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ANALYTICAL DEVELOPMENT TO SUPPORT MANUFACTURING OF A SUSTAINABLE VACCINE AGAINST INVASIVE NONTYPHOIDAL SALMONELLOSIS

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GVGH is developing a candidate trivalent *Salmonella* vaccine to fight invasive nontyphoidal *Salmonellosis* (iNTS) and typhoid fever, especially aimed for sub-Saharan Africa to impact disease burden and to reduce anti-microbial resistance spread. This trivalent vaccine may be the only viable option for a sustainable iNTS vaccine in sub-Saharan Africa over the separate administration of Typhoid Conjugate Vaccines (TCV) and a vaccine against iNTS.

GVGH generated the iNTS-TCV formulation by combining the GMMA technology for the iNTS components, *S.* Typhimurium (STm) and *S.* Enteritidis (SEn) GMMA adsorbed on Alhydrogel, and the Vi-CRM197 glycoconjugate, originally developed by GVGH and recently WHO prequalified as TCV TYPHIBEV by Biological E Ltd (Hyderabad, India).

A set of analytical methods to support the vaccine lot release and characterization have been developed by GVGH. In particular, to quantify the key active ingredients of iNTS components a competitive ELISA-based method (FAcE, Formulated Alhydrogel competitive ELISA assay) has been setup and characterized in terms of specificity, accuracy and precision. Vi component is instead characterized by means of HPAEC-PAD method, able to specifically identify and quantify the total polysaccharide in the final drug product. With regard to safety assessment, a Monocyte Activation Test (MAT) has been developed as to monitor the intrinsic pyrogenicity of GMMA-based vaccines and applied as surveillance test for the Phase 1 clinical lot, with the plan to set release criteria based on clinical experience.

In vivo potency assay has been set to characterize the immunogenicity of vaccine lots in comparison to freshly formulated material at the time of release and during real-time stability. A significant antibody response to each of the active ingredients of the trivalent vaccine is raised in mice and assessed by Parallel Line Assay. Overall, the applied analytical panel and the results support the development of an iNTS-TCV vaccine as a viable option for a sustainable iNTS vaccine in sub-Saharan Africa.