Table III: Pertussis Vaccine Evidence to Recommendations Table

Questions:
Which type of pertussis vaccine (acelullar pertussis vaccine (aP) or wholecell pertussis vaccine (wP)) should be recommended for use in national immunization programmes?
Policy recommendations are derived from the results of the following comparisons of the profiles of the vaccines in terms of:

- The quality of the evidence on benefits and harms
- The effect of wP vs aP vaccine on clinically important outcomes and harms
- The resource implications related to the cost of aP and wP vaccine
- The values and preferences as well as equity implications

Population: Infant and child population ages 6 weeks to <7 years of age

Intervention: aP primary or secondary vaccine series compared to wP primary or secondary series

Setting (if relevant): Global, with special focus on low and middle income countries

Decision domain	Summary of reason for decision	Subdomains influencing decision
Quality of evidence (QoE) *Is there high or moderate quality of evidence* Yes **X** No ☐	Quality of Evidence for benefits: High **X**[1] Moderate ☐ Low☐ Very Low ☐ Quality of Evidence for harms: High **X**[1] Moderate ☐ Low☐ Very Low ☐	Reasons for rating down: 9 RCTs used for benefits and 10 RCTS used for estimating serious adverse effects (safety), rated as high Quality of Evidence for benefits: high Quality of Evidence for harms: high
Balance of benefits and harms *Is there certainty that the benefits outweigh the harms?* Yes **X** No ☐	**Intervention Effects:** A primary series of wP or aP vaccines reduces the risk for severe pertussis as documented by studies from 19 developing and industrialized countries. A primary series of wP or aP is not associated with serious adverse effects. Local signs and transient relatively benign fever, convulsions, hypotonic hyporesponsive episodes or prolonged crying occur more often as	Is the baseline risk for benefit similar across age, gender, race and SES? Yes **X** No☐ Should there be separate recommendations for subgroups based on risk or disease severity levels? Yes☐ No **X** Is the baseline risk for harm similar across subgroups? Yes **X** No☐ Should there be separate

[1] Jefferson T, Rudin M, Depietrantonj C. Systematic review of the effects of pertussis vaccines in children. Vaccine 2003 May 16; 21 (17-18): 2003-14.

	compared to placebo or diphtheria/tetanus vaccine. There are less such reactions with aP- than with wP-vaccines[1,2] Duration of protection after wP and aP lasts at least 6 years (low quality evidence). However, the duration of protections is longer for wP[3] and this may have equity implications. Data suggest that for aP-containing vaccines used in low incidence settings, a 3-dose primary series plus one booster after about 2 years may not prove sufficient protections for children aged > 6 years. Mathematical modelling studies and baboon models support the hypothesis that transition from wP to aP may be associated with shorter duration of protection and disease resurgence. Evidence indicates that aP vaccines have lower initial efficacy, faster waning of immunity, and possible reduced impact on transmission.	recommendations for subgroups based on harms? Yes☐ No **X**
Values and preferences *Is there confidence in the estimate of relative importance of outcomes and patient preferences?* Yes **X** No ☐	Vaccination and the importance of vaccination, is highly valued in most populations and particularly in low and middle income countries. Compared with aP vaccines, wP vaccines probably induce protection of longer duration without evidence of additional serious adverse effects. This has implications for patients. Infants and unimmunized children are at highest risk to severe pertussis	Are the benefits, harms and costs of the intervention valued differently by disadvantaged populations compared to privileged populations? Yes **X** No☐ **Source**: describe: consultations with disadvantaged populations, direct and indirect research, and/or transparent reflection by guideline panel. **Source of variability**, if any: Methods for determining values satisfactory for this recommendation? Yes☐ No **X** All **critical outcomes** relevant to disadvantaged populations measured?

[2] Bar-ON ES, Goldberg E, Hellmann S, Leibovici L. Combined DTP-HBV-HIB vaccine versus separately administered DTP-HBV and HIB vaccines for primary prevention of diphtheria, tetanus, pertussis, hepatitis B and Haemophilus influenzae B (HIB). Cochrane Database for Systematic Reviews 2012(4):CD005530.

[3] Quinn HE, McIntyre PB. Pertussis epidemiology in Australia over the decade 1995-2005, trends by region and age group. Commun Dis Intell 2007 June 31: 205-15.

		Yes X No ☐
Resource implications *Are the resources worth the expected net benefit?* Yes☐ No X	**Summary Points:** aP vaccine is significantly more expensive than the wP vaccine (difference > 5 US$ per dose with PAHO's revolving fund prices). This has implications for health systems, especially in low and middle income countries Switching from wP to the more expensive aP vaccine would create increased implementation costs, and probably reduce vaccine coverage, at least in the short term. Countries would be left with a more expensive vaccine with potentially shorter duration of coverage. Increased cost without increased benefit could risk health inequities for a LMIC population.	**Feasibility**: Is this intervention accessible, acceptable to patients and providers and affordable to disadvantaged populations? Yes X No ☐ **Is there a risk of discrimination**? Yes☐ No X **Opportunity cost**: Is this intervention and its effects worth withdrawing or not allocating resources from other interventions? Yes☐ No X **Evidence from:** Background information on equity Yes X No ☐ Health equity impact assessment Yes☐ No X Analysis of opportunity cost of equity Yes☐ No X Equity weighing of health outcomes Yes☐ No X Is there variability in resource requirements and feasibility across settings and populations? Yes☐ No X Is there a need for additional recommendations? Yes☐ No X
Overall recommendation:	We recommend the continued use of wP vaccines wherever wP vaccines already exists, and especially in LMIC where increased aP vaccine costs may have negative health system implications.	
Remarks and values and preference and equity statement	wP and aP vaccines are highly effective; between them there is no difference in major adverse events. wP-induced protection appears to last longer and for national health systems, wP vaccine is significantly less costly than aP vaccines. Low costs facilitate high vaccination coverage which is essential for health equity.	
Implementation considerations	wP is less costly for the health system; it will effectively prevent severe pertussis without major adverse events. wP-using countries should not change to aP-vaccine	
Research priorities	There is a need to improve surveillance of disease burden particularly in LMICs and to assess the impact of infant immunization, with a focus on fatalities in infants <1 year of age and on hospital surveillance. Identification of conditions necessary for pertussis resurgence and the effective strategies for resurgence prevention are important for modelling research.	