Claims:

1) A combination vaccine comprising

i) inactivated polio virus antigen (IPV) selected from Salk or Sabin strain;

ii) inactivated rotavirus (IRV) antigen;

wherein the inactivated polio virus antigen is a dose reduced inactivated polio virus antigen selected from a group comprising of:

a) dose composition having Sabin Type 1, Type 2, Type 3 combination selected from 5-16-10 D-antigen units;

b) dose composition having Sabin Type 1, Type 2, Type 3 combination selected from 2.5-8-5 D-antigen units;

c) dose composition having Sabin Type 1, Type 2, Type 3 combination selected from 5-8-10 D-antigen units;

d) dose composition having Salk Type 1, Type 2, Type 3 combination selected from 7.5-16-10 D-antigen units;

e) dose composition having Salk Type 1, Type 2, Type 3 combination selected from 8-2-5 D-antigen units;

f) dose composition having Salk Type 1, Type 2, Type 3 combination selected from 10-2-5 D-antigen units;

g) dose composition having Salk Type 1, Type 2, Type 3 combination selected from 10-2-10 D-antigen units;

h) dose composition having Salk Type 1, Type 2, Type 3 combination selected from 10-2-12 D - antigen units;

i) dose composition having Salk Type 1, Type 2, Type 3 combination selected from 10-2-16 D - antigen units; and

j) dose composition having Salk Type 1, Type 2, Type 3 combination selected from 5-2-5 D-antigen units;

wherein the polio virus antigen is a dose reduced composition having at least one inactivated polio virus strain selected from Type 1, Type 2 or Type 3 of Sabin; or Mahoney type 1, MEF Type 2, or Saukett type 3 of Salk; and is adsorbed on aluminium hydroxide adjuvant having Al3+ concentration between 0.1 — 2.5 mg/dose and percent adsorption of at least 70 %;

wherein the rotavirus antigen is heat inactivated CDC-9 rotavirus strain at a concentration 1-30 µg/dose and is adsorbed on aluminium hydroxide adjuvant having Al3+ concentration between 0.1 — 2.5 mg/dose and percent adsorption of at least 70 %;
wherein the dose reduced composition is reduced as compared to a standard dose of IPV i.e. 40 — 8 — 32 of Type 1, 2, and 3 (as prescribed by the WHO).

2) The vaccine as claimed in claim 1, wherein said combination vaccine comprises one or more antigens selected from group comprising of Diphtheria toxoid (D), Tetanus toxoid (T), Whole cell pertussis (wP), HBsAg, Hib PRP-Carrier protein conjugate (Hib B), *Neisseria meningitidis* A antigen(s), *Neisseria meningitidis* C antigen(s), *Neisseria meningitidis* W-135 antigen(s), *Neisseria meningitidis* Y antigen(s), *Neisseria meningitidis* X antigen(s), *Streptococcus pneumoniae* antigen(s), *Neisseria meningitidis* B bleb or purified antigen(s), *Staphylococcus aureus* antigen(s), Anthrax, BCG, *Hepatitis* A antigen(s), *Hepatitis* B antigen, Human papilloma virus, *Salmonella typhi* antigen(s), Acellular pertussis, Malaria Antigen (RTS,S), Measles, Mumps, Rubella, Dengue, Zika, Ebola, Chikungunya, Japanese encephalitis, and Diarrheal antigens.

3) The vaccine as claimed in claim 2, wherein the Diphtheria toxoid (D) and Tetanus toxoid (T) are adsorbed onto aluminium phosphate adjuvant.

4) The vaccine as claimed in claim 2, wherein the Diphtheria toxoid and Tetanus toxoid are purified using Gel permeation chromatography with resin selected from the group comprising of Sephacryl S-300 HR, PLgel, Sephacryl S-200HR, Sephadex, Bio-Gel (cross-linked polyacrylamide agarose gel) and Styragel.

5) The vaccine as claimed in claim 2, wherein the acellular pertussis antigen (aP) is one or more antigens selected from modified adenylate cyclase, Pertussis toxoid (PT), Filamentous hemagglutinin (FHA), Pertactin (P69 or PRN), and Fimbrial proteins (FIM 1, 2 and 3).

6) The vaccine as claimed in claim 2, wherein the Whole cell pertussis (wP) is inactivated whole cell pertussis comprising one or more of *Bordetella pertussis* strains 134, 509, 25525 and 6229.

7) The vaccine as claimed in claim 2, wherein the Hib B antigen is Hib PRP polysaccharide conjugated to a carrier protein using a cyanylation conjugation chemistry, wherein said cyanylation reagent is selected from 1-cyano-4-dimethylaminopyridinium tetrafluoroborate (CDAP)1-cyano-4-pyrrolidinopyridinium tetrafluorborate (CPPT), 1-cyanoimidazole namely (1-CI), 1-cyanobenzotriazole(1-CBT) or 2-cyanopyridazine-3(2H)one (2-CPO); and carrier protein is selected from a group comprising of CRM197, Diphtheria toxoid, *Neisseria meningitidis* outer membrane complex, fragment C of tetanus toxoid, pertussis toxoid, protein D of *H. influenzae*, *E. coli* LT, *E. coli* ST, and exotoxin A from Pseudomonas aeruginosa, outer membrane complex c (OMPC), porins, transferrin binding proteins, pneumolysin, pneumococcal surface protein A (PspA), pneumococcal surface adhesin A (PsaA), pneumococcal PhtD, pneumococcal surface proteins BVH-3 and BVH-11, protective antigen (PA) of *Bacillus anthracis* and detoxified edema factor (EF) and lethal factor (LF) of *Bacillus anthracis*, ovalbumin, keyhole limpet hemocyanin (KLH), human serum albumin, bovine serum albumin (BSA) and purified protein derivative of tuberculin (PPD), synthetic peptides, heat shock proteins, pertussis proteins, cytokines, lymphokines, hormones, growth factors, artificial proteins comprising multiple human CD4+ T cell epitopes from various pathogen-derived antigens such as N 19, iron-uptake proteins, toxin A or B from *C. difficile* and *S. agalactiae* proteins.

8) The vaccine as claimed in claim 2, wherein HBsAg antigen is a surface antigen of Hepatitis B and is individually adsorbed onto aluminium phosphate.

9) The vaccine as claimed in claim 1, wherein vaccine comprises at least one preservative selected from a group consisting of 2-phenoxyethanol (2-PE), Phenol, Thiomersal, Formaldehyde.

10) The vaccine as claimed in claim 1, wherein the combination vaccine is a bivalent vaccine composition comprising dose reduced IPV and IRV.

11) The Vaccine as claimed in claim 1, wherein concentration of IRV antigen is 2.5 μg/dose.

12) The Vaccine as claimed in claim 1, wherein concentration of IRV antigen is 5μg/dose.

13) The vaccine as claimed in Claim 1, wherein concentration of IRV antigen is 10 μg/dose.

14) The vaccine as claimed in Claim 11-13, wherein Alum (Al^{3+}) is used as an adjuvant in the concentration not greater than 1 mg/dose.

15) The vaccine as claimed in claims 1 or 2, comprising Diphtheria toxoid, Tetanus toxoid, Whole cell pertussis (wP), Hib PRP-Carrier protein conjugate (Hib B), IPV and IRV wherein Diphtheria toxoid is present in an amount in the range of 1-50 Lf; Tetanus toxoid is present in an amount in the range of 1 – 30 Lf; wP is present in an amount in the range of 10 – 50 IOU; Dose reduced inactivated Salk strain of polio virus type 1 is present in an amount in the range of 1 – 20 D antigen units, type 2 in the range of 1 – 20 D antigen units, Type 3 in the range of 1 – 20 D antigen units; IRV is present in an amount in the range of 1 – 30 μg; H. influenzae type b PRP- protein conjugate is in an amount in the range of 2 – 20 μg of PRP content; Total aluminum content (Al^{3+}) is present in an amount in the range of 0.4-1.5 mg; 2-Phenoxyethanol is present in an amount in the range of 2 – 6 mg; L-Histidine is present in the range of 0.5 – 5 mg.

16) The vaccine as claimed in claim 1 or 2 comprising Diphtheria toxoid, Tetanus toxoid, wP, Hib B, IPV and IRV, wherein Diphtheria toxoid is present in an amount of about 22.5 Lf; Tetanus toxoid is present in an amount of about 7.5 Lf; wP is present in an amount of about 15 IOU; Dose reduced inactivated Salk strain of polio virus type 1 is present in an amount of about 10 D antigen units, type 2 is present in an amount of about 2 D antigen units, Type 3 is present in an amount of about 10 or 16 D antigen units; IRV is present in an amount of about 10 μg; H. influenzae type b PRP- TT conjugate is present in an amount of about 5 μg of PRP content; Total aluminum content (Al^{3+}) is present in an amount of not more than 0.9 mg; 2-Phenoxyethanol is present in an amount of about 3.25 mg; L-Histidine is present in an amount of about 1.55 mg.

17) The vaccine as claimed in claim 1 or 2, comprising Diphtheria toxoid, Tetanus toxoid, wP, Hib B, IPV and IRV, wherein Diphtheria toxoid is present in an amount of about 22.5 Lf; Tetanus toxoid is present in an amount of about 7.5 Lf; wP is present in an amount of about 15 IOU; Dose reduced inactivated Salk strain of polio virus type 1 is present in an amount of about 10 D antigen units, type 2 is present in an amount of about 2 D antigen units, Type 3 is

present in an amount of about 10 or 16 D antigen units; IRV is present in an amount of about 10 μg; H. influenzae type b PRP- CRM197 conjugate is present in an amount of about 10 μg of PRP content; Total aluminum content (Al^{3+}) is present in an amount of not more than 0.9 mg; 2-Phenoxyethanol is present in an amount of about 3.25 mg; L-Histidine is present in an amount of about 1.55 mg.

18) The vaccine as claimed in claims 1 or 2, comprising Diphtheria toxoid, Tetanus toxoid, Whole cell pertussis (wP), Hib PRP-Carrier protein conjugate (Hib B), IPV and IRV, wherein Diphtheria toxoid is present in an amount in the range of 1-50 Lf; Tetanus toxoid is present in an amount in the range of 1 – 30 Lf; wP is present in an amount in the range of 10 – 50 IOU; Dose reduced inactivated Sabin strain of polio virus type 1 is present in an amount in the range of 1 – 20 D antigen units, type 2 in the range of 1 – 20 D antigen units, Type 3 in the range of 1 – 20 D antigen units; IRV is present in an amount in the range of 1-30 μg; H. influenzae type b PRP- protein conjugate is in an amount in the range of 2-20 μg of PRP content; Total aluminum content (Al^{3+}) is present in an amount in the range of 0.4-1.5 mg; 2-Phenoxyethanol is present in an amount in the range of 2 – 6 mg; L-Histidine is present in the range of 0.5 – 5 mg.

19) The vaccine as claimed in claim 1 or 2, comprising Diphtheria toxoid, Tetanus toxoid, wP, Hib B, IPV and IRV, wherein Diphtheria toxoid is present in an amount of about 22.5 Lf; Tetanus toxoid is present in an amount of about 7.5 Lf; wP is present in an amount of about 15 IOU; Dose reduced inactivated Sabin strain of polio virus type 1 is present in an amount of about 5 D antigen units, type 2 is present in an amount of about 16 D antigen units, Type 3 is present in an amount of about 10 D antigen units; IRV is present in an amount of about 10 μg; H. influenzae type b PRP- TT conjugate is present in an amount of about 5 μg of PRP content; Total aluminum content (Al^{3+}) is present in an amount of not more than 0.9 mg; 2-Phenoxyethanol is present in an amount of about 3.25 mg; L-Histidine is present in an amount of about 1.55 mg.

20) The vaccine as claimed in claim 1 or 2, comprising Diphtheria toxoid, Tetanus toxoid, wP, Hib B, IPV and IRV, wherein Diphtheria toxoid is present in an amount of about 22.5 Lf; Tetanus toxoid is present in an amount of about 7.5 Lf; wP is present in an amount of about 15 IOU; Dose reduced inactivated Sabin strain of polio virus type 1 is present in an amount

of about 5 D antigen units, type 2 is present in an amount of about 16 D antigen units, Type 3 is present in an amount of about 10 D antigen units; IRV is present in an amount of about10 μg; H. influenzae type b PRP- CRM197 conjugate is present in an amount of about 10 μg of PRP content; Total aluminum content (Al^{3+}) is present in an amount of not more than 0.9 mg; 2-Phenoxyethanol is present in an amount of about 3.25 mg; L-Histidine is present in an amount of about 1.55 mg.

21) The vaccine as claimed in claims 1 or 2, comprising Diphtheria toxoid, Tetanus toxoid, Whole cell pertussis (wP), Hib PRP-Carrier protein conjugate (Hib B), HBsAg, IPV and IRV, wherein Diphtheria toxoid is present in an amount in the range of 1-50 Lf; Tetanus toxoid is present in an amount in the range of 1 – 30 Lf; wP is present in an amount in the range of 10 – 50 IOU; Dose reduced inactivated Salk strain of polio virus type 1 is present in an amount in the range of 1 – 20 D antigen units, type 2 in the range of 1 – 20 D antigen units, Type 3 in the range of 1 – 20 D antigen units; IRV is present in an amount in the range of 1 – 30 μg; H. influenzae type b PRP- protein conjugate is in an amount in the range of 2 – 20 μg of PRP content; Hepatitis B surface antigen (HBsAg) is in an amount in the range of 5 – 30 μg; Total aluminum content (Al^{3+}) is present in an amount in the range of 0.4-1.5 mg; 2-Phenoxyethanol is present in an amount in the range of 2 – 6 mg; L-Histidine is present in the range of 0.5 – 5 mg.

22) The vaccine as claimed in claim 1 or 2, comprising Diphtheria toxoid, Tetanus toxoid, wP, Hib B, HBsAg, IPV and IRV, wherein Diphtheria toxoid is present in an amount of about 22.5 Lf; Tetanus toxoid is present in an amount of about 7.5 Lf; wP is present in an amount of about 15 IOU; Dose reduced inactivated Salk strain of polio virus type 1 is present in an amount of about 10 D antigen units, type 2 is present in an amount of about 2 D antigen units, Type 3 is present in an amount of about 10 or 16 D antigen units; IRV is present in an amount of about10 μg; H. influenzae type b PRP- TT conjugate is present in an amount of about 5 μg of PRP content; Hepatitis B surface antigen (HBsAg) is in an amount of about 12.5 μg; Total aluminum content (Al^{3+}) is present in an amount of not more than 0.9 mg; 2-Phenoxyethanol is present in an amount of about 3.25 mg; L-Histidine is present in an amount of about 1.55 mg.

23) The vaccine as claimed in claim 1 or 2, comprising Diphtheria toxoid, Tetanus toxoid, wP, Hib B, HBsAg, IPV and IRV, wherein Diphtheria toxoid is present in an amount of about 22.5 Lf; Tetanus toxoid is present in an amount of about 7.5 Lf; wP is present in an amount of about 15 IOU; Dose reduced inactivated Salk strain of polio virus type 1 is present in an amount of about 10 D antigen units, type 2 is present in an amount of about 2 D antigen units, Type 3 is present in an amount of about 10 or 16 D antigen units; IRV is present in an amount of about 10μg; H. influenzae type b PRP- CRM197 conjugate is present in an amount of about 10 μg of PRP content; Hepatitis B surface antigen (HBsAg) is in an amount of about 12.5 μg; Total aluminum content (Al^{3+}) is present in an amount of not more than 0.9 mg; 2-Phenoxyethanol is present in an amount of about 3.25 mg; L-Histidine is present in an amount of about 1.55 mg.

24) The vaccine as claimed in claims 1 or 2, comprising Diphtheria toxoid, Tetanus toxoid, Whole cell pertussis (wP), Hib PRP-Carrier protein conjugate (Hib B), HBsAg, IPV and IRV, wherein Diphtheria toxoid is present in an amount in the range of 1-50 Lf; Tetanus toxoid is present in an amount in the range of 1 – 30 Lf; wP is present in an amount in the range of 10 – 50 IOU; Dose reduced inactivated Sabin strain of polio virus type 1 is present in an amount in the range of 1 – 20 D antigen units, type 2 in the range of 1 – 20 D antigen units, Type 3 in the range of 1 – 20 D antigen units; IRV is present in an amount in the range of 1 – 30 μg; H. influenzae type b PRP- protein conjugate is in an amount in the range of 2 – 20 μg of PRP content; Hepatitis B surface antigen (HBsAg) is in an amount in the range of 5 – 30 μg; Total aluminum content (Al^{3+}) is present in an amount in the range of 0.4-1.5 mg; 2-Phenoxyethanol is present in an amount in the range of 2 – 6 mg; L-Histidine is present in the range of 0.5 – 5 mg.

25) The vaccine as claimed in claim 1 or 2, comprising Diphtheria toxoid, Tetanus toxoid, wP, Hib B, HBsAg, IPV and IRV; wherein Diphtheria toxoid is present in an amount of about 22.5 Lf; Tetanus toxoid is present in an amount of about 7.5 Lf; wP is present in an amount of about 15 IOU; Dose reduced inactivated Sabin strain of polio virus type 1 is present in an amount of about 5 D antigen units, type 2 is present in an amount of about 16 D antigen units, Type 3 is present in an amount of about 10 D antigen units; IRV is present in an amount of about 10 μg; H. influenzae type b PRP- TT conjugate is present in an amount of

about 5 μg of PRP content; Hepatitis B surface antigen (HBsAg) is in an amount of about 12.5 μg; Total aluminum content (Al^{3+}) is present in an amount of not more than 0.9 mg; 2-Phenoxyethanol is present in an amount of about 3.25 mg; L-Histidine is present in an amount of about 1.55 mg.

26) The vaccine as claimed in claim 1 or 2, comprising Diphtheria toxoid, Tetanus toxoid, wP, Hib B, HBsAg, IPV and IRV; wherein Diphtheria toxoid is present in an amount of about 22.5 Lf; Tetanus toxoid is present in an amount of about 7.5 Lf; wP is present in an amount of about 15 IOU; Dose reduced inactivated Sabin strain of polio virus type 1 is present in an amount of about 5 D antigen units, type 2 is present in an amount of about 16 D antigen units, Type 3 is present in an amount of about 10 D antigen units; IRV is present in an amount of about10 μg; H. influenzae type b PRP- CRM197 conjugate is present in an amount of about 10 μg of PRP content; Hepatitis B surface antigen (HBsAg) is in an amount of about 12.5 μg; Total aluminum content (Al^{3+}) is present in an amount of not more than 0.9 mg; 2-Phenoxyethanol is present in an amount of about 3.25 mg; L-Histidine is present in an amount of about 1.55 mg.

27) The vaccine as claimed in any one of claims 15-26, wherein the IPV and IRV antigens are individually adsorbed on Aluminum hydroxide; and other antigen(s) are either unadsorbed or adsorbed on aluminum salt selected from one or more of Alum Phosphate, Alum hydroxide, and their combination thereof.

28) The vaccine as claimed in any one of claims 15-26, wherein the vaccine comprises of excipients selected from the group comprising of Histidine, Sucrose, Glycine, & Sodium Chloride; and wherein the concentration of Histidine is in range of 5 – 40 mM.

29) A process of manufacturing a combination vaccine as claimed in claim 1, comprising the steps of:

i) Adsorbing Sabin/Salk strain IPV bulk and IRV bulk individually on Aluminum hydroxide; and

ii) Mixing Monovalent bulks of IPV and IRV and keeping the mixture at 2 – 8 °C on rocker for 2 hours.

30) A process of manufacturing a hexavalent combination vaccine as claimed in any one of claims 15- 20, comprising the steps of:

a. adsorbing Sabin/Salk strain IPV bulk and IRV bulk individually on Aluminum hydroxide, followed by pH adjustment to 6.2 – 6.6;

b. adsorbing Diphtheria toxoid on Aluminum phosphate, followed by pH adjustment to 5.5 – 6.5 and addition of Tetanus toxoid and blending by agitation at room temperature for 18 – 24 hours;

c. adding the above mixtures obtained in step a and step b, followed by pH adjustment to 6.4 – 6.6 and agitation at room temperature for 60 minutes;

d. adding wP antigen and a stabilizer to the above mixture, followed by agitation for 60 minutes and left in static condition for overnight at 2 – 8 °C;

e. adding Hib PRP conjugate and 2-phenoxyethanol (2-PE) to the mixture obtained in step d at 2 – 8 °C, followed by pH adjustment to 6.4 – 6.6; and

f. adding NaCl and WFI (q.s.) to the mixture obtained in step e, followed by agitation for 2 hours.

31) A process of manufacturing a heptavalent combination vaccine as claimed in any one of claims 21 - 26, comprising the steps of:

a. adsorbing Sabin/Salk strain IPV bulk and IRV bulk individually on Aluminum hydroxide, followed by pH adjustment to 6.2 – 6.6;

b. adsorbing HBsAg on Aluminium phosphate, followed by pH adjustment to 6.0 – 6.5;

c. adsorbing Diphtheria toxoid on Aluminum phosphate, followed by pH adjustment to 5.5 – 6.5 and addition of Tetanus toxoid;

d. blending mixtures obtained in step b and c, by agitation at room temperature for 18-24 hours;

e. adding the above mixtures obtained in step a and d, followed by pH adjustment to 6.4 – 6.6 and agitation at room temperature for 60 minutes;

f. adding wP antigen and stabilizer to the above mixture, followed by agitation for 60 minutes and left in static condition for overnight at 2 – 8 °C;

g. adding Hib PRP conjugate and 2-phenoxyethanol (2-PE) to the mixture obtained in step d at 2 – 8 °C, followed by pH adjustment to 6.4 – 6.6; and

h. adding NaCl and WFI (q.s.) to the mixture obtained in step e, followed by agitation for 2 hours.