Centre for Health & Population Research	RRC APPLICATION FORM

RESEARCH PROTOCOL NUMBER: 2006-030	FOR OFFICE USE ONLY		
	RRC Approval:	☒ Yes /	☐ No	Date:18.6.06
	ERC Approval:	☐ Yes /	☐ No	Date:23.7.06
	AEEC Approval:	☐ Yes /	☐ No	Date:

Protocol Title: Long-term effects of prenatal Omega-3 (ω-3) fatty acid supplementation on Child Development in Bangladeshi Children

Short title (in 50 characters including space): Long-term effects of ω-3 on child development

Theme: (Check all that apply)

- ☒ Nutrition
- ☐ Emerging and Re-emerging Infectious Diseases
- ☐ Population Dynamics
- ☐ Reproductive Health
- ☐ Vaccine Evaluation
- ☐ HIV/AIDS
- ☐ Environmental Health
- ☐ Health Services
- ☒ Child Health
- ☐ Clinical Case Management
- ☐ Social and Behavioural Sciences

Key words: fish oil supplementation, cognitive development, Bangladesh, children

Relevance of the Protocol:

In the developing countries many children are at risk of sub-optimal intake of the micronutrients, including poly unsaturated fatty acids (PUFAs), necessary for optimal brain and cognitive development. A study has observed no benefit of α-linolenic acid (LNA) supplementation to influence maternal DHA status, which raises the question if mothers under prevailing dietary conditions are able to meet the high foetal requirements of DHA and if they need additional supplementation for optimal development of foetal brain. Despite the importance of DHA, there is limited research to assess the impact of supplementation of DHA during pregnancy on development of infants. In a randomized, double –blind, controlled trial, pregnant mothers were supplemented with DHA from 17-19 weeks gestation until 3 months after delivery. Although no difference was observed in the cognitive development of their infants, as measured at 6 or 9 months, a developmental benefit became apparent at the age of 4 years. An earlier study at ICDDR,B assessed the effects of prenatal fish oil supplementation on children's psychomotor development at 10 months of age, and observed no significant differences among children in the fish oil and soy oil supplemented groups. Since the children were tested at 10 months of age, the global cognitive measures may not have been sensitive to the subtle changes that might have occurred as a result of fish oil supplementation. We, therefore, believe that it is worthy to follow-up these children at their preschool age to determine if there are any benefits from the fish oil supplementation on these children's development at a later age.

Centre's Priority (as per Strategic Plan, to be imported from the attached Excel Sheet):
#12: Conduct studies to evaluate the effect of improving maternal nutrition as well as non-nutritional interventions on foetal growth and birth weight. #5: Strengthen child health and development interventions through research on effective child caring, stimulation and health-seeking practices in the homes.

Programmes:

- ☒ Child Health Programme
- ☒ Nutrition Programme
- ☐ Programme on Infectious Diseases & Vaccine Science
- ☐ Poverty and Health Programme
- ☐ Health and Family Planning Systems Programme
- ☐ Population Programme
- ☐ Reproductive Health Programme
- ☐ HIV/AIDS Programme

Principal Investigator (Should be a Centre's staff)	**DIVISION:**
Dr. Jena D. Hamadani Division: Phone: 2331 **Address (including e-mail address):** Mahakhali, Dhaka jena@icddrb.org	☒ CSD ☐ LSD ☐ HSID ☐ PHSD
Co-Principal Investigator(s): Internal Dr. Fahmida Tofail	
Co-Principal Investigator(s): External: (Please provide full official address including e-mail address and Gender) NA	
Co-Investigator(s): Internal: Dr Iqbal Kabir	
Co-Investigator(s): External (Please provide full official address including e-mail address and Gender) NA	
Student Investigator(s): Internal (Centre's staff):	
Student Investigator(s): External: (Please provide full address of educational institution and Gender) Farhana Sharmeen (female)	

Collaborating Institute(s): Please Provide full address

Institution # 1

Country	USA
Contact person	Farhana Sharmeen
Department (including Division, Centre, Unit)	Department of Psychology
Institution (with official address)	Harvard University, Cambridge, Ma
Directorate (in case of GoB i.e. DGHS)	
Ministry (in case of GoB)	

Institution # 2

Country	
Contact person	
Department (including Division, Centre, Unit)	
Institution (with official address)	
Directorate (in case of GoB i.e. DGHS)	
Ministry (in case of GoB)	

Institution # 3

Country	
Contact person	
Department (including Division, Centre, Unit)	
Institution (with official address)	
Directorate (in case of GoB i.e. DGHS)	
Ministry (in case of GoB)	

Note: If more than 3 collaborating institutions are involved in the research protocol, additional block(s) can be inserted to mention its/there particular(s).

Population: Inclusion of special groups (Check all that apply):

Gender

☒ Male
☒ Female

Age

☐ 0 – 4 years
☒ 5 – 9 years
☐ 10 – 19 years
☐ 20 – 64 years
☐ 65 +

☐ Pregnant Women
☐ Fetuses
☐ Prisoners
☐ Destitutes
☐ Service Providers
☐ Cognitively Impaired
☐ CSW
☐ Others (specify)
☐ Animal

NOTE It is the policy of the Centre to include men, women, and children in all research projects involving human subjects unless a clear and compelling rationale and justification (e.g. gender specific or inappropriate with respect to the purpose of the research) is there. Justification should be provided in the `Sample Size' section of the protocol in case inclusiveness of study participants is not proposed in the study.

Project/study Site (Check all the apply):

- ☐ Dhaka Hospital
- ☐ Matlab Hospital
- ☐ Matlab DSS Area
- ☐ Matlab non-DSS Area
- ☐ Mirzapur
- ☒ Dhaka Community
- ☐ Chakaria
- ☐ Abhoynagar
- ☐ Mirsarai
- ☐ Patyia
- ☐ Other areas in Bangladesh
- ☐ Outside Bangladesh

  Name of Country:
- ☐ Multi Centre Trial

(Name other countries involved):

Type of Study (Check all that apply):

- ☐ Case Control Study
- ☐ Community-based Trial/Intervention
- ☐ Program Project (Umbrella)
- ☐ Secondary Data Analysis
- ☐ Clinical Trial (Hospital/Clinic)
- ☒ Family Follow-up Study
- ☐ Cross Sectional Survey
- ☐ Longitudinal Study (cohort or follow-up)
- ☐ Record Review
- ☐ Prophylactic Trial
- ☐ Surveillance/Monitoring
- ☐ Others:

NOTE: Does the study meet the definition of clinical studies/trials given by the International Committee of Medical Journal Editors (ICMJE)? Yes ☒ No ☐

Please note that the ICMJE defined clinical trial as "*Any research project that prospectively assigns human subjects to intervention and comparison groups to study the cause-and-effect relationship between a medical intervention and a health outcome*".

If YES, after approval of the ERC, the PI should complete and send the relevant form to provide required information about the research protocol to the Committee Coordination Secretariat for registration of the study into websites, preferably at the www.clinicaltrials.gov. It may please be noted that the PI would require to provide subsequent updates of the research protocol for updating protocol information in the website.

Targeted Population (Check all that apply):

- ☒ No ethnic selection (Bangladeshi)
- ☐ Bangalee
- ☐ Tribal group
- ☐ Expatriates
- ☐ Immigrants
- ☐ Refugee

Consent Process (Check all that apply):

- ☒ Written
- ☒ Oral
- ☐ None
- ☒ Bengali Language
- ☐ English Language

Proposed Sample Size:

Sub-group (Name of subgroup (e.g. Men, Women) and Number

Name	Number	Name	Number
(1) Young children	150	(3)	
(2)		(4)	

Total sample size:150

Determination of Risk: Does the Research Involve (Check all that apply**):**

- ☐ Human exposure to radioactive agents?
- ☐ Fetal tissue or abortus?
- ☐ Investigational new device?
  (specify:)
- ☒ Existing data available from Co-investigator
- ☐ Human exposure to infectious agents?
- ☐ Investigational new drug
- ☐ Existing data available via public archives/sources
- ☐ Pathological or diagnostic clinical specimen only
- ☐ Observation of public behaviour
- ☐ New treatment regime

Yes	No	
☒	☐	Is the information recorded in such a manner that study participants can be identified from information provided directly or through identifiers linked to the study participants?
☐	☒	Does the research deal with sensitive aspects of the study participants' behaviour; sexual behaviour, alcohol use or illegal conduct such as drug use?

Could the information recorded about the individual if it became known outside of the research:

Yes	No	
☐	☒	Place the study participants at risk of criminal or civil liability?
☐	☒	Damage the study participants' financial standing, reputation or employability, social rejection, lead to stigma, divorce etc.?

Do you consider this research (Check one):

- ☐ Greater than minimal risk
- ☐ Only part of the diagnostic test
- ☒ No more than minimal risk

Minimal Risk is "a risk where the probability and magnitude of harm or discomfort anticipated in the proposed research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical, psychological examinations or tests. For example, risk of drawing a small amount of blood from a healthy individual for research purposes is no greater than the risk of doing so as a part of routine physical examination".

Yes/ No

☐ ☒ Is the proposal funded?

If yes, sponsor Name: (1)

(2)

Yes/No

☐ ☒ Is the proposal being submitted for funding?

If yes, name of funding agency: (1)

(2)

Do any of the participating investigators and/or member(s) of their immediate families have an equity relationship (e.g. stockholder) with the sponsor of the project or manufacturer and/or owner of the test product or device to be studied or serve as a consultant to any of the above?

IF YES, a written statement of disclosure to be submitted to the Centre's Executive Director.

Dates of Proposed Period of Support **Cost Required for the Budget Period ($) 4,657.8**

(Day, Month, Year - DD/MM/YY)

Beginning Date : 25/06/06

End Date : 31/08/06

Years	Direct Cost	Indirect Cost	Total Cost
Year-1	**4,657.8**	0	**4,657.8**
Year-2	0	0	0
Year-3	0	0	0
Year-4	0	0	0
Year-5	0	0	0
Total	**4,657.8**	0	**4,657.8**

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 the responsibility for the scientific conduct of the project and to provide the required progress reports including updating protocol information in the SUCHONA (Form # 2) if a grant is awarded as a result of this application.

_____ _____

Signature of PI **Date**

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 reviewers' comments and is approved.

Dr. MA Salam

Name of the Division Director Signature Date of Approval

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. Also 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. **(Please keep as brief as possible).**

Principal Investigator(s): **Jena D. Hamadani**
Research Protocol Title: Long-term effects of prenatal Omega-3 fatty acid supplementation on Cognitive Development of Bangladeshi Children
Total Budget US$: 4,657.8 Beginning Date : 25/06/06 Ending Date: 31/08/06
Global micronutrient deficiency, known as the "hidden hunger," has imposed detrimental consequences in developing countries. Specifically, omega-3 fatty acids directly affect the neurodevelopment and cognitive functioning of infants; however, studies assessing effects of integral fatty acids such as docosahexaenoic acid (DHA) on infant cognitive development demonstrate inconsistencies in their results. Also, the lack of follow-up trials during an age when more sensitive tools can be implemented, limits the understanding of the long-term effects of omega-3 fatty acids on specific domains of cognitive development. The purpose of this study is to conduct a follow-up trial of a randomized, double blind, controlled study conducted in Dhaka, Bangladesh in 2001, which assessed the effects of prenatal DHA supplementation on infant development. Although the original study found no significant difference between the treatment and placebo groups at 10 months of age of the infants, this proposed follow-up study will assess the effects of omega-3 fatty acid supplementation at 6 years of age of 150 children by implementing the Wechsler Preschool & Primary Scale of Intelligence – III (WPPSI-III), a sensitive and appropriate measure of cognitive functioning for this age group. The results of such a study will have implications on the effectiveness and necessity of dietary recommendations and intervention programs to counteract a major detriment to the advancement of underdeveloped nations.

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

Name	Professional Discipline/ Specialty	Role in the Project
1. Jena Hamadani	Pediatrics/child development	PI
2. Fahmida Tofail	Child development	Co-PI
3. Dr Iqbal Kabir	Nutrition	Co-I
4. Farhana Sharmeen	Psychology student	Student investigator

Description of the Research Project

Hypothesis to be Tested:

Concisely list in order, 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.

The children who received prenatal DHA will exhibit increased cognitive abilities compared to the placebo group who received prenatal soy oil.

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.

To determine long-term effects of Fish oil (ω-3 fatty acid) supplementation during pregnancy on verbal and problem solving abilities of preschool children.

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.

Micronutrient deficiencies remain an enormous problem leading to poor growth, anaemia, developmental delays, blindness and even death (Etcheverry et al. 2005), and many children in the developing countries are at risk of sub-optimal intake of micronutrients, including omega-3 polyunsaturated fatty acids (PUFAs), necessary for optimal brain and cognitive development, Individuals who consume inadequate energy, protein, vitamins, and minerals may be less able to metabolize long-chain (PUFAs) from dietary precursors, which in turn may compromise their optimal brain and cognitive development (Richardson and Puri 2000). The longer-chain omega-3 PUFA, docosahexaenoic acid (DHA) is an integral component of cell membranes and is most beneficial in the functioning of the central nervous system, and considered important to maintain an optimal state of neural membranes (Carlson and Neuringer 1999).

Studies have shown that vision, memory, and cognitive performance measures in early infancy are significantly affected by Omega-3 fatty acid deficiency in human pre-term infants (Kretchmer et al. 1996; Carlson 1993). Humans consume the ready form of DHA from marine fish oil, and young infants receive DHA through breast milk (Kurlak and Stephenson 1999; Clandinin et al. 1980). DHA is accrued in the fetal brain primarily during the last trimester of pregnancy and continues through early postnatal period (Wainwright 2000). A decline in maternal DHA status has also been observed in the later half of pregnancy, although research on the impact of prenatal DHA supplementation on infant development is limited (Hornstra 2000).

The study of DHA supplementation during pregnancy in developing countries is an important area of research because mothers from poorer nations tend to have low hepatic and adipose tissue stores of fatty acids due to chronic maternal undernutrition. Tofail et al (2006 in press) conducted a randomized, double blind, controlled study to assess the effects of prenatal DHA supplementation on infant development in Dhaka, Bangladesh, where serious health and nutrition problems,

characterized by half the population living below the poverty line exist. The study is a follow up of an intervention that aimed to improve pregnancy outcomes by supplementing women with fish oil during their last trimester of pregnancy. The sample population was chosen from a community in Dhaka city, where illiteracy, poverty, overcrowding, poor housing and poor hygiene are common. A house-to-house survey was conducted between January and March of 2000 and 400 eligible pregnant women at 25 weeks of gestation (based on first date of their last menstruation period) were enrolled, and were randomly assigned to the treatment or placebo group after obtaining informed consent.

Both the treatment and placebo group received fish oil and soy oil, respectively daily. Soy oil was selected as a control because of its common use in Bangladesh. Mothers in the treatment group took 4 one-gram capsules on a daily basis. The fish oil contained a ready form of the omega-3 fatty acids DHA and eicosapentaenoic acid (EPA). The soy oil capsules were also administered daily and were of equal quantity. The total daily supplement of fish oil contained 1.2 grams of DHA and 1.8 grams of eicosapentaenoic acid (EPA) and the daily dosage of soy oil capsules contained 2.25 grams of linoleic acid (LA) and 0.27 grams of lenolenic acid (LNA). The capsules were identical in appearance, and mothers were given clear instructions on taking them. The intervention period continued from 25 weeks of gestation until delivery. Of the 400 mothers, 249 infants were available for assessment at ten months post-partum. The infants (10 mos. $\pm$ 15 days), were brought to ICDDR,B: Centre for Health and Population Research and were tested in a quiet room in the presence of their mothers. Developmental assessments were conducted using the Bayley Scales of Infant Development II (BSID-II), which includes 2 subscales: mental developmental index (MDI), and psychomotor development index (PDI) (Bayley 1993). Also, infant's behavior, quality of stimulation at home, socio-economic status, and anthropometry measures were performed. The experimental and control groups were similar in parental schooling, paternal occupation, breast-feeding and socio-economic status except that mothers in the fish oil group were younger ($p<0.02$) and had fewer children ($p< 0.008$). MDI, PDI, behavior ratings, and the quality of psychosocial stimulation at home (HOME) (Caldwell 1967) were also similar in the two groups. There were also no significant group differences in any anthropometric measurements at birth or at 10 months. A multiple regression analysis, controlling for the possible confounders, found no difference between the DHA and soy oil samples. Age, quality of home stimulation and birth weight were significant predictors of MDI, while, sex, gestational age, mothers' BMI, presence of utilities at home, birth length and quality of home stimulation significantly predicted PDI (Tofail et al. 2006 in press).

Inconsistent and lack of significant results in assessing the effects of PUFAs on cognitive development may be due to the implementation of global measures insensitive to specific features of cognitive development as well as very little focus on the link between PUFAs and cognitive performance in children after infancy (Carlson and Neuringer 1999). The importance of continuing research on the health and developmental benefits and risks associated with omega fatty acids cannot be underestimated. Although there has been very little focus on the link between PUFAs and cognitive performance in children after infancy, there is some evidence that fatty acid metabolism may have implications on a cluster of neuro-developmental disorders, including attention deficit-hyperactivity disorder (ADHD), dyslexia, dyspraxia, and autism. The mechanism may be related to inefficiency in the synthesis of long-chain PUFAs from their precursors (Richardson and Ross 2000). Richardson et al. (2000) suggest that the clinical signs of PUFA deficiency (i.e. polydipsia, polyuria, dry scaly skin, and behavioral abnormalities) are also common in children with ADHD. Furthermore, long-chain PUFA deficiency, as evidenced in the plasma of boys with ADHD, has been found to correlate with a range of behavioral, learning, and health problems (Stevens et al. 1996). DHA, a long-chain omega-3 PUFA, maintains an optimal state of neural membranes, enabling membrane fluidity and thickness that in turn affects cell signaling (Uauy et al. 2001).

This study will assess the long-term effects of prenatal fish oil supplementation on the cognitive development of Bangladeshi children at 6 years of age. We hypothesize that relative to the children in the placebo group whose mothers received prenatal soy oil, those in the DHA group will exhibit increased cognitive abilities in the verbal and problem solving domains of the WPPSI-III (Wechsler 2002).

Conducting cognitive developmental research on a population suffering severe malnutrition is a great opportunity to address important health problems on an international scale. A nation can't progress if its people are being barred from receiving adequate nutrition and, therefore, from developing on a basic cognitive level. The results of a follow-up study assessing the long-term effects of omega-3 fatty acid supplementation will have implications about the form of and effectiveness of making specific dietary recommendations such as pharmaceutical supplementation, food fortification, or consumer education as a solution to the global problem of micronutrient deficiencies.

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.

Method

Participants

The original sample population was chosen from a community in Dhaka city, where illiteracy, poverty, overcrowding, poor housing and poor hygiene are common. Of the original population, it has been surveyed that approximately 150 of the children will still be available for assessment in the follow-up study. The Bangladeshi children will be 6 years old and will be recruited from the fish oil and soy oil cohorts.

Measures

The Wechsler Preschool & Primary Scale of Intelligence – III (WPPSI-III, Wechsler, 2002), created by David Wechsler, is one of the major instruments for assessing the cognitive abilities of young children. The WPPSI-III has two parts, the Verbal Scale and the Performance Scale and each of these scales has several subtests. The Verbal Scale measures language expression, comprehension, listening, and the ability to apply these skills to solving problems. The examiner gives the questions orally, and the child gives a spoken response. The Performance Scale assesses nonverbal problem solving, perceptual organization, speed, and visual-motor proficiency through the use of tasks like puzzles, analysis of pictures, imitating designs with blocks, and copying.

The WPPSI-III employs the Deviation IQ (M = 100, SD = 15) for the Verbal, Performance, and Full Scale IQs and scaled scores (M = 10, SD = 3) for the subtests. A raw score is first obtained on each subtest and then converted to a scaled score within the examinee's own age group through use of a table in the WPPSI-III manual. From ages 3 through 6.5 years, the reliabilities for Performance, Verbal, and Full Scale IQs range from 0.90 to 0.97. Also, the WPPSI-III has adequate test-retest reliabilities for each of the three IQs as well as construct, concurrent, and predictive validity for many types of normal and handicapped children in the age range from 4 to

6.5 years. The scale has already been modified and validated for use in Bangladeshi children by Prof. Frances Aboud in her earlier research (personal communication).

The Home Observation for Measurement of the Environment (HOME) Inventory (Caldwell, 1967) will be implemented to assess and control for the quality of emotional, social, and cognitive support available to the participants at home. The instrument has been modified for cultural content, and validated through pilot studies in several of projects conducted by Child Development Unit of Clinical Sciences Division at ICDDR,B. Participants will also be assessed for height, weight, mid-upper-arm circumference and head circumference using standard procedures (WHO, 1983).

Procedure

The participants will be assessed in a quiet testing room in the Child Development Unit of ICDDR,B. They will participate in the verbal and performance subtests of the WPPSI-III (Wechsler, 2002) under the supervision of their parent and upon informed parental consent. The tests will be conducted by the psychologist at Child Development Unit who is trained in performing the test. Their homes will also be visited to assess the quality of psychosocial stimulation at home (HOME) (Caldwell, 1967). HOME interview will be conducted by a SFRA at Child Development Unit who is also trained in this test and has conducted several such interviews in the previous projects of Child Development Unit.

We have estimated a total of 150 children who will be available for this follow-up. The WPPSI takes about 45 minutes and the HOME about 40 minutes. We have estimated that on average they can test 4-5 children everyday. To test 150 children we'd need about 30-40 working days. The duration of the project is about 2 months and we should be able to finish the tests by then.

Sample Size Calculation and Outcome Variable(s)

All available subjects out of 249 children whose mothers had participated and were randomized to receiving either fish-oil or soy-oil supplementation during pregnancy and assessed for developmental measures at the age of 10 months.

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 equipment that will be required for the study. For field studies, describe the field area including its size, population, and means of communications.

Child development unit of ICDDR,B has got all the required instruments available and there are rooms for testing. In addition the Unit members will help the conduct of the study.

Data Safety Monitoring Plan (DSMP)

All clinical investigations (biomedical and behavioural intervention research protocols) should include the Data and Safety Monitoring Plan (DSMP) to provide the overall framework for the research protocol's data and safety monitoring. It is not necessary that the DSMP covers all possible aspects of each elements. When designing an appropriate DSMP, the following should be kept in mind.

a) All investigations require monitoring;
b) The benefits of the investigation should outweigh the risks;
c) The monitoring plan should commensurate with risk; and
d) Monitoring should be with the size and complexity of the investigation.

Safety monitoring is defined as any process during clinical trails that involves the review of accumulated outcome data for groups of patients to determine if any treatment procedure practiced should be altered or not.

Study questionnaires will be recorded on paper forms, which will be kept in a secure facility under the responsibility of the Principal Investigator of this study. All questionnaires and data forms will be reviewed for inconsistencies and missing data points. Edited data will be entered on to a personal computer using Microsoft Access data base specifically designed for this project.

Data Analysis

Describe plans for data analysis. Indicate whether data will be analyzed by the investigators themselves or by other professionals. Specify what statistical software 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.

Analysis
To examine the treatment effect, a series of analyses of covariance will be conducted to determine if the IQ scores differ significantly between treatment groups, controlling for potential confounding variables such as socio-demographic characteristics, home environment, and sex. The significance level will be set at $p<0.05$, two-tailed, for all hypothesis contrasts.

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.

Approval of the Ethical Review Committee of ICDDR,B will be sought for the study.
This study is non-invasive. Subjects will be assigned study identification numbers and their identities will be protected during data analysis and study reporting. There is no benefit or risk to subjects, but information from this study may help shape future nutritional interventions for children in Bangladesh.
Written informed consent of one of the parents will be obtained after thorough explanation of the purpose of the study, requirements of participation, study procedures, and the risks and benefits to the child. Another person will be acting as witness at the time of consent signing.
Some of the information collected may be considered sensitive in nature. Therefore, measures will be taken to ensure strict confidentiality of the information obtained.

Use of Animals

Describe in the space provided the type and species of animals 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.

NA

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.

Bayley N. Bayley scales of infant development.3rd ed. San Antonio, TX: The Psychological Corporation (1993).

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Etcheverry, P., Griffin, I.J., Abrams, S.A. (2005). Micronutrient deficiencies: New solutions to a seemingly irresolvable problem. Harvard Health Policy Review, 6(1), 2005.

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Richardson, A.J., Ross, M.A. (2000). Fatty acid metabolism in neurodevelopmental disorder: a new perspective on associations between attention-deficit/hyperactivity disorder, dyslexia, dyspraxia and the autistic spectrum. Prostaglandins Leukot EssentFatty Acids, 63, 1–9.

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Stevens, L.J., Zentall, S.S., Abate, M.L., Kuczek, T., Burgess, J.R. (1996). Omega-3 fatty acids in boys with behaviour, learning, and health problems. Physiological Behavior, 59, 915–920.

Uauy, R., Calderon, F., Mena, P.(2001). Essential fatty acids in somatic growth and brain development. World Rev Nutr Diet, 89, 134–160.

Wainwright, P. (2000). Invited commentary, Nutrition and behavior: the role of n-3 fatty acids in cognitive function. British Journal of Nutrition, 83, 337-339.

Wechsler, D, (2002). Wechsler preschool and primary scale of intelligence. San Antonio, TX: Psychological Corp.

World Health Organization (1983) Measuring change in nutritional status. Guideline for assessing nutritional impact of supplementary feeding programme for vulnerable groups. Geneva: World Health Organization.

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 the People's Republic of Bangladesh through a training programme.

The student investigator plans to present results in undergraduate thesis paper at Harvard University. Moreover the results of the study will be presented at the national, regional and international conferences and will be published in peer-reviewed journals.

Collaborative Arrangements

Describe briefly if this study involves any scientific, administrative, fiscal, or programmatic arrangements with other national or international organizations or individuals. Indicate the nature and extent of collaboration and include a letter of agreement between the applicant or his/her organization and the collaborating organization.

This is a collaborative study concerning child development unit of ICDDR,B and the Harvard University, where the PI of the project is the mentor of the student from Harvard University.

Biography of the Investigators

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

(Note: Biography of the external Investigators may, however, be submitted in the format as convenient to them)

1 Name: Dr. Jena D. Hamadani

2 Present Position: Associate Scientist

3 Educational background:
(last degree and diploma & training relevant to the present research proposal)

PhD in Child Development; 2004, MBBS; 1984

4.0. List of ongoing research protocols
(start and end dates; and percentage of time)

As Principal Investigator

Protocol Number	Starting date	End date	Percentage of time
Head of Child Development Unit at ICDDR,B.	November, 2001	31 October, 2006	20

4.1. As Co-Principal Investigator

Protocol Number	Starting date	End date	Percentage of time
2003-033	March 2005	December 2007	10
2004-052	March 2005	December 2007	20

4.2. As Co-Investigator

Protocol Number	Starting date	Ending date	Percentage of time
2003-023	AUG 2003	JUL 2006	10

5 Publications

Types of publications	Numbers
a) Original scientific papers in peer-review journals	25
b) Peer reviewed articles and book chapters	
c) Papers in conference proceedings	3
d) Letters, editorials, annotations, and abstracts in peer-reviewed journals	12
e) Working papers	1
f) Monographs	1

6 Five recent publications including publications relevant to the present research protocol

1) Hamadani JD, Huda SN, Khatun F, Grantham-McGregor SM. Psychosocial Stimulation Improves the Development of Malnourished Children In Rural Bangladesh. Submitted to Journal of Nutrition on 26th March 2006.

2) **Hamadani JD.** Effect of psychosocial stimulation on mental development and behaviour of malnourished children. ICDDR,B's Health and Science Bulletin 2005 Dec;3(4):5-10.

3) Hamadani JD, Khatun F, Huda SN, Grantham McGregor SM. Effects of psychosocial stimulation on development and behaviour of malnourished children in Bangladesh. Trans Royal Soc Trop Med Hyg 2005:99, 947.

4) Hamadani JD, Fuchs GJ, Osendarp SM, Huda SN, Grantham-McGregor SM. Zinc supplementation during pregnancy and effects on mental development and behavior of infants: a follow-up study. Lancet. 2002;360(9329):290-4.

5) Hamadani JD, Fuchs GJ, Osendarp SM, Khatun F, Huda SN, Grantham-McGregor SM. Randomized controlled trial of the effect of zinc supplementation on mental development of Bangladeshi infants. Am Clin Nutr. 2001;74:381–6.

Biography of the Investigators

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

(Note: Biography of the external Investigators may, however, be submitted in the format as convenient to them)

1 Name: Dr. Fahmida Tofail

2 Present Position: Assistant scientist/Senior Medical Officer

3 Educational background:
(last degree and diploma & training relevant to the present research proposal)

PhD, Child Health (Field Child Development and Nutrition), Institute of Child Health, University College London (UCL), UK; Jan 2005
MBBS (Mymensingh Medical College, Dhaka University, Bangladesh); Jan 1992

4.0 List of ongoing research protocols
(start and end dates; and percentage of time)

4.1. As Principal Investigator

4.2. As Co-Principal Investigator (PI of Child Development Part)

Protocol Number	Starting date	End date	Percentage of time
2002-031	Oct, 2002	Dec, 2004	Full time as a PhD student
2000-002	Jan, 2001	Sep, 2001	10%

4.3. As Co-Investigator

Protocol Number	Starting date	Ending date	Percentage of time
2003-023	AUG 2003	JUL 2006	10

5 Publications

Types of publications	Numbers
a. Original scientific papers in peer-review journals	5
b. Peer reviewed articles and book chapters	
c. Papers in conference proceedings	
d. Letters, editorials, annotations, and abstracts in peer-reviewed journals	7
e. Working papers	
f. Monographs	1

6 Five recent publications including publications relevant to the present research protocol

1) **Tofail F**. PhD Thesis on "Effect of food and micronutrient supplementation during pregnancy on subsequent development of infants in Bangladesh: A randomized trial", January, 2006.
2) **Tofail F**, Kabir I, Hamadani JD, Chowdhury F, Yesmin S, Mehreen F, Huda SN. Fish Oil and Soy Oil Supplementation during Pregnancy and Infant's Psychomotor Development. Accepted by JHPN, 2006
3) Osendarp SJM, Fuchs GJ, van Raaj JMA, Mahmud H, **Tofail F,** Black RE, Prabhakar H, Santosham M. The effect of zinc supplementation during pregnancy on immune response to Hib and BCG vaccines in Bangladesh. J Trop Ped, Advance Access, April, 2006.
4) Yesmin S, Mehrin F, Hilaly A, Irfan LD, Hamadani JD, Huda SN, **Tofail F**. Association of Malnutrition with Mental, Motor and Behaviour Development in Bangladeshi Infants. Published in the Proceedings of the 2nd World Congress on Childhood disabilities in December, 2005.
5) **Tofail F**, Huda SN, Hamadani JD, Kabir I, Chowdhury F, Mehrin F, Yesmin S, Grantham McGregor S. Factors associated with child development in Bangladeshi infants. Poster presented at 'Research in progress' at Royal Society of Tropical Medicine and Hygiene- in London, December, 2004.

Biography of the Investigators

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

(Note: Biography of the external Investigators may, however, be submitted in the format as convenient to them)

1 Name: Dr. Iqbal Kabir

2 Present Position: Scientist

3 Educational background:

(last degree and diploma & training relevant to the present research proposal)

PhD

4.0 List of ongoing research protocols

(start and end dates; and percentage of time)

4.1 As Principal Investigator

Protocol Number	Starting date	End date	Percentage of time

4.2. As Co-Principal Investigator

Protocol Number	Starting date	End date	Percentage of time

4.3. As Co-Investigator

5 Publications

Types of publications	Numbers
a. Original scientific papers in peer-review journals	64
b. Peer reviewed articles and book chapters	4
c. Papers in conference proceedings	3
d. Letters, editorials, annotations, and abstracts in peer-reviewed journals	67
e. Working papers	0
f. Monographs	1

6 Five recent publications including publications relevant to the present research protocol

- Hossain MS, Salam MA, Rabbani GH, Kabir I, Biswas R, Mahalanabis D. Rice-ORS versus glucose-ORS in management of severe cholera due to Vibrio cholerae O139 Bengal: a randomized, controlled clinical trial. J Health Popul Nutr. 2003 Dec;21(4):325-31.

- Hossain MS, Salam MA, Rabbani GH, Kabir I, Biswas R, Mahalanabis D. Tetracycline in the treatment of severe cholera due to Vibrio cholerae O139 Bengal. J Health Popul Nutr. 2002 Mar;20(1):18-25.

- Haider R, Kabir I, Huttly SR, Ashworth A. Training peer counselors to promote and support exclusive breastfeeding in Bangladesh. J Hum Lact. 2002 Feb;18(1):7-12.

- Iqbal Hossain M, Yasmin R, Kabir I. Nutritional and immunisation status, weaning practices and socio-economic conditions of under five children in three villages of Bangladesh. Indian J Public Health. 1999 Jan-Mar;43(1):37-41.

- Mazumder RN, Ashraf H, Hoque SS, Kabir I, Majid N, Wahed MA, Fuchs GJ, Mahalanabis D. Effect of an energy-dense diet on the clinical course of acute shigellosis in undernourished children.
- Br J Nutr. 2000 Nov;84(5):775-9.

Biography of the Investigators

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

(Note: Biography of the external Investigators may, however, be submitted in the format as convenient to them)

1 Name: Farhana Sharmeen

2 Present Position: Psychology student

3 Educational background:

(last degree and diploma & training
relevant to the present research proposal)

AB honors degree in Psychology expected in June '07 at Harvard University
Class of 2003. College preparatory curriculum with Advanced Placement courses. GPA 4.3 on a 4.0 scale at Boston Latin School.

4.0 List of ongoing research protocols

(start and end dates; and percentage of time)

None.

Budget Justifications

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

No budget is required for the project. The student investigator will bear the day to day expenses through her university, while child development unit will support her by providing an office, research tools, and expert staff to conduct the tests. The mothers and their children will receive transportation cost plus a toy for the child.

Personnel	Position	no. of staff	Effort%	Salary/mo	1st year	
					Months	Amount US$
PI- Dr. Jena Hamadani	NC-11	1	0.03	1,944	2	116.6
Co-investigator-Dr. Fahmida Tofail	NB-4	1	0.03	1,203	2	72.2
Doctoral student		1	1.00			-
Tester	GS-3	1	0.50	307	2	307.0
Interviewer for HOME	GS-3	1	0.50	307	2	307.0
Field worker	sp level	2	1.00	70	2	280.0
Sub Total						**1,082.8**
	No. of trips	No. of cases		Rate/ trip		
Local Travel						
Transport for bringing the children for Bayley test	1	150		1.5		225.0
Transport for visiting children's home	2	150		0.5		150.0
Sub Total						**150.0**
Equipments						
Computer and its accessories						1,500.0
Anthropomtric equipment						500.0
WPPSI kit						1,000.0
Sub Total						**3,000.0**
Supplies						
Toys for children		150.0		0.5		75.0
Office supply						50.0
Refreshments for mothers/children during tests		150		1		150.0
Subtotal						**275.00**
Total cost required for the project						**4,657.8**

Other Support

Describe sources, amount, duration, and grant number of all other research funding currently granted to PI or under consideration.

All the investigators work at ICDDR,B and are members of Clinical Sciences Division. They are also investigators of other projects.

Appendices

Appendix 1: Voluntary Consent Form

International Centre for Diarrhoeal Disease Research, Bangladesh
Voluntary Consent Form

Title of the Research Protocol: **Long-term Effects of Prenatal Omega-3 Fatty Acid Supplementation on Child Development in Bangladeshi Children**

Principal Investigator: **Jena D. Hamadani**

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.

Name of participant: _____ Age: Sex:

Please feel free to ask any questions you may have about this study and the information given below. You will be given an opportunity to ask questions, and your questions will be answered.

International Centre for Diarrhoeal Disease Research is conducting a research to evaluate the effect of Fish-oil supplementation during pregnancy on mental development of children at 6 years of age.

Purpose of research:
To examine the long-term effects of fish oil supplementation during pregnancy on children's mental development.

Why selected:
You participated in a study approximately 6 years ago when you were pregnant in which you took either fish oil or soy oil capsule. Your child then participated in a follow-up of the study when we measured her/his mental development at 10 months of age. We now would like to assess the mental development of your child at 6 years of age.

Procedures:
If you decide for your/your child's participation in the study, the following would be done:

Growth and developmental assessment
We would like to test your child's mental development by asking her/him some questions and showing her/him some pictures and puzzles which will take about one hour. We will bring your child to our hospital at the age of six years for this test and also measure your child's height and weight.

Home visit
We shall also visit your home to collect information on your living condition, ask some questions about your child's activities at home.

Risks and benefits:
1. Risks: There is no risk to you/your child from this examination/interview.
2. Benefits: your child will enjoy participating in this study and going through the test which is quite fun. In addition we'll give a toy to your child. By participating in this study you and your child will be contributing to the development of science. However, please note that usually the results of the study will not be shared with you, unless you are interested to know or if there is something that should be further evaluated for your child's welfare.

Right not to participate and withdraw:

You/your child are participating in the study voluntarily. You/your child would have the right to refuse to answer any or all questions and also withdraw your consent at any time during the study without showing any cause thereof. You are at liberty to consent to either or both of the measurements but it may not be useful to collect either of measurements without the other

Costs:

We would provide cost for your child's transportation from home to the hospital where we will do the test, and therefore there should be no costs to you/your child for being part of this study.

Confidentiality:

Your/your child's research records will be kept private to the extent allowed by law. The research records and answer sheets will contain information on your child's name and address. However, this information is kept in a locked, secured space. No one other than the researchers will have access to this material. We will use this information only to contact you about the investigation. Your child's name will not be used in any reports or articles that are written about the results of this study.

Questions:

You can ask any questions you have about the study or about your rights. If you have other questions later, you can contact:

Dr. Jena D. Hamadani, CSD, ICDDR, B. Tel 8860523-32, Ext-2331

If you have questions about being part of a research study or you think some harm has been done to you because of the study, you can contact:

Mr. Bejoy Ratan Saha, Committee Co-ordination Secretariat, ERC, ICDDR, B. Tel: 02-8860523-32, Ext-3508

Declaration by the participant:

The investigator(s) of the research project have explained to me the purpose, procedures, risk and benefits of this study; my rights as the study participant; and on confidentiality of my child's medical and personal information. I agree to my child's participation in this study, and I understand that I may end participation at any time, without showing any reason thereof. I agree to the conditions described, and give consent for the

Please tick: Hospital test ☐ Home visit ☐ Both ☐

Guardian's signature/left thumb impression: _____ Date:

Signature of witness/left thumb impression: _____ Date:

Signature of Investigator: _____ Date:

Appendix 1: Voluntary Consent Form

AvŠ:RwZK D`ivgq M‡elYv †K›` (AvB wm wW wW Avi, we), XvKv, evsjv‡`k
‡¯”Qvq AskMn‡Yi AbgwZ cÎ
wcZvgvZv/Awf fveK‡`i AbgwZ cÎ
Voluntary Consent Form in Bengali

Title of the Research Protocol: **Long-term Effects of Prenatal Omega-3 Fatty Acid Supplementation on Child Development in Bangladeshi Children**

Principal Investigator: **Jena D. Hamadani** cavb M‡el‡Ki bvg t Wvt ‡Rbv nvgv`vbx

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.

M‡elYv cK‡íi wk‡ivbvg t evsjv‡`kx wkï‡`i weKv‡k Mfve¯vq I‡gMv-3 d¨wU GwmW Mn‡bi `xN‡gqv`x cfve

AskMnbKvixi bvg ---------- eqm: wj½:

AbMnceK GB M‡elYv m¤ú‡K Ges wb‡æv³ Z_¨vejx m¤ú‡K Avcbvi wKQ Rvbvi _vK‡j †Kvb iKg wØav bv K‡i ck Ki“b| Avcbv‡K ck Kivi m‡hvM †`qv n‡e Ges Avcbvi mKj c‡ki DËi †`qv n‡e|

AvŠ:RwZK D`ivgq M‡elYv †K›` (AvB wm wW wW Avi, we) GKwU M‡elYv cwiPvjbv Ki‡Z hv‡”Q †hLv‡b MfKvjxb Ae¯vq †hme gv‡qiv gv‡Qi †Zj †L‡qwQ‡jb Zv‡`i 6 ermi eqmx wkïi ew× weKv‡ki Dci Gi cfve cix¶v Kiv n‡e|

M‡elYvi D‡Ïk¨
Mfve¯vq gv‡q‡`i gv‡Qi †Zj Lvlqvi d‡j wkïi gvbwmK weKv‡k `xN †gqv`x cfve cix¶v Kiv|

Avcbvi wkï‡K †Kb GB M‡elYvq wbewPZ Kiv n‡q‡Q t
Avbgwb bK 6 ermi Av‡M Mfve¯vq Avcwb GB M‡elbvq AskMnb K‡iwQ‡jb †hLv‡b Avcbv‡K gv‡Qi †Zj A_ev mqweb †Zjh³ K¨vcmj Lvlqv‡bv n‡qwQj| AZ:ci Avcbvi wkï GB M‡elbvi d‡jv Av‡c AskMnb K‡iwQj †hLv‡b Avgiv Avcbvi wkï‡K 10 gvm eq‡m ew× weKv‡ki Rb¨ cix¶v Kwi| GLb Avgiv Avcbvi wkïi 6 ermi eq‡m cbivq ew× weKv‡ki cix¶v Ki‡Z AvMnx|

c×wZ
Avcwb/ Avcbvi wkï GB M‡elYvq AskMnb Ki‡j wb‡æv³ KvR¸‡jv Kiv n‡e:

wkïi weKvk Ges ew× cwigvc
Avgiv Avcbvi ev”Pv‡K wKQ ck wRÄvmv K‡i, wKQ Qwe Ges avavi †Ljv †`wL‡q Zvi ew× cix¶v Kie hv‡Z Avbgwb bK 1 N›Uv mgq jvM‡e| GB D‡Ï‡k¨ Avgiv Avcbvi wkï‡K 6 eQi eq‡m nvmcvZv‡j G‡b ew× cix¶v Ki‡ev Ges Zvi IRb I D”PZv gvc‡ev|

evox cwi`kb
M‡elYvi Ask wnmv‡e Avgiv Avcbvi cwiewiK Ae¯v m¤ú‡K Z_¨ msM‡ni Rb¨ Avcbvi evox‡Z mv¶vr Ki‡ev Ges evox‡Z Avcbvi wkïi wewfb KvhKjvc m¤ú‡K wKQ ck wR‡Äm Kie|

Avcbvi SwK Ges DcKvixZv
1) SwKmgn: GB cix¶v/mv¶vrKvi †_‡K Avcbvi/Avcbvi wkïi †Kvb ai‡bi ¶wZi m¤vebv bvB|

2) DcKvixZv: Avcbvi wkï GB M‡elYvq AskMnb K‡i Le Avb›` cv‡e Ges cix¶v PjvKvjxb mgqUv Le gRvi n‡e| GQvov Avcbvi wkï‡K GKwU †Ljbv †`qv n‡e| GB M‡elbvq AskMnb K‡i Avcwb/Avcbvi wkï weÄv‡bi AMMwZ‡Z ¸i“ZcY fwgKv ivL‡eb| wKš GKwU wel‡q g‡b ivL‡eb, mvavibZ M‡elYvi djvdj Avcbv‡`i‡K Rvbv‡bv nqbv hw` bv Avcbviv Rvb‡Z AvMnx nb A_ev Avcbv‡`i wkïi Kj¨v‡Yi Rb¨ hw` †Kvb wKQ AwZwi³ gj¨vqb Kivi c‡qvRb nq|

AskMnb bv Kivi A_ev cZ¨vnvi Kivi AwaKvi
Avcwb Ges Avcbvi wkïi GB M‡elYvq †¯”Qvq AskMnb Ki‡Qb| Avcbvi/Avcbvi wkïi cY AwaKvi Av‡Q Avgv‡`i ‡h†Kvb c‡ki A_ev me¸‡jv c‡kiB DËi bv †`qvi Ges †Kvb Kvib bv †`wL‡q †h‡Kvb mgqB M‡elYvi ‡_‡K Avcbvi AskMnb cZ¨vnvi Kivi| Avcbvi cY ¯vaxbZv Av‡Q Dfq A_ev †h‡Kv‡bv GKwU cix¶vq AskMnb Kivi, wKš GKwU Qvov Ab¨wU‡Z AskMnb Ki‡j †Zgb †Kvb Kv‡R Avm‡ebv|

LiP t
Avcbv‡K/Avcbvi wkï‡K ewo ‡_‡K nvmcvZv‡j Avmv hvIqvi Rb¨ hvZvqvZ fvov †`qv n‡e Kv‡RB GB M‡elYvq AskMn‡bi Rb¨ Avcbv‡K/Avcbvi wkï‡K †Kvb LiP w`‡Z n‡e bv|

†Mvcbxqvi t
Avcbvi/Avcbvi wkïi cix¶‡Yi djvdj msµvšZ Z_¨vejx AvBbvbhvqx †Mvcb ivLv n‡e| M‡elYvi †iK‡W Ges DËic‡Î Avcbvi wkïi bvg Ges wVKvbv msµvšZ Z_¨vejx Av‡Q| Z‡e †mB Z_¨vejx Zvjve× fv‡e, wbivc` ¯v‡b ivLv n‡e| M‡elK Qvov Ab¨ †KD GB Z_¨ e¨envi Ki‡Z cvi‡ebv| ïagvÎ M‡elbv msµvšZ Kvi‡Y Avcbvi mv‡_ †hvMv‡hvM Kivi Rb¨ GB Z_¨ejx e¨envi Kiv n‡e| M‡elYvi djvdj msµvšZ wi‡cv‡U Avcbvi/Avcbvi wkïi bvg I cwiwPwZ e¨envi Kiv n‡ebv|

ckvejx t
Avcwb GB M‡elYv msµvš welq A_ev Avcbvi/Avcbvi wkïi AwaKvi m¤c‡K †h †Kvb ck Ki‡Z cv‡ib| hw` cieZx‡Z Avcbvi †Kvb ck _v‡K Z‡e wbæwjwLZ e¨w³i mv‡_ †hvMv‡hvM Ki‡Z cv‡ib |
Wvt ‡Rbv wW nvgv`vbx, wm Gm wW, AvB wm wW wW Avi we, †dvb - 8860523-32 G · ‡Ubkb 2331
M‡elYvq Ašf³ e¨w³ wnmv‡e hw` Avcbvi †Kvb ck _v‡K A_ev Avcwb hw` g‡b K‡ib †h GB M‡elYvi Kvi‡b Avcbvi †Kvb ¶wZ n‡q‡Q ‡m‡¶‡Îl Avcwb wbæwjwLZ e¨w³i mv‡_ †hvMv‡hvM Ki‡Z cv‡ib|
Rbve weRq iZb mvnv, KwgwU mgšq ‡m‡µUvix, B, Avi, wm - AvB, wm, wW, wW, Avi, we| †dvb - 8860523-32 G · ‡Ubkb - 3508
AskMnbKvixi weewZ
GB M‡elYvi D‡Ïk¨, c×wZ, SwK, DcKvixZv; AskMnbKvix wnmv‡e Avgvi AwaKvi; Ges Avgvi mšv‡bi †gwWK¨vj Ges e¨w³MZ Z_¨vejxi †Mvcbxqvi m¤ú‡K we¯ZwiZfv‡e Avgv‡K ewS‡q ejv n‡q‡Q| Awg Avgvi mšvb‡K GB M‡elYvq AskMnb Ki‡Z w`‡Z ivRx AwQ Ges Awg eS‡Z cviwQ †h †Kvb ai‡bi KviY bv †`wL‡q †h‡Kvb mg‡q Avgvi AskMnY cZ¨vLvb Ki‡Z cwi| Awg wb‡æv³ wel‡qi mv‡_ GKgZ Ges Abgwz c`vb KiwQ

AbMn K‡i wUK (√) †`b :nvmcvZvj †U÷ /__/ , evox cwi`kb /__/, DfqB /__/----------ZwiL

Awffve‡Ki ¯v¶i/evg e×v½wji Qvc ---------- ZwiL

mv¶xi ¯v¶i/evg e×v½wji Qvc ---------- ZwiL

M‡el‡Ki ¯v¶i ---------- ZwiL

Appendix 2: Comments of External Reviewers
External review is waived.

Appendix 3: Response to External Reviewer's Comments
External review is waived.

Appendix 4: Abstract Summary covering eight points specified by the ERC

INFORMATION TO INCLUDE IN ABSTRACT SUMMARY

The Committee will not consider any application, which does not include an abstract summary. The abstract should summarize the purpose of the study, the methods and procedures to be used, by addressing each of the following items. If an item is not applicable, please note accordingly:

Global micronutrient deficiency, known as the "hidden hunger," has imposed detrimental consequences in developing countries. Specifically, omega-3 fatty acids directly affect the neurodevelopment and cognitive functioning of infants; however, studies assessing effects of integral fatty acids such as docosahexaenoic acid (DHA) on infant cognitive development demonstrate inconsistencies in their results. Also, the lack of follow-up trials during an age when more sensitive tools can be implemented, limits the understanding of the long-term effects of omega-3 fatty acids on specific domains of cognitive development. The purpose of this study is to conduct a follow-up trial of a randomized, double blind, controlled study conducted in Dhaka, Bangladesh in 2001, which assessed the effects of prenatal DHA supplementation on infant development. Although the original study found no significant difference between the treatment and placebo groups at 10 months of age of the infants, this proposed follow-up study will assess the effects of omega-3 fatty acid supplementation at 6 years of age of 150 children by implementing the Wechsler Preschool & Primary Scale of Intelligence – III (WPPSI-III), a sensitive and appropriate measure of cognitive functioning for this age group. The results of such a study will have implications on the effectiveness and necessity of dietary recommendations and intervention programs to counteract a major detriment to the advancement of underdeveloped nations.

1. *Describe the requirements for a subject population and explain the rationale for using in this population special groups such as children, or groups whose ability to give voluntary informed consents may be in question.*

   Inclusion criteria: Children who participated in the study at the age of 10 months and whose mothers participated in the study approximately 6 years ago during pregnancy.

   Exclusion criteria:
   a) Children with any obvious physical or mental disability.
   b) Lack of parental consent

2. *Describe and assess any potential risks – physical, psychological, social, legal or other – and assess the likelihood and seriousness of such risks. If methods of research create potential risks, describe other methods, if any, that were considered and why they will not be used.*

   There are no known physical, pyschological, social, legal or other risks known to the participants in this study. A simple test will be used to assess children's performance

and verbal IQ by showing them puzzles and asking them some questions. Children usually enjoy participating in this test. Children's anthropometry will be measured which is an easy method. A simple questionnaire will be used to interview mothers and observe the mother-child interaction.

3. *Describe procedures for protecting against or minimizing potential risks and an assessment of their likely effectiveness.*

   The procedures to be employed in the study do not involve any risk to the study participants

4. *Include a description of the methods for safeguarding confidentiality or protecting anonymity.*

   As soon as subjects are enrolled, they will be assigned a study identification number on their consent form. This number will be coded on all the measurement forms. Consent forms will be stored under lock and key in the investigator's office.

5. *When there are potential risks to the subject, or the privacy of the individual may be involved, the investigator is required to obtain a signed informed consent statement from the subject. For minors, informed consent must be obtained from the authorized legal guardian or parents of the subject. Describe consent procedures to be followed including how and where informed consent will be obtained.*

   Parents mostly mothers of the children will be given the consent form to read. If the mothers are illiterate, the consent form will be read for them by the research assistant in presence of a witness. Once the mother fully understands all the points mentioned in the consent form, she will be asked to sign or give her left thumb impression on the form. Her signing will be fully voluntary and she will not be compelled to do so.

   a) *If signed consent will not be obtained, explain why this requirement should be waived and provide an alternative procedure:*

      Consent form would be used

   b) *If information is to be withheld from a subject, justify this course of action:*

      No information would be withheld from the participants

   c) *If there is a potential risk to the subject or privacy of the individual is involved in any particular procedure include a statement in the consent form stating whether or not compensation and/or treatment will be available*

      Not applicable since the study including its procedures do not involve any risk.

6. *If study involves an interview, describe where and in what context the interview will take place. State approximate length of time required for the interview.*

   Interviews will take place at home and will last approximately 45 minutes. Measurements of anthropometry and performance and verbal IQ will take place in the Child Development Unit's office at Dhaka hospital of ICDDR,B and will take

approximately 45 minutes.

7. *Assess the potential benefits to be gained by the individual subject as well as the benefits, which may accrue to society in general as a result of the planned work. Indicate how the benefits outweigh the risks.*

   There is no direct benefit to the individual subject. However, the general benefit to society will be a better understanding of effects of fish oil during pregnancy on children's development. Moreover, the children usually enjoy participating in the study.

8. *State if the activity requires the use of records (hospital, medical, birth, death or other), organs, tissues, body fluids, the fetus or the abortus.*

   Not applicable

   The statement to the subject should include information specified in item 2,3,4,5(c) and 7 as well as indicating the approximate time required for participation in the activity.

Check-List

CHECK-LIST FOR SUBMISSION OF RESEARCH PROTOCOL FOR CONSIDERATION OF RESEARCH REVIEW COMMITTEE (RRC)
[Please check (X) appropriate box]

1. Has the proposal been reviewed, discussed and cleared at the Division level?

   Yes ☒ No ☐

   If No, please clarify the reasons:

2. Has the proposal been peer-reviewed externally?

   Yes ☐ No ☒

   If the answer is 'No', please explain the reasons: Has been requested for waiving external review for time constrain

   If yes, have the external reviews' comments and their responses been attached

   ☐ No ☒

Yes

3. Has the budget been cleared by Finance Department?

   Yes ☐ No ☒

   If the answer is 'No', reasons thereof be indicated: Not required

4. Does the study involve any procedure employing hazardous materials, or equipments?

   Yes ☐ No ☒

   If 'Yes', fill the necessary form.

_____ _____

Signature of the Principal Investigator Date