

Annex 1

Unconditional Amendments

1. A betacoronavirus (BetaCoV) messenger RNA (mRNA) vaccine comprising at least one mRNA polynucleotide having an open reading frame encoding at least one BetaCoV antigenic polypeptide;

wherein the at least one BetaCoV antigenic polypeptide is (a) a spike (S) protein or immunogenic fragment thereof, or (b) an S1 subunit or an S2 subunit of S protein or an immunogenic fragment thereof;

wherein the BetaCoV vaccine is formulated in a lipid nanoparticle, wherein the lipid nanoparticle comprises 40-60% cationic lipid, 5-15% non-cationic lipid, 1-2% PEG lipid, and 30-50% cholesterol.

2. The vaccine of claim 1, wherein the open reading frame encodes an S protein.

3. The vaccine of claim 1, wherein the open reading frame encodes an S1 subunit or an S2 subunit of S protein.

4. The vaccine of any of claims 1-3, wherein the BetaCoV is MERS-CoV, SARS-CoV, HCoVOC43, HCoV-229E, HCoV-NL63 or HCoV-HKU1.

5. The vaccine of any of claims 1-4, wherein the at least one mRNA polynucleotide comprises a 5' untranslated region (UTR), a 3' UTR, a 5' cap and a poly(A) tail.

~~6. The vaccine of claim 5, wherein the 5' cap is a 5' terminal cap 7mG(5')ppp(5')NmpNp.~~

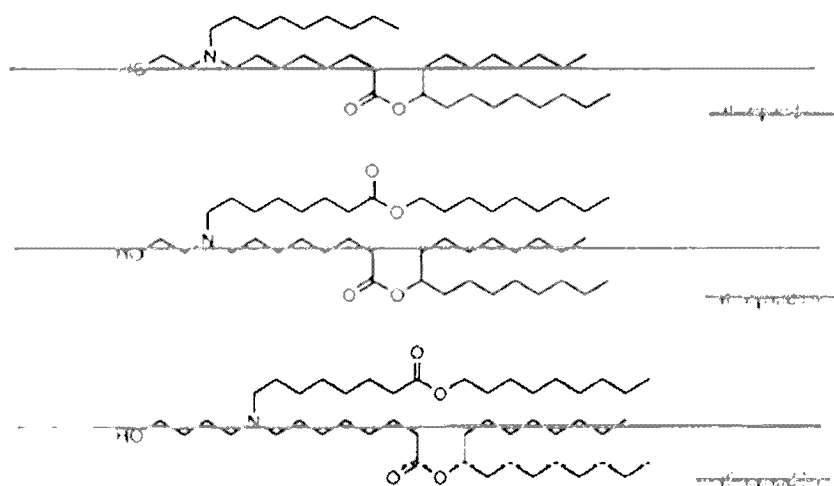
~~76. The vaccine of any of claims 1-65, wherein the at least one mRNA polynucleotide comprises at least one chemical modification; optionally wherein the at least one chemical modification is a N1-methylpseudouridine modification or a N1-ethylpseudouridine modification.~~

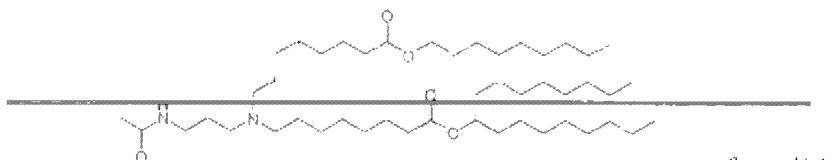
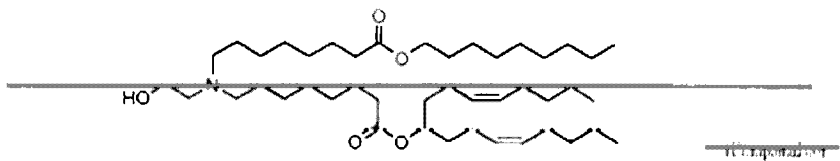
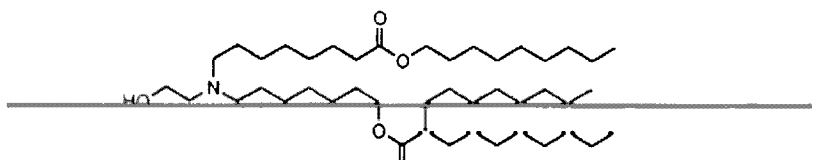
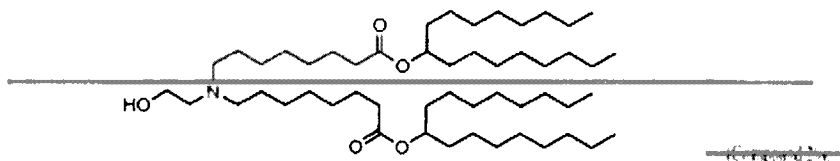
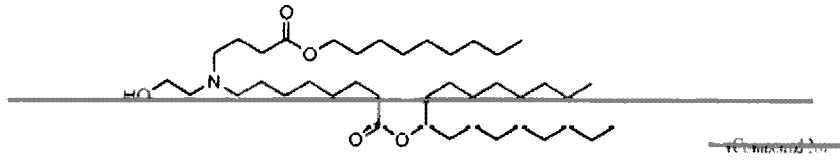
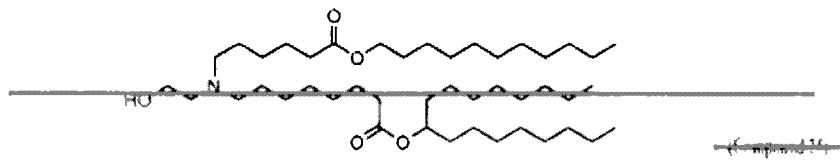
87. The vaccine of claim 76, wherein at least 80% of the uracil in the open reading frame has a chemical modification.

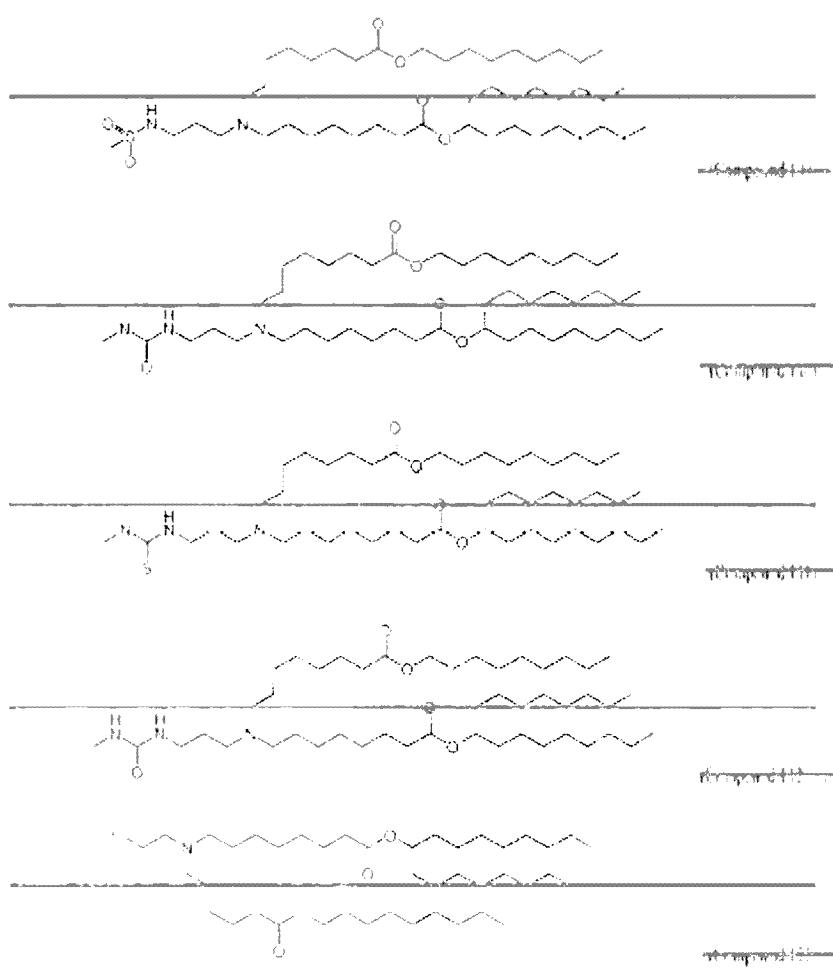
98. The vaccine of any of claims 1-87, wherein the cationic lipid is an ionizable cationic lipid and the non-cationic lipid is a neutral lipid.

109. The vaccine of claim 98, wherein the neutral lipid is selected from DSPC, DPPC, POPC, DOPE and SM.

11. The vaccine of any of claims 1-10, wherein the lipid nanoparticle comprises a compound of Compound 3, 18, 20, 25, 26, 29, 30, 60, 108, 112 or 122:







4210. The vaccine of any of claims 1-419 for use in a method of preventing and/or treating a BetaCoV disease in a subject.

4311. The vaccine for use of claim 4210, wherein the vaccine is administered to the subject by intradermal or intramuscular injection.