

# Pertussis Vaccination Schedules

## Summary and recommendations

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# FOR DECISION

- Review the evidence in support/against different schedules for DTP containing vaccines and the impact of different vaccination strategies.
  1. **Is there enough evidence to support the preferential use of different DTP-(X) immunization schedules?**
    - How does this differ for wP and aP-based vaccines?
  2. **Is there enough evidence to identify criteria supporting the preferential use of different DTP- (X) immunization schedules?**
- Update recommendations on the optimal schedules for DTP containing vaccines
  - with a view to lead to the updating of the pertussis position paper

# Current schedules considered in the analyses

- **Age at first dose:**
  - 6 weeks
  - 8 weeks
  - 12 weeks and onwards
- **Number and timing of primary infant doses**
  - 3 doses using an accelerated schedule (6,10,14 weeks or 2,3,4 months)
  - 3 doses using an extended schedule (2,4,6 months)
  - 2 doses using an extended schedule (2,4 months and 3,5 months)
  - 2 doses using an accelerated schedule (2,3 months and 3,4 months)
- **Infant-toddler booster**
  - None
  - <9 months
  - 9-11 months
  - 12-14 months
  - ≥15 months
- **Preschool booster**
  - None
  - < 4years
  - 4-5 years
  - ≥6 years

# Framing of the policy questions

- **Main incentives for countries to change schedule would be an increase in vaccine impact or reduced costs of the program without loss of vaccine effectiveness.**
- High level criteria taken into consideration to inform the policy questions:
  - Maternal antibodies (initial protection/interference with early responses)
  - Pertussis- diphtheria- tetanus epidemiology and particularly the epidemiology of pertussis in young infants and disease control objectives for all three diseases
  - Coverage (at a given age)
  - Regulatory approval: availability/licensed vaccines and licensing conditions
  - Correlates of protection
  - Degree and duration of protection
  - Safety and particularly reactogenicity in infants when spacing primary doses and booster
  - Potential co-administration of other vaccines (Hib, Hep B, IPV)
  - Number of contacts/ number of shots per visit
  - Number of doses needed with a specific schedule.
  - How criteria differ for wP vs aP-based vaccines
  - Costs of changing schedules and cost-effectiveness

# General conclusions

- **Pertussis vaccine main driver behind considering different schedules**
  - To protect infants against pertussis-related mortality
- **Recommended schedules should ensure flexibility**
  - To enable countries to tailor the schedules based on their local epidemiology, objective of their immunization program, and their programmatic issues.
- **Gap in knowledge: timing of D and T boosters to achieve long term or life long protection.**

# Main conclusions about the impact of different wP schedules

- **From systematic review**

- Evidence for increased immunogenicity with 2p+1 vs 3p
- No evidence for increased clinical protection with 2p+1 vs 3p

- **From modelling work (in selected LMICs)**

- Current evidence is not strong enough to preclude a move to 6w,10w,9m should this be advantageous for other antigens administered as part of the same combined vaccine.
  - However, a move to 6w,10w,9m *could* be detrimental if coverage and timeliness of the 10w dose is adversely affected, so important to carefully assess operational implications.
- 6w,14w,9m is likely to be inferior to 6w,10w,9m unless dramatic improvements can be achieved in the coverage and timing of the current 14w dose visit.

# Conclusions of the pertussis working group about DTP schedules (1 of 2)

- DTP1 should be given as early as possible  $\geq 6$  weeks of age. Thus, later schedules (e.g. 3, 5, 11 m) were not further discussed.
- No evidence in support of any 2p schedule, 2p+1 schedule at 6, 10 w plus toddler booster, or 3p+1 schedule plus adolescent/adult booster.
- Concerning a 2p+1 schedule at 6, 14 weeks plus an infant booster (9-12 months),
  - Given the high effectiveness of 2 doses of wP and aP against pertussis death, the main risk was assessed to be related to excess deaths if DTP2 was only given at 14 weeks (or later, in real life) as this would lead to an increased risk in children having received only 1 dose until the age scheduled for DTP2.
  - Primary series at 6, 10, 14 weeks would likely lead to a higher coverage with DTP2 at an earlier age.

# Conclusions of the pertussis working group about DTP schedules (2 of 2)

- A 3p primary schedule at 6,10,14 weeks carries high vaccine effectiveness against pertussis infant mortality.
- Protection against diphtheria seems to be sufficient with 3 primary doses in most settings. **For tetanus, boosters are needed** to ensure circulating antibodies i.e. continuous protection.
- Concerning the timing of the pertussis booster dose, no revisiting of the current statement was needed nor possible, as there was no new information regarding this schedule.
  - The pertussis booster dose should be administered at 1-6 years preferably in 2nd year of life ( $\geq 6$  months after last primary dose).
  - This contact could further be used as catch-up for other vaccines. This schedule should ensure protection for at least 6 years for countries using wP vaccine.
  - For countries using aP, protection may not last as long as evidenced in the USA and Australia.



# Proposed recommendations (1)

1. **Current schedules with 3 primary infant doses remains the preferred option for countries where it is currently used**
  - **Costs of ANY change...**
  - **No compelling evidence to change to 2p+1 schedule** (6w, 10w, 9m or 6w,14w, 9m).
    - Sustained efficacy during 1<sup>st</sup> year of life = no evidence of early waning which might favour a late dose at 9 months.
    - Evidence indicates additional benefit for pertussis from the 3<sup>rd</sup> dose and delaying its administration until 9 months may impact on course completion and, without rapid waning, would reduce overall protection against severe disease in the first year of life
  - **Hib component:**
    - Benefit from the 3<sup>rd</sup> priming dose if given in 1 month intervals between doses.
    - Pentavalent vaccine on 2p+1 schedule would need 8 week interval between doses
    - Uncertain need for booster to ensure longer term protection with 6w,10w,14w schedule



# Proposed recommendations (2)

- 2. Pertussis booster dose should be administered at 1-6 years**
  - Preferably in the 2<sup>nd</sup> year of life ( $\geq 6$  months after primary doses)
  - This contact can be used as catch up for administration of other vaccines
- 3. Countries should continue using alternate primary vaccination schedule as witnessed by adequate surveillance**
  - Recommendation for countries that currently do this successfully
- 4. Countries should consider their current epidemiological situation and potential impact on pertussis and Hib**
  - In the context of vaccination coverage achieved at different ages and timeliness of immunization
  - Countries should contemplate this before moving from a 3p or 2p+1 schedule
- 5. Any change in schedule and strategy should be informed by data**
- 6. Countries should try to reach the highest coverage possible with the current vaccination strategy and to implement disease surveillance**