

Newsletter New Vaccine Breakthroughs

💉 Next weapons against fatal diarrheal disease

Edition 1 · April 14th, 2025

✉️ Editor's Note / Introduction

Welcome to the first edition of Newsletter New Vaccine Breakthrough—your trusted source for insights into vaccine science, policy, and innovation.

👉 This issue covers:

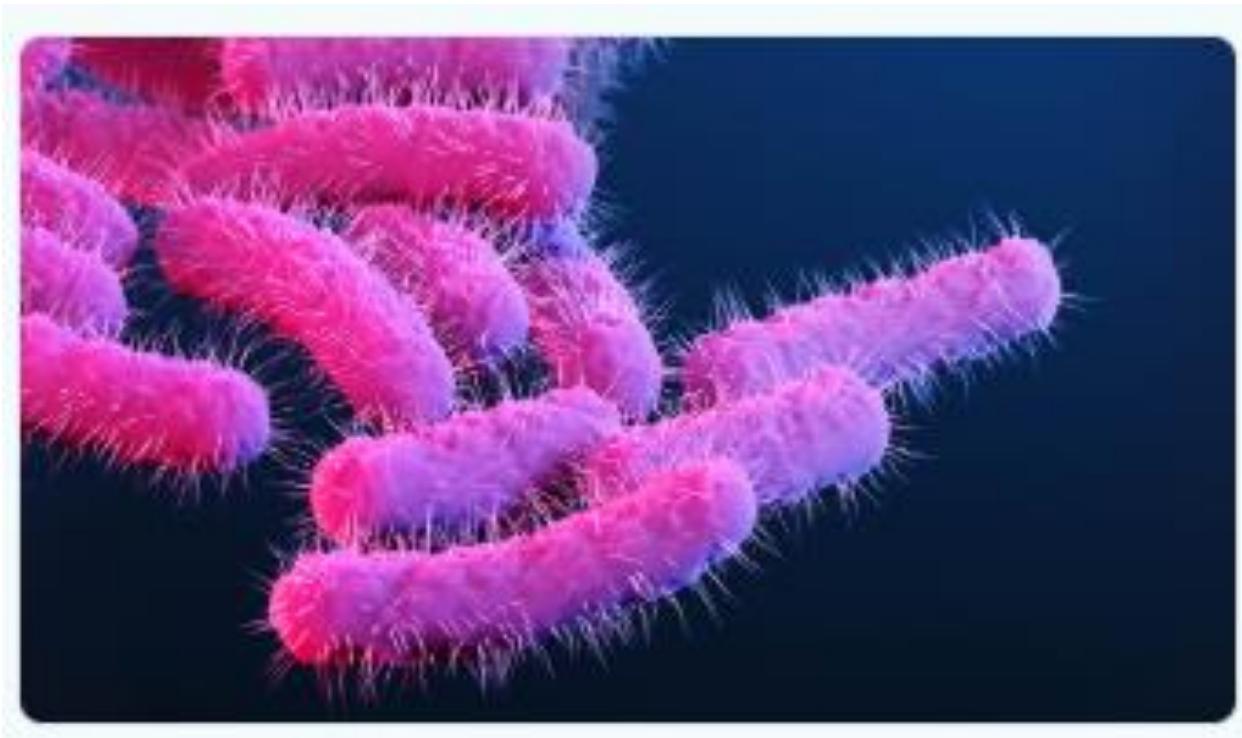
1. The world's most clinically advanced tetravalent bioconjugate vaccine candidate against shigellosis entered in a phase 2 study.
2. Innovative vaccines against ETEC infection in preclinical studies.
3. Next-generation non replicating rotavirus vaccine.

Let's dive in. 💧

📘 1. Spotlight: Topic of the Month:

1 The world's most clinically advanced tetravalent bioconjugate vaccine candidate against shigellosis entered in a phase 2 study.

🧠 Valvena a specialty vaccine company, and Limma Tech biologics AG, a clinical-stage biotech company developing vaccines for the prevention of life-threatening diseases, announced today that the first participant has been vaccinated in a Phase 2 infant safety and immunogenicity study of **Shigella 4V2 (S4V2)**, the world's most clinically advanced tetravalent bioconjugate vaccine candidate against shigellosis. Shigellosis is the second leading cause of fatal diarrheal disease worldwide, strongly contributing to pediatric morbidity and mortality. It is estimated that up to **165 million infections are due to Shigella of which 62.3 million** occur in children younger than five years.



⌚ 2. Global IMD Update:

2 Innovative vaccines against ETEC infection in preclinical studies.

Enterotoxigenic Escherichia coli (ETEC) is a major cause of diarrheal disease worldwide, particularly in children in low- and middle-income countries. Its ability to rapidly colonize the intestinal tract through diverse colonization factors and toxins underpins its significant public health impact. Despite extensive research and several vaccine candidates reaching clinical trials, no licensed vaccine exists for ETEC. **This review** explores the temporal and spatial coordination of ETEC virulence factors, focusing on the interplay between adherence mechanisms and toxin production as critical targets for therapeutic intervention.

Table 3. Innovative vaccines against ETEC infection in preclinical studies.

Animal Model	Vaccine/Toxin	Dose	Route	Main Findings	Reference
Rabbit	MecVax—multiple epitope-fusion-based vaccine composed of STaN12S-mnLTR192G/L211A and CFA/I/II/IV	25 µg CFA/I/II/IV + 25 µg toxoid fusion STa/LT + 0.2 µg dmlT adjuvant	ID	Specific serum IgG, inhibits adherence and neutralizes STa and CT enterotoxicity	[126,127,128]
Mouse	Total ETEC RNA	30, 50, or 70 µg single dose	IM or Oral	IL-1β secretion, specific serum IgG, IgM, and IgA and mucosal IgA. A 75% protection was achieved with 70 µg orally administered	[129]
Mouse	SLS (STa-LTB-STb) recombinant enterotoxin and fimbriae proteins (F4, F5, F6, F18, and F41)		SC	IL-1β and TNF-α secretion, specific serum IgG, 80% protection achieved	[130]
Mouse	Microneedle—LTB subunit	5 µg, single dose	ID	Specific serum IgA, IL-17A production	[86]
Mouse	Chitosan nanoparticles containing LTB, STxB, and CTxB	4 doses of 70 µg	Oral+IP	Specific serum IgG and IgA and mucosal IgA. A 33% survival was achieved	[116]
Mouse	Chitosan nanoparticles containing OMVs	10 or 50 µg single dose	SC or Oral	Serum IgG and mucosal IgA. Toxin and bacteria neutralization	[117]
Mouse	PD alone or PD-O148 conjugate, adjuvanted with aluminum phosphate	50 µg, 3 doses	SC	O-specific serum IgG titers, protection	[131]
Mouse	CFA/I fimbrial antigens, including CfαEB and a CfαE-LTB chimera with dmlT	10 µg CfαEB with 0.1 µg dmlT	ID, sublingual	IgG1, IgG2a, and fecal IgA antibody responses in ID but not in sublingual	[120]

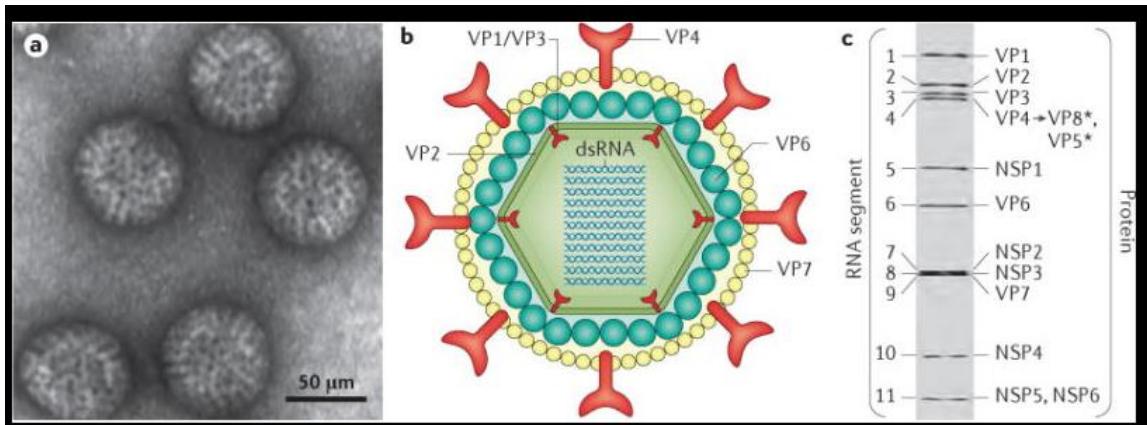
IM: intramuscular, SC: subcutaneous, ID: intradermal, IP: intraperitoneal, OMVs: outer membrane vesicles, CF: colonization factor, LTB: heat-labile toxin B, dmlT: double mutant heat-labile toxin.

3. Science Simplified:

3 Next-generation non replicating rotavirus vaccine.

The goal of **next-generation rotavirus vaccines** is to improve the effectiveness and impact of rotavirus vaccination programs in low-income countries and lower middle-income countries, by further reducing morbidity and mortality associated with rotavirus infection and associated moderate to severe diarrhea. Here after the 3 promising vaccines in phase 1, 2 & 3 studies

- CDC, **CDC-9 inactivated rotavirus vaccine** .
- PATH Trivalent **P2-VP8 Subunit Vaccine**
- Medical Biology, Chinese Academy of Medical Science **Inactivated rotavirus vaccine** . The **phase 2** is ongoing.



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