CLAIMS:

1. An immunogenic composition comprising a *Clostridioides difficile* (*C. difficile*) toxoid A and/or toxoid B, and a CpG adjuvant comprising at least one CpG or a saponin containing liposomal adjuvant.

2. The immunogenic composition of claim 1, wherein the CpG adjuvant comprises a B class CpG; optionally wherein the CpG adjuvant comprises CpG 24555 (SEQ ID NO: 48).

3. The immunogenic composition of claim 1 or 2, comprising about 0.1 to 5 mg/mL or higher, about 0.1 to about 1.0 mg/mL, about 0.5 to about 1.5 mg/mL, about 0.8 to about 1.8 mg/mL, or about 3.0 to about 4.0 mg/mL CpG.

4. The immunogenic composition of any one of claims 1-3, comprising about 0.5 mg/mL, about 1.0 mg/mL, about 1.2 mg/mL, or about 3.6 mg/mL CpG; optionally comprising about 3.6 mg/mL CpG.

5. The immunogenic composition of any one of claims 1-4, wherein the CpG adjuvant further comprises an additional adjuvant; and/or wherein the CpG adjuvant further comprises an aluminum salt selected from aluminum phosphate, aluminum sulfate and aluminum hydroxide ($Al(OH)_3$); optionally wherein the CpG adjuvant further comprises $Al(OH)_3$.

6. The immunogenic composition of any one of claims 1-5, comprising a CpG and about 0.1 to 5 mg/mL, about 0.5 to about 1.5 mg/mL, or about 1.0 to about 2.5 mg/mL $Al(OH)_3$; or comprising a CpG and about 1.0, about 1.5, about 1.7, about 1.8, about 2.0, or about 2.5 $Al(OH)_3$; or comprising about 0.5 to about 3.6 mg/mL CpG and about 0.1 to 5 mg/mL $Al(OH)_3$.

7. The immunogenic composition of any one of claims 1-6, wherein the CpG adjuvant comprises a histidine or phosphate buffer; optionally wherein the histidine or phosphate buffer is at a concentration of about 5 mM to 15 mM, or preferably about 10 mM.

8. The immunogenic composition of any one of claims 1-7, wherein the CpG adjuvant comprises sodium chloride; optionally wherein the sodium chloride is at a concentration of about 20 mM to 100 mM, or preferably about 50 mM or about 60 mM.

9. The immunogenic composition of any one of claims 1-8, wherein the CpG adjuvant has a pH of about 6.0 to 7.0, or preferably about 6.5.

10. The immunogenic composition of any one of claims 1-9, wherein the CpG adjuvant comprises about 3.6 mg/mL CpG 24555; or wherein the CpG adjuvant comprises about 1.0 mg/mL CpG 24555 and about 1.5 mg/mL of $Al(OH)_3$.

11. The immunogenic composition of claim 1, wherein the saponin containing liposomal adjuvant comprises a saponin and a monophosphoryl lipid A (MPLA)-containing liposome composition, wherein the liposome composition comprises i) a lipid bilayer comprising phospholipids and ii) cholesterol; optionally wherein the saponin is selected from QS-7, QS-18, QS-21, or a mixture thereof, further optionally wherein the saponin is QS-21; optionally wherein the phospholipid is selected from dimyristoyl phosphatidylcholine (DMPC), dipalmitoyl phosphatidylcholine (DPPC), distearyl phosphatidylcholine (DSPC), dimyristoyl phosphatidylglycerol (DMPG), dipalmitoyl phosphatidylglycerol (DPPG), and distearyl phosphatidylglycerol (DSPG), further optionally wherein the phospholipids are DMPC and DMPG.

12. The immunogenic composition of claim 11, wherein the saponin containing liposomal adjuvant comprises QS-21, Monophosphoryl Lipid A (MPLA), DMPC, DMPG and cholesterol; optionally wherein the MPLA is Monophosphoryl 3-Deacyl Lipid A.

13. The immunogenic composition of claim 11 or 12, wherein the saponin containing liposomal adjuvant comprises a histidine or phosphate buffer; optinally wherein the phosphate buffer is at a concentration of about 5 mM to 15 mM, or preferably about 10 mM; and/or wherein the saponin containing liposomal adjuvant comprises sodium chloride at a concentration of about 100 mM to 200 mM, or preferably about 150 mM; and/or wherein the saponin containing liposomal adjuvant has a pH of about 5.5 to 7.0, preferably about 6.2.

14. The immunogenic composition of any one of claims 1-13, wherein the *C. difficile* toxoid A comprises the amino acid sequence of SEQ ID NO: 4, wherein the initial methionine is absent, and *C. difficile* toxoid B comprises the amino acid sequence of SEQ ID NO: 6, wherein the initial methionine is absent; and/or wherein the *C. difficile* toxoid A comprises the amino acid sequence of SEQ ID NO: 84, and *C. difficile* toxoid B comprises the amino acid sequence of SEQ ID NO: 86; and/or wherein the composition comprises the *C. difficile* toxoid A and the *C. difficile* toxoid B in a ratio of about 3:1 to about 1:1; and/or wherein the composition comprises 200 µg of toxoid per dose.

15. The immunogenic composition of any one of claims 1-14, wherein the *C. difficile* toxoid A and toxoid B are lyophilized and reconstituted with a CpG adjuvant or a saponin containing liposomal adjuvant; optionally wherein the lyophilized *C. difficile* toxoid A and toxoid B are reconstituted with a CpG adjuvant comprising about 3.6 mg/mL CpG 24555; or wherein the lyophilized *C. difficile* toxoid A and toxoid B are reconstituted with a CpG adjuvant comprising about 1.0 mg/mL CpG 24555 and about 1.5 mg/mL Al(OH)3; or wherein the lyophilized *C. difficile* toxoid A and toxoid B are reconstituted with a saponin containing liposomal adjuvant comprising about 0.2 mg/mL QS-21, about 0.4 mg/mL Monophosphoryl 3-Deacyl Lipid A, about 14 mg/mL DMPC, about 1.6 mg/mL DMPG and about 11 mg/mL cholesterol.

16. The immunogenic composition of any one of claims 1-15, wherein the composition is to be administered at a dose volume of 0.5 mL.

17. The immunogenic composition of any one of claims 1-16, for use as a medicament.

18. The immunogenic composition of any one of claims 1-16, for use as a vaccine.

19. Use of the immunogenic composition of any one of claims 1-16, in the manufacture of a medicament for eliciting an immune response in a human subject against *C. difficile*.

20. Use of the immunogenic composition of any one of claims 1-16, in the manufacture of a medicament for preventing, treating or ameliorating an infection, disease or condition associated with *C. difficile* in a human subject; and/or preventing, treating or ameliorating a medically attended *C. difficile* infection in a human subject.

21. The use of claim 19 or 20, wherein the immunogenic composition is to be administered in a first and second dose; optionally wherein the second dose is to be administered about 2 months after the first dose (e.g. M 0, 2) or about 6 months after the first dose (M 0, 6).

22. The use of any one of claims 19-21, wherein the human subject is 18 years of age or older, 50 years of age or older, 55 years of age or older, 60 years of age or older, 65 years of age or older, or 70 years of age or older.

23. The use of any one of claims 19-22, wherein an immune response is elicited and comprises neutralizing antibodies against *C. difficile* toxin A and/or neutralizing antibodies against *C. difficile* toxin B; and/or wherein neutralizing antibodies elicited against *C. difficile* toxin A and/or B is greater after administration of 2 doses of the immunogenic composition compared to administration of 3 doses of the investigational *C. difficile* vaccine.