29 August 2001

To: Professor Lars Ake Persson
   Associate Director, Public Health Science Division

From: Professor Mahmudur Rahman
   Chairman, Ethical Review Committee (ERC)

Sub: Protocol # 2001-015

Thank you for your memo of 27th August 2001 with the modified copy of the consent form and the questionnaire for your protocol # 2001-015 entitled "Arsenic in tube-well water and health consequences". The modified version of the protocol is hereby approved upon your satisfactory addressing of the issues raised by the ERC in its special meeting held on 16th August 2001.

Thank you.
To: Chairman, ERC

From: Dr. Mohammed Abdu Salam

Subject: Questionnaire and consent forms of the research study entitled “Arsenic in tube well water and health consequences”

Date: August 29, 2001

This has reference to the meeting of the ERC where the committee had requested the investigators to modify the questionnaire and the consent forms, and I took the responsibility to help the investigators in doing so. In response, the investigators have modified the questionnaire per my advice, and I would consider the modified versions as satisfying.

I think that the committee may now consider approval of the latest versions of the questionnaire and the consent forms.

Thanks.
MEMORANDUM

August 28, 2001

To Professor Mahmudur Rahman
Chairman, Ethical Review Committee (ERC)

From Professor Lars Ake Persson,
Associate Director, Public Health Science Division

Sub: Modified copy of the consent forms and questionnaire

This has reference to your memo of 19th August 2001
communicating me the decision of the ERC on the modified
version of the protocol # 2001- 015 entitled "Arsenic in tube well
water and health consequences." As advised by you, consent
forms (both Bangla and English) and questionnaire have been
revised in consultation with Dr. M. A. Salam, a Member of the
ERC. I would much appreciate if you could kindly approve the
protocol.

Thank you
Attachment 1

**ETHICAL REVIEW COMMITTEE, ICDDR,B.**

Principal Investigator: Professor Lars Ake Persson

Applicant No.: 2001-15

Title of Study: ARSENIC IN TUBE WELL WATER AND HEALTH CONSEQUENCES

Trainee Investigator (if any): ______________________

Supporting Agency (if Non-ICDDR,B): ______________________

Project Status: In process

[ ] New Study

[ ] Continuation with change

[ ] No change (do not fill out rest of the form)

<table>
<thead>
<tr>
<th>Circle the appropriate answer to each of the following (If Not Applicable write NA)</th>
</tr>
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<tbody>
<tr>
<td>1. Source of Population:</td>
</tr>
<tr>
<td>(a) Ill subjects</td>
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<tr>
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<td>(c) Minor or persons under guardianship</td>
</tr>
<tr>
<td>2. Does the Study Involve:</td>
</tr>
<tr>
<td>(a) Physical risk to the subjects</td>
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<td>(b) Social risk</td>
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<td>(c) Psychological risks to subjects</td>
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<td>(d) Discomfort to subjects</td>
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<tr>
<td>(e) Invasion of privacy</td>
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<tr>
<td>(f) Disclosure of information damaging to subject or others</td>
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<tr>
<td>3. Does the Study Involve:</td>
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<tr>
<td>(a) Use of records (hospital, medical, death or other)</td>
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<td>(b) Use of fetal tissue or abortus</td>
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<tr>
<td>(c) Use of organs or body fluids</td>
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<tr>
<td>4. Are Subjects Clearly Informed About:</td>
</tr>
<tr>
<td>(a) Nature and purposes of the study</td>
</tr>
<tr>
<td>(b) Procedures to be followed including alternatives used</td>
</tr>
<tr>
<td>(c) Physical risk</td>
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<tr>
<td>(d) Sensitive questions</td>
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<tr>
<td>(e) Benefits to be derived</td>
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<tr>
<td>(f) Right to refuse to participate or to withdraw from study</td>
</tr>
<tr>
<td>(g) Confidential handling of data</td>
</tr>
<tr>
<td>(h) Compensation &amp;/or treatment where there are risks or privacy is involved in any particular procedure</td>
</tr>
<tr>
<td>5. Will Signed Consent Form be Required:</td>
</tr>
<tr>
<td>(a) From subjects</td>
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<tr>
<td>(b) From parents or guardian (if subjects are minor)</td>
</tr>
<tr>
<td>6. Will precautions be taken to protect anonymity of subjects</td>
</tr>
<tr>
<td>7. Check documents being submitted herewith to Committee:</td>
</tr>
</tbody>
</table>
| [ ] Umbrella proposal - Initially submit an overview (all other requirements will be submitted with individual studies)
| [ ] Protocol (Required)
| [ ] Statement given or read to subjects on nature of study, risks, types of questions to be asked, and right to refuse to participate or withdraw (Required)
| [ ] Informed consent form for subjects
| [ ] Informed consent form for parent or guardian
| [ ] Procedure for maintaining confidentiality
| [ ] Questionnaire or interview schedule

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

__________________________  ____________________________
Principal Investigator Trainee
**ICDDRB: Centre for Health & Population Research**

**RRC APPLICATION FORM**

**RESEARCH PROTOCOL**

**Protocol No.: 2001-15**

**FOR OFFICE USE ONLY**

<table>
<thead>
<tr>
<th>Approval</th>
<th>Yes/No</th>
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**Project Title:** Arsenic in tube well water and health consequences

(Revised August 28, 2001)

**Theme:** (Check all that apply)

- Nutrition
- Emerging and Re-emerging Infectious Diseases
- Population Dynamics
- Reproductive Health
- Vaccine evaluation
- Environmental Health
- Health Services
- Child Health
- Clinical Case Management
- Social and Behavioural Sciences

**Key words:** Arsenic, drinking water, epidemiology, exposure, health effects, skin lesion

**Principal Investigator:** Lars Ake Persson  
**Division:** PHSD  
**Phone:** 9885155

**Address:** Public Health Sciences Division  
ICDDR,B, Mohakhali, Dhaka

**Email:** persson@icddrb.org

**Co-Principal Investigator(s):** Mahfuzar Rahman

---

**Co-Investigator(s):**

1. Shams El Arifeen
2. SM Akramuzzaman
3. Abbas Bhuiya
4. Eva-Charlotte Ekström
5. Md. Khalequzzaman
6. Peter Kim Sreetfield
7. Nigar Shahid
8. MA Wahed
9. Md Yunus
10. Mushtaque Chowdhury
11. Marie Vahter

**Student Investigator/Intern:**

**Collaborating Institute(s):** Research Division, BRAC and Institute of Environmental Medicine, Division of Metal and Health, Karolinska Institute, Sweden
### Population: Inclusion of special groups (Check all that apply):

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<td>Fetuses</td>
<td>Prisoners</td>
<td>Destitutes</td>
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<tr>
<td>Females</td>
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<td>Age</td>
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<td>20 +</td>
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<td>&gt; 65</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Animal</td>
</tr>
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</table>

### Project / study Site (Check all the apply):

- Dhaka Hospital
- Matlab Hospital
- Matlab DSS area
- Matlab non-DSS area
- Mirzapur
- Dhaka Community
- Chakaria
- Abhoynagar
- Mirsarai
- Patya
- 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 up
- 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

### Targeted Population (Check all that apply):

- No ethnic selection (Bangladeshi)
- Banglasee
- Tribal groups
- Expatriates
- Immigrants
- Refugee

### Consent Process (Check all that apply):

- Written
- Oral
- None
- Bengali language
- English language

### Proposed Sample size: Total sample size: 190,000

Sub-group 2850 (Case-reference)
Determination of Risk: Does the Research Involve (Check all that apply):

- Human exposure to radioactive agents?
- Fetal tissue or abortus?
- Investigational new device?
  - archives/source
  - (specify__________________________)
- specimen only
- Existing data available from Co-investigator
- Human exposure to infectious agents?
- Investigational new drug
- Existing data available via public
- Pathological or diagnostic clinical
- Observation of public behaviour
- New treatment regime
- Exposure to arsenic in water

Yes/No

☐ ☑ Is the information recorded in such a manner that subjects can be identified from information provided directly or through identifiers linked to the subjects?

☐ ☑ Does the research deal with sensitive aspects of the subject's 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:

a. place the subject at risk of criminal or civil liability?

b. damage the subject's financial standing, reputation or employability; social rejection, lead to stigma, divorce etc.

Do you consider this research (Check one):

- greater than minimal risk
- no risk
- no more than minimal risk
- only part of the diagnostic test

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, the 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: Sida (funding received) and WHO (committed)
Yes/No

☒ ☐ Is the proposal being submitted for funding?

If yes, name of funding agency: (1) ___________ WHO (committed)

(2) ___________ USAID

Do any of the participating investigators and/or 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, submit a written statement of disclosure to the Director.

<table>
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<th>Dates of Proposed Period of Support</th>
<th>Cost Required for the Budget Period (S)</th>
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<td>(Day, Month, Year - DD/MM/YY)</td>
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<td>Beginning date 01/07/2001</td>
<td>b. Direct Cost : US $ 540253 Total Cost : US $ 789,655</td>
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<td>End date 30/06/2003</td>
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Approval of the Project by the Division Director of the Applicant

The above-mentioned project has been discussed and reviewed at the Division level as well by the external reviewers.

The protocol has been revised according to the reviewer's comments and is approved.

Name of the Division Director ____________________________
Signature ____________________________
Date of Approval ____________________________

Certification by the Principal Investigator

I certify that the statements herein are true, complete and accurate to the best of my knowledge. I am aware

Signature of PI ____________________________
Date: ____________________________
that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. I agree to accept responsibility for the scientific conduct of the project and to provide the required progress reports if a grant is awarded as a result of this application.

Name of Contact Person (if applicable)
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</tbody>
</table>

Consent Forms in English
Consent Forms in Bangla

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

Principal Investigator Lars Ake Persson

Project Name **Arsenic in tube well water and health consequences**

<table>
<thead>
<tr>
<th>Total Budget USD 789,655</th>
<th>Beginning Date July 2001</th>
<th>Ending Date June 2003</th>
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The discovery of arsenic in groundwater in Bangladesh has aroused widespread concern. A major proportion of tube wells for drinking water in the country is contaminated with arsenic. Experiences from other countries indicate that the consequences of this exposure will be extensive and include excess incidence and mortality in cancers and cardio-vascular diseases. However, the knowledge base is weak on the weight of this new burden of diseases and on the speed by which it develops. Little is known about the reproductive health consequences, and about the possible aggravating role of the widespread malnutrition in Bangladesh on arsenic-induced health effects.

The overall objective of this project is to establish a strong epidemiologic platform of research on levels of arsenic exposure through drinking water, occurrence of arsenic skin lesions, consequences for reproductive outcome, effect on adult mortality, modifications of effects by the nutritional status, and effects of an intervention with alternative water sources.

ICDDR,B is running a health and demographic surveillance system in 142 villages of the Matlab thana. The surveillance system contains demographic information, reproductive outcomes, health information, nutritional and health data as well as a linked geographic information system. This area is heavily affected by the arsenic contamination of drinking water. We propose screening for skin lesions in the 220,000 population, assessment of arsenic content of the 9000 tube wells of the Matlab surveillance area, and an establishment of a data base for epidemiological studies of levels of arsenic exposure and manifestations of arsenicosis in the population. Immediate analyses will be performed on the risk for arsenic related skin lesions and effects on reproductive outcome and mortality. A village-based arsenic mitigation activity is coordinated with the surveillance, and priority will be given to the areas with the highest exposure. Reversibility of skin changes will be assessed. The consequences of a shift to other water sources will also be evaluated, including monitoring of diarrhoeal diseases through the surveillance system in Matlab.

The mitigation activity is collaborated with BRAC, a major national NGO with the longest experience of arsenic mitigation programmes in Bangladesh. Collaboration is suggested with the Institute of Environmental Medicine, Division of Metals and Health, Karolinska Institutet (professor Marie Vahter) in the area of arsenic biochemistry.
KEY PERSONNEL (List names of all investigators including PI and their respective specialties)

<table>
<thead>
<tr>
<th>Name</th>
<th>Professional discipline/speciality</th>
<th>Role in the project</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Lars Åke Persson</td>
<td>Epidemiologist, professor, head of Public Health Sciences Division, ICDDR,B</td>
<td>Principal investigator</td>
</tr>
<tr>
<td>2. Shams El Arifeen</td>
<td>Epidemiologist and head, Child Health Programme</td>
<td>Co-investigator</td>
</tr>
<tr>
<td>3. SM Akramuzzaman</td>
<td>Senior Medical Officer, Clinical Sciences Division</td>
<td>Co-investigator</td>
</tr>
<tr>
<td>4. Abbas Bhuiya</td>
<td>Social scientist, head, Social and Behavioural Sciences Programme</td>
<td>Co-investigator</td>
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<tr>
<td>5. Eva-Charlotte Ekström</td>
<td>Nutrition epidemiologist, Clinical Sciences Division</td>
<td>Co-investigator</td>
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<tr>
<td>6. Md. Khalequzzaman</td>
<td>Epidemiologist, senior physician, Child Health Programme</td>
<td>Co-investigator</td>
</tr>
<tr>
<td>7. Mahfuzar Rahman</td>
<td>Environmental epidemiologist, Public Health Sciences Division</td>
<td>Co-investigator</td>
</tr>
<tr>
<td>8. Peter Kim Streatfield</td>
<td>Demographer, head of Health and Demographic Surveillance Programme</td>
<td>Co-investigator</td>
</tr>
<tr>
<td>9. Nigar Shahid</td>
<td>Senior scientist, Child Health Programme, Public Health Sciences Division</td>
<td>Co-investigator</td>
</tr>
<tr>
<td>10. MA Wahed</td>
<td>Head, Nutrition Biochemistry Section, Clinical Sciences Division</td>
<td>Co-investigator</td>
</tr>
<tr>
<td>11. Md Yunus</td>
<td>Scientist and head, Matlab Health Research Programme</td>
<td>Co-investigator</td>
</tr>
<tr>
<td>12. Mushtaque Chowdhury</td>
<td>Director Research, BRAC</td>
<td>Co-investigator and co-ordinator of mitigation activities</td>
</tr>
<tr>
<td>13. Marie Vahter</td>
<td>Professor, Division of Metals and Health, Institute of Environmental Health, Karolinska Institutet, Stockholm</td>
<td>Co-investigator</td>
</tr>
</tbody>
</table>

DESCRIPTION OF THE RESEARCH PROJECT

Hypothesis to be tested:

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

The overall objective of this project is to establish a strong epidemiologic platform of research on arsenic toxicity and health effects, intervention with arsenic mitigation, and follow-up to evaluate effects of the intervention, such as reversibility of arsenic-related skin lesions and possible consequences for contamination of drinking water and diarrhoeal disease morbidity.

The primary hypotheses we will test are:
• Although several studies have demonstrated dose-effect relationship between arsenic in drinking water and various health effects, such as skin changes, the knowledge base is weak for assessment of burden of arsenic induced disease and projections into the future in Bangladesh, especially considering the possible influence of wide-spread malnutrition and the general health conditions of the population. We postulate that the individual susceptibility to develop arsenic-related skin changes (melanosis, keratosis, leucomelanosis and hyperkeratosis) for a given dose and duration of arsenic exposure is a) higher for younger individuals as compared to older, b) higher for boys and men as compared to girls and women, c) higher for those with anthropometric signs of chronic protein energy deficiency as compared to normal anthropometry and d) higher for those with micronutrient deficiencies (especially selenum, zinc and antioxidants) as compared to those without deficiencies.

• Laboratory-based studies and a few population-based, mainly ecological studies, indicate that arsenic exposure may increase risk for spontaneous abortions and stillbirths. We postulate that women who have higher arsenic concentrations in their drinking water and report consumption of water from those tube wells during previous pregnancies have a higher rate of negative pregnancy outcome, i.e. miscarriages, stillbirths and early neonatal deaths.

• Studies from other countries have shown that long-term exposure to arsenic in drinking water increases the mortality risk for cardiovascular diseases and selected cancers. Given the relatively long use of tube-well water in the Matlab area and the arsenic concentration levels measured in pilot studies there may be reasons to anticipate an arsenic-related excess mortality by such causes. We postulate that individuals with higher dose-time levels of arsenic exposure have a higher mortality in malignant neoplasms and/or cardio-vascular diseases as compared to those with low arsenic concentration in drinking water.

• There is only anecdotal information about reversibility of skin changes after shift to arsenic-free water. Follow-up of patients with skin changes including monitoring of arsenic concentrations in urine may provide the needed knowledge. We postulate that a cessation of arsenic intake through drinking water in individuals with arsenicosis of skin will result in some degree of reversibility of these skin changes.

• An arsenic mitigation programme with a shift to alternative, arsenic-low or arsenic-free water sources might potentially imply an increased exposure to pathogen-contaminated water, e.g. unclean surface water. However, this does not necessarily imply an increased rate of diarrhoeal diseases, for example in children. We postulate that a shift to alternative, arsenic-low or arsenic-free water sources as part of a mitigation program will not imply an increased incidence of diarrhoeal diseases in children under five years of age in these households.
In addition, there are other secondary objectives with the proposed activities. The tube wells in the surveillance area are already having their coordinates in the Geographic Information System (GIS), which is part of the Matlab databases. An update of all newly constructed tube wells is under way. The GIS also includes satellite images of the area at different time periods, and this may be expanded in order to characterise the surface (flooding areas, landscape characteristics) and to study these spatial pattern and geographical and seasonal variation of arsenic contamination of ground water. This part of the databases may also offer opportunities for other scientists in hydrology and geochemistry to link their studies to the population and the health effects.

Another obvious secondary objective is to establish a prospective database for studies of arsenic and health based on the Matlab surveillance system, including individual information on water consumption and arsenic concentration in that water, GIS information on the tube wells, presence or absence of skin changes, interventions with arsenic mitigation activities. This information will easily be linked to other types of information (socio-economic conditions, health data) in the system.

---

**Background of the Project including Preliminary Observations**

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

---

**Background and significance**

A major proportion of the tube wells in the large delta region of Bangladesh is contaminated with arsenic, showing levels high above the safety limits (WHO permissible limit 10µg/L and Bangladesh limit is 50µg/L) (1-3). This implies that, according to estimates based on nation-wide surveys, more than 20 million people are exposed to arsenic in drinking water above current safety limits (4). Arsenic exposure through drinking water is known to cause a number of serious health consequences. Skin lesions, i.e. diffuse melanosis followed by spotted melanosis, hyperpigmentation, and keratosis are common and the first recognised health effects — and also believed to be a marker for increased risk for other, more serious malignant and non-malignant consequences. In spite of a vast number of studies from other countries there is still lack of knowledge on the dose-effect relationships between arsenic in drinking water and skin lesions and other health effects. Similarly, there is insufficient knowledge on the possible modifications by age, sex, and nutritional status, and on the possible reversibility of some
of the health effects. Epidemiological information of this type is much needed for proper planning of countrywide interventions in Bangladesh.

**Arsenic in the human body**

Arsenic is absorbed in the gastrointestinal tract in humans. Inorganic arsenic is methylated during metabolism and is excreted mainly as mono-methylarsenic acid (MMA) and dimethylarsenic acid (DMA) in humans, but only as DMA in animals. Trivalent arsenic (As$_{III}$) is most readily methylated, and the reduction of As$_V$ to As$_{III}$ seems to involve oxidation of glutathione (GSH) and has been proposed to be a critical step in arsenic metabolism. Absorbed arsenic interferes with the activity of several enzymes in the heme biosynthesis pathway and modifies urinary excretion of porphyrins in both animals and humans. Chronic occupational exposure to arsenic results in an increase in total coproporphyrin (I+III) in urine. Thus it may be possible to use this parameter, as well as urinary arsenic, MMA, and DMA, as a means of biological monitoring.

**Rationale for investigating the variation in individual susceptibility to arsenic-related skin lesions**

The latency (i.e. the time from first exposure to manifestation of disease) for arsenic-caused skin lesions, in particular keratosis, is typically of the order of 10 years (5). However, latency much shorter as well as longer than 10 years may occur, and the rapidity of the appearance of skin lesions seems to be dose dependent. In order to assess the burden of arsenic-induced health problems age- and gender-specific information on the occurrence of such effects is needed, as well as an improved understanding of the exposure to arsenic over time.

The ingested arsenic is methylated and excreted in urine. Children have reportedly a lower degree of methylation of arsenic than adults. Anecdotal information from arsenic mitigation activities in affected areas indicates that children are found to have arsenic skin lesions long before expected latency periods. Some studies indicate a lower degree of arsenic methylation in men than in women, especially as compared to pregnant women (6). This may be part of the reason why men are described to show arsenic-related skin lesions more frequently than women, under seemingly equal exposure levels to arsenic in drinking water (5).

Poor nutritional status might increase the health effects of arsenic through variations in the arsenic methylation capability (7-9). Vitamin A status in the population may be related to susceptibility to arsenic related diseases. The risk of skin cancer in arsenic-exposed individuals has been associated to beta-carotene levels (8, 10). Such associations have also been shown for cardio-vascular disease risks (7). The general nutritional status (as expressed by anthropometry), the antioxidant status and other micronutrients such as zinc status may play an important role in modifying the body’s response to arsenic exposure. No information is available on the role of general malnutrition in relation to arsenic-related diseases in a society like Bangladesh, where malnutrition is wide-spread (almost half of the births <2500 grams, more than half of the children stunted, wide-
spread malnutrition among adult women, vitamin A deficiency still common in spite of supplementation programmes, iron deficiency in adult women almost fifty per cent).

Rationale for investigating effects on reproductive outcome

Very little is known about the human effects of arsenic contaminated water on foetal growth, miscarriages and stillbirth. Animal experiments have shown that arsenic exposure increases the risk for foetal death and growth retardation (11). Human data are limited to a few ecological studies of populations exposed to arsenic from drinking water or from work near smelters. Associations with spontaneous abortions and stillbirths have been shown, but are difficult to interpret due to multiple chemical exposures in those groups, or due to the weak study design (12, 13).

Even a relatively low excess risk of abortions, stillbirths and early neonatal deaths related to arsenic in drinking water would have a major public health impact in Bangladesh, due to the vast number of pregnant women exposed to the arsenic contaminated water.

Rationale for investigating effects on mortality in cancer and cardio-vascular diseases

Lifetime excess risk of skin cancer if exposed to arsenic in drinking water has been assessed to be 1.3/1000 for men and 0.6/1000 for women per microgram of arsenic per day. In its latest document on arsenic in drinking water, the U.S. National Research Council (NRC) concluded that there is a combined cancer risk of 1 in 100 at the level of 50 μg/L and 1/10 at the level of 500 μg/L (11). If this is true also for the Bangladeshi population the public health consequences are frightening, since more than a 20 million population currently is estimated to be exposed to have arsenic in their drinking water above the level of 50 μg/L (4).

In Matlab more than half the population have got their drinking water from tube wells for almost 20 years, and one quarter of the population had tube wells as their source of drinking water almost 30 years ago (see figure 1 in preliminary results). This implies that a major part of the population has had a sufficiently long period of exposure to cause arsenic-related deaths in cancers and cardio-vascular diseases (given a relatively constant arsenic level in the tube wells over time). Thus, there are reasons to use the health and demographic surveillance system and assess the current and recent mortality in cardio-vascular diseases and cancers in relation to arsenic exposure. Such information may be used for projections of the nation-wide mortality impact of the arsenic exposure.

Rationale for investigating the reversibility of skin changes

The appropriate treatment for arsenic-induced skin changes is a shift to arsenic-free drinking water. However, there is insufficient knowledge to what extent these skin changes disappear when the individual is no longer drinking the contaminated water. There is anecdotal information available that less advanced skin changes are reversible, but unknown if this also is the case for more advanced lesions. Measurements of urine arsenic levels are needed to judge if the exposure has ceased. A better understanding of
the potential reversibility is needed from a clinical as well as a public health point of view.

Rationale for investigating any change in diarrhoeal disease incidence when implementing arsenic mitigation activities
A shift to alternative arsenic-free water sources may potentially imply a shift to pathogen-contaminated water. This is especially the case when surface water will be used as the new water source, but may also be the case when harvesting rainwater. In most mitigation projects so far some control of pathogens has taken place, e.g. by cultivating samples from the new drinking water source. This is an important intermediate step, but a monitoring of diarrhoeal diseases in vulnerable groups, i.e. infants and children, is also needed. The Matlab surveillance system has included a monitoring of diarrhoeal diseases in all children below 5 years of age. This information can be used in order to evaluate if the shift to alternative water sources increases the risk for diarrhoea.

Preliminary results
Matlab, a field research area of ICDDR,B: Centre for Health and Population Research, has been chosen for field activities of this project. It is situated 53 km south east of Dhaka, accessible by road and river transport. The positioning of Matlab is highly affected by the sedimentation process of arsenic laden soil, as it is situated near the Meghna River, where it joins the confluents streams of the Brahmaputra and Ganges rivers. The area is low-lying delta plain intersected by branches of the rivers and numerous canals. During the monsoon essentially all land is flooded, except clusters of houses built on earthen mound. In 1988-89, a 60-km long embankment was built alongside the bank of the Dhonagoda and Meghna rivers. The embankment was built primarily to protect the area from monsoon flooding so that agricultural activities might be carried out throughout the year.
**Start of use of tube wells as drinking water**

During the latest decades a radical shift in drinking water sources have taken place (Figure 1). In 1974 one quarter of the Matlab population got their drinking water from drilled tube wells, increasing to a bit more than half in 1982 and 95% in 1996. Thus, potential exposure times to arsenic in tube well water may have a median around 15-20 years for the adult population. The tube well water is only to a limited extent used for washing.

![Graph showing percentage of households using tube wells as drinking water from 1974 to 1996](image)

*Figure 1. Sources of drinking water in Matlab over time. Based on information from Health and Demographic Surveillance System, Matlab (ICDIN,B. Demographic surveillance system – Matlab. 1996 Socio-economic census. Volume 29: Dhaka, iCDIN,B, 1998).*

**Arsenic concentration**

A pilot study was performed in 1997 with a strategic sample of 60 tube wells from all areas in the Matlab surveillance system. More than three quarters of these samples had total arsenic above the GoB maximum permissible limit of 50 µg/L. In 2001, 20 tubewell water samples were further analyzed and the arsenic concentration was on the same level as in 1997.
Figure 2. Arsenic concentrations in pilot study of tube wells in Matlab, Bangladesh. Cumulative frequency curve. Median arsenic level 144 ug/L water. Thirty-two per cent of the samples above 50 ug/L.

The Matlab area is located in the central part of the areas in Bangladesh showing the highest arsenic concentrations in tube wells, according to the information provided by the British Geological Survey (4).

Skin changes
No systematic evaluation of the presence of arsenic-related skin changes have so far been performed in Matlab. Linked to the pilot study of tube well water (see above) members of households with a high arsenic content in their water were examined and arsenic-related skin lesions were confirmed in some individuals, and these individuals and households were given appropriate advice. The ICDDR.B staff clinic in Matlab has also diagnosed a number of staff with skin lesions, their tube wells have been tested and appropriate measures have been taken. This more anecdotal information underlines the probability that arsenic-related skin lesions are present in the Matlab area. A survey is needed to assess the prevalence.

Reproductive outcomes
From the information provided by the health and demographic surveillance in Matlab the number and rates of pregnancy outcomes are reported on an annual basis (table 1). Live births constituted 89.1% of the registered pregnancies, miscarriages 8.1% and stillbirths 2.9% (data from 1998).

<table>
<thead>
<tr>
<th>Type of pregnancy outcome</th>
<th>Number</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total pregnancies</td>
<td>6486</td>
<td>120.1 per 1000 women 15-49 years</td>
</tr>
<tr>
<td>Live birth pregnancies</td>
<td>5776</td>
<td>89.1 % of pregnancies</td>
</tr>
<tr>
<td>Total foetal wastage</td>
<td>710</td>
<td>10.0% of pregnancies</td>
</tr>
<tr>
<td>Early (miscarriages)</td>
<td>525&lt;sup&gt;1&lt;/sup&gt;</td>
<td>8.1% of pregnancies</td>
</tr>
<tr>
<td>Late (Stillbirths)</td>
<td>185</td>
<td>2.9% of pregnancies</td>
</tr>
<tr>
<td>Neonatal deaths (first month)</td>
<td>236</td>
<td>40.5 per 1000 live births</td>
</tr>
</tbody>
</table>

<sup>1</sup>Out of this 43% reportedly induced.

**Adult mortality**

Mortality registration is part of the health and demographic surveillance system. A verbal autopsy procedure includes a standardised questionnaire to identify the symptoms preceding death and possible causes. In one year (1998) there were 85 deaths reported due to malignant neoplasms and 160 cardiovascular deaths out of a total of 1111 adult deaths in a population of 134,999 individuals from 15 years and above.

**Nutritional status**

Malnutrition is widespread in Bangladesh, and Matlab is no exception. Forty-five percent of the infants are born with a weight below 2.5 kg (in Sweden 5%). Micronutrient malnutrition is common in children as well as in adults. In a recent supplementation trial in pregnant women in another area of Bangladesh 6 out of 10 women had low serum zinc levels (LA Persson, unpublished data). In a recent survey of women in reproductive ages the average weight was 44 kg, and one quarter was below 40 kg. Thus, there are reasons to believe that a relatively high proportion of individuals have protein and energy deficiencies and micronutrient deficiencies that theoretically may be important for the individual susceptibility to arsenic toxicity.

**Research Design and Methods**

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

Study site
The Matlab study site is briefly described above under preliminary observations. ICDDR,B is running a health and demographic surveillance system in 142 villages of the Matlab thana, encompassing a 220,000 population in 18,386 hectares of land. The Matlab health and demographic surveillance system (HDSS) was initiated already in 1963, and records all vital events, as well as in- and out-migration. Births, deaths, marriage, pregnancies and different pregnancy outcomes are registered and up-dated by community health workers on a monthly basis. In addition, selected information on reproductive and child health, socio-economic conditions, and health interventions etc. has been collected cross-sectionally or continuously. A geographic information system (GIS) is an integrated part of the HDSS, and includes spatial information on households, tube wells, health facilities, landscape characteristics etc.

ICDDR,B has a central health facility in Matlab that receives 15,000 patients per year. This facility is equipped to support clinical and public health research in the area. Clinical examinations, laboratory examinations and treatment efforts of patients with arsenic-related diseases may take place in Matlab health facility. Four sub-centres in half of the surveillance area provide primary health care and support to studies. In the other half of the surveillance area the government provides health services to the population.

Study procedures
The shift in drinking water source from surface water to tube well water in the 1970s and 1980s went with some radical changes in perceptions of drinking water quality, taste, relation between water and health etc. Now, a few decades later, a new change in the understanding of drinking water, its qualities and the relation to health is needed. We intend to start the field activities of the proposed studies by an ethnographic study that will focus the following sectors of information: (a) attitudes towards the different drinking water sources, taste of water, practical issues regarding access to water, handling of water and use of drinking water. Who are the decision makers regarding issues of water sources, and use of water for drinking? (b) Perceptions of water and health, water and illnesses and disease. The arsenic-related health effects are often non-visible but some individuals (unknown frequency) have developed arsenic-related skin lesions. Are there any attitudes formed regarding these skin problems and to what extent are those perceived as related to the water? (c) Are there any attitudes formed on arsenic in drinking water? Is there an awareness of the problem, and how is this problem perceived? This research will be conducted in the initial steps of the project, and probably be supplemented by additional fieldwork as the project develops. The initial results of the ethnographic study will be used to finalise questionnaires and procedures used in the project.

The project has two phases: (1) covering the 110,000 population in the part of Matlab, where ICDDR,B is providing health services, and (2) including the remaining part of the
HDSS area – another 110,000 population. Depending upon funding both steps will be taken simultaneously, or following after one another. The first step will enable the creation of a database that is sufficient for initial answers to the research questions, while the completion of the entire 220,000 population will offer much better power for the analytical work and therefore better precision in the results. See sample size calculations below.

Study Design

- A retrospective cohort analysis of current exposure (as a proxy for exposure levels over time) and duration of exposure to the arsenic contaminated water on skin changes will be assessed. Information from testing of all 9000 tube wells (4500 in each step), individual information on water used for drinking, and results of screening for arsenic-related skin lesions in the entire 220,000 population (excluding infants) will be entered into a database. This will enable us to analyse the doses of arsenic in relation to presence of arsenic skin lesions and will also enable us to evaluate the individual susceptibility to develop arsenic-related skin changes (melanosis, keratosis, leucomelanosis and hyperkeratosis) for a given dose and duration of arsenic exposure.

- A case-referent study of the modification by current nutritional status on arsenic-induced skin lesions will be nested into the above cohort study. Individuals with arsenic skin lesions (above 5 years of age) will be selected as cases, and two referents without arsenic skin lesions will be randomly selected from the HDSS databases. Nutritional status of cases and referents will be assessed by anthropometry and blood samples will be taken for nutritional biochemistry. Urine samples will be taken from cases and referents as soon as the cases are identified for analysis of arsenic methylation patterns as well as current exposure levels. This approach will be enabling us for testing the hypotheses that individual susceptibility is higher for those with signs of protein energy malnutrition and micronutrient deficiencies compared to individuals with normal nutritional status.

- A second retrospective cohort analysis will be performed to assess current exposure and duration of exposure on reproductive events, such as, spontaneous abortions, still births, and early neonatal deaths during the last three years (1997-2000). The information on reproductive events are available in HDSS database. This approach will enable us to test the hypothesis that women who have higher arsenic concentrations in their drinking water and report consumption of water from arsenic contaminated tube wells during previous pregnancies have a higher rate of negative pregnancy outcome, i.e. miscarriages, stillbirths and early neonatal deaths.

- A third cohort analysis will assess the effect of arsenic exposure on overall adult mortality during the last five years (1995-2000). Mortality information including cause of death is available in the HDSS database, specifically cardio-vascular
diseases and cancer mortalities during the last five years. This approach will enable us to test the hypothesis that individuals with higher dose-time levels of arsenic exposure have a higher mortality from malignant neoplasms and/or cardio-vascular diseases as compared to those with low arsenic concentration in drinking water.

BRAC, a Bangladesh NGO, will be responsible for the arsenic mitigation component. Initial advice of temporary alternative drinking water sources will be given (arsenic-free tube wells in the neighbourhood). In close collaboration with the concerned people this will be followed by promotion of alternative sources of safe drinking water (rainwater harvesting, treated surface water, and treated arsenic contaminated ground water). The safe water options that BRAC is currently implementing are: rain water harvesting (RWH), treatment of pond water with “pond sand filter” (PSF), treatment of ground water with “Safi” candle filter, and dug well.

- A follow-up study will be performed including individuals having skin changes in order to assess the effect of arsenic mitigation on the reduction of arsenic levels in urine (change in exposure), as well as on reversibility of skin lesions, assessed by clinical examination. This will enable us to test the hypothesis that cessation of arsenic intake through drinking water in individuals with arsenicosis of skin will result in some degree of reversibility of these skin changes.

- An arsenic mitigation programme with a shift to alternative, arsenic-low or arsenic-free water sources might potentially imply an increased exposure to pathogen-contaminated water, e.g. unclean surface water. Water quality of all alternate safe water options will be monitored and tested by BRAC, especially for diarrhoeal pathogen contamination. This will enable us to test the hypothesis that a shift to alternative, arsenic-low or arsenic-free water sources as part of a mitigation program will not imply an increased contamination of alternate water source.

Training of field staff

*Training of field team.* Extensive training will be given to the field team on arsenic, its health consequences and skin lesions. The training will be conducted by the staff of ICDDR, B, and assistance will be sought from DCH, NGO- Forum and NIPSOM. The training will especially be focused on how to identify arsenicosis patients.

*Training for FRA and Shastha Sebika (SS, BRAC).* Training will be given about the details of origin and extent of arsenic poisoning in the ground water of Bangladesh. On the second day the FRA and SS will learn about the technique of testing of arsenic in the field using field kit. Later more lessons will be provided on how to collect the water samples, transport and storage.

*Training of Medical Officers.* Training will be given on arsenic and its health consequences at Matlab Training Centre. The training will be conducted by the staff of
ICDDR, B, with assistance from DCH and NGO- Forum. The training will be concentrated on how to identify arsenicosis patients. First, the training will provide details about the origin and extent of arsenic poisoning in the ground water of Bangladesh, health aspects of arsenicosis, and identification of patients. Second, theoretical and practical training will be provided in identifying arsenicosis skin lesions. This training will include patients with different skin manifestation, i.e., keratosis, melanosis and/or leucomelanosis. The participating physicians will examine the identified individuals and classify the skin lesions as arsenic-related lesions, suspected arsenic-related lesions and not arsenic related skin problems. A competent dermatologist will also train the physician in order to have the different diagnoses (DD) for arsenic skin lesions, i.e., Addison’s disease, cirrhosis of liver, pellagra, excessive exposure to sun, xeroderma, corns, warts, etc. Later the physicians can train the field teams in order to identify suspected individuals in the field.

Role of Dermatologist: A competent dermatologist will be recruited for the study. He will train the study personnel on identification of arsenic related skin lesions and he will also validate randomly selected sub-sample of arsenic lesions, diagnosed by health workers and physicians.

Skin screening in the field

Trained field teams with male and female field research assistant (FRA) will perform a clinical screening of skin manifestations in the entire study population from 5 years of age and above (approx. 190,000 population, 97,000 in the first phase). The community health research workers (CHRWs) will introduce the field team to the community. There will be 10 teams (each consisting of one male FRA and one female FRA). The team will move from village to village until the entire area is covered. Skin manifestations of arsenicosis (melanosis, keratosis, leucomelanosis and hyperkeratosis) will be confirmed following criteria developed in consultation with expertise in this field. They will work for the whole Matlab DSS area encompassing 220,000 population after finishing the intervention area. Individuals with skin lesions will be invited to the Matlab central health facility for confirmation by physician. The diagnosis of skin lesions by the physicians will be validated by the dermatologist in a randomly selected sub sample of cases. Screening of skin changes will precede the screening of arsenic water concentrations in tube wells, but will be closely linked in time to avoid possible biases. Photographs of the skin lesion will be taken by a digital camera under standardised conditions and used for validation of the findings by an expert panel. The validation will be used for retraining of the field staff and for quality control.

Measurement of blood pressure

The physician will further examine the individuals as well as measure blood pressure. Blood pressure will be taken after rest and relaxation for at least 15 minutes in sitting position according to the protocol recommended by the World Health organization.
Blood pressure will be measured 3 times by mercury column sphygmometer and the lowest value will be taken as the proper value.

Assessment of arsenic in tube wells

Approximately 9000 tube wells (4500 in each phase) in the Matlab area will be screened by use of Merck field kits, and tube wells with concentrations of arsenic above 50 µg/L will be classified as arsenic contaminated. A field team comprising of a FRA (field research assistant) and SS (Sastha Sabika, BRAC) will analyse tubewell water. This screening of water will take place after the screening of arsenicosis in order to avoid biases. On the same occasion water samples will be taken and frozen for analysis by atomic absorption spectrophotometry (AAS) at the ICDDR,B laboratory in Dhaka. The initial semi-quantitative screening test is needed for the interaction with the community members and initial mitigation activities. The AAS analysis is needed for the dose-effect analysis over the whole range of arsenic concentrations in tube wells. A random subsample of 600 tube well water samples will be selected for repeated examination by AAS over time in order to study seasonal variation and time trends (quarterly testing). The arsenic screening activities will be closely co-ordinated with the mitigation activities. The initial advice on alternative water sources will immediately be given and discussed with the affected household when the filed test kit result is ready. The strategy for the long-term mitigation activities is summarised below.

Use of tube well water as drinking water

Information on use of tube wells (initiation of tube well, depth of tube well, GIS coordinates of tube wells, start of use as source of drinking water) is partly available in the current HDSS databases. These data will be checked on the household and individual level in order to generate exposure data for a specific tube well as well as for all individuals. For each individual a retrospective history of sources of drinking water will be taken, based on field experiences from West Bengal. In addition, a 24-recall of water intake will be taken.

Assessment of nutritional status

Some information on nutritional status of the Matlab population is already available in the Matlab databases (arm circumference on all children, weight of women 13-44 years of age in half of the area). Additional information is needed to assess the modifying effect by nutritional status on arsenic-related health problems. Anthropometric status (weight, height) will be measured on all identified cases of arsenicosis and two randomly selected referents for case-referent analysis.

Ascertainment of cause of death in the adult population

As part of the routine HDSS activities all deaths in the surveillance area are registered and a structured interview is performed with the relatives in order to register the symptoms preceding death or known diseases leading to the death of the individual. This
information is used in a standardised way to classify the causes of death. The information on cause of death is an integrated part of the HDSS databases.

**Case-referent study of arsenicosis of skin**

All identified cases from 5 years of age and above with arsenic-related skin lesions will be identified as cases. Arsenic causes a variety of benign skin lesions including hyperpigmentation, hyperkeratosis, leucomelanosis, and, more rarely, squamous cell carcinomas (14). Referents will be randomly selected from the HDSS databases (from 5 years of age).

Cases and referents will be invited to the Matlab central facility or, when appropriate, to the sub-centres. Photographs will be taken of skin lesions under standardised conditions and used for validation of the findings by an expert panel. Anthropometric measurements will be taken (weight, height). Blood samples will be taken for haemoglobin assessment by HemoCue® and for later analyses of relevant micronutrient status. The cases will be carefully re-examined in order to identify suspected skin cancer. Blood pressure will be measured, urine will be tested for glucose and protein, and evaluation will be done for peripheral vascular disease and peripheral neuropathy. Patients with arsenic-related diseases demanding proper treatment (e.g. skin cancers) will be referred to appropriate level of care for treatment.

**Laboratory analyses**

Water samples from tube wells will be collected in the villages and frozen to -20°, thereafter transported to Dhaka and analysed for total arsenic by AAS at the ICDDR,B laboratory.

First-morning urine samples will be collected with assistance from Community Health Research Workers, frozen and stored in -86° C freezers. Samples will be transported on dry ice to Karolinska Institutet, Sweden for analysis of inorganic arsenic and its methylated metabolites. These analyses will be conducted at Division of Metals and Health, Institute of Environmental Medicine, Karolinska Institutet, Sweden (Professor Marie Vahter). From the case-referent study all urine samples will be analysed for total arsenic. In a subsample with elevated values (estimated to 75%) speciation will be performed. In the clinical follow up of cases with skin lesions urine samples will be taken on a quarterly basis to evaluate the cessation of exposure to arsenic. We estimate that two such follow up urine collections will be done per patient during a 2-year period.

Blood samples from the case-referent study will be analysed for S-zinc and selenium (atomic absorption spectrophotometry). Parts of the samples will be stored for additional analyses (follic acid, β-carotene).
Sample size calculations

Cohort analyses. In the 220,000-population sample, 190,000 are 5 years of age and above, according to our demographic surveillance, and included in the skin screening. A conservative estimate, based on local data from other arsenic-exposed Bangladeshi communities, indicates that 0.5% of the population may have arsenic-related skin changes, i.e. 950 individuals. If the average exposure periods are 15 years and three quarters of the population are exposed to “toxic” levels, relative risks for skin changes among exposed (using 50µg/L as cut off for exposure) down to the level of 1.2 may be demonstrated, and with a dichotomous stratification (e.g. by gender) down to the level of 1.3. This implies that the sample size will allow for stratification and still maintain enough power to demonstrate the anticipated and even lower relative risks.

If three years of data on pregnancies and reproductive outcomes are included in the analysis, using a case-referent approach in the analysis, relative risks on the level of 1.4 may be detected for the outcomes miscarriage, stillbirth or neonatal death, respectively. Including a longer time period than 3 years provides more pregnancies for the retrospective analysis and increases the power. The disadvantage may be a potentially decreased quality of the exposure information.

A 5-year retrospective cohort analysis of cancer and cardiovascular deaths would allow for a detection of excess risks on the level of OR 1.4 and 1.2, respectively, given the mortality reported in those diagnoses 1996-2000 and a cut-off exposure level of 500 µg/L. If the duration of exposure and the latency periods so allows a longer period for the analysis may be included.

Case-referent analysis. Assuming that 75% of non-cases are “exposed” (e.g. to arsenic levels >50µg/L) and that 2 referents are selected per case of skin lesions an OR of 1.2 may be detected. If stratifying into two groups, e.g. by sex, an OR of 1.3 may be detected (given that α=0.05 and 1-β=0.80). The sample size in the case-referent study will suffice to detect any clinically relevant differences between (two) groups in hemoglobin, S-ferritin, S-zinc and S-β-carotene, according to our experience and available information on serum levels and variances from anemia studies in Bangladesh.

A random sub-sample of water from 600 tube wells will be assessed repeatedly on a quarterly basis in order to monitor time trends and evaluate seasonal variation. This sample size will allow a detection of overall seasonal differences of 30 µg/L (based on a mean of 212 µg/L, and a SD of 184 µg/L).

After a short period of mitigation activities, e.g. when 1/10 households have shifted to alternative water sources, a difference of a few percent in the point prevalence of diarrhoeal diseases caused by the intervention may be detected (presuming an overall point prevalence in under-five children of 8%).

Exposure assessment. Arsenic exposure level will be categorized on different levels and will account for duration in order assess dose-effect relations.
<table>
<thead>
<tr>
<th>Design</th>
<th>Population</th>
<th>Outcome, estimated number of cases</th>
<th>Exposure level</th>
<th>Proportion exposed in population</th>
<th>Lowest detectable RR (figure for phase 1* between brackets)</th>
<th>Sample size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cohort</td>
<td>190,000</td>
<td>Skin lesions (0.5% of the sample = 950)</td>
<td>&gt;50 µg/L</td>
<td>75%</td>
<td>1.17; 95% CI 1.01-1.36; (1.3)</td>
<td>Total population surveyed</td>
</tr>
<tr>
<td>Cohort, case-referent</td>
<td>19,000 pregnancies (3 years of surveillance)</td>
<td>Miscarriages (n = 662)</td>
<td>&gt;500 µg/L</td>
<td>10%</td>
<td>1.37; 95% CI 1.02-1.82; (2.0)</td>
<td>Case-referent analysis: 662 cases, 1324 referents</td>
</tr>
<tr>
<td>Cohort, case-referent</td>
<td>19,000 pregnancies (3 years of surveillance)</td>
<td>Stillbirths (n = 551)</td>
<td>&gt;500 µg/L</td>
<td>10%</td>
<td>1.40; 95% CI 1.02-1.91; (2.0)</td>
<td>Case-referent analysis: 551 cases, 1102 referents</td>
</tr>
<tr>
<td>Cohort, case-referent</td>
<td>17,300 live births (3 years of surveillance)</td>
<td>Neonatal deaths (n=702)</td>
<td>&gt;500 µg/L</td>
<td>10%</td>
<td>1.36; 95% CI 1.03-1.80 (1.8)</td>
<td>Case-referent analysis: 702 cases, 1404 referents</td>
</tr>
<tr>
<td>Cohort</td>
<td>ICDDR,B surveillance 1996-2000</td>
<td>Cancer deaths &gt;14 years of age during last 5 years (n=425)</td>
<td>&gt;500 µg/L (assuming sufficiently long exposure)</td>
<td>10%</td>
<td>1.37; 95% CI 1.03-1.82; (1.55)</td>
<td>5 years surveillance, 675,000 person years</td>
</tr>
<tr>
<td>Cohort</td>
<td>ICDDR,B surveillance 1996-2000</td>
<td>Cardio-vascular deaths &gt; 14 years of age during last 5 years (n=840)</td>
<td>&gt;500 µg/L</td>
<td>10%</td>
<td>1.23; 95% CI 1.00-1.51; (1.46)</td>
<td>5 years surveillance, 675,000 person years</td>
</tr>
<tr>
<td>Case-referent</td>
<td>190,000</td>
<td>Skin lesions, n = 950</td>
<td>&gt;50 µg/L</td>
<td>75%</td>
<td>1.20; 95% CI 1.00-1.45; (1.3)</td>
<td>950 cases, 1900 referents. When stratifying for 1 background factor OR ≥ 1.3 detectable</td>
</tr>
</tbody>
</table>

* Phase 1: study in the 110,000 population with 97,000 individuals >4 years.

**Arsenic mitigation intervention by BRAC**

BRAC, one of the largest national non-governmental organizations, has a proven capacity for field-level programme implementation, socio-economic research, a strong institutional network and experience in training community members in testing tube well water for arsenic. BRAC’s action research on community based arsenic mitigation includes the following major components.

**The safe water option implementation plan**

This component of the project aims at installing safe water options in arsenic affected areas in Matlab. Priority will be given to villages where the arsenic problem is acute. The safe water options will be installed after testing of tube wells is completed and the
alternative options are evaluated. Monitoring of the water quality and social acceptance of the alternative options will be carried out during the project period.

Situation analysis and participatory decision making

The BRAC Community Health Workers from each village in the area will be jointly trained by BRAC and ICDDR,B in the health effects of arsenic, arsenic testing, and alternative water sources. This training will also be co-ordinated with the government arsenic project BAMSWP. ICDDR,B and BRAC staff will jointly perform the testing of tube wells, described above. Villages meetings will be held with a cross section of villagers as part of the testing process. Once all tube wells have been tested, the results will be presented to the village community in a second meeting. At that meeting, alternative sources of safe drinking water will also be discussed. A limited list of solutions is approved by the project and will be promoted. This list of options may change over time, if indicated and advised by government and other stakeholders. Since villagers have little or no experience with alternative safe water sources, demonstration of different alternative safe water systems will be done, with no cost to the community. However, the community would decide where the system would be located, and commit themselves to maintain the system.

System implementation

Identified alternative safe water options will be construction of BRAC’s Technical Advisor. BRAC engineer will oversee the construction and commissioning of the process.

Table. Different safe water options initially selected for the project.

<table>
<thead>
<tr>
<th>Option</th>
<th>Water sources</th>
<th>Location</th>
<th>Families served</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ponds sand filter (PSF)</td>
<td>Surface water</td>
<td>Community</td>
<td>40-60</td>
</tr>
<tr>
<td>Rain water harvesting (RWH)</td>
<td>Rain water</td>
<td>Family</td>
<td>1</td>
</tr>
<tr>
<td>Two chamber treated unit</td>
<td>Surface water</td>
<td>Community</td>
<td>6-10</td>
</tr>
<tr>
<td>Safi filter</td>
<td>Ground water</td>
<td>Family</td>
<td>1</td>
</tr>
</tbody>
</table>

Pond and sand filters. In areas where deep tube wells are not feasible, it is possible to treat surface water from ponds, that are exclusively reserved for drinking purposes and to make it safe for drinking and cooking. DPHE, supported by UNICEF, has designed a community-based slow sand filtration system, called pond sand filter, which can remove bacteria from surface water by filtering it through a large tank filled with sand and gravel. It is now being successfully used in arsenic-effected areas. Community members must periodically clean pond sand filters by washing the top layers of sand.

Deep wells. Deep wells, deeper than 80 meters, are free from arsenic. Dhaka city water and the water sources of the southern part of Bangladesh (where salt water enters the shallow aquifer) are therefore mostly free from arsenic. Although more expensive than shallow wells, deep wells could be an alternative. If such wells are dug carelessly, there is a possibility of "shunting" the aquifers and allowing water from the higher, arsenic-
contaminated aquifer contaminate the lower aquifer. It is unclear whether, in a longer perspective, pumping would increase the arsenic content in those wells.

Rainwater harvesting. Like pond sand filters rainwater-harvesting systems have been used in the coastal districts for years, and are being introduced in arsenic-affected areas. Rainwater harvesting system use a tin rooftop or sometimes a sheet of plastic, to collect rainwater and store it in large cement tanks. Users let the first few minutes of rainfall without collecting the water, to clean roof and gutters. Once in the tank, the rainwater can be safely stored indefinitely without being contaminated by bacteria. With a large enough tank, a family can store enough water for drinking and cooking all through the dry season.

Monitoring of water quality and use of water. Water quality of all alternate safe water options will be monitored and tested, especially for diarrhoeal pathogen contamination. BRAC staff will visit each village on a regular basis to monitor the operation and maintenance of alternative water systems and motivate to promote safe water use. After distribution or construction of any option among the villagers it requires continuous monitoring of the use of each and every option at least for few months because people are used to the tube well water and may find the alternative options more complicated.

Evaluation of impact and possible negative consequences of intervention

The operation and maintenance of the alternative water systems will be monitored by BRAC, see above. The shift to alternative arsenic-free water sources might imply an increased exposure to pathogens that could result in increased rates of diarrhoeal diseases in vulnerable groups, i.e. infants and children. The occurrence of diarrhoeal diseases is monitored as part of the health and demographic surveillance, by monthly home visits and interviews. The occurrence of diarrhoeal diseases in children of households with new water sources will be compared to households without such changes, considering possible confounding, e.g. by age.

Potential impact

This project will generate new knowledge on doses of arsenic exposures and effects on health, i.e. the occurrence of skin lesions and negative reproductive outcomes, such as miscarriages, stillbirths, and neonatal mortality. The toxic effects on skin will be evaluated in relation to age, sex, and nutritional status. Further, the studies will provide answer to the question if the arsenic contamination of the drinking water already is resulting in excess mortality among adults. Such information is much needed in the discussion and forecasting of the arsenic-related health consequences in Bangladesh. The results would further give a solid epidemiological platform for a better understanding of the speed by which arsenic-related diseases and health manifestations develop in the currently arsenic-exposed Bangladeshi population, and the effect of an arsenic mitigation intervention. ICDDR,B and the Matlab surveillance system offer unique possibilities for such studies. Due to the already collected health data of that system the answers to these important questions may be provided within a 2-year project period.
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. (TYPE WITHIN THE PROVIDED SPACE).

The Matlab research and services infrastructure is presented in the text above. These facilities are unique and make this project possible. The health and demographic surveillance system will provide a lot of the necessary information needed. A strong research team has been formed with strong competence in epidemiology, arsenic epidemiology, nutrition, clinical sciences, reproductive epidemiology and biochemistry. Excellent partners have been identified in the area of arsenic mitigation (BRAC) and arsenic biochemistry (professor Marie Vahter, Karolinska Institutet). The ICDDR,B biochemistry laboratory has already an AAS equipment for arsenic analysis (only total arsenic), but the procurement of another AAS equipment would considerably increase the capacity.

Data Analysis

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

The investigators will review all questionnaires and data forms for accuracy, consistency and completeness. After editing, data will be entered for editing and cleaning. Periodical checks will be performed by running and reviewing frequency distributions and cross-tabulations. The HDSS has a series of data quality controls that will further ensure the completeness and correct identities of the information. Cohort analysis, and multivariable modelling of doses and effect will be done by use of SPSS 10.0 or other appropriate software, as well as case-referent analysis and logistic regression modelling.

The modelling of doses and effects will include some different options in order to demonstrate alternative approaches and how robust the estimates are. It will include calculations of standardized morbidity ratios (SMR), standardized rate ratios (SRR), and Cox regression analyses catering for possible influence by age, sex and other confounding factors.
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.

The study will include invitation for testing of tube well water, inspection of skin for arsenic skin lesions, and, in a sub-set of the population, blood sampling for micronutrients, and urine sampling for arsenic analyses. The water testing and the screening for skin lesions will benefit the persons in the affected households and proper advice will be given to affected households and individuals. The blood sampling is not of immediate benefit to the individual participant, although the assessment of haemoglobin may be useful for anaemic individuals who may benefit from iron therapy. The urine sampling is not of immediate benefit to the participants, although the assessment of total arsenic will be useful for some individuals in getting further advice to change to arsenic-free drinking water. However, due to logistic reasons there will be a delay in the analysis of arsenic in urine. Informed consent will be sought, and participants will be free to refrain totally from participation or from some part of the study. The study is linked to a mitigation activity for which a major national NGO, BRAC, is responsible. To benefit from that activity will not be conditionally linked to the participation in the study. The proposal will be reviewed by the Ethical Review Committee at ICDDR,B, Dhaka, Bangladesh.

Use of Animals

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

Not applicable
Literature Cited

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


Dissemination and Use of Findings

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

The findings will be communicated to other actors and stakeholders in the area of arsenic contamination of ground water and its health effect in Bangladesh. This will be done through reports (more popular as well as scientific reports) and through a workshop with invited participants at the Matlab training Centre during the second year of the project.

The findings will be used for the projections of health effects caused by the arsenic catastrophe in Bangladesh (burden of arsenic-induced diseases, disabilities and death). The findings will also be used in order to recommend appropriate actions in order to protect foetuses and newborns, in order to plan some aspects of the health services to arsenic-exposed communities, and in order to evaluate appropriate alternative water sources.

A narrative and a financial report will be submitted to the funding partners every 6 months. After completion of the project (at 24 months) a final report will be submitted to donors within another 2 months.

Collaborative Arrangements

Describe briefly if this study involves any scientific, administrative, fiscal, or programmatic arrangements with other national or international organisations 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. (DO NOT EXCEED ONE PAGE)

The mitigation program will be collaborated with Research and Evaluation Division, BRAC, Bangladesh (Director research, Dr Mushtaque Chowdhury). BRAC, a non-governmental organisation, has initiated an arsenic mitigation program. The organisation has gained considerable experience of field-testing of tube wells by field kits used by trained village health workers (VHW). BRAC has been running projects with UNICEF/DPHE (with participation by Grameen Bank and Dhaka Community Hospital) to involve communities in finding safe sources of drinking water once unacceptable arsenic levels in tube well water have been detected.

The arsenic biochemistry is collaborated with professor Marie Vather, Institute of Environmental Medicine, Division of Metals and Health, Karolinska Institutet, Stockholm. Professor Marie Vather is a leading expert on health effects of arsenic exposure and arsenic biochemistry. She has been involved in the planning of the project,
and will be responsible for overseeing the arsenic biochemistry activity. Her laboratory will be running the analysis of the urine samples.
Biography of the Investigators

May 2001

CURRICULUM VITAE

NAME
Lars Åke Persson
Born 1947-07-23 (ID 470723-1439)

CURRENT POSITIONS

Professor, International Public Health, Umeå University, Sweden (leave of absence since March 1, 1999)
Director, Public Health Sciences Division, ICDDR,B: Centre for Health and Population Research, Dhaka, Bangladesh

ADDRESS

Public Health Sciences Division, ICDDR,B
GPO Box 128, Mohakhali CA, Dhaka 1000, Bangladesh
Phone +880 2 9885155
Fax +880 2 8826050
E-mail persson@icddrb.org

EDUCATION/TRAINING

<table>
<thead>
<tr>
<th>INSTITUTION AND LOCATION</th>
<th>DEGREE (if applicable)</th>
<th>YEAR(S)</th>
<th>FIELD OF STUDY</th>
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<tbody>
<tr>
<td>Uppsala University, Sweden</td>
<td>MD</td>
<td>1973</td>
<td>Medicine</td>
</tr>
<tr>
<td>Sandvikskolan, Sweden</td>
<td>Certificate</td>
<td>1972-73</td>
<td>Aid and disaster relief training</td>
</tr>
<tr>
<td>Swedish Board of Health and Welfare</td>
<td>Certificate</td>
<td>1973</td>
<td>Tropical/international medicine</td>
</tr>
<tr>
<td>Gävle Hospital and Västernorrlands landsting, Sweden</td>
<td>Internship</td>
<td>1973-74</td>
<td>Medicine, Surgery, General practice</td>
</tr>
<tr>
<td>Dept Paediatrics, Örnsköldsviks sjukhus, Sweden</td>
<td>Residency</td>
<td>1974-76</td>
<td>Paediatrics</td>
</tr>
<tr>
<td>Dept Paediatrics, Umeå University, Sweden</td>
<td>Residency</td>
<td>1978-79</td>
<td>Paediatrics</td>
</tr>
<tr>
<td>Dept Child Psychiatry, Umeå University, Sweden</td>
<td>Residency</td>
<td>1979</td>
<td>Paediatrics/child psychiatry</td>
</tr>
<tr>
<td>Dept Infectious Diseases, Umeå University, Sweden</td>
<td>Residency</td>
<td>1979</td>
<td>Paediatrics/inf dis</td>
</tr>
<tr>
<td>Swedish Board of Health and Welfare</td>
<td>Specialist</td>
<td>1980</td>
<td>Paediatrics</td>
</tr>
<tr>
<td>Umeå University, Sweden</td>
<td>PhD</td>
<td>1984</td>
<td>Paediatrics/Paediatric Nutrition</td>
</tr>
<tr>
<td>Dept Paediatrics, Umeå University, Sweden</td>
<td>Docent</td>
<td>1990</td>
<td>Paediatrics</td>
</tr>
<tr>
<td>Umeå University, Sweden</td>
<td>Professor</td>
<td>1998</td>
<td>International Public Health</td>
</tr>
</tbody>
</table>

PROFESSIONAL EXPERIENCE

1976-1978  Medical Officer, Ndolage Hospital, Tanzania
1980-1983  Fellow, Social Medicine, Umeå University, Sweden
1983-1984  Fellow, Dept Paediatrics, Umeå University, Sweden
1984-1985  Medical Advisor, Institute for Protection of Children's Health, Hanoi, Vietnam
1985-1986  Fellow, Dept Paediatrics, Umeå University, Sweden
1986-1990  Senior lecturer/researcher in Paediatrics/Epidemiology, Umeå University, Sweden
1990-1997  Associate professor, Dept Epidemiology and Public Health, Umeå University, Sweden
1998-     Professor in International Public Health, Umeå University, Sweden
1999-     Director, Public Health Sciences Division, ICDDR,B, Dhaka, Bangladesh

LANGUAGES

Swedish - mother-tongue; English – fluent; Kiswahili – fluent; Spanish – fair; German – fair; French – fair

RESEARCH ADVISOR

Completed theses

<table>
<thead>
<tr>
<th>Title</th>
<th>Degree</th>
<th>Student</th>
<th>Year</th>
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</thead>
<tbody>
<tr>
<td>Infant mortality in transitional Nicaragua</td>
<td>PhD</td>
<td>Rodolfo Peña</td>
<td>1999</td>
</tr>
<tr>
<td>Adolescent pregnancies in Nicaragua. The importance of education.</td>
<td>PhD</td>
<td>Elmer Zelaya Bladon</td>
<td>1999</td>
</tr>
</tbody>
</table>
### Current research students

<table>
<thead>
<tr>
<th>Title of project/planned thesis</th>
<th>Intended degree</th>
<th>Student</th>
<th>Planned year of defence</th>
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<tbody>
<tr>
<td>Effectiveness of iron supplementation programmes in pregnancy. The impact of dose frequency on compliance, side effects and haematological outcome</td>
<td>PhD</td>
<td>Zia Hyder</td>
<td>2001</td>
</tr>
<tr>
<td>Trauma exposure, resilience factors and mental health of refugee children in Sweden.</td>
<td>PhD</td>
<td>Stephen Goldin</td>
<td>2002</td>
</tr>
<tr>
<td>Equity in child health in Vietnam</td>
<td>PhD</td>
<td>Dinh P Hoa</td>
<td>2002</td>
</tr>
</tbody>
</table>

### RESEARCH PROJECTS

<table>
<thead>
<tr>
<th>Project</th>
<th>Role in project</th>
<th>Funding agency</th>
<th>Year(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arsenic in tube well water and health consequences in Matlab, Bangladesh</td>
<td>Principal investigator</td>
<td>Sida, WHO</td>
<td>2001-</td>
</tr>
<tr>
<td>Socioeconomic determinants of child survival during warfare and rapid social transition. Infant mortality in Bavi district, Vietnam, 1965-98 (Collaborative project with Department of Social Paediatrics, Institute for Protection of Children’s Health, Hanoi)</td>
<td>Principal investigator</td>
<td>SAREC</td>
<td>1999-</td>
</tr>
<tr>
<td>Pilot studies of arsenic exposure through drinking water and health consequences in Matlab, Bangladesh</td>
<td>Principal investigator</td>
<td>USAID</td>
<td>2000-</td>
</tr>
<tr>
<td>Combined interventions to promote maternal and infant health (Collaborative project between ICDDR,B, UNICEF, and Cornell University, USA)</td>
<td>Principal investigator</td>
<td>UNICEF, National Institute of Health (NIH) and Fogarty</td>
<td>2000-</td>
</tr>
<tr>
<td>Studies of the public health consequences of violence against women in Bangladesh (Collaboration ICDDR,B, Naripokkho, Bangladesh and WHO)</td>
<td>Co-investigator</td>
<td>Asian Development Bank (ADB)</td>
<td>2000-</td>
</tr>
<tr>
<td>Development of a questionnaire instrument for evaluation of causes of adult female deaths and maternal mortality, and the evaluation of causes of death in a nation-wide survey in Bangladesh (Collaboration with Johns Hopkins University)</td>
<td>Principal investigator</td>
<td>USAID through Johns Hopkins</td>
<td>2000-</td>
</tr>
<tr>
<td>Iron and zinc deficiency during infancy - causes,</td>
<td>Principal investigator</td>
<td>SAREC, MFR</td>
<td>1995-</td>
</tr>
<tr>
<td>Functional outcomes and the effect of an intervention, A cohort study in central Java. (Collaboration with Gadjah Mada University and Dept Nutrition UC Davis)</td>
<td>Investigator</td>
<td>SAREC</td>
<td>1997-</td>
</tr>
<tr>
<td>---</td>
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<td>---</td>
</tr>
<tr>
<td>Determinants of compliance with iron and zinc supplementation in infancy. A cohort study in Central Java</td>
<td>Principal investigator</td>
<td>SAREC</td>
<td>1997-</td>
</tr>
<tr>
<td>Vitamin A supplementation and immunisation in practice in Bangladesh. A cohort study of the equity and effectiveness in preventing under five mortality (Collaboration with Research and Evaluation Division, BRAC, Bangladesh)</td>
<td>Principal investigator</td>
<td>SAREC</td>
<td>1997-</td>
</tr>
<tr>
<td>Effectiveness of iron supplementation programmes in pregnancy. The impact of dose frequency on compliance, side effects and haematological outcome (Collaborative project with BRAC, Bangladesh and Dept Nutrition, UC Davis)</td>
<td>Co-investigator</td>
<td>SAREC</td>
<td>1996-</td>
</tr>
<tr>
<td>Exposure to trauma, resilience factors, and mental health of refugee children in Sweden (Collaboration with Dept Child Psychiatry, Umeå university)</td>
<td>Principal investigator</td>
<td>Swedish Council for Planning and Co-ordination of Research (FRN), and from Swedish Council for Social Research (SFR)</td>
<td>1994-</td>
</tr>
<tr>
<td>Swedish Multicentre study of the incidence and aetiology of coeliac disease</td>
<td>Co-investigator, member of the steering committee</td>
<td>Swedish council for forestry and agricultural research (SJFR), The Swedish Foundation for Health Care Sciences and Allergy Research (Vårdal), and &quot;Front-line research funds&quot; of the Västerbotten county council</td>
<td>1991-</td>
</tr>
<tr>
<td>Swedish participation in the multi centre study &quot;Euro Growth Study&quot; regarding feeding, growth and micronutrient health of infants 0-3 years of age</td>
<td>Principal investigator</td>
<td>Umeå university research funds (Central component financed by European union)</td>
<td>1991-1998</td>
</tr>
<tr>
<td>Health systems research in Vietnam (Collaborative project with Ministry of Health, Vietnam, Medical Faculty, Hanoi, IH CAR, KI, Nordic School of Public Health, Göteborg, and Epidemiology, Umeå University, Sweden)</td>
<td>Co-principal investigator</td>
<td>SAREC</td>
<td>1991-1999</td>
</tr>
<tr>
<td>Reproductive and child health in Nicaragua (Collaborative project with the Municipality Health Services, the Autonomous Nicaraguan University, and the Movimiento Comunal, León, Nicaragua)</td>
<td>Principal investigator</td>
<td>SAREC</td>
<td>1990-1999</td>
</tr>
<tr>
<td>Risk indicators in adolescence for future cardiovascular diseases, the Umeå Youth Study</td>
<td>Co-principal investigator</td>
<td>Swedish council for social research (SFR)</td>
<td>1988-1995</td>
</tr>
<tr>
<td>The epidemiology of Epidemic Spastic Paraparesis (Konzo) in Zaire (Collaborative project between Nutrition Institute in Kinshasa (CEPLANUT), ICH, Uppsala University, and Epidemiology, Umeå University, Sweden)</td>
<td>Co-investigator</td>
<td>SAREC</td>
<td>1988-1994</td>
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<tr>
<td>Swedish Childhood Diabetes Study</td>
<td>Co-investigator</td>
<td>MFR</td>
<td>1986-1991</td>
</tr>
<tr>
<td>Epidemiology in the planning of Primary Health Care (Collaboration with Community health department, Medical Faculty, Somali National University, Mogadishu, Somalia)</td>
<td>Co-investigator, later principal investigator</td>
<td>SAREC</td>
<td>1982-1992</td>
</tr>
</tbody>
</table>
Swedish multicentre study on food habits and nutrient intake in childhood in relation to health and socioeconomic conditions (Collaborative study with Swedish Food Administration and Uppsala University)  | Co-investigator | Swedish Food Administration | 1979-1986

TEACHING

- Course organiser and teacher at international course in Health and Demographic Surveillance and Advanced Analysis of Longitudinal Data, in Matlab, Bangladesh (2001)
- Course organiser and teacher at International Training Course in Epidemiology for Public Health in Matlab and Dhaka, Bangladesh (2000)
- Teacher in Epidemiology at courses in Epidemiology and research methodology at ICDDR,B, Dhaka (1999-)
- Course co-organiser and teacher at 5 credit course in nutritional epidemiology at Umeå University (1997-1998).
- Production of the textbook "Epidemiology for Public Health" (by Lars Åke Persson and Stig Wall) based on the teaching experiences and international courses during the 1980s and 1990s. See publication list number 100.
- Course organiser and teacher in 5 credit course in public health, epidemiology and biostatistics as part of the introductory semester for biomedicine students at the medical faculty, Umeå University (1996-1998).
- Director of studies at the Department of Epidemiology and Public Health, Umeå University and development of the curriculum and core course content of the Masters’ of Public Health program at Umeå University (1994-95).
- Course organiser and teacher at courses in Epidemiology, 10 credits, which is part of the post graduate program in Public Health at Umeå University (1991-present). This course as well as the entire Public Health program is given in English with course participants from many countries. Also organiser and teacher in Advanced Epidemiology (10 credits) from 1994 to 1998.
- Invited teacher in nutritional epidemiology at the ESPGAN summer school in Austria, 1995.
- Teacher in international health, nutrition and epidemiology at 10 credit courses in International Health at Umeå University. (1991-present).
- Teacher in international health and nutrition at courses at the Swedish Agricultural University. (1986-1996).
- Organiser and teacher in international health (2 credits) within a multidisciplinary course (10 credits) on "Conditions in low income countries" at Umeå University. (1989)
- Co-ordinator and teacher at yearly research training courses (summer school) in "Epidemiology and Field Research Methods" with participants from Africa, Asia and Latin America as well as European countries in Umeå. (1988-present). These courses are intensive courses of 2-3 weeks duration, including a lot of "hands-on" experience of epidemiology.
- Invited speaker at the SAREC supported research seminar "Infections of the gastrointestinal and respiratory tract" at the National Institute of Hygiene and Epidemiology, Hanoi, Vietnam. (1988).
- Co-ordinator and teacher in courses in "Epidemiology and Field Research Methodology" at the Olof Palme Institute in Hanoi, Vietnam (1986), at King Edward's Medical College in Lahore, Pakistan (1986), at the Medical Faculty in Mogadishu, Somalia (1987), in Luanda, Angola (1987), in Harare, Zimbabwe (1988) and in Matagalpa, Nicaragua (1988). Intensive courses of 1-2 weeks duration. The teaching methods developed have been evaluated and reported in the Bulletin of the World Health Organization (see publication list number 25). Course material developed in English and Spanish (see publication list number 82 and 88).
- Teacher and course organiser for the courses in paediatrics at Medical Faculty, Umeå University. (1985-1987). Responsible for three courses of three months duration each.
- Teacher/organiser of seminars, courses and weekly post-graduate training of paediatricians and nurses at the Olof Palme Institute for Protection of Children’s Health, Hanoi, Vietnam and at various regional hospitals in Vietnam. (1984-85). Several hours of teaching each week. Development of course material, which was replicated in training activities on lower levels in the health care system.
- Teacher and co-organiser of a research training course supported by SAREC "Epidemiology in Primary Health Care" in Mogadishu, Somalia. (1984). Intensive course of one week's duration.
• Teacher in Social Medicine and Epidemiology for medical students at the Department of Social Medicine Medical Faculty, Umeå University. (1980-83). Course organiser, a few weeks of teaching per semester.  
• Teacher in International Health and International Paediatrics for medical students at the Medical Faculty, Umeå University. (1978-1995).  
• Teacher in Paediatrics and Child Health Care at Ndoge Nurses' Training School, Ndoge Hospital, Tanzania. (1976-78).

ADVISORY COMMITTEES, EXPERT MISSIONS ETC.
• Member, Research Evaluation Committee, ICDDR,B (1999-)  
• Executive board member, International Society for Research on Human Milk and Lactation (1998-)  
• Member of the quality assurance group at the Medical Faculty, Umeå University (1997-1999).  
• Faculty opponent at the defence of the PhD thesis of Bo Burström, Karolinska Institutet, "Risk factors for measles mortality. Studies from Kenya and 19th century Stockholm" (1996).  
• Representative of the Medical Faculty in the Equal Opportunity Committee of Umeå University (1996-1999).  
• Member of the research training committee (Forskarutbildningskomittén) at the Medical Faculty, Umeå University (1996-1999)  
• Member of the advisory board for research grant applications to Swedish Medical Society (Svenska Läkarestiftskapet) (1996-1999)  
• Chairman of the advisory group for research grants from the Joint Committee of the Northern County Councils at Umeå University. (1995)  
• Co-ordinator of the program support by the Swedish Public Health Institute to Umeå University for research on Child and Adolescent Health. (1993-1999)  
• Advisor to SIDA in its support to Tanzania Food and Nutrition Centre, Dar es Salaam. (1993-1999)  
• Member of the research ethics committee at the Medical Faculty, Umeå University. (1993-1999).  
• Member of the SAREC advisory board for research in health and nutrition. (1990-1997)  
• Member of the board of the Working group of paediatric epidemiology of the Swedish Paediatric Association. (1990-1994)  
• Faculty opponent at the defence of the PhD thesis of Redda Tekle-Haimanot's "Epidemiology of neurological disorders in Ethiopia" at Umeå University. (1990).  
• Secretary and member of an evaluation team for the SAREC supported Pakistani-Swedish research project "Breast feeding in a developing country" at King Edward Medical College, Lahore, Pakistan. (1989)  
• Member of a working group of the Swedish Board of Heath Welfare regarding the "Biological Development of Swedish Children". (1988-1990)  
• Temporary WHO Adviser (Epidemiology) regarding "Research and action for the promotion of oral health within primary health care" (1987-1988)  
• Member of the Swedish Research Council's (Forskningsrådsnämndens) advisory group on methodology in dietary studies. (1980-85)  
• Member of the project group "Processing of epidemiological data in a developing country - development of a micro-computer system."

ORIGINAL PUBLICATIONS


ORIGINAL PUBLICATIONS, MANUSCRIPTS


70. Ivarsson A, Hernell O, Nystrom L, Persson LA. Increased coeliac disease risk in children born in the summer reflects causals environmental exposure(s) with a seasonal pattern. Submitted.


73. Andersson T, Persson LÅ, Bergström S, Högberg U. Grand multipara with surviving infants have no increased risk of maternal deaths; a cohort study from 19th century Sweden. Manuscript.


REVIEWS, DISCUSSION PAPERS, BOOKS, CHAPTERS ETC.


BIOGRAPHICAL SKETCH

May 2001

CURRICULUM VITAE

NAME
Mahfuzar Rahman
Born 1966-06-01

CURRENT POSITIONS
Epidemiologist, Public Health Sciences Division, ICDDR,B
Centre for Health and Population Research, Dhaka, Bangladesh

ADDRESS
Public Health Sciences Division, ICDDR,B
GPO Box 128, Mohakhali CA, Dhaka 1000, Bangladesh
Phone +880 2 9885155
Fax +880 2 8826050
e-mail mahfuzar@icddrb.org

EDUCATION/TRAINING

<table>
<thead>
<tr>
<th>INSTITUTION AND LOCATION</th>
<th>DEGREE</th>
<th>YEAR(s)</th>
<th>FIELD OF STUDY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rajshahi Medical college, Rajshahi, Bangladesh</td>
<td>MBBS</td>
<td>1992</td>
<td>Medicine</td>
</tr>
<tr>
<td>Faculty of Health Sciences, Linköping University, Sweden</td>
<td>PhD.</td>
<td>1994-99</td>
<td>Epidemiology</td>
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<tr>
<td>Johns Hopkins University, School of Hygiene and Public Health, Baltimore, MD</td>
<td>Post-graduate Training</td>
<td>1998</td>
<td>Summer Graduate Epidemiology Program (Epidemiology and Biostatistic)</td>
</tr>
</tbody>
</table>

RESEARCH AND PROFESSIONAL EXPERIENCE:
1992-1993 - Internship training, Rangpur Medical College Hospital, Rangpur
1994-1999 - Research Coordinator, SIDA
2000 (Jan-May) - International Fellow, Public Health Sciences Division, ICDDR'B
2000 (June- till) - Arsenic and Environmental Epidemiologist, Public Health Sciences Division, ICDDR, B: Centre for Health and Population Research.

RESEARCH PROJECTS

<table>
<thead>
<tr>
<th>Project</th>
<th>Role in project</th>
<th>Funding agency</th>
<th>Year(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arsenic in tube well water and health consequences</td>
<td>Principal investigator</td>
<td>Sida, WHO</td>
<td>2001-</td>
</tr>
<tr>
<td>Pilot studies of arsenic exposure through drinking water and health consequences in Matlab, Bangladesh</td>
<td>Principal investigator</td>
<td>USAID</td>
<td>2000-</td>
</tr>
<tr>
<td>Arsenic exposure, hypertension and skin lesion in Bangladesh</td>
<td>Principal investigator</td>
<td>Linköping Universitet Grant</td>
<td>1998-</td>
</tr>
<tr>
<td>Arsenic in drinking water and diabetes mellitus</td>
<td>Principal investigator</td>
<td>Planning grant SAREC/SIDA</td>
<td>1996-</td>
</tr>
</tbody>
</table>
ADVISORY COMMITTEES, EXPERT MISSIONS ETC.

- Referee for a number of scientific journals, e.g. Health Policy and Planning.

Original publication


REVIEWs, DISCUSSION PAPERS, BOOKS, CHAPTERS ETC.


Budget Justifications

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

Commitment is expressed in person-time. Project period 24 months.

**Staff.** ICDDR, B has got an excellent group of field staff, public health specialists, epidemiologists, bio-statisticians, social scientists, laboratory scientists and clinicians for the study. This personnel is financed by individual research projects in relation to the time they allocate to the project. Lars Åke Persson is principal investigator for the project and has had the principal role in the planning. He will have the primary responsibility for all parts of the project and will provide scientific expertise on the development and analysis of the results of various outcomes. He is allocating 4 months of his time to the project.

Mahfuzar Rahman is arsenic epidemiologist and will have the day-to-day responsibility for the field work and be involved in all steps of the project. Dr. Mahfuzar Rahman will also ensure co-ordination and will provide scientific expertise within whole project, serves as an expert physician in the field and on the development and analysis of the results of the various outcomes; 24 months.

Drs. Abbas Uddin Bhuyia, will serve as Co-Investigator and will provide scientific expertise in his respective area, responsible for ethnographic study within the project; will be responsible for the qualitative components of the study; involvement 3 months.

Shams El Arifeen is child health epidemiologist and will be involved in the epidemiological analysis of reproductive outcome. His involvement is 1 month.

SM Akramuzzaman is clinical scientist and involved in the planning for skin screening, clinical follow-up and analysis of reversibility of skin lesions; 2 months.

Eva-Charlotte Ekström is nutrition epidemiologist and consultant to the Centre. She has been involved in the design of the nutrition aspects and will lead the analysis of those parts; 3 months.

Md. Khalequzzaman is public health physician and epidemiologist and will be involved in the planning and analysis for skin screening, and patient follow-up, 2 months.

Peter Kim Streetfield is demographer and epidemiologist and will be responsible for the entire arsenic-related HDSS system, the GIS application, and will be involved in the analysis of arsenic effects on reproductive outcomes and mortality outcomes; 3 months.

Our GIS expert recently left, he is being replaced; 4 salary months.

Nigar Shahid will be involved in the analysis of reproductive outcomes; 2 months.

MA Wahed will be in charge of the arsenic analyses at ICDDR,B lab, and will provide scientific and technical expertise on the assessment of arsenic and biochemical outcomes; 3 months.

Md. Yunus is senior public health physician and has the overall responsibility for the Matlab health research program, including the clinical activities and the field activities; 3.5 months.
J Chakraborty is Senior Manager in Matlab, will guide and facilitate the implementation of the project activities in Matlab facilitate the implementation of the project activities in Matlab. 5 months committed.

HR Chowdhury is Senior Medical Officer and will supervise the clinical management of patients with arsenicosis, 5 months.

Four medical officers (2 male and 2 female) will be responsible for the examination of patients with skin changes and other arsenic-related health problems; 48 salary months.

Dr Mushiaque Chowdhury, Director of the Research and Evaluation Division at BRAC, and Co-Investigator, will be co-ordinating the activities with the ICDDR.B team, coordinating the field activities for the arsenic mitigation. Professor Marie Vather, Institute of Environmental Medicine, Division of Metals and Health, Karolinska Institutet, Stockholm, will serve as Co-Investigator and will be responsible for the analysis of the urine samples.

A field laboratory manager is in charge of the handling of the samples of urine, water and blood, 12 months. The field manager is having the responsibility of coordinating and overseeing the activities of the field staff, 24 months. A field research officer (ethnography) is conducting the ethnographic interviews (12 months), supervised by the social scientist. A clerk is managing the project office (12 salary-months). Senior Health Research Assistants perform parts of clinical examination and take blood samples (24 salary-months). Field Research Assistants are performing the skin screening in the field; totally 240 salary months. One Data Managing Assistant manages data entry (24 months), supervised by a data manager (8 months). The role of the ICDDR.B community health research workers in the area is to inform about the project in each household, and to give assistance in the field for the field team (78 salary months).

Analyses will be performed of total arsenic in urine in individuals with arsenicosis and controls, and in clinical follow up of the arsenicosis patients (total 2850 samples) and AAS analysis of arsenic in tube well water (9000 tube wells plus seasonal follow up, 1800 samples). Analysis of Hb will be done immediately in Matlab and of micronutrients later at a biochemistry laboratory.

Funds are allocated for local travel Dhaka-Matlab and within Matlab and, for some international travel, mainly for the contact with partners at Karolinska Institute.

We propose the procurement of -86°C freezers. The very large number of samples (water, urine, serum) makes it necessary to totally procure 3 freezers. The WHO budget also includes funds for procurement of a AAS with auto sampler H-generator (H shimabzu, Japan). Configuration: Atomic Absorption Spectrophotometer, Furnace kit, Auto sampler, High temperature burner head, Hydride vapour generator. Some renovation is needed in the laboratory space in Dhaka and preparation of facilities for the clinical follow-up in Matlab.

The institutional overhead includes managing costs for the project in finance and personnel department, costs of managing the field site in Matlab and the clinical services
linked to the project. (The lower rate in the Sida budget is motivated by the Sida/SAREC core contribution to the Centre).

The arsenic mitigation activity that is performed by BRAC is calculated based on their previous experiences and adjusted for the population size and the estimated arsenic contamination in the area. See separate budget sheet and description in the text above.

**Other Support**

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

<table>
<thead>
<tr>
<th>Source</th>
<th>Amount</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>UNICEF</td>
<td>640,000</td>
<td>3 years</td>
</tr>
<tr>
<td>USAID</td>
<td>20,000</td>
<td></td>
</tr>
<tr>
<td>JHU</td>
<td>20,000</td>
<td></td>
</tr>
</tbody>
</table>
Check List

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

1. Face Sheet Included

2. Approval of the Division Director on Face Sheet

3. Certification and Signature of PI on Face Sheet, #9 and #10

4. Table on Contents

5. Project Summary

6. Literature Cited

7. Biography of Investigators

8. Ethical Assurance

9. Consent Forms

Detailed Budget
## ARSENIC AND HEALTH: Budget ICDDR,B, and BRAC (mitigation component)

**Matlab, 222,000 population**

**Project period 24 months**

Side contribution approximate, depending upon exchange rate (calculated for 1 US$=10 SEK). Salary increase after 1 year 2.5% included.

*Salaries incl. benefits and taxes*

<table>
<thead>
<tr>
<th>Rate/m Person-months/units</th>
<th>Cost</th>
<th>Total cost</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Professional staff</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epidemiologist: PI, D1*</td>
<td>$13125</td>
<td>-</td>
</tr>
<tr>
<td>Child health epidemiologist: Shams El Arifeen</td>
<td>$6930</td>
<td>-</td>
</tr>
<tr>
<td>Clinical scientist NOC*</td>
<td>$1218</td>
<td>-</td>
</tr>
<tr>
<td>Social scientist PS*</td>
<td>$999</td>
<td>-</td>
</tr>
<tr>
<td>Nutrition epid. consultant: P4</td>
<td>$4657</td>
<td>-</td>
</tr>
<tr>
<td>Clinical scientist NOC*</td>
<td>$1471</td>
<td>-</td>
</tr>
<tr>
<td>Arsenic epidemiologist: NOC*</td>
<td>$1016</td>
<td>1.54</td>
</tr>
<tr>
<td>Demographer, PS*</td>
<td>$11677</td>
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</tr>
<tr>
<td>GIS exper: NOC*</td>
<td>$1016</td>
<td>2.0</td>
</tr>
<tr>
<td>Senior scientist NOD</td>
<td>$1858</td>
<td>1.0</td>
</tr>
<tr>
<td>Head, arsenic lab NOC*</td>
<td>$1505</td>
<td>1.5</td>
</tr>
<tr>
<td>Head, Matlab</td>
<td>$2475</td>
<td>2.5</td>
</tr>
<tr>
<td>Senior manager, NOC*</td>
<td>$1457</td>
<td>1.5</td>
</tr>
<tr>
<td>Senior physician, NOC*</td>
<td>$1123</td>
<td>2.0</td>
</tr>
<tr>
<td>Consultant, Dermatologist</td>
<td>$500</td>
<td>2.0</td>
</tr>
<tr>
<td>Medical officers (male &amp; female)</td>
<td>$659</td>
<td>6.0</td>
</tr>
<tr>
<td><strong>Subtotal professional staff</strong></td>
<td>79,447</td>
<td>15,682</td>
</tr>
</tbody>
</table>

| **Field staff**             |      |            |
| Field laboratory management, GS5 | 251 | 9.0 | 3,198 | - | 1,066 | 4,265 |
| Field manager, NOD          | 659 | 24.0 | 16,014 | - | - | 16,014 |
| Field research officer, ethnography GS6 | 456 | 2.0 | 923 | 1,874 | 2,770 | 5,541 |
| Clerk/Admin Assistant, CSA Matlab, GS4 | 256 | 4.0 | 1,089 | 2,179 | - | 3,268 |
| Senior Health Research Assistant, GS4 | 269 | 12.0 | 3,268 | 1,634 | 1,634 | 6,537 |
| Field Research Assistants, water collection, GS3 | 225 | 12.0 | 7,273 | - | - | 7,273 |
| Field Research Assistant, skin screening, GS3 | 225 | 150.0 | 34,172 | 10,252 | 10,252 | 54,875 |
| Data Management: GS6        | 455 | 4.0 | 1,847 | - | 923 | 3,848 |
| Data Management Assistant: GS3 | 225 | 14.0 | 3,401 | - | 1,367 | 4,768 |
| Community health workers, GS2 | 189 | 30.0 | 6,749 | - | - | 6,749 |
| **Subtotal field staff**    | 74,235 | 24,060 | 71,238 | 119,554 |

<table>
<thead>
<tr>
<th>Operating expenses</th>
<th>Rate $</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>15</td>
</tr>
<tr>
<td>--------------------------</td>
<td>----</td>
</tr>
<tr>
<td>Lab supplies water collection</td>
<td></td>
</tr>
<tr>
<td>Lab As species unica Karolinska</td>
<td>15</td>
</tr>
<tr>
<td>Lab As total in unica Karolinska</td>
<td>5</td>
</tr>
<tr>
<td>As field test screening</td>
<td>0.35</td>
</tr>
<tr>
<td>As in water, AAS (ICDDRB)</td>
<td>3</td>
</tr>
<tr>
<td>Analyses Ha, zinc</td>
<td>6</td>
</tr>
<tr>
<td>Analyses selenium, folic acid beta carotene</td>
<td>10</td>
</tr>
<tr>
<td>Subtotal operating expenses</td>
<td>56,125</td>
</tr>
<tr>
<td>Travel</td>
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<tr>
<td>Local travel, inbetween Dhaka Matlab</td>
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<tr>
<td>International travel</td>
<td>1400</td>
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<tr>
<td>Subtotal travel</td>
<td>3,800</td>
</tr>
<tr>
<td>Capital expenditure</td>
<td></td>
</tr>
<tr>
<td>Digital camera for documenting skin lesions</td>
<td>900</td>
</tr>
<tr>
<td>GIS additional equipment and software</td>
<td>1500</td>
</tr>
<tr>
<td>Freezer for samples -86 degree C</td>
<td>10000</td>
</tr>
<tr>
<td>AAS</td>
<td></td>
</tr>
<tr>
<td>Renovation of lab for AAS</td>
<td></td>
</tr>
<tr>
<td>Preparation canical follow up room Matlab</td>
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</tr>
<tr>
<td>Subtotal capital expenditure</td>
<td>12,400</td>
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<tr>
<td>Other expenditures</td>
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<tr>
<td>Printing, photocopics</td>
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<tr>
<td>Training and dissemination</td>
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<tr>
<td>Communication (e mail fax phone)</td>
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<tr>
<td>Subtotal other expenditure</td>
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<tr>
<td>Direct cost</td>
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<tr>
<td>Level of institutional overhead</td>
<td>15%</td>
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<tr>
<td>Institutional overhead cost</td>
<td>34,651</td>
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<tr>
<td>BRAC mitigation component (see separate sheet)</td>
<td>72,510</td>
</tr>
<tr>
<td>Total</td>
<td>338,168</td>
</tr>
</tbody>
</table>
International Centre for Diarrhoeal Disease Research, Bangladesh
Voluntary Consent Form
(Cross-sectional survey)

Title of the Research Project: Arsenic in tube well water and health consequences

Principal Investigator: Prof. Lars Åke Persson

In Bangladesh, water of majority of the tube wells is contaminated with arsenic the levels of which exceed the WHO recommended safe limits of 50 µg/L. The arsenic content of water of some tube wells from all areas of the Matlab Surveillance System of ICDDR,B was tested in 1997 and 2001. It was found that water of over 3/4th of the tested tube wells contained arsenic in quantities that exceeds the WHO-recommended safe limit. High level of arsenic in drinking water may cause many health problems including various types of skin lesions, reproductive and cardiovascular diseases, and even cancers. These problems are more common in relatively younger males and in those suffering from protein energy malnutrition.

We are conducting a research study, and the main purpose of our study are to measure the levels of arsenic in the tube well water and to examine if people have arsenic-related health problems such as skin lesions. We would also investigate if some factors such as general health and nutritional status of people influence arsenic toxicity. Results of this study would help determine arsenic-related health problems and to determine preventive measures against them.

After determining the arsenic content in the tube well water, we would meet people in your community to discuss about its preventive measures including discussion on the ways to get arsenic-free water. This part of the study would be done in collaboration with BRAC.

We request for your permission to enrol you and your family members older than five years into our study. We will examine you and your family members for arsenic-related skin lesions, which would take about 30 minutes. We may refer you and/or your family members to Matlab Health Centre for further examination by a physician, and if we do so, we would bear the travel costs.

We assure you that all information obtained from you and your family members including findings of physical examination would be kept strictly confidential, and none other than the investigations of this study will have an access to the information.

There is no risk involved in the examination of the skin. You may decide not to participate in the study or parts of the study, and may also withdraw from the study at any time without affecting any service provided to you and to your family members by the Centre. You may or may not get any direct benefit by participating in this study; however, the information obtained is likely to help protect the society from arsenic toxicity.

If you are willing your and your family members' participation in the study please indicate that by putting your signature or left thumb impression in the specified space below.

Thank you for your cooperation.

<table>
<thead>
<tr>
<th>Signature of Interviewer</th>
<th>Signature /thumb impression of the participant or guardian of the participant</th>
<th>Signature of Witness</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Date:</th>
<th>Date:</th>
<th>Date:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
অন্তর্জাতিক উদ্যোগায় গবেষণা কেন্দ্র, বাংলাদেশ
সংস্কৃতি-সমাজতন্ত্র পত্র (পরিকল্পনা)

পর্যবেক্ষণ নম্বর নলকুপের পানিতে অর্থনীতিক ও সমাজের উপর তার প্রভাব

প্রধান পর্যবেক্ষক প্রফেসর লার্ড অকে পর্বনি

বাংলাদেশের অধিকাংশ নলকুপের পানি অর্থনীতিক দ্বারা পূর্বাভাস এবং এর মাত্রা বিশ্ব স্থাপত্য সংগ্রহ নির্বাচিত নির্পরাধিক মাত্রা, প্রতি দিছিও ৫০ মাইলের একের চেয়ে বেশি। ১৯৯০ ও ২০০২ সালের আর্থিক দিকের মতান্তর সার্কেলস সিস্টেমের
অতিরিক্ত সকল পানীয় জলের ক্রিয়া এর দুই তৃতীয়াংশেরও অধিক নলকুপের পানিতে বিদ্যমান সম্ভব
নির্বাচিত নির্লিপ্ত মাত্রার দেশী পরিমাণে অর্থনীতিক পাচার হচ্ছে। পানির জলের অলিভিক পরিমাণে আরো থাকে। তবে বিদ্যমান
প্রযুক্তির মাত্রা যেমন তুমিই অত্যন্ত প্রজাতন্ত্র ও কৃষির সমস্যা, এমনকি বাংলাদেশের ঘটনাটি।

আমার এক পর্যবেক্ষণ করার যাদু উদ্যোগ নলকুপের পানিতে অর্থনীতিক পরিমাণ নির্ধারন করা ও লক্ষ্য মাত্রা
অর্থনীতিক কারণ সৃষ্টি সম্প্রুতি সমস্ত ক্ষেত্রে অনুশীলন একটি পর্যবেক্ষণ করা। এ গবেষণায় আমার যে দেশের চাই যে মনোনীত সমাজের স্বাভাবিক জনসংখ্যা পুষ্টি অর্থনীতিক কারণ সৃষ্টি সংস্করণের প্রতিক করা।
আমার এই পর্যবেক্ষণ অর্থনীতিক কারণ সৃষ্টি সংস্করণের বিষয় ভাবে ও আমার প্রতিরোধকৃত বাল্য নিশ্চিত হয়ে যাবে।

নলকুপের পানির অর্থনীতিক পরিমাণের পর আমরা অপনার এলাকার লক্ষ্যের সাথে এর প্রতিরোধকের বাল্য
সম্ভব আলোচনা করা। এ অর্থনীতিক ক্রিয়া পার্থক্য উপর এর প্রতিরোধকৃত অনুচ্ছেদ বিষয়ে বাল্যবোধ বহনা করুন।
পর্যবেক্ষণ এই ভাবে প্রাক আমাদের সহযোগী হিসেবে কাজ করবে।

আমার আমাদের এই পর্যবেক্ষণ অপনার এবং অপনার পরিবারের ও বেচারের দেশী কাজের সমস্যা অসমান বিকল্পের জন্য।
আমরা অকার্যকালের পছন্দী অর্থনীতিক অর্থনীতিক অনুপ্রেরণার মাধ্যমে কেন সমাজে অন্তর্ভুক্ত করার কারণ সমাজে অন্তর্ভুক্ত করা।
আমরা আমাদের ও আমাদের অর্থনীতিক অর্থনীতিক অর্থনীতিক অনুপ্রেরণার সংস্করণের অর্থনীতিক জনিত
তুলুকে কেন সমাজে অন্তর্ভুক্ত করা। এই ক্ষেত্রে আমাদের অন্তর্ভুক্ত ও আমাদের প্রতিপত্তিসম্পূর্ণ বাল্য নিশ্চিত হয়ে যাবে।

আমার আমাদের প্রতিপত্তি দিয়ে আমাদের অপনার কারণ সমাজের শান্তির পরিকল্পনার ফলের সমস্ত সংস্করণ প্রদর্শন ও কৃত্রিম এ পর্যবেক্ষণ পর্যবেক্ষণ হয়ে তার অনুচ্ছেদ পরিবর্তন।

এই পর্যবেক্ষণ তুলে পরিকল্পনার ফলে আপনার অপনার পরিবারের সমস্যার কেন রকম বিপর্যয় সমাধান করছে? আপনি
এই পর্যবেক্ষণ অথবা পর্যবেক্ষণ মেয়ে কেন অনুশীলন নাও করতে পারছি, এমন্যকি প্রস্তাবনা করে।
অন্য পর্যবেক্ষণ করার কাজের সমস্ত ক্ষেত্রে আলোচনা কর পরামর্শ করতে পারে।

c

আপনি এই পর্যবেক্ষণ অপনার এবং অপনার পরিবারের সমস্যার অসমান বিকল্পের আমাদের প্রস্তাবে রাও ধারণা দিয়ে করে
নীতির নির্দেশ হয়ে অপনার প্রচেষ্টার অনুমোদন দিন।

আপনার সহযোগিতার জন্য ধন্যবাদ।

সাক্ষাতকার প্রখরের স্থায় অ্যাপ্রেনরকের/ অ্যাডভাইসরকের/ স্থায়িত্বকর

ফারাহ ফারাহ ফারাহ
International Centre for Diarrhoeal Disease Research, Bangladesh  
Voluntary Consent Form (Referent for further examination)

**Title of the Research Project:** Arsenic in tube well water and health consequences

**Principal Investigator:** Prof. Lars Åke Persson

Thank you for participating in the study and coming today to the clinic. Let us remind you about the purpose of the study in case you do not remember.

The purpose of our research study is to understand if and to what extent, arsenic-contaminated drinking water has resulted in adverse health effects, especially skin lesions in the population. We will also study if other factors such as general health and nutritional status help protect people against the arsenic toxicity. Such information will be useful for prevention of arsenic-related health problems in Bangladesh.

We request you/your family member to help us by participating in the study. We have not found any arsenic-related skin lesions during your physical examination, but we would like to examine your general health and nutritional status for the purpose of our study. We will similarly examine general health and nutritional status of other people who have suspected arsenic-related skin lesions.

A medical doctor at the Matlab Health Centre will examine your general health, measure your blood pressures, and examine your skin. A trained senior research assistant will collect 4.0 ml blood (less than one teaspoonful) from a vein of your forearm under aseptic precautions. There is minimal risk associated with this procedure, and you will feel momentary mild pain during the needle prick. The blood will be examined for haemoglobin concentration, and levels of some vitamins and minerals. We will also request you to provide us with small amount of your urine (about 5.0 ml i.e. one teaspoonful) for determining presence of arsenic. If you have arsenic-related disease(s) that require proper treatment, we will refer you to appropriate health care facilities.

We assure you that we shall strictly maintain confidentiality of the information we collect from you/your family members, and none other than the investigators of this study would have access to the information.

Your participation in our study is voluntary. You may decide not to participate in the study or parts of the study, and also to withdraw from the study at any time without affecting any of the services offered to you and your family members by the Centre.

You may ask any question about this study, and I shall be happy to provide answer to them. If you have any problem or further question you may also contact your healthy care worker or Dr. Hafizur Rahman Chowdhury at the Matlab Hospital of ICDDR, B or Prof. Lars Ake Persson in Dhaka at the following phone number 9885155.

If you/ your family member is willing to participate in the study, please sign your name or give left thumb impression below.

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আত্মজীবিত উদ্যোগের গবেষণা কার্য, বাংলাদেশ

সম্পর্কে সম্মান পত্র (অতিরিক্ত পরিকল্পনা জন্য)

গবেষণার নাম নলকুঁপের পানিতে আদর্শিক ও স্থায়ীর উপর তাঁর প্রভাব

প্রধান গবেষক প্রফেসর লাল অকে পার্ক

গবেষণার অর্থপ্রাপ্তির জন্য আমাদের সহায়তা চান। আমাদের হাতেও মনে নাও থাকতে পারে, সেজন্য আমার এ গবেষণার উদ্ধৃতি আমাদের মনে করিয়ে দিতে চাই।

আমাদের এ গবেষণার উদ্ভাবন হচ্ছে আদর্শিক-সৃষ্টিতে পানির জল বোকার্যের স্থায়ির উপর কৌশল কর্তিত প্রচার কর্মে বিন্যাস রাখা হয়েছে, বিস্তার ভুকের সমস্যার আলটালে বুদ্ধির কাছে। আমার আরেক দেখতে চাই যে, আদর্শিকের কাছে সৃষ্টি স্থায়ি সমস্যায় লোকজনের সাধারণ স্থায়ি ও পুটির কৌশল প্রচার আর জানা কিছু। এই তথ্য বাংলাদেশ অন্যতমকের কাছে সৃষ্টি স্থায়ি সমস্যা প্রতিষ্ঠানে সহায়তা করতে পারে।

আমারা এই গবেষণার অনুরূপ এবং অন্যান্য পরিবর্তন সমস্যার অন্তর্ভুক্ত মাধ্যমে আমাদের সহায়তা করার জন্য আমাদের অনুরোধ করি। আমরা আমাদের এই জন্য পরিচালন সম্মানে আমাদের তুলে আদর্শিক-সংশোধিত কৌশল সমন্বয় দেখতে পারিনি। কিন্তু আমার আমাদের সাধারণ স্থায়ি ও পুটির অস্ত্র নিয়ন্ত্রণের জন্যে আমাদের রাখাও প্রচার করাতে চাই।

একইভাবে, আমার যাত্রার মাধ্যমে আদর্শিক-পরিষ্কার ভুক্তের সৃষ্টি দেখতে পেয়েছি, আমাদের পরিকল্পনা করতে।

মতলব স্থায়ির কেন্দ্র একজন চিকিৎসক অন্যদিকের সাধারণ স্থায়ি, রোকাচার ও ভুক্ষের পরিষ্কার করতে পারেন। একজন লক্ষ্য-প্রতিষ্ঠান স্থায়ি-সহকারীর সম্পর্কে ধারণার সাথে, বীর্যা-জুড়ে অস্ত্র ও আদর্শিক/আমাদের পরিপূর্ণ সমন্বয় শুধু একটি সমান্তরাল সূচনা করেন কষ্ট ও প্রতিষ্ঠানের সমন্বয়ের জন্যে আমার কৌশল সম্পর্কে সূচনা করা হয়। এই সূচনা হলো প্রমাণিত, ইতিহাসশাস্ত্র, ও কর্মনির্দেশ পরিপালনের জন্যে যেমন পরিপূর্ণ মূল সমন্বয় সৃষ্টি করে। আদর্শিক/আমাদের পরিপূর্ণ সমন্বয় আদর্শিক-সংশোধিত কৌশল সমন্বয় আচার্য হলেন আমরা তার যথাযথ চিকিৎসা জন্য উপযুক্ত স্থায়ি করতে পারবো।

আমার আমাদের সমন্বয় নির্দেশনা দিচ্ছি যে, আমার এবং আমাদের সমন্বয়ের সকল সমন্বয়ের শরীরকের পরিমাণ সহ সমান তথা প্রস্তুত রাখো এবং আমার এ গবেষণার চিকিৎসার ছাড়া অন্য কোথাও তা জন্মন পাওয়া যাবে।

গবেষণার অন্তর্ভুক্ত সমন্বয়ের অর্থনৈতিক সম্পর্কভাবে আমার অগ্রণী। আমার ইচ্ছা করলে সমন্বয় বা অর্থ করা যে গবেষণার অর্থনৈতিক সৃষ্টি চিকিৎসার সাহায্য করতে, অন্তর্ভুক্ত সমন্বয় এ বিষয়ে হাসপাতাল যে কৌশল অন্য সমন্বয়ের সাধারণ করার কারণে অন্তর্ভূক্ত সমন্বয় করতে পারাও। লেখার ফল আদর্শ ও আমাদের পরিপূর্ণ সমন্বয়ের কৌশল এ প্রতিষ্ঠানের প্রক্রিয়া যে কিছুর সময় হুকুম হবে না।

আদর্শিক গবেষণা সমস্ত জন্য কৌশল প্রচার করতে পারেন। এবং আদর্শ জন্য উত্তর দেখে। আদর্শের কৌশল সমন্বয় হুলে অন্য কৌশল গবেষণা অন্তর্ভুক্ত আদর্শের প্রতিষ্ঠান অর্থনৈতিক সাহায্য করতে পারেন।

আদর্শ এই গবেষণার অন্তর্ভুক্ত ও আদর্শের পরিপূর্ণ সমন্বয়ের অন্তর্ভুক্ত আদর্শের প্রতিষ্ঠানে রাতি থাকবে দেখা করে নীচের বিভাগীয় ব্যবসা আদর্শের স্থায়ি অথবা টিনসই দিন।

আদর্শ সমন্বয়ীর জন্য কার্যকর।

সাক্ষাতকার গবেষকের নাম
অন্তর্ভূক্তরা/অভিধানকরের নাম/টিনসই
সাক্ষাতের কার্যকর

তারিখ
তারিখ
তারিখ
International Centre for Diarrhoeal Disease Research, Bangladesh
Voluntary Consent Form (Cases for further examination)

Title of the Research Project: Arsenic in tube well water and health consequences

Principal Investigator: Prof. Lars Åke Persson

Thank you for participating in the study and coming today to the clinic. Let us remind you about the purpose of the study in case you do not remember.

The purpose of our research study is to understand if and to what extent, arsenic-contaminated drinking water has resulted in adverse health effects, especially skin lesions in the population. We will also study if other factors such as general health and nutritional status help protect people against the arsenic toxicity. Such information will be useful for prevention of arsenic-related health problems in Bangladesh.

Our recent investigation showed that the tube well water in your area contains high amount of arsenic. In the recent examination at your home we found skin lesions in you/your family member(s) that could be due arsenic. If you agree your/your family members’ participation in the study, a medical doctor will examine your general health, measure your blood pressures, and further examine your/your family members’ skin lesions. We will take pictures of your skin lesions using a camera for final diagnosis by an external expert. A trained senior research assistant will collect 4.0 ml blood (less than one teaspoonful) from a vein of your forearm under aseptic precautions. There is minimal risk associated with this procedure, and you will feel momentary mild pain during the needle prick. The blood will be examined for haemoglobin concentration, and levels of some vitamins and minerals. We will also request you to provide us with small amount of your urine (about 5.0 ml i.e. one teaspoonful) for determining presence of arsenic. If you have arsenic-related disease(s) that require proper treatment, we will refer you to appropriate health care facilities.

We assure you that we shall strictly maintain confidentiality of the information we collect from you. All records from this study at the Matlab Hospital or the Dhaka Offices of ICDDR,B will be kept under lock and key and only the researchers responsible for this study will have access to the information. The study records will not have your personal identification, and we would use a code number instead.

Your participation in our study is voluntary. You may decide not to participate in the study, and also to withdraw from the study at any time without affecting any of the services offered to you and your family members by the Centre. You may ask any question about this study and I shall be happy to provide answer to them. If you have any problem or further question you may also contact your healthy care worker or Dr. Hafizur Rahman Chowdhury, at the Matlab Hospital of ICDDR, B or Prof. Lars Ake Persson in Dhaka at the following phone number 9885155.

If you/your family member is willing to participate in the study, please sign your name or give left thumb impression below.

Signature of Interviewer

Signature/thumb impression of the participant or guardian of the participant

Signature of Witness

Date:

Date:

Date:
আন্তর্জাতিক উদরাময় গবেষণা কেন্দ্র, বাংলাদেশ
সংস্থা-সম্পাদিত পত্র (বিষয় পরিকার জন্য)

প্রান্তন গবেষণা প্রফেসর বাহাদুর আজীব

গবেষণার নামকরণ নলকুফের পাশে আন্তর্জাতিক ও স্থানীয় উপর তার প্রবণতা

গবেষণার প্রধান প্রফেসর লালু আজীব।

গবেষণার অংশগ্রহণের জন্য আপনাকে ধনাদান। আপনার হতাওয়া মন নাও থাকতে পারে, কিন্তু আমার এ গবেষণার উদ্দেশ্য অপরাধ মন করিয়ে দিতে চাই।

আমাদের এ গবেষণার উদ্দেশ্য হচ্ছে আন্তর্জাতিক দৃষ্টিত বিষয়টি জন লোকজনের স্বাস্থ্যের উপর কেন্দ্রিত প্রভাব ফেলতে বিন্যাস বা তার পরিস্কারণ করা নিশ্চয় করার মাধ্যমে অন্তর্জাতিক পরিবেশের সমস্যাতে সম্ম্যক সমাধান পান।

সম্প্রতি একটি পরিকারে আমাকে সে একাডেমিক সুপার করে যে একাডেমিক নলকুফের পাশে অনিশ্চিততায় আন্তর্জাতিক পাওয়া গেছে। এটি সাধারণভাবে আপনার/আমার পরবর্তী সময়ের পরিবর্তে সাহিত্যিক রীতি ও তত্ত্বের পরিক্রমায়। এর মাধ্যমে আমাদের আন্তর্জাতিক দৃষ্টিত বিষয়টি দখল করা হয়নি বা পর্যবেক্ষিত বিষয়ের একজন তত্ত্ব—বিশেষজ্ঞ পরিক্রমা তার আন্তর্জাতিক জন্য বিশেষ সাহিত্যিক পরিক্রমা।

একজন প্রশাসনিক আমন্ত্রণ নেয়া সে হচ্ছে আপনাকে সাহিত্যিক পরিবেশের সাহিত্যিক বিষয়ের পরিক্রমায় একজন প্রকাশক। এবং আমিন তত্ত্ববিদ অবশ্যই তার অংশগ্রহণের জন্য জনপ্রিয়। আমাদের মূল সমস্ত প্রতিকৃতির জন্য সাক্ষর প্রতিকৃতির কোন সমস্যায় অংশগ্রহণ আমাদের তার সাহিত্যিক চিত্রিত জন্য উপযুক্ত স্থায়ী করার চেষ্টা করছে।

আমার অংশগ্রহণ সম্পন্ন হয়ে নির্দেশিত হল যে আমার এবং আপনার পরবর্তীর সরকার সমাজের শারীরিক পরিক্রমার ফলাফল সহ সমাজে পড়াল্লার ধারাতে এবং রূপান্তর।

প্রধান আমাদের পরিবর্তী সময়ের অংশগ্রহণের সম্পূর্ণতা অন্তর্জাতিক ইচ্ছামত। আমার ইচ্ছা করল সম্পন্ন বা আংশিকভাবে এই গবেষণার অংশগ্রহণের মাধ্যমে বিভিন্ন ধারাতে পান, এবং এই অংশগ্রহণের মাধ্যমে, যে কোন সময় আমাদের সম্প্রতি প্রতিষ্ঠানের কারণে পান।

এর মাধ্যমে আমি কেন না আমাদের পরিবারের সমস্যার একটি এ প্রতিষ্ঠানের প্রচারণা করা কীভাবে সম্ভবপ্রায় হবে জানাতে পারি।

আমার আয়োজন গবেষণা সম্পন্ন হলে কেন প্রস্তাব করতে পারেন, এবং আমি জীবন মন তার উপর দেখি। আপনার কোন সময় হয়নি তিনি আপনার স্মৃতি বা অন্তর্জাতিক অবৈধতা যা অন্তর্জাতিক হবে টার্মিনালের সাথে মেধাজনী হয়নি।

এখানে আমি বলছি আপনার উপরের কোন একটি এই প্রতিষ্ঠানের প্রচারণার কেন কীভাবে সম্ভবপ্রায় হবে জানাতে পারি।

আমার প্রতিষ্ঠান আমাদের একটি দৃষ্টি আমাদের পরিবারের অন্তর্জাতিক আমাদের প্রস্তাব নির্দেশনা করার জন্য সম্ভবপ্রায় হবে নিয়ে সে সম্ভব হবে না।

আমার আয়োজন গবেষণা সম্পন্ন করা যে কন্ট্রুকশন করতে পারেন, এবং আমি জীবন মন তার উপর দেখি। আপনার কোন সময় হয়নি তিনি আমার স্মৃতি বা অন্তর্জাতিক অবৈধতা যা অন্তর্জাতিক হবে টার্মিনালের সাথে মেধাজনী হয়নি।

এখানে আমি বলছি আপনার উপরের কোন একটি এই প্রতিষ্ঠানের প্রচারণার কেন কীভাবে সম্ভবপ্রায় হবে জানাতে পারি।

আমার প্রতিষ্ঠান আমাদের একটি দৃষ্টি আমাদের পরিবারের অন্তর্জাতিক আমাদের প্রস্তাব নির্দেশনা করার জন্য সম্ভবপ্রায় হবে না।

______________________________
সাক্ষ্যার্থে গবেষণার স্থানকারী
আশ্রমবাড়ি/ অভিজাতবাড়ি স্থানকারী/স্মৃতির স্থানকারী

তারিখ:
তারিখ:
তারিখ:
### DRAFT OUTLINE FOR QUESTIONNAIRE

**Arsenic in tubewell water and health consequences**

<table>
<thead>
<tr>
<th>Interviewer: Please record the following</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Village: .................................................................</td>
</tr>
<tr>
<td>2. Union: .................................................................</td>
</tr>
<tr>
<td>3. Date of interview: .................................</td>
</tr>
<tr>
<td>4. Interviewer name ..............................</td>
</tr>
<tr>
<td>5. Time of commencement of the interview: ..........</td>
</tr>
<tr>
<td>6. Time of ending of this interview: ...............</td>
</tr>
</tbody>
</table>

**Notes if any:** .................................................................

.................................................................

.................................................................

(Note to interviewer: The next pages refer to houses lived in and water sources during the years in each house. The purpose is to identify each house a participant lived in, the major water sources used in the house, and significant changes in the water sources such as a new tube-well.)
PART 1
QUESTIONNAIRE FOR SKIN LESION

1a. Does the participant show signs of hyperpigmentation, hypopigmentation of skin, or both? (Yes=1, No=2)

1b. If participant has pigmentation changes, write down the extent of it in this area (where was it most prominent?) (Body=1, Trunk=2, Palm=3, Sole=4)

1c. If participant has pigmentation changes, write down the extent of it in this area (where was it most prominent?)
   No pigmentation=0, Melanos (early stage)=2, Hyperpigmentation=3, Hypopigmentation=4, Both occurring side-by-side=5

2. If participant has pigmentation changes: (Yes=1, No=2)
   2a. আপনার শরীরে প্রথম কবে এই হ্যালোর দোগ দেখা গিয়েছিল (বছর)?
   2b. শরীরে কোন জায়গায় প্রথম এরকম দোগ দেখা গিয়েছিল (বর্ষা দিন)?

2c. তখন আপনার বয়স কত ছিল?

3. গত দুই বছরে আপনি ফি দোগের কোন রকম পরিবর্তন দেখেছেন?
   (Improved=1, Worsened=2, Not changed=3)

4. Does the participant shows the signs of keratoses on the palms or soles or both, and or other areas (s). (please enter responses here, Yes=1, No=2)

4a. If the participant has keratoses, write down the extent of it in this area (where was it most prominent or marked)
   (Palms=1, Soles=2, Both=3)

5. If participant shows signs of keratoses: Is it nodular, elevated or flat?
   (Nodular=1, Elevated=2, Flat=3)

6a. তিন বছর আগে আপনি আপনার তুকের শক্ত হওয়া যথেষ্ট লক্ষ্য করেন?
   6b. শরীরে কোন ক্ষেত্রে প্রথম তুক শক্ত হয়েছিল (বর্ষা দিন)?
   6c. তখন আপনার বয়স কত ছিল?
PART 2. QUESTIONNAIRE for First Clinic Visit *(performed by physician)*

- Participant has no skin lesions → Go to Physical Exam

### Physical Examination for Skin Lesions

<table>
<thead>
<tr>
<th>Melanosis</th>
<th>Palm</th>
<th>Sole</th>
<th>Trunk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Keratosis</td>
<td>Spotted</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diffuse</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leucomelanosis</td>
<td>Spotted</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diffuse</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperkeratosis</td>
<td>Spotted</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diffuse</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Physical Examination Protocol

<table>
<thead>
<tr>
<th>Clubbing</th>
<th>Present/Absent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vyanosis</td>
<td>Present/Absent</td>
</tr>
<tr>
<td>Basal</td>
<td>Present/Absent</td>
</tr>
</tbody>
</table>

### Vascular System

<table>
<thead>
<tr>
<th>Right Extremity</th>
<th>Left Extremity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Pressure</td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>Diastolic</td>
</tr>
<tr>
<td>Edema</td>
<td>Grade as millimeters of depression at distal shin just above ankle</td>
</tr>
<tr>
<td></td>
<td>Grade as millimeters of depression at distal shin just above ankle</td>
</tr>
<tr>
<td>Pulse</td>
<td>Rate/minute</td>
</tr>
</tbody>
</table>

### Hepatic System

<table>
<thead>
<tr>
<th>Hepatomegally</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade as Cm below costal margin at mid-clavicular line in expiration</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Asotes</th>
<th>Absent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Spider Telangectasias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absent</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Jaundice</th>
<th>Absent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td></td>
</tr>
</tbody>
</table>
### Neurologic System

<table>
<thead>
<tr>
<th></th>
<th>Right Lower Extremity</th>
<th>Left Lower Extremity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pinprick sensation</td>
<td>Yes/No</td>
<td>Yes/No</td>
</tr>
<tr>
<td>Distribution</td>
<td>Normal/Hypoesthesia/Hyperesthesia/ Dysthesia</td>
<td>Normal/Hypoesthesia/Hyperesthesia/ Dysthesia</td>
</tr>
<tr>
<td>Kinaesthesia</td>
<td>Normal/Abnormal</td>
<td>Normal/Abnormal</td>
</tr>
</tbody>
</table>

### Standing height (m) /
### Weight (kg) /
### Ambient temperature (deg. C) /

### Respiratory System

#### Preamble

এখন আপনার কুচের পোষা সময়ীত্ব কিছু প্রশ্ন ডাকার করবো। প্রশ্নগুলি হ'লঃ আপনা “না” হতে উভয় দিন।

#### Cough

1. আপনার কাশির কোন সময় আছে হয়?
   - Yes
   - No

2. কত মাস/বছর ধরে আপনার কাশির অসুখ আছে?
   - Month
   - Year

3. বছরের শীতের তিন মাসের কৌশল ভাব দিনেই কি আপনার কাশি হয়?
   - Yes
   - No

#### Phlegm

4. বছরের মাঝে অস্ত্রোল তিন মাস ধরে প্রতিদিনই কি কাশিতে কোষেন?
   - Yes
   - No

#### Periods of cough and phlegm

5. পর তিন বছরের অস্ত্রোল তিন সাল ধরে বা তার কৌশল সালের যখন আপনি কাশিতে কোষিয়ে হয়?
   - Yes
   - No

If Yes

4b. কাশির ওত্তরের সময় কি আপনার একাধিকবার হয়েছে? Yes No

#### Breathlessness

5a. আপনি অত্যন্ত হরিয়ে গেলে বা একটি উঠতে উঠতে গেলে কি প্রশ্ন হয়?
   - Yes
   - No

If Yes

5b. আপনি কি আপনার সময়ীত্ব কৌশলের সাথে একই তালে হাটতে গেলে হরিয়ে যায়?
   - Yes
   - No

If Yes

5c. আপনি কি বান্ধবীকে সময় হরিয়ে হাটাতে গেলে বাস-কর্দমের কারণে বিশাল করেন?
   - Yes
   - No
Draft questionnaire for pilot testing
26/08/01

Wheeze

6. যদি এক বছরের মধ্যে কখনো দিনগুলো নিয়মিত হয়ে থাকে সেকথা সাই সহ শরীর হয় কি?
   Yes  No

7a. কখন একবার শরীর কোথা দিনগুলো নির্ধারি দেন যখন কি হাসপাতাল রোগ করেন?
   Yes  Not appreciable

If Yes
7b. হাসপাতাল যখন ঘায়েন তখন কি আপনার শাস্ত্র-প্রশাসন বাধায় ধরে বিরাম কি?
   Yes  No

7. যদি এক বছরের মধ্যে যায়ে এই কারণের জন্য করলে মৃত্যুর কাজের কথা আপনার মৃত্যু কোথা দেখতে পারেন?
   Yes  No

Chest illnesses

8. যদি চিন যেসব আপনার কি একবার কোথা রেখেছিল সেই হলে আপনি এক স্বাস্থ্য কেন্দ্র কাজ করতে পারেন?
   Yes  No

If Yes
8a. এই সময় কি আপনার কথা রেখেছে?
   Yes  No

If Yes
8c. যদি তিনি বছরের মধ্যে একবারের কষ্ট একবারের কষ্ট মৃত্যু ঘটে তো কিনা?
   Yes  No

Past illnesses

নিচের এই দিনগুলো সময়ে আপনার কাজ করেছিল কি?
9a. তাকে কোথা আমার নাম সহ আপনে করেছি কি?
   Yes  No

9b. হার্ট অস্থি (Cardiac disease)
   Yes  No

9c. তিনি বছরের মধ্যে এক স্বাস্থ্যকর মৃত্যু কথা উঠে কিনা (Bronchitis)
   Yes  No

9d. নিউমনিয়া (pneumonia)
   Yes  No

9c. দূষন নেতার সময় কোথা কোথা যা গুল্ম করা যা করা কথা (Pleurisy)
   Yes  No

9f. বুদ্ধির বর্ণ থেকে TB
   Yes  No

9g. ইথামা (Asthma)
   Yes  No

9h. অন্যান্য কোষের রোগ (Other respiratory disease)
   Yes  No

9i. এলাকায়, হীরি ও কোষের রোগ (Allergy & Corneal congestion)
   Yes  No

Tobacco smoking

10a. আপনি কি একবার মৃত্যু করেন?
   Yes  No

If No
10b. এই জন্য একবারের কষ্ট করেছি করেছি পান করেছি?
   exsmoker

   never smoked
Draft questionnaire for pilot testing
26/08/01

If participant never smoked, omit question on smoking → Go to Spirometry
If participant is a smoker or is an ex-smoker, complete the table below:

<table>
<thead>
<tr>
<th>14c. অপর্নি এক্ষেত্রে অপর্নি এক্ষেত্রে ছিল কি</th>
<th>14d. পূর্বে হিসেব আগে এক্ষেত্রে ছিল কি</th>
<th>14e. অপর্নি ছিল সত্যিকারে এক্ষেত্রে ছিল কি</th>
</tr>
</thead>
<tbody>
<tr>
<td>-----</td>
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</tr>
<tr>
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<tr>
<td>-----</td>
<td>-----</td>
<td>-----</td>
</tr>
</tbody>
</table>

BIOLOGICAL SAMPLE

URINE
1. Was a urine sample taken from this participant? Yes ___ No ___
2. Result of urinary protein test  
3. Result of urinary glucose  
4. If no urine sample could be obtained give an explanation. If participant has blood in urine ask about menstruation if female or about urinary tract infections or other possible causes if male.
5. If positive for glucose ask participant following questions
6. Do you have diabetes? Yes ___ No ___ Don’t Know ___
7. Do you have blood sister or brother who has diabetes? Sister ___ Brother ___ Don’t know ___
8. Do you have a mother or father who has diabetes? Mother ___ Father ___ Don’t know ___
9. At what age did you develop diabetes? Yrs. ___

BLOOD
1. Was a blood sample taken from this participant? Yes ___ No ___
2. If not, explain why blood sample could not be collected

PHOTOGRAPHS OF SUBJECTS WITH SKIN LESIONS
1. Were photographs taken of this participant? Yes ___ No ___
2. If no, explain why photograph could not be taken
PART 3. Questionnaire on Tubewell Water History

1. আপনার বর্তমান ঢিবিটি কি?
Para / Village: ____________________________________________
Union: __________________________________________________

2. আপনি এবং অন্যান্য সকলে ফি একই কল, নাকি একের বেশী কল, নাকি অন্য কল / উৎস থেকে জল পান করেন?
   Just one
   কোথায় থেকে জল পান?
   (Probe: What is it? For example, which tubewell, pond? What is the location?)
   কল, পাতা হুয়া, পুতুল, না টাইম কল?
   More than one
   কারণের আলোচনা থেকে জল পান করেন?
   Sample collected?
   Y  N

3. পাবিত্র প্রাপ্ত উত্তর 'হা' বিবেচনা না তুলে নিন।
   আপনি এই বাড়িতে এখানে আসা তখন থেকে কি আপনার বাড়ির উৎস একই আছে যা আপনি বর্তমানে ব্যবহার করেন?

CURRENT HOUSE (first change in water source)

[Note: This page is for the current house. To know if there was a change in the water source while the participant was resident in it. If there was more than one change then add separate page for each change].

1a. এই বাড়িতে থাকার সময় আপনি কত বছর জল পান করেন?

1b. কত বছরের আগে আপনি বর্তমান জলের জায়গা কল করেন?

Tubewell Identification number (ID) ________________
Duration (years) _____________________________
Draft questionnaire for pilot testing
26/08/01

SECOND TO LAST HOUSE (or house before last)

আমাদের পরের প্রাপ্ত হচ্ছে আপনি আগে বাস করেন কোন বাড়িতে?

1. কর্তব্য বাড়ির আগে আপনি কোথায় বাস করতেন?
2. আপনার আগের বাড়িতে আপনি / আপনার বাড়ির সমস্ত কিছু যে একটি, না একের বেশী কল, না কল কোন জায়গা থেকে হল পড়তেন?
   - Just one
   - একটি জায়গা যে হল?
   - (probe: What is it? For example, which tubewell, pond? What is the location?)
   - More than one
   - কম্পিউটার জায়গা থেকে হল পড়তেন?

3a. আপনি এই বাড়িতে কত বছর বসা হয়েছে?

Tubewell Identification number (ID) / / / / / / / / / /
Duration (years) / / / /

THIRD TO LAST OR PRESENT HOUSE

পরের প্রাপ্ত হচ্ছে আপনার আগে এবং তার আগে বাস করেন কোন বাড়ি?

1. কর্তব্য বাড়ির আগের বাড়িতে আগে আপনি কোথায় বাস করতেন?
Village .................................................................
Union .................................................................

2. এই বাড়িতে আপনি এবং আপনার বাড়ির সকলে যে এক, না কয়েক বছর লাগ খোল হয়েছিলেন?
   - Just one
   - একটি জায়গা যে হল?
   - (probe: What is it? For example, which tubewell, pond? What is the location?)
   - More than one
   - কম্পিউটার উল্লেখ থেকে জায়গা হয়েছিলেন?

3. বাড়িতে আপনি এবং আপনার বাড়ির সকলে যে এক বা কয়েকের বেশী হল জায়গা থেকে হল পড়তেন?
   - Just one
   - একটি জায়গা যে হল?
   - (probe: What is it? For example, which tubewell, pond? What is the location?)
   - More than one
   - কম্পিউটার উল্লেখ থেকে জায়গা হয়েছিলেন?

Tubewell Identification number (ID) / / / / / / / / / /
Duration (years) / / / / / / / / / /
WATER SAMPLES

THIS SECTION IS TO BE COMPLETED BY FIELD ASSISTANTS
WATER
1. Total water samples collected for this participant: ________________

2. [fill in with the code for the residence or work; e.g., current house, current water source would be

<table>
<thead>
<tr>
<th>Residence</th>
<th>Tubewell ID</th>
<th>Duration of use</th>
</tr>
</thead>
<tbody>
<tr>
<td>residence (current)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>option 1 [explain]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>option 2 [explain]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Residence (previous 1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>option 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>option 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Residence (previous 2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>option 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>option 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Residence (previous 3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>option 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>option 2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

VOLUMES OF WATER CONSUMED

In the next questions ask about the volumes of fluids currently consumed. Ask about what the participants first drink after getting up from sleep this morning. Then ask about the rest of the morning. When you get to the time of interview, switch to asking about previous days up to the last drink of last night. For the size of container, a small cup is of 100 cc, a small glass is of 250 cc, medium 500 cc, and large mug 750 cc.
<table>
<thead>
<tr>
<th></th>
<th>Glass, Cup, Bowl</th>
<th>in cc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breakfast</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bread</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fruits, Jam</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tea/Coffee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lunch</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sandwich</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fruits, salty snacks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tea/Coffee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dinner</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rice, Dal, Kichrani</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vegetable Subzi</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tea/Coffee</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Total**

**PAST VOLUMES CONSUMPTION**

1. I usually drink **less** (same) (more) **than** (as much as) a cup of water or tea/coffee. *More*

<table>
<thead>
<tr>
<th></th>
<th>Glass, cup</th>
<th>in cc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Example: more</td>
<td>1 medium glass</td>
<td>500 cc</td>
</tr>
</tbody>
</table>

2. I usually drink **less** (same) (more) **than** (as much as) a cup of water or tea/coffee. *More*

<table>
<thead>
<tr>
<th></th>
<th>Glass, cup</th>
<th>in cc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Example: more</td>
<td>1 medium glass</td>
<td>500 cc</td>
</tr>
</tbody>
</table>
Arsenic in tube well water and health consequences

Abstract Summary for Ethical Review Committee

The discovery of arsenic in groundwater in Bangladesh has aroused widespread concern. Major proportions of tube wells for drinking water in the country are contaminated with arsenic. Experiences from other countries indicate that the consequences of this exposure will be extensive and include excess incidence and mortality in cancers and cardiovascular diseases. However, the knowledge base is weak on the weight of this new burden of diseases and on the speed by which it develops. Little is known about the reproductive health consequences, and about the possible aggravating role of the widespread malnutrition in Bangladesh on arsenic-induced health effects.

The overall objective of this project is to establish a strong epidemiologic platform of research on levels of arsenic exposure through drinking water, occurrence of arsenic skin lesions, consequences for reproductive outcome, effect on adult mortality, modifications of effects by the nutritional status, and effects of an intervention with alternative water sources.

We propose screening for skin lesions in the 220,000 population, and assessment of arsenic content by atomic absorption spectrometry (AAS) of the 9000 tube wells of the Matlab surveillance area. Information from testing of all 9000 tube wells, individual information on water used for drinking, and results of screening for arsenic-related skin lesions in the entire 220,000 population (excluding infants) will be entered into the data bases of Matlab HDSS. This information will enable analysis of doses of arsenic in relation to presence of arsenic skin lesions. Efforts will be made to assess the calendar time at start of the identified skin lesion, enabling a retrospective cohort analysis of current exposure (as a proxy for exposure levels over time); duration of exposure to the arsenic contaminated water, and onset of skin changes. A second retrospective cohort analysis will be performed on current exposure, duration of exposure, and reproductive events, such as spontaneous abortions, still birth, and early neonatal deaths during the last three years (this information is also available in HDSS system). This will enable us to evaluate the effects of arsenic exposure as a reproductive toxin in humans. A third cohort analysis will relate the arsenic exposure to overall adult mortality (mortality information including cause of death from the HDSS system) and specifically to mortality in cardiovascular diseases and cancers during the last five years. A case-referent study of the modification by current nutritional status on arsenic-induced skin lesions will be nested into the first cohort analysis. Individuals with arsenic skin lesions (above 5 years of age) will be selected as cases, and two referents will be randomly selected from the HDSS databases. Nutritional status of cases and referents will be assessed by anthropometry and blood samples will be taken for nutritional biochemistry. Urine samples will be taken from cases and referents as soon as the cases are identified for analysis of arsenic methylation patterns as well as current exposure levels. BRAC, a Bangladesh NGO, will be responsible for the arsenic mitigation component. Initial advice of temporary alternative drinking water sources will be given (arsenic-free tube wells in the
neighbourhood) followed by promotion of alternative sources of safe drinking water (rainwater harvesting, treated surface water, and treated arsenic contaminated ground water). A follow-up will be performed of individuals with skin changes as to levels of arsenic species in urine (change in exposure), as well as to assessment of reversibility of skin lesions, assessed by clinical examination. The consequences of a shift to other water sources will also be evaluated, including monitoring of diarrhoeal diseases through the surveillance system in Matlab.

Strategies to address ethical issues

1. The latency (i.e. the time from first exposure to manifestation of disease) for arsenic-caused skin lesions, in particular keratosis, is typically of the order of 10 years. However, latency much shorter as well as longer than 10 years may occur. In order to assess the burden of arsenic-induced health problems age- and gender-specific information on the occurrence of such effects is needed, as well as an improved understanding of the exposure to arsenic over time. The ingested arsenic is methylated and excreted in urine. Children have reportedly a lower degree of methylation of arsenic than adults. Children are found to have arsenic skin lesions long before expected latency periods. Some studies indicate a lower degree of arsenic methylation in men than in women, especially as compared to pregnant women. Poor nutritional status might increase the health effects of arsenic through variations in the arsenic methylation capability. Vitamin A status in the population may be related to susceptibility to arsenic related diseases. The risk of skin cancer in arsenic-exposed individuals has been associated to beta-carotene levels. The general nutritional status (as expressed by anthropometry), the antioxidant status and other micronutrients such as zinc status may play an important role in modifying the body’s response to arsenic exposure. Due to the vast number of pregnant women exposed to the arsenic contaminated water, even a relatively small risk of abortions, stillbirths and early neonatal deaths related to arsenic in drinking water would have a major public health impact in Bangladesh. The appropriate treatment for arsenic-induced skin changes is a shift to arsenic-free drinking water. However, there is insufficient knowledge to what extent these skin changes disappear when the individual is no longer drinking the contaminated water. There is anecdotal information available that less advanced skin changes are reversible, but unknown if this also is the case for more advanced lesions. Measurements of urine arsenic levels are needed to judge if the exposure has seized. A better understanding of the potential reversibility is needed from a clinical as well as a public health point of view. A shift to alternative arsenic-free water sources may potentially imply a shift to pathogen-contaminated water. This is especially the case when surface water will be used as the new water source, but may also be the case when harvesting rainwater. In most mitigation projects so far some control of pathogens has taken place, e.g. by cultivating samples from the new drinking water source. This is an important intermediate step, but a monitoring of diarrhoeal diseases in vulnerable groups, i.e. infants and children, is also needed. The Matlab surveillance system has included a monitoring of diarrhoeal diseases in all
children below 5 years of age. This information can be used in order to evaluate if the shift to alternative water sources increases the risk for diarrhoea.

2. There may be minimal risks involved in this study. Medical doctors will examine all subjects participate in Matlab health centre for general health, measure blood pressure and examine skin. A trained senior research assistant will collect 4 ml blood (less than one teaspoonful) from veins of forearm with all aseptic precautions. There is minimal risk associated with this procedure. There is no risk involving skin examination.

3. Standardised procedure of collection of blood, and urine samples will be used.

4. Identification of all study participants will remain confidential. Study staff will use records only. Every effort will be made to keep the records confidential as possible. All data forms will be kept in a locked file cabinet. Data will be analysed and published without reference to any name or identity.

5. The participants will be signing a consent form informing them of the nature of the study, its rationale, and its risks and benefits. The informed consent document will embody the elements of the consent as described in the Declaration of Helsinki, and the ICH Harmonized Tripartite Guidelines for Good Clinical Practices. The investigator or designate will describe the protocol to the participant or the legal guardians of potential subjects face to face. The subject information and consent form may be read to the participants of all participants, but in any event, the investigator will give the parent's ample opportunity to inquire about the details of the study and ask questions before signing the consent form. We will insure that health research workers and physicians are trained to recognise symptoms and clinical signs of arsenicosis.

6. The suspected individuals of arsenicosos will be interviewed in the Matlab health centre as well as to their houses. The interview will not take more than 15 minutes.

7. This study will assist in understanding to what extent arsenic-contaminated drinking water have resulted in adverse health effects, especially skin lesions. We will also study if other factors, i.e. general health and nutritional status help protect the individual against the arsenic toxicity. Such information will be useful for prevention of arsenic-related health problems in Bangladesh.

8. We will use the records from ICDDR, B health and demographic surveillance system at Matlab.