

AN 85-DAY REPEAT DOSE TRANSCUTANEOUS TOXICITY STUDY
OF AN ENTEROTOXIGENIC *E. COLI* VACCINE
IN NEW ZEALAND WHITE RABBITS

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ABSTRACT

A vaccine against enterotoxigenic *E. coli* (ETEC) is being developed for travelers and young children at high risk of ETEC diarrhea. The purpose of this study was to determine the potential toxicity and immunogenicity of the vaccine when administered alone or with an enterotoxin adjuvant to New Zealand White (NZW) rabbits by the transcutaneous route. This study was also designed to determine the persistence, late onset, or reversibility of any toxic effects over a 20-day no-treatment recovery period. NZW rabbits (14/sex/group) were assigned to the study and were treated via wet skin patch with either PBS vaccine adjuvant, or both vaccine and adjuvant on Study Days (SD) 1, 22, 43, and 64. Two animals/sex/group were sacrificed on SD 3 (interim), six animals/sex/group were sacrificed on SD 66 (terminal), and the remaining animals were sacrificed following the recovery period on SD 85 (recovery). Parameters evaluated included mortality, physical examinations, cageside observations, dermal Draize observations, measurement of induration at dosing sites, body weight and changes, body temperatures, humoral responses to the vaccine and adjuvant, clinical pathology (serum chemistry, hematology, coagulation, and C-reactive protein), gross pathology, organ weight data, and microscopic pathology. When administered alone or together, treatment with the adjuvant or vaccine did not produce systemic toxicity. Treatment with the adjuvant alone or in combination with the vaccine was associated with dose site reactions, including erythema, edema, and inflammation; however, these findings were transient and non-adverse. Treatment with the vaccine alone was not associated with dose site reactogenicity. Both the vaccine and adjuvant were highly immunogenic.