INTRODUCTION

Typhoid fever is an acute febrile communicable disease caused by the obligate human pathogen *Salmonella typhi*, a gram negative bacterium belonging to the family Enterobacteriaceae. It is one of the major public health problems in many developing countries of the world and causes considerable morbidity and mortality. It is estimated that more than 12 million people are affected annually by typhoid fever, worldwide. Man is the only natural host and reservoir for *S. typhi*. The bacterium enters the body via gastrointestinal tract, usually by ingestion of food or water contaminated by human feces and causes a generalized systemic infection producing fever accompanied by intense headache, general weakness, diarrhea, abdominal pain and other manifestations. Although less frequent, intestinal perforation may also occur, contributing to about 25% of the deaths associated with the illness. Even with antibiotics, convalescence without complications produces impaired activity in patients for at least three weeks, with a substantial loss of productivity. While the priority is to develop better methods of disease prevention, there
is also an urgent need to develop assays that will allow early and definite diagnosis of typhoid fever. Currently, typhoid fever is diagnosed by culture or by Widal's (serological) test. Confirmatory bacteriological cultures are time consuming and take two to three days. Widal's agglutination test detects antibodies capable of agglutinating fixed, killed bacteria. Since a rise in titre must be demonstrated, at least two samples taken several weeks apart are required. Furthermore, due to high endemicity of the disease, agglutinins are frequently found in normal healthy subjects and are also produced in response to vaccination. Hence, the value of a single sample obtained from a patient in a typhoid endemic-area or from a putative typhoid patient who has been vaccinated is limited. Thus there is a need for a sensitive test for diagnosis of typhoid which can put in evidence the causative microorganism specifically. Work presented in this thesis seeks to

i) Study the complexity of somatic (O), flagellar (H) and capsular (Vi) antigens of *S. typhi* with monoclonal antibodies raised against these antigens.

ii) Develop enzyme immunoassays for the detection of *S. typhi* employing specific anti-*S. typhi* monoclonal antibodies.