5.0 Summary and Conclusion

The Vi conjugate vaccine developed and tested in this study has proved to be immunogenic in raising efficient immune responses in all age groups. The production of Vi polysaccharide was carried out with all optimized parameters in fermenter at 100L scale which yielded high amounts of Vi antigen with maximum O-acetyl content when determined by Hestrin method. All the purification steps were processed through different stages that included hydrophobic interaction, elimination of residual and other host cell impurities with different molecular weight cut-offs. The processed polysaccharide was checked for bacterial endotoxins (BET) value so that the endotoxins content was very negligible in the final purified lots. The purified polysaccharide was further allowed to couple with tetanus toxoid to accomplish the purpose of the present invention.

Different polysaccharide-protein conjugation methods were studied to optimize an appropriate coupling technique that could yield maximal amount of Vi-TT conjugate with specified polysaccharide to protein ratio. Conjugation experiments were carried out and concluded that attachment of an aldehyde activated polysaccharide with immunogenic protein molecule was appropriate and the technique was used in the present study. The final lot of Vi polysaccharide-Tetanus toxoid conjugate bulk was well characterized and formulated as a final vaccine to test the novel antigen in laboratory animals for evaluation of Non-clinical toxicity.
and in human volunteers for immunogenicity and safety profiles when compared with available native polysaccharide vaccine.

The safety of the vaccine was studied in mice and rabbits for acute and systemic toxicity to detect any toxic effects of the test vaccine. Results proved that no abnormalities were seen and no signs of ill health or deaths were observed in animals. Immunogenicity test was carried with an available reference vaccine; the seroconversion in the lab animals proved high in animals immunized with the test vaccine.

All the above data supported to conduct human clinical trial with different dosage schedule. The percentages of seroconversion (≥ 4-fold titer rise) in all the age groups of 13-17 yrs, 6-12 yrs with single dose and in 2-5 yrs (two doses) of ViPs-TT conjugate vaccine at strength of 25 µg were 100%.

The percentage of seroconversion (≥ 4-fold titer rise) in the age group of 2-5 years with two doses of ViPs-TT conjugate vaccine at strength of 15 µg was also 100%.

**In conclusion** Typhoid Vi polysaccharide-Tetanus toxoid conjugate vaccine developed and tested in lab animals and subjected to Human clinical trial was proved to be safe and immunogenic and superior to existing typhoid native Vi polysaccharide vaccine.