

# Proposed recommendations for discussion

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# Working Group Conclusions

- No policy change on age of vaccination (birth) is justified
- Continue **universal BCG vaccination** in high incidence TB settings and **to expand to countries with high leprosy burden**
- Added recommendations for vaccination of HIV infected **children/individuals clinically well and immunologically stable on anti-retroviral therapy (ART)**
- Urgent need for research in the development of **new vaccines**
- Encourage **molecular characterization** of currently available BCG vaccines in terms of strain and product specific aspects

# 1. Universal vaccination at birth

- In countries or settings with high\* incidence of TB **and/or leprosy**, BCG should be given to neonates at birth, or as soon as possible thereafter, for prevention of TB and leprosy
- Newborns also receive hepatitis B vaccine as soon as possible after birth, ideally within 24 hours, therefore co-administration with BCG is strongly recommended as it is safe to do so
- If the birth dose was missed, catch-up vaccination of unvaccinated is recommended

\*Countries with high incidence of TB are those with a TB notification rate >40 TB cases per 100,000 population per year.



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## 2. Selective risk group vaccination at birth

- Countries with low\* incidence of TB or leprosy may choose to **selectively** vaccinate neonates in recognized risk groups
- High-risk groups to be considered include:
  - Neonates of parents (or other close contacts/relatives) with previous TB or leprosy disease
  - Neonates in immigrant populations from countries with high incidence of TB and/or leprosy
  - Neonates in any other locally identified risk group for TB and/or leprosy

\*Countries with low-incidence of TB are those with a TB notification rate of  $<100$  TB cases (all forms) per 1 million population per year.



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### 3. Switching from universal to selective risk group vaccination at birth

- Countries should consider the impact of a switch on prevention of leprosy and consideration should be given to other mycobacterial infections, as well as any potential non-specific effects of BCG vaccination on all-cause infant mortality.
- Essential to have an efficient disease **surveillance system** capable of showing:
  - the current notification rate of bacteriologically confirmed pulmonary TB cases
  - the average annual rate of tuberculous meningitis in children aged under five years should be monitored
  - routine leprosy notification rates at national and sub-national level and burden of other mycobacterial infections e.g. Buruli ulcer should be assessed

## 4. Vaccination of older age groups

- BCG vaccination of unvaccinated/tuberculin skin test (TST) or IGRA\*, negative school-children provides long-term effectiveness (up to 20+ years)
- BCG vaccination of older age groups should be considered in:
  - Unvaccinated older children, adolescents and adults living in high incidence settings of TB and/or leprosy
  - Unvaccinated older children, adolescents and adults moving from low incidence to high incidence TB/leprosy settings
  - Unvaccinated/TST- or IGRA negative persons at risk of occupational exposure in low and high TB incidence areas

\* Interferon gamma release assay



## 5. HIV exposed and other immunocompromised

- BCG vaccination is **contraindicated** for persons:
  - with impaired congenital or acquired immunity
  - known or suspected congenital immunodeficiency
  - under immunosuppressive treatment
  - **for HIV infected persons**
- **However**, if HIV infected individuals are on **anti-retroviral therapy (ART)**, clinically well and **immunologically stable** (CD4% > 25% for children under 5 years or CD4 count ≥200 if age > 5 years), **BCG administration can be considered**, especially for those living in high incidence TB settings



## 6. Populations with a high prevalence of HIV infection

- The following guidance is provided to facilitate national and local decisions on the use of BCG vaccine in infants at risk for HIV infection:
  - Neonates born to women of unknown HIV status should be vaccinated.
  - Neonates born to known HIV-infected women and whose HIV infection status is unknown but who demonstrate no signs or reported symptoms suggestive of HIV infection should be vaccinated particularly if the mother is already on ART.





## 6. Populations with a high prevalence of HIV infection (cont..)

- Neonates who are born to HIV-infected mothers and whose HIV infection status is unknown but who have signs or reported symptoms suggestive of HIV infection should not be vaccinated.
  - *However, only applicable to infants who have not yet received BCG in the first few weeks of life, since clinical manifestations typically occur after the neonatal period.*
- For newborns who are confirmed HIV infected through early virologic testing, although evidence is limited, BCG should not be administered until the infant has started on ART and confirmed to be immunologically stable (CD4% > 25%).

## 7. Vaccination of special populations, contraindications & precautions

- **No contraindications** for **low birth weight or preterm infants\***, or **lactating women**
- **Pregnant women** – BCG is **contraindicated** during pregnancy
- **Travelers**
  - An individual risk-strategy based on age, duration of travel and the TB incidence in the country to be visited should be considered before vaccination of travelers from non TB endemic countries to TB endemic countries.
  - For young children traveling to TB endemic countries, particularly those under 2 years of age and those likely to have repeated travel during childhood, should be vaccinated.

\*not including extreme LBW (< 1000g) and preterm infants (< 30 weeks gestation)



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# Recommendations for specific measures including surveillance

- Currently, reporting of childhood TB cases by countries to WHO is broken into two age ranges: 0-4 years and 5-14 years. To better understand the effectiveness of BCG vaccination at various ages, it should be encouraged to report TB cases by age in years, (and if possible by months for those less than 1 year) including status of BCG vaccination of cases (preferably with information with used product/batch).

## 8. Research needs

- Development of **new vaccines** against TB and leprosy is recommended; assessment might include their potential non-specific effects on all-cause mortality.
- More evidence is needed on the influence of **BCG vaccine strain/product on efficacy, effectiveness, and adverse effects**.
- The implementation of **BCG vaccination of HIV infected children** including those on ART should be monitored and research on effectiveness and safety should be considered.
- Research for **strategies to improve timeliness** of BCG vaccination should be conducted.

## 8. Research needs (cont.)

- Long-term studies to explore BCG **vaccine effectiveness**, **duration of protection** particularly in low latitudes could be useful.
  - Studies on BCG vaccine efficacy and effectiveness should be carefully assessed when BCG is not given soon after birth or after stringent testing if given in childhood.
- Granted that such studies are **difficult and expensive**, further investigations rigorously designed and implemented may however help clarify outstanding questions.