We claim:

1. A vaccine composition for prophylaxis against Hand Foot and Mouth Disease caused by Enterovirus -71 ~~[~~(EV71~~]~~) and Coxsackievirus A16 (CVA16) comprising:
    a. a vaccine antigen, ~~the said vaccine antigen~~that is a synthetic construct ~~is the~~selected from recombinant protein sequences as represented by SEQ ID No. 2 (named as MEV1) ~~-~~or SEQ ID No. 4 (named as MEV2);
    b. at least one adjuvant~~s~~;
    c. at least one stabilizer~~s~~; and
    d. a physiologically acceptable buffer selected from a phosphate ~~and~~ or a citrate buffer;

wherein the said vaccine ~~formulation~~ composition is stable for at least 2 years at 5 ±3^{o}C and up to 2 weeks at 37^{o}C.

2. The vaccine composition ~~as claimed in~~according to claim 1, wherein ~~the vaccine antigen having protein~~ SEQ ID 2 is obtained from a codon optimized gene sequence as represented by SEQ ID No. 1.

3. The vaccine composition ~~as claimed in~~according to claim 1, wherein ~~the vaccine antigen having protein~~ SEQ ID 4 is obtained from a codon optimized gene sequence as represented by SEQ ID No. 3.

4. The vaccine composition ~~as claimed in~~according to claim 1, wherein the at least one adjuvant is ~~selected from a group of~~ alum, ~~(aluminium phosphate, aluminium hydroxide),~~ a squalene-based adjuvant~~s such as MF59~~, a montanide, a RIBI adjuvant, a complete Freud's adjuvant, an ~~and~~ incomplete Freud's, MPL, muramyl dipeptide, an oil-in-water emulsion, a TLR ligand-~~-~~based adjuvant~~s~~, a CpG oligonucleotide~~s~~, a ~~Non~~non-CpG oligonucleotide~~s~~, a saponin~~s such as QS-1, ISCOM, ISCOMATRIX~~, a vitamin~~s~~, ~~and~~ or an immunomodulant~~s such as cyotkines~~.

5. The vaccine composition ~~as claimed in~~according to claim 1, wherein the at least one stabilizer~~s~~ is~~are selected from~~a sugar ~~5-60% sucrose or 5-40% Trehalose~~ or a sugar alcohol~~s like 5-40% Glycerol or 5-40% Sorbitol~~ .

6. The vaccine composition as claimed in claim 1, wherein the said vaccine antigens SEQ ID No. 2 or SEQ ID No. 4 is prepared by a process comprising:
    a. expression of the protein sequences SEQ ID No. 2 or SEQ ID No. 4 from codon optimized gene sequences, namely SEQ ID No. 1 and SEQ ID No. 3 respectively with 0.2-0.75 mM IPTG between 15 °C-37°C, in the form ofas inclusion bodies in a suitable host selected from *E. coli* BL21 (DE3) cells or Rosetta cells;
    b. centrifugation at 10,000 rpm for 5 minutes to obtain the protein of interest, that is either MEV-1 or MEV-2 in the a cell pellet;
    c. wherein preparing the said vaccine antigen SEQ ID No.2 comprising comprises the steps of;:
        i) suspending the cell pellet of step (b) with a lysis buffer-I, the said lysis buffer-I for MEV1 comprising 50mM Na_2HPO_4, 0.3M NaCl, 1% TritonX-114, 0.5mg/ml lysozyme, 1mM AEBSF, simultaneously performing freeze thaw cycles for at least 3 times followed by ultrasonication for 20 seconds thrice with at least 30 seconds intervals in between;
        ii) undergoing cell lysis with a lysis buffer-II for MEV1, the said lysis buffer-II for MEV1 comprising 3-6M Urea, 5-10mM imidazole, 50mM Na_2HPO_4, 0.3M NaCl, and 1mM AEBSF at 4°C for 3-16 hours to recover at pH 7.4 the an insoluble protein at pH of 7.4 for MEV1 to obtain a denatured protein solution of MEV1;
        iii) adding the denatured protein solution of MEV1 of step (ii) above to a Ni-NTA Immobilized Metal Affinity Chromatography column followed by washing with a Wwash Bbuffer-I comprising 50mM Na_2HPO_4, 0.3M NaCl, 1mM AEBSF, 3M urea at pH 7.4 with 0.1% Triton X-114 and 5-10 mM Imidazole;
        iv) again performing washing after step (iii) above for MEV1 washing the column from step (iii) with a Wash Buffer–II comprising 50mM Na_2HPO_4, 0.3M NaCl, 1mM AEBSF, 3-6M urea at pH 7.4 with 0.1% Triton X-114 and 20mM imidazole; followed by washing by a Wash Buffer–– III, the said Wwash Bbuffer-III comprising 50 mM Na_2HPO_4, 0.3 M NaCl, 1 mM AEBSF additionally with 20mM imidazole with decreasing concentrations of urea;
        v) eluting the target protein MEV1 from the column in step (iv) with an elution buffer, the said elution buffer comprising 50mM Na_2HPO_4, 0.3M NaCl, 1mM AEBSF by using increasing concentrations of imidazole (250-500 mM) optionally with 3-6 M urea;

vi) undergoing dialysis of washed Ni-NTA column-based affinity purified protein MEV-1 against phosphate buffer saline using 10 kDa cutoff, membrane and refolding with a refolding buffer~~s~~ comprising 0.1-0.3M NaCl, 10% glycerol and 0.2-0.5 M Arginine or 0.2-0.5 M Arginine-HCl optionally followed by size exclusion chromatography to obtain ~~the final protein~~ MEV-1 with at least 92% to 96% purity;

d) wherein preparing the ~~said~~ vaccine antigen SEQ ID No.4 ~~comprising~~ comprises the steps of:

i) suspending the cell pellet of step (b) undergoing lysis with lysis buffer-I for MEV2, comprising 50 mM Tris, 0.3 M NaCl, 1% Triton X114, 0.5 mg/ml lysozyme, 1mM AEBSF at pH 8-8.5;

ii) or, alternatively, suspending the cell pellet of step (b) undergoing cell lysis with lysis buffer-II for MEV2, the ~~said~~ lysis buffer-II for MEV2 comprising 50 mM Tris, 0.3 M NaCl, 1 mM AEBSF in presence of 6M urea and 10-20 mM DTT;

iii) undergoing refolding of MEV-2 after step (ii) above in decreasing concentration of urea and DTT concentration in the presence of ~~–~~0.2-1M Arginine or Arginine-HCL, redox pair reagents selected from Cysteine/Cystine, GSSG/GSH, oxidized DTT/reduced DTT or cystamine/cysteamine with concentration between 0.05mM to 10mM to obtain ~~the final protein~~ MEV-2 with at least 96% purity.

e) optionally storing ~~the said protein~~ MEV1 or MEV2 in a solution comprising polyols or ~~Sugars~~sugars~~,~~ ~~examples being~~selected from~~,~~ 5-40% Glycerol, ~~or~~ 5-60% Sucrose, ~~or~~ 5-40% Trehalose or 5-40% Sorbitol at -20 degree C wherein the solution protects MEV1 or MEV2 ~~to protect~~ from thermal stress.

7. A method of preparing the vaccine antigens SEQ ID No. 2 or SEQ ID No. 4 of claim 1 comprising the steps of:
   a. ~~expression of~~expressing ~~the~~ protein sequences SEQ ID No. 2 or SEQ ID No. 4 from codon optimized gene sequences, namely SEQ ID No. 1 and SEQ ID No. 3

respectively with 0.2-0.75 mM IPTG between 15 °C-37°C, ~~in the form of~~as inclusion bodies in a suitable host selected from *E. coli* BL21 (DE3) cells or Rosetta cells;

b. ~~centrifugation~~ centrifuging at 10,000 rpm for 5 minutes to obtain ~~the protein of interest~~MEV1 or MEV2 in ~~the~~ a cell pellet;

c. wherein preparing the ~~said~~ vaccine antigen SEQ ID No.2 ~~comprising~~ comprises the steps of~~;~~:

i) suspending the cell pellet of step (b) with a lysis buffer-I, the ~~said~~ lysis buffer-I for MEV1 comprising 50mM Na_2HPO_4, 0.3M NaCl, 1% TritonX-114, 0.5mg/ml lysozyme, 1mM AEBSF, simultaneously performing freeze thaw cycles for at least 3 times followed by ultrasonication thrice for 20 seconds with at least 30 seconds intervals in between;

ii) undergoing cell lysis with a lysis buffer-II for MEV1, the ~~said~~ lysis buffer-II for MEV1 comprising 3-6M Urea, 5-10mM imidazole, 50mM Na_2HPO_4, 0.3M NaCl, and 1mM AEBSF at 4°C for 3-16 hours to recover at pH 7.4 an ~~the~~ insoluble protein ~~at pH of 7.4~~ for MEV1 to obtain a denatured protein solution of MEV1;

iii) adding the denatured protein solution of MEV1 of step (ii) ~~above~~ to a Ni-NTA Immobilized Metal Affinity Chromatography column followed by washing with a wash buffer-I comprising 50mM Na_2HPO_4, 0.3M NaCl, 1mM AEBSF, 3M urea at pH7.4 with 0.1% Triton X-114 and 5-10 mM Imidazole;

iv) washing the column from step (iii) ~~again performing washing after step (iii) above for MEV1~~ with a Wash Buffer–II ~~-~~comprising 50mM Na_2HPO_4, 0.3M NaCl, 1mM AEBSF, 3-6M urea at pH7.4 with 0.1% Triton X-114 and 20mM imidazole; followed by washing ~~by~~ with a Wash Buffer – III, the ~~said~~ W~~w~~ash B~~b~~uffer-III comprising 50 mM Na_2HPO_4, 0.3 M NaCl, 1 mM AEBSF additionally with 20mM imidazole with decreasing concentrations of urea;

v) eluting the ~~target protein~~ MEV1 from the column in step (iv) with an elution buffer, the ~~said~~ elution buffer comprising 50mM Na_2HPO_4, 0.3M NaCl, 1mM AEBSF by using increasing concentrations of imidazole (250-500 mM) optionally with 3-6 M urea;

vi) undergoing dialysis of ~~washed Ni-NTA column-based affinity purified protein~~ MEV-1 against a phosphate buffer saline using 10 kDa cutoff, membrane and refolding with a refolding buffer~~s~~ comprising 0.1-0.3M NaCl,

10% glycerol and 0.2-0.5 M Arginine or 0.2-0.5 M Arginine-HCl optionally followed by size exclusion chromatography to obtain ~~the final protein~~ MEV-1 with at least 92% to 96% purity;

d) wherein preparing the ~~said~~ vaccine antigen SEQ ID No.4 ~~comprising~~ comprises the steps of;

i) suspending the cell pellet of step (b) undergoing lysis with a lysis buffer-I for MEV2~~, the said lysis buffer-I for MEV1 comprising Lysis Buffer-I for MEV2 comprised~~ comprising 50 mM Tris, 0.3 M NaCl, 1% Triton X114, 0.5 mg/ml lysozyme, 1mM AEBSF at pH 8-8.5;

ii) or, alternatively undergoing cell lysis with lysis buffer-II for MEV2, the said lysis buffer-II for MEV2 comprising 50 mM Tris, 0.3 M NaCl, 1 mM AEBSF in presence of 6M urea and 10-20 mM DTT;

iii) undergoing refolding of MEV-2 after step (ii~~f~~) above in decreasing concentration of urea (from 6 M to 0.1 M) and DTT concentration (from 20 mM to 0.1 mM) in presence of 0.2-1M Arginine or Arginine-HCL, redox pair reagents selected from Cysteine/Cystine, GSSG/GSH, oxidized DTT/reduced DTT or cystamine/cysteamine with concentration between 0.05mM to 10mM to ~~obtain the final protein~~ MEV-2 with at least 96% purity.

e) optionally storing ~~the said protein~~ MEV1 or MEV2 in a solution comprising a polyol~~s~~ or ~~Sugars~~a sugar, ~~examples being,~~selected from 5-40% Glycerol, ~~or~~ 5-60% Sucrose, ~~or~~ 5-40% Trehalose or ~~or~~ 5-40% Sorbitol at -20 degree C to protect MEV1 or MEV2 from thermal stress.

8. A composition comprising a multi-epitope synthetic protein sequence as disclosed in SEQ ID No. 2 with at least 92% - 96% purity.

9. A composition comprising a multi-epitope synthetic protein sequence as disclosed in SEQ ID N~~n~~o. 4 with at least 96 % purity.

10. The immunogenic composition of claim 4, wherein the alum is aluminium hydroxide or

11. The immunogenic composition of claim 4, wherein the saponin is QS-1, ISCOM, or ISCOMATRIX.

12. The immunogenic composition of claim 4, wherein the immunomodulant is a cytokine.

13. The immunogenic composition of claim 4, wherein the squalene-based adjuvant is MF59.

14. The immunogenic composition of claim 5, wherein the sugar is 5-60% sucrose or 5-40% trehalose.

15. The immunogenic composition of claim 5, wherein the sugar alcohol is 5-40% glycerol or 5-40% sorbitol.