

## Mucosal Immunization Technologies

### Health need

AIDS, tuberculosis, acute respiratory-tract infections, and diarrheal diseases account for millions of deaths annually worldwide. All are caused by pathogens that enter the body via the mucosa, tissue linings found in the oral cavity and the reproductive and gastrointestinal tracts. Vaccines administered directly to the mucosa can trigger key antibodies and preferentially activate specific cells. Yet, mucosal vaccines face significant barriers to success due to in situ dilution and dispersion, interference from inert food and dust particles, enzymatic degradation, and low pH in the stomach. These and other factors can limit the ability of the vaccine to reach its target immune cells, resulting in a suboptimal immune response. To more effectively protect people from pathogens that enter the body via the mucosa, new technological approaches are needed.

### Technology solution

PATH recently developed a mucosal immunization technology platform—viable in two formats—that builds on several proven formulation, adjuvant, and delivery technologies to enable the efficient sublingual administration of subunit vaccines. The first format is a thermoresponsive gel (TRG) that begins as a liquid solution at room temperature and transforms into a gel upon contact with the oral mucosa. Its gel matrix enables it to adhere to mucosal surfaces and protects the vaccine antigen from degradation caused by salivary enzymes. The second is a fast-dissolving tablet (FDT) that disintegrates instantly in a small amount of saliva. The FDT can also be reconstituted in diluents or a buffer and then administered orally with a liquid dropper.

### Current status and results

PATH and our technical collaborators recently demonstrated the applicability of the TRG technology for sublingual immunization in animal models using a dmLT-adjuvanted TRG formulation of poliovirus vaccine, which elicited protective mucosal immunoglobulin A responses in all mucosal secretions tested. In previous animal studies advanced by PATH, tetanus toxoid vaccine formulated as a TRG also elicited a high level of relevant antibodies in serum and in the secretions of the oral cavity and the gastrointestinal and reproductive tracks.

In addition, PATH has developed a FDT formulated with a candidate enterotoxigenic *Escherichia coli* (ETEC) vaccine. The lead ETEC FDT formulation is stable at 12 months under refrigeration. Ongoing work has produced an ambient temperature-stable ETEC FDT formulation with maintained viability for at least 3 months. The FDT presentation has also been successfully adapted for use with a veterinary vaccine against Newcastle disease.

Additional assessments are under way as PATH continues to research the two formats as value-added product presentations for human and veterinary vaccines.



PATH/Scott Areman

**Novel methods to induce mucosal immunity.**

**“The best defense against these predominantly mucosal pathogens would be vaccines, preferably mucosal vaccines capable of inducing both systemic and mucosal immunity.”**

van Ginkel F, Nguyen H, McGhee J. Vaccines for mucosal immunity to combat emerging infectious diseases. *Emerging Infectious Diseases*. 2000;6(2):123–132.

### Availability

For more information regarding this project, contact Dexiang Chen at [dchen@path.org](mailto:dchen@path.org).

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