

AN 85-DAY REPEAT DOSE INTRADERMAL TOXICITY STUDY OF AN ENTEROTOXIGENIC *E. COLI* VACCINE IN GUINEA PIGS

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ABSTRACT

A vaccine against enterotoxigenic *E. coli* (ETEC) is being developed to protect travelers and young children that are at risk from this disease. The purpose of this study was to determine the immunogenicity, local skin reactogenicity, and potential toxicity of the ETEC vaccine candidate, when administered alone or in combination with an adjuvant derived from *E. coli*, to Dunkin Hartley guinea pigs by the intradermal route on Study Days 1, 22, 43, and 64. Guinea pigs were treated with 100 µL of the vaccine given alone or the adjuvant mixed with either PBS or the vaccine. Parameters evaluated included mortality, cageside observations, physical examinations, body weights, body temperatures, dermal Draize scores, dose site induration measurements, gross pathology, organ weights, and histopathology. Treatment with vaccine with or without adjuvant had no effect on mortality, cageside observations, physical examinations, body weights, body temperature, gross pathology, or organ weights. Administration of the vaccine alone resulted in a few observations of mild erythema but no induration. Administration of the adjuvant resulted in a dose-related increase in severity of erythema and edema but the severity appeared to decrease with repeated dosing. In addition, the incidence of positive Draize scores appeared to be lower in those animals that received vaccine in combination with adjuvant. Administration of adjuvant alone or in combination with vaccine resulted in areas of induration following the first dose that increased with dose level. However, only animals receiving the adjuvant without vaccine developed areas of induration at subsequent intervals. The tested vaccine components all produced variable inflammation at the inoculation site that was evident two days post-inoculation but which had resolved completely by three weeks post-inoculation.