The said excipients and stabilizers are selected from- (a) sugars such as maltodextrin, sucrose, lactose, sorbitol, mannitol and trehalose; (b) divalent metal ions structural stabilizers such as Zn (II) and Ca (II); (c) buffering agents such as 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid (HEPES), Tris, Phosphate or Histidine; (d) salts such as Sodium Chloride (NaCl); (e) bulking agents such as low particle size Sugar spheres, Maltodextrin, Sorbitol, Mannitol, Dextran or Lactose; (f) activating agents such as Arginine, Glutamic acid, sodium glutamate; (g) dispersants such as Tween® 20 and Tween® 80; and (h) surfactants such as sodium dodecyl sulfate (SDS), Poly ethylene glycol (PEG) 400, PEG-300, PEG-400 and PEG-600, Pluronic® 68, and F127. In a preferred embodiment, said formulation of spray dried vaccine is formed using the liquid vaccine feed comprising: rotavirus serotype, 1 % to 15 % (w/v) either sucrose or trehalose or combinations thereof; 10 mM to 100 mM pH buffering component(s) or combinations thereof at a pH ranging from 6.0 to 8.0; 0.001 % to 0.08 % surfactants, 0.1 mM to 5mM of a divalent cation, and 0.5 % to 10 % bulking agent.

The rotavirus vaccine formulation of the present invention comprises of at least one rotavirus serotypes in the range of 8.18×10^6 to 2.0×10^6 per dose administered, said at least one excipient in the range of 1% to 15% (w/v), said at least one buffering agent in the range of 10 mM to 100 mM, said at least one surfactant in the range of 0.001% to 0.08 % and pH of 6 - 8.

The excipients and stabilizers, especially the buffering agents, are chosen to allow maximum solubility to the divalent ions, such as Zn (II) and Ca (II), which are principally required for maximum process stability and also

We claim:

1. An improved thermostable spray dried rotavirus vaccine formulation wherein said vaccine formulation comprises of :
   - at least one rotavirus serotype;
   - at least one excipient being selected from a sugar, a buffering agent, a structural stabilizer, a salt, a bulking agent, an activating agent, a detergent, a surfactant, an antacid, a blending agent, either alone or in combination.

2. The improved thermostable spray dried rotavirus vaccine formulation as claimed in claim 1 wherein said rotavirus serotype is selected from at least one rotavirus strains being selected from bovine, rhesus, human, ovine, rhesus/human reassortants, or bovine/human reassortants.

3. The improved thermostable spray dried rotavirus vaccine formulation as claimed in claim 1 wherein said rotavirus serotype is selected from the human-bovine rotavirus ressortants serotypes G1, G2, G3, G4, and P1 either alone or in combination.

4. The improved thermostable spray dried rotavirus vaccine formulation as claimed in claim 1 wherein
   - said sugar is selected from maltodextrin, sucrose, lactose, sorbitol, mannitol and trehalose;
   - said buffering agent is selected from HEPES, Tris, Phosphate or Histidine;
   - said structural stabilizer is divalent metal ions being selected from Zn (II) and Ca (II);
   - said salt is Sodium Chloride (NaCl);

- said bulking agent is selected from low particle size sugar spheres, maltodextrin, sorbitol, mannitol, dextran or lactose;
- said activating agent is selected from arginine, glutamic acid, sodium glutamate;
- said detergent is selected from dispersants being selected from Tween® 20 and Tween® 80;
- said surfactant is selected from sodium dodecyl sulfate (SDS), Poly ethylene glycol (PEG) 400, PEG-300, PEG-400 and PEG-600, Pluronic® 68, and F127;
- said antacid with predetermined acid neutralizing capacity is selected from HEPES, citrate, histidine, calcium carbonate, sodium carbonate, potassium carbonate, sodium bicarbonate, calcium bicarbonate, potassium bicarbonate, aluminium hydroxide, magnesium hydroxide;
- said blending agent are sugars and sugar alcohols selected from cyclodextrin, maltodextrin, dextrose, glucose, mannitol, starch, sorbitol, maltitol, xylitol and lactose, either alone or in combination with said antacid.

5. The improved thermostable spray dried rotavirus vaccine formulation as claimed in claim 4 wherein said acid neutralizing capacity is in the range of 0.4 to 0.5 meq / dose.
6. The improved thermostable spray dried rotavirus vaccine formulation as claimed in claim 1 wherein said formulation comprises of at least one rotavirus serotypes in the range of 2.0 x 10^6 to 8.18 x 10^6 IU/ml per dose administered, said at least one excipient in the range of 1% to 15% (w/v), said at least one buffering agent

in the range of 10 mM to 100 mM, said at least one surfactant in the range of 0.001% to 0.08 % v/v and pH of 6 - 8.

7. The improved thermostable spray dried rotavirus vaccine formulation as claimed in claim 4, wherein said formulation preferably comprises of :
   - said sugar is Trehalose or sucrose or combination thereof;
   - said buffering agent is HEPES or Histidine or combination thereof;
   - said divalent cation is $Ca^{+2;}$
   - said salt is Sodium Chloride (NaCl);
   - said bulking agent is maltodextrin ;
   - said activating agent is Glutamic acid;
   - said dispersant is Tween® 20;
   - said blending agent is Maltodextrin with dextrose.

8. The improved thermostable spray dried rotavirus vaccine formulation as claimed in claim 1 wherein said vaccine formulation comprises of the following in the range of :

Ingredients	**%**
rotavirus serotypes titre	1×10^4 IU/mL to 1×10^9 IU/mL
sugar	1% to 15% (w/v)
buffering agent	10mM to 100 mM
divalent metal ions	0.1 mM to 5 mM
salt	0 % to 0.88 % w/v
bulking agent	0.5% to 10 % w/v
activating agents	0% to 0.131 % (w/v)
dispersants	0% to 0.02%w/v
surfactant	0.001% to 0.08% v/v

blending agent 0-90% w/w

9. The improved thermostable spray dried rotavirus vaccine formulation as claimed in claim 1 wherein optimum value of said rotavirus serotypes titre is 0.818 x 10^7 IU/mL in 1 X dose and 8.18 x 10^7 IU/mL in 10 X dose.

10. The improved thermostable spray dried rotavirus vaccine formulation as claimed in claim 1 wherein said thermostable spray dried rotavirus vaccine formulation manifests potency loss not exceeding Log_{10} = [0.5] for at least 24 months.

11. The improved thermostable spray dried rotavirus vaccine formulation as claimed in claim 1 wherein said vaccine formulation is powder or granule based formulation.

12. A process of preparing improved thermostable spray dried rotavirus vaccine formulation as claimed in claim 1, said process comprising the steps of:

(a) selecting said at least one rotavirus serotype;

(b) adding said at least one excipient to said selected rotavirus serotype of step (a) to prepare a liquid feed with optimal potency retention;

(c) spray drying of said liquid feed of step (b) in a spray dryer with two fluid nozzle using an atomization gas at predetermined process parameters to obtain a spray dried rotavirus vaccine formulation;

(d) blending of said spray dried rotavirus vaccine formulation of step (c) with said at least one blending agent to obtain a rapid

dispersible form of said spray dried rotavirus vaccine formulation;

(e) reconstituting said spray dried rotavirus vaccine formulation obtained in step (d) with an aqueous diluent to obtain liquid rotavirus vaccine ready for administration;

wherein

- said spray dried rotavirus vaccine formulation comprises of rotavirus strains in monovalent or multivalent rotavirus serotypes mixtures,
- said spray dried rotavirus vaccine formulation is reconstituted immediately prior to administration,
- said reconstituted vaccine formulation is to be administered orally.

13. The process of preparing improved thermostable spray dried rotavirus vaccine formulation as claimed in claim 12 wherein said process parameters and their operational range comprises

Process parameters	**operational range**
Inlet temperature	0 to 200 ^{0}C
Outlet temperature	35^{0}C to 60 ^{0}C
Aspirator	65 to 80 %
Feed rate	0.3mL/min to 10 mL/min
Spray gas flow	25 Nm^3/hr to 35 Nm^3/hr
Atomization pressure	4 bar to 7 bar
Nozzle orifice diameter	0.7mm to 1.2 mm
Feed solids	10% g/mL to 25 % g/mL

14. The process of preparing improved thermostable spray dried rotavirus vaccine formulation as claimed in claim 12 wherein said process parameters and their optimum range comprises

Process parameters	optimum range
Inlet temperature	70^{0}C to 75 ^{0}C
Outlet temperature	43 ^{0}C to 48 ^{0}C
Aspirator	70% to 75 %
Feed rate	0.4 mL/min
Spray gas flow	30 Nm^3/hr
Atomization pressure	5 bar
Nozzle orifice diameter	1 mm
Feed solids	21 % g/mL.

15. The process of preparing improved thermostable spray dried rotavirus vaccine formulation as claimed in claim 12 wherein said atomization gas being selected from Nitrogen, Argon, Carbon dioxide or atmospheric air or combinations thereof, with purity of not less than 95% v/v and moisture content not more than 2% w/w.

16. The process of preparing improved thermostable spray dried rotavirus vaccine formulation as claimed in claim 12 wherein said blending is being carried out with said blending agent either alone or in combination with said antacid in a manner wherein
    - said blending agent individually or in combination with said antacid confers Tg of not less than 50 °C,
    - said antacid in acid neutralizing capacity in the range of 2.0 mEq/g to 5.0 mEq/g of powder.

17. The process of preparing improved thermostable spray dried rotavirus vaccine formulation as claimed in claim 12 wherein said vaccine formulation is stable for 24 hours after reconstitution.

18. The improved thermostable spray dried rotavirus vaccine formulation as claimed in claim 1 wherein said thermostable spray dried rotavirus vaccine maintains potency with potency loss of less than Log_{10}=[0.5] for 4 weeks at 37^{0}C and for 24 months at 2°C to 8°C.

19. The improved thermostable spray dried rotavirus vaccine formulation as claimed in claim 1 wherein said thermostable spray dried rotavirus vaccine maintains potency with potency loss of less than Log_{10} = [0.5] for 24 weeks at 37^{0}C and for 24 months at 2 °C to 8°C.

20. The improved thermostable spray dried rotavirus vaccine formulation as claimed in claim 1 wherein said thermostable spray dried rotavirus vaccine maintains potency with potency loss of less than Log_{10} = [0.5] for 4 weeks at 45 ^{o}C, 24 weeks at 37 ^{o}C and for 24 months at 2 °C to 8 °C.