

Advantages of Mucosal Delivery Systems

- **Oral or intranasal products avoid the need for needles/syringes or skilled health care personnel for administration.**
- **Live, attenuated bacterial vaccines have been particularly effective against intracellular pathogens (e.g. BCG, Ty21a) and require less knowledge of immune protective mechanisms.**

Challenges For Mucosal Delivery Systems - 1

- **Lack of available clinically proven adjuvants (e.g. could increase the small window between immunogenicity and reactogenicity).**
- **Lack of knowledge of specific protective immune mechanisms may limit the use of targeted subunit delivery methods.**
- **Attenuation of bacteria for use as live vaccines - difficult to balance between good immunogenicity, low reactogenicity, and limited shedding in stool (i.e. to avoid unintended dissemination).**
- **Manufacturing consistency of live bacterial vaccines offers unique challenges - retaining high viability, stabilization of lyophilized product for storage outside the cold-chain.**
- **Development of potency assays that are clearly linked to efficacy.**

Challenges For Mucosal Delivery Systems - 2

- **The delivery system should protect the subunit antigen(s) from degradation and facilitate its transport to lymphoid tissue for presentation to immunocompetent cells.**
- **The vaccine product/delivery vehicle combination should trigger the appropriate type of immune response for protection.**
- **The delivery system should not adversely affect immunogenicity of the vaccine product and ideally should aid in long term stability of the subunit antigen(s).**
- **The design and formulation of the product (e.g. powder vs. liquid) as well as route of delivery should be considered to minimize adverse events while maximizing vaccine uptake to specific target sites and immunogenicity.**
- **Use of human challenge models where appropriate to compare formulations, dosing schedules, modes of administration for differences in reactogenicity/efficacy.**

Optimal Vaccine for Mucosal Delivery

- **Would require one or few doses.**
- **Could be disseminated for administration without need for skilled health care personnel.**
- **Packaged formulation would be stable for distribution without refrigeration.**
- **Would provide protection for >5 years.**
- **Manufacturing methodologies are currently available and easy to validate.**
- **Reasonable cost for vaccine.**