV if INDICATED, and if they are ASYMPTOMATIC, with a CD4+ T cell count of > 200 cells/mm3

Vaccine	Dose	Route	Schedule of Immunization	Indications	Adverse reactions
1. Measles, mumps, rubella	Two doses	Deep SC or IM injection preferably in the deltoid	Second dose given at any time but at least one month after the first	- PLHIV who wants to be protected and immune against measles, mumps and rubella infections - Rubella IgG seronegative women with CD4+ counts >200cells/uL - Second MMR dose if the patient remains rubella IgG seronegative - Measles, mumps and rubella susceptible and healthy close contacts of HIV infected individuals should receive two doses of MMR vaccine	- Fever and rash occur usually 7-12 days after vaccination and lasting 1-2 days. These are usually attributable to the measles component - Arthalgia and / or arthritis are reported in up to 25% of vaccinated women and are usually mild and transient. - Transient lymphadenopathy sometimes occurs and is associated with rubella vaccination. - Parotitis and deafness occur rarely and are attributable to the mumps component.
2. Varicella	0.5 mL two doses	SC injection, preferably in the deltoid	3 months interval between doses if HIV (+)	- VZV IgG negative, - PLHIV with uncertain history of varicella infection - PLHIV who are at risk of exposure (e.g. HCW)	- Rash, localized at the site of injection or generalized, within one month of immunization - Fever
3. Yellow fever	0.5 ml - Single dose	SC injection, preferably in the deltoid	- Booster after 10 years for those at risk, provided that the CD4+ count is >200 cells/uL - Other live-virus vaccines may be given concurrently; alternatively 4 weeks should be allowed to elapse between sequential vaccinations		- Most common: Injection site reactions - An influenza-like illness, characterized by fever, headache and muscle ache, occurs in 2-10% of vaccine recipients 5-14 days after immunization. - Severe: risk of encephalitis to PLHIV - Rare: Hypersensitivity or anaphylaxis, neurotropic disease and viscerotropic disease

Table 4. Vaccines contraindicated in PLHIV regardless of CD4+ T cell count

Vaccines
1. Oral polio vaccine 2. BCG 3. Ty 21 – oral typhoid vaccine 4. Influenza – intranasal 5. Herpes zoster

Table 5. Schedule of pre-exposure vaccinations in PLHIV

Vaccine	Primary Course	Boosting
Cholera	2 doses	2 years
Haemophilus influenzae type B	1 dose	None
Hepatitis A2 or 3 doses	5 years	
Hepatitis B3 or 4 doses	Anti-HBs <10 IU	
Human papilloma virus	3 doses	
Influenza-parenteral	1 dose	Repeat yearly
Japanese B encephalitis	3 or 4 doses	3 years
Measles, mumps, rubella	1 or 2 doses	None
Meningococcus (MenC)	1 or 2 doses	None
(ACWY)	1 dose	5 years
Pneumococcus (PPV23)	1 dose	Generally none
Poliomyelitis	3 doses	5-10 years
Rabies	3 doses	1 year (first): 3-5 years (subsequent)
Tetanus, diphtheria, pertussis	1-5 doses	10 years
Typhoid Fever (ViCPS)	1 dose	2-3 years
Varicella	2 doses	None
Yellow Fever	1 dose	10 years

VACCINES THAT MUST BE GIVEN TO ALL PLHIV REGARDLESS OF CD4 + T CELL COUNT

Hepatitis B
Influenza
Pneumococcus

A. Hepatitis B

1. The vaccine

General description

- Monovalent hepatitis B vaccine uses recombinant DNA technology to express HBsAg in yeast.

Dose, route and schedule of administration for PLHIV

- 20 ug/ml/vial, administer 2 vials intramuscularly on a 3-dose schedule at day 0, 1 month, and 6 months
- Alternative regimens:
  - Accelerated schedule using 4 doses IM route given at day 0, 1 month, 2 months and 12 months
  - If combined with hepatitis A, doses at days 0, 7, and 21 and a booster dose should be given at 1 year

Vaccine efficacy in PLHIV

- Response rates varies between 17%- 59% (Table 5)
- Immunogenicity is impaired in HIV-infected patients especially those with low CD4+ T cell count

Table 6: Immunogenicity of different HBV vaccine preparations (AIDS Reviews, 2007)

Study	Year	Vaccine	Subject(n)	Response rates
Collier et al	1988	Plasma-derived	16	56%
Keet et al	1992	Recombinant	32	28%
Bruguerra	1992	Recombinant	21	24%
Tayal et al	1994	Recombinant	12	17%
Wong et al	1996	Recombinant	14	43%
Rey et al	2000		20	55% 3 injections, 78% of non-responders after 3 additional doses
Ahuja et al	2005	Recombinant	116	53%
Pasricha et al	2005	Same	40	100% if CD4+>200, 47% if CD4+ <200
Overton et al	2005	Same	194	17.5% response associated with HIV RNA copies of < 400
Fonseca et al	2005	Same	210	34% with 20 ugm, and 47% 40 ugm
Cornejo-Juarez et al	2006	Same	79	CD4+ > 350, 64% seroconvert with 40 ug, 39% standard dose CD4+ <350, 24% 40 ug, 26% standard dose 61.5% with 10 ug and 60% with 40 ug; response rate is associated with CD4+ >200
Velga et al	2006	Same	55	59% response if CD4+ >450 and undetectable HIV RNA (< 400 copies)

Vaccine safety and adverse events

- The vaccine is safe and well-tolerated and no significant adverse clinical reactions to HBV vaccination distinctive to PLHIV have been reported.
- Common adverse events: transient soreness, erythema and induration at injection site
- Uncommon systemic early onset events temporally related to vaccination include:
  - Fatigue, dizziness, syncope, hypotension, arthritis, arthralgia, lymphadenopathy, rash and urticaria
  - Influenza-like symptoms, such as low-grade fever, malaise, headache, myalgia
  - Gastrointestinal upsets, such as abdominal pain, diarrhea, vomiting, nausea and abnormal liver function tests
  - Neurological manifestations include rarely paresthesia and extremely rarely paralysis, neuropathy, and neuritis (including Guillain-Barre syndrome, multiple sclerosis and optic neuritis)
  - Severe skin disorders such as erythema multiforme

Precautions and contraindications

- Hypersensitivity to any component of the vaccine, including yeast
- Should **not** be administered to subjects with severe febrile infection
- General vaccination of pregnant women **cannot** be recommended because the effect of the antigen on fetal development is unknown. However, neither pregnancy nor lactation should be considered a contraindication for vaccination.
- The effect on breastfed infants of the administration of the vaccine to their mother has not been evaluated in clinical studies.
- As with all injectable vaccines, a solution of 1 in 1,000 adrenaline should always be readily available for immediate use in case of a rare anaphylactic reaction.

Vaccine Storage and Handling

- Vaccine must be stored at +2o C to +8o C. Do **not** freeze; discard if vaccine has been frozen.

2. Recommendations for pre-exposure and post-exposure prophylaxis in PLHIV

Pre-exposure prophylaxis

- Routine vaccination in all PLHIV, regardless of CD4+ T cell count and those who belong to the high risk population
- Post-vaccination follow-up
  - AntiHBs level should be measured yearly. A single booster should be considered when antiHBs concentrations decline to <10 mIU/ml, and consider 3 further double doses (20ugm/vial) at 0, 1 and 2 months for non-responders.

Post-exposure prophylaxis

- Following a high-risk exposure, those who have NOT been vaccinated previously should be offered a rapid course of vaccination (0, 1, and 2 months and Hepatitis B immune globulin (HBIG).
  - Persons who have responded to previous vaccination with antiHBs level >10 IU/L should be offered a booster dose (2 vials of 20 ugm) of the vaccine.
  - Post-exposure prophylaxis should be given preferably within 2 days and up to 7 days after exposure.

3. Hepatitis B in PLHIV

- In PLHIV with HBV, the lifetime risk of progression to either cirrhosis and liver cancer is 25-30% and is associated with accelerated progression to hepatic cirrhosis, end-stage liver disease, greater levels of HBV viremia, and increased liver-related mortality
- 3-fold higher increased risk of liver disease especially those with low CD4 T cell counts
- Co-infection rates with HIV infected is 8.7% overall, with co-infection rate in men having sex with men ranging from 9-17%, injecting drug users 7-10%, and multiple partners heterosexual contact 4-6%
- Among the estimated 36 million PLHIV worldwide, nearly 4 million (10%) are chronically infected with HBV
- No available local data on PLHIV with HBV infection

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B. Influenza

1. The vaccine

General description

- Inactivated trivalent vaccine containing 3 strains - one influenza A (H3N2), one influenza A (HIN1) and one influenza B serotype
- Prepared yearly using virus strains or genetic reassortants similar to those likely to be circulating in the forthcoming year
- For the Philippines, current recommendations state that the formulation for the Southern Hemisphere be used.
- Two types are available. These are equivalent in efficacy and adverse reactions.
  - Split virus vaccine – contains virus components prepared by treating whole viruses with organic solvents followed by centrifugation
  - Surface antigen vaccine – contains highly purified hemagglutinin and neuraminidase antigens prepared from disrupted virus particles

Dose, route and schedule of immunization

- Given intramuscularly (or by deep subcutaneous injection in case of bleeding disorders)
- Single dose, every year

Vaccine efficacy in PLHIV

- Vaccine-induced antibody responses correlate with CD4+ cell counts
- Vaccine-induced antibody responses are lower in PLHIV compared to HIV-negative controls, especially among those with CD4+ counts < 200 cells/uL
- Vaccine efficacy was reduced from 65% in those with CD4+ counts > 100/uL to 11% in those with lower counts; efficacy was 52% in those with plasma HIV RNA levels below 30,000 copies/ml and 40% in those with higher viral load
- PLHIV with CD4+ counts >300 cells/uL while on cART have humoral and cellular responses to influenza vaccination similar to healthy controls. Reconstitution of the immune response against influenza antigens occurs during treatment. Hence, improved antibody response rates are expected in PLHIV with cART-induced immune reconstitution.
- In PLHIV receiving cART with CD4+ count >200 cells/uL, vaccine efficacy is 69-100% against laboratory-confirmed infection; protection against respiratory disease is 73-100%.

- In PLHIV with CD4+ counts < 200 cells/uL, protective effect is significantly reduced but protection against severe disease is observed compared to unvaccinated persons
- Pooled relative risk reduction of 66% (95% CI 36-82%) for the development of symptomatic disease in PLHIV was reported in a systematic review of prospective studies to assess the efficacy of influenza vaccines in PLHIV
- Moderately effective in reducing the incidence of influenza in PLHIV – a randomized controlled trial in 102 HIV patients (mean CD4+ T-cell count 400/mm3, with 13% having values < 200/mm3 showed significant reduction in respiratory symptoms from 49% to 29% and laboratory-confirmed seasonal influenza from 21% to 0%.

Vaccine safety and adverse events

- Safe and well-tolerated in PLHIV
- Adverse effects
  - Most frequent: soreness at the injection site
  - Rare: fever, malaise, muscle pain, arthralgia (beginning 6-12 hrs after immunization and lasting up to 48 hrs); allergic reactions may occur most likely due to hypersensitivity to residual egg protein; Guillain-Barre syndrome has been reported but causal relationship with the vaccine has not been established

Precautions and contraindications

- Immediate anaphylactic reaction to a previous dose of influenza vaccine
- Severe allergy to eggs
- Moderate to severe illness with or without a fever
- Active neurologic disorder or a history of developing neurologic symptoms or illness following a previous dose
- History of Guillian-Barre Syndrome within 6 weeks of receiving an influenza vaccine
- No evidence that inactivated influenza vaccine causes damage to the fetus. Inactivated influenza vaccine can be administered during pregnancy, and influenza vaccine is recommended for all pregnant women who will be pregnant during influenza season. Live attenuated influenza vaccine should **not** be used in pregnancy. Because administration of vaccines might be associated with a transient rise in plasma HIV RNA levels, immunization of pregnant women is best done after cART has been

initiated to minimize increases in plasma HIV RNA levels that might increase the risk of perinatal HIV transmission.

Vaccine storage and handling

- Store at refrigerator temperature (2-8o C). Vaccine **must not** be frozen.
- Ship in insulated containers with coolant packs

2. Recommendations for pre-exposure and post-exposure prophylaxis in PLHIV

Pre-exposure prophylaxis

- Vaccination using the inactivated trivalent influenza vaccine is recommended annually for ALL PLHIV irrespective of immunologic status, viral load, age, and comorbidities.
- Intranasal live attenuated influenza vaccine (LAIV) is **not** recommended for PLHIV. Immunocompromised PLHIV should avoid close contact with anyone who has received the LAIV within the previous 21 days.

Post-exposure prophylaxis

- Post-exposure vaccination is **not** indicated but chemoprophylaxis may be given.
- Post-exposure chemoprophylaxis with either oseltamivir or zanamivir within 48 hrs of a high-risk contact given for 10 days should be considered in the following groups:
  - Unvaccinated persons
  - Vaccinated persons in whom the vaccine is not expected to be effective, i.e., CD4+ counts <200 cells/uL or poor match between vaccine and circulating influenza strain
  - Persons in institutional settings
- Oseltamivir 75 mg orally once daily or Zanamivir 10 mg once daily by inhalation with Diskhaler for 10 days is recommended.
- Chemoprophylaxis is expected to be 80% effective in preventing severe illness but the efficacy in PLHIV is unknown.

3. Influenza in PLHIV

- Limited information on the impact of HIV on the natural history of influenza
- Among PLHIV increased risk of complications, impairment of respiratory function with hypoxemia, prolonged duration of illness and increased rates of hospitalization, increased risk of mortality and influenza-related death have been reported.

- Data from the pre-cART era showed substantial excess mortality due to pneumonia during influenza seasons
- No data on whether the magnitude of risk has been reduced by the introduction of cART

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C. Pneumococcus

1. The vaccine

General description

For adults, 23-valent polysacharide vaccine (PPV23) is available

- Composed of purified preparations of pneumococcal capsular polysaccharide from 23 different serotypes, which account for around 90% of IPD cases. The vaccine induces cross-reactivity against serotypes that account for an additional 8% of IPD cases.
- A 7-valent pneumococcal conjugate vaccine (PCV-7) is locally available, but is indicated only for children.

Dose, route and schedule for immunization

- 0.5 ml single dose by subcutaneous or intramuscular injection, preferably into the deltoid
- Indications for revaccination
  - Those >65 years who received their first dose more than 5 years ago and before they reached age 65
  - After 5-10 years of the first dose in high-risk groups in whom antibody levels are likely to decline
  - Persons less than 65 years old who received the vaccine more than 5 years ago and who have the following:
- Anatomical or functional asplenia
- HIV, leukemia, lymphoma, malignancy, multiple myeloma
- Chronic renal failure or nephrotic syndrome
- Receiving immunosuppressive therapy, including corticosteroids
- Received solid organ or bone marrow transplant

Vaccine Efficacy in PLHIV

- Pneumococcal vaccination significantly reduced the risk of pneumonia by 35% (HR 0.65, 95%CI 0.42-1.00) among PLHIV in a matched cohort study in USA
- Pneumococcal vaccination (OR 0.44, 95% CI 0.22 to 0.88) and current use of cART (OR 0.23, 95% CI 0.14 to 0.36) were associated with reduced risk of pneumococcal disease regardless of CD4+ counts in a case-control study in Spain
- Lower antibody responses in those with CD4+ cell counts <500 cells/mm3 compared to those with higher CD4+ counts
- Among low-level responders, revaccination with a double dose of pneumococcal vaccine does not stimulate antibody response

- In PLHIV on cART with >200 CD4+ count, immunogenicity might be at least as good as that observed in healthy persons. Case-control studies in developed countries have generally shown protection from IPD. One large multicenter observational study in the USA in vaccine recipients with CD4+ >500 cells/mm3 showed reduced incidence of pneumococcal disease, but not in those with lower CD4+ counts.

Vaccine safety and adverse effects

- Most frequent: Soreness, swelling and redness at injection site; resolves within 48 hrs
- Rare: Fever, malaise and muscle pain
- Allergic reactions may occur
- Local reactions reported more frequently following a second dose of PPV-23 than after the first dose, especially if <3 years interval from the first injection

Precautions and contraindications

- Immediate anaphylactic reaction to a previous dose of pneumococcal vaccine
- Allergy to a vaccine component: anaphylaxis to phenol or thimerosal
- Moderate to severe illness with or without a fever
- Vaccination given within the previous 3 years
- Pneumococcal vaccine can be administered during pregnancy. Although its safety during the first trimester of pregnancy has not been evaluated, no adverse consequences have been reported among newborns whose mothers were inadvertently vaccinated during pregnancy.

Vaccine storage and handling

- Store at refrigerator temperature (2-8^{o} C). Vaccine must not be frozen.
- Ship in insulated containers with coolant packs.

2. Recommendations for pre-exposure and post-exposure prophylaxis in PLHIV

Pre-exposure prophylaxis in PLHIV

- Vaccination using PPV-23 is recommended for all PLHIV regardless of age, CD4+ counts and co-morbid conditions.
- PPV-23 is given as a single dose. Single booster dose is recommended after 5 years

- The duration of the protective effect of primary pneumococcal vaccination is unknown.
- Revaccination can be considered for persons who were initially immunized when their CD4+ counts were <200 cells/μL and whose CD4+ counts have increased to >200 cells/μL in response to cART.
- Revaccination every 5 years may be considered.
- No evidence confirms clinical benefit from revaccination.
- Smoking cessation needs to be aggressively promoted.

Post-Exposure Prophylaxis

- Not recommended

3. Pneumococcal disease in PLHIV

- Significant cause of pneumonia and invasive pneumococcal disease (IPD) in PLHIV despite the advent of cART
- Increased risk for mortality is related to CD4 count
- Incidence of Invasive Pneumococcal Disease(IPD) higher in PLHIV
  - Increased incidence of bacteremia accompanying pneumonia compared to persons without HIV infection. Estimated rate of pneumococcal bacteremia (9.4 cases per 1,000 patient-years) in PLHIV was approximately 100-fold greater than in HIV-uninfected historical controls
  - Risk factors for severe disease and IPD
    - Previous hospitalization
    - Presence of comorbidities
    - Alcoholism
    - Current smoking
    - Low CD4 count (< 100 cells/mm3)
    - Low hemoglobin
    - African race
    - HIV acquired through blood transfusion or injecting drug users
    - Previous AIDS-defining opportunistic infections
    - Previous pneumonia

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VACCINES THAT MAY BE GIVEN SAFELY TO PLHIV IF INDICATED, REGARDLESS OF CD4 + T CELL COUNT

Cholera
Hemophilus influenza B
Hepatitis A
Human Papilloma virus
Japanese B Encephalitis
Meningococcus
Poliomyelitis
Rabies
Tetanus, Diphtheria, Pertussis
Typhoid fever

A. Cholera

1. The Vaccine

General description

- Heat/formalin inactivated *Vibrio cholerae* 01 Inaba and Ogawa, classic and El Tor strains – in 3 ml oral suspension
- Sodium hydrogen carbonate 5-6 grams – 1 sachet – effervescent buffer, in raspberry flavor
- The old parenteral cholera vaccine is no longer recommended because of its short-lived protection.

Indications for immunization

- **Not** given routinely **except** if a PLHIV falls under special situations (Table 2)

Dose, route and schedule of administration

- Oral vaccine (against cholera and enterotoxigenic *Escherichia coli*-ETEC)
- Dissolve buffer in 1 glass water. Add 1 vial vaccine. Mix well and drink.
- Immunocompetent adults: 2 doses at 1–6 weeks interval
- PLHIV: 2 doses at 10–14 days interval
- If >6 weeks has elapsed between doses, repeat course.
- Booster after 2 years if continuous protection is required

Vaccine efficacy in PLHIV

- No specific studies on efficacy
- Promising reports in Mozambique showed that PLHIV with CD4+ counts >100 have improved responses
- Duration of protection in PLHIV is not known

Vaccine safety and adverse events

- Common - upset stomach, nausea, vomiting, loss of appetite
- Rare- fever, malaise, dizziness, runny nose, cough, dizziness
- Very rare - fatigue, joint pains, sweating, sore throat, rash, severe diarrhea, itching, swelling of lymph glands

Precautions and contraindications

- Postpone vaccination in case of acute illness.

- Avoid food and drink 2 hours before and 1 hour after vaccination
- **Cannot** be given to children below 2 years of age
- **Cannot** be administered with other oral vaccines
- May be administered during pregnancy and lactation

Vaccine storage and handling
- Store at 2-8^{o}C (refrigerator)
- Do **not** freeze
- After reconstitution, should be drank in 2 hours.

2. Recommendations for pre-exposure and post-exposure prophylaxis in PLHIV

Pre-exposure prophylaxis
- For travelers visiting areas with ongoing epidemics/outbreaks
- For long-term travelers who drink untreated water, eat poorly cooked or raw seafood in disease-endemic areas under unsanitary conditions and without access to medical care
- Persons with compromised gastric defense mechanisms (achlorydia, prior ulcer surgery, on antacid treatment) visiting cholera-risk areas
- For refugees in countries where cholera is known to be present
- Aid workers assisting in disaster relief or refugee camps

Post-exposure prophylaxis in PLHIV
- Not recommended

3. Cholera in PLHIV
- PLHIV are associated with an increased risk for cholera
- No difference in clinical presentation and complications between immunocompetent individuals and PLHIV

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B. *Haemophilus influenzae* Type B

1. The vaccine

General description

- The Hib vaccines are protein-polysaccharide conjugates. The vaccine is used either as combined diphtheria/tetanus/acellular pertussis/inactivated polio/Hib (DTaP/IPV/Hib) or as a single Hib vaccine.

Dose, route, and schedule of administration

- Dose: single dose
- The vaccine is given by intramuscular injection (or subcutaneous injection in persons with bleeding disorders), preferably in the deltoid.
- Vial: 1 dose + syringe of 0.5 mL diluent

Vaccine efficacy in PLHIV

- Evidence exists that persons with asymptomatic or mildly symptomatic HIV disease achieve adequate antibody responses
- In persons who have not developed a clinical AIDS-defining diagnoses, the conjugated vaccine, which is T cell-dependent, produced better responses than the T cell-independent unconjugated vaccine.
- The unconjugated vaccine produced better responses in persons with advanced HIV disease.

Vaccine safety and adverse events

- Fever, restlessness, prolonged crying, loss of appetite, vomiting and diarrhoea
- Redness and pain at injection site
- Potentially fatal: anaphylaxis

Precautions and contraindications

- Contraindications: Hypersensitivity, acute febrile illness; infants <6 weeks
- Special precautions:
  - Ensure that vaccine does not enter a blood vessel.
  - Expected immune response may **not** be achieved in immunocompromised patients. Insufficient evidence to demonstrate that administration immediately after exposure to *Haemophilus influenzae* type b will prevent illness.
  - Safety and efficacy of the vaccine in infants < 2 months and children > 6 years have not been established.

- For patients with bleeding disorders, SC administration should be used instead of IM.
- If vaccine is co-administered with measles-mumps-rubella vaccine and the diphtheria, tetanus, pertussis, poliomyelitis vaccine, administer at two separate injection sites.
- Pregnancy Category C: Either studies in animals have revealed adverse effects on the fetus (teratogenic or embryocidal or other) and there are no controlled studies in women, or studies in women and animals are not available. Should be given only if the potential benefit justifies the potential risk to the fetus.

Vaccine storage and handling

- Vaccine: Refrigerate immediately upon arrival. Store at 35°- 46°F (2°-8°C). Do not freeze or expose to freezing temperatures.
- Diluent: May be refrigerated or stored at room temperature 68°-77°F (20 -25°C). Do not freeze or expose to freezing temperatures.

2. Recommendations for pre-exposure and post-exposure prophylaxis in PLHIV

Pre-exposure prophylaxis

- Vaccination is **not** routinely recommended in PLHIV **except** in:
  - PLHIV who acquire splenic dysfunction, whether or not they were immunized in infancy.
  - PLHIV who have recovered from Hib disease and have risk factors for further disease, those with recurrent pulmonary infections or other risk factors for severe disease
  - For PLHIV who are scheduled to receive other vaccines, a multivalent vaccine including Hib may be considered.

Post-exposure prophylaxis

- PLHIV who are household contacts of a Hib case should be given rifampicin prophylaxis, regardless of their immunization status. The recommended dose is 20 mg/kg/day (up to a maximum of 600 mg daily) once daily for 4 days.
- Patients on cART may take ciprofloxacin as an alternative to rifampicin.
- HIV-infected contacts of a case of invasive Hib disease should be offered one vaccine dose.

3. Hemophilus influenzae B in PLHIV

- A study of men in San Francisco found that the annual incidence of invasive HiB was 8.1 per 100,000 HIV-infected men between 20 and 49 years old, compared with 0.93 per 100,000 for all men in this age range
- A population-based study in Atlanta identified two cases of invasive HiB in HIV-infected men among an estimated 3,250 HIV-infected adults, yielding an estimated annual incidence rate of 41 per 100,000 HIV-infected persons

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C. Hepatitis A

1. The vaccine

General description

- Inactivated Hepatitis A virus adsorbed to aluminum hydroxide as adjuvant, administered intramuscularly in the deltoid muscle

Dose, route and schedule of administration

- CD4+ count >300 cells/uL: 2-dose IM route (deltoid) schedule at either 0 and 6 through 12 months
- CD4+ count <300/uL: 3-dose IM route schedule over 6-12 months

Alternative dose schedule:

- 4-dose schedule: Days 0, 7, and 21 to 30 followed by a booster dose at month 12 for travelers to endemic areas, vaccine should be given at least 2 weeks before travel
- If combined with hepatitis B vaccine, should be administered at days 0,1 month, and 6 months IM route

Vaccine efficacy in PLHIV

- Response rates are generally reduced in PLHIV ranging from 50-94% overall
- Response rates correlate with CD4+ T cell count at time of vaccination (ranging from 9% at CD4+ T cell count of < 200 cells/uL to 95-100% at CD4+ counts > 300-500 cells/uL) and HIV RNA levels, thus increasing number of doses may improve responses.
- Routine post-vaccination testing is generally **not** recommended
- Duration of protection is unknown, but may be shorter than in HIV-negative persons

Vaccine safety and adverse events

- The vaccine is safe and well tolerated in PLHIV with rates of adverse events comparable to those who are HIV-negative
- Common adverse events: injection site reactions such as soreness, induration, redness and swelling
- Less common: headache, malaise, fatigue, fever, nausea, and loss of appetite
- Rare: serious allergic reactions

Precautions and contraindications

- Hypersensitivity to any component of the vaccine (i.e. 2 phenoxyethanol, yeast)
- Should **not** be administered to subjects with severe febrile illness
- Should be used during pregnancy only when clearly needed. The effect of Havrix on fetal development has not been assessed. However, as with all inactivated viral vaccines, the risks to the fetus are considered to be negligible.
- Vaccine should be used with caution in breastfeeding women. The effect on breastfed infants of the administration of the vaccine to their nursing mothers has not been evaluated in clinical studies.
- As with all biologicals, a solution of 1 in 1,000 adrenaline should be readily available for immediate use in case of anaphylaxis.
- Vaccine should be administered with caution in subjects with bleeding disorder since bleeding may occur following an intramuscular injection.

Vaccine storage and handling

- Vaccine must be stored at 2-8^{o}C. Do not freeze; discard if vaccine has been frozen.

2. Recommendation for pre-exposure and post-exposure prophylaxis in PLHIV

Pre-exposure prophylaxis

- Routinely given regardless of CD4+ T cell if indicated or for those PLHIV who belong to the risk group for infection or its complications (please see above risk groups of infections)

Post-exposure prophylaxis

- Post-exposure prophylaxis is recommended in all HAV-seronegative PLHIV, and should be given within 14 days of exposure.
- Post-exposure prophylaxis using HAV vaccine and human normal immune globulin (500 mg) is recommended.

3. Hepatitis A in PLHIV

- Clinical features does not appear to be worse in PLHIV when compared to HIV negative person although HAV viremia may be prolonged

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D. Human Papilloma Virus

1. The vaccine

General description

Quadrivalent HPV vaccine

- Contains types 6, 11, 16, 18 L1 capsid protein, virus-like particles
- Manufactured in yeast, Saccharomyces cerevisiae
- Adjuvanted with proprietary amorphous aluminum hydroxyphosphate sulfate
- For the prevention of cervical, vulvar and vaginal cancers and genital warts

Bivalent HPV vaccine

- Contains types 16 and 18 LI capsid protein, virus-like particles
- Manufactured in insect cells, baculovirus
- Adjuvanted with ASO4 -aluminum hydroxide plus monophosphoryl lipid A derived from Salmonella minnesota
- For the prevention of cervical cancer

Indication for immunization

Routine use

- Both quadrivalent and bivalent HPV vaccines are routinely given to adolescents males and females 10 to less than 19 years

Catch-up vaccination

- Quadrivalent HPV vaccine for women 19 to 45 years
- Bivalent HPV vaccine for women 19 to 55 years
- Both vaccines have no current recommendation for adult males.
- Both vaccines do not require prior screening before administration of the vaccine. However, routine screening should be continued even after vaccination, as there are other types of HPV types that can cause cervical cancer.

Special situations

Vaccines can be administered to patients with:

- Equivocal or abnormal Pap smear
- Positive HPV DNA test
- Genital warts
- Immunosuppression
- Breastfeeding

Dose, route, and schedule of administration

- Quadrivalent HPV vaccine schedule of vaccination – 3 doses within 6 months at 0, 2, 6 months IM deltoid
- Bivalent HPV vaccine schedule of vaccination – 3 doses within 6 months at 0, 1, 6 months IM deltoid
- Minimum intervals for both vaccines are 4 weeks between doses 1 and 2 and 12 weeks between doses 2 and 3.
- Do not restart the series if the schedule is interrupted
- May be administered at the same visit with other age-appropriate vaccines

Vaccine efficacy in PLHIV

- Clinical trials of the HPV vaccines suggest high efficacy and an excellent safety profile in women who do not have abnormal cervical cytology or HPV infection prior to immunization. However, women with HIV or other immunosuppressive conditions were **not** enrolled in the main HPV vaccine trials and its efficacy and safety in this setting remains unknown.
- However, the immune response and vaccine efficacy might be **less** for PLHIV than in persons who do not have HIV or who are immunocompetent.
- Vaccination is less beneficial for females who have already been infected with one or more of the HPV vaccine types.

Vaccine safety and adverse events

- Local reactions-84% mostly pain and swelling
- Fever-10%
- No serious adverse reactions reported
- Syncope (fainting) may follow any vaccination, especially in adolescents and young adults. Syncope, sometimes associated with falling, has occurred after vaccination with quadrivalent HPV recombinant vaccine. Therefore, vaccinees should be carefully observed for approximately 15 minutes after administration of quadrivalent HPV recombinant vaccine.

Precautions and contraindications

Precautions

- Moderate or severe acute illnesses (defer until symptoms improve)
- If a woman is found pregnant after initiation of the vaccine series, remaining doses should be delayed until after the pregnancy.

- If a vaccine has been administered during pregnancy, there is no indication for intervention

Contraindication
- Severe allergic reaction to a vaccine component or following a prior dose

Vaccine storage and handling
- Store at 2-8^{o}C
- Do not expose to freezing temperatures.
- Protect from light.
- Administer immediately after removing from refrigeration.

2. Recommendation for pre-exposure and post exposure prophylaxis in PLHIV

Pre-exposure prophylaxis
- Because HPV vaccine is not a live-virus vaccine, it may be administered to PLHIV.
- Vaccine should be administered before potential exposure to HPV through sexual activity.

Quadrivalent vaccine
- Male – 10-19 years
- Female – 10-45 years

Bivalent vaccine
Male – 10-19 years
Female - 10 to 55 years
- Females who are sexually active should still be vaccinated consistent with age-based recommendations.
- Sexually active females who have **not** been infected with any of the four HPV vaccine types receive the full benefit of the vaccination.

Post-exposure prophylaxis
- None recommended

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E. Japanese B Encephalitis

1. The vaccine

General description

- Japanese encephalitis vaccine (JEV) is a formalin-inactivated vaccine derived from mouse brain
- Japanese B encephalitis vaccine is **not** available in the Philippines.

Dose, route and schedule of administration

- The recommended vaccine schedule is three doses on days 0, 7–14 and 28.
- The last dose should be administered at least 10 days before the commencement of travel to ensure an adequate immune response and access to medical care in the event of delayed adverse reactions.
- For those aged >60 years, a 4th dose is recommended 1 month after completion of the initial course.
- A booster is recommended after 3 years for those at continued risk.
- Administered by deep subcutaneous route

Vaccine efficacy in PLHIV

- No studies have been published on antibody responses to JEV vaccination in PLHIV.
- No data are available on the immunogenicity of three vaccine doses or on the impact of highly active cART on vaccine responses. It should be assumed that patients with CD4+ count < 400 cells/μL and especially those with CD4+ count < 200 cells/μL are likely to have reduced response rates.

Vaccine safety and adverse events

- The JEV vaccine is moderately reactogenic.
- A history of allergies or urticaria may increase the risk for adverse reactions.
- Adverse reactions tend to occur within 48 hours for the first dose but around 96 hours for the second. The hypersensitivity reaction may occur as late as 10 to14 days after the last dose.
- Common: tenderness, redness, swelling, and other local effects (reported in about 20% of vaccines)
- Less common: fever, headache, malaise, rash, and other reactions such as chills, dizziness, myalgia, nausea, vomiting, and abdominal pain (reported in about 10% of vaccines)

- Rare: severe hypersensitivity, including angioedema or urticaria, (occurs in 0.6% of patients)
- Limited data indicate that the pattern of adverse reactions is not modified by HIV infection.

Precautions and contraindications

- Persons with allergic conditions should be advised about the risk of vaccine-related angioedema and generalized urticaria.
- A risk assessment needs to take into account the likelihood of exposure and the possible adverse effects of the vaccine.
- Anecdotal reports suggest that the JEV vaccine should **not** be used in individuals who have recovered from acute disseminated encephalomyelitis or Guillain–Barré syndrome or who have multiple sclerosis or other demyelinating disorders.

Storage and handling

- Store at 2° – 8°C. Do not freeze or expose to freezing temperatures

2. Recommendations for pre-exposure and post-exposure prophylaxis in PLHIV

Pre-exposure prophylaxis

- People living in endemic areas
- Travellers to Southeast Asia and the Far East who will be staying for more than 30 days in endemic areas, especially if travel will include rural areas
- Travellers to and residents of areas experiencing epidemic transmission
- Persons with extensive outdoor activities in rural areas
- Expatriates whose principal area of residence is an area where JEV is endemic or epidemic

Post-exposure prophylaxis

- None
- The importance of precautions against mosquito bites should be emphasized

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F. Meningococcus

1. The vaccines

General description

- There are two meningococcal polysaccharide vaccines (MPSV) available in the Philippines.
  - Meningococcal polysaccharide A and C
  - Meningococcal polysaccharride A, C, Y and W-135 for use in children (2 years and above) and adults
- Meningococcal polysaccharide B vaccine and meningococcal conjugate vaccines are not available locally
- Protective antibody is achieved within 7-10 days of vaccination.
- In healthy adults, antibody levels decrease but are detectable as long as 10 years after vaccination
- Protection induced by the quadrivalent vaccine lasts for approximately 3 to 5 years.

Dose, route, and schedule of administration

- MPSV is administered as a single dose 0.5ml and can be given concurrently with other vaccines but at different anatomic sites.
- The vaccine is usually administered by deep subcutaneous or intramuscular injection preferably in the deltoid.
- Little boost occurs on repeated vaccination.
- Boosters are recommended after 5 years for those at continuous risk

Vaccine efficacy in PLHIV

- There has been very little data published on either the safety or efficacy of these vaccines in PLHIV.
- In general, better responses are observed in those with less advanced disease, and no major adverse reactions were noted.
- The duration of protection may be reduced in PLHIV, but there is insufficient evidence to modify standard boosting recommendations.

Vaccine safety and adverse events

- Adverse events are generally mild.
- Very common: transient local pain with associated swelling or redness and fever (> 38^{o}C)
- Common: headache, vomiting, irritability, fatigue and loss of appetite
- Rare: serious (neurological) complications or anaphylaxis

Precautions and contraindication

- Those allergic to any component of the vaccine
- Those who experienced a severe reaction after a previous injection of the vaccine
- In those suffering from high fever or acute disease, vaccination should be postponed.
- Meningococcal vaccines may be given to pregnant women when clinically indicated.

Vaccine storage and handling (product insert of polysaccharide A and C)

- Vaccine must be shipped in insulated containers.
- Should be stored at refrigerator temperature (2-8^{o}C)
- Vaccine must not be exposed to freezing temperature.
- Protect vaccine from light
- Single-dose vials must be used immediately after reconstitution or within 30 minutes of reconstitution.
- Multidoses presentation vaccine remains stable for 6 hours when stored in a refrigerator (2-8^{o}C).

2. Recommendations for pre-exposure and post-exposure prophylaxis in PLHIV

Pre-exposure prophylaxis

- If vaccination is indicated, immunization should be administered preferably after cART-induced immunoreconstitution. Responses to the vaccine may be reduced in patients with CD4+ counts < 200 cells/μL.
- Single-dose vaccination is recommended for PLHIV at risk of infection through travel.
- Travelers who will be living or working with local people in an area of risk
- For long stay and rural travelers visiting areas of risk
- Backpackers
- Travelers visiting an area of risk during an outbreak
- Re-immunization is recommended for PLHIV with risk recurrence (a booster dose is recommended every 5 years).
- PLHIV who develop meningococcal disease should be offered one vaccine dose after recovery
- Passive immunoprophylaxis: None recommended

Post-exposure prophylaxis

- Contacts of confirmed cases of meningococcal disease should be offered vaccination, as well as given chemoprophylaxis
- Recommended schedule for prophylaxis:
  - Rifampicin 600mg every 12 hours for two days
  - Ciprofloxacin 500 mg single dose (alternative)
  - Ceftriaxone 250mg IM single dose (alternative)
  - For pregnant contacts
    - Rifampicin 600 mg twice daily for two days OR
    - Ceftriaxone 250 mg IM single dose
- For patients on cART, ciprofloxacin is preferred over rifampicin.
- No recommendations on the use of immunoglobulins

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G. Poliomyelitis

1. The vaccine

General description

- Two types of polio vaccine are currently available:
  - Oral polio vaccine (OPV): A live attenuated vaccine comprised of three poliovirus subtypes
  - Inactivated poliovirus vaccine (IPV)
- It contains three serotypes of formaldehyde-inactivated poliovirus grown on monkey kidney cells.

Dose, route and schedule of administration

- IPV can be administered to adults as individual IPV vaccine or in combination with other vaccines, usually the combination vaccine diphtheria/tetanus/IPV.
- It is administered intramuscularly or subcutaneously in persons with bleeding disorders.
- Primary series should be administered in 3 doses as follows: The first 2 doses of IPV given at a 4-8 week interval and a third dose 6-12 months after the second dose.
- Booster dose is given after 5 and 10 years.
- OPV is contraindicated in PLHIV and their contacts.

Vaccine efficacy in PLHIV

- Both OPV and IPV produce neutralizing antibody responses in HIV-infected children.
- Antibody responses to a primary course of IPV have been studied in children of HIV-infected mothers, comparing those with and without HIV infection. No significant differences were detected between HIV-infected and non-HIV infected children, with 88% developing adequate titers of neutralizing antibody to all three serotypes after two doses of IPV, and 100% to at least two serotypes.
- In patients with advanced HIV infection response to the vaccine is reduced.
- Humoral immune responses to IPV are presumed to be restored in patients with advanced disease who are successfully treated with cART. However, the longevity of protection may be reduced in PLHIV.

Vaccine safety and adverse events

- IPV can be safely administered to immunocompromised adults.
- Injection site reactions are the most common adverse events reported, occurring with greater frequency after subsequent doses.

Precaution and contraindications

- OPV is contraindicated in PLHIV and their contacts.

Vaccine storage and handling

Shipping requirements

- Should be shipped in insulated container. Maintain temperature at 35-46°F (2-8°C). Do not freeze or expose to freezing temperatures.

Storage requirements

- Refrigerate immediately upon arrival. Store at 35-46°F (2-8°C). Do not freeze or expose to freezing temperatures.

Shelf life after opening

- Multidose vials: Withdraw single dose of vaccine into separate sterile needle and syringe for each immunization. The vaccine should be administered shortly after withdrawal from the vial. Unused portions of multidose vials may be refrigerated at 35-46°F (2-8°C) and used until expired, if not contaminated or unless otherwise stated in the manufacturer's product information.
- Manufacturer-filled syringes: The vaccine should be administered shortly after the needle is attached to the syringe.

Special instructions

- Rotate stock so that the earliest dated material is used first.

2. Recommendation for pre-exposure and post-exposure prophylaxis in PLHIV

Pre-exposure prophylaxis

- Infants and children infected with HIV regardless of their immune status
- Household members or other household contacts
- Nursing personnel in close contact with PLHIV
- Unvaccinated or incompletely vaccinated PLHIV who intend to travel to a polio-endemic area such as India, Pakistan, Afghanistan and Nigeria
- PLHIV with a history of incomplete vaccination should receive the remaining doses of IPV to complete a five-dose vaccination course, regardless of the interval since the last dose and type of vaccine received previously.

Post-exposure prophylaxis

- Human normal immunoglobulin (HNIG 750 mg IM, preferably in the deltoid or SC in persons with bleeding disorders) is recommended for PLHIV following exposure to wild-type poliovirus or OPV, regardless of vaccination history.
- HNIG should be given as soon as possible after exposure. Protection lasts for three weeks.
- Where the information is available, HNIG is **not** indicated if the PLHIV is known to be antibody-positive to all three poliovirus types.
- Prior OPV/IPV history should be recorded.
- A serum should be collected for baseline antibody testing, but prophylaxis should not be delayed pending the results. Stool samples should be collected one week apart for analysis. If poliovirus is detected, repeat administration of HNIG at three-weekly intervals will be required until two consecutive stool samples test negative.

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H. Rabies

1. The vaccine

General description

- Cell culture rabies vaccines – These are modern day vaccines prepared from rabies virus grown on tissue culture, free of neuronal tissues, inactivated by B-propiolactone and purified by ultracentrifugation.
  - Human diploid cell vaccine (HDCV) – the gold standard of human rabies vaccines
  - Purified vero cell rabies vaccine (PVRV)
  - Purified chick embryo cell vaccine (PCECV)
  - Purified duck embryo vaccine

Indications for immunization in PLHIV

Routine use

- Pre-exposure vaccination is recommended for:
  - Health care workers in hospitals that handle dog bites and rabies cases (doctors, nurses, paramedical staff)
  - Rabies research and diagnostic lab workers
  - Rabies biologic production workers
  - Veterinarians and vet students
  - Animal control and wildlife handlers
  - Spelunkers and other animal handlers
  - Field workers (bill collectors, mailmen, delivery men)
  - Morticians and embalmers

Dose, route, and schedule of administration

Pre-exposure prophylaxis for PLHIV:

- 1 injection IM on Days 0, 7, and 28

Post exposure prophylaxis for PLHIV

- 1 IM dose each on Days 0, 3, 7, 14, 28 or 30: or
- 2 IM doses on Day 0, and 1 IM dose each on Day 7 and Day 21
- If currently asymptomatic, with CD4+ >400cells/mm, with completed pre-exposure prophylaxis:
  - 1 IM dose on Day 0, and 1 IM dose on Day 3

Note:

- All injections must be given on the deltoids only
- All injections must be given intramuscularly
- Serologic testing like rapid focus flourescent inhibition test (RFFIT),

(if available routinely) should be done between days 14 and 28. If the antibody response is <0.5 IU/ml, a further booster dose of rabies vaccine should be administered

Vaccine efficacy in PLHIV

- Data on the efficacy of rabies vaccine for pre- and post- exposure prophylaxis in PLHIV are very limited. Available evidence indicates that the immune response is affected by the CD4+ cell count and disease stage, with low or absent antibody responses reported in some persons with CD4+ count <200-250 cells/μL.
- In published studies, most vaccine failures occurred in persons who were either not receiving ART or were receiving sub-optimal regimens.

Vaccine safety and adverse events

- Soreness, swelling or itching in duration at injection site
- Headache, dizziness, nausea, abdominal pain
- Rarely, neurologic reactions reported, resolved spontaneously

Precautions and contraindications

Precautions

- Always inject IM vaccines on the deltoid, **never in the buttocks**.
- For persons with bleeding disorders, consider ID route.
- For persons with PLHIV, or on corticosteroids, other immunosupressive agents, or antimalarial prophylaxis agents, give vaccine only by IM route. These drugs can interfere with antibody response and immune response may be inadequate.
- Never administer vaccine intravascularly.

Contraindications

- Presence of moderate and severe acute illnesses
- Allergy to any vaccine component
- An immediate anaphylactic reaction to a previous dose of rabies vaccine
- Pregnancy is **not** a contraindication for post-exposure treatment.

Storage and handling

- Ideal storage conditions are 2-8^{o}C.

2. Recommendations for pre-exposure and post-exposure prophylaxis in PLHIV

Pre-exposure prophylaxis

- All PLHIV who belong to the high-risk population

Post-exposure prophylaxis

All persons exposed to rabid or suspect rabid animals categorized as follows:

Category I*

- Touching or feeding of animals
- Licks on broken skin

Category II**

- Nibbling of uncovered skin
- Minor scratches or abrasions without bleeding
- Minor scratches and abrasions in the head, face or neck

Category III**

- Licks on broken skin
- Single or multiple transdermal bites or scratches
- Contamination of mucous membranes with saliva
- All Category II exposures in the head, face or neck

Notes:

* Pre-exposure prophylaxis may be recommended

** Post-exposure prophylaxis MUST be administered

Available vaccines in the Philippines:

- Purified vero cell rabies vaccine (PVRV)
  - Dose: 0.5 ml IM or 0.1ml ID
- Purified chick embryo cell vaccine (PCECV)
  - Dose – 1.0 ml IM or 0.1 ml ID

3. The role of passive immunization product (immunoglobulins)

Immunoglobulins are administered to:

- All patients with Category III exposure
- All Category II exposure patients who are immunocompromised, including PLHIV

Composition

- Human rabies immune globulin (HRIG) prepared from plasma of hyperimmunized human donors
- Equine rabies immune globulin (ERIG), prepared from serum of horses
- Fractionated equine rabies immune globulin (Favirab) contains F(ab')2 fragments rather than the whole globulin.

Dose and route of administration

- HRIG: 20 IU/kg body weight
- ERIG: 40 IU/kg body weight. Skin test has to be done before administration
- Favirab: 40 IU/kg body weight. Skin test has to be done before administration.
- The entire dose is infiltrated in and around the site of the bite, if anatomically feasible. The remaining solution is injected intramuscularly at a site distant from the vaccine site.

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I. Tetanus-diphtheria-pertussis

1. The vaccines

General description

- Purified inactivated fractional adsorbed tetanus toxoid
- Purified inactivated adsorbed diphtheria-tetanus toxoid (Td)
- A sub-unit fractional inactivated vaccine formulated to contain 5 Lf of tetanus toxoid, 2 Lf diphtheria toxoid, 2.5 Lf ug detoxified pertussis vaccine (Tdap)

Dose and route of administration

- Two doses of Tetanus diphtheria toxoid (Td) 0.5ml at 4 to 8 weeks apart IM followed by 3rd dose of tetanus-diphtheria-pertussis (Tdap) to be given 6 to 12 months later
- Booster every 10 years with Tdap
- Partially immunized pregnant women should complete the series of three doses. In pregnancy, the 3rd dose is given at least two weeks before delivery.

Vaccine efficacy in PLHIV

Tetanus

- The vaccine has been shown to be less immunogenic in PLHIV.
- In general, responses are inversely correlated to the CD4+ cell count. Antibodies in PLHIV may decline to non-protective levels as the immune factors deteriorate.
- There is insufficient evidence to modify recommendations about boosting.

Diphtheria

- Limited data exist on the immunogenicity and clinical efficacy of the vaccine in PLHIV.
- Vaccine responses may be reduced compared to HIV-negative persons, especially in those with advanced disease and low CD4+ cell count.
- Response to vaccine may improve with cART.

Pertussis

- No data on clinical efficacy of the vaccine in PLHIV are available this time.

Vaccine safety and adverse events

Local

- Pain at the injection site

Systemic

- Headache, generalized body aches
- Tiredness, fever in <10%
- Severe systemic reactions such as generalized urticaria, anaphylaxis or neurological complications are rare.
- No increased risk of side effects or adverse reactions in PLHIV

Precautions and contraindications

- Moderate to severe illness with or without fever
- Moderate to severe anaphylactic reaction to any toxoid component like thimerosal
- Per ACIP, history of neurologic or severe hypersensitivity reaction following a prior dose
- Bleeding disorders
- Thrombocytopenia, hemophilia and other coagulation disorders

Vaccine storage and handling

- Store at 2-8^{o}C. Do not freeze.
- The vaccine should not be stored in direct contact with refrigerant.

2. Recommendations for pre-exposure and post-exposure prophylaxis in PLHIV

Pre-exposure prophylaxis

Tetanus /diphtheria

- Tetanus vaccination is recommended in all PLHIV regardless of CD4+ cell count and should be given in accordance with standard recommendations.
- Adults who have **not** been immunized previously or have an uncertain vaccination history require five vaccine doses in order to confer adequate protection.
- Three doses should be given at least 1 month apart (0, 1 month, 2 month) and two further boosting doses should be planned at 5 and 10 years. There is no need to restart a series if more than the recommended time between doses has elapsed.

- Adults who have received a full primary course (three doses) as infants and a booster at preschool age (total of four doses) require a single booster dose.
- Persons who have received five vaccine doses require a booster dose at 10-yearly intervals if with increased risk of exposure or if they are due to travel to remote areas where they may not be able to receive tetanus immunoglobulin (TIG) in the event of a tetanus-prone injury.
- Td vaccines can be administered to PLHIV irrespective of their immune status, using the same schedule and dose for non-HIV-adults .
- Booster doses every 5-10 years

Pertussis

- For individuals at high risk of infection (e.g., those exposed in the household or in high-risk occupations), a single dose of a pertussis-containing vaccine (Tdap) could be considered.

Post-exposure prophylaxis

Tetanus

- In unvaccinated persons, the tetanus vaccine alone is not considered adequate for post-exposure prophylaxis after a high-risk exposure.
- Patients with unknown or uncertain previous vaccination history and those who have not completed the primary vaccine series should also be considered susceptible.
- TIG is used for post-exposure prophylaxis in these patients together with the tetanus vaccine (Table 7). TIG is given by intramuscular injection at the dose of 250 IU, or 500 IU if more than 24 h have elapsed since injury, if there is a risk of heavy contamination and following burns.
- TIG confers protection for approximately 4 weeks. TIG has not been studied in large-scale trials. Evidence of its efficacy has been drawn from retrospective studies in healthy individuals. Efficacy in PLHIV has not been established.
- Wound cleaning, **debridement** (when indicated) and proper immunization are the essential components of wound management in PLHIV. The need for tetanus vaccine and TIG depends on both the condition of the wound and the vaccination history.

Table 7: Tetanus post-exposure prophylaxis in PLHIV

History of tetanus toxoid (no. of doses)	Characteristic			
	Clean, minor wounds		All other wounds	
	Tdap or Td[1]	TIG	Tdap or Td[1]	TIG[2]
Unknown or <3	Yes	No	Yes	Yes
>3	Yes (1 dose) if last dose given >10 years before	No	Yes (1 dose) if last dose given >10 years before or CD4+ count < 200 cells/µl	Yes[3]

[1] Tetanus vaccine is recommended in all PLHIV following a possible exposure.

[2] TIG should be given by intramuscular injection in the deltoid within 24h of possible exposure. When tetanus vaccine and TIG are given concurrently, separate syringes and separate sites should be used.

[3] TIG is not usually indicated for persons who have received at least three vaccine doses including a dose within the previous 10 years.
However, individuals with a high-risk wound who are severely immunosuppressed should receive TIG even if fully vaccinated in the past and where the last vaccine dose occurred within the last 10 years.

Diphtheria

- Individuals who are close contacts of a case of diphtheria should receive vaccination and antibiotic prophylaxis as soon as possible.
- Unimmunized individuals should receive three doses of Td/IPV.
- Previously immunized individuals should receive a single booster dose of Td/IPV unless a booster dose was given within the past year.
- The recommended regimen for antibiotic prophylaxis for adults is a single dose of intramuscular benzylpenicillin (1.2M units) or erythromycin 500 mg every 6 h for 7 days.

Pertussis

- Unimmunized or partially immunized individuals and vulnerable close contacts of a case of pertussis should be offered antibiotic prophylaxis within 21 days of onset of a clinically suspected or confirmed case.
- Post-exposure chemoprophylaxis is recommended in all PLHIV regardless of CD4+ cell count or immunization status.
- The recommended regimens for adults:
  - Erythromycin estolate 500 mg QID for 14 days
  - Azithromycin 500 mg Day 1, 250 mg Days 2-5
  - Cotrimoxazole double strength 1 tablet once daily for 14 days
  - Clarithromycin 500 mg BID for 7 days

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J. Typhoid

1. The Vaccine

General Description

- Two typhoid vaccines are available locally: the parenteral ViCPS vaccine, containing purified Vi ('virulence') capsule polysaccharide and the oral Ty21a vaccine, containing live attenuated S. typhi Ty21a

Dose, route, and schedule of administration

- The oral vaccine is **contraindicated** for use among PLHIVs.
- The dose of ViCPS vaccine is 25 mcg (0.5 ml) given intramuscularly (or subcutaneously in persons with bleeding disorders), preferably in the deltoid (Typherix GSK, Typhim VI Sanofi)
- One dose of the vaccine should be given at least 2 weeks before the expected exposure.
- A booster is recommended every 3 years in those who remain at risk. This interval might be reduced to 2 years if the CD4+ count is <200 cells/μL.

Vaccine efficacy In PLHIV

- Typhoid vaccines are not 100% protective and responses may be further reduced in HIV infection. Travelers should be advised to follow strict food and drink precautions.

Vaccine safety and adverse events

- Serious problems from typhoid vaccine, such as severe allergic reaction, are very rare.
- Mild reactions include:
  - Fever (up to about 1 person per 100)
  - Headache (up to about 3 people per 100).
  - Redness or swelling at the site of the injection (up to 7 people per 100)

Precautions and contraindication

- Use with caution among pregnant and lactating women, those with bleeding disorders
- Contraindicated among patients with acute severe febrile infection
- Do not use among those who had had a severe reaction to a previous dose of the vaccine

Vaccine storage and handling

- Store the vaccine in a refrigerator between 2°-8°C.

2. Recommendations for pre-exposure prophylaxis in PLHIV
   - Those with significant risk of exposure to *S. typhi* (i.e. local outbreaks, travel to high risk areas)
   - Those who will have close contact with a documented *S. typhi* carrier
   - Laboratory workers exposed to *S. typhi*

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VACCINES THAT CAN BE GIVEN SAFELY TO PLHIV IF INDICATED, AND IF THEY ARE ASYMPTOMATIC, WITH A CD4+ T CELL COUNT OF >200 CELLS/ML

Measles-Mumps-Rubella
Varicella
Yellow Fever

A. Measles-mumps-rubella

1. The Vaccine

General description

- Measles vaccine is a live further attenuated strain.
- Mumps vaccine is a live attenuated mumps virus vaccine.
- Rubella vaccine is a live attenuated virus.

Dose, route and schedule of administration

- Two doses should be administered to confer immunity to measles, mumps and rubella with the second dose given at any time but at least one month after the first.
- Administered by deep subcutaneous or intramuscular injection preferably in the deltoid

Vaccine efficacy In PLHIV

- Limited published data show that a minority of measles IgG- seronegative PLHIV seroconvert following vaccination.
- Serocoversion rates for rubella are also diminished in these patients.
- cART-induced immunoreconstitution is likely to improve seroconversion rates.
- Durability of responses may be reduced in PLHIV.

Vaccine safety and adverse events

- Fever and rash occur in 5-15% of vaccine recipients, usually 7-12 days after vaccination and lasting 1-2 days. These are usually attributable to the measles component.
- Arthalgia andor arthritis are reported in up to 25% of vaccinated women and are usually mild and transient. Transient lymphadenopathy sometimes occurs and is associated with rubella vaccination.
- Parotitis and deafness occur rarely and are attributable to the mumps component.
- In general, MMR vaccination is safe in HIV-infected adults. Serious illnesses have **not** been reported in PLHIV in association with mumps or rubella vaccine administration.

Precautions and contraindications

- Persons with severe allergy (i.e. hives, swelling of the mouth or throat, difficulty breathing, hypotension and shock) or who have had a severe

allergic reaction to a prior dose of MMR should not be vaccinated with MMR.

- Pregnant women should **not** receive measles vaccine. Pregnancy should be avoided for 1 month following receipt of measles vaccine/ MMR vaccine.
- Persons receiving large daily doses of corticosteroids (>2mg/kg per day or <20 mg per day of prednisone) for 14 days or more should **not** receive MMR.
- Persons with moderate/severe acute illness should not be vaccinated until the illness has resolved.
- Receipt of antibody-containing blood products (e.g. immune globulin, whole blood or packed red blood cells, intravenous immune globulin) may interfere with seroconversion to measles.
- Patients who are severely immunocompromised for any reason should not be given MMR vaccine.

Vaccine storage and handling

- Ship with refrigerant to maintain 10'C (50'F) or less at all times.
- Refrigerate immediately and protect from light at all times.
- Store at refrigerator temperature 2-8'C (35-45'F), but may be frozen.
- After reconstitution, store in a refrigerator and use immediately or discard after 8 hours.

2. Recommendations for pre-exposure prophylaxis in PLHIV

- The combined MMR vaccine is recommended for PLHIV who want to be protected against measles, mumps and rubella infections.
- The vaccine is indicated for PLHIV who are asymptomatic and with a CD4+ T cell count of >200 cells/μL.
- HIV-infected women of childbearing age should also be screened for rubella IgG and the MMR vaccine offered to rubella IgG-seronegative women with CD4+ counts>200cells/uL.
- Rubella IgG serology should be repeated after vaccination and a second MMR dose administered if the patient remains rubella IgG-seronegative.
- MMR should be administered at least 14 days before or 3 months after the administration of antibody-containing blood products (e.g. immune globulin) because passively acquired antibodies may interfere with the response to the vaccine.

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B. Varicella

1. The Vaccine

General description

- Live attenuated varicella virus vaccine
- Propagated in human or guinea pig cells
- Lyophilized and to be reconstituted when used as directed from package insert
- Either as single antigen or combination (with MMR, at least in U.S.)
- Contains hydrolyzed gelatin, neomycin, fetal bovine serum, sucrose, human-diploid cells (MRC-5) and egg protein (in combination MMR vaccine)
- Does not contain known preservatives
- Duration of protection is uncertain (probably >10 years)

Dose, route and schedule of administration

- Administered by subcutaneous injection, preferably in the deltoid
- 3 months interval between doses in PLHIV
- Pregnancy should be avoided for 1 month after vaccination.

Vaccine efficacy in PLHIV

- Limited data on the efficacy of vaccination among PLHIV
- Among VZV IgG-seropositive persons with CD4+ counts> 400 cells/uL and stable on antiretroviral therapy for at least 3 months, the vaccine has been shown to boost VZV-specific cellular immune responses.
- Less robust responses have been observed in patients with nadir CD4+ count <200 cells/uL restored to >400 cells/uL with cART. By extrapolation of the recent observations in children, expert opinion in the U.S. now advises consideration of VZV vaccination in older children and adults with CD4+ counts >200 cells/uL.

Vaccine safety and adverse events

- Up to 10% of immunocompetent adults develop a vaccine-associated rash, localized at the site of injection or generalized, within one month of immunization; may also have fever.
- In VZV IgG-seropositive PLHIV with CD4+ >400 cells/uL while on cART no excess adverse events have been reported following VZV vaccination; no significant effects on HIV plasma RNA load have been observed.

- Transmission of vaccine virus from vaccines has been documented only rarely and only from individuals with vaccine-associated rashes.

Precautions and contraindications

Precautions

- Acute severe illness
- Untreated tuberculosis
- Thrombocytopenia
- Recent administration of blood, plasma or immune globulin
- Use of salicylates

Contraindications

- History of severe adverse reaction or anaphylactic reaction to the vaccine or any vaccine component
- Pregnancy and breastfeeding
- Malignant condition affecting the bone marrow or lymphatic system
- Family history of congenital or hereditary immunodeficiency in first-degree relatives; significant immunodeficiency including cellular immunodeficiency
- High-dose immunosuppressive therapy or low-dose steroid therapy exceeding 2 weeks' duration
- Persons with acute moderate or severe febrile illness usually should not be vaccinated until their symptoms have abated.

Storage and handling

- Store only in stand-alone freezers or the freezer compartment of refrigerator-freezer combinations, provided that the freezer compartment has its own separate, sealed, and insulated exterior door.
- Use immediately after reconstitution or within 72 hours upon removal from freezer; may not refreeze once out of the freezer; refrigerator temperature- stable up to 3 days from removal in freezer.
- May be transported using dry ice or frozen packs, particularly for field vaccination; combination MMR may not be transported at any time.

2. Recommendation for pre-exposure prophylaxis in PLHIV

- Varicella zoster virus IgG-negative
- PLHIV with uncertain history of varicella infection and who wants to be protected against the infection

- PLHIV who are at risk of exposure
- Tests to demonstrate VZV IgG seroconversion should be performed 4-6 weeks after the second vaccine dose.

3. The role of passive immunization with VZV immune globulin (VZIG)

- Indicated for susceptible immunocompromised patients who have had a significant exposure to VZV to include symptomatic PLHIV and asymptomatic patients with CD4+ count <400 cells/uL
- Given to high-risk persons for whom varicella vaccine is contraindicated
- There is no published evidence of VZIG efficacy in PLHIV.
- Do not use if the person is on regular immune globulin treatment.
- VZIG is given by intramuscular injection.
- This should be administered as soon as possible within 96 hours of exposure. The duration of protection is 3 weeks.
- In the event of a second exposure after 3 weeks, repeat administration of VZIG prophylaxis is recommended.
- Rare anaphylactic reactions have occurred in individuals with hypogammaglobulinemia or prior blood transfusion reactions.
- Where intramuscular injection is contraindicated in individuals with bleeding disorders, intravenous immunoglobulin (0.2 g/kg body weight) may be given instead.

Post-exposure prophylaxis

- Following a significant exposure to varicella or zoster, the VZV IgG status should be ascertained but prophylaxis should not be delayed waiting for the results.
- VZV IgG-seronegative patients should be considered for post-exposure prophylaxis and monitored closely for symptoms of varicella to facilitate prompt institution of antiviral therapy.
- Post-exposure prophylaxis should be tailored to the patient's clinical status.
- For symptomatic HIV infection and/or CD4+ counts <400 cells/μL (with or without cART):
    - VZIG must be given as soon as possible, preferably within 7 days and not later than 10 days after exposure.
    - Antiviral chemoprophylaxis with oral acyclovir (800 mg four times daily or equivalent) for 7 days, commencing 7-10 days post-

exposure, may be considered if VZIG is not available, or given in conjunction with VZIG in profoundly immunocompromised patients.

- Asymptomatic HIV infection and CD4+ counts >400 cells/μL (with or without cART):
  - Vaccination should be considered within 3 days of exposure. The second dose should be normally scheduled after 3 months, with subsequent serological testing to confirm VZV IgG seroconversion 4-6 weeks after the second vaccine dose.

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C. Yellow Fever

1. The Vaccine

General description (YFV- Yellow fever vaccine)

- A live-attenuated virus vaccine
- Vaccination can only be given at designated centers competent in yellow fever vaccination

Dose, route and schedule of administration

- Given by subcutaneous injection, preferably in the deltoid
- Given as a single 0.5 ml dose
- A booster is indicated after 10 years for those at risk, provided that the CD4+ count is >200 cells/μL.
- Other live-virus vaccines may be given concurrently; alternatively 4 weeks should be allowed to elapse between sequential vaccinations.
- Pregnancy should be avoided for 1 month after vaccination

Vaccine efficacy in PLHIV

- Data regarding seroconversion rates after YFV vaccination among PLHIV are limited.
- High seroconversion rates (around 70%) have been observed in PLHIV adults with CD4+ counts >200 cells/μL, most of whom where on cART at the time of vaccination.
- Good responses have also been reported in asymptomatic PLHIV adults with CD4+ counts ranging between 240 and 1300 cells/μL, most of whom where on cART at the time of vaccination.
- The duration of protection in PLHIV is unknown, but may be reduced compared to HIV-negative persons.

Vaccine safety and adverse events

- Most common adverse event: injection site reactions
- An influenza-like illness, characterized by fever, headache and muscle ache, occurs in 2-10% of vaccine recipients 5-14 days after immunization.
- More serious adverse events: very rare and less common in those who have had previous immunization
- Severe: risk of encephalitis to PLHIV
- Rare: Hypersensitivity or anaphylaxis (one per 130,000-250,000),

neurotropic disease (one per 250,000-8 million) and the recently recognized viscerotropic disease (one per 40,000–1,200,000)
- May be safe in PLHIV with less advanced disease, in PLHIV with CD4+ counts > 200 cells/μL, either in early HIV infection or following cART.

Precautions and contraindications

Precautions
- Acute moderate to severe illness with or without a fever usually should not be vaccinated until their symptoms have abated.

Contraindications
- An immediate anaphylactic reaction to a previous dose of yellow vaccine
- Anaphylactic reaction to a vaccine component
- History of anaphylaxis or sensitivity to eggs or egg protein
- Pregnancy and breast-feeding mothers
- Concurrent administration of cholera and yellow fever vaccines leads to a suboptimal immune response to both vaccines. They should be given at least 3 weeks apart. If this cannot be done because of time constraints, then they should be given on the same day.

Vaccine storage and handling
- Store at a temperature between 2-8ºC (refrigerator temperature)
- Do not freeze.

2. Recommendation for pre-exposure prophylaxis in HIV
- All PLHIV who intend to travel or live in areas where yellow fever is endemic (South America or Africa) and are at risk of exposure to the infection, or protection against mosquitoes cannot be guaranteed
- Those PLHIV who will travel to countries where yellow fever vaccine is a requirement

Yellow fever is the only disease for which the WHO requires an International Certificate of Vaccination for travelers. Some countries require a certificate for all travelers, while other countries require it only from travelers coming from endemic areas. The Philippines requires a vaccination certificate form from all travelers over 1 year of age coming from endemic countries. Filipinos traveling to endemic areas can get the vaccine and certificate from the Bureau of Quarantine, Port Area, Manila at telephone number: (632)

527-4678. Vaccination should be undertaken at least 2 weeks before travel and vaccine recipients should be monitored closely after vaccination.

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List of Abbreviations

AEFI	Adverse Event Following Vaccination
AIDS	Acquired Immunodeficiency Syndrome
AntiHBs	Antibody against Hepatitis B Surface Antigen
cART	Combination Antiretroviral Therapy
CSF	Cerebrospinal Fluid
DNA	Deoxyribonucleic Acid
DTaP/IPV/Hib	Combined diphtheria-tetanus-acellular pertussis/ inactivated polio/Haemophilus influenza B
ERIG	Equine Rabies Immune Globulin
ETEC	Enterotoxigenic Escherichia coli
FDA	Food and Drug Administration
H	Hemagglutinin
HAV	Hepatitis A virus
HBIg	Hepatitis B immune globulin
HBsAg	Hepatitis B surface Antigen
HBV	Hepatitis B virus
HCC	Hepatocellular carcinoma
HDCV	Human Diploid Cell Vaccine
Hib	Haemophilus influenzae Type B
HIV	Human Immunodeficiency Virus
HIV-RNA	Human Immunodeficiency Virus- Ribonucleic Acid
HNIG	Human Normal Immune Globulin
HPV	Human Papilloma Virus
HRIG	Human Rabies Immune Globulin
ID	Intradermal
IDU	Injecting drug users
IgG	Immunoglobulin G
IM	Intramuscular
IPD	Invasive Pneumococcal Disease
IPV	Inactivated poliovirus vaccine
IV	Intravascular
JEV	Japanese encephalitis virus
LAIV	Live attenuated influenza vaccine
MMR	Measles, Mumps, Rubella
MPSV	Meningococcal polysaccharide vaccines
MSM	Men who have sex with men

N	Neuraminidase
OPV	Oral polio vaccine
PCECV	Purified Chick Embryo Cell Vaccine
PCV-7	7-valent pneumococcal conjugate vaccine
PLHIV	Persons living with human immunodeficiency virus
PPV23	23-valent pneumococcal polysaccharide vaccine
PVRV	Purified Vero Cell Rabies Vaccine
RFFIT	Rapid Focus Fluorescent Inhibition Test
SC	Subcutaneous
Td/Tdap	Tetanus-Diphtheria/ Tetanus-Diphtheria-acellular Pertussis
TIG	Tetanus immunoglobulin
TY 21a	oral Ty21a typhoid vaccine, containing live attenuated S. typhi Ty21a "strain"
VAPP	Vaccine-associated paralytic polio
ViCPS	Vi ('virulence') capsule polysaccharide
VZV	Varicella-Zoster virus
YFV	Yellow Fever vaccine