2018). Similarly, tetanus and diphtheria antitoxin levels fall over time in individuals completing a pediatric DTaP vaccine regimen.

[0005] The Advisory Committee on Immunization Practices (ACIP) now recommends administration of a single booster dose of a tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine to individuals over the age of 10, and a booster dose of a either a Tdap vaccine or a tetanus and diphtheria (Td) vaccine at 10 year intervals or as needed for wound management (Liang et al., supra, 2018). Clinical trials have shown that two doses of Tdap are safe and immunogenic, but that anti-pertussis antibody titers rapidly decline, generally resulting in loss of protection against pertussis infection within two to three years.

[0006] Thus, improved booster vaccines are needed to provide higher titer and longer lived antibody responses against pertussis antigens to help address the waning immunity observed as a consequence of the switch from whole-cell to acellular pertussis antigens in current vaccine regimens. Improved Tdap booster vaccines are needed, which have a satisfactory safety profile and are not inferior to current vaccines with regard to tetanus and diphtheria toxoid immunogenicity.

SUMMARY

[0007] The present disclosure relates to immunogenic compositions comprising tetanus, diphtheria, and acellular pertussis (Tdap) antigens, and a toll-like receptor 9 (TLR9) agonist, such as oligonucleotide comprising an unmethylated cytidine-phospho-guanosine (CpG) motif. The immunogenic compositions may further comprise an aluminum salt adjuvant to which the Tdap antigens are adsorbed. The immunogenic compositions are suitable for active booster immunization against tetanus, diphtheria, and pertussis in an individual in need thereof.

[0007a] In one aspect, the present disclosure refers to use of an immunogenic composition in the manufacture of a medicament for active booster immunization of a human subject against tetanus, diphtheria, and pertussis, wherein the immunogenic composition comprises tetanus, diphtheria, and acellular pertussis (Tdap) antigens, an aluminum salt adjuvant to which the Tdap antigens are adsorbed, and a toll-like receptor 9 (TLR9) agonist, wherein the TLR9 agonist is an oligonucleotide of from 10 to 35 nucleotides in length comprising an unmethylated cytidine-phospho-guanosine (CpG) motif, wherein the immunogenic composition comprises from about 750 µg to about 6000 µg of the oligonucleotide, wherein the human subject is three years of age

or older, and wherein the Tdap antigens comprise a tetanus toxoid (TT), a diphtheria toxoid (DT), a pertussis toxoid (PT), a pertussis filamentous haemagglutinin (FHA), and pertussis pertactin (PRN).

[0007b] In one aspect, the present disclosure refers to an immunogenic composition, comprising: tetanus, diphtheria, and acellular pertussis (Tdap) antigens, an aluminum salt adjuvant to which the Tdap antigens are adsorbed, and a toll-like receptor 9 (TLR9) agonist, wherein the TLR9 agonist is an oligonucleotide of from 10 to 35 nucleotides in length comprising an unmethylated cytidine-phospho-guanosine (CpG) motif, the immunogenic composition comprises from about 750 µg to about 6000 µg of the oligonucleotide, and the Tdap antigens comprise a tetanus toxoid (TT), a diphtheria toxoid (DT), a pertussis toxoid (PT), a pertussis filamentous haemagglutinin (FHA), and pertussis pertactin (PRN).

[0007c] In one aspect, the present disclosure refers to a kit comprising the immunogenic composition disclosed herein, and instructions for administration of the immunogenic composition to stimulate an immune response against the Tdap antigens in a human subject.

[0007d] In one aspect, the present disclosure refers to a kit comprising: i) a first composition comprising tetanus, diphtheria, and acellular pertussis (Tdap) antigens and an aluminum salt adjuvant to which the Tdap antigens are adsorbed; ii) a second composition comprising a TLR9 agonist; and iii) instructions for mixing the first composition with the second composition to prepare the immunogenic composition disclosed herein.

BRIEF DESCRIPTION OF THE DRAWINGS

[0008] FIG. 1A-C depicts the levels of cytokine secretion by spleen cells in vitro after restimulation with Tdap antigens. Levels of IFN-γ (FIG. 1A), IL-5 (FIG. 1B), and IL-17 (FIG. 1C) are shown.

[0009] FIG. 2A-B shows that inclusion of CpG 1018 in Tdap vaccines results in a substantial reduction in *B. pertussis* burden in the lungs and trachea three days after intranasal challenge of vaccinated mice.