Attachment 1.
(FACE SHEET)

Date 04.10.1998

ETHICAL REVIEW COMMITTEE, ICDDR,B.

Principal Investigator Dr. N.H. Alam

Trainee Investigator (if any) _____

Application No. 98-023

Supporting Agency (if Non-ICDDR,B) _____

Title of Study Evaluation of a dietary treatment algorithm as a home-based ~~management of children with persistent~~ diarrhoea: a community base study

Project status:
(✓) New Study
( ) Continuation with change
( ) No change (do not fill out rest of form)

Circle the appropriate answer to each of the following (If Not Applicable write NA).

1. Source of Population:
   (a) Ill subjects (Yes) No
   (b) Non-ill subjects Yes No
   (c) Minors or persons under guardianship (Yes) No
2. Does the study involve:
   (a) Physical risks to the subjects Yes (No)
   (b) Social Risks Yes (No)
   (c) Psychological risks to subjects Yes (No)
   (d) Discomfort to subjects Yes (No)
   (e) Invasion of privacy Yes (No)
   (f) Disclosure of information damaging to subject or others Yes (No)
3. Does the study involve:
   (a) Use of records, (hospital, medical, death, birth or other) (Yes) No
   (b) Use of fetal tissue or abortus Yes (No)
   (c) Use of organs or body fluids (Yes) No
4. Are subjects clearly informed about:
   (a) Nature and purposes of study (Yes) No
   (b) Procedures to be followed including alternatives used (Yes) No
   (c) Physical risks (Yes) No
   (d) Sensitive questions (Yes) No
   (e) Benefits to be derived (Yes) No
   (f) Right to refuse to participate or to withdraw from study (Yes) No
   (g) Confidential handling of data (Yes) No
   (h) Compensation &/or treatment where there are risks or privacy is involved in any particular procedure NA Yes No
5. Will signed consent form be required:
   (a) From subjects Yes No
   (b) From parent or guardian (if subjects are minors) (Yes) No
6. Will precautions be taken to protect anonymity of subjects (Yes) No
7. Check documents being submitted herewith to Committee:
   ___ Umbrella proposal - Initially submit an overview (all other requirements will be submitted with individual studies).
   ✓ Protocol (Required)
   ✓ Abstract Summary (Required)
   ✓ Statement given or read to subjects on nature of study, risks, types of questions to be asked, and right to refuse to participate or withdraw (Required)
   ___ Informed consent form for subjects
   ✓ Informed consent form for parent or guardian
   ✓ Procedure for maintaining confidentiality
   ___ Questionnaire or interview schedule *

* If the final instrument is not completed prior to review, the following information should be included in the abstract summary:
1. A description of the areas to be covered in the questionnaire or interview which could be considered either sensitive or which would constitute an invasion of privacy.
2. Examples of the type of specific questions to be asked in the sensitive areas.
3. An indication as to when the questionnaire will be presented to the Cttee. for review.

We agree to obtain approval of the Ethical Review Committee for any changes involving the rights and welfare of subjects before making such change.

Principal Investigator

Trainee

International Centre for Diarrhoeal Disease Research, Bangladesh

RESEARCH PROTOCOL

FOR OFFICE USE ONLY
Protocol No: 98-023 Date: 04/10/98
RRC Approval: Yes/ No Date:
ERC Approval: Yes/No Date:

1. Title of Project (Do not exceed 60 characters including spaces and punctuations)
Evaluation of a dietary treatment algorithm as a home-based management of children with persistent diarrhoea: a community based study

2a. Name of the Principal Investigator(s) (Last, Middle, First)	2b. Position / Title	2c. Qualifications
Alam, Nur Haque	Sr. Medical Officer GR I	MBBS, MD

3. Name of the Division/ Branch / Programme of ICDDR,B under which the study will be carried out.
Clinical Sciences Division

4. Contact Address of the Principal Investigator	4a. Office Location: ICDDR, B, Mohakhali, Dhaka 1212 4b. Fax No: 880-2-9885657 4c. E-mail: nhalam@icddrb.org 4d. Phone / Ext: 2311

Use of Human Subjects	5a. Use of Live Animal	5b. If Yes, Specify Animal Species
☑ Yes	☐ Yes	
☐ No	☑ No	

5. Dates of Proposed Period of Support *(Day, Month, Year - DD/MM/YY)*	7. Cost Required for the Budget Period
	7a. Ist Yr ($): 24,905 *2nd Yr ($): 24,906* *3rd Yr ($):*
	7b. Direct Cost ($): 49,811 Total Cost ($):

8. Approval of the Project by the Division Director of the Applicant
The above-mentioned project has been discussed and reviewed at the Division level as well by the external reviewers. The protocol has been revised according to the reviewer's comments and is approved.

Dr. M.A. Salam
Name of the Division Director

Signature

4-10-98
Date of Approval

Certification by the Principal Investigator

I certify that the statements herein are true, complete and accurate to the best of my knowledge. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. I agree to accept responsibility for the scientific conduct of the project and to provide the required progress reports if a grant is awarded as a result of this application.

10. Signature of PI

Date: 4-10-98

Table of Contents

☑ Check here if appendix is included

PROJECT SUMMARY: Describe in concise terms, the hypothesis, objectives, and the relevant background of the project. Describe concisely the experimental design and research methods for achieving the objectives. This description will serve as a succinct and precise and accurate description of the proposed research is required. This summary must be understandable and interpretable when removed from the main application. (TYPE TEXT WITHIN THE SPACE PROVIDED).

Principal Investigator: Dr. N.H. Alam

Project Name: Evaluation of a dietary treatment algorithm as a home-based management of children with persistent diarrhoea: a community based study

Total Budget: US $49,811 Beginning Date Ending Date

Persistent diarrhoea continues to be an important cause of childhood morbidity and mortality in the developing countries. Improved case management might prevent mortality and morbidity due to this childhood illness. This study proposes to evaluate the feasibility and efficacy of a dietary treatment algorithm (shown efficacious in the hospital setting) as a home based management of children with non-severe persistent diarrhoea. This is a randomised, controlled, home-based intervention study. After examining the eligibility criteria the patients will be randomised to either intervention group (dietary treatment algorithm) or control (standard management). Patients in the intervention group, in addition to dietary manipulation, will receive oral rehydration therapy and vitamin-mineral supplementation. The initial diet (diet A) contains rice powder, cow's milk, and vegetable oil, and calorie content of 68 kcal/100 g. The diet B (containing rice powder, vegetable oil, egg white and sugar and calorie content 68 kcal/100 g) will be offered if there is no improvement of diarrhoea on day 7. Diet B will also be fed for 7 days. The patients under control group will receive standard management which include oral rehydration therapy and his/her usual diet or as adivsed by hospital physician, and also they will receive vitamin and minerals. 320 children aged 5 months to 36 months will be included in the study. After completion of the study the success rate with diet A, diet B and overall will be calculated and will be compared with that of the control group. The weight gain or loss of the patients of intervention group will also be compared with that of the control group. The factors related to treatment failure will also be analysed. This treatment alogorithm might help to establish a rationale and effective treatment of persistent diarrhoea at home.

KEY PERSONNEL (List names of all investigators including PI and their respective specialties)

Name	Professional Discipline/Specialty	Role in the Project
1. Dr. N.H. Alam	SMO Gr I/Gastroenterology	Principal Investigator
2. Dr. J.D. Hamadani	SMO Gr II/Paediatrics	Co-Investigator
3. Dr. A.S.G. Faruque	Scientist/Epidemiology	Co-Investigator
4. Dr. G.J. Fuchs	Interim Director/Paediatrician	Co-investigator

DESCRIPTION OF THE RESEARCH PROJECT

Hypothesis to be tested:

Concisely list in order, in the space provided, the hypothesis to be tested and the Specific Aims of the proposed study. Provide the scientific basis of the hypothesis, critically examining the observations leading to the formulation of the hypothesis.

Non-severe persistent diarrhoea patients can be treated at home using a simple dietary treatment algorithm.

Specific Aims:

Describe the specific aims of the proposed study. State the specific parameters, biological functions/ rates/ processes that will be assessed by specific methods (TYPE WITHIN LIMITS).

To evaluate the feasibility and efficacy of a dietary treatment algorithm as home based management of children with non-severe persistent diarrhoea.

Background of the Project including Preliminary Observations

Describe the relevant background of the proposed study. Discuss the previous related works on the subject by citing specific references. Describe logically how the present hypothesis is supported by the relevant background observations including any preliminary results that may be available. Critically analyze available knowledge in the field of the proposed study and discuss the questions and gaps in the knowledge that need to be fulfilled to achieve the proposed goals. Provide scientific validity of the hypothesis on the basis of background information. If there is no sufficient information on the subject, indicate the need to develop new knowledge. Also include the **significance and rationale** of the proposed work by specifically discussing how these accomplishments will bring benefit to human health in relation to biomedical, social, and environmental perspectives. (DO NOT EXCEED 5 PAGES, USE CONTINUATION SHEETS).

Diarrhoea continues to be a major cause of childhood morbidity and mortality worldwide. Persistent diarrhoea (PD), defined as episodes lasting for 14 days or more (1), accounts for only about ten percent of all diarrhoeal episodes but is associated with 30% to 50% of all diarrhoea related deaths (2-4).

Two major clinical categories of persistent diarrhoea can be distinguished (5):

- mild persistent diarrhoea with several daily loose stools but normal hydration status and which leads to growth faltering, more severe malnutrition and sometimes death due to diarrhoeal or nondiarrhoeal illness.
- severe persistent diarrhoea with dehydration and high purging rates (>7ml/kg/hour or very frequently large watery stools).

The pathogenesis of persistent diarrhoea is multifactorial with a wide spectrum of functional disturbances. Suggested mechanisms include in isolation or the combination of persistence of entero pathogens, bacterial overgrowth, continued mucosal injury, delayed mucosal repair, and host susceptibility (6). Delayed repair of mucosal injury and host susceptibility are strongly influenced by malnutrition which frequently precedes and occurs as a result of persistent diarrhoea (7). This

self perpetuating cycle can be broken only through appropriate nutritional rehabilitation. Depending upon the severity of the mucosal damage, changes occur in the digestive, secretory, absorptive and reabsorptive capacities of macro and micronutrients (8). One of the most important absorptive problem is energy malabsorption due to malabsorption of carbohydrate and fat (9). Lack of clear guidelines for effective therapy has contributed to widely practiced but ineffective regimes such as the routine administration of antibiotics and use of low caloric density diets (6). In consideration of the functional disturbances of the small intestine, modified diets have been used for the hospital-based management of persistent diarrhoea according to a dietary algorithm at ICDDR,B and other centres in Bangladesh with good results/success.(10,11). Ideally, these diets should be inexpensive, culturally acceptable, locally available and provide adequate calories. Recent data have indicated that cereal/legume based diets with oil can be successful in treating children with persistent diarrhoea (12,13).

The addition of milk products can enhance the protein quality and micronutrients content of these diets, although the amount of lactose which can be tolerated by these children is not precisely known. The use of a full milk diet (the equivalent of 6 g lactose/kg/day) has resulted in increased stool output in most children with persistent diarrhoea (14). Recent studies indicate that modest amounts of milk products can be tolerated as part of a mixed diet given to treat acute (15,16) and persistent diarrhoea (12). Although not all children improve on this therapy (12,13). Dietary intolerance (continued diarrhoea and/or poor weight gain) has been considered to be the most common cause for failure of these diets, but little exists to indicate which component or components of the diet is not tolerated. Providing a less complex form of carbohydrate by substituting monosaccharide (glucose) or disaccharide (sucrose) for at least some of the starch of a milk cereal diet might result in more effective therapy (17). Data from earlier studies indicate that chicken and egg protein are often well tolerated in children with diarrhoea (13,18) and can be used to replace milk protein. Fewer practical options are available for altering the nature of the fat component of the diet other than substituting vegetable fat for animal fat (19,20).

The International Working Group on Persistent Diarrhoea sponsored by the World Health Organisation and the Applied Diarrhoeal Disease Research Project (ADDR) evaluated a dietary treatment algorithm for use in developing countries. The overall success rate of the treatment algorithm was 80% (21). However, because this study was hospital-based, the study population was based with more severe cases. Although the children that are hospitalized represent as important group of children with PD, a large number of mild and moderate PD cases present to hospitals and clinics with mild or no sign of dehydration but who do not require hospitalisation. Moreover, if hospitalised, these children are at great risk to develop hospital-acquired infection (22). Yet, if these children do not receive appropriate nutritional therapy their diarrhoea may persist or worsen and accelerating their malnutrition with ultimately poor outcome. About 74% of patients presenting with persistent diarrhoea to ICDDR,B hospital are discharged from outpatient dept. (34%) and short-stay ward (39%) without proper nutritional advice (Surveillance data, 1993 to 1995). If a caregiver could use a dietary algorithm containing a simple, locally available diet as a *home-based* approach for the management of persistent diarrhoea, a great many children with PD would be expected to benefit. In addition the potential risk of nosocomial infection associated with hospitalization would be eliminated and the cost of patient care would be markedly reduced. We therefore, propose to evaluate the feasibility and efficacy of a home-based dietary treatment algorithm for the management of non-severe cases of persistent diarrhoea.

Significance

If this study demonstrates the feasibility and efficacy of the home-based nutritional management of persistent diarrhoea in children, then a substantial number of admissions to the hospital will be avoided, thereby reducing health care costs. Further it would also avoid the excess morbidity and mortality due to hospital-acquired infections associated with hospitalized based management of persistent diarrhoea patients. This approach will also help to formulate guidelines for the management of non-severe persistent diarrhoea as one of the components in the Integrated Management of Childhood Illness (IMCI).

Research Design and Methods

Describe in detail the methods and procedures that will be used to accomplish the objectives and specific aims of the project. Discuss the alternative methods that are available and justify the use of the method proposed in the study. Justify the scientific validity of the methodological approach (biomedical, social, or environmental) as an investigation tool to achieve the specific aims. Discuss the limitations and difficulties of the proposed procedures and sufficiently justify the use of them. Discuss the ethical issues related to biomedical and social research for employing special procedures, such as invasive procedures in sick children, use of isotopes or any other hazardous materials, or social questionnaires relating to individual privacy. Point out safety procedures to be observed for protection of individuals during any situations or materials that may be injurious to human health. The methodology section should be sufficiently descriptive to allow the reviewers to make valid and unambiguous assessment of the project. **(DO NOT EXCEED TEN PAGES, USE CONTINUATION SHEETS).**

Design: This is a randomized, controlled, home-based intervention study.

Patients selection: Children attending the out-patient department of ICDDR,B hospital will be considered for selection into the study.

Inclusion criteria:

a) Age 5 months to 36 months
b) Duration of diarrhoea > 14 days
c) Dehydration status-some or nil according to WHO criteria
d) Written informed consent obtained from parents or legal guardian
e) Accessible distance (within 15 km radius from ICDDR,B)

Exclusion criteria:

a) Signs of systemic illness or other severe illnesses requiring hospital-based care (sepsis, severe pneumonia, meningitis, severe hyponatraemia or hypokalaemia)
b) Severe malnutrition - wt/age <60% with or without edema.
c) Patients with severe dehydration
d) Bloody diarrhoea

Observation period:

All patients attending the outpatient department of ICDDR,B from 8 a.m. to 2 p.m. with history of persistent diarrhoea will be screened for eligibility for this study following the inclusion and exclusion criteria. The children who are eligible will initially be observed for 4 hours. A detaialed clinical history will be recorded, and physical examination including anthropometry will be done. Children with some dehydration will be rehydrated with WHO-ORS.

Stool microscopy (*Giardia, Cryptosporidia, E. histolytica*), Stool culture (vibrios, shigella, salmonella and campylobacter) and urine analysis will be done.

Randomization:

After examining the eligibility criteria and informed consent signed by one of the parents/legal guardian, the patients will be randomized to either intervention group (dietary treatment algorithm) or control (standard management). Two strata of randomization list will be prepared by using random table. One stratum will be used for randomization of patients 5 months to 18 months and other stratum 19-36 months. The randomization lists will be prepared and serially numbered in sealed envelopes will be supplied containing the name of the treatment group. The envelopes will be opened by one of the investigators only after a patient has been irrevocably assigned to the study.

Case management

Intervention group

Treatment algorithm:
We have chosen to adapt the WHO algorithm designed for hospitalized children. The components of the treatment algorithm are summarized in Fig. 1, (Adapted from ref. 21) During the observation period, the mothers or other caregivers of the children will be educated to prepare the diet (Table I) and will be advised to feed study Diet (A) containing milk and rice-cereal mixture initially for 7 days. House visits will be done on every alternate days for follow up. During follow-up on day-3, if any treatable stool pathogen was identified from specimen obtained on Day 1, antimicrobial therapy will be provided for administration at home. Any skin infection, mild respiratory tract infection or urinary tract infection will also be treated with antimicrobial orally at home. Patients with skin infection will be treated with cloxacillin 50 mg/kg/day in 4 divided doses. Mild respiratory tract infection will be treated with amoxicillin 100 mg/kg/day in 3 divided doses. Urinary tract infection will be treated according to the culture and sensitivity results. All requisite medicines will be provided to all study patients, and ingredients of diets will be supplied to the mothers of the patients of the intervention group only.

At home, care-givers will record on a diarrhoea diary the frequency of stool each 24 hours, the stool consistency and time of cessation of diarrhoea. (Definitions below). After 7 days if diarrhoea continues, caregivers will be trained to prepare Diet B and will be instructed to feed Diet B - a milk free diet containing rice-cereal, vegetable oil, egg albumin and glucose mixture. The second diet (B) will also be fed for 7 days. For partially breastfed children the diets will be offered to attain energy intake >75 kcal/kg/day and for non-breastfed child the energy intake will be 110 kcal/kg/day. In addition multivitamin drops and zinc acetate are standard therapy for PD patients and will be given routinely to all children from the beginning of the study and for the following three weeks (Table 2). The dosage of multivitamin syrup will be 1 ml twice daily and Zinc acetate 10 mg twice daily. Oral rehydration with standard WHO-ORS will continue to maintain hydration to replace ongoing liquid stool losses until cessation of diarrhoea. The number of ORS packets used will be recorded.

On day 7 after beginning of diet A, if the patients are found to have normal stool (soft or formed), they will continue diet A.

After 7 days of second dietary regime, if diarrhoea persists, the patients will be admitted to the inpatient department for further evaluaition and management according to the standard hospital practice at ICDDR,B.

Control group
The patients under control group will receive standard management which is advised to take WHO-ORS at home for maintenance of hydration and to continue his/her usual diet or as advised by hospital physician.

Follow-up:
All patients will be followed-up by home visits on every alternate day up to day 15 and then every 2 weeks thereafter up to 4 weeks. The children will be examined thoroughly including anthropometry at every follow up. Study personnel will also monitor the preparation of diet at home. Samples of prepared diet will also be collected and stored in deep freezer for quality study (e.g. composition and calories).

Fig. 1

DIETARY TREATMENT ALGORITHM

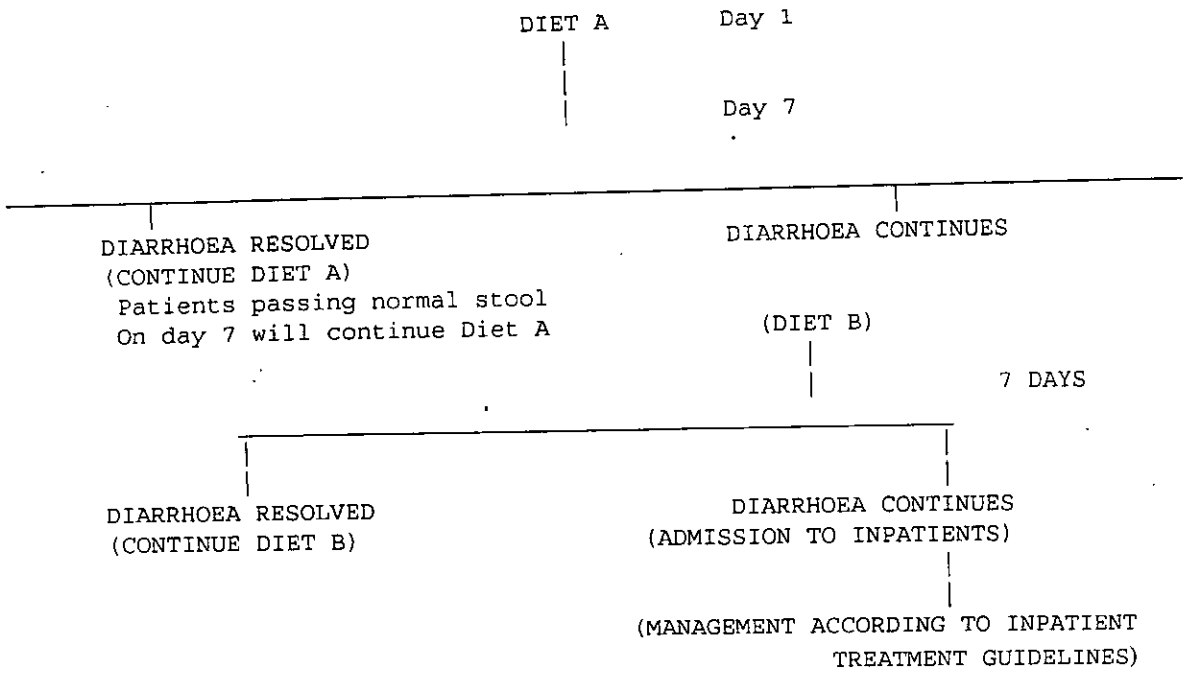

Table 1. Composition of study diets

Diet A		Diet B	
Milk/Suji/Litre (>4 mo age group)		**Full-Strength Rice Suji/L**	
Whole milk powder	40 g	Rice powder	60 g
Rice powder	40 g	Egg white	100 g (four)
Sugar	25 g	Oil (Soya)	30 ml
Oil (Soya)	25 g	Glucose	35 g
Mag. Chloride	0.5 g	Kcl	01 g
Potassium chloride	01 g	Mag. Chloride	0.5 g
Calcium	02 g	Calcium	02 g
After cooked volume	1000 ml	After cooked volume	1000 ml
Energy	67kcal/100ml	Energy	70 kcal/100 ml
Protein	4.4 gm/100ml	Protein	1.88 g/100 ml
PER*	8%	PER	10%

Table 2. Composition of Multivitamin drop (Composition per 1 ml)

Vitamin A U.S.P.	5000 IU
Vitamin D B.P.	640 IU
Ascorbic Acid (C) B.P.	50 mg
Thiamine Hcl (B_1)	1.6 mg
Riboflavin Sodium Phosphate (B_2) B.P.	1.37 mg
Pyridoxine B.P. (B_6) U.S.P.	1.0 mg
Nicotinamide B.P.	10.0 mg
D-Panthenol U.S.P.	5.0 mg
Folic acid	0.25 mg

Justification of selection of diet A in the beginning

Dietary treatment algorithm is a well recognised treatment schedule for the nurtritional management of children suffering from persistent diarrhoea. In ICDDRB hospital, this treatment algorithm is also being followed. Justification of using Diet A initially is that this diet is easy to prepare, culturally acceptable, less modified as compared to Diet B. and less expensive (1 L Diet A costs Tk. 18.00 vs. Tk. 26.00 for Diet B).

Study withdraal

Patients will be considered withdrawn from the study if a) their parents withdraw informed consent, or b) needs hospital care .

Patients will be considered for hospital care for the following reasons:

a) appearance of signs of some dehydration b) signs of severe infections (e.g. fever, cough, respiratory distres, tachycardia, tachypnoea, reluctant to feeding etc. c) signs of electrolyte imbalance (e.g. less responsive to environments or irritabiliy, abdominal distensions etc.). After hospitalisation, the patients will be managed according to the standard hospital practice. Patints wil be followed up even after withdrawn from the study. Data obtained from the withdrawn patients wil also be included in the analysis upto the time of withdrawal.

Sample size

Samle size was calculated on the basis of two major outcome variables:

a) success rate of diet therapy

b) Growth faltering (percentage of patients experiencing weight loss during the stuy periods).

Based on the study (21) the sample size of this study is determined to be of 137 in each group on anticipated success rate (combining success of Diet A and Diet B) of 80% in the intervention group against an arbitrary standard success rate of 65% in the control group, considering a significance level of 5% and power of 80%. Assuming a dropout of 15%, a total sample of 320 patients was calculated.

We are not expecting significant difference in recovery rate on diet A and the control. However, if the difference is 20% or more, then the present sample size will be enough to detect the significant difference.

Thirty percent of children under control group is anticipated to experience weight loss as opposed to 10% in the intervention group during the study periods. Considering a significance level of 5% and 80% power, the sample size in each group is calculated as 60.

Finally, we consider the toal sample size for this study as 320.

Organization of the trial

Patients attending in the treatment centre of ICDDR,B will be evaluated for recruitment for study.

Study Schedule
The study will be started after the approval of RRC and ERC and allocation of budget. The first two month will be utilized for staff recruitment, training and pretrial. 20 months will be needed for patients study. Last 2 month will be utilised for data analysis and reporting of the study results.

Definition

Diarrhoea: Three or more abnormal stool (loose or watery) during a 24 hour period.

Stool consistency: Abnormal stool - loose/watery or abnormal as considered by mother.
Normal stool - soft/formed or normal considered by mother.

Cessation of diarrhoea: Last abnormal stool followed by normal stool at least for three days.

Success of diet therapy: Cessation of diarrhoea within 7 days of starting of the modified diet (diet A or diet B).

Facilities Available

Describe the availability of physical facilities at the place where the study will be carried out. For clinical and laboratory-based studies, indicate the provision of hospital and other types of patient's care facilities and adequate laboratory support. Point out the laboratory facilities and major equipments that will be required for the study. For field studies, describe the field area including its size, population, and means of communications. (TYPE WITHIN THE PROVIDED SPACE).

ICDDR,B treatment centre will be used for patients recruitment, observation, and training of the caregivers of the patients.

Data Analysis

Describe plans for data analysis. Indicate whether data will be analyzed by the investigators themselves or by other professionals. Specify what statistical softwares packages will be used and if the study is blinded, when the code will be opened. For clinical trials, indicate if interim data analysis will be required to monitor further progress of the study. **(TYPE WITHIN THE PROVIDED SPACE).**

Statistical analysis

Statistical analysis will be done using SPSS/PC software. Percentage of success of treatment for each dietary intervention and overall success rate will be calculated. Relative risk ratios and their associated 95% confidence intervals will be calculated to identify variables (e.g. inappropriately making and feeding the diet, associated other infections, education of mothers, family income, no. of children in the family, source of drinking water, antibiotic use before admission, type of dehydration before intervention, frequency of stool etc.) that were related to the treatment failure. Overall success rate (the number of patients recovered at the end of 10 days) in the intervention group will be compared with that of control group. The number of patients lost weight will also be compared between the groups.

Adjusted analysis will be done by constructing life tables of the two groups and will be compared by log rank test.

Ethical Assurance for Protection of Human Rights

Describe in the space provided the justifications for conducting this research in human subjects. If the study needs observations on sick individuals, provide sufficient reasons for using them. Indicate how subject's rights are protected and if there is any benefit or risk to each subject of the study.

This intervention study will be conducted among the children under 5 years of age because these children are the sufferers from this illness of persistent diarrhoea. Written informed consent will be duly signed by the parents or legal guardians.

There is no risk for this intervention on the other hand they might be benefited from this intervention.

Use of Animals

Describe in the space provided the type and species of animal that will be used in the study. Justify with reasons the use of particular animal species in the experiment and the compliance of the animal ethical guidelines for conducting the proposed procedures.

Not applicable.

Literature Cited

Identify all cited references to published literature in the text by number in parentheses. List all cited references sequentially as they appear in the text. For unpublished references, provide complete information in the text and do not include them in the list of Literature Cited. There is no page limit for this section, however exercise judgment in assessing the "standard" length.

1. World Health Organisation (WHO). Persistent diarrhoea in children in developing countries: Memorandum from a WHO meeting. Bull WHO 1988;66(6):709-717.

2. Bhan MK, Arora NK, Ghai KR et al. Major factors in diarrhoea related mortality among rural children. Indian J Med Res 1986;83:9-12.

3. Fauveau V, Henry RI, Briend A, et al. Persistent diarrhoea as a cause of mortality in rural Bangladesh. Acta Paediatr 1992;81(Suppl 381):12-14.

4. Victora (G, Huttly SR, Fuchs SC, et al. Deaths due to dysentery acute and persistent diarrhoea among Brazilian infants. Acta Paediatr 1992;81(Suppl 381):7-11.

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8. Lima Aldo A.M. and Guerrant RL. Persistent diarrhoea in children: Epidemiology, Risk Factors, Patho Physiology, Nutritional Impact, and Management. Epidemiologic Reviews 1992;14:222-242.

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11. Akbar MS, Roy SK and Banu N. Persistent diarrhoea: Management in Algorithmic Approach Using a Low-cost Rice-based Diet in Severely Malnourished Bangladeshi Children. J Trop Pediatr 1993;39:332-337.

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15. Alarcon P, Montoya R, Perez F, et al. Clinical trial of home available, mixed diets versus a lactose-free, so protein formula for the dietary management of childhood diarrhoea J Pediatr. Gastroenterol Nutr 1991;12:224 32.

16. Brown KH, Perez F, et al. Clinical trial of modified whole milk, lactose hydrolysed whole milk, or cereal mill mixtures for the dietary management of acute childhood diarrhoea. J Pedeatr Gastroenterol Nutr 1991;12:340-50.

17. Bhan MK, Arora NK, Khosroo V et al. Chronic diarrhoea in infants and children. Ind J Pediatr 1985;52:483-95.

18. Godard C, Bustos M, Munoz M et al. Value of a chicken based formula for refeeding of children with protracte diarrhoea and malnutrition in a developing country. J Pediatr Gastroenterology Nutr. 1989;9:473-80.

19. Brown KH. Appropriate diets for the rehabilitation of malnourished children in the community settings. Act Paediatr Scand 1991;374(Suppl):151-9.

20. Bardhan PK, Alam NH, Mahalanabis D. Clinical trial of coconut oil vs soy oil based comminuted chicken diet i the treatment of persistent diarrhoea. (Manuscript under preparation).

21. International working group on Persistent diarrhoea: Evaluation of a Algorithm for the treatment of persisten diarrhoea: A multicentre study. Bull WHO 1996;74(5):479-489.

22. Alam NH, Bardhan PK, Haider R, Mahalanabis D. Trimethoprim-Sulphamethoxazole in the treatment o persistent diarrhoea. A double-blind placebo controlled clinical trial. Arch Dis Childhood 1995;72:483-486.

Dissemination and Use of Findings

Describe explicitly the plans for disseminating the accomplished results. Describe what type of publication is anticipated: working papers, internal (institutional) publication, international publications, international conferences and agencies, workshops etc. Mention if the project is linked to the Government of Bangladesh through a training programme.

The findings of the research will be disseminated by reporting in the national and international conferences and peer reviewed journals.

Principal Investigator: Last, first, middle _____

Biography of the Investigators: Dr. N.H. Alam, Principal Investigator

Give biographical data in the following table for key personnel including the Principal Investigator. Use a photocopy of this page for each investigator.

Name	Position	Date of birth
Dr. Nur Haque Alam	Senior Medical Officer Gr I	1.1.1952

Academic Qualifications (Begin with baccalaureate or other initial professional education

Institution and Location	Degree	Year	Field of study
Dhaka Medical College, Dhaka, Bangladesh	M.B.B.S.	1976	Medicine
University of Basel, Switzerland	M.D.	1993	Gastroenterology

Research and Professional Experience

Concluding with the present position, list, in chronological order, positions held, experience, and honours. Indicate current membership on any professional societies or public committees. List, in chronological order, the titles, all authors and complete references to all publications during the past three years and to representative earlier publications pertinent to this application (**Do not exceed two pages, use continuation sheets**).

Publications

1. **N.H. Alam,** T. Ahmed, M. Khatun, A.M. Molla. Effects of food with two oral rehydration therapies: a randomized controlled clinical trial. Gut 1992;33(4):560-562.

2. **N.H. Alam,** P.K. Bardhan, R. Haider, D. Mahalanabis. Trimethoprim-Sulphamethoxazole in the treatment of persistent diarrhoea: a double blind placebo controlled clinical trial. Arch Dis Childhood 1995;72:483-86.

3. **N.H. Alam,** R. Meier, K. Gyr et al. Effects of a partially hydrolised guar gum on intestinal absorption of carbohydrate, protein and fat: a double-blind controlled study in volunteers. Clin Nutr 1998:17:125-129.

4. A.N. Alam, **N.H. Alam**, T. Ahmed, D.A. Sack. Randomised double blind trial of single dose doxycycline for treating cholera in adults. Br Med J 1990;300:1619-1621.

5. B.J. Collins, F.P.L. van Loon, A. Molla, A.M. Molla, **N.H. Alam.** Gastric emptying of oral rehydration solutions in acute cholera. J Trop Med Hyg 1989;92:290-4.

6. A. Islam, T. Butler, S.K. Nath, **N.H. Alam,** K. Stoekel, et al. Randomized treatment of patients with typhoid fever by using ceftriaxone or chloromphenicol. J Infect Dis 1988;158:742-7.

7. A. Islam, T. Butler, I. Kabir, **N.H. Alam.** Treatment of Typhoid fever with Ceftriaxone for 5 days or Chloramphenical for 14 days: a randomized clinical trial. Antimicrob Agents Chem 1993;37(8):1572-4.

8. E. Carniel, T. Butler, S. Hossain, **N.H. Alam,** D. Mazigh. Infrequent detection Yersinia enterocolitica in childhood diarrhoea in Bangladesh. Am J Trop Med Hyg 1986;35(2):370-71.

9. T. Butler, E. Carniel, S. Hossain, **N.H. Alam**, D. Mazigh. Diarrhoea caused by *Yersinia enterocolitica* in children in Bangladesh. Contr Microbiol Immunol 1987;9:117-121.

10. T. Rausch, C. Beglinger, **N.H. Alam,** R. Meier. Effect of transdermal application of nicotine on colonic transit in healthy nonsmoking volunteers Neurogastroenterol. Mot. 1998;10:000-000.

11. S.A. Sarker, D. Mahalanabis, P.K. Bardhan, **N.H. ALAM**, Kh.H. Rabbani, et al. Noninvasive Assessment of Gastric Acid Secretion in Man Application of Electrical Impedence Tomography (EIT). Dig Dis Sci 1997:42(8):1804-1809.

12. P.K. Bardhan, M.J. Albert, **N.H. Alam**, S.M. Faruque, P.K.B. Neogi, D. Mahalanabis. Small Bowel And Fecal Microbiology In Children Suffering from Persistent Diarrhea in Bangladesh. J Pediatr Gastroenterol Nutr 1998;26:9-15.

Abstracts:

1. **N.H. Alam,** R. Meier, E. Minder, C. Bachman et al. The influence of a soluble fiber containing liquid diet on gastrointestinal functions in healthy volunteers. In: Proceedings of the 15th ESPEN Congress on Clinical Nutrition and Metabolism, 12-15 September, 1993, Budapest, Hungary.

2. R. Meier, **N.H. Alam,** T.H. Rousch, C. Beglinger, H. Schneider, K. Gyr. The effect of liquid diets on cholecystokinin (CCK) release and gallbladder motility in healthy male volunteers. In: Proceedings of the 15th ESPEN Congress on Clinical Nutrition and Metabolism, 12-15 September, 1993, Budapest, Hungary.

3. R. Meier, **N.H. Alam,** C. Beglinger, H. Schneider, K. Gyr. Effect of a liquid diet with and without soluble fibers on CCK release and gallbladder contraction. Gastroenterology 1993:A635.

4. S.A. Sarker, D. Mahalanabis, P.K. Bardhan, **N.H. Alam,** K. Gyr et al. Measurement of Gastric acid secretion by a Novel noninvasive test. Dig Dis week, May 14-17, 1975. San Diego, USA. (Abstract No. A236).

5. S.A. Sarker, P.K. Bardhan, S.R. Rabbani, **N.H. Alam**, A. Kibor et al. Noninvassive assessment of gastric acid secretion by applied potential tomography. Gut 1995;37(Suppl 2):A231(Abstract no.1971).

6. **N.H. Alam,** R. Meier, S.A. Sarker, P.K. Bardhan, K. Gyr et al. Effect of a soluble fiber supplemented oral rehydration solution (ORS) in the treatment of acute diarrhoea in children. Dig Dis Week, May 10-16, 1997 (Abstract no. 2735).

7. P.K. Bardhan, T. Ahmed, **N.H. Alam,** A.N. Alam et al. Excrine Pancreatic function in cholera and shigellosis Digestion 1990;46(3):127.

8. **N. H. Alam**, A. S. G. Faruque, N. Dewan, S. A. Sarker, G. J. Fuchs. Risk factors for severe persistent diarrhoea.
9. Commonwealth Congress on Diarrhoea and Malnutrition , Nov. 21- 24, 1997, Karachi, Pakistan

Principal Investigator: Last, first, middle _____

Biography of the Investigators: Dr. J.D. Hamadani, Co-Investigator

Give biographical data in the following table for key personnel including the Principal Investigator. Use a photocopy of this page for each investigator.

Name	Position	Date of birth
Dr. Jena Derakhshami Hamadani	Senior Medical Officer Gr II	18.02.1958

Academic Qualifications (Begin with baccalaureate or other initial professional education

Institution and Location	Degree	Year	Field of study
Rajshahi Medical College Hospital, Rajshahi, Bangladesh	M.B.B.S.	1984	Medicine
Bangladesh Institute of Child Health, Dhaka University, Dhaka, Bangladesh	D.C.H.	1996	Pediatrics

Research and Professional Experience

Concluding with the present position, list, in chronological order, positions held, experience, and honours. Indicate current membership on any professional societies or public committees. List, in chronological order, the titles, all authors and complete references to all publications during the past three years and to representative earlier publications pertinent to this application **(Do not exceed two pages, use continuation sheets).**

Publications

1. Hamadani JD, Tarek MK, Chowdhury J, Kabir I. Case Report: Intestinal Perforation in a child with Shigella Dysenteriae 1 infection - A rare complication. JDDR, Vol 12 No. 3, P 225-6, Sep 1994.

2. Roy SK, Alam AN, Majid N, Khan AM, Hamadani J, Shome G. Persistent Diarrhoea: A Preliminary Report on Clinical Features and Dietary Therapy in Bangladeshi Children. J Trop Med. 1989;35:55-59.

3. Azim T, Qadri F, Hamadani J, Sarkar MS, Haldar RC. Immune Response of Children with Shigellosis and Leukaemoid Reaction. Abstract in proceeding of "7th International Congress of Mucosal Immunology" Aug, 1992, Prague, Czechoslovakia.
Same abstract was also presented in ASCON-II, ICDDR,B.

4. Haider R, Islam A, Hamadani J, Shirazi N, Habte D. Can Mothers of partially breastfed infants be helped to breastfed exclusively? Results from a Diarrhoeal Disease Hospital. Abstract accepted for Third Commonwealth Conference on Diarrhoea and Malnutrition, Nov 1994.

5. Azim T, Islam LN, Haldar RC, Hamadani JD, Khanum N, Sarkar MS, Qadri F, Salam MA, Albert MJ, Sack RB. Neutrophil polarization and phagocytosis in children with shigella dysenteriae type 1 infection. Poster presentation in the 12th European Immunology Meeting" in Barcelona, June, 1994.

6. Azim T, Haldar RC, Sarkar MS, Ahmed S, Hamadani JD, Chowdhury A, Qadri F, Salam MA, Sack RB, Albert MJ. Cytokines in the stools of children with complicated shigellosis. Clin Diag Lab Immun. July 1995;2:492-5.

7. Hamadani JD, Dewan N, Faruque ASG. Entero Pathogens and charactristics of patients readmitted in a diarrhoeal disease hospital - Abstract accepted for 8th ASCODD Meeting Feb '97.

8. Azim T, Quadri F, Ahmed S, Sarker MS, Halder RC, Hamadani JD, Chowdhury A, Wahed MA, Salam MA, Albert MJ. Lipopolysaccharide-Specific antibodies in plasma and stools of children with shigella-associated leukaemoid reaction and hemolytic-uremic syndrome. Clin Diag Lab Immun, Nov 1996;3:701-5.

9. Azim T, Islam LN, Halder RC, Hamadani JD, Khanum N, Sarker MS, Salam MA, Albert MJ. Peripheral Blood Neutrophil responses in children with shigellosis Clin Diag Lab Immun Sep 1995; 2: 616-22.

10. Azim T, Sarker MS, Hamadani JD, Khanum N, Halder RC, Salam MA, Albert MJ. Alterations in lymphocyte phenotype and function in children with shigellosis who develop complications. Clin Diag Lab Immun, Mar 1996; 3:191-6.

11. Haider R, Islam A, Hamadani JD, Amin NJ, Kabir I, Malek MA, Mahalanabis D, Habte D. Breastfeeding counselling in a diarrhoeal disease hospital. Bulletin of WHO 1996;74 (2): 173-9.

12. Faruque ASG, Mahalanabis D, Hamadani JD, Zetterstorm R. Reduced Osmolarity Oral Rehydration Salt in Cholera. Scand J Infect Dis 1996;28:87-90.

13. Unicomb LE, Kilgore PE, Faruque ASG, Hamadani JD, Fuchs GJ, Albert MJ, Glass RI. Anticipating rotavirus vaccines: hospital-based surveillance for rotavirus diarrhoea and estimates of disease burden in Bangladesh. Pediatr Infect Dis J 1997;16:947-51.

14. Azim T, Sarker MS, Hamadani JD, Wahed MA, Halder RC, Salam MA, Albert MJ. Effect of Nutritional Status on Lymphocyte Responses in Children with Shigella Flexneri Infection. Imm and Infec Dis 1996;6:151-8.

15. Faruque ASG, Mahalanabis D, Hamadani JD, Hoque SS. Hypo-osmolar Sucrose Oral Rehydration Solution in Acute Diarrhoea: a pilot study. Acta Paediatr 1996;85:1247-8.

16. Hamadani JD, Dewan N, Faruque ASG. Clinical and etiological characteristics of patients readmitted into a diarrhoea hospital. CAPGAN Abstract in J Pediatr Gastroent Nut 1998;27:247.

17. Azim T, Ahmed SM, Sarker MS, Unicomb LE, De S, Hamadani JD, Salam MA, Faruque SM, Wahed MA, Albert MJ. Raised Interferon Levels in Plasma precede the development of persistent diarrhoea from Rotavirus Infection in Bangladeshi children. Submitted for publication in Clin Diag Lab Immun.

18. Faruque ASG, Hamadani JD, Hoque SS, Mahalanabis D. Picture calendar to promote Oral Rehydration therapy at home for illiterate mothers, a motivational tool. J Trop Paediatr 1998;44:182.

19. Haider R, Kabir I, Hamadani JD, Habte D. Reasons for failure of breastfeeding counselling mothers' perspectives in Bangladesh. Bull WHO 1997;75:191-6.

20. Haider R, Kabir I, Hamadani JD, Habte D. Exclusive breastfeeding initiated during hospitalization of young infants with diarrhoea is sustained at home. Published in the Abstracts of the 16th International Congress of Nutrition. Montreal, Canada, July 27-Aug 1, 1997.

Principal Investigator: Last, first, middle _____

Biography of the Investigators: Dr A.S.G. Faruque, Co-Investigator

Give biographical data in the following table for key personnel including the Principal Investigator. Use a photocopy of this page for each investigator.

Name	Position	Date of birth
Dr. A.S.G. Faruque	Scientist	01.01.1951

Academic Qualifications (Begin with baccalaureate or other initial professional education

Institution and Location	Degree	Year	Field of study
Rajshahi Medical College, Rajshahi, Bangladesh	M.B.B.S.	1973	Medicine
School of Public Health, Johns Hopkins University, Baltimore, Maryland, USA	M.P.H.	1988	Public Health

Research and Professional Experience

Concluding with the present position, list, in chronological order, positions held, experience, and honours. Indicate current membership on any professional societies or public committees. List, in chronological order, the titles, all authors and complete references to all publications during the past three years and to representative earlier publications pertinent to this application **(Do not exceed two pages, use continuation sheets)**.

PUBLICATIONS:

1. Faruque ASG, Hamadani JD, Hoque SS, Mahalanabis D. Picture calendar to promote Oral rehydration therapy at home for illiterate mothers: a motivational tool. J Trop Paediatr 1998;44:182.

2. Dewan N, Faruque ASG, Fuchs GJ. Nutritional status and diarrhoeal pathogen in hospitalized in Bangladesh. Acta Paediatr 1998;87:627-30.

3. Islam S, Faruque ASG, Fuchs GJ, Wahed MA, Mahalanabis M. Shelf-life of precooked rice oral rehydration salt packets. South Asian J Trop Med Pub Hlth 1997;28:862-4.

4. Unicomb LE, Banu NN, Azim T, Islam A, Bardhan PK, Faruque ASG, Hall A, Moe CL, Noel JS, Monroe SS, Albert MJ, Glass RI. Astrovirus infection in association with acute, persistent and nosocomial diarrhoea in Bangladesh. Pediatr Infect Dis J 1998;17:611-14.

5. Hossain MI, Yasmin R, Faruque ASG. Morbidity and mortality pattern of children in a district paediatric hospital of Bangladesh. Bangladesh J Child Health 1997;21:1-5.

6. Albert MJ, Faruque ASG, Mahalanabis D. Association of Providencia alcalifaciens with diarrhoea in children. J Clin Micrbiol 1998;5:1433-35.

7. Faruque ASG, Hoque SS, Fuchs GJ, Mahalanabis D. Randomized controlled clinical trial of rice versus glucose oral rehydration solutions in infants and young children with acute watery diarrhoea. Acta Paediatr 1997;86:1308-11.

8. Fuchs GJ, Tienboon P, Khaled MA, Nimsakul S, Linpisarn S, Faruque ASG, Yutrabootr Y, Dewier M, Suskind RM. Nutritional support and growth in thalassaemia major. Arch Dis Childhood 1997;76:509-512.

9. Bhattacharya MK, Teka T, Faruque ASG, Fuchs GJ. Cryptosporidium infection in children in urban Bangladesh. J Trop Paediatrics 1997;43:282-286.

10. Unicomb LE, Kilgore PE, Faruque ASG, Hamadani JD, Fuchs GJ, Albert MJ, Glass RI. Anticipating rotavirus vaccines: hospital-based surveillance for rotavirus diarrhoea and estimates of disease burden in Bangladesh. Pediatr Infect Dis J 1997;16:947-51.

11. Albert MJ, Bhuiyan NA, Talukder KA, Faruque ASG, Nahar S, Faruque SM, Ansaruzzaman M, Rahman M. Phenotypic and genotypic changes in *Vibrio cholerae* O139 Bengal. J Clin Microbiol 1997;35:2588-2592

12. Faruque ASG, Teka T, Fuchs GJ. Shigellosis in children: a clinico-epidemiological comparison between *Shigella dysenteriae type I and Shigella flexneri.* Ann Trop Pediatr (in press).

13. Faruque ASG, Mahalanabis D, Hoque SS, Fuchs GJ, Habte D. Double blind randomized controlled trial of Zinc and vitamin A supplementation in young children with acute diarrhoea. Acta Paediatrica (in press).

14. Faruque ASG, Salam MA, Faruque SM, Fuchs GJ. Aetiological, clinical, and epidemiological characteristics of a diarrhoea epidemic in Dhaka, Bangladesh. Scand J Infect Dis (in press).

15. Aeromonas-associated diarrhoea in Bangladeshi children: clinical and epidemiological characteristics. Teka T, Faruque ASG, Hossain MI, Fuchs GJ. Ann Trop Paediatr (in press).

16. Haque R, Faruque ASG, Hahn P, Lyerly DM, Petri WA. Entamoeba histolytica and entamoeba dispar infection in children in Bangladesh. J Infect Dis 1997;175:734-6.

17. Faruque ASG, Mahalanabis D, Hamadani JD, Hoque SS. Hypoosmolar sucrose oral rehydration solutions in acute diarrhoea: a pilot study. Acta Paediatr 1996;85:1247-8.

18. Faruque ASG, Mahalanabis D, Hamadani JD, Zetterstrom R. Reduced osmolarity glucose ORS in cholera. Scand J Infect Dis 1996;28:87-90.

19. Faruque ASG, Fuchs GJ, Albert MJ. Changing epidemiology of cholera due to Vibrio cholerae O1 and O139 Bengal in Dhaka, Bangladesh. Epidemiol Infect 1996;116:275-8.

20. Mahalanabis D, Faruque ASG, Islam A, Hoque SS. Maternal education and family income as determinants of severe disease following acute diarrhoea in infants and young children: a case control study. J Biosoc Sci 1996;28:129-139.

21. Teka T, Faruque ASG, Fuchs GJ. Risk factors for deaths in under-age-five children attending a diarrhoea treatment centre. Acta Paediatr 1996;85:1070-5.

22. Unicomb L, Faruque SM, Malek MA, Faruque ASG, Albert MJ. Demonstration of a lack of synergistic effect of rotavirus with other diarrhoeal pathogens on severity of diarrhoea in children. J Clin Microbiol 1996;34:1340-42.

23. Albert MJ, Faruque SM, Faruque ASG, Bettelheim KA, Neogi PKB, Bhuiyan NA, Kaper JB. Controlled study of cytolethal distending toxin-producing *Escherichia coli* infections in Bangladeshi children. J Clin Microbiol 1996;34:717-719.

24. Mahalanabis D, Faruque ASG, Hoque SS, Faruque SM. Hypotonic oral rehydration solution in acute diarrhoea: a controlled clinical trial. Acta Paediatr 1995;84:289-93.

25. Albert MJ, Faruque SM, Faruque ASG, Neogi PKB, Ansaruzzaman M, Bhuiyan NA, Alam K, Akbar MS. Controlled study of *Escherichia coli* diarrhoeal infections in Bangladeshi children. J Clin Microbiol 1995;33: 973-977.

26. Albert MJ, Ansaruzzaman M, Bhuiyan NA, Neogi PKB, Faruque ASG. Characteristics of invasion of HEp-2 cells by Providencia alcalifaciens. J Med Microbiol 1995;42:186-90.

27. Ansaruzzaman M, Kibria AKMG, Rahman A, Neogi PKB, Faruque ASG, Rowe B, Albert MJ. Detection of provisional serovars of *Shigella dysenteriae* and designation as *S. dysenteriae* serotypes 14 and 15. J Clin Microbiol 1995;33:1423-1425.

Principal Investigator: Last, first, middle _____

APPENDIX

International Centre for Diarrhoeal Disease Research, Bangladesh
Voluntary Consent Form

Title of the Research Project: **Evaluation of a dietary treatment algorithm as a home-based management of children with persistent diarrhoea: a community-based study.**

Principal Investigator: Dr. N.H. Alam

Before recruiting into the study, the study subject must be informed about the objectives, procedures, and potential benefits and risks involved in the study. Details of all procedures must be provided including their risks, utility, duration, frequencies, and severity. All questions of the subject must be answered to his/ her satisfaction, indicating that the participation is purely voluntary. For children, consents must be obtained from their parents or legal guardians. The subject must indicate his/ her acceptance of participation by signing or thumb printing on this form.

Your child is suffering from persistent diarrhoea. Major treatment of this disease is dietary management in addition to rehydration therapy. ICDDR,B is carrying out a study to evaluate the feasibility and efficacy of a dietary treatment algorithm as home-based management of children with non-severe persistent diarrhoea. This study will not cause any risk to the patients' health. On the other hand the study patients will get benefit from the supervision and suggestion of the study personnel. If you agree to enrol your child in this study, the following schedule will have to be followed:

1. Your child will be observed for 4 hours in the hospital and will be given oral rehydration solution.

2. Stool will be examined to identify pathogens causing diarrhoea.

3. Mother/caregiver will be trained to prepare the study diets and will be instructed to feed the child at home accordingly or you will feed your child the usual diet.

4. You will be supplied with a diarrhoea diary card to note the number of stool and stool character by making a tick mark on the appropriate box.

5. Our staff will visit and examine your child at home and advise you accordingly.

If at any time you wish to withdraw your child from the study, you are free to do so without any obligation.

If the above conditions are acceptable to you, please sign or give your thumb impression below.

Signature of Investigator/ or agents **Signature of Subject/ Guardian**

Date: **Date:**

Principal Investigator: Last, first, middle _____

Detailed Budget for New Proposal

Project Title: Evaluation of a dietary treatment algorithm as a home-based management of children with persistent diarrhoea: a community based study

Name of PI: Dr. N.H. Alam

Protocol Number: Name of Division: Clinical Sciences Division

Funding Source: Amount Funded (direct): $49,995 Total: Overhead (%)

Starting Date: After approval by RRC /ERC & allocation of fund Closing Date: 2 years from starting

Strategic Plan Priority Code(s):

Sl. #	Account Description	Salary Support			US $ Amount Requested		
	Personnel	**Position**	**Effort %**	**Salary**	**1st Yr**	**2nd Yr**	**Total**
1	Dr. N.H. Alam, PI	Sr. Med. Officer Gr I	15	1345	2307	2400	4707
2	Dr. J.D. Hamadani, Co-Invest.	Sr. Med. Officer Gr II	05	1072	618	634	1252
3	Dr. A.S.G. Faruque, Co-Invest.	Scientist	05	1747	992	1032	2024
4	To be named	Study Med. Officer	100		2700	2700	5400
5	To be named	Research Officer	100		4164	4330	8494
6	To be named	Health Assistant-2	100		5376	5591	10967
7	To be named	Health Worker-2	100		1344	1398	2742
				Sub Total	17501	18085	**35586**
	INTERNATIONAL TRAVEL					2500	
	Sub Total						**2500**
	Supplies and Materials (Description of Items)						
	Office stationery				500	500	**1000**
	Others				200	200	**400**
				Sub Total	700	700	**1400**
	Other Contractual Services						
	Rent, Communications, Utilities				209	200	**409**
	Conveyance for patients and follow-up home visits				2000	2000	**4000**
	Printing and Publication				100	200	**300**
	Contractual services				**200**	**200**	**400**
				Sub Total	**2509**	**2600**	**5109**
	Interdepartmental Services						
	Pathological Tests				400	300	700
	Microbiological tests				600	400	1000
	Biochemistry Tests				300	200	500
	Transport				300	200	500
	Xerox, Mimeographs etc.				100	100	200
				Sub-total:	1700	1200	2900
	Capital Expenditure				**2500**		**2500**
	TOTAL DIRECT COST				**24,910**	**25,085**	**49,995**

Principal Investigator: Last, first, middle _____

Budget Justifications

Please provide one page statement justifying the budgeted amount for each major item. Justify use of man power, major equipment, and laboratory services.

Personnel: Investigators' salary support has been calculated by per cent of effort. Study Physician will help in taking medical history and physical examination in the hospital and also during home visits. Research Officer will organise the facilities in the hospital, arrange equipment and material needed for examination and training. S/he will also do data entry and will help in data analysis. Research assistant will be engaged in patients' recruitment, educate mothers/caregivers about preparation of feeding of diet, and also supervise the caregivers at home.

Equipment: Weighing scale and other measuring equipments will be purchased for anthropometric measurements. Computer accessories will also be needed.

Laboratory services: Cost of laboratory services has been calculated from the existing rates of laboratory services.

Principal Investigator: Last, first, middle _____

Other Support

Describe sources, amount, duration, and grant number of all other research funding currently granted to PI or under consideration. (DO NOT EXCEED ONE PAGE FOR EACH INVESTIGATOR)

1. WHO — 47,000.00 for 1 year
2. Novartis Nutrition — 89,000.00 for 2 years

Principal Investigator: Last, first, middle _____

Check List

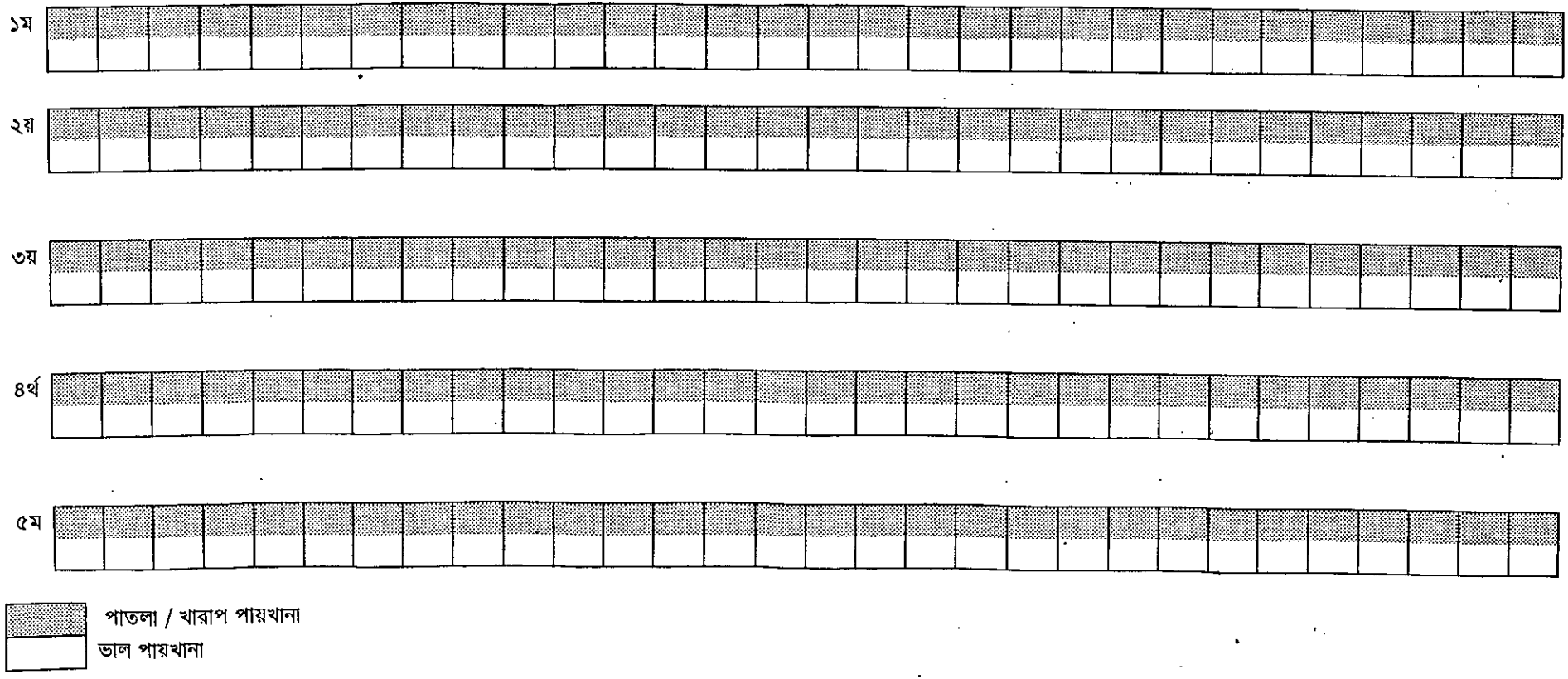
After completing the protocol, please check that the following selected items have been included.

1. Face Sheet Included ☑
2. Approval of the Division Director on Face Sheet ☑
3. Certification and Signature of PI on Face Sheet, #9 and #10 ☑
4. Table on Contents ☑
5. Project Summary ☑
6. Literature Cited ☑
7. Biography of Investigators ☑
8. Ethical Assurance ☑
9. Consent Forms ☑
10. Detailed Budget ☑

Diarrhoea Diary Card

যতবার পায়খানা করবে ততবার নিম্নে বর্ণিত ঘরে (✓) টিক চিহ্ন দিবেন

পায়খানা ভাল মনে করলে সাদা ঘরে টিক চিহ্ন দিবেন এবং খারাপ মনে করলে কাল ঘরে টিক চিহ্ন দিবেন



Answer to Reviewer # I

1. "Demonstrated ability of caregiver" has been omitted from the protocol. All patients fulfilling other entry criteria will be included. Caregivers of the patient who also do not have economic means for providing the advised diets, the ingredients of the study diet will be supplied during the study period.

2. The envelopes will be opened only after a patient has been irrevocably assigned to the study.

3. The mothers will be taught to prepare Diet B on day 6 when there will be no improvement of diarrhoea with Diet A for 5 days.

4. The patients will be followed up for 4 weeks after diarrhoea resolved.

5. Adjusted analysis will be done by construction of life tables of the patients of the study groups and will be compared by log rank test:

6. Addition of 1 g of salt to Diet A has been omitted.

Reviewer # 2: Reviewer no. 2 did not make any written comments.

Reviewer No. 1

Dr. G J Fuchs, M D, DIRECTOR
CLINICAL SCIENCES DIVISION, ICDDR,B, DHAKA
FAX: 008802 883116

Title: #

[illegible] *

Summary of Referee's Opinions: Please see the following table to evaluate the various aspects of the proposal by checking the appropriate boxes. Your detailed comments are sought on a separate, attached page.

	Rank Score		
	High	Medium	Low
Quality of Project	✓		
Adequacy of Project Design	✓		
Suitability of Methodology	✓	✓	
Feasibility within time period		✓	
Appropriateness of budget	✓		
Potential value of field of knowledge	✓		

CONCLUSIONS

I support the application:

a) without qualification ☐

b) ✓ with qualification

- on technical grounds ☑
- on level of financial support ☐

I do not support the application ☐

Name of Referee: DILIP MAHALANABIS Signature: Dilip Mahalanabis

Position: DIRECTOR Date: 11.7.98

Institution: SOCIETY FOR APPLIED STUDIES

* Title : "Evaluation of a dietary treatment algorithm as a home based management of children with persistent diarrhoea: a community based study"

Detailed comments

Please briefly provide your opinions of this proposal, giving special attention to the originality and feasibility of the project, its potential for providing new knowledge and the justification of financial support sought; include suggestions for modifications (scientific or financial) where you feel they are justified).

(Use additional pages if necessary)

Title : Evaluation of a dietary treatment algorithm as a home based management of children with persistent diarrhoea: a community based study

PI : N.H. Alam

Reviewer : Dr. Dilip Mahalanabis

The topic of research is of high public health priority and the results will be valuable in improving the case-management of diarrhoeal disease. The project is well designed and the investigators have demonstrated ability to carry out the work. I, therefore, fully support this proposed research project. I have a few comments which follows :

1. Page 4 under "Inclusion criteria"

   "Demonstrated ability of caregiver"; this point is not clear. If it means, the mother has to have sufficient education and economic means to be included, then large number of poor mothers will be excluded and the findings of the study will not be generalizable.

2. Page 4, last sentence (under "Randomization")

   It should be assured that the envelope will be opened only after a patient has been irrevocably assigned to the study.

3. Page 5, Treatment algorithm

   When do you teach mother to prepare diet B?

4. Page 5, Follow-up : for how long?

5. Page 6: Statistical analysis

   Do the investigators intend to do adjusted analysis? If so, please describe.

6. Page 10, Diet

   The Diet A has a relatively high osmolality. Is it necessary to add 1 g salt to a milk based diet?

Reviewer No. 2

Forwarded to PI (CAD) NH Alan

FAX TRANSMISSION

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AND ALASKAN NATIVE HEALTH
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TO: Dr. Finch

DATE: 8/5/98

FAX#: 011-880-2-883114

PAGES: 2 including this cover sheet.

FROM:

SUBJECT:

COMMENTS:

If there were any problems receiving this transmittal, please contact us.

Title: Evaluation of a dietary treatment algorithm as a home based management of children with persistent diarrhoea: a community based study.

Summary of Referee's Opinions: Please see the following table to evaluate the various aspects of the proposal by checking the appropriate boxes. Your detailed comments are sought on a separate, attached page.

	Rank Score		
	High	Medium	Low
Quality of Project	✓		
Adequacy of Project Design	✓		
Suitability of Methodology	✓		
Feasibility within time period	✓		
Appropriateness of budget	✓		
Potential value of field of knowledge	✓		

CONCLUSIONS

I support the application:

a) without qualification ☑

b) with qualification

- on technical grounds ☐
- on level of financial support ☐

I do not support the application ☐

Name of Referee: M. SANTOSHAM Signature: M. Santosham

Position: PROFESSOR, INTERNATIONAL HEALTH Date:

Institution: JOHNS HOPKINS UNIVERSITY