CLAIMS

1. Use of a vaccine composition in the manufacture of a medicament for booster vaccination for inducing in a human subject a neutralizing antibody response against dengue virus, said composition comprising a dengue antigen of each of serotypes 1 to 4 and wherein each of said dengue antigens is independently selected from the list consisting of: (a) a live attenuated dengue virus and (b) a live attenuated chimeric dengue virus, wherein said live attenuated chimeric dengue virus comprises a genome from a first flavivirus in which the prM-E sequence has been replaced with a prM-E sequence of a dengue virus and wherein said first flavivirus is selected from the group consisting of a yellow fever virus and a dengue virus; wherein at least one of said dengue antigens is said live attenuated chimeric dengue virus

   wherein said subject has previously received a primary vaccination course against each of serotypes 1 to 4 of dengue virus, wherein said primary vaccination course was administered in one dose, two doses 3-6 months apart or three doses wherein the first and the third dose were administered 12 months apart, and wherein said subject was dengue naïve before said primary vaccination course, wherein said subject is at least 9 years old; and

   wherein said booster vaccination is to be administered at least two years after the end of the primary vaccination course and results in at least a 2-fold increase in the neutralizing antibody titre against at least one of dengue serotypes 1 to 4, when compared with the neutralizing antibody titres before administration of the booster vaccination.

2. The use according to claim 1, wherein the booster vaccination is to be administered at least four years after the end of the primary vaccination course.

3. The use according to any claim 1 or 2, wherein said booster vaccination results in at least a 2-fold increase in the neutralizing antibody titre for at least three of the dengue serotypes, when compared with the neutralizing antibody titres before administration of the booster vaccination.

4. The use according to any one of claims 1 to 3, wherein said subject is at least 11 or 12 years old.

5. The use according to any of claims 1 to 4, wherein the subject has, before booster administration, a neutralizing antibody titer against each of serotypes 1 to 4 of at least 10 and less than 150, preferably less than 120.

6. The use according to any one of claims 1 to 5, wherein said 2-fold increase in the neutralizing antibody titre against each of serotypes 1 to 4 is measured between 20 and 60 days after said booster vaccination, preferably 28 days after said booster vaccination.

7. The use according to any one of claims 1 to 6, wherein said neutralizing antibody titre is measured using a dengue Plaque Reduction Neutralization Test ($PRNT_{50}$) test.

8. The use according to any one of claims 1 to 7, wherein said vaccine composition administered for booster vaccination is identical to the vaccine composition previously administered during the primary vaccination course.

9. The use according to any one of claims 1 to 7, wherein said vaccine composition administered for booster vaccination is different from the vaccine composition previously administered during the primary vaccination course.

10. The use according to any one of claims 1 to 9, wherein said subject has not previously been naturally infected by a dengue virus.

11. The use according to one any of claims 1 to 10, wherein the primary vaccination course comprises a vaccine composition which comprises a dengue antigen of each of serotypes 1 to 4 and wherein each of said dengue antigens is independently selected from the list consisting of: (a) a live attenuated dengue virus and (b) a live attenuated chimeric dengue virus, wherein said live attenuated chimeric dengue virus comprises a genome from a first flavivirus in which the prM-E sequence has been replaced with a prM-E sequence of a dengue virus and wherein said first flavivirus is selected from the group consisting of a yellow fever virus and a dengue virus.

12. Use of a vaccine composition in the manufacture of a medicament for inducing in a human subject a neutralizing antibody response against dengue virus, said composition comprising a dengue antigen of each of serotypes 1 to 4, wherein said dengue antigens of serotypes 1 to 4 are each independently selected from the group consisting of a live attenuated dengue virus and a live attenuated chimeric dengue virus, wherein said live attenuated chimeric dengue virus comprises a genome from a first flavivirus in which the prM-E sequence has been replaced with a prM-E sequence of a dengue virus and wherein said first flavivirus is selected from the group consisting of a yellow fever virus and a dengue virus; wherein at least one of said dengue antigens is said live attenuated chimeric dengue virus;
wherein said composition is to be administered as:

(a) a primary vaccination course, wherein said primary vaccination course is to be administered in one dose, two doses 3-6 months apart or three doses wherein the first and the third dose are to be administered 12 months apart; followed at least two years after the end of the primary vaccination course by

(b) a booster vaccination,

and wherein the human subject is initially dengue naive and is at least 9 years old.

13. The use according to claim 12, wherein the booster vaccination is to be administered at least four years after the end of the primary vaccination course.

14. The use according to claim 12 or 13, wherein said booster vaccination results in at least a 2-fold increase in the neutralizing antibody titre against at least one of dengue serotypes 1 to 4, when compared with the neutralizing antibody titres induced after the primary vaccination course.

15. The use according to any one of claims 12 to 14, wherein said booster vaccination results in at least a 2-fold increase in the neutralizing antibody titre against at least three of the dengue serotypes, when compared with the neutralizing antibody titres induced after the primary vaccination course.

16. The use according to claim 14, wherein said 2-fold increase in the neutralizing antibody titre against each of serotypes 1 to 4 is measured between 20 and 60 days after said booster vaccination, preferably 28 days after said booster vaccination.

17. The use according to any one of claims 14 to 16, wherein said neutralizing antibody titre is measured using a dengue Plaque Reduction Neutralization Test ($PRNT_{50}$) test.

18. The use according to any one of claims 1 to 17, wherein said subject is aged between 9 years and 60 years old.

19. The use according to claim 12, wherein said primary vaccination course consists in administration of 3 vaccine doses, wherein the second dose is to be administered about 6 months after the first dose and the third dose is to be administered about 6 months after the second dose.

20. The use according to any one of claims 1 to 19, wherein the booster vaccination is to be administered less than 20 years after the end of the primary vaccination course, preferably less than 10 years.

21. The use according to any one of claims 1 to 20, wherein the human subject is resident in a dengue endemic area.

22. The use according to any one of claims 1 to 21, wherein said composition comprises a dengue antigen of each of serotypes 1 to 4 and wherein each of said dengue antigens is the live attenuated chimeric dengue virus.

23. The use according to any one of claims 1 to 22, wherein said first flavivirus is a yellow fever virus.

24. The use according to any one of claims 1 to 23, wherein (i) the dengue antigens of serotypes 1, 3 and 4 are each a live attenuated chimeric dengue/dengue virus and the dengue antigen of serotype 2 is the live attenuated dengue virus or (ii) wherein the dengue antigens of serotypes 1 to 4 are each the live attenuated chimeric dengue virus.

25. The use according to any one of claims 1 to 24, wherein the dengue antigens of serotypes 1, 2, 3 and 4 comprise nucleic acid sequences having at least 90% identity to SEQ ID NOs: 1, 2, 3 and 4 respectively.

26. The use according to claim 25, wherein the dengue antigen of serotype 2 comprises a nucleic acid sequence having at least 95% identity to SEQ ID NO: 2.

27. The use according to claim 25 or claim 26, wherein the Envelope (E) protein encoded by the nucleic acid sequence of the dengue antigen of serotype 2 comprises a threonine residue at the position within the protein which corresponds to position 226 of SEQ ID NO: 2, a glycine residue at the position within the protein which corresponds to position 228 of SEQ ID NO: 2 and a valine residue at the position within the protein which corresponds to position 251 of SEQ ID NO: 2.