Informed Consent Form
Next generation ORS: ORS with calcium

icddr,b protocol # PR-22091	Version No. 1.0	Version Date: October 16, 2022

Protocol Title
Next generation ORS: Randomized controlled trial comparing ORS with calcium vs standard ORS in reducing severity with acute watery diarrhea of adults.

Investigators' names
Dr. Shafiqul A Sarker (Local PI)
Dr. Dr. Sam Cheng (External PI)
[List of other investigators is available on request]

Funder
The funder of this research is the National Institute of Health, USA.

Organizations
International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b), Dhaka, Bangladesh,
University of Florida, Gainesville, *USA*
University of Kentucky, Lexington, USA

Conflicts of interest
The Principal Investigators, Dr. Sam and Dr. Sarker, and the other research team members, have no conflicts of interest to declare.

Since you have diarrhoea, and admitted in the Short Stay Unit or Longer Stay Unit, you are being asked to provide informed consent. Unless otherwise specified, the words "you" and "your" refer to you (i.e., the person participating in the research). The words "we" or "us" refer to study workers and investigators.

Purpose of the research
We invite you to take part in a clinical trial. Clinical trials are research studies that test if new ways to detect, prevent, or treat diseases work well, are safe, and whether they lead to any unexpected outcomes.

Oral Saline and normal feeding are the most important parts of treatment of diarrhoeal diseases. These simple treatment saves millions of lives each year, but they do not shorten the duration of illness. Diarrhea causes losses of several ions from the body (one kind of salt like Na, K, Hco3 and minerals like Zn & Ca). The losses of Na, K, Hco3 are replaced through rehydration therapy with ORS, but loss of Ca^{++} is not replaced with the present ORS. Recently preliminary studies in animal and humans show that, replacement of Ca^{++} reduced diarrhea. However, so far, no formal randomized controlled trials (RCTs) on Ca^{++} replacement in diarrheal patients have been performed. At icddr,b (Cholera Hospital) we are carrying out a research study to examine if treatment with ORS containing Ca aiming to reduce the severity and/or duration of diarrhoea.

Up to 396 participants will be asked to join this study.

Invitation to participate
You are being invited to join this study because:

- Adult male

- Non-pregnant adult female
- Age between 18 and 60 years
- History of acute watery diarrhea with signs of some OR severe dehydration
- No bloody diarrhea
- No signs of systemic infection that needed intravenous antibiotics

Methods and procedures
If you agree to our proposal of enrolling you, we will ask some questions about your health condition related to the current illness and before this illness; perform a thorough physical examination. Measure your weight, height, count pulse and respiratory rates, body temperature and record findings.

A fresh stool specimen will be collected for detection of cholera. After initial rehydration and randomization, all cholera patients will receive antimicrobial therapy for cholera while all non-cholera patients will not. Immediately after completion of rehydration participants will consume the assigned ORS after randomization (standard ORS or the investigational ORS; the Ca^{++} ORS) according to standard of care WHO/icddr,b guidelines for 72 hours or up to the time when the patients fulfill the criteria of cessation of diarrhea. Which of the products you will receive will depend on a process called "Randomization" (like flipping a coin) that will give you an equal chance to receive either of them. Neither any one of us nor you know which of the product you will have received. It will be disclosed only after analysis of the results.

Two and half millilitre (half of a teaspoon) of venous blood will be collected if you are severely dehydrated (enrolled in Aim 1) on enrolment and after 24 hours of full rehydration for various laboratory tests that will allow us to assess disease condition and test results may help the doctors to treat you. A repeat sample will be drawn only when clinically indicated. A spot urine sample also will be collected 2 times: one prior to and at the end of 72 hr intervention for laboratory assessment urine Ca^{++}/creatinine ratio.

If diarrhoea ceased, you will be discharged. If your diarrhea continues beyond 72 hours or consume more than 30 L of the assigned ORS we will withdraw you from the study (after declaring failure). But we will continue to provide the standard protocols of the hospital until you fully recover.

Risks and Potential benefits
We do not expect any problem from ingesting the test ORS. At the time of collection of blood, you will feel a momentary pain due to needle prick. There also is a rare chance of bluish discolouration (bruish) surrounding the prick site, due to mild leaking of blood in the skin, which may result in a small bruise or swelling of the skin, and there is a very low chance of bleeding or infection. However, we will take required precaution including the use of disposable syringes and needles to prevent these problems and only well-trained personnel will collect this sample. You will be monitored closely. If any deterioration of your health, we will provide the best possible treatment at the Dhaka hospital of icddr,b at our own cost. If necessary, you will be referred for medical care to other hospital.

You may benefit from the medical care that will be provided by the study up to next 7 days. The medical care provided to you during this period will be free of charge. If you require treatment for any injuries or illness related to your participation in the study, you should contact the investigators or icddr,b immediately. The information we learn may help your community and in similar places around the world by providing important information on whether the this ORS with Ca is effective to reduce diarrhoea severity and duration.

Privacy, anonymity and confidentiality
We will respect your privacy. No identifying information about you will be given to anyone or be published without your permission, unless the law requires us to do this. If you join this study, we will collect only

the information we need for this study including some personal information that identifies you (name, address, phone number) for the purposes of contacting you. Data and samples related to the study will only be accessed by the research team or by people or institutions authorized by the Principal Investigators. Data Safety Monitoring Board (DSMB) that will particularly look at the reliability of data and safety of the test products, and the Ethical Review Committee (ERC) of icddr,b will have access to those information, which will be kept in a secured place under the supervision of the principal investigator of the study. However, we would also like to inform you that disclosure of such information is subject to the laws of Bangladesh. At the time of publishing the results of this study, we will not use your name or identity.
Signing this consent form does not give up your legal rights and does not change the legal and professional responsibilities of the study doctor(s) or involved institutions.

Future use of information
Your data collected during this study will be kept by the International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b), according to institutional policies for at least five years after the main study report is published. Data will only be used for scientific purposes to benefit society.

Right not to participate and withdraw
Participation is voluntary, meaning it is your choice to take part or not in this study. You can change your mind at any time. You will also be able to withdraw consent of participation at any time during the study without paying any penalty or effect on your/your family member treatment at the Dhaka hospital in future. If you decide to leave the study, you can contact the Principal Investigator or a member of the study team to let them know. The investigators will also have the right to withdraw you from the study if it is deemed to be in your best interest.

Communication
If you have any question you can ask me right now or at any time later on. If you want to know anything about rights and benefits for participation in this study you can ask Mr M A Salam Khan, IRB Coordinator. The addresses are as follows:
The addresses are as follows:

Purpose of contact	Name and address	Address for communication
For any question related to the study, or any problem	Local PI :Shafiqul Alam Sarker	Address: Nutrition and Clinical Services Division, icddr,b, 68 Shaheed Tajuddin Ahmed Sarani, Mohakhali, Dhaka 1212 Mobile No.+8801713039813 (to be open 7/24 hours)
To know the rights or benefits or to log any complaint or dissatisfaction	M A Salam Khan (IRB Coordinator)	IRB Secretariat, Research Administration, icddr,b, Mohakhali, Dhaka-1212 Phone: (+88-02) 9827084 or Mobile: 01711428989

I am giving my consent to the investigator to join this study ☐ Yes ☐ No

I am giving my consent to the investigator to obtain photos and videos ☐ Yes ☐ No

I am giving my consent to give my provided information to other researchers on condition that my identifiable information cannot be disclosed or shared with anybody. ☐ Yes ☐ No

I am giving consent to be contacted about additional research opportunities in the future. ☐ Yes ☐ No

Participant's name	Participant's signature or thumbprint	Date (DD/MMM/YYYY)

Name of witness to the consent discussion	Signature of witness	Date (DD/MMM/YYYY)

Name of person who explained consent (representative of the PI)	Signature of person who explained consent	Date (DD/MMM/YYYY)