PHARMACOVIGILANCE AND CLINICAL TRIALS DIVISION

CLINICAL TRIAL APPLICATION PUBLIC ASSESSEMENT REPORT

PART 1: ADMINSTRATIVE DETAILS

Title of Study and Protocol Version: A Phase 3, randomized, double-blind, placebo-controlled trial to evaluate the effect of *Bifidobacterium longum subsp. infantis* DSM33361 (Bifin02) administered together with *Lacticaseibacillus rhamnosus* GG DSM33156 (LGG®) versus placebo on weight gain in underweight infants, Version 1.0 dated 18 June 2025	**Study Ref:** MCAZ Ref: CT286/2025
Date of receipt of the application: 12 May 2025	
Clinical trial Phase: Phase 3	
Study Site(s): Mutala Trust, 52 Alpes Road Vainona, Harare, Zimbabwe	
Applicant/Principal Investigator name and address: Professor Chiratidzo Ellen Ndhlovu 52 Alpes Road Vainona, Harare, Zimbabwe	
Sponsor name and address: Africa Clinical Research Network (ACRN) C1-402, 4th Floor, Block C, Grand Baie La Croisette, Grand Baie, Mauritius	
Study duration: 43 months	
Date of Commencement (Expected or Actual):	
Clinical trial authorisation validity period: 15 October 2025 to 31 March 2029	

PART 2: SUMMARY OF EVALUATION
Study design:

This is a Phase 3, randomized, double-blind, placebo-controlled trial to evaluate increased weight gain with, and safety of, co-administration of Bifin02 and LGG®, versus placebo in underweight infants ($-4.5 \leq WAZ < -2.0$) recently discharged from the hospital following acute non-surgical illness. Eligible participants between 30 and 120 days of age will be randomized at or after hospital discharge to receive daily supplements of Bifin02 and LGG®, or placebo for 28 days with a total trial duration of approximately 90 days.

Population:
100 participants will be recruited from Zimbabwe, an additional 100 participants will be recruited from Kenya. This brings the total sample size to 200 participants.

Study Objectives:
Primary objectives:

1. To evaluate the change in weight standardized for age

Key Secondary Objectives:

1. To evaluate the change in weight of infants receiving Bifin02 and LGG® vs placebo

Other Secondary Objectives:

1. To estimate the group response over time associated with Bifin02 and LGG® vs placebo.
2. To assess the proportion of infants who achieve a specified change in WAZ from baseline to Day 56 in infants receiving Bifin02 and LGG® vs placebo.
3. To assess the proportion of infants who achieve a specified WAZ at Day 56 in infants receiving Bifin02 and LGG® vs placebo.
4. To assess the re-hospitalization rate of infants receiving Bifin02 and LGG® vs placebo
5. To assess the safety of the intervention through End of Trial (EoT, Day 90 visit)
6. To measure engraftment in participants
7. To assess the cost-effectiveness of Bifin02 and LGG® supplementation compared to standard care.
8. To evaluate the budget impact of adopting probiotic supplementation within the healthcare system
9. To analyse the long-term economic benefits of improved weight gain and health outcomes in underweight infants.
10. To assess the equity and access implications of implementing probiotic supplementation.

Exploratory Objectives:

1. To describe stool biomarkers in response to the intervention in terms of stool composition (e.g., microbiome)
2. To describe the blood biomarkers (e.g., inflammation, metabolomics), in response to the intervention
3. To assess whether baseline nutritional status (WAZ) or baseline *B. infantis* abundance modifies the effect of Bifin02 and LGG® compared to placebo on WAZ change through Day 56 and Day 90.

Eligibility Criteria:

Inclusion Criteria

1. Participant must be between 30 days and 120 days of age (inclusive), at the time of randomization (Day 1)
2. Hospitalized for acute nonsurgical illness at screening or history of hospitalization for acute nonsurgical illness within 60 days prior to randomization
3. Completed fluid rehydration, pedal oedema (if present) has resolved, discharged from hospital, and no longer receiving antibiotics prior to randomization (Day 1)
4. WAZ at randomization (Day 1) is greater than or equal to negative 4.5 and less than negative 2.0 ($-4.5 \leq WAZ < -2.0$)
5. Any Sex
6. Participant's parent(s)/legally acceptable representative (LAR) is capable of giving informed consent which includes agreement to comply with the requirements and restrictions listed in the informed consent form (ICF) and in this protocol
7. Participant's parent(s)/LAR agrees to stay in contact with the trial site for the duration of the trial, provide updated contact information as necessary, and have no current plans to relocate from the trial area for the duration of the trial.
8. Participant's parent(s)/LAR is reliably able to store the investigational product under refrigerated conditions.
9. Participant receives some feedings from breastmilk and mother intends to continue breast-feeding.

Exclusion Criteria

1. Congenital condition (suspected or confirmed) that the Investigator considers likely to interfere with feeding or with normal growth and development.
2. Infant has not been discharged from hospital since birth or has not been at home for at least one week since birth.
3. Infant hospitalized with septic shock during current hospitalization.
4. Infant required invasive mechanical ventilation during current hospitalization.
5. Infant with acute kidney injury on hospital admission
6. Infant with severe jaundice or suspected kernicterus
7. Infant with short bowel syndrome
8. Infant receiving treatment for suspected or confirmed HIV infection
9. Infants with suspected or confirmed TB infection at the time of screening or enrolment, regardless of treatment status
10. Ongoing or planned infant antibiotic (e.g., as prophylaxis in sickle cell disease) and/or probiotic usage
11. Ongoing or planned maternal antibiotic and/or probiotic usage for breast-feeding infants
12. Inability of participant's parent(s)/LAR to comply with protocol requirements, as per Investigator assessment
13. Concurrent or planned participation in another clinical trial.
14. Infants who are part of a twin pair, where the other twin is also eligible for enrolment, will be excluded to prevent cross-contamination arising from shared living environments, feeding practices, physical contact, or caregiver-administered probiotics.
15. Participants whose primary residence is located at a distance that would impede the study team's ability to conduct required home visits and follow-up assessments, as determined by the research team, will be excluded from the study.

Vulnerable Populations:

Children aged between 30 to 120 days will be enrolled. Only participants for whom informed consent/assent has been provided will be enrolled. Justification for conducting the study in the vulnerable population was acceptable.

Informed Consent, Decision-making & Confidentiality
Shona and English Informed Consent Forms were provided which were satisfactory. Adequate proof of participant insurance was provided.

Scientific and Technical Issues
The study design was found to be scientifically sound, the justification for the study was acceptable and follow up procedures were satisfactory. All the scientific and technical aspects were satisfactory.

Other materials, documents and study instruments (Patient recruitment materials, Questionnaires)
Recruitment materials, and questionnaires were satisfactory.

Clinical Trials/Study Medicines

1. Bifin02 Sachets
2. LGG® Sachet
3. Placebo for Bifin02 and for LGG®

Manufacturer of study medicines: CHR. HANSEN A/S, Denmark

The justification for the study products was acceptable.

Summary of review of:

1. Quality
2. Safety
3. Efficacy

Quality, safety, efficacy and benefit risk analysis data were assessed and were satisfactory.

Application Review Process
The application was reviewed under the normal pathway.

Status after review:
The clinical trial was authorised on the 15 October 2025.

PART 3: OVERALL COMMENTS AND CONCLUSION:

The Principal Investigator (PI) was required to address queries raised by the MCAZ Pharmacovigilance and Clinical Trials Committee after initial review, second review cycle and third review cycle of the application. The PI responded and addressed all the queries. The PI was subsequently authorised, with the approval of the Secretary for Health and Child Care, to conduct the trial subject to the contents of the application and the following conditions:

1. Reporting of all adverse events to MCAZ;
2. Submission of all amendments to the protocol for approval by MCAZ;
3. Submission of a progress report of the clinical trial by the 31st of January annually;

4. Submission of the final report and copy of any publication of the clinical trial prior to publication of results;
5. In compliance with the current Good Clinical Practices (cGCP) and all other relevant MCAZ guidelines;
6. Submission of the completed indemnity form for conducting clinical trials to the Director-General prior to commencement of the clinical trial;
7. Publication of summarised public assessment report for the clinical trial application and public inspection report for GCP inspections on the MCAZ website and/or Clinical Trials Registry platform by MCAZ;
8. Listing of the clinical trial on the MCAZ public Clinical Trials Registry;
9. Expiry date of this authorisation 31 March 2029.

Name of Evaluator: Tracey Matambo Signature:  Date: 29/10/2025

Name of 2nd Evaluator: Tatenda Nyamandi Signature:  Date: 11/11/2025