CLAIMS

1. Use of a first immunogenic composition and of a second immunogenic composition in the manufacture of a medicament ~~A method for~~ inducing an immune response in a human subject, wherein the first immunogenic composition is to be administered to the subject followed by the second immunogenic composition, wherein the ~~comprising administration of a~~ first immunogenic composition comprises~~ing~~ one or more antigens and a first adjuvant, ~~to the subject followed by administration of a~~ wherein the second immunogenic composition comprises~~ing~~ one or more antigens and a second adjuvant to the subject, wherein the first and second composition have at least one antigen in common, wherein the first and second adjuvant comprise a TLR agonist and/or an immunologically active saponin and have at least one of these two components in common and wherein

- the second adjuvant contains a lower amount of at least one common component than the first adjuvant,

and/or

- the common antigen is RTS,S and the second composition contains a lower amount of RTS,S than the first composition,

with the proviso that the first and second compositions do not both comprise RTS,S and QS21 and 3D-MPL associated with an oil-in-water emulsion formulation

2. The use~~method~~ of claim 1, wherein first adjuvant and second adjuvant consist of the same components.

3. The use~~method~~ of any one of the preceding claims, wherein the first and second adjuvants consist of the same components in the same relative proportions.

4. The use~~method~~ of any one of the preceding claims, wherein the second adjuvant contains a lower amount of at least one common component than the first adjuvant.

5. The use~~method~~ of any one of the preceding claims, wherein the lower amount in the second adjuvant is an at least 10% lower, such as an at least 25% lower, e.g. an at least two fold lower, such as an at least three fold lower, e.g. an at least four fold lower, such as an at least five fold lower, e.g. an at least six fold lower, such as an at least seven fold lower, e.g. an at least eight fold lower, such as an at least nine fold lower, e.g. an at least ten fold lower, such as an at least 15 fold lower, e.g. an at least 20 fold lower amount than in the first adjuvant.

6. The usemethod of any one of the preceding claims, wherein the lower amount in the second adjuvant is a between 2 and 50 fold lower, such as a between 2 and 20 fold lower, e.g. a between 2 and 15 fold lower, such as a between 2 and 10 fold lower, e.g. a between 3 and 7 fold lower, such as a between 4 and 6 fold lower amount than in the first adjuvant.

7. The usemethod of any one of the preceding claims, wherein the first and second adjuvant comprise a TLR agonist, and wherein the TLR agonist is a TLR4 agonist, such as 3D-MPL.

8. The usemethod of any one of the preceding claims, wherein the first and second adjuvant comprise an immunologically active saponin, such as QS21, optionally further comprising a sterol.

9. The use~~method~~ of any one of the preceding claims, wherein the first and second adjuvant comprise 3D-MPL and QS21 in a liposomal formulation.

10. The usemethod of claim 9, wherein the first adjuvant comprises between 25 and 75, such as 50 micrograms, of 3D-MPL and between 25 and 75, such as 50 micrograms of QS21 and the second adjuvant comprises between 5 and 15, such as 10 micrograms of 3D-MPL and between 5 and 15, such as 10 micrograms of QS21.

11. The usemethod of claim 9, wherein the first adjuvant comprises between 12.5 and 37.5, such as 25 micrograms, of 3D-MPL and between 12.5 and 37.5, such as 25 micrograms of QS21 and the second adjuvant comprises between 2.5 and 7.5, such as 5 micrograms of 3D-MPL and between 2.5 and 7.5, such as 5 micrograms of QS21.

12. The use~~method~~ of any one of the preceding claims, wherein the first adjuvant and/or the second adjuvant does not comprise aluminium.

13. The use~~method~~ of any one of the preceding claims, wherein the second composition contains a lower amount of the common antigen than the first composition.

14. The usemethod of any one of the preceding claims, wherein the lower amount of common antigen in the second composition is an at least 10% lower, such as an at least 25% lower, e.g. an at least two fold lower, such as an at least three fold lower, e.g. an at least four fold lower, such as an at least five fold lower, e.g. an at least six fold lower, such as an at least seven fold lower, e.g. an at least eight fold lower, such as an at least nine fold lower, e.g. an at least ten fold lower, such as an at least 15 fold lower, e.g. an at least 20 fold lower amount of antigen than in the first composition.

15. The usemethod of any one of the preceding claims, wherein the lower amount of common antigen in the second composition is a between 2 and 50 fold lower, such as a between 2 and 20 fold lower, e.g. a between 2 and 15 fold lower, such as a between 2 and 10 fold lower, e.g. a between 3 and 7 fold lower, such as a between 4 and 6 fold lower amount of antigen than in the first composition.

16. The use~~method~~ of any one of the preceding claims, wherein all antigens in the first and second compositions are the same.

17. The use~~method~~ of any one of the preceding claims, wherein a common antigen is a Plasmodium antigen, such as a *P. falciparum* or a *P. vivax* antigen.

18. The use~~method~~ of any one of the preceding claims, wherein a common antigen is circumsporozoite protein or an immunogenic fragment of variant thereof.

19. The usemethod of any one of the preceding claims, wherein the common antigen is selected from the group consisting of: RTS, CSV-S, RTS,S and CSV-S,S and mixed particles comprising RTS and CSV-S.

20. The usemethod any one of the preceding claims, wherein the time interval between administration of the first composition and administration of the second composition is between 1 and 24 months, e.g. between 1 and 18 months, such as between 1 and 12 months, e.g. between 2 and 24 months, e.g. between 2 and 18 months, such as between 2 and 12 months, between 2 and 10 months, such as between 3 and 9 months, e.g. between 4 and 8 months, such as between 7 and 8 months.

21. The usemethod of any one of the preceding claims, wherein the first immunogenic composition is administered twice before administration of the second immunogenic composition.

22. The usemethod of any one of the preceding claims, wherein at a time interval of at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, or at least 20, or more months after administration of the second composition, the second composition is administered one or more further times.

23. The usemethod of any one of the preceding claims, wherein the human subject is more than 18 years of age when the first composition is administered.

24. The usemethod of any one of claims 1 to 21, wherein the human subject is less than five years of age when the first composition is administered.

25. The usemethod of any one of the preceding claims, wherein the second administration is given intradermally.

~~26. An immunogenic composition for use in a method for inducing an immune response in a human subject, wherein the method comprises administration of a first immunogenic composition comprising one or more antigens and a first adjuvant to the subject followed by administration of a second immunogenic composition comprising one or more antigens and a second adjuvant to the subject, wherein the first and second composition have at least one antigen in common and the first and second adjuvant comprise a TLR agonist and/or an immunologically active saponin and have at least one of these two components in common and wherein~~

- ~~the second adjuvant contains a lower amount of at least one common component than the first adjuvant, and/or~~
- ~~the common antigen is RTS,S and the second composition contains a lower amount of RTS,S than the first composition,~~

~~with the proviso that the first and second compositions do not both comprise RTS,S and QS21 and 3D-MPL associated with an oil-in-water emulsion formulation.~~

~~27. The immunogenic composition of claim 26 comprising one or more of the further features of any one or more of claims 2 to 25.~~

~~28.~~26. Use of a second immunogenic composition comprising one or more antigens and a second adjuvant in the manufacture of a medicament for inducing an immune response in a human subject wherein that subject has previously received a first immunogenic composition comprising one or more antigens and a first adjuvant, wherein the first and second composition have at least one antigen in common and the first and second adjuvant comprise a TLR agonist and/or an immunologically active saponin and have at least one of these two components in common and wherein

- the second adjuvant contains a lower amount of at least one common component than the first adjuvant,

and/or

- the common antigen is RTS,S and the second composition contains a lower amount of RTS,S than the first composition,

with the proviso that the first and second compositions do not both comprise RTS,S and QS21 and 3D-MPL associated with an oil-in-water emulsion formulation.

~~29.~~27. The use of claim 26~~28~~ comprising one or more of the further features of any one or more of claims 2 to 25.

~~30.~~28. Use of a first immunogenic composition and of a second immunogenic composition in the manufacture of a medicament ~~A method~~ for inducing an immune response in a human subject, wherein the first immunogenic composition is to be administered to the subject followed by the second immunogenic composition, ~~comprising administration of a~~ wherein the first immunogenic composition comprise~~s~~ing one or more antigens and a first adjuvant, wherein the ~~to the subject followed by administration of a~~ second immunogenic composition comprise~~s~~ing one or more antigens and a second adjuvant ~~to the subject~~, wherein the first and second composition have at least one antigen in common and wherein the first and second adjuvants consist of 3D-MPL and QS21 in a liposomal formulation in the same relative proportions, wherein the second composition contains a lower amount of antigen and/or a lower amount of adjuvant than the first composition.

~~31.~~29. The ~~method~~ use of claim 28~~30~~ comprising one or more of the further features of any one or more of claims 2 to 25.

~~32.~~30. Use of a first immunogenic composition and of a second immunogenic composition in the manufacture of a medicament ~~A method~~ for inducing an immune response in a human subject against malaria ~~comprising administration of a~~, wherein the first immunogenic composition is to be administered to the subject followed by the second immunogenic composition, wherein the first immunogenic composition comprises~~ing~~ RTS,S and a first adjuvant ~~to the subject followed by administration of a~~, wherein the second immunogenic composition comprises~~ing~~ RTS,S and a second adjuvant ~~to the subject~~, wherein the first and second adjuvant comprise a TLR4 agonist and/or a immunologically active saponin in the same relative proportions, wherein the second composition contains a lower amount of adjuvant than the first composition, with the proviso that the first composition is not a composition comprising RTS,S and QS21 and 3D-MPL associated with an oil-in-water emulsion formulation.

~~33.~~31. The ~~method~~ use of claim ~~32~~30 comprising one or more of the further features of any one or more of claims 2 to 25.

~~34.~~32. Use of a first immunogenic composition and of a second immunogenic composition in the manufacture of a medicament ~~A method~~ for inducing an immune response in a human subject against malaria, wherein the first immunogenic composition is to be administered to the subject followed by the second immunogenic composition, wherein the ~~comprising administration of a~~ first immunogenic composition comprises~~ing~~ RTS,S and a first adjuvant ~~to the subject followed by administration of a~~, wherein the second immunogenic composition comprises~~ing~~ RTS,S and a second adjuvant to the subject, wherein the first and second adjuvants consist of 3D-MPL and QS21 in a liposomal formulation in the same relative proportions, wherein the second composition contains a lower amount of antigen and/or a lower amount of adjuvant than the first composition.

~~35.~~33. The ~~method~~ use of claim 32~~34~~ comprising one or more of the further features of any one or more of claims 2 to 25.

~~36.~~34. Use of a first immunogenic composition and of a second immunogenic composition in the manufacture of a medicament ~~A method~~ for inducing an immune response in a human subject, wherein the first immunogenic composition is to be administered to the subject followed by the second immunogenic composition, wherein the ~~comprising administration of a~~ first immunogenic composition comprises~~ing~~ RTS,S and an adjuvant ~~to the subject followed by administration of a~~, wherein the second immunogenic composition comprises~~ing~~ RTS,S ~~to the~~

subject, wherein the adjuvant comprises a TLR agonist and/or an immunologically active saponin and wherein the second immunogenic composition does not comprise an adjuvant.

~~37.~~35. The method use of claim 34~~36~~, wherein the adjuvant comprises or more of the further features of any one or more of claims 7 to 9 or 12.

~~38.~~36. The ~~method~~ use of claim 34~~36~~ or 35~~37~~, comprising one or more of the further features of any one or more of claims 13 to 25.

~~39.~~37. The method use of any one of claims 34 to 36~~36 to 38~~, wherein the first and the second composition both comprise 25 micrograms of RTS,S or both comprise 50 micrograms of RTS,S.