




# Combination Vaccines for Global Health: Why their importance continues to grow

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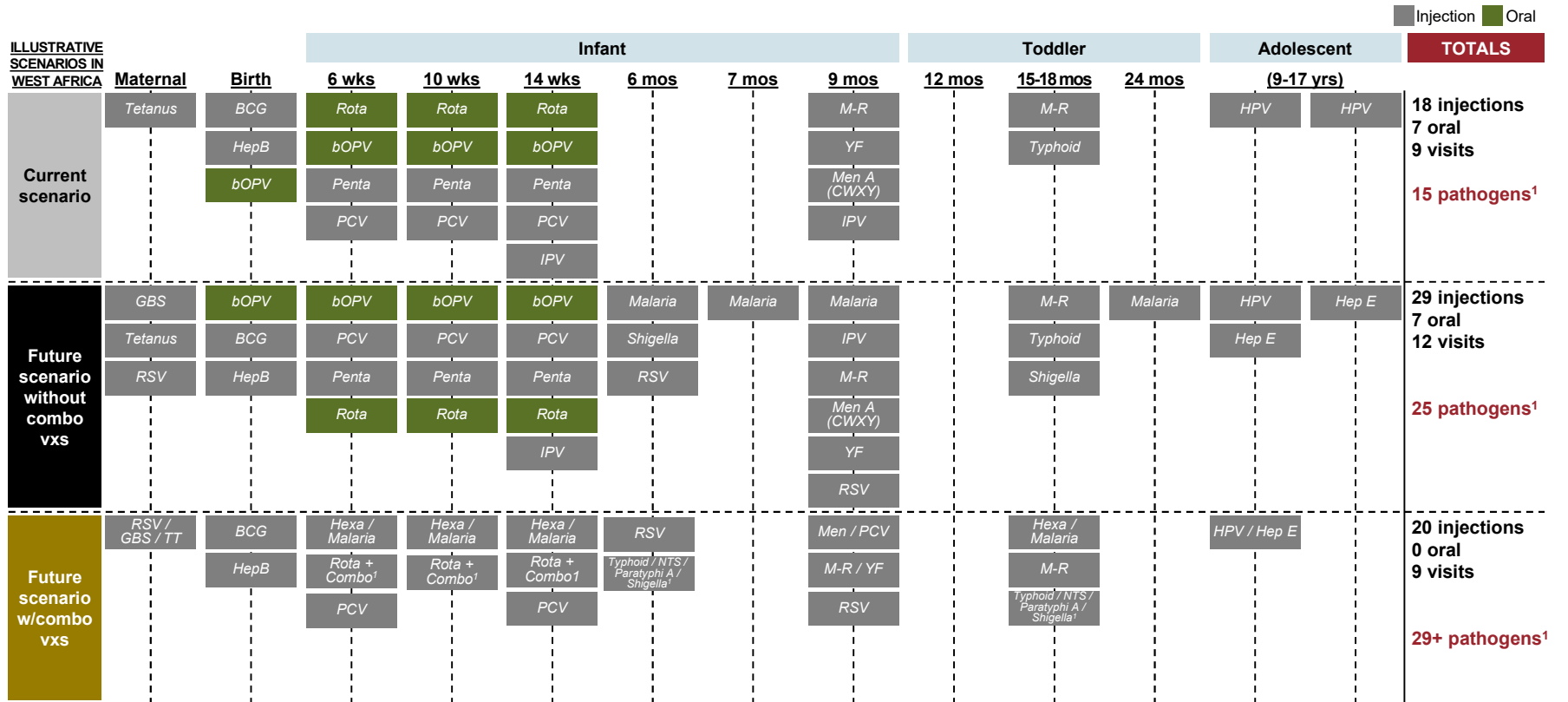
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# COMBINATION VACCINES HAVE POTENTIAL TO ADDRESS SEVERAL BARRIERS --- BUT PRODUCT DEVELOPMENT CHALLENGES EXIST

Challenges with vaccine delivery risk successful roll-out of high-impact candidates...	...combination vaccines are part of the solution but difficult for countries and developers to evaluate...	...important to develop a shortlist prioritizes combinations with direct impact & product enablement
 <p><b>Increased costs</b> to countries &amp; tightening fiscal constraints</p>	<p>Technical and market requirements are complex and require understanding of interplay of several factors.....</p>	<p>1 Combinations that allow us address delivery challenges</p>
 <p>More <b>complex schedules</b> with new immunization platforms required</p>	<p><b>“Must have” compatibility</b>      Epidemiology, dosing, route of administration</p>	<p>2 Combinations that enable pull-through of additional products (e.g., regional vaccines, enteric vaccines for lower burden diseases)</p>
 <p><b>Crowded “space on limbs”</b> and delivery challenges (e.g., storage)</p>	<p><b>Technical feasibility</b>      CMC complexity, regulatory pathways</p>	
<p>Challenges put vaccines in development at-risk of limited or unsuccessful roll-out: RSV, GBS, HEV, Paratyphi A, malaria, Shigella, HIV, next-gen TB and Rota</p>	<p>...but can result in big advantages:</p> <p><b>Impact</b>      Reduction in number of injections / increase in coverage</p>	

# THE PRESENT, FORESEEN FUTURE, AND POTENTIAL ALTERNATIVE FUTURE WITH OPTIMIZED COMBINATION VACCINES



<sup>1</sup> 1. Hypothesis for 2 potential antigens to combine with a novel injectable Rotavirus which could include Adenovirus 40/41 and Norovirus 2. Includes Typhoid, Shigella (quadrivalent), Paratyphi A, Nontyphoidal Salmonella. IPV and OPV are not counted twice. Pathogens only counted once during entire schedule

## ■ COMBINATION VACCINES – CHALLENGES AND OPPORTUNITIES

1. **Administrative incompatibility** – All antigens must live on same schedule/same # of doses
2. **Chemical incompatibility** – Some require adjuvants (e.g., Alum); some are incompatible with Alum; Ph stability; varying tonicity requirements; compatibility of excipients, potential for precipitation/flocculation of antigens
3. **Epidemiological incompatibility** – Particularly for vaccines with limited persistence, need for vaccines to be timed with peak onset of diseases, e.g., Rota peak precedes Typhoid peak
4. **Intellectual property incompatibility** – Who owns the patents? Tech transfer issues/legal around IP
5. **Economic incompatibility** – Combination vaccines may be more expensive than stand alone
6. **Manufacturing incompatibility** – Likelihood of technical failure increases with each additional antigen, particularly for heterogeneous combos (i.e., less challenging than adding PCV valences)
7. **Regulatory challenges** – Licensing based on clinical endpoints may be unrealistic, can you “pull through” new antigens affixed to a licensed product. “The typhoid tugboat?”
8. **Market uncertainties** – If you build it, will they come?? Expensive and hard to develop so must have confidence it will be taken up.



## Combination Vaccines for Global Health ---- Summary

- Hard, but necessary task with big and disruptive impact upside
- Recent successes remind us they can be done --- e.g., wP-based Hexas
- New platforms (e.g., mRNA) may be more amenable to combinations

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- Recent successes remind us they can be done --- e.g., wP-based Hexas
- New platforms (e.g., mRNA) may be more amenable to combinations
- Regulatory “creativity” needs to be embraced ---- with scientific backing ---- to realize the potential for novel combinations

? Typhoid conjugate

? Penta / Hexa

? Meningitis



Novel  
add-on