

A photograph showing a group of women and children in a community setting. In the foreground, a woman with a colorful patterned shawl holds a baby wrapped in a yellow cloth. Behind her, another woman holds a baby, and a third woman is visible. The background shows a simple structure with a corrugated metal roof and trees.

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GATES *foundation*

GLOBAL VACCINE AND IMMUNIZATION RESEARCH FORUM NEW COMBINATION VACCINES: HOW AND WHY?

POTENTIAL FUTURE STATES

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■ INTRO - WHAT PROBLEM ARE WE TRYING TO SOLVE?

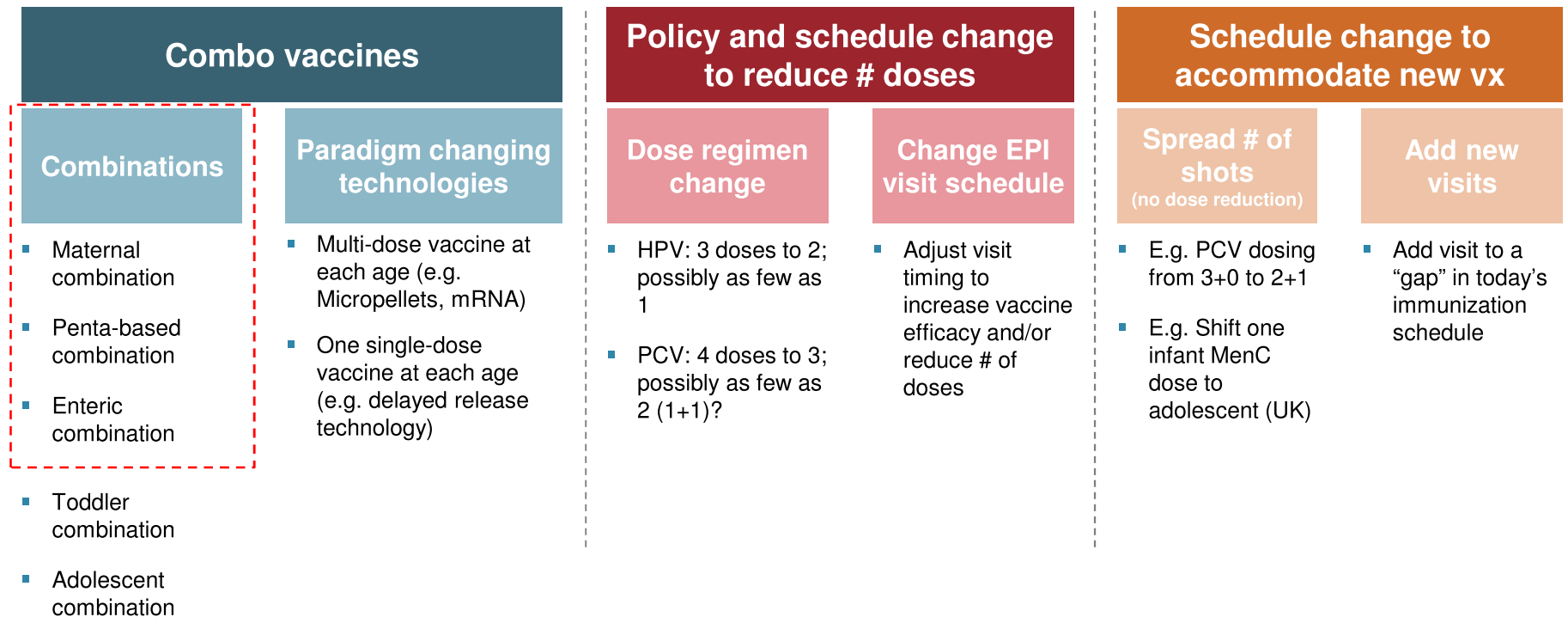
Problem statement


- Planning to **add new vaccines to a system already challenged** to deliver current ones
- Concern that countries might be reaching “**dual max**”: # and timing of “shots” and budget constraints
 - New vaccines in development will require different immunization platforms (e.g., maternal RSV) or will lead to more simultaneous administrations (e.g., ETEC, Shigella)
 - 50% of GAVI countries graduating by 2030. Significant budget increases required to pay for vaccines



Which vaccines could feasibly be combined (new or existing) to mitigate headwinds in the developing world?

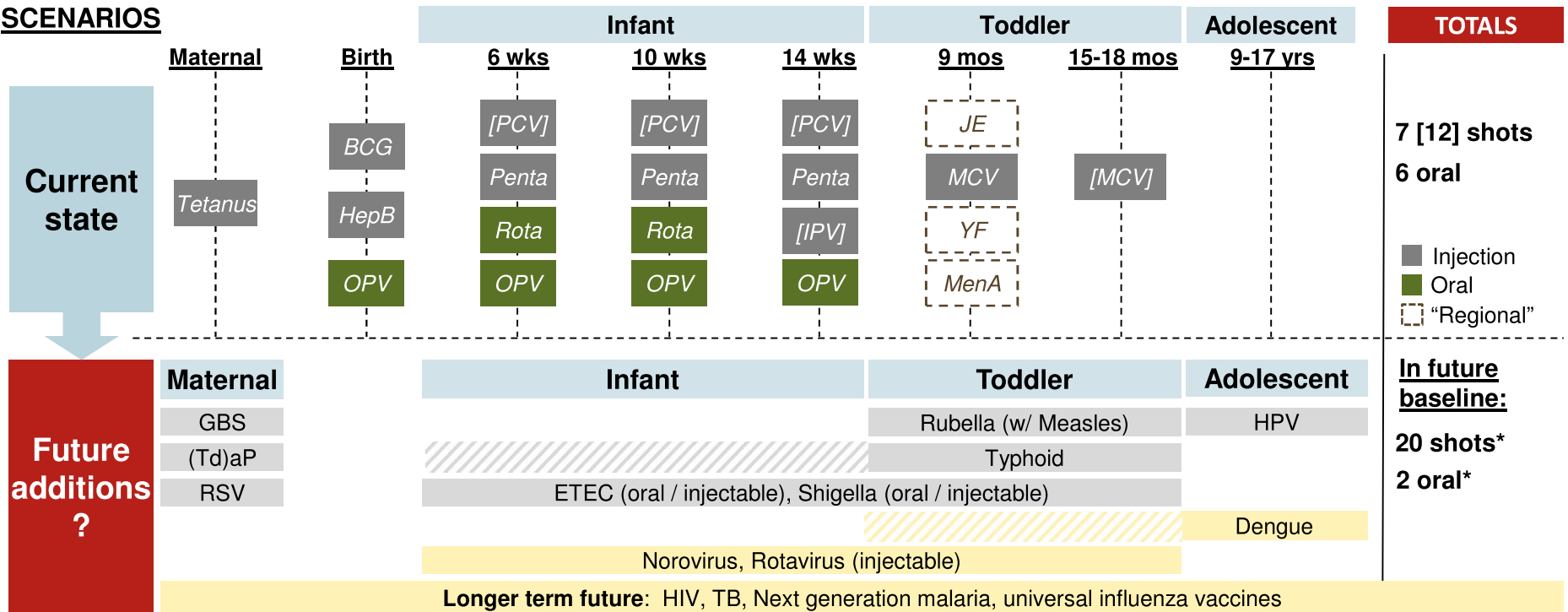
IMPORTANT TO EVALUATE VARIOUS LEVERS TO MITIGATE THE “DUAL MAX” ISSUE



 Key topics for today’s discussion

A FUTURE SCHEDULE COULD INVOLVE UP TO 13 ADDITIONAL SHOTS OVER AN ALREADY CROWDED SCHEDULE

SCENARIOS



Injection burden and delivery challenges preclude future additions from being all standalone vaccines

NOTE: *Calculation assume ETEC and Shigella are injectable. Excludes some regional vaccines and long-term development vaccines (HIV, malaria, TB, universal flu); Totals ignore regional vaccines in current state

FOR TODAY'S DISCUSSION: POTENTIAL COMBINATIONS FOR THREE MAJOR PLATFORMS


	1 Maternal	Birth	2 Infant: Penta-based	3 Infant: Enterics	Toddler	Adolescents
Global	<ul style="list-style-type: none"> • RSV (Td)aP • Flu (Universal) • CMV 	<ul style="list-style-type: none"> • BCG • HBV 	<ul style="list-style-type: none"> • Penta • IPV • Rota (NRRV) • PCV 	<ul style="list-style-type: none"> • Rota • Norovirus 	<ul style="list-style-type: none"> • M-R 	<ul style="list-style-type: none"> • HPV • CMV • TB • HIV
Regional	<ul style="list-style-type: none"> • Tetanus • GBS 		<ul style="list-style-type: none"> • MenA (C,W,X) or fHBP 	<ul style="list-style-type: none"> • ETEC • Shigella • Typhoid • Cholera 	<ul style="list-style-type: none"> • Typhoid • JE • YF • MenA (C,W,X) 	<ul style="list-style-type: none"> • HEV

Why not a first priority platform for combination?

Long-acting immunoglobulins as an alternative (e.g., RSV)

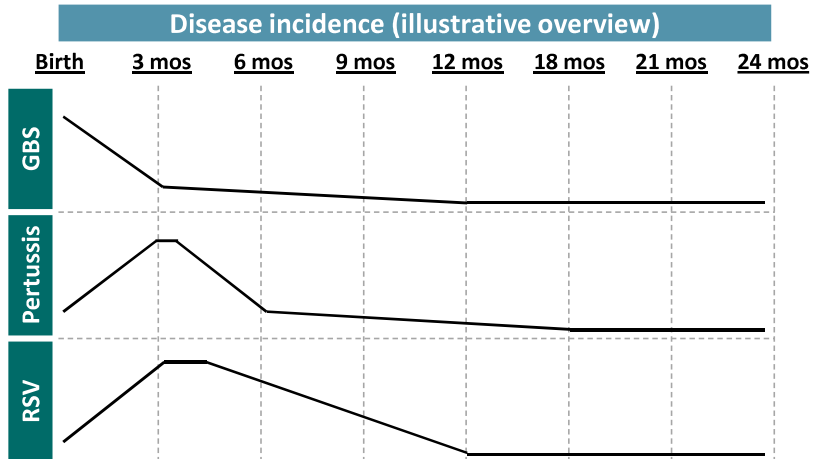
No clear global combination to develop

Beyond HPV, no near term candidates to combine

 Areas of focus for today's discussion

1 MATERNAL PLATFORM

Current state



- Tetanus is the only vaccine given to mothers in the developing world. High maternal coverage rates difficult without supplemental immunization activities (SIAs)
- 2015 maternal tetanus coverage (based on large catch-up programs, not routine immunization):
 - India: 59%; Nigeria: 44%; Pakistan: 65%

Rationale for novel combo

- True burden of these pathogens in developing world under active investigation
- Epidemiology clustered in time, supportive of similar vaccine delivery strategy
- Maternal immunization may be more acceptable if higher impact can be anticipated with combination products
- Similar protein-based and glycoconjugate vaccines have been successfully combined in other licensed products (e.g., DTaP-HBV-Hib based combos)

Scope

- **Priority antigens:** Tetanus, RSV, Pertussis, GBS
- **Other potential antigens:** Universal flu, CMV, HEV

2 INFANT: PENTA PLATFORM

Current state

MARKET DYNAMICS:

- Today's Penta market is healthy, with adequate supply and low price
- In 2015, there were six suppliers of Penta, with average price under \$2 / dose
 - Crucell, Shantha, Panacea, Serum, BioE, BioFarma, and BBIL

COVERAGE:

- Global estimates:
 - Penta: 86% (third dose)
 - IPV: 86% (third dose)
 - Oral Rota: 19% -- early in global roll-out

Rationale for novel combo

- Penta is a well-established vaccine delivered at established visits; an antigen added to this existing platform would be expected to achieve similar coverage rates
 - **Rota:** An injectable rota under development with potential efficacy, safety and cost benefits vs. current oral vaccines
 - **Polio:** Lower antigen IPV may mitigate cost increase; Reduce # infant injections post-polio elimination if antigen maintained
 - **Meningitis:** MenA-TT (MenAfrivac) introduction into EPI but non-MenA outbreaks occurring (C, W); Penta-Men combo could address # shots and changing epidemiology

Scope

- **Priority antigens:** Penta, IPV, NRRV (P2-VP8*), MenACW
- **Other antigens to consider:** PCV?, fHBP ("MenB"), Typhoid conjugate

3 INFANT: ENTERICS PLATFORM

Current state

Epidemiological incidence (highest to lowest)	
0-11 months of age	12-23 months of age
• Rotavirus	• Shigella / EIEC
• Shigella	• Rotavirus
• ST-ETEC	• ST-ETEC
• Norovirus GII	• V. cholerae
• V. cholerae	• Norovirus GII

Increasing incidence

Rationale for novel combo

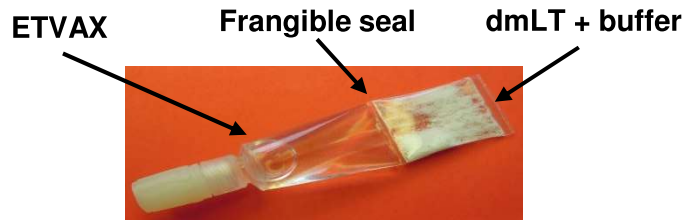
- Diarrheal disease burden is clustered across geographies and pathogens, making combination particularly attractive
- Individually, pathogens have modest to high disease burden
- Combination could better support argument for new product development
- Lead candidates developed sequentially, with plan for combination product after ETEC licensure. Is a more aggressive development strategy viable?

Scope

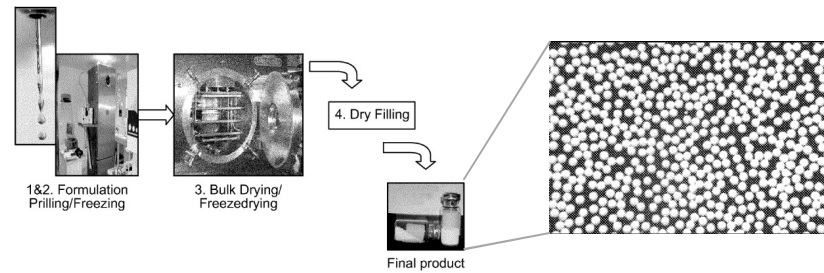
- **Priority antigens:** Rota, ETEC, Shigella, (Typhoid)
- **Other antigens under consideration:** Norovirus, Cholera

NEW TECH. HAS POTENTIAL TO CHANGE LONG-TERM PARADIGM OF COMBINATION VACCINES, ENABLING 'BLUE SKY' SCENARIOS

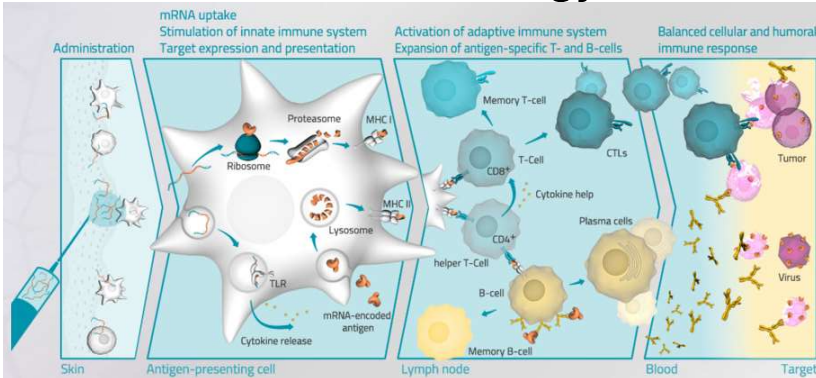
1 Frangible seal



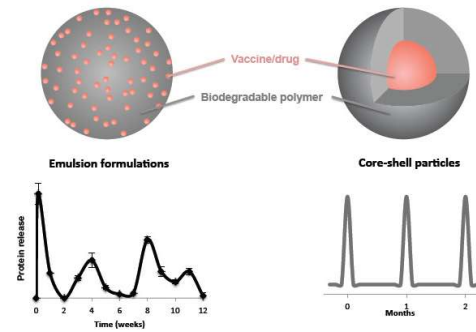
2 Micropellets



3 mRNA technology



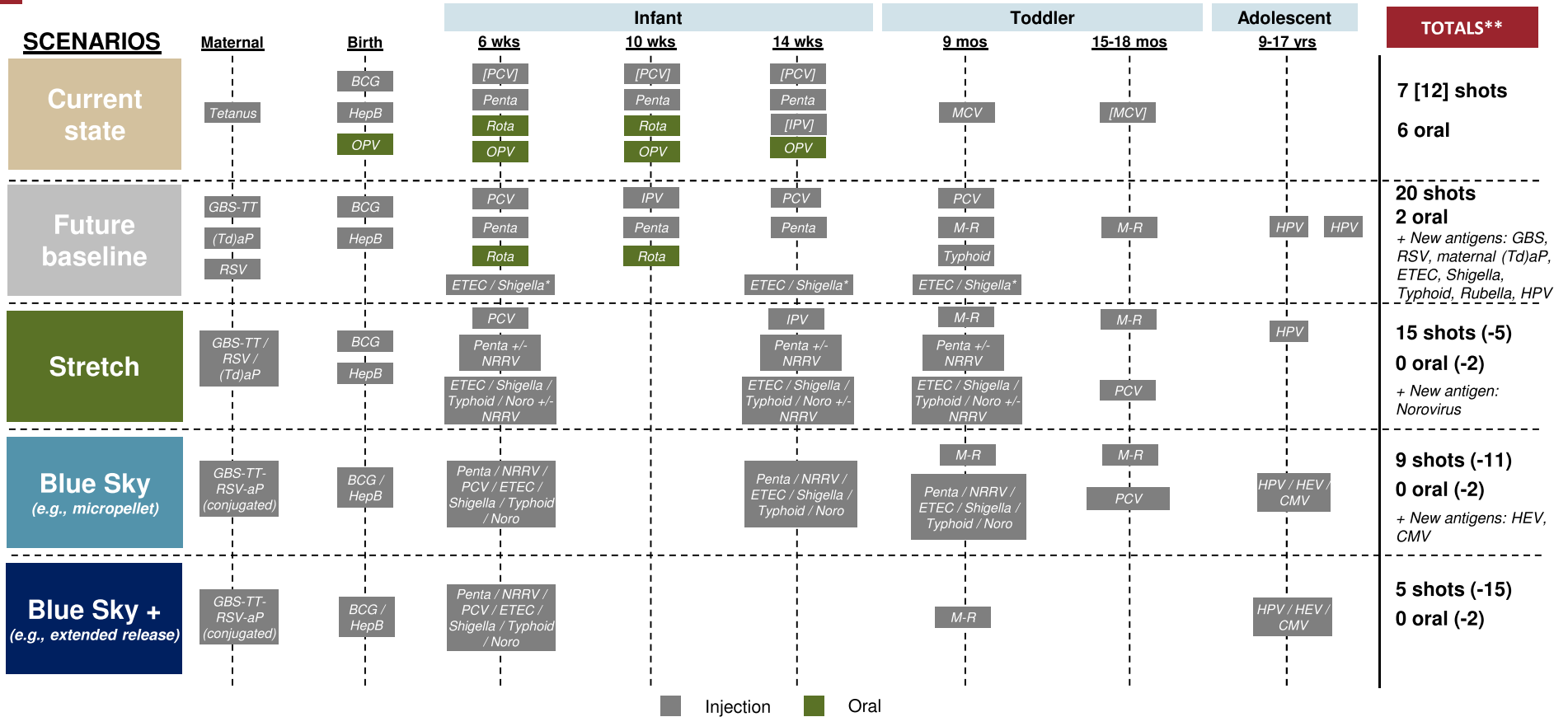
4 Delayed release



Source: Process for Stabilizing an Adjuvant Containing Vaccine Composition (US20090232894)

COMBO VACCINES: SEVERAL SCENARIOS FOR REDUCTION IN SHOTS

DEPEND ON DEGREE OF SUCCESS OF COMBOS AND NOVEL TECHNOLOGIES



NOTE: Excludes regional vaccines and long-term development vaccines (HIV, malaria, TB, universal flu); *ETEC / Shigella may be oral in future baseline; **Changes in totals based on changes from future baseline schedule

■ CONCLUSIONS

- Vaccine development targeting developing world diseases will increase
- Current products in pipeline represent both opportunities and challenges
- To maximize impact and reduce timeframe, must leverage recent vaccinology learnings (# of doses, optimal schedules and combination vaccines)
- Must strategically identify the right combination products (epidemiology, vaccinology, technical and commercial) and seek partnership opportunities early