International Centre for Diarrhoeal Disease Research, Bangladesh
CENTRE FOR HEALTH AND POPULATION RESEARCH
Mail : ICDDR,B, GPO Box 128, Dhaka-1000, Bangladesh
Phone: 880-2-8811751-60, Telex : 642486 ICDD BJ
Fax : 880-2-8823116, 8812530, 8811568, 8826050, 9885657, 8811686, 8812529
Cable : Cholera Dhaka

Memorandum

26 January 2003

HSD 2003

To : Dr. Robert F. Breiman, MD
Principal Investigator of protocol # 2003-001, and
Associate Director, Health Systems and Infectious Diseases Division

From: Professor Mahmudur Rahman
Chairperson, Ethical Review Committee

Sub : Approval of protocol # 2003-001

Thank you for your memo dated 23rd January 2002 with the modified version of your research protocol # 2003-001 entitled "Outbreak Investigation of a Cluster of Deaths in Chandpur Village, Meherpur District, Bangladesh, during April-May 2001" incorporating the observations made on the protocol. The protocol is hereby approved subject to:

a) inclusion of one virologist and one epidemiologist from government in the study.

b) ratification of the approval by the ERC in its next meeting scheduled to be held on 5th February 2003.

You shall conduct the study in accordance with the ERC-approved protocol; and shall be responsible for protecting the rights and welfare of the subjects and compliance with the applicable provisions of ERC Guidelines. You shall also submit report(s) as required under ERC Guidelines. Relevant excerpt of ERC Guidelines and *'Annual/Completion Report for Research Protocol involving Human Subjects'* are attached for your information and guidance.

Thank you and I wish you all success in running the above-mentioned study.

Copy: Director, ICDDR,B, and
Chairman, Research Review Committee

International Centre for Diarrhoeal Disease Research, Bangladesh
CENTRE FOR HEALTH AND POPULATION RESEARCH
Mail : ICDDR,B, GPO Box 128, Dhaka-1000, Bangladesh
Phone: 880-2-8811751-60, Telex : 642486 ICDD BJ
Fax : 880-2-8823116, 8812530, 8811568, 8826050, 9885657, 8811686, 8812529
Cable : Cholera Dhaka

Memorandum

22 January 2003

To : Dr. Robert F. Breiman, MD
Principal Investigator of protocol # 2003-001, and
Associate Director, Health Systems and Infectious Diseases Division

From: Professor Mahmudur Rahman
Chairperson, Ethical Review Committee

Sub : Protocol # 2003-001

Thank you for your protocol # 2003-001 entitled "Outbreak Investigation of a Cluster of Deaths in Chandpur Village, Meherpur District, Bangladesh, during April-May 2001". As requested by you, the Ethical Review Committee has undertaken expedited review of the protocol and following are the comments on it:

a) The same title of the protocol should be used throughout the protocol (p6 and p35).

b) Since the outbreak investigation is to support the Government of Bangladesh, it is strongly recommended that one virologist and one epidemiologist from government should be included in the research team. In future, the government will be able to use the trained manpower for effective handling of such outbreak.

c) On the ERC Face Sheet, item # 3(c) and 5(b) should be marked "YES".

d) The Bangla version of three consent forms should be provided. In absence of Bangla version of the consent forms, no comments could be made on them.

e) Consent form:

i. In forms B1-B3, para-1, it has been stated that ICDDR,B and CDC are doing the study. CDC, USA, should be written instead of CDC only.

ii. Under 'permission to store blood specimen', section the statement 'I give .... for future research' should be deleted as the statement has wider implication.

iii. The statement 'I agree to have my blood sample saved for future testing' should be replaced by a more explicit and clear statement such as 'I agree to have my blood sample saved for the tests as mentioned above.'

iv. No provision for thumb impression has been kept in any consent form. Provision for thumb impression should be included in all consent forms.

f) The budget of the protocol was not processed through the Finance Department.

You are, therefore, advised to modify the protocol incorporating the above observations; and submit the modified version of the protocol for consideration.

ERC approval of the protocol will be accorded upon your addressing the above issues. It may, however, be noted that approval is subject to ratification by the ERC meeting in its scheduled to be held on 5th February 2003.

Thank you.

Copy: Acting Chairman
Research Review Committee

Prof A K M Nurul Anwar
MBBS, MPhil, PhD, FCPS
Vice-Principal

IBRAHIM MEDICAL COLLEGE
An Institution of Diabetic Association of Bangladesh
Ibrahim Sarani, Segunbaghicha, Dhaka-1000.
Tel: 9567623

21 January 2003

Prof. Mahmudur Rahman
Chair, Ethical Review Committee, ICDDR-B

Sub: Review of Protocol # 2003-001: Investigation of an outbreak of Encephalitis in Meherpur District.

Thank you for your memo of 15 January 2003 on the above subject.

The protocol is an outbreak investigation without any intervention and will determine prevalence of antibodies to Nipah/Hendra viruses among the surviving case patients, health workers & others who were in close contact with ill patients. Other healthy individuals in the same village will act as case control. Risk factors, reservoirs and mode of transmission will be evaluated, which may suggest future prevention strategies. A standardized instrument will be used to collect demographic and past medical history of the participants. 5-10 ml of blood will be collected after obtaining informed consent. Permission will also be obtained to store part of the blood sample for future testing, which however will not be used for HIV & genetic tests.

Informed consent forms have been suitably developed, which addressed all issues of ethical concern. However, Bengali translation of the consent forms should be provided.

In the face sheet, 3(c) and 5 (b) should be marked 'yes'.

The protocol is recommended for ethical clearance subject to above modifications.

Thanking you

21/1/03

(Prof. A.K.M. Nurul Anwar)
Member, ERC

To,
Chairman
ERC, ICDDR,B Dhaka.

21.01.2003

From : Prof. J. Ashraful Haq
Department of Microbiology, BIRDEM

Ref.: Comments on the protocol entitled " Outbreak investigation of a cluster of deaths in Chandpur village. Meherpur district, Bangladesh, during April-May 2001 (2003-01)"

The above protocol intends to investigate the possible cause of death that occurred during April-May 2001 at Chandpur village of Meherpur district. It was a suspected outbreak of viral encephalitis. The objectives of the study include determination of antibody to Nipah/Hendra virus among the survivors and their contacts and mode of transmission of infective agents.

The following points may be noted:

a. The investigation will be done jointly by ICDDR, B and CDC, Atlanta, USA. The DGHS-MOHFW will provide support to carry out the investigation. Since this outbreak investigation is to support the government of Bangladesh, it is strongly recommended that one virologist and one epidemiologist from government should be included in the research team. In future, the government will be able to use this trained manpower for effective handling of such outbreak.

b. Ten and 5 ml of blood will be collected from adult and children population respectively. Half of the collected blood sample will be sent to CDC, USA for determination of antibody to Nipah/Hendra virus. Other half will be stored at ICDDR,B for future study. If the samples are negative for antibody to Nipah/Hendra virus then the samples will be tested further for antibodies to other arboviruses and dengue viruses. No genetic and HIV tests will be done with these samples.

c. There are three consent forms namely B1, B2 and B3 for adult, child and healthcare professionals. All these consent forms are in English. No Bengali consent forms have been provided and therefore no comment can be made. Bengali version of consent forms should be included.

In form BI-B3, para-1 - It has been stated that ICDDR,B and CDC are doing the study, CDC, USA should be written instead of CDC only.

Under "permission to store blood specimen" section the statement ' I give.....for future research' should be deleted as the statement has wider implication.

The statement ' I agree to have my blood sample saved for future testing' should be replaced by more explicit and clear cut statement such as " I agree to have my blood sample saved for the tests as mentioned above"

No provision for thumb impression has been kept in any consent forms. Provision for thumb impression should be included in all consent forms.

Recommendation

Subject to the above modifications, the protocol may be considered for ethical clearance.

Date: 21st January 2003

To: The Chairperson, ERC

From: Mohammad Ullah

Sub: Review of the protocol # 2003-001 entitled, "Investigation of an outbreak of encephalitis in Meherpur District".

Thank you for sending me the above protocol for review. This is a cross-sectional and case control study to obtain epidemilogical data from the residents of Chandpur village under Meherpur District. This is a study of great public health importance in Bangladesh. After a through review, however, following observations are made:

01. The PI used different title in the protocol (p 6 and p 35).
02. The PI submitted a budget with the approval of the appropriate authority of the Centre (p 26).

Comments: Unified title of the study should be used throughout the protocol and approved budget should be submitted for consideration. In addition to the above, any observation(s) by the other ERC Members should be addressed. Finally, the protocol may please be approved after addressing the above observations.

Thank you.

Duration of Study: The duration of the study is about 6 months. We anticipate starting the study at the beginning of September 2002 and finishing in by the beginning of March 2003

Limitations and anticipated difficulties

Until the data collection has been started and later during the analysis phase the limitations of this study cannot be wholly predicted. From past experience, however, we anticipate the study requiring special attention to be given to move beyond the negative attitude of nurses, patients and other health care professionals that exists implying that nurses are not doing the work they are 'supposed' to be doing. The sample size may appear ambitious but the use of the previous studies, particularly in the area of observation of nursing activities is expected to make the workload more appropriate.

ACTION PLAN

Major Activities of the study	Duration in Weeks
1. Preparatory work of the study	4
2. Development and finalization of research instruments	4
3. Training of interviewers	1
4. Data collection and compilation	12
5. Data processing and editing	10
6. Publication of quarterly report	2
7. Coding and analysis	6
8. Preparation draft report for review	4
9. Incorporation of comments and observations	1
10. Preparation of final report and submission	1

Working weeks are non-exclusive

Facilities Available

The International Centre for Diarrheal and Disease Research, Bangladesh (ICDDR,B) has a long history of carrying out research with collaboration from national institutions. For the proposed study, the Centre has the necessary reputation and contacts to facilitate links with the hospitals that will be included in the study. Several presently employed field research officers will be recruited to participate in the study. Additional field staff will need to be hired and all field workers will be trained in the various data collection techniques used to carry out the study. Strong supervision of the quality of the data collection will be maintained, which will include ongoing review of the field notes.

Data Analysis

Qualitative

Qualitative data analysis is an iterative process, involving ongoing data collection and analyses. As data is collected, a coding system will be developed by the investigators for the qualitative data analyses. The coding system will be based on the initial research questions and objectives, as well as emergent themes. Qualitative interview data will be entered into a word processing program compatible with use in Atlas.ti, a text-organizing program and texts will be coded in Atlas.ti. In order to ensure the validity of the coding, during the initial stages all coded texts will be reviewed by a second individual. Subsequently, a sample of

International Centre for Diarrhoeal Disease Research, Bangladesh
CENTRE FOR HEALTH AND POPULATION RESEARCH
Mail : ICDDR, B, GPO Box 128, Dhaka-1000, Bangladesh
Phone : 880-2-8811751-60, Telex : 642486 ICDD BJ
Fax : 880-2-8823116, 8812530, 8811568, 8826050, 9885657, 8811686, 8812529
Cable : Cholera Dhaka

Memorandum

15 January 2003

To : Professor AKM Nurul Anwar
Member, Ethical Review Committee

Prof. J. Ashraful Haq
Member, Ethical Review Committee

From: Professor Mahmudur Rahman
Chairman, Ethical Review Committee

Sub : **Proposal for giving expedited decision**

Attached please find a memo dated 14th January 2003 from Dr. Robert F. Breiman with the protocol # 2003-001 entitled "Investigation of an Outbreak of Encephalitis in Meherpur District". The PI requests for expedited decision on the grounds mentioned in his memo. The January 2003 ERC meeting has been scheduled on 5th January 2003 and convening of a special ERC meeting for such small proposal is not considered to be justifiable. Further:

a) The proposal is an outbreak investigation without having any intervention, and the anticipated harm or discomfort to the study subjects in the proposed proposal is minimal.

b) The investigation was recommended by the Directorate of Health Services, Government of the People's Republic of Bangladesh; and the WHO. This protocol represents technical assistance to the DGHS and WHO to investigate this outbreak.

c) The proposal has been reviewed and approved by the CDC's IRB.

d) Acting ICDDR,B Director and RRC Chairman has waived review of the proposal in the RRC meeting.

e) CDC team has been awaiting ERC's approval of the proposal and the CDC has scheduled its visit Bangladesh early next month.

P.T.O.

In view of the above, I would appreciate if you could undertake review of the proposal and provide me with your comments on the proposal as early as possible. I propose to take decision on the basis of your comments, subject to the ratification of the action by the ERC in its next meeting.

I am sending copy of the proposal to the Co-Chairperson and other members of the Committee and they are also most welcome to provide their comments on the proposal.

I hope this meets your approval and other members of the Committee.

DISTRIBUTION

Dr. Halida H. Akhter
Prof. Hamida Akhtar Begum
Dr. AKM Iqbal Kabir
Prof. Hajera Mahtab
Dr. MA Salam
Mr. Mohammad Ullah
Prof. Md. Abdul Baqi
Brig. (Retd.) QMS Hafiz
Prof. Barkat-e-Khuda
Barrister (Dr.) Rafiqur Rahman
Dr. Nigar S. Shahid

Attachment I

Date:

(FACE SHEET)

ETHICAL REVIEW COMMITTEE, ICDDR,B.

Principal Investigator: Dr. Robert F. Breiman, M.D.

Trainee Investigator (if any): _____

Application No. 2003-001

Supporting Agency (if Non-ICDDR,B) _____

Title of Study: Outbreak Investigation of a Cluster of Deaths in Chandpur Village, Meherpur District, Bangladesh, during April-May 2001

Project Status: _____

[ ] New Study

[ ] Continuation with change

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

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

1. Source of Population:
   - (a) Ill subjects — Yes (No)
   - (b) Non-ill subjects — (Yes) No
   - (c) Minor or persons under guardianship — (Yes) No

2. Does the Study Involve:
   - (a) Physical risk to the subjects (minor (blood draw)) — (Yes) No
   - (b) Social risk — Yes (No)
   - (c) Psychological risks to subjects — Yes (No)
   - (d) Discomfort to subjects — (Yes) No
   - (e) Invasion of privacy — Yes (No)
   - (f) Disclosure of information damaging to subject or others — Yes (No)

3. Does the Study Involve:
   - (a) Use of records (hospital, medical, death or other) — (Yes) No
   - (b) Use of fetal tissue or abortus — Yes (No)
   - (c) Use of organs or body fluids — Yes (No)

4. Are Subjects Clearly Informed About:
   - (a) Nature and purposes of the study — (Yes) No
   - (b) Procedures to be followed including alternatives used — (Yes) No
   - (c) Physical risk — (Yes) No
   - (d) Sensitive questions — (Yes) No
   - (e) Benefits to be derived — (Yes) No
   - (f) Right to refuse to participate or to withdraw from study — (Yes) No
   - (g) Confidential handling of data — (Yes) No
   - (h) Compensation &/or treatment where there are risks or privacy is involved in any particular procedure — (Yes) No RB

5. Will Signed Consent Form be Required:
   - (a) From subjects — (Yes) No
   - (b) From parents or guardian (if subjects are minor) — (Yes) No

6. Will precautions be taken to protect anonymity of subjects — (Yes) No

7. Check documents being submitted herewith to Committee:
   - ____ Umbrella proposal - Initially submit an with overview (all other requirements will be submitted with individual studies
   - ✓ Protocol (Required)
   - ✓ Abstract Summary (Required)
   - ✓ Statement given or read to subjects on nature of study, risks, types of questions to be asked, and right to refuse to participate or withdraw) (Required
   - ✓ Informed consent form for subjects
   - ✓ Informed consent form for parent or guardian
   - ✓ Procedure for maintaining confidentiality
   - ____ Questionnaire or interview schedule*

* If the final instrument is not completed prior to review, the following information should be included in the abstract summary

1. A description of the areas to be covered in the questionnaire or interview which could be considered either sensitive or which would constitute an invasion of privacy
2. Example of the type of specific questions to be asked in the sensitive areas
3. An indication as to when the questionnaire will be presented to the Committee for review

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

_____
Principal Investigator

_____
Trainee

International Centre for Diarrhoeal Disease Research, Bangladesh
CENTRE FOR HEALTH AND POPULATION RESEARCH
Mail : ICDDR, B, GPO Box 128, Dhaka-1000, Bangladesh
Phone: 880-2-8811751-60, Telex : 642486 ICDD BJ
Fax : 880-2-8823116, 8812530, 8811568, 8826050, 9885657, 8811686, 8812529
Cable : Cholera Dhaka

Memorandum

To: Professor Mahmudur Rahman
Chairman, Ethical Review Committee (ERC)
ICDDR,B: Centre for Health & Population Research

From: Robert F. Breiman, M.D.
Associate Director & Head
Health Systems and Infectious Diseases Division

Date: January 14, 2003

Subject: **Investigation of an Outbreak of Encephalitis in Meherpur District (2003-001)**

In May 2001, an outbreak of encephalitis with 18 cases and 9 deaths occurred in Chandpur Village, Meherpur District. A limited investigation at that time suggested that the outbreak was caused by Nipah/Hendra virus. A larger outbreak investigation, involving international institutions, was planned but was interrupted by the events surrounding and following September 11.

WHO is now requesting (see enclosed letter) that CDC-Atlanta and ICDDR,B assist WHO and the DGHS-MOHFW in an investigation to define the scope and characterize the epidemiology of the outbreak and to determine whether a risk for continued transmission and lethal disease persists.

Enclosed is a protocol developed in collaboration with CDC to conduct this investigation. As mentioned above, the investigation involves technical support to the government and WHO to understand the nature of the outbreak. There will be no intervention and the small investigation involves minimal risk to the participants. The protocol has been reviewed and approved by CDC's IRB. The CDC investigation team is working through other time commitments and they hope to begin this investigation in February, 2003. We would appreciate ERC review of the proposal. Because of the nature of the outbreak investigation, the Acting Chair, RRC has waived the requirement for RRC consideration.

Thank you.

Enclosures:

ICDDR,B: Centre for Health & Population Research **RRC APPLICATION FORM**

RESEARCH PROTOCOL
Protocol No. 2003-001

FOR OFFICE USE ONLY

RRC Approval: ☐ Yes / ☐ No Date:

ERC Approval: ☐ Yes / ☐ No Date:

AEEC Approval: ☐ Yes / ☐ No Date:

Project Title: Outbreak Investigation of a Cluster of Deaths in Chandpur Village, Meherpur District, Bangladesh, during April-May, 2001

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

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

Key words: Nipah virus, encephalitis, serosurvey

Relevance of the protocol: Between 26 April and 11 May 2001, nine unusual deaths were reported in the village of Chandpur located in the District of Meherpur in Bangladesh. An investigative team led by the DGHS began an investigation of this outbreak on 18 May; this was followed by a second investigation from 26 May to 1 June by a team that also included personnel from the World Health Organization (WHO). Analysis of sera from surviving patients suggested that Nipah/Hendra virus was responsible for this outbreak. We will conduct further studies to ascertain the magnitude of the outbreak, identify risk factors for infection, identify the source of transmission, including potential animal reservoirs. The data from our investigation will help guide the public health response to this outbreak, including the assessment of possible continuing risk for Nipah/Hendra infection and possible disease prevention strategies. This investigation is intended to improve current understanding of this recently identified and emerging lethal pathogen.

Programmes

☐ Child Health Programme
☐ Nutrition Programme
☑ Programme on Infectious Diseases & Vaccine Sciences
☐ Health and Family Planning Systems Programme
☐ Population Programme
☐ Reproductive Health Programme

Principal Investigator: Dr. Robert F. Breiman
Phone: 8811751-60, Ext-2500,
Email: breiman@icddrb.org
Division: HSID
Address: HSID, GPO Box-128, Dhaka-10000

Co-Principal Investigator(s): Dr. Vincent Hsu, Medical Epidemiologist, Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, CDC
Dr. Kanak Talukder, Head, Disease Control, DGHS, Dhaka.
Dr. Jahangir Hossain, Medical Officer, Clinical Sciences Division, ICDDR,B
Thomas Ksiazek, Head, Special Pathogens, Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, CDC

Co-Investigator(s): Joseph Bresee

ICDDR,B:; Dr. Tasnim Azim, Head, Virology Laboratory, Laboratory Sciences Division (LSD); Dr. Goutam Podder, Laboratory Scientist, LSD; Dr. AK Siddique, Head, Epidemic Control and Preparedness Unit

CDC: Charles Rupprecht, DVM, PhD, Umesh Parashar, MBBS, MPH, Joseph Bresee, MD, William Bellini, MD,, Pierre Rollin, PhD, Larry Anderson, MD,

Directorate General of Health Services, Bangladesh: Dr. Kanak Ranjan Talukder, Director, Communicable Disease Control; Dr. Abdul Mannan Bangali, Assistant Director, Malaria & other Parasitic Disease Control (M & PDC).

Student Investigator/Intern: None

Collaborating Institute(s): Centers for Disease Control and Prevention, USA

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

Gender
☑ Male
☑ Females
Age
☑ 0 – 4 years
☑ 5 – 9 years
☑ 10 – 19 years
☑ 20 +
☑ > 65
☑ 15—55 yrs

☐ Pregnant Women
☐ Fetuses
☐ Prisoners
☐ Destitutes
☐ Service providers
☐ Cognitively Impaired
☐ CSW
☑ Others (specify: 1 to 4 years_____)
☐ Animal

Project / study Site (*Check all that apply*):

☐ Dhaka Hospital
☐ Matlab Hospital
☐ Matlab HDSS area
☐ Matlab non-HDSS area
☐ Mirzapur
☐ Dhaka Community
☐ Chakaria
☐ Abhoynagar
☐ Mirsarai
☐ Patyia
☑ Other areas in Bangladesh __Meherpur district _
☐ Outside Bangladesh
name of country: _____
☐ Multi centre trial
(Name other countries involved)
_____

Type of Study *(Check all that apply)*:

☑ Case Control study
☐ Community based trial / intervention
☐ Program Project (Umbrella)
☐ Secondary Data Analysis
☐ Clinical Trial (Hospital/Clinic)
☐ Family follow-up study
☑ Cross sectional survey
☐ Longitudinal Study (cohort or follow-up)
☐ Record Review
☐ Prophylactic trial
☐ Surveillance / monitoring
☐ Others

Targeted Population *(Check all that apply)*:

☑ No ethnic selection (Bangladeshi)
☐ Bangalee
☐ Tribal groups
☐ Expatriates
☐ Immigrants
☐ Refugee

Consent Process *(Check all that apply)*:

☑ Written
☐ Oral
☐ None
☑ Bengali language
☐ English language

Total sample size: 150-200

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

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

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 more than minimal risk
☐ no 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: Centers for Disease Control and Prevention

---

Yes/No

☐ ☑ Is the proposal being submitted for funding ?

If yes, name of funding agency: (1) _____

(2) _____

Do any of the participating investigators and/or 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.

Dates of Proposed Period of Support	Cost Required for the Budget Period ($)			
(Day, Month, Year - DD/MM/YY)	*a. Ist Year*	*2nd Year*	*3rd Year*	*Other years*
Beginning date February 17, 2003	**7,661**			
End date August, 2003	*b. Direct Cost* **6,080**	*Total Cost:* **7,661**		

Approval of the Project by the Associate Director of the Applicant

Dr. Robert F. Breiman

Name of the Associate Director

Signature

14-1-03

Date of Approval

Certification by the Principal Investigator

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

Signature of PI

Date: 14-1-03

Name of Contact Person (if applicable)

Table of Contents

		Page #
Face Page	.....	1
Project Summary	.....	6
Description of the Research Project	.....	7
Hypothesis to be tested	.....	7
Specific Aims	.....	7
Background of the Project Including Preliminary Observations	.....	8
Research Design and Methods	.....	10
Facilities Available	.....	15
Data Analysis	.....	16
Ethical Assurance for Protection of Human Rights	.....	17
Use of Animals	.....	19
Literature Cited	.....	20
Dissemination and Use of Findings	.....	21
Collaborative Arrangements	.....	21
Biography of the Investigators	.....	22
Detailed Budget	.....	26
Budget Justifications	.....	27
Other Support	.....	27
Appendix	.....	28
Consent Forms in English	.....	29
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: Dr. Robert F. Breiman

Project Name: Outbreak Investigation of a Cluster of Deaths in Chandpur Village, Meherpur District, Bangladesh, during April-May, 2001

Total Budget: US$ 7,661 Beginning Date: February 17, 2003 Ending Date: August, 2003

Between 26 April and 11 May 2001, nine unusual deaths were reported in the village of Chandpur located in the District of Meherpur, Bangladesh. An international team organized by World Health Organization in collaboration with a national team investigated this outbreak from 26 May to 1 June. They reported that all people who dies had mild to severe fever, almost half had headache and vomiting, 6 out of 9 had cough and seven had convulsion at the terminal stage. Two persons with febrile illnesses had IgM and IgG antibodyies against Nipah/Hendra virus. The investigators concluded that Nipah/Hendra virus was the likely etiology of the outbreak. Other than these possible cases in Bangladesh, Nipah virus infection of humans has been described only in Malaysia and Singapore during an epidemic that occurred in 1998-1999 where 104 patients died out of 265 cases; the major risk factor for Nipah virus infection of humans was close contact with pigs. By contrast, the cases in Chandpur restricted appeared to be restricted to a small geographic area and pigs did not appear to be involved in transmission.

We will conduct further cross sectional and a case-control studies to ascertain the extent of and identify risk factors for infection, identify the source of infection including potential animal reservoirs, and determine characteristics of the infecting virus. Briefly, we will conduct surveys among a sample of the residents of Chandpur village who are 1 year or older and health care professionals from Meherpur General Hospital and the Thana Health Clinic where several fatal cases were cared for at the time of outbreak. Following informed consent, demographic information, history of illnesses occurring since 1st April 2001, and detailed animal exposure history will be collected. Serum will be tested at a laboratory of the National Center for Infectious Diseases at CDC. The principal objectives will be to determine the prevalence of antibodies to Nipah/Hendra virus among surviving case patients, case-contacts and other people within the same village where the outbreak occurred, assess the clinical features among persons with antibodies to Nipah/Hendra virus, and to evaluate potential risk factors and modes of transmission for Nipah/Hendra virus during and following the outbreak.

The data from our investigation will help guide the public health response to this outbreak, including the assessment of possible continuing risk for Nipah/Hendra infection and the need for additional studies of local human and animal populations. In addition, the data will improve our current understanding of this recently identified highly lethal illness, and may assist in the development of effective prevention and control strategies.

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

Name	Professional Discipline/ Specialty	Role in the Project
	ICDDR,B Investigators	
1. Robert F. Breiman	Head, Programme on Infectious Diseases and Vaccine Sciences	Study design , analysis and monitoring
2. Dr. AK Siddique		
3. Dr. Md. Jahangir Hossain	Clinical Sciences Division	Study design and analysis
4. Dr. Tasnim Azim	Head, Virology Laboratory	
5. Dr. Goutam Podder	Laboratory Scientist	

CDC Investigators

6. Vincent Hsu, MD, MPH, EIS Officer (Study design, epidemiologic field investigation [survey implementation, blood drawing])
7. Umesh Parashar, MBBS, MPH, Medical Epidemiologist (Study design, epidemiologic investigation)
8. Joseph Bresee, MD, Medical Epidemiologist (Study design, epidemiologic investigation)
9. William Bellini, PhD, Chief, Measles Section, REVB (Nipah virus antibody laboratory testing)
10. Larry Anderson, MD, Chief, REVB (Study design, epidemiologic investigation)
11. Pierre Rollin, PhD, Supervisory Research Microbiologist (epidemiologic investigation, Nipah virus laboratory testing)
12. Thomas Ksiazek, PhD, Chief, SPB (Nipah virus laboratory testing)
12. Charles Rupprecht, DVM, PhD, Supervisory Research Veterinarian (animal epidemiologic investigations)

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 scope of transmission of Nipah/Hendra virus during and following the outbreak May 2001 was wider than determined during the initial investigations. Risk factors or reservoirs will be identifiable which will suggest prevention strategies.

Specific Aims:

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

1. Determine the prevalence of antibodies to Nipah/Hendra virus among the following:
   a. Surviving case-patients,
   b. Household contacts, healthcare workers, and others who were in close contact with ill patients,
   c. Other individuals in the same village where the outbreak occurred.

2. Assess the clinical features of disease among persons with antibodies to Nipah/Hendra virus.

3. Assess evidence of late onset or recurrent encephalitis among persons with antibodies against Nipah/Hendra virus.

4. Define mode(s) of transmission--Evaluate potential risk factors for acquisition of antibody to Nipah/Hendra virus, including contact with other case-patients and domestic or wild animals, and evaluate person-to-person transmission.

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).

Between 26 April and 11 May 2001, nine unusual deaths were reported in the village of Chandpur located in the District of Meherpur in Bangladesh. An investigative team led by the DGHS began an investigation of this outbreak on 18 May; this was followed by a second investigation from 26 May to 1 June by a team that also included personnel from the World Health Organization (WHO)(1, 2).

The village of Chandpur, population 802, is located approximately 17 kilometers from the border with India, close to the district town of Meherpur. The area is flat and mainly agricultural, with abundant trees and bushes. The houses are constructed from mud, and many have separate kitchens, cowsheds, and toilets. Each of the houses has a shallow tube well which is the main source of water. Houses usually have a variety of domestic animals, such as goats, chicken, and ducks. A few pigs are present in the village. Fruit bats are present in large numbers in this area.

All of the 9 fatal cases were adults (mean age: 44 years; range: 30-60 years), and 5 were male. Six of the 9 fatal cases were related and the other 3 lived in close proximity to these 6 patients. Clinical features included fever (9 of 9 patients), terminal disorientation and seizures (7 of 9), dry cough (6 of 9), vomiting (5 of 9), and headache (4 of 9). Another 10 nonfatal cases were identified in Chandpur that met a broad case definition of fever with either cough or vomiting or change in mental status during the period from April 1 through May 30, 2001. Another 9 nonfatal cases in addition to those meeting a case definition were identified by the investigative team. No unusual illnesses in the local animal population were identified.

A total of 141 blood smears were taken from cases, contacts, and villagers in mid-May; all were negative for malarial parasites. A total of 47 blood samples were collected from mild cases, contacts and neighbours, of which 2 showed IgM and IgG antibodies against Nipah/Hendra virus. One of the positive specimens was from a 32-year-old female who was the sister of 4 fatal cases. On May 3, she had onset of an illness characterized by fever, headache, cough, vomiting, and drowsiness. The other positive specimen was from the 20-year-old wife of the index fatal case. She had onset of a mild illness (fever and headache) on 5 May and recovered fully. Based on these laboratory findings, it was presumed that Nipah/Hendra virus caused this outbreak. While other patients with encephalitis during the same period did not have demonstrable Nipah/Hendra virus antibodies at the time of the outbreak, follow-up late convalescent sera were not collected to determine if antibodies developed late in the course of convalescence.

Other than these possible cases in Bangladesh, Nipah virus infection of humans has been described only in Peninsular Malaysia and Singapore during an epidemic that occurred in 1998-1999 (3,4). In this epidemic, a total of 265 patients (104 [40%] fatal) with viral encephalitis and 11 patients (1 fatal) with laboratory-confirmed Nipah virus illness were reported in Malaysia and Singapore, respectively. Most patients had features of encephalitis, characterized by fever and neurological abnormalities. Relapses of, and late-onset, Nipah encephalitis have been described in patients (6, 7). The major risk factor for Nipah virus infection of humans was close contact with pigs (3-5, 8, 9), but a few patients had no direct contact with pigs (3). No evidence exists linking ingestion of pork with development of Nipah infection. Antibodies to Nipah virus were found in other animals (e.g., dogs, cats, and flying foxes) (10-12), but transmission from these animals to humans was not documented. Bats were considered to be the primary reservoir of Nipah virus. Person-to-person transmission of Nipah virus appeared to be uncommon (13-14).

Hendra virus, closely related to Nipah virus, had been primarily a disease of horses. However, two human deaths in Australia were due to Hendra virus between 1994 and 1995. (15-16). Clinical manifestations include neurological symptoms consistent with meningitis, myalgias, headaches and lethargy. Horses appeared to be the primary source of human Hendra virus infection.

While the Chandpur village deaths represent the second possible outbreak of Nipah virus in humans, several features of this outbreak were strikingly different from the Nipah virus outbreak in Malaysia and Singapore and more similar to Hendra cases. The cases appear to have been restricted to a small geographic area and limited chains of transmission raise the possibility that the virus was transmitted person-to-person. Second, no concurrent illness was noted in the local animals that came in contact with humans. Although a few pigs were identified in the village, no sick pigs were observed and none of the patients reported any contact with pigs, which were the primary source of human infection in the Malaysia/ Singapore outbreak. Because the Chandpur outbreak raises several issues of public health significance, we propose to conduct a detailed investigation of this outbreak, focusing on issues not fully addressed in the previous investigations.

Specifically, we will conduct further studies to ascertain the extent of and identify risk factors for infection, identify the source of infection including potential animal reservoirs, and determine characteristics of the infecting virus. The data from our investigation will help guide the public health response to this outbreak, including the assessment of possible continuing risk for Nipah/Hendra infection and the need for additional studies of the local human and animal populations. In addition, the data will improve our current understanding of this recently identified illness with a high fatality and may assist in the development of effective prevention and control strategies.

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).**

STUDY DESIGN

We will conduct a cross-sectional and case-control study of the residents of Chandpur village and of health care workers who cared for the fatal cases. We will interview participants to obtain epidemiologic data using standardized instruments and collect blood specimens to test for antibodies to Nipah/Hendra virus.

The proposed timeline for the 24-weeks investigation that will be conducted in February 2003 is in the following table. However, if more extensive population sampling is needed, it may be necessary to extend the time spent in Chandpur/Meherpur. Many additional months will be needed in the laboratory to analyze specimens and data analysis will take several additional months. It is anticipated that the investigation will be completed in August 2003.

Table 1. Proposed timeline for investigation of cluster of deaths in Chandpur / Meherpur, Bangladesh

Day/Week	Activity
Days	
1	Meeting with WHO, ICDRRB, CDC, and government officials in Dhaka; formation of team and agreement on programme of work
2-9	Population survey in Chandpur village and listing of health care professional in Meherpur District Hospital by Two Field Research Assistant
10-12	Data entry and making a list of population
13	Travel to and arrival in Meherpur by Study Team
14-21	Study activities as described in this protocol including training of personnel and data collection
22	Travel back to and arrival in Dhaka
23	Data cleaning
24	Wrap-up meetings with team members
25-28	Begin specimen shipping to CDC for laboratory testing
Weeks	
5	Data entry screen creation, Finish data entry in computer, Begin data cleaning
8	Preliminary data results from CDC expected
12	Begin data analysis
24	Finalize analysis, begin report writing

STUDY POPULATION

The survey will be conducted among a sample of the residents of Chandpur village who are ≥1 year of age. A total of 802 persons live in Chandpur village, including 422 males and 380 females. A survey will also be completed on behalf of individuals who died in the outbreak by relatives of the deceased.

We will also study a sample of health care workers from Meherpur General Hospital, where several of the fatal cases were treated. The sample will include some workers who provided care to the patients and some who did not. This evaluation will be helpful to determine whether person-to-person transmission of the offending virus occurred.

CASE DEFINITION

A ***confirmed*** case will be defined as a person with either IgM or IgG antibodies against Nipah/Hendra virus in serum specimens. A ***possible*** case will be defined as a person with fever and either cough or vomiting or neurologic symptoms (e.g., headache, change in level of consciousness, seizures) between 01 April and 30 May 2001.

SAMPLING TECHNIQUE AND SAMPLE SIZE FOR CASE DETECTION AND CASE CONFIRMATION

Selection of village cases: The objective for case selection is to identify as many confirmed cases (those with positive Nipah/Hendra antibody titers) as possible without having to survey and draw blood from every village resident. Because antibody results will not be available until after the study team leaves Chandpur, we must try to identify factors that will give us the greatest yield of identifying confirmed cases. We will focus serum collection from the following groups of residents in the area: (1) all possible surviving individuals who had an illness meeting the "possible" case definition, (2) contacts of individuals who died in the outbreak, (3) contacts of individuals who had previous positive antibody titers to Nipah/Hendra virus, and (4) contacts of possible cases meeting the case definition. If interviews from groups 1 through 4 suggest a strong exposure(s) to possible risk factor, e.g. occupational, geographic, or animal exposure, then we will also extend the survey and serology study to (5) all others in the village with that/those particular exposure(s) associated with becoming a case. We estimate that pool (1) will give us approximately 15 cases; although it is uncertain how many other individuals pools (2) through (5) we will identify, a rough estimate would be about 35, for a total of 50. Identifying, surveying, and obtaining serum from these targeted groups will provide the greatest yield of people with positive Nipah/Hendra serologies.

Identification of surviving cases: A list of surviving cases from the outbreak (group 1) will be provided by Government and WHO staff involved in the 2001 investigations. We will use the list to contact those individuals to enroll in the study. Medical records from hospitals or clinics, if available, will be reviewed from these patients only after they have been contacted and they have consented to participate in the investigation. These records will be used to confirm that they meet the "possible" clinical case definition and provide clinical information, about their illnesses.

Population Survey: A population survey in Chandpur village will be carried out to collect information on name, age sex, occupation, family number. The data entry and analysis will be done in Epi-info 6. A list of age and their corresponding sex, occupation and family will be prepared. This survey and analysis will be carried out before arrival of the investigation team at Meherpur.

A list of physicians, nurses and other health workers will be obtained from the Civil Surgeon of Meherpur Hospital.

Selection of village controls: All persons meeting the possible case definition will be considered to be "cases" for the case-control study, until serologic results are available. Two controls will be selected for each case, if

possible. This ratio may need to be reduced to 1:1 ratio, depending upon the number of village cases enrolled and availability and willingness of residents to participate as controls. Controls will be age-matched to the selected presumed cases (+ or – 5 years for persons >18 years of age, + or – 2 years for 11 to 18 years of age, + or -1 year for 2 to 10 years of age, + or - 2 months for <2 years of age. The age -matched control will be selected by simple random sampling from the list of the population surveyed.

Selection of health care staff: We will attempt to identify and enroll as many health care staff that cared for the admitted cases from Chandpur village with possible case definition. Such staff include physicians, nurses, ward boys or girls, phlebotomists, and other workers that had potential exposure to the cases at Meherpur Hospital and at the Thana Health Clinic. The determination of the final number of persons to be included in the sample will depend on the ability to identify and contact all health care personnel that had contact with confirmed and possible cases, but we aim to include all available health care personnel who were exposed to the fatal cases or admitted with possible case definition.

Any health care staff meeting any of the following criteria will be defined as exposed to the patient:

1) A needle stick injury from a needle which was in contact with the patient's blood.
2) Splashed in the eye, nose or mouth with respiratory secretions, stool, urine, or blood from the patient
3) Direct skin contact with respiratory secretions, stool, urine, or blood from the patient
4) Any contact including activities such as dressing or washing the patient, skin contact, handling of patient items such as utensils or cups, or handling of hospital equipment used by the patient such as ventilator masks or nasal prongs

Additional health care staffs without exposure to cases may be enrolled at a later time as controls only if there are sufficient numbers of antibody positive health care workers (cases) to conduct a case-control study with sufficient power. Controls will be age-matched within five years and randomly selected from the list of health care personnel of Meherpur Sadar Hospital who were not exposed to cases as defined above. Controls will be selected with a 2:1 ratio to cases. If it is determined that an insufficient numbers of cases to perform a case-control study exists, then a cross-sectional analysis will be done.

ENROLLMENT

For all participants included in the investigation sample, written, informed consent will be obtained for both the interview and the collection of a blood sample (Appendix B). For children (equal to or less than 18 years of age), the parent or guardian will sign the consent form. (For children 7 years of age or older, assent to participate will be obtained (Appendix C). A copy of the forms will be placed in the patient's study folder and a copy will be provided to the participant.

Once enrolled, each subject will be assigned a unique study ID number and entered on the appropriate enrollment log (Appendix D). For village cases, the study ID number will have a 2-alphabet prefix to identify it as a village case (i.e., "VL" for village), followed by a 4 digit numerical suffix. For instance, the first village subject will be assigned the study ID number "VL-0001." Village controls will be assigned the same 2-alphabet prefix, but the 4 digit numerical suffix will begin with a "1", e.g. "VL-1001." For heath care workers who are cases, the study ID number will have a prefix "HC", followed by a 4 digit numerical suffix beginning with "0" and with controls, the study ID number will begin "HC-1001."

DATA COLLECTION

Subject interviews: A standardized instrument will be used to collect information from the participants. The survey for Chandpur village residents (Appendix E) will collect data on:

- Demographic characteristics, such as age, sex and occupation
- Past medical history, particularly about illnesses since April 1, 2001
- Exposure history, particularly to persons who were ill with a neurologic disease during the past year and to a variety of domestic and wild animals

For health care workers, we will inquire about occupational details, history of exposure to fatal cases, and illness history (Appendix F).

Questionnaire modifications:

Details of possible exposures among the study population will not be fully known until the study team reaches the field site and assesses the situation; thus, the questionnaires may be slightly modified to meet the study objectives. Modifications to the questionnaire will only include additional details about exposures and activities that might be related to the risk of infection with Nipah/Hendra virus such as certain animal exposures not previously thought to be associated with Nipah/Hendra virus, occupational exposures, and/or travel history to certain areas where exposure to animal reservoirs may be more likely. For example, answers to questionnaires may indicate that many persons who were ill had exposure to dogs. If ill persons appeared to have more contact with dogs than non-ill, we would re-interview subjects to ask additional questions including type of contacts, times of contacts, and location of contacts with dogs. These modifications will be done on site. These changes / additions will have no effect upon risk towards the participants. Because it is uncertain what types of communication resources (telephone, fax, or email) are available at the study site, we will report any changes to the IRB as soon as communication resources are available.

Medical records:

If a subject has indicated on the survey that he/she was hospitalized for an illness compatible with a possible case, we will review his/her hospital record to confirm the illness and abstract clinical information using a medical abstraction form (Appendix G). We will obtain appropriate informed consent from each individual prior to obtaining hospital records. If necessary, we will obtain written permission from the hospital(s) to obtain medical records (Appendix H).

COLLECTION OF BLOOD SPECIMENS AND SPECIMENS LABELLING :

After obtaining informed consent, a single specimen of 10 ml of blood will be obtained from each adult participant and 5 ml of blood from all children 1 to 12 years of age. The specimen will be labeled with the patient's unique study ID number with pre-made adhesive labels according to the nomenclature discussed above.

DATA MANAGEMENT:

All data collection forms will be photocopied; one copy each will be retained by the investigation team from Bangladesh and one copy will remain with the CDC investigators. Data will be entered into a central database by staff members of ICCDR,B assisted by CDC epidemiologists. Copies of the data will be shared with all investigators, once they are entered and cleaned. Laboratory data will be entered into a relational database and merged with the survey data at the end of the study.

WITHDRAWAL FROM INVESTIGATION:

A person is free to not participate in the investigation. A subject may refuse to participate at any point after consenting to be in the investigation. Refusal to participate will in no way affect the subjects' or families' medical care or standing at the health care facility.

TIMING OF SPECIMEN COLLECTION:

The blood specimen will be obtained either immediately prior to or immediately after administration of the interview survey. If a specimen cannot be obtained on the same visit, a follow-up visit will be arranged at the convenience of the participant.

SPECIMEN HANDLING:

Approximately 10 ml of blood will be obtained from adults and 5 ml from children equal to or less than 12 years of age. The Field Team will carry a cooler equipped with ice packs with them and the specimen will be placed in the cooler after collection. At the end of each day, or more frequently if possible, the cooler will be transported to a local hospital laboratory. At the laboratory, the blood specimens will be centrifuged/decanted to separate serum. Sera for each patient will be divided into two aliquots. Each aliquot will be placed in a different tube that will be labeled with the patient's unique investigation ID number. The tubes will then be frozen at -20^0C. At the end of the investigation, all the sera will be will be transported to the laboratory of the ICDDRB and kept frozen at -70^0C. One aliquot of sera for each patient will be retained at the ICDDRB laboratory and one aliquot will be transported to the laboratory at CDC to test for antibodies against Nipah/Hendra virus.

SPECIMEN TESTING:

Sera will be tested for the presence of IgM and IgG antibodies against Nipah/Hendra virus. IgM antibodies will be detected by using an IgM-capture enzyme immunoassay (EIA) and IgG antibodies by using an indirect EIA. Serum specimens that are positive or that give a borderline positive result for Nipah/Hendra virus antibodies by EIA will be tested by one or more confirmatory assays: (1) a neutralization assay, (2) western blot testing, and/or (3) immunoprecipitation of radiolabeled expressed viral antigens. For the neutralization assay, the heat-inactivated sera will be tested in a biosafety level-4 laboratory in duplicate at dilutions of 1:10 to 1:640 against a virus challenge of 30 to 300 median tissue culture infectious doses of prototype Nipah virus in Vero E-6 cells. Replication of virus will be determined at 6 days by fixing the cells with formaldehyde, staining the cell monolayers with crystal violet, and using microscopy to detect syncytial formation. Neutralization titer will be considered to be the highest dilution with complete inhibition of syncytium formation. Western blot and immunoprecipitation techniques can be tested in a biosafety level-2 laboratory.

STORAGE OF SPECIMENS:

Permission will be obtained from the participants to store part of their blood sample for future testing. The sample will be labeled with the unique patient identification number. The samples will only be tested for other potential agents that may have caused the illness and deaths in Chandpur village in April-May 2001. These other agents include antibodies to other arboviruses, such as Japanese encephalitis, West Nile, or other viral encephalitis, or dengue fever. The blood sample will not be tested for the HIV virus and no genetic tests will be done. If permission is not obtained to store part of their blood sample for further testing, the sample will be discarded within one week of obtaining final results for Nipah / Hendra virus and other potential agents that may have caused the outbreak. Because antibody test results obtained do not have any clinical impact on the care of enrolled subjects, results of these tests will not be given individually to enrolled subjects.

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).

This investigation will be conducted in the village of Chandpur and Meherpur Central (Sadar) hospital where sick patients were treated.

Chandpur village: The village of Chandpur, population 802, is located about 7 km from Meherpur town and on both side of Dhaka-Meherpur highway. The village is located approximately 17 kilometers from the Indian border.

Meherpur Sadar (central) Hospital: From the capital city of Dhaka, it takes about 7 hours journey by bus and about 3 hours by air and bus (half an hour by air, then two and half an hour by car) to Meherpur. Meherpur District has a population of 546,000 (1995) and the people from Meherpur district mainly seek medical care in this hospital. The hospital provides both primary and secondary care. The hospital has about 100 beds but accommodates about double patients of hospital bed. The hospital has adequate freezer storage space for sera, which can be temporarily stored until sent to ICDDR,B.

Centre for Health and Population Research (ICDDR,B): ICDDR,B has extensive experience with epidemiological and clinical research. The ICDDR,B laboratory has facilities to carry out research in Clinical Microbiology, Clinical Biochemistry, Immunology, and Virology.

Data Analysis

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

Data will be entered in relational databases and analyzed using Epi-Info 6.04, 2000, and/or SAS v8.0. The major outcome variable is the prevalence of antibodies to Nipah/Hendra virus. Once the results of serologic testing are available, risk factors for acquisition of antibodies against Nipah/Hendra virus will be analyzed in a nested case-control study. For the nested case control study, cases will be defined as individuals with evidence of antibody to Nipah/Hendra virus and controls will be persons without identifiable Nipah antibodies. Thus for purposes of analysis, individuals enrolled as possible cases but who are antibody negative may be used as a control, in addition to other enrolled controls.

The power of the study will depend upon the prevalence of antibodies (number of cases) in the study sample, the prevalence of the particular exposure in question, and the strength of the association with a particular exposure (table 2). For example, a minimum of 15 Nipah/Hendra virus antibody-positive patients and 30 controls would be required by presuming 10% expected frequency of exposure among control and OR of 10 with 2:1 control to case matching and considering 80% power of achieving a significant result at the 5% level.

For a matched case control study, the required number of cases would be less. If it is determined that not enough power exists to analyze as a case-control study because of insufficient cases with antibody to Nipah/Hendra virus, and or the rarity of the risk factor in question, the study will be analyzed as a cross-sectional study with prevalence and other descriptive data.

Table 2. Required number of cases given odds ratios and expected prevalence of a particular exposure among controls with a 2:1 ratio of controls to cases in an unmatched study.

Expected prevalence of exposure among control (%)	Odds ratios			
	3	4	5	10
2.0	326	185	127	49
5.0	141	82	57	23
10.0	81	48	34	15

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.

RESEARCH AND ETHICAL REVIEW COMMITTEES AND BOARDS

This investigation will be submitted for approval and approved by the CDC Institutional Review Committee prior to enrollment of any patients. The protocol will be also submitted for approval of Research Review Committee (RRC) and Ethical Review Committee (ERC) at the International Center for Diarrhoeal Diseases Research, Bangladesh (ICDDR, B).

Although we had previously been informed that approval of this investigation is not required by the ICDDR,B IRB (as this is considered technical assistance to the government investigation of an outbreak), we are working closely with the CDC Human Subject Manager on the best way to assure the coordinated activities between all collaborators on human subject activities.

INFORMED CONSENT

Informed consent will be obtained from all individuals who agree to participate in the investigation prior to administering the survey and drawing blood (Appendix B). For children between 1 and 7 years of age, consent for participation will be obtained from the parents/guardian. Children 7 to 17 years will be asked to give assent to participate in the investigation (Appendix C). A subject may refuse to participate in either the interview survey or the serologic investigation. It will be stressed that participation in the investigation is voluntary and participants may withdraw at any time. Trained professionals will translate the consent form into the local language (Bangla) and the form will be back translated to English to validate its contents. Investigation personnel will read out the consent form to participants who are unable to read. A copy of the form will be given to each participant who agrees to participate in the investigation.

BENEFITS & RISKS TO PARTICIPANTS

The participants will get no direct benefit from taking part in the investigation. Society may benefit by learning more about the causes of the unusual illnesses and deaths in Chandpur village during April-May 2001.

The collection of blood specimens may cause some discomfort to the participants. Bruising, bleeding, and rarely, infection could occur where the needle enters the vein. Emotional distress may occur among relatives or contacts who are asked to recall the circumstances of the illness and death of a loved one.

HANDLING OF ADVERSE EVENTS

Should a complication occur to a participant as a result of drawing blood, such as bleeding or infection, immediate medical aid will be given at no cost to the individual. If necessary treatment is not available locally, the participant will be taken to the nearest medical facility that can appropriately treat the complication at no charge to the patient.

COSTS

There is no monetary cost to the participant for taking part in the investigation. The participants will not be compensated for their time and inconvenience, consistent with the local policies for medical research and in order to avoid any coercion to participate in the trial in a country with a high poverty level. If the subjects incur any cost to take part in the investigation (e.g., transportation to hospital for treatment of possible adverse events), they will be reimbursed for these costs.

SUBJECT IDENTIFICATION

Investigation subjects will be identified only by investigation number in all materials that are used for analysis of investigation data, including all materials that are sent to the principal investigator or to any site other than the site at which the data are collected. No patient identifiers will be used in the analyses, nor will any identifying information be used in any reports or publications that may arise from this investigation.

Subjects may be provided the results of any testing conducted on specimens that they provide for the investigation. To obtain information, they will be asked to call the investigation coordinator for the site at the conclusion of the investigation.

PROTECTION OF PRIVACY

Efforts will be made to protect confidentiality to the extent allowed by law. All data and forms collected for investigation purposes that remain at the investigation site after completion of the investigation will be retained as part of the investigation records at each investigation site in a locked office. Access to investigation records will be restricted to investigation coordinators.

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.

Testing of animals will not occur during this study

Literature Cited

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

1. "Brief rapid-communication report of the investigation on 'Meherpur-Chandpur-Fever-Deaths Episode' by the team of Directorate General of Health Services" Unpublished paper written by Bangladesh National Team investigating cluster of deaths in Meherpur district, Bangladesh, 22 April 2001
2. "Draft report of the investigation of a cluster of deaths in Meherpur District, Bangladesh." Unpublished paper by WHO and National Team investigating cluster of deaths in Meherpur District, Bangladesh, undated
3. Parshar UD, Lye MS, Ong F. et al. Case control study of risk factors for human infection with a new zoonotic Nipah virus during a 1998-1999 outbreak of severe encephalitis in Malaysia. J Infect Dis 2000; 181: 1755-9
4. Chew MHL, Arguin PM, Shay DK, et al. Risk factors for Nipah virus infection among abattoir workers in Singapore. J Infect Dis 2000; 181:1760-3
5. Tan KS, Tan CT, Goh KJ. Epidemiological aspects of Nipah virus infection. Neurol J Southeast Asia 1999; 4:77-81
6. Wong SC, Ooi, MH, Wong MNL et al. Late presentation of Nipah virus encephalitis and kinetics of the humoral immune response. J Neurol Neurosurg Psychiatry 2001; 71:552-554
7. Tan CT, Goh KJ, Wong KT et al. Relapsed and late-onset Nipah encephalitis. Ann Neurol 2002; 51:703-708
8. CDC. Outbreak of Hendra-like virus—Malaysia and Singapore, 1998-1999. MMWR 1999; 48:265-269
9. Goh KJ, Tan CT, Chew NK et al. Clinical features of Nipah virus encephalitis among pig farmers in Malaysia. NEJM 2000; 342: 1229-35
10. Hooper PT, Williamson MM. Hendra and Nipah virus infections. Vet Clin North Am Equine Pract 2000; 16:597-603
11. Chua KB, Koh CL, Hooi PS et al. Isolation of Nipah virus from Malaysian island flying-foxes. Microbes and Infection 2002; 4:145-51
12. Johara MY, Field H, Rashdi AM et al. Nipah virus infection in bats (order Chiroptera) in Peninsular Malaysia. Emerg Infect Dis 2001; 7:439-41
13. Mounts AW, Kaur HJ, Parashar UD et al. A cohort study of health care workers to assess nosocomial transmission of Nipah virus, Malaysia, 1999. J Infect Dis 2001; 183:810-3
14. Tan CT, Tan KS. Nosocomial transmissibility of Nipah virus. J Infect Dis 2001; 184:1367
15. Murray K, Selleck P, Hooper P et al. A morbillivirus that caused fatal disease in horses and humans. Science 1995;268:94-97
16. O'Sullivan JD, Allworth AM, Paterson DL. Fatal encephalitis due to novel paramyxovirus transmitted from horses. Lancet 1997;349:93-95

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.

Because antibody test results obtained do not have any clinical impact on the care of enrolled subjects, results of these tests will not be given individually to enrolled subjects. All data generated by the study will be shared among the study collaborators. After data collection and analysis has been complete, a final report will be prepared and shared among the collaborators. The report might also be submitted for publication to a peer-reviewed journal. Any reports arising from these data and this collaboration will be reviewed and approved by each study site that generates data for the report.

Collaborative Arrangements

Describe briefly if this study involves any scientific, administrative, fiscal, or programmatic arrangements with other national or international organizations or individuals. Indicate the nature and extent of collaboration and include a letter of agreement between the applicant or his/her organization and the collaborating organization. **(DO NOT EXCEED ONE PAGE)**

This study will represent a collaboration between ICDDR,B and CDC, including the Division of Vector-Borne and Infectious Diseases and The Division of Viral and Rickettsial Diseases. ICDDR,B will collaborate with Directorate General of Health and Meherpur Sadar Hospital to facilitate the study.

Biography of the Investigators

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

1. Name: **Robert F. Breiman, M.D.**

2. Present position: Associate Director, ICDDR,B and Head, Health Systems and Infectious Diseases Division (HSID)

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

Institution and Location	Degree	Year	Field of Study
University of Arizona	B.A.	1975	Political Science
University of Arizona	M.D.	1979	Medicine
UCLA Affiliated Hospitals	**Residency**	**1979-1982**	**Internal Medicine**
UCLA Affiliated Hospitals	**Chief Resident**	**1982-1983**	**Internal Medicine**
UCLA	**Fellowship**	**1984-1987**	**Infectious Diseases**
CDC	**Fellowship**	**1987-1989**	**EIS Program**

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

4.1. As Principal Investigator

Protocol Number	Starting date	End date	Percentage of time
2000-023	10/00	12/02	15%
2000-011	1/02	6/02	20%

4.2. As Co-Principal Investigator

Protocol Number	Starting date	End date	Percentage of time
2001-021	1/02	9/04	5%
2001-029	1/01	6/03	5%

4.3. As Co-Investigator

Protocol Number	Starting date	Ending date	Percentage of time
2001-14	5/02	10/02	10%
2002-10	4/02	7/02	2%
2002-28	10/01	9/03	10%

5. Publications

Types of publications	Numbers
a) Original scientific papers in peer-review journals	90
b) Peer reviewed articles and book chapters	9
c) Papers in conference proceedings	>50
d) Letters, editorials, annotations, and abstracts in peer-reviewed journals	10
Working papers	
Monographs/books	6

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

i) Feikin DR, Elie CM, Goetz MB, Lennox JL, Carlone GM, Romero-Steiner S, Holder PF, O'Brien WA, Whitney CG, Butler JC, **Breiman RF**. Randomized trial of the quantitative and functional antibody responses to a 7-valent pneumococcal conjugate vaccine and/or 23-valent polysaccharide vaccine among HIV-infected adults. *Vaccine*. 2001;20:545-53.

ii) **Breiman RF,** Keller DW, Phelan MA, Sniadack DH, Stephens DS, Rimland D, Farley MM, Schuchat A, Reingold AL Evaluation of effectiveness of the 23-valent pneumococcal capsular polysaccharide vaccine for HIV-infected patients. *Arch Intern Med*. 2000;160:2633-8.

iii) Lieu TA, Ray GT, Black SB, Butler JC, Klein JO, **Breiman RF**, Miller MA, Shinefield HR. Projected cost-effectiveness of pneumococcal conjugate vaccination of healthy infants and young children. *JAMA* 2000;283(11):1460-8.

iv) Metlay JP, Hofmann J, Cetron MS, Fine MJ;,Farley MM, Whitney C, **Breiman RF.** Impact of penicillin susceptibility on medical outcomes for adult patients with bacteremic pneumococcal pneumonia. *Clin Infect Dis* 2000;30:520-528.

v) Nuorti JP, Butler JC, Farley MM, Harrison LH, McGeer A, Kolczak MS, **Breiman RF.** Cigarette smoking and invasive pneumococcal disease. *N Engl J Med* 2000;342:681-689.

Biography of the Investigators

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

1 Name : Vincent P. Hsu

2 Present position : EIS Officer, Respiratory and Enteric Virus Branch, CDC

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

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

4.4. As Principal Investigator

Protocol Number	Starting date	End date	Percentage of time

4.5. As Co-Principal Investigator

Protocol Number	Starting date	End date	Percentage of time

4.6. As Co-Investigator

Protocol Number	Starting date	Ending date	Percentage of time
3416	June 2002	June 2003	15%

5. Publications

Types of publications	Numbers
Peer-reviewed journal	2
Handbook for Medical Personnel	1
Published abstracts	4

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

Hsu VP, Lukacs SL, Handzel T, Hayslett J Harper S, Hales T, Semenova VA, Romero-Steiner S, Elie C, Quinn C, Khabbaz R, Khan A, Schuchat A, Martin G, Eisold J, Hajjeh R. **Opening a *Bacillus anthracis*-Containing Envelope, Capitol Hill, Washington, D.C.: The Public Health Response**. *Emerg Infect Dis 2002; 8:1039-43*

Hsu VP, Ed. **Tuberculosis Control Manual 2002—Los Angeles County**. *In press*

Sewell G, Hsu V, Jones SR. Zoster Gangrenosum: **A Case Report of Necrotizing Fasciitis as a Complication of Herpes Zoster**. *American Journal of Medicine 2000; 6:520-1*

Hsu V, Harper S, Simpser E, Niven B, Fukuda K, Uyeki T. **Outbreak of Influenza A in a Pediatric Chronic Care Facility.** [Abstract K-455]. *In: 42nd Interscience Conference on Antimicrobial Agents and Chemotherapy, San Diego, CA, September 27 to 30, 2002. Washington, DC: American Society for Microbiology, 2002.*

Hsu V, Rodrigue D, Otaya M, Rayos E, Qian D, Currier J, Jones BE. **The Effect of Supervised Antiretroviral Therapy in Coinfected Persons with Human Immunodeficiency Virus (HIV) and Tuberculosis (TB).** *Programs and Abstracts, 37th Annual Metting of the Infectious Disease Society of America, 1999*

Detailed Budget for new proposal:

Project Title: Outbreak Investigation of a Cluster of Deaths in Chandpur Village, Meherpur District, Bangladesh, during April-May, 2001

Name of PI: Dr. Robert F. Breiman

Protocol no: Name of Division: HSID

Funding Source: CDC	Operating Cost (Direct): US $	**6,080**
	Indirect cost (26% of direct cost): US $	**1,581**
	Total cost: US $	**7,661**

Starting Date:17 February, 2003 Ending Date: August, 2003

Personnel	# of staff	% of effort	Daily rate	Per Person Days	1st Year Feb-Mar
Field Research Assistants	2	100	16	25	800
Subtotal					**800**
Supplies		#	Unit price		
Syringe		200	0.1		20
Butterfly needle		100	0.4		40
Sterile gloves		250	0.2		50
Office supplies					100
Other					300
SubTotal					**510**
Travel/site visits			Person		
Dhaka-Meherpur by Field Research Assistant			2		30
Meherpur-Dhaka by Field Research Assistant			2		30
Dhaka-Meherpur for Study Team			4		280
Meherpur-Dhaka for Study Team			4		280
Other travel					300
Other cost					500
SubTotal					**1,420**
Specimen Transport and International Shipping					3,000
Sub Total					**3,000**
Other Contractual services					
Communications (Fax, DHL, telephone, postage etc)					100
Trainining, workshop					50
Printing and publication					200
Sub Total					**350**
Total direct cost					**6,080**
Indirect cost					**1,581**
Total cost					**7,661**

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.

Field Research Assistant: Two Field Research Assistant will be recruited on daily basis for population survey, data collection, data cleaning and data entry

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)

APPENDIX
International Centre for Diarrhoeal Disease Research, Bangladesh
Voluntary Consent Form

Title of the Research Project: Investigation of a Cluster of Deaths in Chandpur Village, Meherpur District, Bangladesh, during April-May, 2001

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

See following appendices:

B1-B3. Consent forms for adult village resident, child village resident, health care professional
C. Assent form for child
D. Enrollment logs
E. Survey for Chandpur village resident
F. Survey for health care professional
G. Hospital medical record abstraction form
H. Permission to review medical records

Appendix B1. Consent to participate in a research study
ADULT VILLAGE RESIDENT

Fleisch-Kincade Reading level = 7.0

Investigation of a Cluster of Deaths in Chandpur Village, Meherpur District, Bangladesh

Introduction
We are asking you to take part in a research study. The International Center for Diarrhoeal Diseases Research, Bangladesh (ICDDR,B) and the Centers for Disease Control and Prevention (CDC) are doing this study. The goal of the study is to learn more about the unusual illnesses and deaths that happened in the village of Chandpur, Meherpur District between 26 April and 11 May 2001. This study may help learn more about diagnosing, treating, and preventing the disease.

We are asking you to take part in this study because you live in or near Chandpur and fall in one of the following groups:

1. You may have had this disease
2. You may have been at risk for getting this disease
3. You are not believed to have the disease and will be used as a comparison group.

Right to Withdraw
You are free to join the study or not. If you do not join, you will not lose any health care service that you expect to get apart from this study. If you decide to join the study, you are also free to drop out later for any reason. In that case too, you will not lose any health care service that you expect to get apart from this study.

You may choose to have your blood sample stored. If so, you may choose to have the blood sample removed from storage at any time.

Procedures
If you take part in the study, we will ask you some questions about your health, your household, and your lifestyle. You may refuse to answer any question that you wish for any reason. Answering these questions will take about 15 minutes.

We will also collect 10 ml (2 teaspoonfuls) of blood from you by placing a sterile small needle in the vein of your arm. We will test your blood to see if you have been previously exposed to a virus called Nipah or Hendra virus. It will take about 5 minutes to get the blood sample.

Benefits
You will get no direct benefit from taking part in this study. We will not inform you of your individual test result. Society may benefit by learning more about the causes of the unusual illnesses and deaths in Chandpur village in April-May 2001.

Risks
You may have slight pain when the blood sample is taken. A bruise or small blood clot may occur in the area where the blood is drawn. Some people may have minor bleeding from the site. There is a rare chance that infection may occur at or near the area where blood is drawn. A friend or relative of someone who died may have some emotional distress.

Confidentiality

Our discussion about the study and your test results will be kept private to the extent allowed by law. To protect your privacy, we will keep your records under a patient number and not by name. We will keep the records in locked files and only study staff will be able to look at them.

Medical Records

If you were in the hospital for an illness that might be due to the disease, we will try to review your hospital medical record. Again, we will keep your records private.

Costs and Compensation

This study will be done at no direct cost to you. The only cost to you for being in our study is the time you must spend to take part. We will not repay you for the time you took to take part in the study.

If you are injured as a result of this study, we will arrange for medical care at no cost to you. If you believe you have been harmed as a result of this study, you may contact Dr. Robert Breiman, of ICDDR,B, at 2-988-1761.

Availability of Information

Any questions you have about this study can be answered by Dr. Robert Breiman, of ICDDR,B, at 2-988-1761. If you later choose to not take part in the study, or if you choose to remove your blood sample for storage, you can contact Dr. Breiman.

For information about your rights as a participant in this research study, you may contact the IRB Chairperson of ICDDR,B, at 2-8811751.

CONSENT TO PARTICIPATE IN A RESEARCH STUDY
ADULT VILLAGE RESIDENT

Name of participant_____

Permission to take part in the research study
I have read and understand the statements above. The information has been explained to me. I understand the goals of the study. I understand the benefits and risks that are involved. All my questions have been answered. My signature below indicates that I voluntarily agree to take part in this study. I will receive a copy of this consent form.

Signature of Study Participant Date

_____ _____

Permission to store blood specimen
I give permission to save my blood sample for future research. This blood sample will be tested for the presence of antibodies to Nipah/Hendra virus and possibly other agents such as Japanese encephalitis, other viral encephalitis, or dengue, but will never be tested for the HIV virus. Genetic testing will not be performed. If I change my mind later, I can choose to have the blood samples removed from storage at a later date for any reason.

_____ I agree to have my blood sample saved for future testing

_____ I disagree. Do not save my blood sample after testing in this study.

Signature of study participant Date

_____ _____

Appendix B2. Consent to participate in a research study
CHILD VILLAGE RESIDENT

Fleisch-Kincade Reading level = 7.5

Investigation of a Cluster of Deaths in Chandpur Village, Meherpur District, Bangladesh

Introduction
We are asking your child to take part in a research study. The International Center for Diarrhoeal Diseases Research, Bangladesh (ICDDR,B) and the Centers for Disease Control and Prevention (CDC) are doing this study. The goal of the study is to learn more about the unusual illnesses and deaths that happened in the village of Chandpur, Meherpur District between 26 April and 11 May 2001. This study may help learn more about diagnosing, treating, and preventing the disease.

We are asking your child to take part in this study because your child lives in or near Chandpur and fall in one of the following groups:

1. Your child may have had this disease
2. Your child may have been at risk for getting this disease
3. Your child is not believed to have the disease and will be used as a comparison group.

Right to Withdraw
Your child is free to join the study or not. If your child does not join, he or she will not lose any health care service that you expect to get apart from this study. If you or your child decides to join the study, you or your child is also free to drop out later for any reason. In that case too, your child will not lose any health care service that you expect to get apart from this study.

You or your child may choose to have your child's blood sample stored. If so, you or your child may choose to have the blood sample removed from storage at any time.

Procedures
If your child takes part in the study, we will ask you and your child some questions about your health, your household, and your lifestyle. You may refuse to answer any question that you wish for any reason. Answering these questions will take about 15 minutes.

We will also collect 10 ml of blood (for children greater than 12 years of age) or 5 ml (for the children equal to or less than 12 years) of blood from your child by placing a sterile small needle in the vein of his/her arm. We will test your child's blood to see if he/she has been previously exposed to a virus called Nipah or Hendra virus. It will take about 5 minutes to get the blood sample.

Benefits
Your child will get no direct benefit from taking part in this study. We will not inform you or your child of his/her individual test result. Society may benefit by learning more about the causes of the unusual illnesses and deaths in Chandpur village in April-May 2001.

Risks
Your child may have slight pain when the blood sample is taken. A bruise or small blood clot may occur in the area where the blood is drawn. Some people may have minor bleeding from the site. There is a rare chance that infection may occur at or near the area where blood is drawn. A friend or relative of someone who died may have some emotional distress.

Confidentiality

Our discussion about the study and your child's test results will be kept private to the extent allowed by law. To protect your privacy, we will keep your child's records under a patient number and not by name. We will keep the records in locked files and only study staff will be able to look at them.

Medical Records
If your child was in the hospital for an illness that might be due to the disease, we will try to review your hospital medical record. Again, we will keep your records private.

Costs and Compensation
This study will be done at no direct cost to you or your child. The only cost to you or your child for being in our study is the time you must spend to take part. We will not repay you for the time you took to take part in the study.

If your child is injured as a result of this study, we will arrange for medical care at no cost to you. If you believe your child has been harmed as a result of this study, you may contact Dr. Robert Breiman, of ICDDR,B, at 2-8811751.

Availability of Information
Any questions you have about this study can be answered by Dr. Robert Breiman, of ICDDR,B, at 2-8811751. If your child later chooses to not take part in the study, or if your child chooses to remove his/her blood sample for storage, you can contact Dr. Breiman.

For information about your child's rights as a participant in this research study, you may contact the IRB Chairperson of ICDDR,B, at 2-8811751.

CONSENT TO PARTICIPATE IN A RESEARCH STUDY

PARENT CONSENT FORM FOR CHILD VILLAGE RESIDENT AGED 1-17 YEARS

Name of parent_____

Name of child_____

Permission to take part in the research study

I have read and understand the statements above. The information has been explained to my child and me. I understand the goals of the study. I understand the benefits and risks that are involved. All my and my child's questions have been answered. My signature below indicates that my child voluntarily agrees to take part in this study. I will receive a copy of this consent form.

Signature of parent Date

_____ _____

Permission to store blood specimen

I give permission to save my child's blood sample for future research. This blood sample will be tested for the presence of antibodies to Nipah/Hendra virus and possibly other agents such as Japanese encephalitis, other viral encephalitis, or dengue, but will never be tested for the HIV virus. Genetic testing will not be performed. If my child changes his/her mind later, I can choose to have the blood samples removed from storage at a later date for any reason.

_____ I agree to have my child's blood sample saved for future testing

_____ I disagree. Do not save my child's blood sample after testing in this study.

Signature of parent Date

_____ _____

Appendix B3. Consent to participate in a research study
HEALTH CARE PROFESSIONAL

Fleisch-Kincade Reading level = 7.3

Investigation of a Cluster of Deaths in Chandpur Village, Meherpur District, Bangladesh

Introduction
We are asking you to take part in a research study. The International Center for Diarrhoeal Diseases Research, Bangladesh (ICDDR,B) and the Centers for Disease Control and Prevention (CDC) are doing this study. The goal of the study is to learn more about the unusual illnesses and deaths that happened in the village of Chandpur, Meherpur District between 26 April and 11 May 2001. This study may help learn more about diagnosing, treating, and preventing the disease.

We are asking you to take part in this study because you work in a health care facility and may have been exposed to a person with this disease:

1. You may have taken care of a person with the disease
2. You may have been working near a person with the disease
3. You were not near a person with the disease and will be used as a comparison group.

Right to Withdraw
You are free to join the study or not. If you do not join, you will not lose any health care service that you expect to get apart from this study. If you decide to join the study, you are also free to drop out later for any reason. In that case too, you will not lose any health care service that you expect to get apart from this study.

You may choose to have your blood sample stored. If so, you may choose to have the blood sample removed from storage at any time.

Procedures
If you take part in the study, we will ask you some questions about your health, your work, and your workplace. You may refuse to answer any question that you wish for any reason. Answering these questions will take about 15 minutes.

We will also collect 10 ml (2 teaspoonfuls) of blood from you by placing a sterile small needle in the vein of your arm. We will test your blood to see if you have been previously exposed to a virus called Nipah or Hendra virus. It will take about 5 minutes to get the blood sample.

Benefits
You will get no direct benefit from taking part in this study. We will not inform you of your individual test result. Society may benefit by learning more about the causes of the unusual illnesses and deaths in Chandpur village in April-May 2001.

Risks
You may have slight pain when the blood sample is taken. A bruise or small blood clot may occur in the area where the blood is drawn. Some people may have minor bleeding from the site. There is a rare chance that infection may occur at or near the area where blood is drawn. A friend or relative of someone who died may have some emotional distress.

Confidentiality

Our discussion about the study and your test results will be kept private to the extent allowed by law. To protect your privacy, we will keep your records under a patient number and not by name. We will keep the records in locked files and only study staff will be able to look at them.

Medical Records

If you were in the hospital for an illness that might be due to the disease, we will try to review your hospital medical record. Again, we will keep your records private.

Costs and Compensation

This study will be done at no direct cost to you. The only cost to you for being in our study is the time you must spend to take part. We will not repay you for the time you took to take part in the study.

If you are injured as a result of this study, we will arrange for medical care at no cost to you. If you believe you have been harmed as a result of this study, you may contact Dr. Robert Breiman, of ICDDR,B, at 2-8811751.

Availability of Information

Any questions you have about this study can be answered by Dr. Robert Breiman, of ICDDR,B, at 2-8811751. If you later choose to not take part in the study, or if you choose to remove your blood sample for storage, you can contact Dr. Breiman.

For information about your rights as a participant in this research study, you may contact the IRB Chairperson of ICDDR,B, at 2-8811751.

CONSENT TO PARTICIPATE IN A RESEARCH STUDY
HEALTH CARE PROFESSIONAL

Name of participant_____

Permission to take part in the research study
I have read and understand the statements above. The information has been explained to me. I understand the goals of the study. I understand the benefits and risks that are involved. All my questions have been answered. My signature below indicates that I voluntarily agree to take part in this study. I will receive a copy of this consent form.

Signature of Study Participant Date

_____ _____

Permission to store blood specimen
I give permission to save my blood sample for future research. This blood sample will be tested for the presence of antibodies to Nipah/Hendra virus and possibly other agents such as Japanese encephalitis, other viral encephalitis, or dengue, but will never be tested for the HIV virus. Genetic testing will not be performed. If I change my mind later, I can choose to have the blood samples removed from storage at a later date for any reason.

_____ I agree to have my blood sample saved for future testing

_____ I disagree. Do not save my blood sample after testing in this study.

Signature of study participant Date

_____ _____

Appendix C. Assent Form
Acceptance to participate by children aged 7 to 17 years.

Fleisch-Kincade Reading level = 5.3

We are asking you to take part in a research study. The goal of the study is to learn more about the unusual illnesses and deaths that happened in the village of Chandpur, Meherpur District between 26 April and 11 May 2001.

If you take part in the study, we will ask you some questions about your health and your lifestyle. You may refuse to answer any question that you wish for any reason. Answering these questions will take about 15 minutes. We will also draw 5-10 ml (about 1-2 teaspoons) of blood from your arm. It will take about 5 minutes to get the blood sample.

You will get no direct benefit from taking part in this study. We will not inform you of your test result. You may have slight pain when the blood sample is taken. A bruise or small blood clot may occur in the area where the blood is drawn. There is a rare chance that infection may occur at or near the area where blood is drawn.

You are free to join the study or not. In certain emergent cases, the parent has a right to force you to take part in a study. But in this case, you make the choice to be in the study or not. You can stop being in the study by telling your parents to tell us that you no longer want to take part. If you have questions, you can ask your parents to talk to the doctors.

You may choose to have your blood sample stored. If so, you may choose to have the blood sample removed from storage at any time. If you were in the hospital for an illness, we may want to look at your hospital medical record.

I have been told about this study. All my questions about this study have been answered. I agree to take part in this study. My father/mother has said that it is all right for me to take part in this study.

_____	_____	_____
Name (print)	Signature	Date

Permission to store blood specimen

I allow the doctors to save my blood sample for future research. This blood sample will be tested antibodies to Nipah/Hendra virus. It may be tested for another viral disease but will never be tested for the HIV virus. Genetic testing will not be done. If I change my mind, I can choose to have the blood samples removed from storage at a later date for any reason.

_____ I agree to have my blood sample saved for future testing

_____ I disagree. Do not save my blood sample after testing in this study.

Signature Date

_____ _____

Appendix D. Enrollment Logs

Village Case Log

Study ID	Name	Age	Sex	Date of enrollment	Cat* (1-5)	Blood draw date/ time
CH - 0001						
CH - 0002						
CH - 0003						
CH - 0004						
CH - 0005						
CH - 0006						
CH - 0007						
CH - 0008						
CH - 0009						
CH - 0010						
CH - 0011						
CH - 0012						

*Categories: (1) all possible surviving cases from individuals who had an illness meeting the case definition, (2) contacts of individuals who died in the outbreak, (3) contacts of individuals who had previous positive antibody titers to Nipah virus, (4) contacts of other possible surviving cases, (5) all others in the village with that/those particular exposure(s) associated with becoming a case

Village Control Log

Study ID	Name	Age	Sex	Date of enrollment	Case Study ID	Blood draw date/ time
CH - 1001						
CH - 1002						
CH - 1003						
CH - 1004						
CH - 1005						
CH - 1006						
CH - 1007						
CH - 1008						
CH - 1009						
CH - 1010						
CH - 1011						
CH - 1012						

Healthcare Professional Case Log

Study ID	Name	Age	Sex	Date of enrollment	Case study ID	Blood draw date / time
HW - 0001						
HW - 0002						
HW - 0003						
HW - 0004						
HW - 0005						
HW - 0006						
HW - 0007						
HW - 0008						
HW - 0009						
HW - 0010						
HW - 0011						
HW - 0012						

Healthcare Professional Control Log

Study ID	Name	Age	Sex	Date of enrollment	Case study ID	Blood draw date/time
HW – 1002						
HW – 1003						
HW – 1004						
HW – 1005						
HW – 1006						
HW – 1007						
HW – 1008						
HW – 1009						
HW – 1010						
HW – 1011						
HW – 1012						
HW – 1013						

Appendix E. Survey for Chandpur Village Residents

Study ID_____

Check one: ☐ Case, deceased (list name and relationship of interviewee to subject)

☐ Case, survived

☐ Family member / contact of case _____(study number of case)

☐ Possible case based on identified risk factor_____

☐ Control _____(study number of case)

Interviewer _____

Date of survey _____/_____/_____ (dd/mm/yy)

Is respondent completing survey for subject? ☐ **Yes** ☐ **No**

If **no**, name of interviewee_____ _____and

relationship to subject _____

Demographic data

Interview subject full name_____

Date of birth _____/_____/_____ (dd/mm/yy) or age in years _____

Sex ☐ **Male** ☐ **Female**

Ethnicity

Village or Union Ward_____

Address_____

GPS coordinates:_____N, _____E

Number of people in subject's household _____

Occupation_____

Occupation address or location_____

GPS coordinates:_____N, _____E

Past Medical History

Have you been ill since April 1, 2001? ☐ **Yes** ☐ **No** ☐ **Don't know**

If **yes**, when did you fall ill? _____/_____/_____ (dd/mm/yy)

Which of the following symptoms did you have? (check all that apply

☐ Fever ☐ Vomiting

☐ Cough ☐ Lethargy / drowsiness

☐ Difficulty breathing ☐ Seizures

☐ Headache ☐ Diarrhea

☐ Other_____

Did you require hospitalization for your illness? ☐ **Yes** ☐ **No** ☐ **Don't know**

If **yes**, when were you hospitalized? _____/_____/_____ (dd/mm/yy)

Which hospital were you admitted to?_____

Was a blood sample taken during hospitalization? ☐ **Yes** ☐**No** ☐ **Don't know**

Exposure History

The following questions refer to the period between 01 April and 30 May 2001

Did you live in the same household as someone who was ill? ☐ **Yes** ☐ **No** ☐ **Don't know**

If yes, name of person_____

Did you care for someone who was ill? ☐ **Yes** ☐ **No** ☐ **Don't know**

If yes, name of person_____

Did you share items of a personal nature with that person? (eating utensils, cups, toothbrush, etc.)

☐ **Yes** ☐ **No** ☐ **Don't know**

Did you have physical contact with that person? ☐ **Yes** ☐ **No** ☐ **Don't know**

Did you come in physical contact with that person's secretions? ☐ **Yes** ☐ **No** ☐ **Don't know**

The following questions refer to the period after 01 April 2001 to the present

Do you live in a household where animals are kept? ☐ **Yes** ☐ **No** ☐ **Don't know**

If **yes**, Which animals are in your household? (check all that apply)

☐ Chickens ☐ Goats

☐ Ducks ☐ Pigs

☐ Dogs ☐ Other_____

☐ Cats ☐ Other_____

Which of the following animals do you have contact with (at least an average of twice a month)? (check all that apply)

☐ Chickens ☐ Goats

☐ Ducks ☐ Pigs

☐ Dogs ☐ Bats

☐ Cats ☐ Squirrels

☐ Other_____ ☐ Other _____

Which of the following animals have you had contact with during the time the animal was sick? (check all that apply)

☐ Chickens ☐ Goats

☐ Ducks ☐ Pigs

☐ Dogs ☐ Bats

☐ Cats ☐ Squirrels

☐ Other_____ ☐ Other _____

Have you had any known contact with living bats? ☐ **Yes** ☐ **No** ☐ **Don't know**

Have you had any known contact with dead bats? ☐ **Yes** ☐ **No** ☐ **Don't know**

Have you noticed bats near or inside your home? ☐ **Yes** ☐ **No** ☐ **Don't know**

Appendix F. Health Care Professional Survey

Study (specimen) Number: _____

Interviewer: _____

Date of Interview: ___/___/___
dd/mm/yy

Hospital: _____

Name: _____

Reg. Number: _____

Personal information:

1. What is your age? _____ years

2. Sex *(circle one)*: 1. Male 2. Female

Work related questions:

3. What is your occupation? *circle one:*

   a. nurse
   b. respiratory therapist/physiotherapist
   c. doctor
   d. pathologist
   e. other _____

4. Did you provide patient care for a patient from Chandpur Village who was admitted during April 1 – May 30 1999 and died in the hospital?

   ☐ Yes ☐ No ☐ Don't know

   IF YES, answer the following:

   4a) In working with this patient, did you ever receive a needle stick injury from a needle which was in contact with the patient's blood?

   ☐ Yes ☐ No ☐ Don't know

   4b) In working with the patient, were you ever splashed in the eye, nose or mouth with respiratory secretions,stool, urine, or blood from the patient?

   ☐ Yes ☐ No ☐ Don't know

   4c) In working with the patient, did you ever have direct skin contact with respiratory secretions, stool, urine, or blood from the patient?

   ☐ Yes ☐ No ☐ Don't know

   4d) What type of protection have you worn **most of the time** when suctioning or doing other procedures involving contact with body fluids of encephalitis patients? *(circle one)*

   a. no protection
   b. gloves only
   c. gloves and surgical mask
   d. surgical mask alone
   e. gloves, mask and gown
   f. gloves, mask, gown and eye protection

g. other *(specify)*: _____

Illness history:

5) Did you have any illness during 1 April to 31 May, 2001? ☐ Yes ☐ No

if yes:

what was the date of your first symptoms? ___/___/___
(Put 88/88/88 if no illness) dd/mm/yy

which of the following symptoms did you have: *(circle one answer for each symptom)*

fever	☐ Yes	☐ No
sore throat	☐ Yes	☐ No
vomiting	☐ Yes	☐ No
cough	☐ Yes	☐ No
headache	☐ Yes	☐ No
stiff neck	☐ Yes	☐ No
eyes sensitive to light	☐ Yes	☐ No
rash	☐ Yes	☐ No

other: (please describe): _____

Appendix G. Hospital Medical Record Abstraction Form

Date_____ Study number_____

Patient's name: _____Age: Years |___|___| Months |___|___| Date of birth_____

Sex ☐ **M** ☐ **F** · Medical record number_____

Admission data

Date of admission_____ Admission diagnosis_____

Admission vital signs: Temp_____ HR_____ BP____/_____R_____

Symptom				
Fever > 38 C	Y	N	U	Comments_____
Headache	Y	N	U	Comments_____
Nuchal rigidity	Y	N	U	Comments_____
Mental status change	Y	N	U	Comments_____
Seizures	Y	N	U	Comments_____
Vomiting	Y	N	U	Comments_____
Diarrhea	Y	N	U	Comments_____
Cough	Y	N	U	Comments_____
Dyspnea	Y	N	U	Comments_____

Laboratory data
Chemistries:

CBC:

Lumbar puncture:

Radiographic and other:

Hospital course

Day 1 Vitals: Tmax_____ HR_____ BP____/_____R_____

Development of symptoms not mentioned above_____

Lab (Chem, CBC, LP, other)_____

Day 2 Vitals: Tmax_____ HR_____ BP____/_____R_____

Development of symptoms not mentioned above_____

Lab (Chem, CBC, LP, other)_____

Day 3 Vitals: Tmax_____ HR_____ BP____/_____R_____

Development of symptoms not mentioned above_____

Lab (Chem, CBC, LP, other)_____

Day 4 Vitals: Tmax_____ HR_____ BP____/_____R_____

Development of symptoms not mentioned above_____

Lab (Chem, CBC, LP, other)_____

Day 5 Vitals: Tmax_____ HR_____ BP____/_____R_____

Development of symptoms not mentioned above_____

Lab (Chem, CBC, LP, other)_____

Day 6 Vitals: Tmax_____ HR_____ BP____/_____R_____

Development of symptoms not mentioned above_____

Lab (Chem, CBC, LP, other)_____

Day 7 Vitals: Tmax_____ HR_____ BP____/_____R_____

Development of symptoms not mentioned above_____

Lab (Chem, CBC, LP, other)_____

Discharge data

Date of discharge_____ Discharge diagnosis_____

Status at discharge Alive Deceased

Appendix H. Permission to Review Medical Records

Date:_____ Patient ID number_____

Patient's name_____ Age: Years |___|___| Montsh |___|___| Date of birth_____

Hospital name_____District _____

Dates of hospitalization _____ to _____

The International Center for Diarrhoeal Diseases Research, Bangladesh (ICDDR,B) and the Centers for Disease Control and Prevention (CDC) are doing a study to learn more about the unusual illnesses and deaths that happened in the village of Chandpur, Meherpur District between 26 April and 11 May 2001. This study may help learn more about diagnosing, treating, and preventing the disease.

The person named above has indicated that he/she was a patient at your hospital and has given us written consent to review his/her medical records at your hospital. ICDDR,B and CDC would like to request permission to review all medical records pertaining to the hospitalization dates above.

As a representative of ICDDR,B and the U.S. CDC, I request permission from the hospital named above to release all medical records pertaining to the hospitalization dates above for our review.

_____
Name of authorized representative

_____ _____
(Signature of authorized representative) (Date)

Check List

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

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

International Centre for Diarrhoeal Disease Research, Bangladesh
CENTRE FOR HEALTH AND POPULATION RESEARCH
Mail : ICDDR,B, GPO Box 128, Dhaka-1000, Bangladesh
Phone : 880-2-8811751-60, Telex : 642486 ICDD BJ
Fax : 880-2-8823116, 8812530, 8811568, 8826050, 9885657, 8811686, 8812529
Cable : Cholera Dhaka

Protocol No. 2003-001

Memorandum

To: Acting Chairman
Research Review Committee (RRC)
ICDDR,B: Centre for Health & Population Research

From: Robert F. Breiman, M.D.
Associate Director & Head
Health Systems and Infectious Diseases Division

Date: January 06, 2003

Subject: **Investigation of an Outbreak of Encephalitis in Meherpur District**

ICDDR,B has been asked by WHO to participate with CDC-Atlanta in assisting the Government of Bangladesh in investigating an outbreak of encephalitis which occurred in Meherpur District in May, 2001. A protocol has been developed for this technical assistance by CDC and ICDDR,B. CDC's IRB has requested that the protocol for the outbreak investigation be reviewed by the Ethical Review Committee (ERC). We request that the need for RRC approval be waived, so that we may submit the proposal for expedited review by the ERC.

Thank you.

WORLD HEALTH ORGANIZATION
SOUTH-EAST ASIA REGION

ORGANISATION MONDIALE DE LA SANTE
REGION DE L'ASIE DU SUD-EST

OFFICE OF THE WHO REPRESENTATIVE FOR BANGLADESH
Tel.: (880-2) 864653-55, 866097-98
E-mail:registry@whoban.org or info@whoban.org

Dr. Rob Brieman 19/12

In reply please refer to : CPC007/D
Prière de rappeler la référence : Date: 19.12.002

Dr. James Hughes
Director
National Center for Infectious Diseases
(CDC)
1600 Clifton Road
Atlanta, GA 30333

Dear Dr Huges,

Subject: Follow-up Action on Out-break of Unknown Disease in Meherpur District (April-May 2001)

In April / May 2001, an outbreak of an unknown disease probably of Viral Origin was reported in Meherpur District of Bangladesh. The outbreak resulted in high morbidity and fatality. A team comprising of CDC and WHO was fielded to investigate the outbreak. Laboratory investigations of specimen collected identified NIPAH/HENDRA Virus. Similar virus was also isolated in specimen collected from cases reported from a neighbouring district.

In order to provide a clear epidemiological chart of this outbreak, the Director of Diseases Control of the Directorate General of Health Services has formally requested WHO to invite a CDC and WHO Team to conduct a follow-up investigation, (copy enclosed). Objective of the follow-up investigation would include the following:

1. To determine the prevalence of antibodies to NIPAH/HENDRA Virus among:
   a) Surviving cases;
   b) Household contacts, health workers and others who were in Close-contact with known cases;
   c) Population in the same village where the outbreak occurred.
2. To assess the clinical features of disease among persons with antibodies to NIPAH/HENDRA Virus.
3. To assess evidence of late onset or recurrent encephalitis among persons with antibodies against NIPAH/HENDRA Virus.
4. To evaluate potential risk factors for acquisition of antibodies to NIPAH/HENDRA, including contact with other cases, domestic and wild animals.

Continued P/2

5. The possibility of neutralizing antibodies in serum of surviving cases should also be explored. The presence of such neutralizing antibodies will be useful in the treatment of cases in future outbreaks using hyper immune plazma.

By copy of this memorandum, CDC HQ/SEARO and ICDDR,B are requested to field a team of epidemiologists to join the CDC team in this follow-up investigation.

Thank you for your cooperation.

Yours sincerely

Dr Suniti Acharya
WR, Bangladesh.

cc: 1 Dr G. Rodier, Director, CDC WHO/HQ
2. Dr Kandebure O' Bai Kamar, in Charge of Outbreaks/Epidemics, CDC Unit, WHO/HQ
3. Dr Kumara Rai, Director, CDS, WHO-SEARO.
4. Director, ICDDRB

RECEIVED
26 DEC 2002
Office

Government of the Peoples Republic of Bangladesh
Directorate General of Health Services
DGHS, Mohakhali, Dhaka.

Memo No.DGHS/Dir.DC/Mehrpur(outbreak)/2001/ 11850 Dated: 1/12/2002

To
WHO Representative, Bangladesh
House No. 12, Road No.7
Dhanmondi R/A
Dhaka-1205.

Sub: Follow-up action on Outbreak of unknown disease in Meherpur District (April-May/2001)

Dear Madam,

Thank you for the opportunity to discuss the above subject. As discussed, we feel that further investigation is needed to investigate the outbreak of unknown diseases which occurred in Meherpur last year. In particular, it would be helpful to investigate the following:

1. Determine the prevalence of antibodies to Nipah/Hendra virus among the following:
    a. Surviving case-patients,
    b. Household contacts, healthcare workers, and others who were in close contact with ill patients,
    c. Other individuals in the same village where the outbreak occurred.
2. Assess the clinical features of disease among persons with antibodies to Nipah/Hendra virus.
3. Assess evidence of late onset or recurrent encephalitis among persons with antibodies against Nipah/Hendra virus.
4. Evaluate potential risk factors for acquisition of antibody to Nipah/Hendra virus, including contact with other case-patients and domestic or wild animals.

We would appreciate your inviting a CDC Atlanta Team to assist us in this investigation. We propose that the investigation begin on 5 January, 2003. Such an invitation to CDC should be sent to Dr. James Hughes, Director, National Center for Infectious Diseases, 1600 Clifton Road, Atlanta, GA 30333. Given the urgency of the matter, it would be better to fax and/or e-mail the request. FAX number is 1-404-639-3039 and e-mail address is: jmh2@cdc.gov.

This request has the concurrence of the Director General of Health Services.

Thanking you.

1/12/2002

(Dr. Kanak Ranjan Talukder)
Director (Disease Control)
Directorate General of Health Services
Mohakhali, Dhaka-1212.

CC:
1. Director General of Health Services, DGHS, Dhaka. (Attn: Asst. Director, Coordination)
2. Director, IEDCR, , Dhaka.
3. Director, ICDDR'B, Dhaka. (Atten: Dr. R. Breiman)

RECEIVED
01 DEC 2002
Director's Office
ICDDR, B