

PD-A BW-854

Trip Report

Bangladesh: JiVita

August 9-20, 1999

Keith P. West Jr., Dr.P.H.
Professor

Parul Christian, Dr.P.H.
Assistant Scientist

**Johns Hopkins School of Public Health
Baltimore, MD**



This trip was undertaken as a research activity under Cooperative Agreement No. HRN-A-00-97-00015-00 between the Center for Human Nutrition, Johns Hopkins School of Public Health, Baltimore, MD and the Office of Health and Nutrition, US Agency for International Development, Washington DC.

Report submitted September 8, 1999

BEST AVAILABLE COPY

Purpose

The purpose of this trip to Bangladesh was to advance preparations for the large JiVitA maternal vitamin A and micronutrient supplementation trial, due to begin by October 1, 2000. Specifically, we were to:

- (1) meet with Mission representatives to update them on progress and plans for the trial (and thank them for their support);
- (2) meet with the National Technical Review Committee to resolve any outstanding issues in order to secure a timely approval of the JiVitA protocol;
- (3) submit the protocol for ethical review by the Bangladesh Medical Research Council;
- (4) continue building the study organization, in terms of personnel, facilities, structure, other resources, and esprit de corps among our partner agencies in-country;
- (5) review and adjust the budget to fit within the financial limits for the CA beginning FY 00; and
- (6) develop a new timeline for starting up the study.

Dr. West was in-country from August 9-20; Dr. Christian was in-country from August 9-17, 1999.

Accomplishments

1) Meetings with USAID Mission Representatives

A very productive briefing was held with Matt Friedman and Molly Mort in the Health and Population Office at the Mission on August 11. We outlined our planned scope of work for the present trip and provisional timetable leading up to the planned start-up of the trial around this time next year, and thanked the Mission for its recent financial support provided to our CA in support of the JiVitA trial. We discussed possible mechanisms for importing equipment and vehicles into country duty-free and the need for us to formally request a waiver to purchase non-American 4WD vehicles (we will need 3) and motorcycles (we will need ~30 of these). Before departing Dhaka, I spoke with Molly and Matt separately by phone to keep them informed of our progress.

Next Steps: Our next series of steps are to gather prices of specific vehicle models from Toyota dealerships in Dhaka and pass these prices onto the Dhaka Mission, draft

letters that request a waiver from USAID/W to purchase Toyota Landcruisers for JiVitA.

2) National Technical Review Committee

Once GOB representatives learned of our arrival in-country through our main counterpart, BIRPERHT, the Line Director for the National Nutrition Programme within the Directorate of Health Services and Member Secretary of the National Committee, Prof Mamunar Rashid, organized the 3rd convening of the National Technical Committee on Thurs, August 12 at the Institute of Public Health Nutrition. The Committee last met on July 21 at which time most technical questions about the study were satisfactorily addressed (*Appendix A*). We had prepared a summary, with references, of evidence on the safety of the proposed vitamin A dose of 1000 ug retinol equivalents. The document (*Appendix B*) was circulated to all committee members by BIRPERHT 3-4 weeks before that meeting. After some discussion, the proposed dosage of vitamin A was cleared as acceptable and safe. The only outstanding issues remaining after the July meeting were questions about the dosages of vitamin C (we proposed 100 mg, or about 1.5 times the RDA for pregnancy but approximately the RDA during lactation, in the US) and iron (we proposed 60 mg per day, following regional, WHO and INACG guidelines). The committee felt that both dosages were too high.

At the August 12 meeting, further discussions were held about vitamin A, after which attention turned to the nutrients in question, and by its association with iron with respect to optimizing absorption, zinc. Minutes of this meeting are attached (*Appendix C*).

In response to member concerns, it was agreed that the concentration of vitamin C in the multinutrient supplement would be lowered to 70 mg, a level that also corresponds to the amount of vitamin C provisionally recommended at a meeting on antenatal micronutrient supplementation formulation held at UNICEF, New York on July 9, 1999. After some discussion about iron and zinc, and in light of a recommendation to lower iron to 30 mg and zinc to 15 mg at the UNICEF meeting, it was also agreed that the JiVitA micronutrient supplement would be limited to 30 mg of elemental iron and 15 mg of zinc. With these changes in place, the committee formally approved the formulation of the proposed micronutrient supplement and the technical aspects of the trial. The formula for the micronutrient supplement, which was originally patterned after that currently in use in NNIPS-3, resembles a compromise among the NNIPS-3 and proposed UNICEF formulations, and that represents responses to specific concerns of the national committee. A table that lists the present RDA values the US and India, micronutrient contents of certain leading brands of antenatal supplements, the NNIPS-3 supplement currently being provided to women in one arm of that trial and the proposed JiVitA supplement is given in *Appendix D*.

Next Steps: Formal approval from the national committee was expected by the end of August or early September. Following this, there will be no further need for a technical review of the protocol; however, the national committee will likely be a standing committee throughout the duration of JiVitA, meeting periodically to review its progress and provide guidance.

3) Protocol Review by the Bangladesh Medical Research Council (BMRC)

The Member Secretary of the National Technical Committee agreed to forward the protocol for ethical review and approval by the Ethical Research Council of the BMRC, which provides institutional review of health research in the country. Before leaving, we worked with BIRPERHT and INFS colleagues to prepare the JiVitA proposal, disclosure statements and drafts of forms for submission to the BMRC following its guidelines (*Appendix E*). The review process is expected to take about 2 months. During this time, the proposal will also be submitted for review to the Committee on Human Research at Johns Hopkins School of Public Health.

4) Organization of JiVitA

A great deal of time was spent planning the coming year's strategy, within fiscal constraints expected during FY 00, and taking several concrete steps toward formally organizing the JiVitA project. Supporting material for these developments can be found in *Appendix F*.

Collaborating Partners. The following organizations are collaborating in JiVitA: the Center for Human Nutrition/Department of International Health at the Johns Hopkins School of Public Health (JHU), the Bangladesh Institute of Research for Promotion of Essential Reproductive Health and Technologies (BIRPERHT), the Institute of Nutrition and Food Science at Dhaka University (INFS), Helen Keller International/Bangladesh (HKI) and the Institute of Public Health Nutrition (IPHN) within the Directorate of Health Services of the GOB.

BIRPERHT, as a parastatal organization, will serve as the main national organization that provides the institutional "umbrella" under which JiVitA will operate. Dr. Halida Akhter will serve as the Country Director and a co-principal investigator. Dr. Akhter, who is an alumnus of the doctoral program at the School and a highly experienced reproductive health researcher in Bangladesh, was recently appointed as a Senior Associate in the Department of International Health at JHU in recognition of the senior in-country roles she and her organization are assuming in the trial. BIRPERHT will support the trial with several key personnel assigned to help set up and manage the

organization.

Next Steps: JHU will begin to support BIRPERHT level of effort for several key staff involved in JiVitA preparations effective August 15, 1999. Initial activities will include engaging the GOB in establishing the legal and official basis of JiVitA and JHU in-country through a formal government order ("G.O.") with accompanying memorandums of understanding, monitoring and assisting as needed the review process of the JiVitA protocol at the BMRC, acting as the in-country JiVitA liaison with the USAID mission, the National Technical Committee and other governmental and NGO agencies, beginning to set up field offices, conducting market surveys for equipment and supply availability and costs, developing lists of potential candidates for key positions, hiring lower level positions as needed to support start up activities, and setting up an accounting system for managing the multiple functional "nodes" of JiVitA (Rangpur office, Gaibandha Field Station, BIRPERHT/Dhaka, INFS/Dhaka and the IPHN/Dhaka).

JHU will be formally recognized as the lead international collaborator under a government order that establishes the JiVitA project in-country under BIRPERHT. Details of managing the collaboration, that will recognize JHU's lead investigative role and primary financial accountability to USAID, and permit JHU investigators to enter and work in-country, import equipment and supplies as needed, set up and oversee financial accounts in accordance with JHU/USAID regulations, etc will be formalized in a memorandum of understanding, currently being drafted. However, the G.O. and associated memoranda can not be formalized until the study protocol is fully approved. At present, plans are proceeding in parallel such that full operational status is anticipated by the end of 1999, by which time the protocol is expected to have been fully approved by the GOB.

The INFS will be collaborating in JiVitA, under the direction of Professor Faruk Ahmed. Dr. Ahmed, as a nutritional biochemist, is one of the country's leading micronutrient researchers. He and his staff will oversee the collection, processing, transport and analysis of serum and breastmilk for retinol, carotenoids, serum ferritin and hemoglobin concentrations. Training and laboratory quality control support will be provided by the JHU micronutrient laboratory. We will arrange for Dr. Ahmed and Dr. Tianan Jiang from our JHU CHN laboratory to work together to develop and standardize simultaneous retinol, carotenoid and tocopherol determinations in the laboratory of Dr. Ahmed's prior to start-up of the subsample activities (planned for Jan 2001). Archives of serum and breast milk from JiVitA will be maintained at JHU. Dr. Ahmed will be a co-investigator in JiVitA. The INFS will be formally recognized within the JiVitA G.O. and will operate under the terms of a memorandum of understanding between JHU and the INFS, that will be administered by BIRPERHT in its Dhaka office.

HKI/Bangladesh has continued to play a strong, supportive role in helping JHU and BIRPERHT set up JiVitA. Particularly helpful have been the assistance of highly

APPENDIX A

July 21, 1999

Minutes of the Second meeting of Technical Committee on
'Maternal Vit A Supplementation study' in Bangladesh'

The second meeting of the above Technical Committee was held on 19th July 1999 in the library room of the Institute of Public Health and Nutrition (IPHN), Mohakhali, Dhaka. It was chaired by Prof. M-Q.K Talukdar, Director, Institute of Child and Mother Health, and Member, Technical Committee as decided by Prof. A.K.M. Nurul Anwar in his absence. The meeting was attended by the following members:

1. Prof. Mamunar Rashid, Line Director, National Nutrition Programme, (Micronutrient Supplementation), Dte. of Health Services
2. Prof. T.A. Chowdhury, Chief Consultant, BIRDEM and Professor of Ob/Gyn.
3. Dr. Halida Hanum Akhter, Director, BIRPERHT
4. Prof. Quazi Salamat Ullah, Acting Director, INFS, Dhaka University, Dhaka
5. Dr. A.M.M Anisul Awal, Local Advisor (IEC), BINP
6. Dr. Shamim Ahmed, Clinical Nutritionist, IPHN
7. Ms. Lynda Keiss, Representative, Helen Keller International

Regrets were obtained from -

1. Prof. Shahla Khatun, Professor & Head of the Department, Dept. of Ob/Gyn, Bangabandhu Sheikh Mujib Medical University
2. Prof. Nazmun Nahar, Head of the Department, Dept. of Child Health Dhaka Medical College Hospital
3. Dr. Asirul Haque, Deputy Project Director (Training), BINP
4. Representative, ICDDR,B
5. Representative of Johns Hopkins University (Center for Human Nutrition, Baltimore, MD, USA)

Agenda 1: Confirmation of the minutes of the first Technical Committee meeting

The Chairman welcomed the members of the Technical Committee and narrated the background of formation of the technical committee. In order to confirm the minutes of the first Technical Committee he requested Prof. Mamunar Rashid, Member Secretary of the Technical Committee to share the minutes of the 1st meeting. The Chairperson wanted to know whether there was any comments on the documentation of the minutes, before confirmation. Dr. Anisul Awal mentioned that in the last meeting he requested to have the complete proposal of the Nepal study to learn the details of their study design, which he did not receive yet. In response Dr. Halida Hanum Akhter, Director, BIRPERHT, mentioned that one copy of a British Medical Journal (BMJ) publication on Nepal study, which had already been sent to the members of the Technical Committee in May 99, include the methodology of the Nepal Study.

As there was no further comments on the minutes, the minutes of the 1st Technical Committee meeting held on 17 February 1999 was confirmed.

Agenda 2: Review the status of implementation of the decisions

The status of implementation of the decisions made in the 1st Technical Committee meeting was reviewed. Dr. Halida Akhter mentioned that in the first meeting responsibility was given to Dr. West and herself to provide relevant papers and additional literature on the effects of synthetic Vit-A supplementation among pregnant women. She mentioned that an eight page safety note based on relevant literature review on effects of Vit-A was already distributed among the members in late June 1999.

Agenda 3: Consideration of approval of the research proposal

| Comments from members | Responses & discussion |
|--|--|
| <p>Dr. Anisul Awal expressed his concern about the confounding effect of repeated worker contacts on supplementation outcome.</p> | <p>Dr. Halida Hanum Akhter mentioned that since this is a placebo control double masked trial and all three study groups will be equally visited, the contact effects will be equally distributed among the three study groups.</p> |
| <p>Dr. Anisul Awal mentioned that a baseline study needs to be conducted before initiating this large study.</p> | <p>Ms. Linda Keiss responded that this is a follow-up intervention study. In case of cross sectional study sometimes we need to do baseline study to compare of pre and post intervention findings. In this study placebo group will serve as constant baseline.</p> |
| <p>Dr. Anisul Awal questioned whether there is a cumulative effect of daily dosing of Vit-A and micronutrient supplementation for a long period, starting 6-8 weeks of pregnancy upto 3 months postpartum. Dr. Awal proposed Vit-A supplementation should not exceed 500-μgm RE daily since the women get Vit-A from food intake.</p> | <p>The chairperson clarified that if it is not overdose, it will not be stored in the liver. Prof. Salamat Ullah mentioned that in Bangladesh Vit-A food consumption level is 600-700 IU and Vit-A availability in food is 200-300 μgm RE which is only 25% of daily requirement. As there has been no Vit-A absorption study nor fat intake study in Bangladesh it was assumed that Vit-A level in the body is very low. Dr. Salamat Ullah opined that Vit-A supplementation of 1000 μgm RE daily would be safe for pregnant and lactating women.</p> |
| <p>Dr. Shamim Ahmed pointed out that according to International Vit-A Consultative Group (IVACG) the safety level of Vit-A is 3000 μg RE or 10,000 IU daily. He enquired whether there is any scope to increase the dose of supplementation upto 10,000 IU daily to meet global commitment.</p> | <p>The Chairperson mentioned that as the research group is proposing a dose of 1,000 μg, we should consider the safety of that dose and it is one third of the IVACG recommended safety dose for Vit-A supplementation.</p> |
| <p>Prof. M-Q.K Talukdar expressed his concerns about higher dosage of Iron and Vit-C and low dose of calcium in the proposed micronutrient supplementation for this study.</p> <p>The concern remains that if this high dose is shown effective in reduction of maternal mortality, recommendation for program supplementation of a much higher dose than RDA may ensue.</p> | <p>It was decided that during next visit of Prof. Keith P. West of Johns Hopkins University this issue should be further discussed.</p> |

Agenda 4: Miscellaneous

Since this committee can co-opt members Dr. Mamunar Rashid recommended the name of Dr. Syeeda Begum, Health and Nutrition Section, UNICEF to be included as member of this Technical Committee. Committee members and the Chairman agreed to the proposition.

The chairman concluded the meeting with following remarks-

1. After threadbare discussion the committee feels that 1000 RE Vit-A is a safe dose for supplementation to pregnant and lactating women as proposed in the study and the technical committee will recommend this to the ministry in its final recommendation.
2. However, some concerns, in terms of dosage in the micronutrient supplementation which need to be discussed and settled, include-
 - a) dose of iron, Vit-C in the proposed micronutrient supplementation for the study
 - b) the proposed 100 mg dose is much higher than recommended RDA for US (30mg), for India (60 mg) etc.
3. This committee suggests that another meeting could be convened with Prof. Keith West to discuss the dosage of some micronutrients during his next Dhaka visit in last week of July. The discussions may cover the relationship between food intake levels, RDA and proposed supplement dosage, as well as possible synergistic effects of the micronutrients when given together in combination.

Having no issues for discussion the Chairperson ended the meeting with thanks to the members for their valuable comments.

Prof. Mamunar Rashid
Line Director
National Nutrition Programme
Dte. of Health Services, and
Member Secretary
Technical Committee
on behalf of the Chairman,
Technical Committee

Distribution list

1. Prof. M-Q. K. Talukdar, Project Director, Institute of Child and Mother Health
2. Prof. Md. Abdullah, Director, INFS, Dhaka University
3. Prof. Shahla Khatun, Professor & Head of the Department, Dept. of Ob/Gyn, Bangabandhu Sheikh Mujib Medical University
4. Prof. T.A. Chowdhury, Chief Consultant, BIRDEM and Ex. Professor of Ob/Gyn.
5. Prof. Nazmun Nahar, Head of the Department, Dept. of Child Health, Dhaka Medical College Hospital
6. Dr. A.M.M Anisul Awal, Local Advisor (IEC), BINP
7. Dr. Md. Asirul Haque, Deputy Project Director (Training), BINP
8. Dr. Shamim Ahmed, Clinical Nutritionist, IPHN
9. Dr. Halida Hanum Akhter, Director, BIRPERHT
10. Representative, ICDDR,B
11. Ms. Lynda Keiss, Representative, Helen Keller International
12. Prof. Mamunar Rashid, Line Director, National Nutrition Programme, Dte. of Health Services
13. P.A to Director General, Directorate of Health Services
14. Dr. Keith P. West, Representative, JHU, Baltimore, USA

APPENDIX B



**BANGLADESH INSTITUTE OF RESEARCH FOR PROMOTION OF
ESSENTIAL & REPRODUCTIVE HEALTH AND TECHNOLOGIES**

Formerly : Bangladesh Fertility Research Programme (BFRP)

fax-410-955-0196

June 24, 1999

To : Please see distribution list
From : Dr. Halida Hanum Akhter
Director, BIRPERHT

Sub: A review of current literature on Vitamin A supplementation safety

As per discussion with Prof. A.K.M. Nurul Anwar, Director General, Health Services on 23 June 1999, and also according to the decision made in the 1st meeting of the Technical Committee on 'Maternal Vit-A Supplementation study in Bangladesh' held on 17 February 1999, I am pleased to share with you a review of current literature on Vitamin A supplementation safety (enclosure-I). I would request your kind comments for discussion in the 2nd Technical Committee meeting which will be convened soon.

With best regards,

Distribution List

1. Prof. Mamunar Rashid, Line Director, National Nutrition Programme, Dte. of Health Services, & Member Secretary, Technical Committee on 'Maternal Vit-A Supplementation study in Bangladesh'
2. Prof. M-Q. K. Talukdar, Project Director, Institute of Child and Mother Health
3. Prof. Abu Abdullah, Director, INFS, Dhaka University
4. Prof. Shahla Khatun, Professor & Head of the Department, Dept. of Ob/Gyn, Bangabandhu Sheikh Mujib Medical University
5. Prof. T.A. Chowdhury, Chief Consultant, BIRDEM and Ex. Professor of Ob/Gyn.
6. Prof. Nazmun Nahar, Head of the Department, Dept. of Child Health, Dhaka Medical College Hospital
7. Dr. A.M.M Anisul Awal, Local Advisor (IEC), BINP
8. Dr. Asirul Haque, Deputy Project Director (Training), BINP
9. Dr. Shamim Ahmed, Clinical Nutritionist, IPHN
10. Dr. Halida Hanum Akhter, Director, BIRPERHT
11. Representative, ICDDR,B
12. Ms. Lynda Keiss, Country Director, Helen Keller International
13. P.A to Director General, Directorate of Health Services
- ✓ 14. Dr. Kieth West, Representative, JHU

comments (Jv2-4)HI

House # 105, Road # 9/A (New), Dhanmondi R/A,
Dhaka-1209, GPO Box-279, Bangladesh

Phone : 327588, 10792, 13034
Fax : 880-2-812376

Effects of Vitamin A Supplementation of Women during Pregnancy on Teratogenicity: A Review of Current Literature and Response to the National Technical Review

In its review of the potential benefits and risks of the maternal vitamin A and multiple micronutrient supplementation trial being proposed by Johns Hopkins University (JHU), the Bangladesh Institute of Research for the Promotion of Essential and Reproductive Health Technologies (BIRPERHT), the Institute of Nutrition and Food Science of Dhaka University (INFS) and Hellen Keller International (HKI)/Dhaka, the national technical committee has expressed understandable concern about the safety of supplementing pregnant women with vitamin A beginning early in gestation.

We offer the national committee the following response, in the context of the trial's purpose, target group, proposed dosage of vitamin A in relation to recommendations, its likely efficacy to improve status, and its safety to the fetus.

Purpose. Following a marked reduction in mortality related to pregnancy in the east-central plains of Nepal with vitamin A or beta-carotene supplementation (1), the proposed trial will assess the impact of daily, antenatal and postpartum vitamin A or multiple micronutrient supplementation on maternal, fetal and early infant mortality, and other health outcomes.

Target Group. The trial will enroll rural, pregnant women in northwestern Bangladesh, an area where vitamin A deficiency appears to be a public health problem (5). Women in this poor, rural region are likely to be at risk, given estimated usual intakes of vitamin A by rural women that are usually less than that recommended (2,3), serum retinoid concentrations that are low for 20-50% of women (3,4,5,6), and a national prevalence of gestational night blindness of ~14% (7).

Dosage. In two of its three supplement arms, the trial proposes to administer, either alone or in combination with other micronutrients, 1000 µg retinoid equivalents (RE, or 3333 IU per day) to pregnant women, beginning at ~6-8 weeks' gestation through ~3 months post partum. The third group will receive a placebo. All supplements will be given to women as tablets.

Dosage in Relation to Dietary and Supplement Recommendations. The proposed dosage is within the range of vitamin A intake currently recommended for healthy, non-deficient pregnant (800 µg RE or 2666 IU) or lactating (1200-1300 µg RE, or 4000-4333 IU) women in the United States (8). It is approximately 1.7 and 1.2 times the current recommended daily allowances for healthy pregnant and lactating women, respectively, living in India (9), other countries in Southeast Asia (10), and levels presently recommended during pregnancy and lactation by FAO/WHO (11).

As an antenatal supplement, 1000 µg RE (or 3333 IU) per day is below levels of vitamin A found in most antenatal supplements (12). The proposed dosage is about -

2/3s of the 1500 µg RE (5000 IU) safe dosage limit recommended by the American College of Obstetrics and Gynecology (13) and - 1/3 of the 3000 µg RE (10,000 IU) upper limit of safety for pregnant women advised by the international Vitamin A Consultative Group (14).

Efficacy of Proposed Dosage to improve Vitamin A Status. It is our intention to improve vitamin A status of women with a daily dose of vitamin A that is within safe, conventional limits. The proposed dosage will deliver the same amount of vitamin A to women as the weekly supplement used in the Nepal trial, or 1000 µg RE (3333 IU) per day. In that study, the prevalence of low serum retinol (< 20 µg/dl) was reduced from 19% in controls to 3% in vitamin A-supplemented women(1). In Indonesia, a daily supplement of 2400 µg RE (8000 IU), a dose that is 2.4 times larger, reduced the prevalence of deficient serum retinol in lactating women from 30% to 9% (15). In India, a trial that provided pregnant women each day with 1800 µg RE (or 6000 IU), representing nearly twice the proposed dose, showed an increase in mean serum retinol concentration of initially deficient women (16). These and other studies suggest that our proposed dose of 1000 µg RE given daily will be as effective as larger doses of vitamin A that have been given to women in studies and projects throughout South and Southeast Asia.

Teratogenicity of Vitamin A Deficiency. Vitamin A is an essential nutrient that participates in the regulation of embryonic development (17), that include such diverse structures such as the eye, limb, heart, face and nervous system (18). As a result, maternal deficiency of vitamin A can lead to developmental abnormalities. Vitamin A deficiency was the first known nutritional teratogen, as reported by Hale in the early thirties, in which vitamin A-depleted pigs gave birth to offspring without or with only rudimentary eyes (19). Numerous reports of experimental vitamin A depletion in multiple species, supported by case reports in human populations, reveal the potential for maternal vitamin A deficiency to be a cause of birth defects (20). Affected structures appear to be roughly comparable to those observed with retinoid toxicity (ie, eye, face, ear, limb, urogenital system, skin, lungs, heart) (21).

Safety of Proposed Dosage. The proposed dosage of 1000 µg RE is approximately equivalent to a recommended allowance of vitamin A for women during pregnancy and lactation, especially when one considers less than 100% compliance, that has no known associated toxicity. On the contrary, in a high risk population such as rural women in northwest Bangladesh, this dose is likely to confer additional protection to the fetus. Unpublished data from Nepal provide, perhaps, the most relevant findings for assessing the risk associated with women consuming the proposed dose of 1000 µg RE per day before and during pregnancy (Table 1). The Nepal trial administered weekly to women supplements containing vitamin A at this dosage, beta-carotene (42 mg per week or ~1000 µg RE per day) or a placebo. The preliminary (and confidential) findings in Table 1 suggest that, overall, supplementing women with vitamin A had no measurable effect on risk of birth defects. A relative risk = 0.76, while suggesting protection (1-0.76 *100 = 24% reduction), the effect was not statistically significant (p =

0.38). Most estimates of relative risk (RR) estimates for types of birth defects in the Table appear protective, but they lack statistical significance. The one comparison that is statistically significant relates to the effect of vitamin A on abnormalities of the eye (including corneal opacities, microtia (small eye), and a lid defect), for which a RR = 0.21 represents a 79% reduction ($p=0.05$). The finding is in agreement with the observations of Hale 60 years ago, suggesting that maternal vitamin A deficiency may be an ocular teratogen in human populations and that normal dietary intakes of vitamin A can markedly reduce this risk.

The weight of epidemiologic studies to date provide evidence that vitamin A intakes at least up to 3333 $\mu\text{g RE}$ (10,000 IU), or more than 3 x the proposed dose, per day are safe, as implied by the conservative limits set by international organizations (13,14). An observational study among women in Boston reported in 1996 that a daily, periconceptional intake as low as 3333 $\mu\text{g RE}$ (10,000 IU), but not lower, consumed as preformed vitamin A from supplements could increase risk of cranio-facial birth defects by about 2-fold (22). The study was roundly criticized for its design, potential for defect misclassification and overinterpretation of the results by its authors (23,24,25), but it had the beneficial effect of stimulating additional studies.

Since then, several large studies in Europe and the United States have demonstrated the safety of maternal intake of up to (and, in some studies, above) 3333 $\mu\text{g RE}$ (10,000 IU) of vitamin A per day. Shaw et al reported findings of a large US case-control study (N=899) that suggests maternal supplemental vitamin A intake up to 10,000 IU poses no risk of neural tube defects (26). Case-control findings from the Atlanta Congenital Defects Program reported a 26% decrease in the risk of birth defects (odds ratio = 0.74) related to daily periconceptional vitamin A intakes up to 2400 $\mu\text{g RE}$ (8000 IU) (27). A case-control study nested into the Human Development Neural Tube Defects Study (in California and Illinois) found that the percentage of women consuming doses of 2400 to 7500 $\mu\text{g RE}$ (8000 to 25,000 IU) daily was similar among women having normal offspring (n=573), infants with neural tube defects (n=548) and infants with other major abnormalities (n=387). Protective odds ratios (-0.75) were observed for birth defects among women consuming >2400 $\mu\text{g RE}$ (23). While none of the protective associations were statistically significant in the above studies, they provided evidence that such intakes of vitamin A would be unlikely to pose harm.

Recent findings from the Case-Control Surveillance of Congenital Abnormality Registry in Hungary, that enrolled 35,727 health control infants and 20,830 infants with 23 categories of congenital defects, show a significantly higher proportion of mothers of normal infants (9.5%) than mothers of cases (7.6%) supplementing their diet during pregnancy with up to 3000 $\mu\text{g RE}$ (10,000 IU) of vitamin A during pregnancy. Risk factor analyses suggested that supplemental vitamin A intake $\leq 10,000$ IU per day during pregnancy was associated with protective odds from poly/syndactyly (OR=0.5), hydrocephaly (OR=0.3), cardiovascular (OR=0.6) and ear (OR=0.3) defects (29). Finally, a recent study from the European Network of the Teratology Information

Services, based in Rome, Italy, found no evidence of increased risk of major malformations among women who took >3000 µg RE (range: 10,000 IU to 300,000 IU) per day during the first nine weeks of organogenesis. The study included 120 and 32 women who routinely consumed over 50,000 IU and 100,000 IU per day, respectively, among whom no birth defects were observed (30).

The Teratology Society (31), American College of Obstetrics and Gynecology (13), the European Teratology Society (32) and the IVACG (14) allow for uncertainty in estimating the threshold of periconceptional maternal vitamin A intake above which birth defects may occur, but all suggest that the threshold is almost certainly far above 2400 to 3000 µg RE (6000 to 10,000 IU) per day. Recent reports among cynomolgus monkeys and modeled analyses suggest that the minimum teratogenic dose is likely to be above 10,000 µg RE (30,000 IU) (33,34).

Summary remark. Based on the above we believe that the proposed dosage of 1000 µg RE (3333 IU) per day as an antenatal and postpartum supplement will be efficacious in improving the vitamin A status of women and safe, for both fetus/infant and mother. We ask that the National Technical Committee view the proposed supplement favorably in terms of its potential benefit:risk ratio.

References

1. West KP Jr, Katz J, Khattry SK et al. Double blind, cluster randomized trial of low dose supplementation with vitamin A or β carotene on mortality related to pregnancy in Nepal. *BMJ* 1999;318:570-5.
2. Bloem MW, Huq N, Gorstein J et al. Production of fruits and vegetables at the homestead is an important source of vitamin A among women in rural Bangladesh. *European J Clin Nutr* 1996;50(Suppl 3):S62-S67.
3. Ahmed F. Vitamin A deficiency in Bangladesh: A review and recommendations for improvement. *Publ Health Nutr* 1999;1: (in press).
4. Ahmed F, Hasan N, Kabir Y. Vitamin A deficiency among adolescent female garment factory workers in Bangladesh. *European J Clin Nutr* 1997;51:698-702.
5. Rice A, Stoltzfus RJ, de Francisco A, Chakroborty J, Kjelhede CL, Wahed MA. Maternal vitamin A or β carotene supplementation in lactating Bangladeshi women benefits mothers and infants but does not prevent subclinical deficiency. *J Nutr* 1999;129:356-65.
6. Hussain AH, Lindtjorn B, Kvale G. Protein energy malnutrition, vitamin A deficiency and night blindness in Bangladeshi children. *Ann Tropical Paediatr*

1996;16:319-25.

7. Progotir Patey: Achieving the Goals for Children in Bangladesh. Dhaka:UNICEF. October 1998.
8. Recommended Dietary Allowances, 10th edition. Food and Nutrition Board, Committee on Life Sciences, National Research Council. Washington DC: National Academy Press. 1989.
9. Gopalan C, Sastry BVR, Balasubramanian SC et al. Nutritive Value of Indian Foods. National Institute of Nutrition, Indian Medical Research Council. Hyderabad, India, 1989.
10. Tee and Florentino. Recommended Dietary Allowances for Southeast Asia. Nutrition Reviews, 1994.
11. Requirements of Vitamin A, Iron, Folate and Vitamin B12. Report of a Joint FAO/WHO Expert Consultation. Rome:Food and Agriculture Organization of the United Nations, 1988.
12. Huffman SL, Baker J, Shumann J, Zehner ER. The case for promoting multiple vitamin/mineral supplements for women of reproductive age in developing countries. Linkages Project. Washington DC:Academy for Educational Development, November, 1993.
13. Vitamin A supplementation during pregnancy. ACOG Committee Opinion: Committee on Obstetrics: Maternal and Fetal Medicine. Int J Gynecol Obstet 1993;40:175.
14. IVACG Statement. Safe doses of vitamin A during pregnancy and lactation. International Vitamin A Consultative Group. Washington DC:ILSI Research Foundation, 1998.
15. Tanumihardjo SA, Muherdiyantiningsih, Permaesih D et al. Daily supplements of vitamin A (8.4 μ mol, 8000 IU) improve vitamin A status of lactating Indonesian women. Am J Clin Nutr 1996;63:32-35.
16. Sivakumar B, Panth M, Shatrugnia V, Raman L. Vitamin A requirements

19. Hale F. The relation of vitamin A to anophthalmos in pigs. *Am J Ophthalmol* 1935;18:1087.
20. Hanson JW. Letter of the Public Affairs Committee of the Teratology Society, reviewed and approved by the Council of the Teratology Society, concerning likely risks and benefits of maternal vitamin A supplementation in the NNIPS-2 trial in Nepal, Bethesda, MD 24 March 1994.
21. Gerster H. Vitamin A - Functions, dietary requirements and safety in humans. *Internat J Vit Nutr Res* 1996;67:71-90.
22. Rothman KJ, Moore LL, Singer MR et al. Teratogenicity of high vitamin A intake. *NEJM* 1995;333:1369-73.
23. Werler MA, Lammer EJ, Mitchell AA. Letter to editor. *NEJM* 1996;334:1195.
24. Brent RL, Hendrickx AG, Holmes LB, Miller RK. *NEJM* 1996;334:1195.
25. Watkins M, Moore C, Mulinare J. *NEJM* 1996;334:1196.
26. Shaw GM, Velie EM, Schaffer D, Lammer EJ. Periconceptional intake of vitamin A among women and risks of neural tube defect-affected pregnancies. *Teratology* 1997;55:132-3.
27. Khoury MJ, Moore CA, Mulinare J. Do vitamin A supplements in early pregnancy increase the risk of birth defects in the offspring? A population-based case-control study. *Teratology* 1996;53:91(Abstract).
28. Mills JL, Simpson JL, Cunningham GC et al. Vitamin A and birth defects. *Am J Obstet Gynecol* 1997;177:31-6.
29. Czeizel AE, Rockenbauer M. Prevention of congenital abnormalities by vitamin A. *Internat J Vit Nutr Res* 1998;68:219-31.
30. Mastroiacovo P, Mazzone T, Addis A et al. High vitamin A intake in early pregnancy and major malformations: A multicenter prospective controlled study. *Teratology* 1999;59:7-11.
31. Teratology Society position paper: Recommendations for vitamin A use during pregnancy. *Teratology* 1987;35:269-75.
32. Dolk HM, Nau H, Hummler H, Barlow SM. Dietary vitamin A and teratogenic risk: European Teratology Society discussion paper. *European J Obstet Gynecol* 1999;83:31-36.

33. Miller RK, Hendrickx AG, Mills JL, Hummler H, Wiegand U-W. Periconceptional vitamin A use: How much is teratogenic? *Reproductive Toxicology* 1998;12:75-88.
34. Wiegand U-W, Hartmann S, Hummler H. Safety of vitamin A: Recent results. *Int J Vit Nutr Res* 1998;68:411-416.

Table 1. Effects of Weekly Maternal Vitamin A or Beta-carotene Supplementation on Cranio-Facial (C-F) Birth Defects, NNIPS-2, Nepal (DRAFT, May 1999)

| | Placebo | Vitamin A | Beta-carotene |
|---------------------------|---------|-----------|---------------|
| No. Live Births | 5597 | 5657 | 6023 |
| Ear/Presacral tags | | | |
| No. | 7 | 3 | 6 |
| Rate per 1000 | 1.25 | 1.45 | 1.06 |
| Relative risk | 1.00 | 1.19 | 0.85 |
| P-value (v placebo) | | 0.72 | 0.77 |
| Eye Defects | | | |
| No. | 9 | 2 | 4 |
| Rate per 1000 | 1.61 | 0.33 | 0.71 |
| Relative risk | 1.00 | 0.21 | 0.44 |
| P-value (v placebo) | | 0.95 | 0.26 |
| Cleft Lip/Palate | | | |
| No. | 8 | 4 | 3 |
| Rate per 1000 | 1.43 | 0.65 | 1.24 |
| Relative risk | 1.00 | 0.45 | 0.27 |
| P-value (v placebo) | | 0.20 | 0.78 |
| Other C-F defects | | | |
| No. | 3 | 6 | 3 |
| Rate per 1000 | 0.54 | 1.00 | 0.71 |
| Relative risk | 1.50 | 1.85 | 1.32 |
| P-value | | 0.37 | 0.72 |
| Total C-F defects | | | |
| No. | 22 | 18 | 18 |
| Rate per 1000 | 3.93 | 2.99 | 3.18 |
| Relative risk | 1.00 | 0.75 | 0.81 |
| P-value | | 0.38 | 0.45 |

APPENDIX C

**Minutes of the Second meeting of Technical Committee on
'Maternal Vit A Supplementation study' in Bangladesh'**

The second meeting of the above Technical Committee was held on 19th July 1999 in the library room of the Institute of Public Health and Nutrition (IPHN), Mohakhali, Dhaka. It was chaired by Prof. M-Q.K Talukdar, Director, Institute of Child and Mother Health, and Member, Technical Committee as decided by Prof. A.K.M. Nurul Anwar in his absence. The meeting was attended by the following members:

1. Prof. Mamunar Rashid, Line Director, National Nutrition Programme, (Micronutrient Supplementation), Dte. of Health Services
2. Prof. T.A. Chowdhury, Chief Consultant, BIRDEM and Professor of Ob/Gyn.
3. Dr. Halida Hanum Akhter, Director, BIRPERHT
4. Prof. Quazi Salamat Ullah, Acting Director, INFS, Dhaka University, Dhaka
5. Dr. A.M.M Anisul Awal, Local Advisor (IEC), BINP
6. Dr. Shamim Ahmed, Clinical Nutritionist, IPHN
7. Ms. Lynda Keiss, Representative, Helen Keller International

Regrets were obtained from -

1. Prof. Shahla Khatun, Professor & Head of the Department, Dept. of Ob/Gyn, Bangabandhu Sheikh Mujib Medical University
2. Prof. Nazmun Nahar, Head of the Department, Dept. of Child Health Dhaka Medical College Hospital
3. Dr. Asirul Haque, Deputy Project Director (Training), BINP
4. Representative, ICDDR,B
5. Representative of Johns Hopkins University (Center for Human Nutrition, Baltimore, MD, USA)

Agenda 1: Confirmation of the minutes of the first Technical Committee meeting

The Chairman welcomed the members of the Technical Committee and narrated the background of formation of the technical committee. In order to confirm the minutes of the first Technical Committee he requested Prof. Mamunar Rashid, Member Secretary of the Technical Committee to share the minutes of the 1st meeting. The Chairperson wanted to know whether there was any comments on the documentation of the minutes, before confirmation. Dr. Anisul Awal mentioned that in the last meeting he requested to have the complete proposal of the Nepal study to learn the details of their study design, which he did not receive yet. In response Dr. Halida Hanum Akhter, Director, BIRPERHT mentioned that one copy of a British Medical Journal (BMJ) publication on Nepal study, which had already been sent to the members of the Technical Committee in May 99, include the methodology of the Nepal Study.

As there was no further comments on the minutes, the minutes of the 1st Technical Committee meeting held on 17 February 1999 was confirmed.

Agenda 2: Review the status of implementation of the decisions

The status of implementation of the decisions made in the 1st Technical Committee meeting was reviewed. Dr. Halida Akhter mentioned that in the first meeting responsibility was given to Dr. West and herself to provide relevant papers and additional literature on the effects of synthetic Vit-A supplementation among pregnant women. She mentioned that an eight page safety note based on relevant literature review on effects of Vit-A was already distributed among the members in late June 1999.

Agenda 3: Consideration of approval of the research proposal

| Comments from members | Responses & discussion |
|---|---|
| <p>Dr. Anisul Awal expressed his concern about the confounding effect of repeated worker contacts on supplementation outcome.</p> <p>Dr. Anisul Awal mentioned that a baseline study needs to be conducted before initiating this large study.</p> <p>Dr. Anisul Awal questioned whether there is a cumulative effect of daily dosing of Vit-A and micronutrient supplementation for a long period, starting 6-8 weeks of pregnancy upto 3 months postpartum. Dr. Awal proposed Vit-A supplementation should not exceed 500-μgm RE daily since the women get Vit-A from food intake.</p> | <p>Dr. Halida Hanum Akhter mentioned that since this is a placebo control double masked trial and all three study groups will be equally visited, the contact effects will be equally distributed among the three study groups.</p> <p>Ms. Linda Keiss responded that this is a follow-up intervention study. In case of cross sectional study sometimes we need to do baseline study to compare of pre and post intervention findings. In this study placebo group will serve as constant baseline.</p> <p>The chairperson clarified that if it is not overdose, it will not be stored in the liver. Prof. Salamat Ullah mentioned that in Bangladesh Vit-A food consumption level is 600-700 IU and Vit-A availability in food is 200-300 μgm RE which is only 25% of daily requirement. As there has been no Vit-A absorption study nor fat intake study in Bangladesh it was assumed that Vit-A level in the body is very low. Dr. Salamat Ullah opined that Vit-A supplementation of 1000 μgm RE daily would be safe for pregnant and lactating women.</p> |
| <p>Dr. Shamim Ahmed pointed out that according to International Vit-A Consultative Group (IVACG) the safety level of Vit-A is 3000 μg RE or 10,000 IU daily. He enquired whether there is any scope to increase the dose of supplementation upto 10,000 IU daily to meet global commitment.</p> | <p>The Chairperson mentioned that as the research group is proposing a dose of 1,000 μg, we should consider the safety of that dose and it is one third of the IVACG recommended safety dose for Vit-A supplementation.</p> |
| <p>Prof. M-Q.K Talukdar expressed his concerns about higher dosage of Iron and Vit-C and low dose of calcium in the proposed micronutrient supplementation for this study.</p> <p>The concern remains that if this high dose is shown effective in reduction of maternal mortality, recommendation for program supplementation of a much higher dose than RDA may ensue.</p> | <p>It was decided that during next visit of Prof. Keith P. West of Johns Hopkins University this issue should be further discussed.</p> |

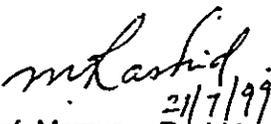
Agenda 4: Miscellaneous

Since this committee can co-opt members Dr. Mamunar Rashid recommended the name of Dr. Syeeda Begum, Health and Nutrition Section, UNICEF to be included as member of this Technical Committee. Committee members and the Chairman agreed to the proposition.

The chairman concluded the meeting with following remarks-

1. After threadbare discussion the committee feels that 1000 RE Vit-A is a safe dose for supplementation to pregnant and lactating women as proposed in the study and the technical committee will recommend this to the ministry in its final recommendation.
2. However, some concerns, in terms of dosage in the micronutrient supplementation which need to be discussed and settled, include-
 - a) dose of iron, Vit-C in the proposed micronutrient supplementation for the study
 - b) the proposed 100 mg dose is much higher than recommended RDA for US (30mg), for India (60 mg) etc.
3. This committee suggests that another meeting could be convened with Prof. Keith West to discuss the dosage of some micronutrients during his next Dhaka visit in last week of July. The discussions may cover the relationship between food intake levels, RDA and proposed supplement dosage, as well as possible synergistic effects of the micronutrients when given together in combination.

Having no issues for discussion the Chairperson ended the meeting with thanks to the members for their valuable comments.


21/7/99
Prof. Mamunar Rashid
Line Director
National Nutrition Programme
Dte. of Health Services, and
Member Secretary
Technical Committee
on behalf of the Chairman,
Technical Committee

Distribution list

1. Prof. M-Q. K. Talukdar, Project Director, Institute of Child and Mother Health
2. ~~Prof. Md. Abdullah, Director, IICS, Dhaka University~~
3. Prof. Shahla Khatun, Professor & Head of the Department, Dept. of Ob/Gyn, Bangabandhu Sheikh Mujib Medical University
4. Prof. T.A. Chowdhury, Chief Consultant, BIRDEM and Ex. Professor of Ob/Gyn.
5. Prof. Nazmun Nahar, Head of the Department, Dept. of Child Health, Dhaka Medical College Hospital
6. Dr. A.M.M Anisul Awa, Local Advisor (IEC), BINP
7. Dr. Asirul Haque, Deputy Project Director (Training), BINP
8. Dr. Shamim Ahmed, Clinical Nutritionist, IPHN
9. Dr. Halida Hanum Akhter, Director, BIRPERHT
10. Representative, ICDDR,B
11. Ms. Lynda Keiss, Representative, Helen Keller International
12. Prof. Mamunar Rashid, Line Director, National Nutrition Programme, Dte. of Health Services
13. P.A to Director General, Directorate of Health Services
14. Dr. Keith P. West, Representative, JHU, Baltimore, USA

11 July 1999

Ref:

From : Prof. Mamunar Rashid
Line Director, National Nutrition Programme,
and Member Secretary of the Technical Committee
Dte. of Health Services
Mohakhali, Dhaka-1212

To : The distribution list below

The first meeting of the Technical Committee formed as per Govt. order (জনস্বাস্থ্য-২/৫-১৯/৯৫/৩৮
জাঃ-১৪/২/৯৯) was convened on 17th February, 1999 in the Conference Room of Dte. of Health
Services, Mohakhali, Dhaka to review the research proposal entitled "Effect of Vit A and
Micro-nutrient Supplementation during Pregnancy and Lactation on Maternal, Fetal and Infant
Mortality." The minutes of this meeting has already been distributed to the members.

The second meeting of the same Technical Committee will be held on 19th July 1999 at
11.30 A.M. in the Conference Room of Institute of Public Health and Nutrition (IPHN),
Mohakhali, Dhaka. The meeting will be Chaired by Prof. A.K.M. Nurul Anwar, Director General,
Directorate of Health Services and the Chairman of the Technical Committee. The agenda of
the meeting are as follows:

1. Confirmation of the minutes of the first Technical Committee meeting.
2. Review the status of implementation of the decisions.
3. Consideration of approval of the research proposal.

You are kindly requested to attend the meeting.

Representatives of the Johns Hopkins University are also requested to be present in the
meeting for necessary discussion and clarifications.



Prof. Mamunar Rashid
Line Director
National Nutrition Programme
Dte. of Health Services

Distribution list:

1. Prof. M-Q. K. Talukdar, Project Director, Mother and Child Health, Matuile, Dhaka
2. Director, INFS, Dhaka University, Dhaka.
3. Professor & Head of the Department, Dept. of Ob/Gyn, Bangabandhu Sheikh Mujib
Medical University, Shahbagh, Dhaka.
4. Prof. T.A. Chowdhury, Chief Consultant (Ob/Gyn), BIRDEM, Shahbagh, Dhaka.
5. Prof. Nazmun Nahar, Head of the Department, Dept. of Child Health,
Dhaka Medical College Hospital, Dhaka.
6. Dr. Anisul Awal, Advisor, BINP, Dhaka.
7. Dr. Asirul Haque, Deputy Director, BINP, Dhaka.
8. Dr. Shamim Ahmed, Clinical Nutritionist, IPHN, Mohakhali, Dhaka [BINP office]
9. Director, BIRPERHT, House 105, Road 9/A (new), Dhanmondi R/A, Dhaka
10. Representative, ICDDR,B, Mohakhali, Dhaka.
11. Representative, Helen Keller International, Dhanmondi, Dhaka.
12. Representatives of Johns Hopkins University.
13. P. A to Director General, Dte. of Health Services, and Chairman, Technical Committee.
14. P. A. to Prof. Mamunar Rashid, Line Director, National Nutrition Programme,
Dte. of Health Services and Member-Secretary of the Technical Committee.

APPENDIX D

20/8/99

Recommended dietary allowances (RDA) of nutrients and composition in currently marketed and propose prenatal/postnatal supplements

| Nutrient | US RDA -preg | US RDA- lact-6 | Indian RDA -preg | Indian RDA -lact-6 | Centrum Brand | Giant Brand | * Prenatal- Roche Brand | NNIPS3 (Nepal) | JIViA Bangladesh (proposed)* |
|--------------------------------|-----------------|-------------------|---------------------|-----------------------|------------------|----------------|----------------------------|-------------------|------------------------------------|
| Vitamin A RE | 800 | 1300 | 600 | 950 | 900 | 1125 | 1200 | 1000 | 1000 |
| β-carotene RE | - | - | 2400 | 3800 | 600 | 375 | - | - | - |
| Vitamin D µg | 10 | 10 | na | na | 10 | 10 | 12.5 | 10 | 10 |
| Vitamin E mg | 10 | 12 | na | na | 10 | 10 | 5 | 10 | 10 |
| B ₁ (Thiamin) mg | 1.5 | 1.6 | 1.3 | 1.4 | 1.5 | 1.5 | 1.6 | 1.5 | 1.6 |
| B ₂ (Riboflavin) mg | 1.6 | 1.8 | 1.5 | 1.6 | 1.7 | 1.7 | 1.8 | 1.6 | 1.8 |
| Niacin mg | 17 | 20 | 16 | 17 | 20 | 20 | 19 | 20 | 20 |
| Folate µg | 400 | 240 | 400 | 150 | 400 | 400 | 800 | 400 | 400 |
| B ₆ mg | 2.2 | 2.1 | 2.5 | 2.5 | 2 | 2 | 2.6 | 2.2 | 2.2 |
| B ₁₂ µg | 2.2 | 2.6 | 1.0 | 1.5 | 6 | 6 | 4 | 2.2 | 2.6 |
| Vitamin C mg | 70 | 95 | 40 | 80 | 60 | 60 | 100 | 100 | 70 |
| Vitamin K µg | 65 | 65 | na | na | 25 | 25 | - | 65 | 65 |
| Zinc mg | 15 | 19 | na | na | 15 | 15 | 7.5 | 30 | 15 |
| Iron mg | 30 | 15 | 38 | 30 | 18 | 18 | 60 | 60 | 30 |
| Calcium mg | 1200 | 1200 | 1000 | 1000 | 162 | 162 | 125 | 125 | 125 |
| Phosphorous mg | 1200 | 1200 | na | na | 109 | 109 | 125 | - | - |
| Magnesium mg | 320 | 355 | na | na | 100 | 100 | 100 | 100 | 100 |
| Iodine mg | 175 | 200 | na | na | 150 | 150 | - | - | - |
| Selenium µg | 75 | 75 | na | na | - | - | - | - | - |
| Copper mg | 1.5-2.0 | na | na | na | - | - | - | 1.5 | 2.0 |

*Prenatal/postnatal supplement

RDA(19-8-99) hi

APPENDIX E

31 August, 1999

From : Prof. Mamunar Rashid
Line Director
National Nutrition Programme,
Director, IPHN
Dte. of Health Services
and
Member-Secretary
Technical Committee on 'Effect of Vitamin A and
Multiple Micronutrient Supplementation during Pregnancy
and Lactation on Maternal, Fetal and Infant Mortality'
Mohakhali, Dhaka

To : Dr. Harunur Rashid
Director
Bangladesh Medical Research Council (BMRC)
Mohakhali, Dhaka

Subject: Submission of research proposal entitled "Effect of Vitamin A and Multiple Micronutrient Supplementation during Pregnancy and Lactation on Maternal, Fetal and Infant Mortality" for ethical review.

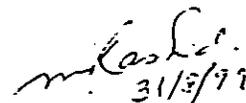
I am hereby sending three complete set of research proposals entitled 'Effect of Vitamin A and Multiple Micronutrient Supplementation during Pregnancy and Lactation on Maternal, Fetal and Infant Mortality' for Ethical Review Committee (ERC) clearance (appendix-1). The proposal has been developed following the prescribed format of Bangladesh Medical Research Council (BMRC).

To give a report to the MOHFW by examining the justification and methodology of the above research proposal a Technical Committee was formed by the Ministry of Health & Family Welfare (MOHFW) (appendix-2). The committee has met three times and has approved the proposal considering in detail its technical aspects. The committee has also decided that ethical clearance should be obtained from BMRC. The minutes of the first, second and third technical committee meetings are enclosed (appendices - 3A, 3B, 3C) for information of the members of the ERC.

Since the technical committee has to obtain the ERC clearance before it submits a report to the MOHFW, I would appreciate your arranging the ethical review of the proposal at the earliest.

Please contact me at IPHN if you need any additional information or clarification to expedite the process.

Many thanks in anticipation.


31/8/99

Prof. Mamunar Rashid

Appendices – as stated

APPLICATION FOR ETHICAL CLEARANCE

from

**Bangladesh Medical Research Council (BMRC)
Mohakhali, Dhaka, Bangladesh**

A Proposal on

**Effect of Vitamin A and Multiple Micronutrient
Supplementation during Pregnancy and Lactation
on Maternal, Fetal and Infant Mortality**

Submitted by

**The Technical Committee of Ministry of Health & Family Welfare
on the research to study
'Effect of Vitamin A and Multiple Micronutrient Supplementation during
Pregnancy and Lactation on Maternal, Fetal and Infant Mortality'**

August 1999

BANGLADESH MEDICAL RESEARCH COUNCIL
Mohakhali, Dhaka - 1212, Bangladesh
Tel: 871395

Application for Ethical Clearance

1. Principal Investigator(s):

Dr. Halida Hanum Akhter, MBBS, MCPS, MPH, Dr.PH
Director
Bangladesh Institute of Research for Promotion of Essential and Reproductive Health
and Technologies (BIRPERHT)
House 105, Road 9/A (New)
Dhanmondi R/A
Dhaka-1209 Bangladesh

Professor Keith P. West, Jr., DrPH
Center for Human Nutrition
Department of International Health
School of Hygiene and Public Health
Johns Hopkins University
Baltimore, MD 21205, USA

2. Co-investigators:

Dr Parul Christian, MS, Dr.P.H.
Assistant Scientist
Center for Human Nutrition
Department of International Health
School of Hygiene and Public Health
Johns Hopkins University
Baltimore, MD 21205, USA

Professor Faruk Ahmed, Msc, PhD
Institute of Nutrition and Food Science
University of Dhaka
Dhaka-1000, Bangladesh

Additional co-investigators will join the study from BIRPERHT, Johns Hopkins University, the INFS, HKI and the IPHN.

3. Place of the Study/Institution(s):

Place of Study:

Gaibandha and Rangpur Districts (Thanas of Sundarganj, Sadullahpur, Gaibandha Sardar and Pirgaccha)

Institutions:

Bangladesh Institute of Research for Promotion of Essential & Reproductive Health and Technologies (BIRPERHT)
Dhanmondi, Dhaka, Bangladesh

The Center for Human Nutrition (CHN) of
The Johns Hopkins University
School of Hygiene and Public Health
Baltimore, MD, USA

Institute of Nutrition and Food Science
University of Dhaka
Dhaka, Bangladesh

Hellen Keller International
Dhaka, Bangladesh

Institute of Public Health Nutrition
Moakhali, Dhaka

4. Title of Study: Effect of Vitamin A and Multiple Micronutrient Supplementation during Pregnancy and Lactation on Maternal, Fetal and Infant Mortality

5. Type of Study: Double-masked, randomized community trial

6. Duration: 5 years

7. Total Cost: USD 3.6 million

Abstract for Ethical Review Committee

Background. Vitamin A and other micronutrient deficiencies are prevalent throughout rural Bangladesh but their role in reproductive health and survival is poorly understood. Recently, a large trial in the Terai of Nepal reported a 44% reduction in mortality of women during and following pregnancy with weekly vitamin A or β -carotene supplementation at normal dietary levels. The trial was carried out in a population where maternal mortality is high (~650 per 100,000 live births) and where night blindness during pregnancy is common, conditions that are similar to Bangladesh. The findings raise the important question of whether maternal supplementation with vitamin A, or other essential micronutrients, at recommended levels, could improve the health and survival of mothers and infants in rural Bangladesh.

Purpose. The proposed study will determine whether daily maternal supplementation with either vitamin A alone or multiple micronutrients (that also contain vitamin A) during pregnancy through the first three months postpartum, at recommended dietary levels, can reduce mortality of women related to pregnancy by at least 35%. Secondly, the trial will examine the impact of maternal supplementation on fetal loss, early infant death and other health outcomes such as birth weight, infant growth and morbidity, and maternal and infant micronutrient status.

Methods. The proposed study is a randomized, double-masked, community trial. It will be carried out in an area of ~650 sq km with a total population of ~570,000 in 21 unions located in the thanas of Sundarganj, Gaibandha, Sadullapur and Pirgaccha of the Districts of Gaibandha and Rangpur. Approximately 600 communities will be randomized for pregnant women, to receive daily supplements of vitamin A providing 1000 ug retinol equivalents or ~1 recommended dietary allowance (RDA), multiple micronutrients (vitamins A, D, E, C, K, B-complex, folate, iron, zinc, calcium, magnesium and copper), or a placebo through 3 months postpartum. The trial expects to enroll, supplement and follow ~18,000

consenting women with their infants in each group each year for a 3-4 year period, providing a total of 54,000 pregnancies, or ~18,000 per supplement group. Informed consent will be sought from women throughout stages of participation. Nearly 110,000 women of reproductive age are expected to be enumerated and canvassed for pregnancy on a monthly basis, by questioning about menstruation in the previous month and conducting urine-based testing among amenstrual women to confirm pregnancy status. Women identified as pregnant will be enrolled and interviewed about previous pregnancy history, current morbidity, diet, work habits, and socioeconomic status. Arm circumference will be measured as an indicator of nutritional status. Supplementation will commence, which will be monitored weekly. Miscariages, stillbirths and live births will be reported to the study staff each week. Mothers and their infants will be visited at home 3 months after a live birth to collect data on third trimester morbidity, complications during labor and delivery, postpartum morbidity, diet, infant vital and health status, and breast feeding and complementary feeding practices. Infants will be screened for obvious birth defects, subsequently confirmed by a physician. Women and infants reporting during home visits to be seriously ill will be referred to nearby health facilities. Maternal and postpartum infant survival will be ascertained weekly from the time of enrollment until the end of supplementation. Following death of an enrolled woman or infant, a death audit will be conducted to ascertain cause of death.

In a 3% subsample of women (and their infants), changes in maternal and infant biochemical and anthropometric status and other reproductive health outcomes will be assessed. Among this sample, venous blood will be drawn from the mother at home visits during the first and third trimesters and again at three months of postpartum. Breast milk and infant blood using heel prick will be collected at the 3-month postpartum visit. Hemoglobin levels will be measured at the time of each blood draw. A data safety and monitoring meeting will be held (in Bangladesh and at JHU) after the first 18000 birth outcomes to review mortality findings and provide guidance about continuation of the trial.

Items for Consideration by the Ethical Review Committee

Point 1. Subject population. The proposed trial will enumerate married women of reproductive age and enroll and follow consecutive pregnancies, with infants, over a planned 4-year recruitment and follow-up period. This is the relevant population at risk for whom answers about the health and survival benefits of vitamin A and micronutrient supplementation are being sought.

Points 2 and 3. Potential risks and procedures for minimizing potential risks. Each of the study micronutrients is essential but has a wide range of normal intake. The levels at which they are included in the supplements are approximately one or slightly more than an RDA for pregnant women. These amounts are considered safe and potentially effective in meeting nutritional needs of a population. Thus, the intervention is not expected to induce pregnancy-related morbidity, birth defects or other adverse health outcomes. Iron, being given at a relatively low dose of 30 mg per day, is not expected to cause gastrointestinal discomfort typically found in some women at higher levels of supplementation (eg, 60 to 120 mg per day). Risk of taking large numbers of supplements at one time will be minimized by usually providing women with only enough supplements for one week and by placing tablets in a child-proof plastic bottle. Intravenous blood drawing in women in the subsample. Infant blood draw will be done using heel prick. Both methods may cause momentary discomfort in drawing blood; however neither pose more than minimum risk when carried out according to standard medical practice. Maternal hemoglobin will be assessed from the same venous blood sample; thus, requiring no further discomfort to the woman. Disposable syringes and needles and gloves will be used and trained phlebotomists will perform the blood draws from women and infants. Disposal of biohazardous material will also be according to the guidelines specified for Bangladesh.

Point 4. Methods for safeguarding confidentiality. All data that can be linked to identifying information of individual study subjects will be treated with strict confidentiality throughout the duration of the trial and beyond by each responsible collaborating institute.

Completed data collection forms will only be handled by authorized study staff. Confidentiality will be protected by tracking the movement of all forms between study stations with transmittal lists. Data entry will take place in the data entry center located in the Rangpur Office. After editing and entry, data forms with identifiers will be kept in locked file cabinets in the Rangpur office. All forms handling and data management will be done by trained staff under the supervision of the study data manager. Individual data and forms with identifiers will be available only to designated study staff and investigators. All findings will be presented only in aggregate form, stripped of identifiers. Forms not in use will be stored under lock and key throughout the period of study and for approximately 3 years after completion of the study, after which paper forms will be incinerated.

Point 5. Informed consent procedures. During the year before the trial, a process of community consent will be undertaken whereby meetings will be held to inform leaders and community groups about the purpose, various activities, requirements and potential benefits and risks of participating in the study, and to obtain their consent to work in their respective unions and mauzas. At an initial census and pregnancy screening survey, a general disclosure statement will be read to eligible women, who are married and between the ages of ~13 to 45 years of age. This statement will inform women about the purpose of the study, including the current census and subsequent pregnancy surveillance. Their verbal consent will be sought for being enrolled into a monthly home surveillance. Because of their marital status, women < 18 years will be considered "emancipated minors". Women who either report to be pregnant or amenstrual during the previous month will be eligible for a pregnancy test to confirm status. Following a separate disclosure statement concerning implications of testing, eligible women will be asked to provide a small amount of urine for a pregnancy test. Women will be informed immediately of the test result. Those who test positive will be informed of the purpose, requirements, potential benefits and risks of participating in the supplementation trial. Verbal consent will be obtained at the enrollment interview; however, a signature or thumb impression will be obtained at that time from women willing and able to do so.

Three percent of all newly enrolled pregnant women will be asked to provide a small amount of blood for nutritional assessment early and late in pregnancy. Their permission will also be sought for a home visit shortly after birth to assess birth weight and other outcomes related to labor and delivery, and at 3 months to collect breast milk and a small amount of blood from the mother and her infant (by heelstick). A separate informed consent will be read prior to asking women to participate in this substudy.

We believe that, in a population and culture where only about 25% of women can read or write and where signing forms is not a conventional practice, especially among women, forcing a written signature for consent may be inappropriate. However, this will be encouraged for those able to do so at the time of actual enrollment of pregnant women into the supplementation trial. All verbal disclosures will be informative and simple in language. Spouses, to the extent possible, will be involved in the consent process. Participants may withdraw from the study at any time. The four, planned disclosure statements are appended for review.

Point 6. Place of interview. Pregnancy testing, informing her its results and all pregnancy interviews will be conducted in the privacy of a woman's home in order to protect the confidentiality of information obtained. An interview will normally take no longer than 30 minutes to minimize the inconvenience of participation.

Point 7. Potential benefits to individuals and society. Among the benefits of participation, approximate 2/3 of the pregnant women will receive an RDA of one or more of essential nutrients. Severely ill women, regardless of treatment code, will be offered a referral to the nearest Thana Health Complex for appropriate health care and follow-up. To improve the effectiveness of referral and as a means to improve general health care in the study area, a program of periodic continuing education for thana health complex and family welfare workers on a variety of primary health care topics will be conducted over time (1-2 times per year). Participating pregnant women will receive counseling on the importance of antenatal care at the time of the enrollment interview, and be advised to

receive tetanus toxoid vaccines. In addition, infant of women in the sub sample will undergo birth assessment and referrals for severe complications, indicated by collected data using standard algorithms. Mothers tested for Hb level and found to be severely anemic (Hb < 7 g/dl) during pregnancy will be treated with iron- folate supplements following WHO guidelines.

Rural women of reproductive age in Bangladesh and the South Asian region stand to gain from the results of this trial, particularly if the findings show a substantial reduction in maternal, fetal or infant mortality risk with vitamin A or micronutrient supplementation. Such findings could be used by the MOH of the Government of Bangladesh to develop or refine dietary and nutritional supplement use guidelines for protecting the health and survival of pregnant women and their offspring. These guidelines could be followed outside the health system, thus empowering women to improve their own chances of a safe and healthy pregnancy through diet or supplement use. These findings, combined with those of maternal micronutrient supplement trials completed (Nepal) or being planned (Indonesia, Ghana) elsewhere could set the stage for forging global policies that assure the availability of appropriate antenatal supplements (in terms of nutrient composition and cost) to women during and following pregnancy, a choice that has long been available to women in industrialized countries. Thus, the benefits to individual women and society appear to far outweigh minimal risks posed by the study.

Point 8. Experimental drug use. No experimental drugs are planned for use in the trial. The proposed amounts of vitamin A and other micronutrients per dose are consistent with recommended intakes and ranges of doses found in antenatal supplements throughout the world (*see attached table*).

Point 9. New drugs registration. Not applicable.

Point 10. Conventional opinion favors the sole use of antenatal care and emergency obstetric care for reducing maternal mortality. Nutritional interventions have played little formal role in protecting women from dying from pregnancy-related causes. Based on the

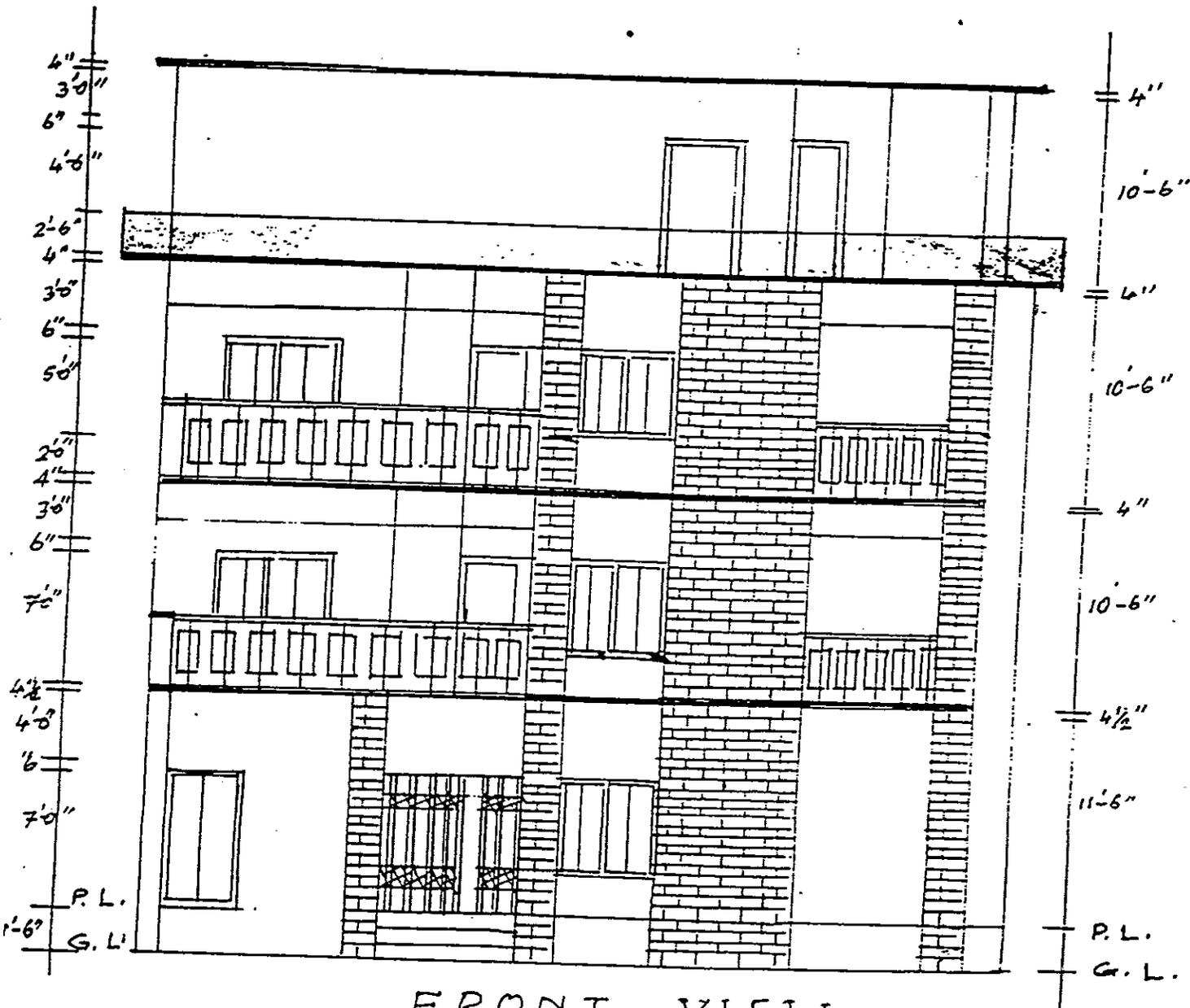
findings in Nepal, there is an urgency to confirm the effects of vitamin A and simultaneously advance knowledge about the benefits of a micronutrient supplement on antenatal and postnatal reproductive health outcomes. Answers to these questions are needed in as time-efficient and a definitive manner as possible. The placebo-controlled trial, in the absence of policy and current availability of such supplements for use, will provide the fastest and most interpretable approach for determining these nutritional effects. In the absence of a placebo group, factors that are variable in the study population, and that can not be controlled in historical control designs, may confound any beneficial effect of supplementation.

Point 11. Experimental drug sponsorship. Not applicable.

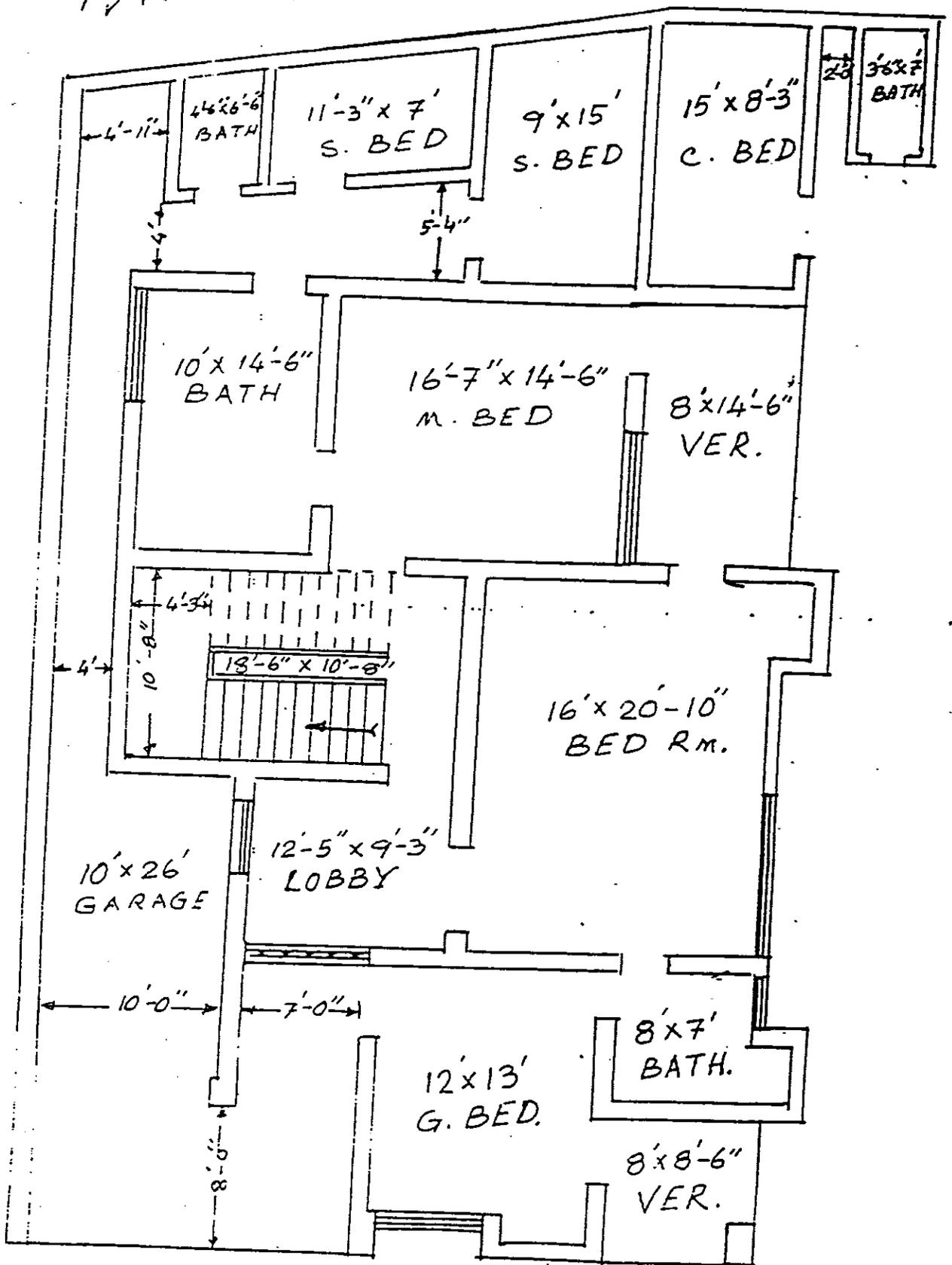
Point 12. Use of records, organs, tissues, etc. No clinic or hospital records are anticipated to be used in the study. In a 3% subsample of pregnant women, approximately 5 ml of maternal blood will be drawn and 15 ml of breastmilk will be taken postpartum for assessing micronutrient status of the mother. A small amount of infant blood will be obtained by heelstick for assessing serum retinol levels. Fetal survival will be ascertained by history of pregnancy outcome from the mother but no fetal tissue will be accessed.

APPENDIX F

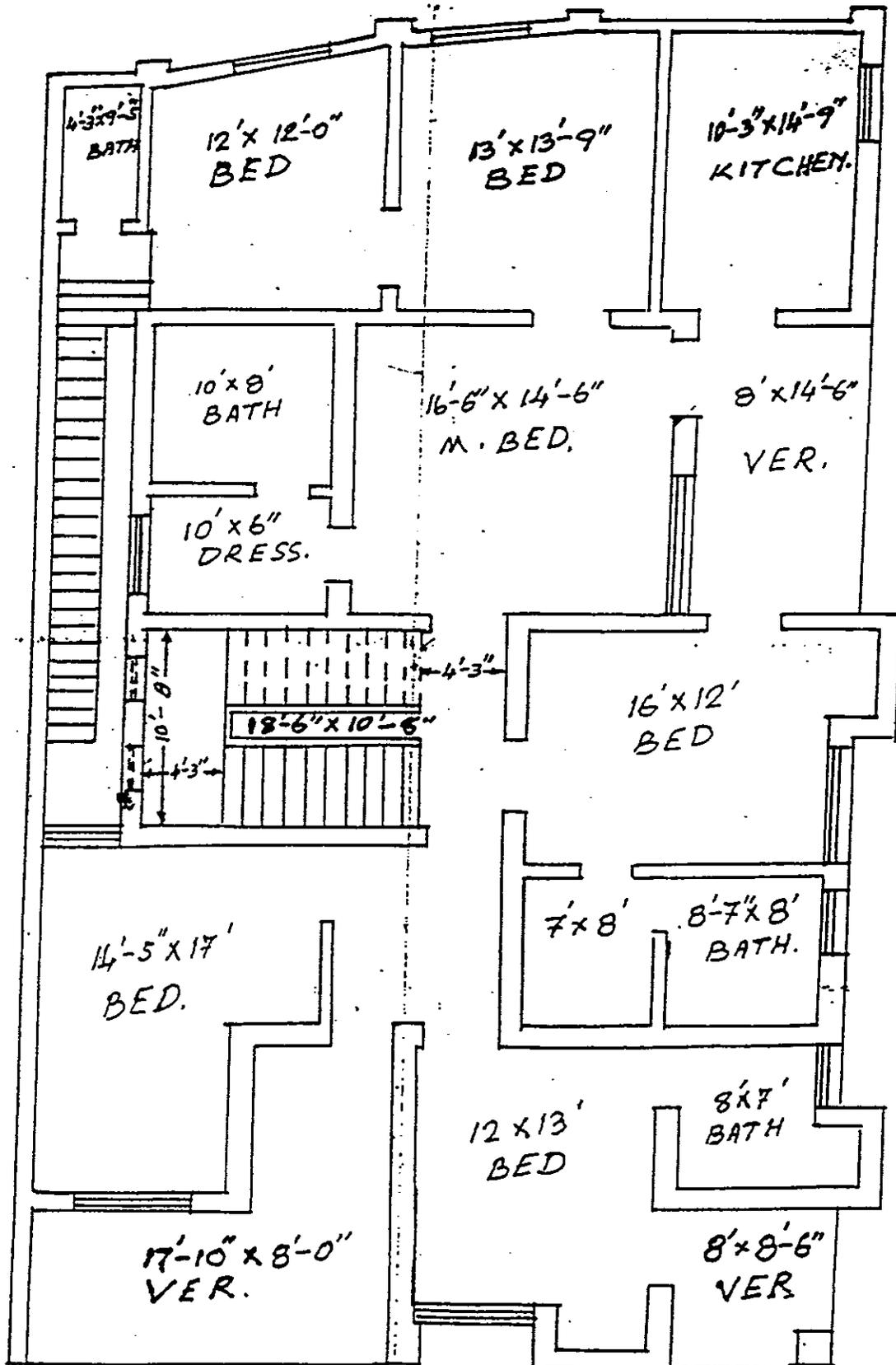




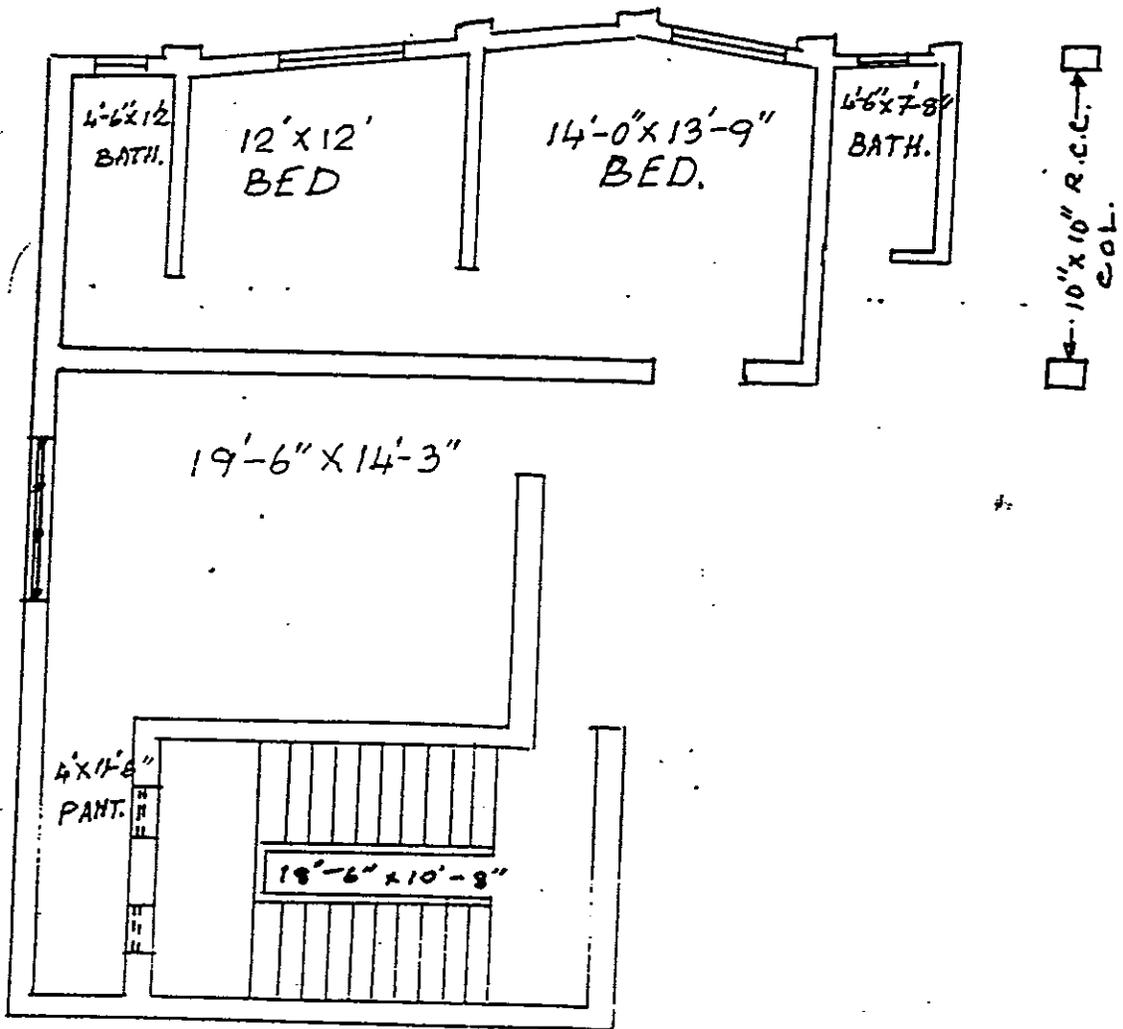
FRONT VIEW.
SCALE: - 8' = 1"



GROUND FLOOR PLAN.
 SCALE: $8' = 1''$

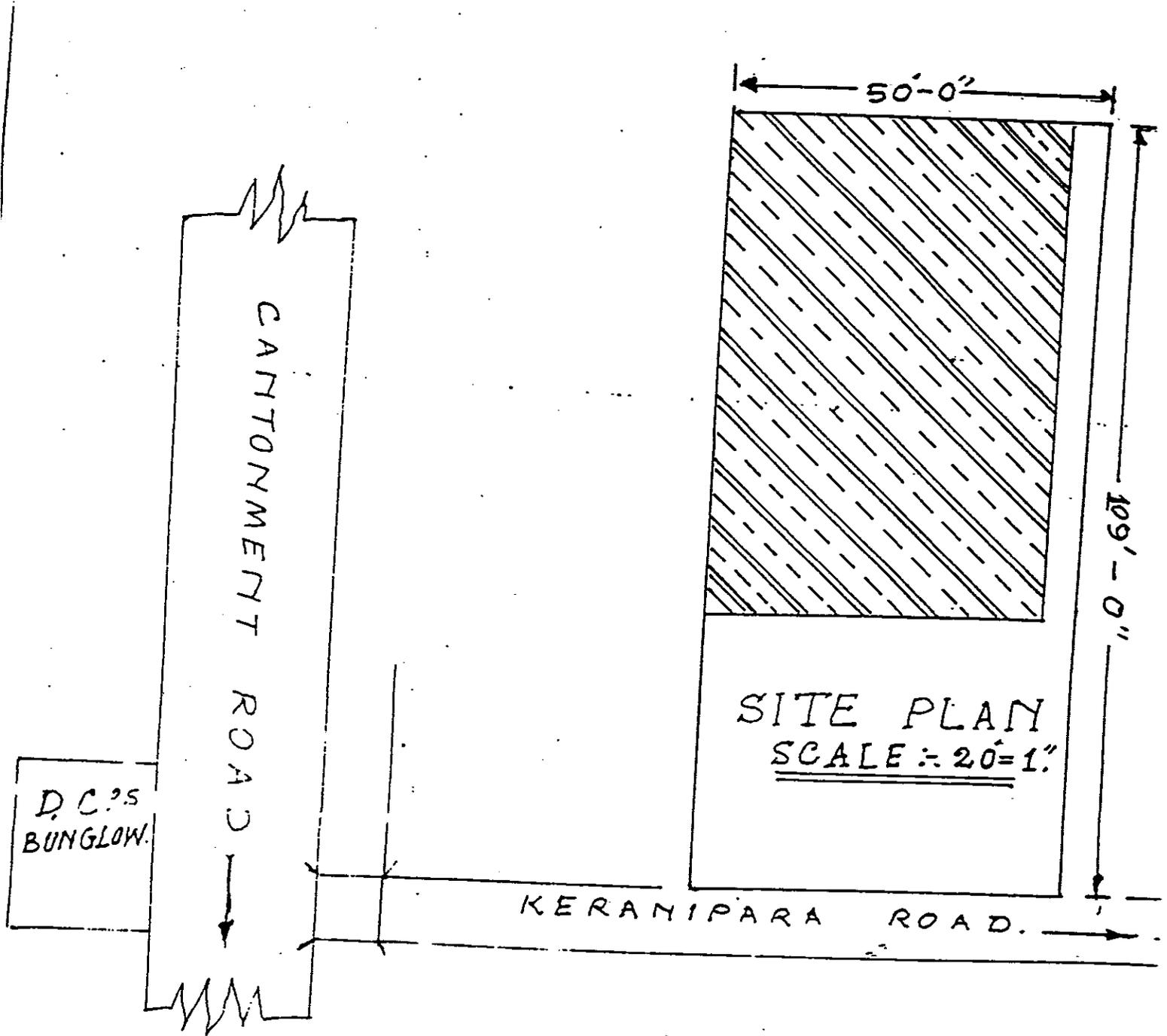


1ST. & 2ND. FLOOR PLAN



3RD. FLOOR PLAN.
SCALE: - 8' = 1"

SIG. OF OWNERS.
 DATE: -



গণপ্রজাতন্ত্রী বাংলাদেশ সরকার

৳৫০



৳৫০

পঞ্চাশ টাকা

জ ০০৭৬৬৬

PRECONTRACT AGREEMENT

THE MATERNAL HEALTH & NUTRITION PROJECT (NAMED "SIVITA"), HEREAFTER CALLED THE LESSEE, AGREES TO LEASE THE PROPERTY LOCATED AT GOLDENVIEW, THE THREE-STORY BUILDING PROVIDED WITH COMPOUND WALL SITUATED AT KERANIPTA, RANGPUR, MURGA STATE RA JL NO. 94, PLOT NO. 3011, LITATION NO. 246 FROM MR. ALTAFER RAHMAN, HEREAFTER CALLED THE LESSOR, BEGINNING 1 SEPT 1999 AT A RATE OF TK 22,000 PER MONTH PENDING THE PROPERTY IS PROPERLY FUNCTIONING AND AGREED UPON CONDITIONS HAVE BEEN MET TO THE SATISFACTION OF THE LESSEE. IN THE EVENT THAT ALL CONDITIONS, EXCEPT NETTING ON THE 2ND FLOOR (WHICH WILL BE DONE BY 30 SEPT 1999 TO THE LESSEE'S SATISFACTION) ARE NOT MET BY 1 SEPT 1999, THE LEASE WILL BEGIN ON THE DATE ON WHICH THE SAID CONDITIONS HAVE BEEN MET TO THE LESSEE'S SATISFACTION. ^{THE LESSEE} ~~THE LESSOR~~ A FURTHER HEALTHY PROVIDES TO MR. HABIBUR RAHMAN, ^{REPRESENTATIVE OF THE LESSEE,} THE SUM OF TK 22,000 AS AN INITIAL PAYMENT IN GOOD FAITH TO BE APPLIED TO THE SIX MONTH ADVANCE FOR RENT. THE LESSEE FURTHER AGREES TO INCUR A 15% INCREASE IN THE MONTHLY RENT FEE EVERY TWO YEARS.

WITNESS: St. Mahabub Khan 16/8-99

(সি: ওয়াশ)

30/8/99

WITNESS: _____

LESSOR: MD. ALTAFER RAHMAN

MD. HABIBUR RAHMAN
16/8/99

LESSEE: Karely Purost A 16 AUG 1999

(সি: ওয়াশ)

16/8/99

Halida Hanum Akhter
16 Aug 1999

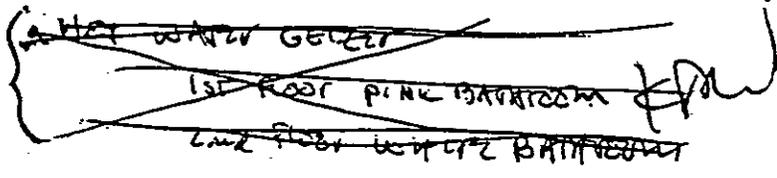
ATTACHMENT TO FACILITATE AGREEMENT DATED 16 SEP 99

CONDITIONS FOR RENTING PROPERTY "GOLDENVIEW",
KELANIPALA, RANGPUR, MOUJA SATGARA JL NO 94,
PLOT NO. 3011, KHATAJIN NO. 746

16 Aug 99

- 1 COAT DISCREPANT PAINT - SAME COLORS / INCL IRON WORKS / INSIDE AND OUTSIDE

NE
APPLY



- NO LEAKS ANYWHERE - CHECK EVERY FAUCET FOR PROPER FUNCTION
- ALL TOILETS FLUSH PROPERLY
- GROUND WATER PROTECTION RING
- FIX WATER PUMP LINE
- NEW WATER PUMP

- NETTING ON ALL 1ST FLOOR WINDOWS / DOORS
- REPAIR EXISTING NETTING
- ALL ELECTRICAL SOCKETS, EACH ROOM, WORKING
- ALL LIGHT FIXTURES WORKING EACH ROOM

- ALL WINDOWS REPAIR / CLEAN

- MOTORCYCLE STAND CLEAN OUT

- CLEAN HOUSE

LESSEE: Kabir Prasad
16 AUG 99

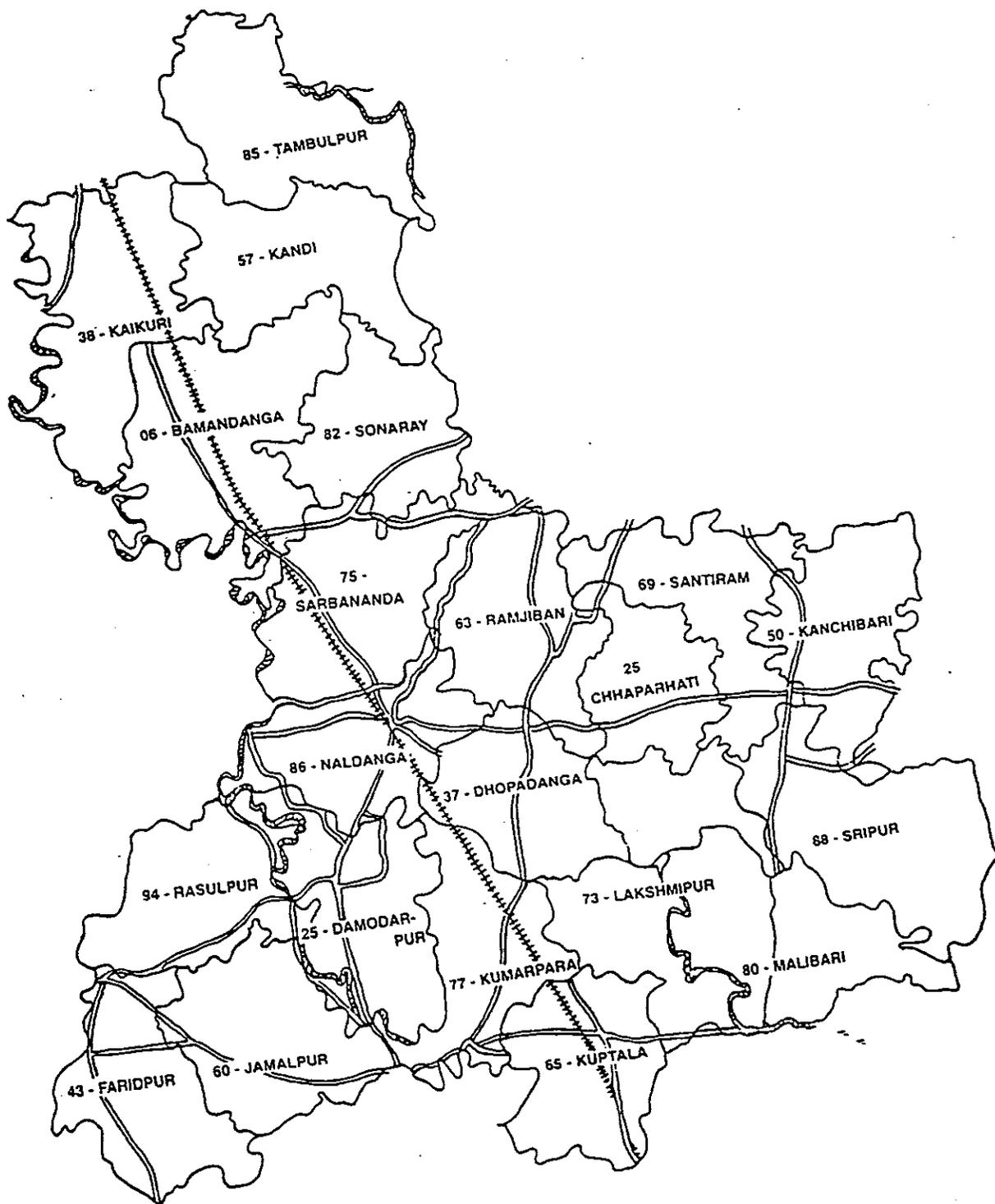
LESSOR: HABIBUR RAHMAN
14/8/99

Names and addresses of personnel contacted during Rangpur & Gaibandha visit (13-8-99 to 16-8-99)

| Name | Designation | Phone |
|--|---|--|
| Gaibandha Civil Surgeon office: | | |
| 1. Dr. Yusuf Ahmed | Civil surgeon | 538 |
| 2. Dr. Nuruzzamn | MO | - |
| Gaibandha DD office | | |
| 1. Mr. Goizar Hossain Ansari | DD FP | 4928 (res, Rangpur) 443 (office, Gaibandha) |
| 2. Dr. Jane Alam | AD (cc) | 443 (office, Gaibandha) |
| 3. Dr. Matiur Rahman | THFPO | - |
| 4. Dr. Ferdous Hossain (Manju) | - | 5395 (res) |
| Rangpur DD office | | |
| 1. Mr. Kabiruddin | DD FP | 3541 (office) 4599, 3060 (res) |
| Sundarganj Thana Health Complex | | |
| 1. Dr. Nazrul Islam | THFPO (Sundarganj T&T office and ext. to THC) | |
| 2. Dr. Shafiqul Islam | RMO | |
| 3. Dr. Abdul Aziz | MO | |
| 4. Dr. Rafiqul Islam | MC | |
| 5. Mr. Habibur Rahman | TFPO | |
| 6. Mr. Abdur Razzak | FPI | |
| Other officials | | |
| 1. - | TNO | 2 (office) 17 (res) |
| House owner (Golden View) | | |
| 1. Mr. Altafur Rahman (Ranju) | Owner | 9125151 (office) 814365 (res, Dhaka) |
| 2. Mr. Habibur Rahman (Raza) | Brother of owner | 3423 (res, Rangpur) |
| 3. Mr. Mohammad Ali | Care taker | |
| Roy Ballav Palace | | |
| 1. Mr. Moezuddin | Care taker | 2733 (res) |
| Tajhat Palace | | |
| 1. Mr. Abdul Latif Pramanik | Curator | 2779 |
| 2. Mr. Hossain Ali | Care taker | |
| 3. Mr. Ahmed Ali | Care taker | |

Sundarganj(jivita-4)

APPENDIX G



APPENDIX H

DISTRICT: GAIBANDEHA

| Name of Thana | Name of Union | Name of Mauza | Total # of sheet map | Collection of sheet map |
|---------------|--------------------|--|----------------------|-------------------------|
| Sundarganj | Bamandanga | 1. Deodoba 2. Baldipara 3. Hatibhandha 4. Jamal 5. Maniram 6. Maniram Kazi 7. Maniram Khamar 8. Manmahta 9. Nagar Kathgara 10. Paikapara 11. Phalgachha Taluk 12. Phalgachha 13. Ramdhan 14. Satgiri 15. Talukramdeb | 29 | 28 |
| | Chhaparhati | 1. Dakshin Maruadaha 2. Khamar Panchgachhi 3. Paschim Chhaparhati 4. Purba Chhaparhati 5. Uttar Maruadaha | 17 | 17 |
| | Dahabanda | 1. Arazi Dahaband 2. Bamanjal 3. Dhumaitari 4. Gopalcharan 5. Hurabhayakhan 6. Jaramandi 7. Jhinia 8. Sundarganj | 17 | 14 |
| | Kanchibari | 1. Bajra Kanchibari 2. Chhaygharia 3. Dulal 4. Kalir Khamar 5. Kanchibari 6. Satirjan | 15 | 14 |
| | Ramjiban | 1. Bazar Para 2. Bekatari 3. Bhabanippur 4. Kashdaha 5. Kekai Kashdaha 6. Nijpara 7. Ramgiban 8. Subarnadaha | 16 | 16 |
| | Shantiram | 1. Khamar Dhubni 2. Panchgachhishantiram 3. Paran 4. Shantiram | 13 | 13 |
| | Sarbananda | 1. Bachh Hati 2. Kismat Sarbananda 3. Taluk Bajit 4. Taluk Rambhadra 5. Taluk Sahabaz 6. Taluk Sarbananda | 16 | 13 |
| | Sonaray | 1. Baidyanath 2. Balaram 3. Chandra | 13 | 13 |

| | | | | |
|-------------------|-------------------|--|----|----|
| | | 4. Fatekhan 5. Sibram 6. Sonaray | | |
| | Sripur | 1. Bholaray 2. Boalia 3. Dakshin Sripur 4. Dharmapur 5. Samas 6. Uttar Sripur | 19 | 19 |
| Sadullapur | Damodarpur | 1. Bhangamor 2. Damodarpur 3. Jamudanga 4. Kismat Barabari 5. Kismat Dasalia 6. Kismat Kheju 7. Marudaha | 16 | 7 |
| | Faridpur | 1. Aldadpur 2. Badalkhan 3. Bishnupur 4. Chak Gobindapur 5. Chand Karim 6. Dari Jamalpur 7. Dari Tajpur 8. Faridpur 9. Isabpur 10. Jamalpur 11. Kismat Anantapur 12. Mahespur Krishnapur 13. Mirpur 14. Nayanpur 15. Sabek Jamalpur 16. Sabek Tajpur 17. Serpur 18. Taherpur Pirojpur | 20 | 20 |
| | Jamalpur | 1. Arazi Jamalpur 2. Bara Jamalpur 3. Buzruk Rasulpur 4. Chak Salaipur 5. Chikni 6. Daudpur 7. Durgapur 8. Enayetpur 9. Gayonpur 10. Gopalpur 11. Hamidpur 12. Kandarpar Manoharpur 13. Khorda Rasulpur 14. Patilakurachakdaria 15. Patila Kura 16. Srikala 17. Taraf Bazit | 20 | 20 |
| | Kumarpara | 1. Dhankuti 2. Hat Bamni 3. Hiali 4. Kesalidanga 5. Khamar Bagchi 6. Kismat Bagchi 7. Lakshmipur 8. Nurpur | 15 | 15 |

| | | | | |
|----------------------------|-------------------|---|----|---|
| | | 9. Uzir Dharanibari | | |
| | Paldanga | 1. Daslia 2. Khamar Dasalia 3. Kismat Hamid 4. Manduarpara 5. Naldanga 6. Pratab 7. Srirampur | 15 | |
| | Rasulpur | 1. Arazi Chhandiapur 2. Arazi Taraf Kamal 3. Baishtamdas 4. Chak Narayan 5. Chhandiapur 6. Jaydeb 7. Junidpur 8. Kismat Tajpur 9. Mahishbandi 10. Rasulpur 11. Taraf Fazil 12. Taraf Kamal 13. Bora Daudpur | 16 | 5 |
| Gaibandha | Kuptala | 1. Beradanga 2. Chapadaha 3. Durgapur 4. Kuptala 5. Ramprasad | 12 | |
| | Lakshmipur | 1. Gobindapur 2. Khorda Malibari 3. Malibari | 11 | |
| | Malibari | 1. Barbaidia 2. Kachuar Khamar 3. Khidir 4. Kismat Malibari 5. Kismat Malibari Dharampur | 14 | |
| District: Pirgachha | | | | |
| Pirgachha | Tambulpur | 1. Arazi Debu 2. Birbiria 3. Ghagoa 4. Gopal 5. Paran 6. Paschim Debu 7. Pratipal 8. Purba Debu 9. Rahamat 10. Ramgopal 11. Salmara 12. Sonaray 13. Taluk Kandi Digtari 14. Tambulpur | 21 | |
| | Kaikuri | 1. Aladipara 2. Atsattipara 3. Balihar 4. Chalnina 5. Chaudhu Rani 6. Dilal Para 7. Jamirjan 8. Kaikuri 9. Kutipara | 24 | |

| | | | | |
|--|--------------|--|----|--|
| | | <ul style="list-style-type: none"> 10. Kutubbas 11. Makram Pur 12. Mangala Kuti 13. Mirapara 14. Muksudkhan 15. Nazar Mohammad 16. Ramchandara Para 17. Subid 18. Sulli Para 19. Umarkhan | | |
| | Kandi | <ul style="list-style-type: none"> 1. Arazikanditaluk Nijpara 2. Chapra 3. Dadan 4. Digtari 5. Doani Maniram 6. Harideb 7. Majbari 8. Manirampur 9. Patak Sikar 10. Purba Pataksukar 11. Satantara 12. Taluk Kandi 13. Talukkandi Kabilapara 14. Talukkandi Nijpara 15. Teani Maniram | 21 | |