CLAIMS

1. A recombinant *Bordetella pertussis* bacterium which comprises:

(i) at least one genomic LpxA gene encoding an LpxA protein, wherein the LpxA protein comprises a mutation at position 170 and/or a mutation at position 229 relative to SEQ ID NO: 1; and/or

(ii) at least one genomic insertion of a heterologous LpxD gene.

2. The recombinant *Bordetella pertussis* bacterium of Claim 1 which comprises at least one genomic LpxA gene encoding an LpxA protein, wherein the LpxA protein comprises a substitution at position 170 and/or a substitution at position 229 relative to SEQ ID NO: 1.

3. The recombinant *Bordetella pertussis* bacterium of Claim 1 or 2 wherein the LpxA protein comprises a Serine residue at position 170 and/or an Alanine residue at position 229 relative to SEQ ID NO: 1.

4. The recombinant *Bordetella pertussis* bacterium of Claim 3, wherein the LpxA protein comprises (i) a Serine residue at position 170 and (ii) an Alanine residue at position 229 when numbered in accordance with SEQ ID NO:1.

5. The recombinant *Bordetella pertussis* bacterium of Claim 4 which comprises an LpxA gene that encodes an LpxA protein having at least 80% amino acid sequence identity to SEQ ID NO: 1 or 2.

6. The recombinant *Bordetella pertussis* bacterium of Claim 4 which comprises an LpxA gene that encodes an LpxA protein having the amino acid sequence of SEQ ID NO: 2.

7. The recombinant *Bordetella pertussis* bacterium of any preceding claim, wherein the heterologous LpxD gene encodes an LpxD protein having at least 90% amino acid sequence identity with SEQ ID NO:3 or SEQ ID NO: 4.

8. The recombinant *Bordetella pertussis* bacterium of Claim 6, wherein the heterologous LpxD gene encodes an LpxD protein having at least 95% amino acid sequence identity with SEQ ID NO:3 or SEQ ID NO: 4.

9. The recombinant *Bordetella pertussis* bacterium of Claim 7, wherein the heterologous LpxD gene encodes an LpxD protein having an amino acid sequence selected from the group consisting of SEQ ID NO:3 or SEQ ID NO: 4.

10. The recombinant *Bordetella pertussis* bacterium of any preceding claim, wherein the endogenous LpxA gene is inactivated and/or the endogenous LpxD gene is inactivated.

11. The recombinant *Bordetella pertussis* bacterium of any one of the preceding claims which produces lipid A wherein (i) at least 30% of the C3' acyl chains are from C_{10} to C_{12} in length; and/or (ii) at least 30% of the C2' acyl chains are from C_{10} to C_{12} in length; and/or (iii) at least 30% of the C2 acyl chains are from C_{10} to C_{12} in length.

12. The recombinant *Bordetella pertussis* bacterium of any one of the preceding claims that produces Lipid A with reduced endotoxic activity compared to that of the Lipid A produced by the parental strain, particularly when measured using TLR4 stimulation assays, particularly human TLR4 stimulation assays.

13. The recombinant *Bordetella pertussis* bacterium of any one of the preceding claims, wherein the growth curve of a bacterial population of said bacteria is comparable to the growth curve of a population of the parental strain.

14. An isolated outer membrane vesicle (OMV) prepared from the recombinant *Bordetella pertussis* bacterium of any one of Claims 1 to 12 which comprises modified Lipid A incorporated into the membrane wherein substantially all of C3' acyl chains of the Lipid A have a length of C_{10} and/or wherein substantially all of C2 and C2' acyl chains of the Lipid A have a length of C_{12}.

15. The isolated outer membrane vesicle according to Claim 13 which is substantially free of dermonecrotic toxin and/or which contains endogenous genetically detoxified pertussis toxoid.

16. An immunogenic composition comprising at least one isolated OMV according to any one of Claims 13 to 15 and a pharmaceutically acceptable excipient.

17. The immunogenic composition of Claim 16, further comprising at least one additional antigen selected from the group consisting of (1) pertussis toxoid (PT), (2) FHA, (3) pertactin (PRN), (4) FIM2/FIM3, (5) adenylate cyclase, (6) diphtheria toxoid (DT), (7)

tetanus toxoid (TT), (8) inactivated polio virus (IPV), (9) hepatitis B surface antigen and (10) Hib PRP.

18. The OMV of any one of claims 13 to 15 or the immunogenic composition of claim 16 or claim 17 for use in inducing an immune response in a suitable mammal, for example a human.

19. The OMV of any one of claims 13 to 15 or the immunogenic composition of claim 16 or 17 for use in prophylaxis or as a vaccine.

20. A method of modulating the reactogenicity of the Lipid A of a *Bordetella pertussis* bacterium, comprising stably integrating into the genome of the bacterium at least one gene selected from the group consisting of LpxA and LpxD, wherein:

    (i) the LpxA gene encodes an LpxA protein having at least 80% sequence identity with SEQ ID NO: 1 or 2 and wherein the protein comprises Serine at position 170 (S170) and/or Alanine at position 229 (A229) when numbered in accordance with SEQ ID NO: 1 or 2; and/or

    (ii) the LpxD gene encodes an LpxD protein having at least 90% amino acid