SYNOPSIS AND TRIAL ABSTRACT

Name of Company: Alimentary Health Ltd. **Name of Active Substance(s):** ***Bifidobacterium Longum 1206***		(For National Authority Use only)
Title: A double-blind, randomised, placebo-controlled trial to establish the safety of a probiotic in subjects with Irritable Bowel Syndrome {IBS}		
Investigator: Professor Eamonn MM Quigley MD,FRCP,FACP,FACG Professor of Medicine and Human Physiology, Department of Medicine, CUH, Cork,		
Study centre: Alimentary Health Ltd, Clinical Trials Unit. Suite 2.6, Consultants Private Clinic, Bishopstown Road, Wilton, Cork, Ireland.		
Publication (reference): Not applicable		
Study period: Study commenced :5th July 2010 Study ended: July 2012	**Clinical Phase**: Phase 11	
Objectives of the study: The objective of this study is to determine the safety and efficacy profile of a probiotic in patients with Irritable Bowel Syndrome (IBS).		
Number of subjects (planned and analysed): Approximately 400 subjects will be screened to complete a target of 76 evaluable subjects for efficacy analysis. **Disposition**: 99 IBS subjects were screened for entry into the study of which 56 were enrolled. Of the 56 randomized, 27 completed the study. 12 of the subjects were from the AH1206 group and 15 subjects from the placebo group, see Table 7-1.		
Diagnosis and main criteria for inclusion: Females 18 to 65 years of age, who meet inclusion/exclusion criteria and have symptoms of IBS consistent with the Rome III Diagnostic Criteria, will be enrolled into the Run-in Phase. To be eligible for the Treatment Phase, subjects must meet the following criteria based on symptom data collected electronically from the last week (7 days) of the run-in phase: 1) complete at least 5 days of symptom data; 2) record at least 1 bowel movement; 3) have an		

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average abdominal pain/discomfort score ≥1 and ≤4; and 4) have an average Bristol Stool Form score >2 and <7.

Test product and dose, *Bifidobacterium longum 1206* in a 1 gram aluminium sachets[23x 90mm],packaged under GMP conditions contains 1 gram of white, free flowing, soluble powder. The active medicinal sachets contain approx. 333 mg b. longum freeze –dried powder blended with a standard excipient {Maltodextrin}.Active sachets contain approx. 1 x 10{^{9}}Colony forming units{CFU}.Placebo sticks contains standard excipient { Maltodextrin} only.

Duration of treatments:
Once daily for 8 weeks (56 days).

Criteria for evaluation:
The objective of this study was to investigate the safety and efficacy profile of a probiotic, in subjects with Irritable Bowel Syndrome (IBS).
However, due to insufficient subject numbers in the trial the efficacy profile (leading to primary and secondary endpoints) was not analyzed. The SAP was updated 16 July 2014.

Statistical methods: All statistical analyses were carried out using SPSS Version 22 for Windows. Results of analyses are presented in this report as in-text tables of hypothesis test results, estimates of treatment differences and associated confidence intervals. All statistically significant results are supported with the strength of the result (effect size, Table 7-30) and the power of the result (carried out using G*Power}

SUMMARY CONCLUSIONS:
Safety:

In relation to the reported adverse events:

- The majority of moderate adverse events were in the AH1206 group, while the majority of moderate adverse events were from the placebo group (p = 0.003);
- No adverse event was classified as probably or definitely related to the study. 63.9% of adverse events were either unrelated or unlikely to be related to the study (based on both subject groups);
- A statistically insignificant relationship was found between the type of action taken towards an adverse event and the treatment, p = 0.216;

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- The majority of adverse events were transient and the subject recovered fully (p = 0.950);
- No subject in the study suffered from a serious adverse event.

In relation to laboratory data:

- There was no statistical change in the either biochemistry and haematology blood results between Visits 01 and 04.

In relation to the physical exam:

- There was no statistical change in the vital signs (heart rate, blood pressure, temperature) checked between the physical exams performed at Visits 01 and 05.

In relation to the product

- Both the *Bifidobacterium longum 1206* and the placebo were well tolerated.

Date of the report: 16th April 2016