SUMMARY

In one aspect, the present disclosure relates to a use of a vaccine composition in the manufacture of a medicament for protecting a human subject against symptomatic dengue disease, wherein said composition comprises:

a dengue antigen of serotype 1, a dengue antigen of serotype 2, a dengue antigen of serotype 3 and a dengue antigen of serotype 4, wherein said dengue antigens 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 is a recipient flavivirus in which the genetic backbone has been modified by exchanging the sequences encoding the prM and E proteins by the corresponding sequences of a dengue virus; wherein said recipient flavivirus is selected from the group consisting of a yellow fever virus and a dengue virus; and wherein said dengue antigen of serotype 2 comprises an Envelope (E) protein comprising the sequence of SEQ ID NO: 13 or SEQ ID NO: 26.

The present disclosure relates to a vaccine composition for use in a method of protecting a human subject against dengue disease, wherein said composition comprises:

(i) a dengue antigen selected from the group consisting of:
  (a) a live attenuated dengue virus;
  (b) an inactivated dengue virus;
  (c) a live attenuated or inactivated chimeric dengue virus;
  (d) a dengue virus-like particle (VLP); and
  (e) a combination of two or more of (a) to (d);

or

(ii) a nucleic acid construct or viral vector which is able to express in a human cell a dengue antigen which is a dengue VLP.

The present disclosure further relates to the use of a vaccine composition of the present disclosure for the manufacture of a medicament for protecting a human subject against dengue disease.

The present disclosure further relates to a method of protecting a human subject against dengue disease, wherein said method comprises administering to said

CLAIMS

1. Use of a vaccine composition in the manufacture of a medicament for protecting a human subject against symptomatic dengue disease, wherein said composition comprises:

   a dengue antigen of serotype 1, a dengue antigen of serotype 2, a dengue antigen of serotype 3 and a dengue antigen of serotype 4, wherein said dengue antigens 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 is a recipient flavivirus in which the genetic backbone has been modified by exchanging the sequences encoding the prM and E proteins by the corresponding sequences of a dengue virus;

   wherein said recipient flavivirus is selected from the group consisting of a yellow fever virus and a dengue virus;

   and wherein said dengue antigen of serotype 2 comprises an Envelope (E) protein comprising the sequence of SEQ ID NO: 13 or SEQ ID NO: 26.

2. A use according to claim 1, wherein said human is 9-45 years of age.

3. A use according to any preceding claim, wherein said subject is dengue immune.

4. A use according to any preceding claim, wherein said medicament results in a statistically significant reduction in the incidence or likelihood of symptomatic virologically-confirmed dengue disease.

5. A use according to any preceding claim, wherein said dengue disease is caused by a dengue virus of serotype 1, serotype 3 or serotype 4.

6. A use according to any preceding claim, wherein said composition is to be administered in multiple doses.

7. A use according to claim 6, wherein said composition is to be administered in two doses.

8. A use according to claim 7, wherein said doses are to be administered six months apart.

9. A use according to claim 6, wherein said composition is to be administered in three or more doses.

10. A use according to claim 9, wherein said composition is to be administered in a first dose, a second dose and a third dose and wherein said second dose is to be administered six months after said first dose and wherein said third dose is to be administered twelve months after said first dose.

11. A use according to any preceding claim, wherein said dengue antigens of serotypes 1, 3 and 4 are each a live attenuated chimeric dengue virus and said dengue antigen of serotype 2 is selected from the group consisting of a live attenuated dengue virus and a live attenuated chimeric dengue virus.

12. A use according to any preceding claim, wherein said dengue antigens of serotypes 1, 3 and 4 are each a live attenuated chimeric dengue virus and said dengue antigen of serotype 2 is selected from the group consisting of a live attenuated dengue virus and a live attenuated chimeric dengue virus, and wherein said live attenuated chimeric dengue viruses are each a recipient flavivirus in which the genetic backbone has been modified by exchanging the sequences encoding the prM and E proteins by the corresponding sequences of a dengue virus and wherein said recipient flavivirus is selected from the group consisting of a yellow fever virus and a dengue virus.

13. A use according to any preceding claim, wherein said dengue antigens of serotypes 1, 3 and 4 are each a live attenuated chimeric dengue virus and wherein said dengue antigen of serotype 2 is a live attenuated dengue virus which comprises a nucleic acid sequence having at least 99% sequence identity to the sequence as set forth in SEQ ID NO: 24.

14. A use according to any one of claims 1 to 12, wherein said dengue antigens of serotypes 1, 2, 3 and 4 are each a live attenuated chimeric dengue virus.

15. A use according to any one of claims 1 to 14, wherein said composition comprises a live attenuated chimeric dengue virus.

16. A use according to any one of claims 1 to 15, wherein said live attenuated chimeric dengue virus is a recipient flavivirus in which the genetic backbone has been modified by exchanging the sequences encoding the prM and E proteins by the corresponding sequences of a dengue virus and said recipient flavivirus is a yellow fever virus.

17. A use according to any one of claims 1 to 15, wherein said chimeric dengue virus comprises one or more proteins from a dengue virus of one serotype and one or more proteins from a dengue virus of a different serotype.

18. A use according to any one of claims 1 to 17, wherein said composition comprises the prM-E sequences of CYD-1, CYD-2, CYD-3 and CYD-4.

19. A use according to any one of claims 1 to 16 and 18, wherein said composition comprises CYD-1, CYD-2, CYD-3 and CYD-4.

20. A use according to any preceding claim, wherein said dengue antigen of serotype 2 comprises an Envelope (E) protein comprising the sequence of SEQ ID NO: 13.

21. A use according to any preceding claim, wherein said dengue disease is severe dengue disease.

22. A use according to any preceding claim, wherein said protecting said human subject against symptomatic dengue disease results in a reduction in the incidence of hospitalisation due to dengue disease caused by dengue virus of any serotype.