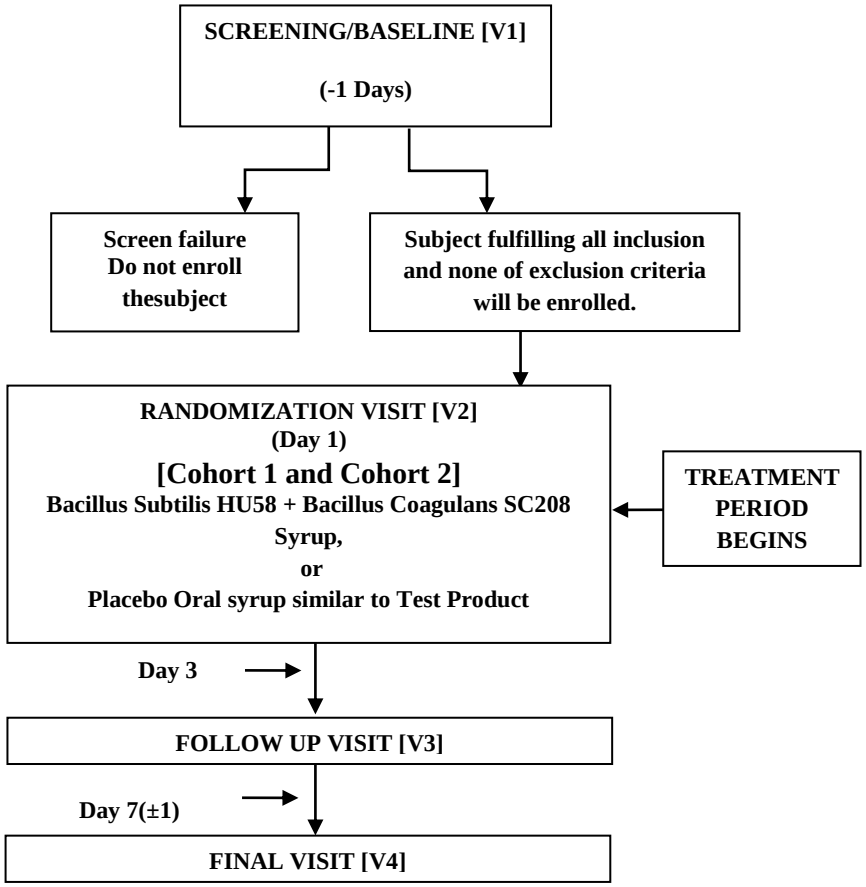
SCIENTIFIC TITLE	A Multicentre, Randomized, Double Blind, Parallel Group, Placebo Controlled Clinical Trial to Evaluate Efficacy and Safety of *Bacillus subtilis* HU58 + *Bacillus coagulans* SC208 Syrup in Treatment of Acute Diarrhoea in Children.
TEST PRODUCT	*Bacillus subtilis* HU58 + *Bacillus coagulans* SC208 Syrup
REFERENCE PRODUCT	• Placebo syrup
ARM	• Arm A- *Bacillus subtilis* HU58 + *Bacillus coagulans* SC208 Syrup • Arm B- Placebo syrup
DOSE	Each subject will receive 5 ml once a day by oral route of either test product or Placebo Syrup for a period of 7 days.
SPONSOR	**Synergia Life Sciences, Pvt. Ltd.,** Universal Majestic, 1503, PL Lokhande Marg, Chembur, Mumbai, Maharashtra 400071, India.
CRO Name	**Biosphere Clinical Research Pvt. Ltd.,** Office No. 02, 03 & 04, Second Floor, Highland Corporate Center, Kapurbawdi Junction, Thane (W) 400 607, Maharashtra, India
PROTOCOL ID/NO.	BCR-SYN-001
VERSION/DATE	V1.0/23 Aug 2021
INDICATION	Acute diarrhoea in Children.
OBJECTIVES	**Primary objective:** • To evaluate the efficacy of *Bacillus subtilis* HU58 + *Bacillus coagulans* SC208 Syrup in treatment of Acute diarrhoea in Children. **Secondary objectives:** • To evaluate the safety of *Bacillus subtilis* HU58 + *Bacillus coagulans* SC208 Syrup in treatment of Acute diarrhoea in Children.

STUDYSCHEDULE	A Multicentre, Randomized, Double Blind, Parallel Group, Placebo Controlled Clinical Trial to Evaluate Efficacy and Safety of *Bacillus subtilis* HU58 + *Bacillus coagulans* SC208 Syrup in Treatment of Acute Diarrhoea in Children. The schedule of the subject's visit at study site will be as follows: a. Visit 1 - Screening visit/Baseline visit (-1 Days) b. Visit 2 - Randomization visit (Day 1) c. Visit 3 - Follow Up visit Day 3 d. Visit 4 - Follow Up visit/End of study visit Day 7±1
INCLUSION CRITERIA	To be eligible for the study, Subjects must meet the following criteria: 1. Male or Female subjects between ≥1 to ≤ 12years of age both inclusive. 2. The investigator believes that the parent(s) or Legally Acceptable Representative(s) (LAR(s)) of the child will comply with the requirements of the protocol. 3. Written informed consent /assent obtained from the subject and parent(s)/LAR(s) of the subject for participation in the study. **Cohort 1:** 1. Subjects undergoing treatment with antibiotics irrespective of indication and the type of antibiotics. 2. Subject suffering from Antibiotic associated diarrhoea defined as passage of three or more liquid or watery stools occurring in a 24-hour period. **Cohort 2:** 1. Subject with confirmed diagnosis of acute infective diarrhoea defined as passage of three or more liquid or watery stools occurring in a 24-hour period and lasting for less than three days).
EXCLUSION CRITERIA	Subjects will be excluded if ANY of the following conditions apply: 1. History of pre-existing diarrhoea within the previous 4 weeks. 2. Subjects requiring hospitalisation. 3. Subjects with Severe dehydration requiring intravenous rehydration. 4. Subjects with bloody and/or purulent stools 5. Subjects with symptoms or suspicion of an organic lesion of the digestive tract, or with undiagnosed abdominal pain or rectal bleeding or other GI disorder especially ulcerative colitis, Crohn's disease, history of carcinomas of the bowel, malabsorption syndrome, intolerance to certain food types (lactose), functional diarrhoea and functional constipation. 6. Subjects with gastrointestinal surgery. 7. History of severe chronic systemic diseases, critical/life-threatening illness or immunodeficiency diseases. 8. Known hypersensitivity to any of the ingredients in the probiotic product or

	the placebo. 9. Use of proton-pump inhibitors, laxatives or anti-diarrhoeal drugs, as well as use of a probiotic 14 days before and during the study 10. Participation in another clinical study within 30 days before the beginning or anytime during the duration of the current clinical study. 11. Any other condition which, in the opinion of the Investigator, prevents the child from participating in the study.
RANDOMIZATION	The subjects would be assigned to Arm A and Arm B in the ratio of 1:1
DISCONTINUATION CRITERIA	1. Subjects at their own request voluntarily or at the request of their legally acceptable representative can be withdrawn from the study. 2. The subject experiences serious adverse effects and withdrawal would be in the best interest of the subject. 3. If at any point of the study subject is found to be non-compliant with the study protocol. 4. Any other criteria as per the investigator that does not justify continuation of the subject in the study.
PROHIBITED MEDICATIONS	Any Probiotic or Prebiotic containing formulations
CONCOMITANT MEDICATIONS	Oral rehydration therapy as per the requirement will be permitted during the study as per the PI discretion.
STUDY DESIGN	

	After obtaining consent, the screening period will be for -1 days. After Randomization, the drug treatment will be for 7days
EVALUATION VARIABLES	**EVALUATION PARAMETERS:** **Primary End Point:** • Stool consistency (as assessed by Bristol Stool Scale (BSS)[including 7 types as follows: type 1 to 2 indicates constipation; type 3 to 5 suggests normal stools; and type 6 to 7 means liquid stool] • Duration of diarrhoea in days (time between the start of treatment until last diarrheal/watery stool before recovery or end of study treatment). **Secondary End Point:** • Abdominal pain intensity (as measured by visual analogue scale (VAS). **Safety End Point:** • The assessment of safety of Investigational Product will be based on the frequency of Adverse Events and changes in laboratory values. All safety variables will be summarized using descriptive statistics.
SAMPLE SIZE	Total 64 randomized subjects will be considered for the study (32 subjects each in each cohort). The subjects would be assigned to Arm A or Arm B in the ratio of 1:1 (16:16 subjects per Arm) for both the cohorts.

Study Schedule:

Study procedures	Screening/ Baseline	Randomization	Follow-up	Follow-up/End of study
	V1	V2	V3	V4
	-1 Days	Day 1	Day 3	Day 7 (±1)
ICF/Assent Signing	X	-	-	-
Inclusion/Exclusion Criteria	X	X	-	-
Randomization	-	X	-	-
Demographics	X	-	-	-
Medical History	X	-	-	-
Vitals (Pulse, RR, Temp.)	X	X	X	X
Physical Examination	X	X	X	X
Laboratory Test (CBC)	X	-	-	X
Bristol Stool Scale (BSS)	X	X	X	X
VAS Scale Assessment	X	X	X	X
Drug Dispensing	-	X	X	-
Drug Accountability	-	-	X	X
Drug Dosing Card Dispensing	-	X	-	-
Drug Dosing Card Accountability for Compliance	-	-	X	X
AE	X	X	X	X
Concomitant Medication	X	X	X	X
Assessment of Efficacy	-	-	X	X
Assessment of Safety	-	X	X	X