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
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Cable : Cholera Dhaka

Memorandum

PHSD 2002

2 December 2002

To : Dr. Mahfuzar Rahman
Principal Investigator of protocol # 2002-017
Public Health Sciences Division

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

Sub : **Approval of protocol # 2002-017**

Thank you for your memo dated 2nd December 2002 with the modified version of your protocol # 2002-017 entitled "Efficacy of flocculent technology as an arsenic mitigation strategy". The modified version of the protocol is hereby approved upon your satisfactory addressing of the issue raised by the ERC.

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.

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

Thank you.

copy: Acting Chairman, Research Review Committee
Associate Director, Public Health Sciences Division

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Cable : Cholera Dhaka

MEMORANDUM

Date: December 2, 2002

To: Chairman, Ethical Review Committee

From: Mahfuzar Rahman, PHSD MRahman

Re: Protocol # 2002-017, "Efficacy Flocculent Technology as an Arsenic Mitigation Strategy".

We sincerely appreciate the thoughtful comments and observations from the Chair. We hereby attached the revised Bangla consent forms.
The revised Bangla consent forms now include:

Appendix 1A: General Voluntary Consent Form for adult household members
Appendix 1B: Head of Household on Behalf of Children and other Household Members
Appendix 1C: Sentinel Mother for collection of urine specimens
Appendix1D: Consent form for Environmental Testing of Discarded Flocculent (required by CDC).

We sincerely appreciate the careful review and consideration of the Committee and the Chair of this proposed evaluation.

With sincere appreciation,
Many thanks

Appendix- 1A

আর্ন্তজাতিক উদারাময় গবেষনা কেন্দ্র , বাংলদেশ

সম্মতি পত্র

প্রধান গবেষক ঃ ডা: মাহফুজার রহমান

সূচনা উদ্দেশ্যঃ

আস্সালামু আলাইকুম, আমি..... । আমি (আমরা) আই,সি,ডি,ডি,আর,বি / ব্র্যাক এ চাকরী করি। আমার এই কাজে আই,সি,ডি,ডি,আর,বি / ব্র্যাক দ্য সেন্টার ফর ডিজিজ কন্টোল এন্ড প্রিভেনসন্ ইন দ্য ইউনাইটেড স্টেটস এবং দ্য প্রক্টর এন্ড গ্যাম্বল কোম্পানী যৌথ উদ্যোগে এই রিসার্চ করছি। এই প্রজেক্ট এর উদ্দেশ্য হল একটি নতুন প্রজেক্ট এর মাধ্যমে পানিতে আর্সেনিক এর পরিমান কমানো যায় কিনা তা পরীক্ষা করা।

এই গবেষনা কাজটি চলবে চার মাস। প্রতিটি ঘরকেই একটি নতুন পাউডারের প্যাকেট দেয়া হবে তদের টিউবওয়েলের পানিতে মেশানোর জন্য,এবং আমরা আপনার রান্না ও খাওয়ার পানি ব্যবহারের জন্য বলব এবং আমরা বলব যে, ব্যবহাব এর সব পানিই যেন এই পদ্ধতির অর্ন্তভূক্ত হয়।

আপনারা যদি এই গবেষনা কাজে যোগ দিতে সম্মত হন তাহলে আপনাদেরকে নিম্নে বর্নিত কাজ গুলো করতে বলা হবেঃ
প্রথমত, আমরা আপনার পরিবার স্বাস্থ্য এবং পানি সর্ম্পকে প্রশ্ন করবো। আমাদের প্রশ্নের উত্তর দিতে ২০ মিনিটের মত সময় লাগবে। দ্বিতীয়ত, আমরা আবার এসে এই দ্রব্য দ্বারা কি করে পানি বিশুদ্ধ কবা যায় তা শিখিয়ে দিয়ে যাবো। এতে প্রায় ৩০ মিনিট থেকে ১ ঘন্টার মত সময় লাগবে। তৃতীয়ত, এই প্রজেক্টের যে কেউ প্রতি সপ্তাহে ১০ মিনিটের জন্য আপনাদের বাড়ী আসবেন। তারা আপনাকে জিজ্ঞেস করবেন যে বিগত সাপ্তাহে আপনাদের বাড়ীর কারোর ডায়রিয়া হয়েছিল কিনা, তারা এই নতুন প্রোডাক্ট যা আপনারা আপনাদের পানিকে আরও নিরাপদ করার জন্য ব্যবহার করছেন, সে সংক্রান্ত যেকোন প্রশ্নের জবাব দেবেন। । চতুর্থত, এই প্রজেক্ট এর যে কেউ যেকোন সময় এসে বাড়ীতে রান্না ও খাওয়ার জন্য ব্যবহৃত পানির নমুনা নিয়ে যাবেন। এটা আমাদের বুঝতে সাহয্য করবে যে এই প্রোডাক্টি কত ঘন ঘন ব্যবহার করা হয়েছিল ।এই গবেষণার ফলাফল বিশ্লেষণ করতে আমাদের কয়েক মাস সময় লাগবে। কিন্তু বিশ্লেষণ এর পর আমরা আপনাদের কাছে এসে তা ব্যাখা করে যাবো।

এই প্রজেক্ট এ অংশগ্রহনের সিদ্ধান্ত সম্পূর্ণ আপনার উপর নির্ভর করে। যদি আপনি এই গবেষণায় অংশ নিতে আগ্রহী / ইচ্ছুক হন তাহলে তা আপনার ও আপনার পরিবারের কাজে আসতে পারে। এই গবেষণার জন্য ব্যবহৃত পদ্ধতির দ্বারা এবং আপনার পরিবারের রান্না এবং খাবারের জন্য যে পানি ব্যবহার করেন তাতে আর্সেনিক গ্রহন এর মাত্রা কমিয়ে আনতে পারে। এই গবেষণায় সামান্য ঝুঁকির সম্ভাবনা রয়েছে।যদি কোন বাচ্চা এই পাউডারের প্যাকেট থেকে কিছু খেয়ে ফেলে তাহলে এই দ্রব্য এর আয়রন এর মাত্রার জন্য সে বাচ্চা অসুস্থ্য হয়ে পড়তে পারে। এই ঝুঁকি এড়ানোর জন্য এই নমুনাটি একটি প্যাকেটে রয়েছে যা কাঁচি বা অন্যান্য ধারালো জিনিরেস সাহায্যে খোলা যায় এবং আমাদের পরামর্শ হল যে এই প্যাকেটগুলো বাচ্চাদের নাগালের বাইরে রাখা ভালো।

আইন অনুযায়ী আপনাদের পরীক্ষা সমূহের ফলাফল গোপন রাখা হবে। আমরা ফলাফল সমূহ একটি বন্ধ রুমে রাখব। এবং শুধু মাত্র গবেষণা কাজের কর্মীগণ এই গবেষণার ফলাফল দেখতে পাবেন। আপনি / আপনাদের নাম ও অন্যান্য ব্যক্তিগত তথ্যসমূহ কখনই জনসম্মুখে উপস্থাপন করা হবেনা। এই গবেষণার জন্য করা পরীক্ষা সমূহের প্রোডাক্ট, এবং এই প্রোডাক্ট ব্যবহারের জন্য উপকরন সমূহ সর্ম্পূণ বিনামূল্যে আপনাদের সরবরাহ করা হবে।

আমরা আপনাকে একটি সম্মতি পত্র দেব। ইন্টারভিউর সময়ে আপনার আমার / আমাদের প্রতি যদি কোন প্রশ্ন াকে তাহলে তা যেকোন সময়ে করতে পারেন। আপনার যদি ইচ্ছা না করে তহলে আপনি যেকোন প্রশ্নের উত্তর দিতে অস্বীকৃতি জানাতে পারেন। এই গবেষণা কার্যে অংশগ্রহণ না করার সিদ্ধান্ত সম্পূর্ণ আপনার অথবা এই কাজের মাঝামাঝি সময়ে চাইলেও অগ্রহন করা বাদ দিতে পারেন। আপনি যদি এই গবেষণার অংশ নিতে না চান তাহলে এই কাজে অংশগ্রণের সুযোগ সুবিধা থেকে বঞ্চিত হবেন। কিন্তু এর জন্য আপনারা অপরাপর সুযোগ সুবিধা বা সাহায্য থেকে বঞ্চিত হবেন না

এই গবেষণা প্রসঙ্গে আপনার যদি আর কোন প্রশ্ন থাকে তাহলে আপনি ডঃ মাহফুর রহমান, টেলিঃ ৮৮১১৭৫১- ৬০, এক্স - ২২৩৬ এর সাথে যোগাযোগা করতে পারেন। এই গবেষণার গবেষিত জনগান হিসাবে যদি আপনার আর কোন প্রশ্ন থাকে তাহলে আপনি ডা ঃ মো ঃ ইউনুস এর সংগে যোগাযোগা করতে পারেন।

আপনি যদি এই গবেষণায় সম্মত হন তাহলে দয়া করে আপনার নাম সই করুন বা বাম হাতের বৃদ্ধাঙ্গুলির ছাপ দিন।

অংশগ্রহনকারীর স্বাক্ষার	ইনটারভিয়ার স্বাক্ষর	স্বাক্ষীর স্বাক্ষর
নাম ঃ ----------	নাম ঃ ----------	নাম ঃ ----------
তাং ----------	তাং ----------	তাং ----------

Appendix- 1B

আর্ন্তজাতিক উদারাময় গবেষনা কেন্দ্র , বাংলদেশ

সম্মতি পত্র

প্রধান গবেষক ঃ ডাঃ মাহফুজার রহমান

সুচনা উদ্দেশ্যঃ

আস্সালামু আলাইকুম, আমি..... । আমি (আমরা) আই,সি,ডি,ডি,আর,বি / ব্র্যাক এ চাকরী করি। আমার এই কাজে আই,সি,ডি,ডি,আর,বি / ব্র্যাক দ্য সেন্টার ফর ডিজিজ কন্টোল এন্ড প্রিভেনস্ন ইন দ্য ইউনাইটেড স্টেটস এবং দ্য প্রক্টর এন্ড গ্যাম্বল কোম্পানী যৌথ উদ্যোগে এই রিসার্চ করছি। এই প্রজেক্ট এর উদ্দেশ্য হল একটি নতুন প্রজেক্ট এর মাধ্যমে পানিতে আর্সেনিক এর পরিমান কমানো যায় কিনা তা পরীক্ষা করা।

এই গবেষনা কাজটি চলবে চার মাস। প্রতিটি ঘরকেই একটি নতুন পাউডারের প্যাকেট দেয়া হবে তদের টিউবওয়েলের পানিতে মেশানোর জন্য.এবং আমরা আপনার রান্না ও খাওয়ার পানি ব্যবহারের জন্য বলব এবং আমরা বলব যে, ব্যবহাব এর সব পানিই যেন এই পদ্ধতির অর্ন্তভূক্ত হয়।

আপনারা যদি এই গবেষনা কাজে যোগ দিতে সম্মত হন তাহলে আপনাদেরকে নিম্নে বর্নিত কাজ গুলো করতে বলা হবেঃ
প্রথমত, আমরা আপনার পরিবার স্বাস্থ্য এবং পানি সর্ম্পকে প্রশ্ন করবো। আমাদের প্রশ্নের উত্তর দিতে ২০ মিনিটের মত সময় লাগবে। দ্বিতীয়ত, আমরা আবার এসে এই দ্রব্য দ্বারা কি করে পানি বিশুদ্ধ কবা যায় তা শিখিয়ে দিয়ে যাবো। । এতে প্রায় ৩০ মিনিট থেকে ১ ঘন্টার মত সময় লাগবে। তৃতীয়ত, এই প্রজেক্ট যে কেউ প্রতি সপ্তাহে ১০ মিনিটের জন্য আপনাদের বাড়ী আসবেন। তারা আপনাকে জিজ্ঞেস করবেন যে বিগত সাপ্তাহে আপনাদের বাড়ীর কারোর ডায়রিয়া হয়েছিল কিনা, তারা এই নতুন প্রোডাক্ট যা আপনারা আপনাদের পানিকে আরও নিরাপদ করার জন্য ব্যবহার করছেন, সে সংক্রান্ত যেকোন প্রশ্নের জবাব দেবেন। । চতুর্থত, এই প্রজেক্ট এর যে কেউ যেকোন সময় এসে বাড়ীতে রান্না ও খাওয়ার জন্য ব্যবহৃত পানির নমুনা নিয়ে যাবেন। এটা আমাদের বুঝতে সাহয্য করবে যে এই প্রোডাক্টি কত ঘন ঘন ব্যবহার করা হয়েছিল।

এই প্রজেক্ট এ অংশগ্রহনের সিদ্ধান্ত সম্পূর্ণ আপনার উপর নির্ভর করে। যদি আপনি এই গবেষণায় অংশ নিতে আগ্রহী / ইচ্ছুক হন তাহলে তা আপনার ও আপনার পরিবারের কাজে আসতে পারে। এই গবেষণার জন্য ব্যবহৃত পদ্ধতির দ্বারা এবং আপনার পরিবারের রান্না এবং খাবারের জন্য যে পানি ব্যবহার করেন তাতে আর্সেনিক গ্রহন এর মাত্রা কমিয়ে আনতে পারে। এই গবেষণায় সামান্য ঝুঁকির সম্ভাবনা রয়েছে।যদি কোন বাচ্চা এই পাউডারের প্যাকেট থেকে কিছু খেয়ে ফেলে তাহলে এই দ্রব্য এর আয়রন এর মাত্রার জন্য সে বাচ্চা অসুস্থ্য হয়ে পড়তে পারে। এই ঝুঁকি এড়ানোর জন্য এই নমুনাটি একটি প্যাকেটে রয়েছে যা কাঁচি বা আন্যান্য ধারালো জিনিরেস সাহায্যে খোলা যায় এবং আমাদের পরামর্শ হল যে এই প্যাকেটগুলো বাচ্চাদের নাগালের বাইরে রাখা ভালো।

আইন অনুযায়ী আপনাদের পরীক্ষা সমূহের ফলাফল গোপন রাখা হবে। আমরা ফলাফল সমূহ একটি বন্ধ রুমে রাখব। এবং শুধু মাত্র গবেষণা কাজের কর্মীগণ এই গবেষণার ফলাফল দেখতে পাবেন। আপনি / আপনাদের নাম ও অন্যান্য ব্যক্তিগত তথ্যসমূহ কখনই জনসম্মুখে উপস্থাপন করা হবেনা। এই গবেষণার জন্য করা পরীক্ষা সমূহের প্রোডাক্ট, এবং এই প্রোডাক্ট ব্যবহারের জন্য উপকরন সমূহ সর্ম্পূণ বিনামূল্যে আপনাদের সরবরাহ করা হবে।

আমরা আপনাকে একটি সম্মতি পত্র দেব। ইন্টারভিউর সময়ে আপনার আমার / আমাদের প্রতি যদি কোন প্রশ্ন াকে তাহলে তা যেকোন সময়ে করতে পারেন। আপনার যদি ইচ্ছা না করে তহলে আপনি যেকোন প্রশ্নের উত্তর দিতে অস্বীকৃতি জানাতে পারেন। এই গবেষণা কার্যে অংশগ্রহণ না করার সিদ্ধান্ত সম্পূর্ণ আপনার অথবা এই কাজের মাঝামাঝি সময়ে চাইলেও অংগ্রহন করা বাদ দিতে পারেন। আপনি যদি এই গবেষণার অংশ নিতে না চান তাহলে এই কাজে অংশগ্রণের সুযোগ সুবিধা থেকে বঞ্চিত হবেন। কিন্তু এর জন্য আপনারা অপরাপর সুযোগ সুবিধা বা সাহায্য থেকে বঞ্চিত হবেন না

এই গবেষণা প্রসঙ্গে আপনার যদি আর কোন প্রশ্ন থাকে তাহলে আপনি ডঃ মাহফুর রহমান, টেলিঃ ৮৮১১৭৫১- ৬০, এক্স - ২২৩৬ এর সাথে যোগাযোগা করতে পারেন। এই গবেষণার গবেষিত জনগন হিসাবে যদি আপনার আর কোন প্রশ্ন থাকে তাহলে আপনি ডা ঃ মো ঃ ইউনুস এর সংগে যোগাযোগা করতে পারেন।

আপনি যদি আপনার শিশু ও পরিবারের অন্যান্য সদস্যদের এই গবেষণায় অংশগ্রহনে সম্মত হন তাহলে দয়া করে আপনার নাম সই করুন বা বাম হাতের বৃদ্ধাঙ্গুলির ছাপ দিন।

অভিভাবকের স্বাক্ষার	ইনটারভিয়ার স্বাক্ষর	স্বাক্ষীর স্বাক্ষর
নাম ঃ ----------	নাম ঃ ----------	নাম ঃ ----------
তাং ----------	তাং ----------	তাং ----------

Appendix- 1C

আর্ন্তজাতিক উদারাময় গবেষনা কেন্দ্র , বাংলদেশ

সম্মতি পত্র

প্রধান গবেষক ঃ ডা: মাহফুজার রহমান

সূচনা উদ্দেশ্যঃ

আস্সালামু আলাইকুম, আমি..... । আমি (আমরা) আই,সি,ডি,ডি,আর,বি / ব্র্যাক এ চাকরী করি। আমার এই কাজে আই,সি,ডি,ডি,আর,বি / ব্র্যাক দ্য সেন্টার ফর ডিজিজ কন্টোল এন্ড প্রিভেনস্ন ইন দ্য ইউনাইটেড স্টেটস এবং দ্য প্রক্টর এন্ড গ্যাম্বল কোম্পানী যৌথ উদ্যোগে-এই রিসার্চ করছি। এই প্রজেক্ট এর উদ্দেশ্য হল একটি নতুন প্রজেক্ট এর মাধ্যমে পানিতে আর্সেনিক এর পরিমান কমানো যায় কিনা তা পরীক্ষা করা।

এই গবেষনা কাজটি চলবে চার মাস। প্রতিটি ঘরকেই একটি নতুন পাউডারের প্যাকেট দেয়া হবে তদের টিউবওয়েলের পানিতে মেশানোর জন্য.এবং আমরা আপনার রান্না ও খাওয়ার পানি ব্যবহারের জন্য বলব এবং আমরা বলব যে, ব্যবহাব এর সব পানিই যেন এই পদ্ধতির অর্ন্তভূক্ত হয়।

প্রথমত, আমরা আপনার পরিবার স্বাস্থ্য এবং পানি সর্ম্পকে প্রশ্ন করবো। দ্বিতীয়ত যিনি পানি বিশুদ্ধ করা এবং রান্না করার কাজে নিয়োজিত তাঁর মূত্র গ্রহন করার জন্য আমরা একটি নমুনা পাত্র দিব। এই প্রশ্নোত্তর পর্ব ও মূত্র গ্রহনের জন্য ২০ মিনিটের মত সময় লাগবে। তৃতীয়ত, আমরা আবার এসে এই দ্রব্য দ্বারা কি করে পানি বিশুদ্ধ কবা যায় তা.শিখিয়ে দিয়ে যাবো। এতে প্রায় ৩০ মিনিট থেকে ১ ঘন্টার মত সময় লাগবে। চতুর্থত, এই প্রজেক্ট যে কেউ প্রতি সপ্তাহে ১০ মিনিটের জন্য আপনাদের বাড়ী আসবেন। তারা আপনাকে জিজ্ঞেস করবেন যে বিগত সাপ্তাহে আপনাদের বাড়ীর কারোর ডায়রিয়া হয়েছিল কিনা, তারা এই নতুন প্রোডাক্ট যা আপনারা আপনাদের পানিকে আরও নিরাপদ করার জন্য ব্যবহার করছেন, সে সংক্রান্ত যেকোন প্রশ্নের জবাব দেবেন। প্রতি চতুর্থ ভিজিটে বা মাসে একবার করে তিন মাসের জন্য যারা এই পানি ব্যবহার করেন, প্রজেক্ট কর্মীগণ তাদের মূত্র সংগ্রহের জন্য একটি নমুনা কাপ দেবেন । পনচমত, এই প্রজেক্ট এর যে কেউ যেকোন সময় এসে বাড়ীতে রান্না ও খাওয়ার জন্য ব্যবহৃত পানির নমুনা নিয়ে যাবেন। এটা আমাদের বুঝতে সাহয্য করবে যে এই প্রোডাক্টি কত ঘন ঘন ব্যবহার করা হয়েছিল।এই গবেষণার ফলাফল বিশ্লেষণ করতে আমাদের কয়েক মাস সময় লাগবে। কিন্তু বিশ্লেষণ এর পর আমরা আপনাদের কাছে এসে তা ব্যাখা করে যাবো।

এই প্রজেক্ট এ অংশগ্রহনের সিদ্ধান্ত সম্পূর্ণ আপনার উপর নির্ভর করে। যদি আপনি এই গবেষণায় অংশ নিতে আগ্রহী / ইচ্ছুক হন তাহলে তা আপনার ও আপনার পরিবারের কাজে আসতে পারে। এই গবেষণার জন্য ব্যবহৃত পদ্ধতির দ্বারা এবং আপনার পরিবারের রান্না এবং খাবারের জন্য যে পানি ব্যবহার করেন তাতে আর্সেনিক গ্রহন এর মাত্রা কমিয়ে আনতে পারে।

এই গবেষণায় সামান্য ঝুঁকির সম্ভাবনা রয়েছে।যদি কোন বাচ্চা এই পাউডারের প্যাকেট থেকে কিছু খেয়ে ফেলে তাহলে এই দ্রব্য এর আয়রন এর মাত্রার জন্য সে বাচ্চা অসুস্থ্য হয়ে পড়তে পারে। এই ঝুঁকি এড়ানোর জন্য এই নমুনাটি একটি প্যাকেটে রয়েছে যা কাঁচি বা অন্যান্য ধারালো জিনিরেস সাহায্যে খোলা যায় এবং আমাদের পরামর্শ হল যে এই প্যাকেটগুলো বাচ্চাদের নাগালের বাইরে রাখা ভালো।

আমরা রেকর্ড সমুহ বন্ধ ঘরে রাখব এবং শুধু মাত্র গবেষণা কাজের কর্মীগণ তা দেখতে পাবেন।

এই গবেষণার জন্য করা পরীক্ষা সমূহের দ্রব্য, এবং এই দ্রব্য ব্যবহারের জন্য উপকরন সমূহ সর্ম্পূণ বিনামূল্যে আপনাদের সরবরাহ করা হবে।

এই গবেষণা প্রসঙ্গে আপনার যদি আর কোন প্রশ্ন থাকে তাহলে আপনি ডঃ মাহ্ফুর রহমান, টেলিঃ ৮৮১১৭৫১- ৬০, এক্স - ২২৩৬ এর সাথে যোগাযোগা করতে পারেন। এই গবেষণার গবেষিত জনগন হিসাবে যদি আপনার আর কোন প্রশ্ন থাকে তাহলে আপনি ডা ঃ মো ঃ ইউনুস এর সংগে যোগাযোগা করতে পারেন।

আপনি যদি এই গবেষণায় আপনার মূত্র নমুনা দিতে সম্মত হন তাহলে দয়া করে আপনার নাম সই করুন বা বাম হাতের বৃদ্ধাঙ্গুলির ছাপ দিন।

অংশগ্রহনকারীর স্বাক্ষার	ইনটারভিয়ার স্বাক্ষর	স্বাক্ষীর স্বাক্ষর
নাম ঃ ----------	**নাম ঃ** ----------	**নাম ঃ** ----------
তাং ----------	তাং ----------	তাং ----------

Appendix- 1D

আর্ন্তজাতিক উদারাময় গবেষনা কেন্দ্র , বাংলাদেশ

সম্মতি পত্র

প্রধান গবেষক ঃ ডা: মাহফুজার রহমান

সূচনা উদ্দেশ্যঃ

আস্সালামু আলাইকুম, আমি..... । আমি (আমরা) আই,সি,ডি,ডি,আর,বি / ব্র্যাক এ চাকরী করি। আমার এই কাজে আই,সি,ডি,ডি,আর,বি / ব্র্যাক দ্য সেন্টার ফর ডিজিজ কন্টোল এন্ড প্রিভেনসন্ ইন দ্য ইউনাইটেড স্টেটস এবং দ্য প্রক্টর এন্ড গ্যাম্বল কোম্পানী যৌথ উদ্যোগে এই রিসার্চ করছি। এই প্রজেক্ট এর উদ্দেশ্য হল একটি নতুন প্রজেক্ট এর মাধ্যমে পানিতে আর্সেনিক এর পরিমান কমানো যায় কিনা তা পরীক্ষা করা।

এই গবেষনা কাজটি চলবে চার মাস।প্রতিটি ঘরকেই একটি নতুন পাউডারের প্যাকেট দেয়া হবে তদের টিউবওয়েলের পানিতে মেশানোর জন্য.এবং আমরা আপনার রান্না ও খাওয়ার পানি ব্যবহারের জন্য বলব এবং আমরা বলব যে, ব্যবহাব এর সব পানিই যেন এই পদ্ধতির অর্ন্তভূক্ত হয়।

আপনার বাড়ী নির্বাচিত হয়েছে সেই গ্রুপে যে আপনারা আপনাদের ব্যবহৃত টিউবওয়েলের পানিতে প্যাকেট করা নতুন পাউডার ব্যবহার করবেন। আমরা খাবার এবং রান্না করার সকল পানি এই পাউডার দিয়ে পরিশোধন করার জন্য বলব।

কার্যপ্রনালী:

আপনি যদি পানি পরিশোধনের জন্য প্যাকেটের পাউডার ব্যবহার করেন তাহলে আপনাকে নিম্নলিখিত কাজগুলো করার জন্য বলা হবে ঃ

আপনার বাড়ীর নিকটে একটি গর্ত করে তাতে ব্যবহারকৃত ফ্লকুলেন্ট ফেলুন।

কেবলমাত্র ব্যবহারকৃত ফ্লকুলেন্টই উক্ত গর্তে ফেলুন।

গবেষনার ফলাফলের জন্য আমাদের কয়েক মাস সময় লাগবে। কিন্তু যখনই ফলাফল পাওয়া যাবে তখনই আপনাদের তা জানান হবে।

ঝুঁকি এবং উপকারিতাসমুহ:

ব্যবহৃত ফ্লকুলেন্ট আলাদা গর্তে ফেলানো সম্পূর্ণ আপনার উপর নির্ভর করছে। আপনি যদি ব্যবহৃত ফ্লকুলেন্ট আলাদা গর্তে ফেলান তাহলে পরিত্যক্ত ফ্লকুলেন্ট শেষ পর্যায়ে কি অবস্থায় পরিনত হয় তা আমাদের বুঝতে সাহায্য করবে। এই সামগ্রীটি আর্সেনিকের পরিমান কমানোর ব্যাপারে কতটুকু কার্যকরী এই প্রক্রিয়ার মাধ্যমে আমরা তা জানতে পারবো।

গর্তে ব্যবহারকৃত ফ্লকুলেন্ট ফেলানো ঝুঁকিপূর্ণ কিনা আমরা তা জানি না।

গোপনীয়তা:

আইন অনুযায়ী গর্ত থেকে নেয়া উপকরনের পরীক্ষা সমূহের ফলাফল গোপন রাখা হবে। আমরা ফলাফল সমূহ একটি বদ্ধ রুমে রাখব। এবং শুধু মাত্র গবেষণা কাজের কর্মীগণ এই গবেষণার ফলাফল দেখতে পাবেন। গবেষনাটি জনসম্মুখে আলোচনার সময় অথবা ফলাফল প্রকাশের সময় আপনি / আপনাদের নাম ও অন্যান্য ব্যক্তিগত তথ্যসমূহ কখনই জনসম্মুখে উপস্থাপন করা হবেনা।

খরচ/মূল্য পরিশোধ:

এই গবেষণার জন্য করা পরীক্ষা সমূহের প্রোডাক্ট, এবং এই প্রোডাক্ট ব্যবহারের জন্য উপকরন সমূহ সর্ম্পূণ বিনামূল্যে আপনাদের সরবরাহ করা হবে।

না করার/ ত্যাগ করার অধিকার:

আমরা আপনাকে একটি সম্মতি পত্র দেব। ইন্টারভিউর সময়ে আপনার আমার / আমাদের প্রতি যদি কোন প্রশ্ন াকে তাহলে তা যেকোন সময়ে করতে পারেন। আপনার যদি ইচ্ছা না করে তহলে আপনি যেকোন প্রশ্নের উত্তর দিতে অস্বীকৃতি জানাতে পারেন। এই গবেষণা কার্যে অংশগ্রহণ না করার সিদ্ধান্ত সম্পূর্ণ আপনার অথবা এই কাজের মাঝামাঝি সময়ে চাইলেও অংগ্রহন করা বাদ দিতে পারেন। আপনি যদি এই গবেষণার অংশ নিতে না চান তাহলে এই কাজে অংশগ্রণের সুযোগ সুবিধা থেকে বঞ্চিত হবেন। কিন্তু এর জন্য আপনারা অপরাপর সুযোগ সুবিধা বা সাহায্য থেকে বঞ্চিত হবেন না

এই গবেষণা প্রসঙ্গে আপনার যদি আর কোন প্রশ্ন *াকে তাহলে আপনি ডঃ মাহফুর রহমান, টেলিঃ ৮৮১১৭৫১- ৬০, এক্স - ২২৩৬* অথবা ডা ঃ মো ঃ ইউনুস, মতলব এর সাথে যোগাযোগা করতে পারেন। এই গবেষণার গবেষিত জনগন হিসাবে আপনার অধিকার সম্পর্কিত যদি কোন প্রশ্ন থাকে তাহলে আপনি আই,সি,ডি,ডি,আর,বি সেক্রেটারী, মিঃ বিজয় সাহা (ফোনঃ ৮৮১০১১৭)এর সংগে যোগাযোগা করতে পারেন।

আপনি যদি আলাদা গর্তে ব্যবহারকৃত ফ্লকুলেন্ট ফেলতে এবং তা হতে নমুনা দিতে সম্মত হন তাহলে দয়া করে আপনার নাম সই করুন বা বাম হাতের বৃদ্ধাঙ্গুলির ছাপ দিন।

অংশগ্রহনকারীর স্বাক্ষার	ইনটারভিয়ার স্বাক্ষর	স্বাক্ষীর স্বাক্ষর
নাম ঃ ----------	নাম ঃ ----------	নাম ঃ ----------
তাং ----------	তাং ----------	তাং ----------

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Memorandum

2 December 2002

To : Dr. Mahfuzar Rahman
Principal Investigator of protocol # 2002-017
Public Health Sciences Division

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

Sub : **Protocol # 2002-017**

Thank you for your memo dated 27th November 2002 with the modified version of your protocol # 2002-017 entitled "Efficacy of flocculent technology as an arsenic mitigation strategy". After review, the following observation is made on the modified version of the protocol:

The sentence "আমরা লটারির মাধ্যমে নির্বাচন করবো যে আপনার বাড়ি কোন গ্রুপে পড়বে" should be deleted from the Bengali version of the consent forms (Appendix 1A, 1B and 1C).

You are, therefore, advised to address the above issues and submit the modified version of the protocol for consideration of the Chair.

Thank you.

copy: Acting Chairman, Research Review Committee
Associate Director, Public Health Sciences Division

01 December 2002

Review of the revised protocol # 2002 – 017, " Efficacy of Flocculent Technology as an Arsenic Mitigation Strategy".
PI: Dr. Mahfuzur Rahman.

I am happy to report that PI has finally responded positively to the issues of ethical concern raised by ERC in its earlier meetings and modified the protocol appropriately to reflect the following changes:

- The protocol now includes the study of efficacy only of the intervention product (combined chlorination- flocculent water treatment method) in 100 households (one household for tube well).
- Fully consented study participants (members of 100 households) will only receive instruction and education regarding safe use of the intervention product. There will be no promotional activities conducted in the community during the study.
- 'Control' group (use of an alternate BRAC brand arsenic mitigation strategy) have been dropped and will not be part of the proposed study. Instead the study will detect a difference in individual women of their pretreatment level of urinary arsenic compared to their level of urinary conc. after 12 weeks of use of the intervention product.

However from the Bengali versions of the consent forms (Appendix – 1A, 1B and 1C) the sentence, ' আমরা লটারীর মাধ্যমে নির্বাচন করব যে আপনার বাড়ী কোন গ্রুপে পড়বে' should be omitted.

The revised protocol with the suggested modification in the consent form is recommended for approval. Since the protocol has now been extensively modified, I wonder if RRC's fresh approval is mandated or may simply be informed of the changes.

Thanking you

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

Acty Chair: RRC
Kindly advise ERC whether Revised protocol may be approved by ERC.
Thanks & Regds
Zaman

2/12 2002 If ERC is satisfied with these revisions I consider it sufficiently revised also for RRC — it will be reported to the next RRC meeting 02-12-02
PERSON Acting chair RRC

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Cable : Cholera Dhaka

To
Professor A.K.M. Nurul Anwar
Member, Ethical Review Committee

For your review and comments, please.
Thank you.

MEMORANDUM

Date: November 27, 2002

To: Chairman, Ethical Review Committee

From: Mahfuzar Rahman, PHSD MRahman

Re: Protocol # 2002-017, "Efficacy Flocculent Technology as an Arsenic Mitigation Strategy".

We sincerely appreciate the thoughtful comments and observations from the Chair, which have resulted in significant revisions and improvements in the protocol. We attempted to address each of the issues and concerns raised by the chair in the insightful response from the Chair dated 17 November 2002.

a) We appreciate the concerns of the Committee regarding the simultaneous examination of efficacy of the intervention product and its promotion in the community before efficacy and safety are established. We have undertaken extensive revision of the protocol to remove all discussion of promotion of the intervention product. Fully consented study participants will only receive instruction and education regarding safe use of the intervention product. There will be no promotional activities conducted during this study.

b) At the request of the Chair and the Committee, we have extensively modified the study design of the protocol to address the ethical concerns regarding achievement of the study objectives. The revised protocol reflects a design that specifies the random selection of **one** household per tubewell to receive the intervention flocculent-chlorination product. Each member of the randomly selected household will provide an informed consent. The randomly selected sentinel mother will additionally provide consent to provide urine samples for arsenic analysis during the study period. The study will be limited to the 100 households who will receive the intervention product. Field workers as described in the protocol to monitor safety and use of the product will follow each of the 100 households with weekly visits. The objective of the visits will be the collection of data and the collection of urine and water samples. Activities promoting the product will not be a component of these visits or of any other part of this proposed study.

c) We appreciate the Chair's comments regarding the control arsenic mitigation strategy. Following reconsideration of the study design, we have eliminated the "control" group of 100 households from this evaluation. The revised protocol will now include a total sample size of 100 households who will all receive the intervention product. This revised sample size will allow us to detect a difference in individual women of their pretreatment level of urinary arsenic compared to their level of urinary arsenic after 12

weeks of use of the intervention chlorination-flocculent product with 70% substantial reduce and 95% confidence. The references to an alternative, standard arsenic mitigation strategy have been eliminated from the revised protocol and will not be a part of the proposed study.

The protocol has been modified to address the concerns of the Chair and the ERC as reflected in the responses from 17 November 2002. We sincerely appreciate the careful review and consideration of the Committee and the Chair of this proposed evaluation.

With sincere appreciation,
Many thanks

cc: Associate Director, PHSD

Attachment 1 Date: 27/11/02

(FACE SHEET)

ETHICAL REVIEW COMMITTEE, ICDDR,B.

Principal Investigator: Mahfuzar Rahman, MBBS, PhD

Application No. 2002-17

Title of Study: Efficacy of Flocculent Technology as an Arsenic Mitigation Strategy

Trainee Investigator (if any): _____

Supporting Agency Proctor & Gamble

Project Status: _____

[x] 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 — 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

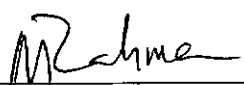
5. Will Signed Consent Form be Required:
   - (a) From subjects — Yes No
   - (b) From parents or guardian (if subjects are minor) — Yes No

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

7. Check documents being submitted herewith to Committee:
   - _x_ Umbrella proposal - Initially submit an with overview (all other requirements will be submitted with individual studies
   - _x__ Protocol (Required)
   - _x__ Abstract Summary (Required)
   - _x__ 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
   - _x__ Informed consent form for subjects
   - _x__ Informed consent form for parent or guardian
   - _x__ Procedure for maintaining confidentiality
   - _x__ 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

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

RESEARCH PROTOCOL

Protocol No. **2002-017**

FOR OFFICE USE ONLY

RRC Approval: Yes/ No Date:

ERC Approval: Yes/No Date:

AEEC Approval: Yes/No Date:

Project Title: Efficacy of Flocculent Technology as an Arsenic Mitigation Strategy
(Revised 27 November, 2002)

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

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

Key words: arsenic mitigation, flocculent treatment, water quality

Relevance of the protocol: This study is designed to evaluate the effectiveness and assess the acceptance and use pattern of a point-of-use water treatment method to improve the microbiological and chemical composition of drinking water. The investigation will be conducted in rural Bangladesh in villages where the water supply contains arsenic levels above the national standard of 50 ppb. It is estimated that 65% of the 4 million tubewells constructed in an attempt to provide a microbiologically safe drinking water source, may contain toxic levels of arsenic in their water. To date, approximately 25 million persons have been exposed to arsenic-contaminated drinking water and over 7,000 patients have been identified with the manifestations of arsenicosis. A number of arsenic mitigation strategies, predominantly consisting of structural and filtering treatments, have been recommended to those at risk; however acceptance and use rates have been less than optimal despite active educational efforts. The use of alternative sources including surface water, reintroduces the risk of illness from diarrheal disease resulting from the ingestion of pathogenic organisms known to inhabit untreated surface water sources. As tubewell water is accessible and acceptable as a drinking source, it would be beneficial to implement a method that would remove arsenic from the tubewell water thus reducing the exposure of the population at risk to elevated arsenic levels. Additionally the flocculent technology proposed for use in this efficacy study has the advantage of reducing the microbiological contamination of treated water through its chlorination activity. Therefore, the problems of both arsenic contamination and microbiological contamination of tubewell water would be addressed with the use of the proposed technology.

Principal Investigator: Mahfuzar Rahman, MBBS, PhD **Division:** PHSD, ICDDR,B: Centre for Health and Population Research,
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Co-Investigator(s):
Andi Shane, NCID, Centers for Disease Control and Prevention, USA
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M.A. Wahed, ICDDR, B
Md. Yunus, ICDDR,B
K Zaman, ICDDR,B
Md. Jakaariya, BRAC, Bangladesh

Collaborating Institute(s): Bangladesh Rural Advancement Committee (BRAC), Bangladesh and Centers for Disease Control and Prevention, Atlanta, GA, USA

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

Gender :
- ☒ Males
- ☒ Females

Age
- ☐ 0 – 5 years
- ☐ 5 – 9 years
- ☐ 10 – 19 years
- ☐ 20 +
- ☐ > 65

- ☐ Fetuses
- ☐ Prisoners
- ☐ Destitutes
- ☐ Service providers
- ☐ Cognitively Impaired
- ☐ CSW
- ☐ Others (specify _____)
- ☐ Animal

Project / study Site *(Check all the apply)*:
- ☐ Dhaka Hospital
- ☐ Matlab Hospital
- ☐ Matlab DSS area

_____
- ☐ Matlab non-DSS area
- ☐ Mirzapur

_____
- ☐ Dhaka Community
- ☐ Chakaria
- ☐ Abhoynagar

_____
- ☐ Mirsarai
- ☐ Patyia
- ☐ Other areas in Bangladesh
- ☐ Outside Bangladesh
  name of country:
- ☐ Multi ☐enter 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

Proposed Sample size: population sharing 100 tubewell water sources; the unit of randomization will be the tubewell, therefore the total sample size will be dependent on the number of persons deriving their drinking water from a tubewell.

Total sample size: persons sharing 100 tubewells

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
- ☒ New treatment regime
- ☐ Human exposure to infectious agents?
- ☐ Investigational new drug
- ☐ Existing data available via public archives/source
- ☐ Pathological or diagnostic clinical specimen
- ☒ Observation of public behaviour

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

Do you consider this research *(Check one)*:

☐ greater than minimal risk

☐ no risk

☐ no more than minimal risk

☐ only part of the diagnostic test

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

Yes/No

☐ ☐ Is the proposal funded?

If yes, sponsor Name: Procter & Gamble Company, Cincinnati, OH, USA

Yes/No

☐ ☐ Is the proposal being submitted for funding ?

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? No

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Dates of Proposed Period of Support

(Day, Month, Year – DD/MM/YY)

Beginning date 01/01/03

End date 30/09/03

Cost Required for the Budget Period ($)

a. *Ist Year* *2nd Year* *3rd Year* *Other*

b. ***Direct Cost: US $ 79,177*** ***Total Cost : US $ 98,971***

Approval of the Project by the Division Director of the Applicant

The above-mentioned project has been discussed and reviewed at the Division level as well by the external reviewers. The protocol has been revised according to the reviewer's comments and is approved.

PERSSON	[signature]	28/11 2002
Name of the Division Director	Signature	Date of Approval

Certification by the Principal Investigator

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

Date: 28/11 2002

Name of Contact Person (if applicable) _____

Table of Contents

[x] 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: **Mahfuzar Rahman, MBBS, PhD**

Project Name: **Efficacy Flocculent Technology as an Arsenic Mitigation Strategy**
Total Budget US$ 98,971 Beginning Date: After obtaining ERC permission Ending Date:

This proposed study is designed to evaluate the effectiveness of a point-of-use combined chlorination-flocculent water treatment method to improve the microbiological and chemical composition of water used for drinking and other household purposes. The investigation will be undertaken in two phases; an initial stage that will consist of the collection of baseline data followed by an intervention stage that will evaluate the efficacy, the acceptance and use pattern of chlorination-flocculent product as a means of improving drinking water quality and will be conducted in the Matlab area. Following the identification of communities with arsenic contamination of their drinking water supply (>50μg/L), baseline data will be collected in the selected communities. This will include information pertaining to the demographics of households, diarrhea incidence, healthcare utilization, assessment of water use in the household, laboratory evaluation of water sources, and measurement of biological parameters for arsenic content. During the intervention phase of twelve-week duration, a total of 100 tubewells and one associated household per tubewell will be identified. One hundred households deriving their water from arsenic-contaminated tubewells will be randomly assigned to receive the point-of-use intervention chlorination-flocculent product and necessary supplies for its use. Baseline and follow-up measurements of biological parameters and of water composition will be obtained in both study groups. Weekly evaluation of intervention households' drinking water for residual chlorine levels and the incidence of diarrheal episodes will complement the monthly measurements of urine arsenic content in the mother of the household and measurements of the arsenic content of household drinking water. Measurements of the microbiological contamination of household water will be conducted at baseline, at mid-study, and at the conclusion of the intervention phase. Individual discussions with households using the flocculent product will assess use (problems & advantages) and the acceptability at the conclusion of the intervention phase. If less than half of the intervention households are using the product at 2 weeks following introduction of the intervention, the rationale for non-use will be explored, and additional activities to promote use will be undertaken before collecting subsequent urine samples. An assessment of the potential consequence of exposure to used, discarded flocculent product will be undertaken in 10 randomly selected households receiving the intervention product. Samples of discarded flocculent will be collected in a designated container with soil. This soil-flocculent mixture will be evaluated for arsenic content at mid-study and at conclusion of the intervention period. An additional 10 households who will not receive the intervention product will similarly collect soil from areas where they might dispose of flocculent, in designated containers. This soil will be evaluated at mid-study and at conclusion of the study period for arsenic content as a comparison to the discarded flocculent-soil mixture collected by the intervention group.

The principal analysis of this study will be a comparison in individual women of their pre-treatment level of urinary arsenic compared to their level of urinary arsenic after 12 weeks of use of the intervention chlorination-flocculent product. Appropriate statistical methods will be applied to account for repeated observations of a single individual over time and clustering within communities.

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

Name	Professional Discipline/ Specialty	Role in the Project
Mahfuzar Rahman	Arsenic and Environmental Epidemiologist, PHSD, ICDDR,B	Principal Investigator
Andi Shane	Epidemic Intelligence Service Officer, Foodborne and Diarrheal Diseases Branch, CDC	Co-Investigator
Steve Luby	Acting Section Chief, Diarrheal Diseases Section, Foodborne and Diarrheal Diseases Branch, CDC	Co-Investigator
Alden Henderson	Health Scientist, National Centers for Environmental Health, Centers for Disease Control and Prevention.	Co-Investigator
Rob Breiman	Associate Director and Head, HSID, ICDDR, B	Co-Investigator
Robert M. Hoekstra	Mathematical Statistician, Division of Bacterial and Mycotic Diseases, Centers for Disease Control and Prevention	Co-Investigator
Md. Sirajul Islam	Head, Environmental Microbiology Laboratory, LSD	Co-Investigator
M.A. Wahed	Head, Nutrition Biochemistry Laboratory, LSD	Co-Investigator
Md. Yunus	Senior Scientist and Head, Matlab Health Research Unit, PHSD	Co-Investigator
Md Jakariya	Environmental Specialist, BRAC, Dhaka,	Co-Investigator
K Zaman	Child Health Epidemiologist, PHSD, ICDDR,B	Co-Investigator
Abbas Bhiuya	Social Scientist, Head, SBSU, PHSD, ICDDR,B	Co-Investigator

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.

We postulate that villagers consuming arsenic and microbiologically contaminated water who utilise this combined flocculent chlorination product will have a substantially lower body burden of arsenic and will consume water with an improved chemical and microbiological composition.

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).**

The objectives of the proposed study are to introduce a home water treatment that combines precipitation, coagulation, flocculation, and chlorination into villages in Bangladesh where the water supply is contaminated with arsenic and other microorganisms and to:

1. assess the acceptance and use pattern of chlorination-flocculent product.
2. assess whether village residents are willing to use the water treatment regularly through weekly evaluations that will determine if available drinking water in households assigned to the intervention chlorination-flocculent product has residual chlorine present.
3. evaluate the effectiveness of the product in decreasing the body burden of arsenic through the measurement of biological parameters including spot urine samples for total and organic arsenic content from a sentinel woman, representing a single tubewell. Urine samples will be analysed for total and organic arsenic content via atomic absorption spectrophotometry (AAS).
4. evaluate if consistent use of the product results in improved chemical and microbiological quality by measuring chemical parameters including arsenic (total and organic) content of water used for drinking and cooking before and after treatment. Microbiological contamination of water used for cooking and drinking will be assessed via membrane-filtration analysis both at baseline and during the intervention period.
5. explore the potential for arsenic leaching from the discarded flocculent by analyzing the arsenic content of soil collected with discarded flocculent.

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).**

The major source of drinking water for persons in Bangladesh prior to the early 1970's was surface water, which although accessible, was frequently not potable[1]. Consumption of microbiologically contaminated water from surface sources has been associated with morbidity and mortality from *enteric* diseases, both in Bangladesh and other areas of the world[2]. In an attempt to provide a safer source of drinking water to the inhabitants of the area, approximately 4 million tubewells consisting of pipes that are sunk into water-bearing strata, fitted with a strainer below the surface and a hand pump above the surface, were placed. Despite the regular use of tubewell water for drinking, a consistent decrease in gastrointestinal disease in Bangladesh was not observed[3]. In many communities, immediate environmental conditions including the close proximity of tubewells to sewage contaminated areas, results in contamination of tubewell water with enteric pathogens[4]. In 1993, chemical analyses of groundwater and tubewell water revealed elevated arsenic content. Simultaneously, persons who were reliant on the tubewell water as a drinking source were noted to have dermatological lesions consistent with arsenicosis, and further investigation yielded an association between the chronic ingestion of tubewell water and the development of arsenicosis[5]. Estimates from field-testing suggest that up to 65% of the 4 million tubewells may be contaminated with harmful levels of arsenic[6].

As with other heavy metals, the toxicity of arsenic is dependent on the form ingested, route of ingestion, chronicity of exposure, and condition of the host[7]. The element is ubiquitous in nature and organic and inorganic forms may be found in foods and beverages, but the inorganic form is most commonly associated with detrimental health effects. Arsenic exerts its damage in the body by inhibiting enzymatic reactions and by inhibiting the formation of peptides, and by reacting with sulfhydryl groups thus accumulating in keratin containing tissues such as hair and nails[9]. A triexponential excretion yields a half-life in the human of approximately 3-4 days[10]. A two-year intervention study following 8 family members in West Bengal who were provided with arsenic-free drinking water yielded an overall decline in measured urine, hair, and nail metabolites during the 2-year period of observation. However, variation in point measurements of the biological markers was noted, especially in those of the urine, with its comparatively shorter half-life. It is hypothesized that in addition to arsenic exposure from drinking water, that the study participants may have encountered additional arsenic burden from the ingestion of foodstuffs irrigated with arsenic contaminated water[8].

The clinical manifestations of arsenic ingestion are diverse involving multiple organ systems. In addition to the characteristic keratoses, hyperpigmentation and hypopigmentation seen with chronic exposure, hypertension, diabetes mellitus, pulmonary and dermatological malignancies may be observed [11,12,15]. The ramifications of these sequelae extend beyond the clinical, as the disfiguring lesions often render persons unable to participate in community and work activities.

Mitigation strategies have been implemented by over 35 organizations to reduce contamination of drinking water supplies, however issues surrounding accessibility, acceptability, and cost have not made these efforts universally available. During a comprehensive program of field-testing and research, the Bangladesh Rural Advancement Committee (BRAC) in cooperation with UNICEF and other partners initiated a pilot project to raise community awareness, introduce a variety of mitigation strategies and evaluate their use in a community of 44,000 households. Initial acceptance of

alternatives to the 25,000 conveniently located tubewells was poor. Active educational efforts by village health workers and promotion of systems including distribution of 10,000 units of the 3-pitcher filter system yielded a rate of use of the intervention of approximately 5%, at 12 months following introduction[16].

Out of the quest to improve water quality, the Procter & Gamble Company (P&G) developed a product for point-of-use water treatment that combines precipitation, coagulation, flocculation, and chlorination. In joint collaboration, CDC, MERTU (Medical Entomology Research and Training Unit) and P&G have instituted field trials of the product in San Juan Sacatepéquez, Guatemala where microbiological contamination of water is prevalent. Results from a pilot in home study reveal decreased microbiological contamination of drinking water, as well as reductions in turbidity and improvements in water quality. Interim analysis of the full health outcome study shows a decreased prevalence of diarrhea among users of the product compared to controls.

The Procter & Gamble Company has developed Hydropure, a technology that uses coagulation, flocculation and chlorination to remove organic material and toxic heavy metals, including lead and arsenic from drinking water, and leaves a chlorine residual to ensure microbiologic potability of water. Their goal was to produce treated water which would not only look clearer and smell better than untreated water, which might facilitate its sustained use, and also be safer than untreated water or water treated only with bleach. Hydropure is a chemical product that treats source water to make it potable by incorporating coagulation, flocculation and disinfection technologies. Hydropure is formulated to reduce the levels of microbial, heavy metal and organic contaminants, while clarifying and lowering the turbidity of the source water. A chlorine residual in the treated water provides protection during storage. The current Hydropure formulation to treat 10 liters of water includes; Ferric Sulfate (2g), Sodium Carbonate (1.34g), Bentonite (1.8g), Chitosan (0.1 g), Magnafloc LT25 (0.05 g) and Calcium Hypochlorite (80 mg).The reformulated flocculent will also contain potassium permanganate (2 mg).

Each PUR sachet contains approximately 5.4 g powder (dose for purifying 10 liter source water) with the following components (Table 1).

Table 1

Chemical	Typical Level of use in DW[1] (mg/L)[2]
Iron (III) sulphate (i.e. ferric)	100-600
Sodium carbonate	50-150
Bentonite	200
Chitosan*	-
Polyacrylamide	1/4[3]
Calcium hypochlorite	10[2], 0.5-5[4]
Potassium permanganate	15

Procter & Gamble has developed a flocculation and chlorination technology (combined product) that not only reduces microorganisms and heavy metals but also removes organic material to render murky water clear. In August 2001, a yearlong study was launched to evaluate the combined product's effect on diarrhea. We now report results from the dry season. We assigned 492 rural Guatemalan households randomly to 1 of 5 groups: bleach, combined product, bleach plus a narrow-mouthed vessel, combined product plus specialized tools, and control. At baseline, 40 (10%) of available water samples from households randomized to intervention were potable and 1 (0.25%) was appropriately chlorinated. After intervention, 330 (63%) of samples from households given intervention were potable (<1 CFU Escherichia coli /100 ml) and 281 (54%) were appropriately chlorinated (>0.08-5.0 mg of free bleach/L). Households given combined product, alone or with a vessel, had less turbid water (49% reduction in median) than controls. After adjustment for age, sex, week of study, and repeated measurements, persons in households receiving combined product, with or without a vessel, had significantly less (25%, P=0.002 and 20%, P=0.01) diarrhea than controls, as did those given bleach but no vessel (22%, P=0.005). During the dry season, despite sub-optimal use, both combined product arms and bleach alone reduced diarrhea. To receive maximum benefit from in-home water treatment, households must consistently prepare and consume treated water. The visual appeal of clear water and the potential for profit-funded continual promotion of the combined product could result in sustained use, thereby empowering households to reduce diarrheal illness. (Reller M. *et. al.* 2002, personal communication)

Arsenic contaminated water sources from Bangladesh before and after treatment with the combination chlorination-flocculent product was evaluated under laboratory conditions. A reduction in mean arsenic level in waters from Bangladesh from a mean of 229 μg/L to a mean of 1.2 μg/L was noted following treatment with the flocculent product in the laboratory. This reduction effected by the product reduced the levels of arsenic below those of the WHO standard (10 μg/L) and below those set by the government of Bangladesh (50 μg/L).

During a pilot trip to Bangladesh, members of the collaborative study team from CDC and P&G met with members of the Public Health Sciences Division of the International Centre for Diarrhoeal Research Bangladesh (ICDDR, B) to obtain an increased selection of water samples for laboratory evaluation before and after treatment with the point-of-use product. Additionally, community demonstrations in villages in two centers, Sonargoan and Matlab, revealed initial acceptance of the product by community members. Focus groups conducted in five rural villages elicited the participation of inhabitants in the preparation of drinking water with the product. Households appeared to have the necessary implements for the preparation of water and members appeared willing to use the product to decrease the arsenic content and reduce the microbiological contamination of their water sources. Demonstrations to community members in which a visible reduction in water turbidity and an improvement in water clarity were particularly well received. Taste and odour of treated waters were deemed acceptable to community members.

Two rounds of field-testing of water samples in rural communities from arsenic contaminated wells revealed improved water quality as post-treatment waters were shown to be low in arsenic content. Of eight water samples collected from arsenic-contaminated tube-wells in January 2001 and sent to a laboratory for evaluation in Newcastle, England, the level of arsenic was reduced from a mean of 229μg/L pre-treatment (49-430) μg/L to 1.2 μg/L (0.4-5) μg/L post-treatment. Subsequent collection of 10 samples of tubewell water in February 2002 from villages in rural Bangladesh revealed a 96% reduction in the concentration of arsenic from 246-8.6μg/L following treatment with the intervention product. Three of the 10 samples had arsenic levels above the WHO threshold but below the Bangladesh government threshold post-treatment. This may be attributed to their origin from infrequently used tubewells with highly reducing conditions that may have prevented optimum flocculation.

Microbiological analyses of tubewell water from two field sites revealed significant decreases in total and fecal coliform counts and *E. coli* counts to levels below detection following treatment with the intervention product. The proposed study is an efficacy study. It asks the question: if villagers with arsenic contaminated water supplies are provided this product and encouraged to use it, will they have a substantially lower body burden of arsenic? The results are uncertain, because foodstuffs, especially rice, can be a significant source of arsenic. Also, it is unclear that even when the product is provided without cost, whether or not families will be willing to devote the time to treat their water. If the intervention does not substantially reduce urinary arsenic we will try to discern whether this is a result of the failure of the product to remove arsenic in the water, the ingestion of other sources of arsenic, the unwillingness to use the product or some other reason. This would involve additional study, likely as an amendment to the currently proposed study.

Alternatively, if the intervention does substantially reduce urinary arsenic, then the next important question becomes: Can this efficacious product be widely used in Bangladesh? Three primary issues would need to be addressed to permit wider use: 1) What would be the long term effect of human exposure to arsenic if this product was widely used throughout Bangladesh and arsenic contaminated flocculent was disposed in latrines or the surrounding environment? 2) How can persons drinking contaminated water be encouraged to use the product? 3) Can the product be manufactured and distributed at a cost that is low enough so that it is affordable to persons exposed to arsenic contaminated and microbiologically contaminated water?

Studies to date of the environmental degradation of arsenic contaminated flocculent suggest that the arsenic remains bound to the iron; therefore it is unlikely that arsenic would reenter food or water supplies. During the intervention phase of this efficacy study, we propose to assess the impact on the local environment of the areas surrounding the discarded, used flocculent product. At mid-study and at the conclusion of the 12 week period, samples of used, discarded flocculent from 10 randomly selected households receiving the intervention will be collected from their dedicated flocculent disposal sites. The second question, pertaining to use of the intervention product, is a scientific question that would involve additional study, some of which could be initiated as an amendment to the currently proposed study.

The third issue of affordability is not a straightforward scientific question. The product is designed to be affordable in low-income countries. It is a product being developed specifically to meet the needs of persons living in low-income countries. The price has not been set and will depend on a number of issues, including sales volume and the particular issues related to each country. Approaches that could improve affordability include bulk supply of the product to non-government organizations that would manage marketing and distribution, non-government organization subsidies, and licensing technology for local manufacture. All of these are possibilities that Procter & Gamble has suggested, but getting the support within Procter & Gamble and the support of institutional partners to work towards resolving these issues depends on sound efficacy data. If this study demonstrates reduced body burden of arsenic with use of the product, we envision negotiating with partners and undertaking a district level demonstration project. A successful district level project could, in turn, lead to a national level program.

Research Design and Methods

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

Methods

The proof of concept study will be undertaken in two phases; an initial stage that will consist of collection of baseline data followed by an intervention stage that will evaluate the efficacy of the product as a means of improving drinking water quality.

Setting

The study will be conducted in Matlab, a field-study area of ICDDR, B located 70km southeast of Dhaka in a low-lying deltaic region. In this site of 149 villages, 190,000 residents derive their drinking water from tubewells that draw water contaminated with arsenic. In addition to widespread arsenic contamination, surveillance has identified diarrheal disease as a leading cause of morbidity and mortality in children less than five years in this area.

Following the identification of communities, a baseline data collection phase, with an estimated duration of three weeks will commence. This will include the collection of information including demographics and structure of communities, household structure, incidences of diarrheal illness, healthcare utilization, assessment of drinking water and household water use, laboratory evaluation of water sources including arsenic content of drinking water, and urine samples for arsenic content.

Exclusion criteria:

1. Households that decline to participate in the study will be excluded.
2. Households who derive their drinking water from tubewells with water containing less 50ppb of arsenic will be excluded from the study.
3. Woman with visible skin lesions suspected to be associated with chronic arsenicosis will not be designated as sentinel women in this proposed sudy and will not provide urine samples for evaluation of total and organic arsenic content. These individuals when identified, will be enrolled in an ongoing study, "*Arsenic in tubewell water and health consequences" RRC 2001-015.*

Interventions

The intervention product, a combination chlorination-flocculent product, containing the active ingredients calcium hypochlorite and iron sulfate will be provided by the Procter & Gamble (P&G) Company. The same formulations of this product have been used in field trials in Guatemala and other areas. The product is contained in a child-resistant packaging to prevent unintentional ingestion. The intervention will be administered by ICDDR, B and BRAC both of whom have a presence and have been involved in the provision of community-based care in the communities of Matlab.

One household per tubewell with arsenic contamination of their tubewell water supply

- (>50 μg/L) will be randomly selected to receive the intervention chlorination-flocculent product and associated necessary implements for its use
    - main ingredients of the intervention product include calcium hypochlorite and iron sulfate
    - child-resistant packaging

Households will be followed weekly for use of the intervention product, safety and adverse effects. Urine samples will be collected from one randomly selected sentinel woman in each of the 100 households selected to use the intervention product. Education and instruction, as well as monitoring for compliance, will occur during the weekly visits. Households deriving their water from a single tubewell will be classified as being affiliated with that tubewell.

Eligibility

Eligible households will be those which:

- are located in the study communities
- have associated household members who provide informed consent
- draw water with arsenic levels $\geq$ 50 μg/L, measured by in-field analysis
- are not regularly using an arsenic mitigation strategy to treat their household water

Measurements

- Baseline:
    - demographics including household and community structure, household water use, diet of household members, healthcare utilization (Appendix 2)
    - biological parameters including a urine sample for arsenic content from the mother of the household. The mother will be followed because she is expected to be at home most of the day and so potentially has treated water available for all of her drinking and cooking. If there is more than one household that derives their water from a single tubewell, a sentinel mother will be randomly selected by the field health worker enrolling the households to provide urinary samples for assessment of arsenic content
    - arsenic (total and organic) content of water
    - microbiological contamination of water
    -
- Follow-up:
    - weekly evaluation to assess if available drinking water in households using the intervention product have residual chlorine present
    - weekly incidence of diarrheal episodes of members residing in the study households
    - monthly measurements of arsenic content of urine of the sentinel mother associated with a tubewell
    - monthly measurements of total and organic arsenic content of household drinking water
    - measurements of microbiological contamination of household drinking water at mid-study and upon study conclusion
    - observations of the use of the chlorination -flocculent product

Scheduled activities for enrolled households

- *Baseline*
  - Seek informed consent
  - Complete baseline survey
  - Test and subsequently randomly select eligible tubewells.
  - Randomly select a single household per eligible tubewell to receive the flocculent-chlorination intervention product
  - Identification and collection of urine sample from sentinel mother associated with each tubewell
  - Collection of drinking water sample and analysis for microbiological contamination
  - Selection of 10 households receiving the flocculent-chlorination product to collect flocculent sludge byproduct. Corresponding selection of 10 households not receiving arsenic mitigation to collect soil samples in dedicated containers.
- *Before initiating intervention*
  - training of health workers
  - preparation of households for intervention
- *Intervention*
  - distribution of intervention product and supplies required for use
- *Weekly*
  - surveillance for diarrheal disease in household members
  - replenishment of supplies
  - encouragement of product use
  - unannounced visits to measure free-chlorine levels of drinking water
  - assessment of product use and acceptability
- *At 2 weeks following introduction of the intervention product*
  - If less than half of the intervention product households are using the product at two weeks following introduction of the intervention, we will explore the rational for non-use in greater detail and will undertake additional activities to promote use, before collecting subsequent urine samples.
- *Monthly*
  - collection of urine samples for analysis of total and organic arsenic levels
  - at mid-study: collection of samples from the 10 households collecting used flocculent byproduct and soil, and from the 10 comparison households collecting soil samples
- *At 3 months*
  - collection of post-intervention urine for analysis of total and organic arsenic levels
  - collection of water samples from 20 households selected to evaluate flocculent disposal effects
  - assessment of use and acceptability (Appendix 4)
- *At study conclusion*

  Selected house hold members will be interviewed to assess attitudes regarding the use of the intervention product (problems and advantages) and understand perceptions and ideas regarding use of the product and water-use as outlined in Appendix 4. Comments about the product and its use as well as questions about ease of use and acceptability of the product will be elicited from participants. Qualitative data analyses will be performed by combining responses into an overall summary and by incorporating quotations and explanations from participants. Frequencies of responses and demographic data will be compiled and

incorporated into the summary. The analyses will be conducted by the PI, BRAC, and study team, (World Health Organization, Tool "A" Assessment and Evaluation of Injection Practices, Draft 4.0, October 2000, pp. 1-14, (www.injectionsafety.org).

Variables

The study team will conduct a pre-intervention baseline survey identifying demographics including household and community structure, household water use, diet of household members, and healthcare utilization. Additionally, water use, storage, and purification practices will be surveyed, (Appendix 2). Community health workers will visit study households at a minimum weekly interval during the intervention phase to assess product use and to monitor diarrheal disease, (Appendix 3). Diarrhea will be defined as 3 or more loose stools in a 24 hour period and an episode of diarrhea will include all days of diarrhea that occur within 72 hours of each other.

Primary outcome measurements will include

- urinary levels of arsenic

Secondary outcome measurements will include

- arsenic levels in treated water
- water microbiology of treated water
- the incidence of diarrhea

Laboratory Methods

Urinary arsenic measurements

Urine samples will be collected for arsenic content in sterile pre-washed polyethylene urine collection cups[13] by study personnel who will gather the samples, add nitric acid (0.1%v/v), and transport them to ICDDR,B for flow injection hydride generation atomic absorption spectrophotometry Every tenth urinary arsenic sample will be divided and sent to a contract laboratory in Newcastle, England for validation via hydride generation followed by ion coupled plasma detection (ICP). Urinary samples will be collected at baseline and at monthly intervals. The urine samples would be stored in cold chests with ice distributed to the households in which urine samples will be collected. This has shown to be adequate for storage. [18]

Water arsenic measurements

Water samples will be collected in polyethylene bottles pre-washed with nitric acid water, and nitric acid (0.1%v/v) will be added after collection as a preservative. Samples will be transported to ICDDR,B for flow injection hydride generation atomic absorption spectrophotometry. Every tenth water sample will be divided and sent to a contract laboratory in Newcastle, England for validation. Water samples will be collected at baseline and at monthly intervals during the intervention period.

Water microbiological analyses

Water samples will be collected in pre-sterilised 500ml Nalgene® plastic bottles. Adherence to sterile technique will be ensured through the use of 70% ethyl alcohol for surface cleansing and the use of disposable gloves during sample collection and processing. Samples will be transported to the microbiological laboratories in insulated coolers with ice packs. Qualitative and quantitative microbiological analyses will be carried out for total and faecal coliforms. A 100ml sample will be filtered through a 0.22µM Millipore®filter followed by the placement of the filter on MFC agar plates. The plates will be incubated at 37°C and 44°C to evaluate total and faecal coliform counts. E. *coli* and faecal normal *streptococci* will also be assessed following the procedures described by Islam *et. al.* 2001[14].

Analyses of flocculent-sludge byproduct

Ten households receiving the intervention product will be randomly selected and requested to collect and store all discarded flocculent accumulated during the intervention portion of the study. The used flooculent byproduct will be stored with equal volumes of soil in designated containers. At baseline, mid-study, and conclusion of the study, analyses of the flocculent-soil samples will simulate arsenic that may be leached from the discarded flocculent via rainwater and other natural conditions. Furthermore, ten randomly selected households whom are not receiving the intervention product and therefore will not have discarded flocculent, will be asked to collect daily soil samples into designated containers. Similar analyses will occur from these collections that will not contain discarded flocculent product; these analyses will serve as non-intervention comparisons.

Sample Size Calculations to Assess Arsenic Burden:

Assuming:

- the intervention product will substantially reduce measured urinary arsenic levels among 70% (±10%) of persons who use the product regularly
- an unmatched design
- a single follow-up evaluation from a sentinel mother who will represent a single tubewell
- 95% confidence

We require 94 tubewells (≈100) to estimate this level of reduction with 20% loss to follow up. This is a conservative estimate insofar as multiple post-intervention measurements will be collected. However, the central uncertainty in home-based water treatment is generally how frequently the water treatment is used. One hundred tubewells would be expected to provide sufficient power to assess differences. One sentinel woman from a single tubewell will be randomly selected for urine arsenic measurements.

Sample size for Arsenic Leaching from Discarded Floc

The environmental assessment for arsenic leaching from the discarded flocculent is an exploratory component of the study. Arsenic is tightly bound to iron, and so the chemistry suggests that leaching will not be a problem. However, given the history of the arsenic problem in Bangladesh, we are seeking some additional reassurance that discarded flocculent will not represent a substantive environmental hazard.

The sample size of 10 households per arm is not intended to definitively demonstrate that there is zero risk for leaching of arsenic from the flocculent. Rather, it will provide some data to guide further thinking. If none of the samples collected from the group with discarded flocculent show elevated levels of arsenic, this result provides reassurance that consistent with our understanding of the chemistry, leaching is unlikely to be a major problem. On the other hand, if several samples with discarded flocculent show elevated levels of arsenic, and especially if these levels are markedly higher than samples without discarded flocculent, then we have identified a substantial problem that will need further attention. If the results are somewhere between these two outcomes, we will at least have some data to guide decision making and further evaluation.

Ethical Issues

Informed Consent

Initially, the proposed study activities will be explained to household members. Many families will hear about the study from these community discussions and from relatives or neighbors. Next, when going house to house for recruitment, project workers will specifically explain the project to all adults who are available in the household at the time of the visit. Members of the household will discuss participation

amongst themselves, and with others in the community. They will be free to withdraw from the study at any point without consequence.

Accepting family consent from a head of household departs from standard U.S. guidelines for informed consent. Regulation 45 CFR 46.116 notes that an IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in 45 CFR 46.116, or waive the requirements to obtain informed consent provided the IRB finds and documents that:

1. The research involves no more than minimal risk to the subjects;
2. The waiver or alteration will not adversely affect the rights and welfare of the subjects;
3. The research could not practicably be carried out without the waiver or alteration; and
4. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

This project involves no more than minimal risk to the subjects. Consent is voluntary; potential subjects will be fully informed, and the process of deciding whether or not to be in the study is a process appropriate to the local culture and process of decision-making. Consent will be obtained from each adult in the family/household members and assent from each child. Should any additional pertinent information become available after enrollment, for example from the study itself or other study of the product, this information will be shared with study subjects.

All potential study participants will receive information about the intervention product.

The consent form will be composed in English, translated and administered in Bengali and back translated into English to ensure that the translation is accurate.

Risks/ Benefits

Risks

The studies and interventions proposed in this protocol present minimal risk to participants, including children and pregnant women. Minimal risk is defined by the Human Assurances Committee of the CDC and in this study as, "the probability and magnitude of harm or discomfort anticipated in research is not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical psychological examinations or tests".

The combination flocculent-chlorination product is composed of traditional chemicals used in drinking water treatment. Sodium carbonate is used as a flavorant and antioxidant in foods. Bentonite is used in dental materials, cosmetics and in pharmaceuticals as a binding or suspending agent. Magnafloc is routinely used in commercial water treatment systems. The World Health Organization recognizes calcium hypochlorite as equivalent to sodium hypochlorite and as an effective and safe drinking water disinfectant. Chitosan is derived from chitin, a polysaccharide found in the exoskeleton of shellfish such as shrimp, lobster, and or crabs. Chitosan is currently being sold as a "fat absorber" through various nutrition outlets. Clinical studies have shown no adverse health effects from ingestion of chitosan.

At the dosage in the individual sachets, the chemicals are generally safe and inherently exhibit a low order of acute and chronic toxicity, except for iron sulfate. The sachet contains 425 mg of ferric iron. This amount of iron if accidentally ingested by a young child has the potential to cause iron toxicity. Ingestion of 30 mg/kg elemental iron is usually required to cause toxicity. A fatal dose is usually >250 mg/kg; however, deaths have occurred from ingestion of as little as 60 mg/kg. In the United States, child resistant packaging has markedly decreased accidental iron ingestions in children.

Iron supplementation is commonly given to women during pregnancy and post-partum in Bangladesh. Thus, similar concentrations of iron as would be found in the intervention chlorination-flocculent product are already present in many Bangladeshi households.

The treatment for acute iron ingestion is immediate medical attention. Instructions will be provided to households receiving the intervention flocculent-chlorination product to proceed immediately to the nearest sub-centre or Matlab central hospital for evaluation in the event of suspected or actual ingestion of the product.

To minimize the possibility of accidental ingestion in this larger and longer study, the intervention flocculent product will be packaged in sealed single use sachets that are difficult for young children to open (child resistant packaging will also be followed in this study). To communicate the potential hazard from ingestion, adults will receive verbal instructions to keep the sachets away from young children and to dispose of the sludge away from children. The printing on the sachets will clearly communicate that the contents are not to be ingested directly. No ingestions have occurred in the Guatemala field study where packets have been supplied to 200 households for 8 months.

The treated water does not have excessive iron concentration (0.1- 0.3 mg/liter) because the hydrous oxide form of iron precipitates out of solution. The used flocculent looks like mud and will likely be discarded on the ground with other refuse. After water treatment, the vast majority of the iron in the intervention product is converted from the more soluble ferric sulfate to the much less soluble and less bioavailable ferric oxide and ferric hydroxide. Thus, the predominant hazardous material in the discarded flocculent will be the hazardous material that was previously in the water; in this study, arsenic. Moving the materials from drinking water to refuse would be expected to markedly decrease the exposure of family members to arsenic. During previous studies in Guatemala, the used flocculent was consistently discarded far away from children and no accidental ingestions have occurred.

Safety of Intervention
It is hypothesized that naturally occurring arsenic bound to iron in sediment was released into shallow aquifers under strongly anaerobic and reducing conditions, thus contaminating tubewell water sources. The intervention combination chlorination-flocculent product creates a strongly oxidizing environment that drives the arsenic in water to bind quickly with the iron in the product. The sludge byproduct containing the bound arsenic will be discarded on the soil surface and thus will not likely be subject to the strong anaerobic and reducing conditions present at several layers beneath the surface. There is the potential that over several hundred years, the sludge may become buried and subject to the strongly reducing, anaerobic conditions that may result in dissociation of arsenic from the iron, however this is a possibility that cannot be currently predicted.

Benefits
The study participants will benefit from receiving an intervention to reduce the arsenic content of their drinking water. Additionally, all study participants will benefit from improved surveillance of diarrhea that according to verbal autopsy reports is the leading cause of death among children less than five years of age in rural Bangladesh. Community health workers will act as a resource, providing educational interventions during regular visits to study families. If children are identified who have diarrhea, oral rehydration solution and instructions for its use will be provided.

Benefits to households assigned to the intervention product include the possibility of a lower incidence of diarrhea and gastrointestinal illness as the intervention product contains a chlorine derivative that reduces the microbiological contamination of water. Households in the intervention product study arm will also receive materials required for the treatment of water with the product including 10 litre buckets, suitable stirring utensils, scissors, filtering cloths, and a supply of the intervention product that will be replenished during the intervention phase of the study. The supplies and training are necessary to insure proper use of the intervention product and are not considered a payment for participation.

Confidentiality

Each participating household and members within each household will be assigned unique identification numbers. These household and member identifiers will be collected on assessments to be used during the project during repeat visitations. These alphanumeric identifiers are needed to ensure accurate linkage of data. Personal identifiers will be removed from all computer files and only the identification number will be included in data analyses.
A list linking the identification codes to the households and household members will be stored with restricted access at ICDDR,B offices. Professionals on the study team who require the information for assessing data validity will be provided with access. The list will be destroyed once data analysis is complete.

Protocol Review
This protocol will be reviewed by the RRC and ERC committees of ICDDR,B and the Institutional Review Board of the CDC.

Reporting
The results of the study will be shared with the participating institutions. The findings, whether or not they demonstrate a substantial health benefit, will be drafted as a scientific manuscript for publication in a peer-reviewed international scientific journal.

Adverse Events
Each of the adverse events and deaths occurring during the study period will be investigated and evaluated to determine if the adverse event was related to the study intervention or procedures. The health of study participants will be protected should any adverse event arise from participation in the study. If the adverse event(s) suggest a substantial ongoing risk to study participants, the study will be terminated.
All participating institutions, i.e. ICDDR,B (Dr. Mahfuzar Rahman, 8811751-60 ext. 2236), BRAC (Md. Jakariya 988 1265 x2702), the Centers for Disease Control and Prevention (Drs. Steve Luby and Andi Shane 404 639 2206), Procter & Gamble (Dr. Bruce Keswick 513 662-4333, Dr. Roy Kulick (513) 662-4501), the RRC and ERC of ICDDR,B, and the CDC IRB will be notified of adverse events and protocol deviations.

Serious adverse events, considered life threatening, judged to be possibly related to study activities will be reported within 24 hours and less serious events within two weeks of their occurrence.

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 equipments 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).**

Field Study Setting

The study will be conducted in Matlab, a field-study area of ICDDR,B located 70km southeast of Dhaka in a low-lying deltaic region. In this site of 149 villages, 190,000 residents derive their drinking water from tubewells that draw water contaminated with arsenic. In addition to widespread arsenic contamination, surveillance has identified diarrheal disease as a leading cause of morbidity and mortality in children less than five years in this area. The intervention will be administered by ICDDR,B and BRAC both of whom have a presence and have been involved in the provision of community-based care in the communities of Matlab.

The resources of the arsenic mitigation research activities group based at the Matlab field station will serve as local support for the activities in the study. Communication among field sites, the Matlab research facility, and ICDDR,B Bangladesh will be achieved through email, mobile telephone communication, and two-way radio devices.

Laboratory Support

The ICDDR, B laboratory will perform the microbiological analyses of collected well and drinking waters. Additional chemical analyses of well and drinking waters and collected urine will be conducted via atomic absorption spectrophotometry, (AAS) at ICDDR,B laboratories. A contract laboratory in Newcastle, England will provide confirmatory arsenic profiles of a selected number of urine and water samples.

Data Analysis

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

Analytic Plan

The primary analysis will be a comparison in individual women of their pre-treatment level of urinary arsenic compared to their level of urinary arsenic after 12 weeks of use of the intervention combination chlorination-flocculent product. Appropriate statistical methods including General Estimated Equations will be applied to account for repeated observations of a single individual over time and clustering within communities.

Interim analyses: At two weeks following the introduction of the intervention, acceptability and use data will be reviewed. If less than half of the intervention product households are using the product, we will explore the rational for non-use in greater detail and will undertake additional activities to promote use, before collecting subsequent urine samples. Data will be entered into a database program and analysed using the EpiInfo 2000, (version 1.1.2, November 2001, CDC, Atlanta, GA) and SAS, (version 8.2, 1991-2001 SAS Institute, Cary, NC) statistical packages.

Data management: Questionnaires will be reviewed by a supervisor in the field for errors, and any apparent errors will be resolved after discussion with both the respondent and the interviewer. A sufficient random sample of forms will be checked by personnel not directly involved with data entry to ensure that fewer than 3 data entry errors occur per 1000 entered fields. Data will be double-entered if an increased rate of errors is noted. Data will be entered into an appropriate data management software package.

Following analysis of the data collected during the study period, the team will present the results to the community leaders. Community health workers will also visit the study households and discuss the results and recommendations that emerge from the analysis. Results will be shared with collaborators including ICDDR,B, BRAC, the Bangladeshi Ministry of Health, and the Procter & Gamble Company. In addition, a manuscript will be prepared for inclusion in the international scientific literature.

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.

This protocol does not involve the use of laboratory animals.

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]Water, Sanitation and Health Electronic Library, World Health Organisation (WHO), November, 2001.01 CD – ISBN 92 4 154459 6

[2]Mintz ED, Reiff FM, Tauxe RV. Safe water treatment and storage in the home: a practical new strategy to prevent waterborne disease. *JAMA* 1995; **273**(12):948-53.

[3]Levine R. Failure of sanitary well to protect against cholera and other diarrhoeal diseases in Bangladesh. *Lancet1976* **ii**:86-89

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[7]Gebel T. Confounding variables in the environmental toxicology of arsenic. *Toxicology* **144** (2000): 155-62.

[8]Mandal TK, Chowdhury TR, Samanta DP, Mukherjee DP, Chanda CR, Saha KC, Chakraborti D. Impact of safe water for drinking and cooking on five arsenic-affected families for 2 years in West Bengal, India. *The Science of the Total Environment, 1998,* **218**: 185-201.

[9]Apostoli P. Bartoli D. Alessio L. Buchet JP. Biological monitoring of occupational exposure to inorganic arsenic. *Occupational and Environmental Medicine* 1999, **56**(12): 825-32.

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[11]Tondel M, Rahman M, Magnuson A, Chowdhury IA, Faruquee MH, Ahmad SA. The Relationship of arsenic levels in drinking water and the prevalence of skin lesions in Bangladesh. *Environmental Health Perspectives*, 1999, **107**: 727-9.

[12]Subramanian KS and Kosnett MJ. Human exposures to arsenic from consumption of well water in West Bengal, India. *Int J Occup Environ Health1998,* **4**:217-30.

[13]Abedin MJ, Cresser MS, Mehrag AA, Feldman J, Cotter-Howells J. Arsenic accumulation and metabolism in rice (*Oryza sativa), Environ Sci Technol2002,* **36**: 962-8.

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[15]Rahman M, Tondel M, Chowdhury IA, Axelson O. Relations between exposure to arsenic, skin lesions, and glucosuria. *Occup Environ Med, 1999,* **56:**277-81.

[16]BRAC Arsenic Mitigation Project – Sonargaon in collaboration with DPHE and UNICEF, preliminary data, 2001.

[17]Samanta G, Chowdhury TR, Badal KM, *et.al.* Flow Injection Hydride Generation Atomic Absorption Spectrometry for Determination of Arsenic in Water and Biological Samples from Arsenic-Affected Districts of West Bengal, India, and Bangladesh. *Microchemical Journal* **62**: 174-191, 1999.

[18] Calderon RL, Hudgens E, Le XC, Schreinmachers D, and Thomas DJ. Excretion of arsenic in urine as a function of exposure to arsenic in drinking water. *Environmental Health Perspectives* 107(8); 663-667, 1999.

Dissemination and Use of Findings

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

The results of the study will be shared with the collaborating institutions and the communities whose members participated in the study. The findings, whether or not they demonstrate a substantial health benefit, will be drafted as a scientific manuscript for publication in a peer-reviewed international scientific journal.

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 be conducted under a cooperative research agreement with fiscal support from the Procter & Gamble Company (P&G), Cincinnati, Ohio. P&G developed the technology that will be used in the intervention arm of this study. This technology is a combination of coagulation, flocculation, and chlorination that removes organic material and toxic heavy metals including lead and arsenic from drinking water, leaving a chlorine residual that ensures microbiological potability.

Biography of the Investigators

May 2002

CURRICULUM VITAE

NAME	CURRENT POSITIONS	ADDRESS
Mahfuzar Rahman Born 1966-06-01	Epidemiologist, Public Health Sciences Division, ICDDR, B: Centre for Health and Population Research, Dhaka, Bangladesh	Public Health Sciences Division, ICDDR, B: Centre for Health and Population Research, GPO Box 128, Mohakhali CA. Dhaka 1000, Bangladesh Phone +880 2 9885155 Fax +880 2 8826050 E-mail mahfuzar@icddrb.org

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Rajshahi Medical college, Rajshahi Bangladesh	MBBS	1992	Medicine
Faculty of Health Sciences, Linköping University, Sweden	PhD.	1994-99	Epidemiology
Johns Hopkins University, School of Hygiene and Public Health, Baltimore, MD	Post-graduate Training	1998	Summer Graduate Epidemiology Program (Epidemiology and Biostatistics)

RESEARCH AND PROFESSIONAL EXPERIENCE:

1992-1993	*Internship training*	Rangpur Medical College Hospital, Rangpur
1993-1994	*Public Health Physician*	Bangladesh Red Crescent Society.
1994-1999	*Research Coordinator*	SIDA
2000 (Jan-May)	*International Fellow*	Public Health Sciences Division, ICDDR, B: Centre for Health and Population Research.
2000 (June- till date)	*Arsenic and Environmental Epidemiologist,*	Public Health Sciences Division, ICDDR, B: Centre for Health and Population Research.

RESEARCH PROJECTS

Project	Role in project	Funding agency	Year(s)
Arsenic in tube well water and health consequences	Principal Co-investigator	Sida	2001-
The case control study of skin lesions and exposure to arsenic	Principal Co-investigator	WHO	2001-
Pilot studies of arsenic exposure through drinking water and health consequneces in Matlab, Bangladesh	Principal Co-investigator	USAID	2000-

Arsenic expsoure, hypertension and skin lesion in Bangladesh	Principal investigator	Linköping Universitite Grant	1998-
Arsenic in drinking water and diabetes mellitus	Principal investigator	Planning grant SAREC/SIDA	1996-

ADVISORY COMMITTEES, EXPERT MISSIONS ETC.

- Referee for a scientific journal, e.g. Health Policy and Planning.
- Technical consultant for Nutrition and Population Unit, South Asia Health, World Bank.
- Technical consultant for SEARO, WHO, New Delhi, India.
- Technical consultant for Some Drinking Water Disinfectants and Contaminants including Arsenic, International Agency for Research on Cancer (IARC), Lyon, France.

ORIGINAL PUBLICATION

1. Rahman M, Axelson O. Arsenic exposure and diabetes mellitus- a second look at case-control data from Swedish copper smelter. *Occupational Environmental Medicine 1995; 52:773-774.*

2. Rahman M, Wingren G and Axelson O. Diabetes mellitus among Swedish art glass workers- an effect of arsenic exposure? *Scandinavian J Work Environmental Health 1996; 22:152-155.*

3. Rahman M, Tondel M, Ahmad AS, Axelson O. Diabetes mellitus associated with arsenic exposure in Bangladesh. *American Journal Epidemiology 1998; 148:198-203.*

4. Rahman M, Tondel M, et al. Hypertension and arsenic exposure in Bangladesh. *Hypertension 1999; 33:74-78.*

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9. Smith AH, Lingas EO, Rahman M. Contamination of drinking water by arsenic in Bangladesh: a public health emergency. *Bulletin World Health Organization 2000; 78: 1093-1103.*

10. Rahman M. Nonmalignant Health Effects of Arsenic Exposure. Doctoral Thesis. *Linköping University Medical Dissertation. No 612, Linköping, 1999, Sweden.*

11. Rahman M, Axelson O. Arsenic ingestion and health effects: Some epidemiological observation. In: W Chappell, CO Abernathy and RL Calderon (eds.): Arsenic exposure and health effects: proceedings of the Forth International Conference on Arsenic Exposure and Health Effects, June, 2000, San Diego, California. *Oxford: Elsevier Science, Ltd., 2001. 193-199.*

12. Milton AH, Hasan Z, Rahman A, Rahman M. Chronic Arsenic Poisoning and Respiratory Effects in Bangladesh. *Journal Occupational Health 2001; 43:136-140.*

13. Rahman M. The Bangladesh arsenic catastrophe-clinical manifestations. *Tropical Doctors 2003* January (Volume 33) *(In Press).*

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15. Milton AH, Rahman M. Respiratory effects and arsenic contaminated well water in Bangladesh. *International Journal Environmental Health Research 2002; 12: 175-179.*

16. Rahman M. Public Health Responses to Arsenic contamination of The Well Water in Bangladesh. *Journal Environmental Science and Health 2002 (Invited commentary).*

REVIEWS, DISCUSSION PAPERS, BOOKS, CHAPTERS ETC.

17. Rahman M, Chowdhury IA. Arsenic in drinking water. How much is too much? *In Touch* 1998; Feb: 1-2

18. Chowdhury IA, Rahman M. Counseling in family planning perspectives. *In Touch* 1998; May:1-3

19. Tondel M, Rahman M. Arsenic poisoning in Bangladesh- the largest disaster in our time? Folkhälsovetenskapligt Centrum Nyhetsblad; 1998:8. *(Swedish).*

20. Rahman M, Street Field K, Persson LA. Addressing the public health crisis. Caused by arsenic contamination of drinking water in Bangladesh. South Asia Health, Nutrition, and Population Unit, *World Bank. 2001.*

21. Smith AH, Rahman M. Arsenic in drinking water: A public health concern. *Medicine Digest 2001;Jan-March.*

22. Rahman M, Tondel M, Chowdhury IA. Arsenic Levels in Drinking Water and Prevalence of Skin Lesions. [Abstract]. *J Diarrhoeal Diseases Research, 1999; 17 (2). 103.*

23. Rahman M, Tondel M, Axelson O. Chronic Arsenicism and Squamous Cell Carcinoma: A Case Study. [Abstract]. *J Diarrhoeal Diseases Research, 1999; 17 (2). 131-132.*

24. Rahman M, Söderkvist P, Rozell BL, Axelson O. Arsenic-induced Keratosis and Squamous Cell Carcinoma. [Abstract]. *J Diarrhoeal Diseases Research, 1999; 17 (2). 132-133.*

25. Rahman M. Epidemiological assessment of arsenic contamination in SEARO countries and elsewhere. *South East Asia Regional Office (SEARO), WHO, New Delhi, 2001.*

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: Steve Luby, MD

2 Present position: Acting Section Chief, Diarrheal Diseases Section, Foodborne and Diarrheal Diseases Branch, Division of Bacterial and Mycotic Diseases, National Centers for Infectious Diseases, Centers for Disease Control and Prevention.

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

University of Texas--Southwestern Medical School at Dallas
MD 1986

University of Rochester--Strong Memorial Hospital
Internship and residency in Internal Medicine.

Centers for Disease Control -- Epidemic Intelligence Service 1990
Completed Preventive Medicine Residency 1993

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
Karachi Soap Health Outcome Study	1/1/02	1/1/04	20%
Home Water Flocculation in Guatemala	1/7/01	1/7/03	15%

4.2 As Co-Principal Investigator

Protocol Number	Starting date	End date	Percentage of time

4.3 As Co-Investigator

Protocol Number	Starting date	Ending date	Percentage of time
HomeWater Flocculation in Kenya	1/6/02	1/6/03	5%

Biography: S. Luby (continued)

5 Publications

Types of publications	Numbers
a) Original scientific papers in peer-review journals	55
b) Peer reviewed articles and book chapters	
c) Papers in conference proceedings	2
d) Letters, editorials, annotations, and abstracts in peer-reviewed journals	2
e) Working papers	
f) Monographs	

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

1. Luby S, Agboatwalla M, Raza A, Sobel J, Mintz E, Baier K, Rahbar M, Qureshi S, Hassan R, Ghouri F, Hoekstra R, Gangarosa E. A low-cost intervention for cleaner drinking water in Karachi, Pakistan. *International Journal of Infectious Diseases*. 2001; 5(3):144-150.

2. Marsh D, Husein K, Lobo M, Ali Shah M, Luby S. Verbal autopsy in Karachi slums: comparing single and multiple cause of child deaths. *Health Policy and Planning*, 1995 10(4) 395-403.

3. Luby S, Syed A, Atiullah N, Faizan K, Fisher-Hoch S. The limited effectiveness of home drinking water purification efforts in Karachi, Pakistan. *International Journal of Infectious Diseases*. 2000 Jan; 4(1):3-7.

4. Dunne EF, Angoran-Biene YH, Kamelan-Tano Y, Sibailly T, Monga B, Kouadio L, Roels TH, Wiktor SZ, Lackritz EM, Mintz ED, Luby S. Is Drinking Water in Abidjan, Côte d'Ivoire, Safe for Infant Formula? *Journal of the Acquired Immune Deficiency Syndromes*. 2001 Dec; 28(4):393-8.

5. Luby S, Agboatwalla M, Raza A, Sobel J, Mintz ED, Baier K, Hoekstra RM, Rahbar MH, Hassan R, Qureshi SM, Gangarosa EJ. Microbiologic effectiveness of hand washing with soap in an urban squatter settlement, Karachi, Pakistan. *Epidemiology and Infection*. 2001 Oct;127(2):237-44.

Biography of the Investigators (continued)

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: Andi L. Shane, MD MPH :

2 Present position: Epidemic Intelligence Service (EIS) Officer, Foodborne and Diarrheal Diseases Branch, Division of Bacterial and Mycotic Diseases, National Centers for Infectious Diseases, Centers for Disease Control and Prevention. :

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

Columbia University School of Public Health, New York City, NY
MPH 1992

Louisiana State University School of Medicine in New Orleans
MD 1997

Albert Einstein College of Medicine -- Montefiore Medical Centre, Bronx, NY
Internship, residency, and chief-residency in Pediatrics, 1997-2001.

Centers for Disease Control -- Epidemic Intelligence Service 2001-present

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

4.1. As Principal Investigator

Protocol Number	Starting date	End date	Percentage of time

4.2. As Co-Principal Investigator

Protocol Number	Starting date	End date	Percentage of time

Biography: A. Shane (continued)

5 Publications

Types of publications	Numbers
a) Original scientific papers in peer-review journals	2
b) Peer reviewed articles and book chapters	
c) Papers in conference proceedings	3
d) Letters, editorials, annotations, and abstracts in peer-reviewed journals	
e) working papers	
f) Monographs	

Five recent publications including publications relevant to the present research protocol

1. Roels TH, Shane A, Goldoft M, Herikstad H, Hedberg C, Angulo F. Foodborne disease in our global village: a multinational investigation of an outbreak of *Salmonella* serotype Enteritidis Phage Type 4 (SE PT 4)Infection in Puerto Vallarta, Mexico. Poster presentation at the Infectious Disease Society of America, 35th annual meeting, September, 1997, *International Journal of Infectious Diseases*, Sept. 2002.

2. Shane, AL, Schroeder, SA , King, D. Respiratory tract infections in children with tracheostomies, poster presentation at American Thoracic Society (ATS 2001) meeting, San Francisco, CA, and platform presentation at the New York Academy of Medicine, June 2001.

3. Joyce JN, Shane A, Lexow N, Winokur A, Casanova MF, Kleinan JE. Serotonin uptake sites and serotonin receptor sites are alteres in the limbic system of schizophrenics. *Neuropsychopharmacology*, 1993, Jun 8(4):315-36.

***ARSENIC AND FLOCCULENT, M* Matlab 9th month**

***Salaries incl. benefits and taxes**

28/11/2002

		Rate/m	Person-months/	Cost
		$		ICDDR,B
Professional staff	**Name**			Total
Arsenic epidemiologist, NOC*	Mahfuzar Rahman	1016	2.0	2,032
Head, Matlab, NOE	Md Yunus	2475	1.0	2,475
Head, HSID, D1	Rob Brieman	0	-	-
Head, Environment Microbilogy, P4	Sirajul Islam	8836	0.5	4,418
Child Health epidemiologist, NOC	Khalequzaman	1471	0.5	736
Social Scientist	Abbas Bhuiya	9091	0.5	4,546
Head, Nutrion Biochemistry	MA Wahed	1505	0.5	753
Subtotal professional staff				*14,959*

Field staff				
Sr. Lab Tech, Matlab, GS4		269	6.0	1,614
Field Research Officer, GS5		353	6.0	2,118
Field manager, NOA		676	9.0	6,084
Field research officer, ethnography GS GS6		459	3.0	1,377
Admin Officer, GS5		353	9.0	3,177
Field Research Assistants, water collection,GS3		225	24.0	5,400
Field Research Assisstant, urine collection, GS3		225	18.0	4,050
Progmamer, NOA		676	3.0	2,028
Data Management Assistant, GS 3		225	12.0	2,700
Porter 3, Dhaka (1) and Matlab (2)		65	18.0	1,170
Subtotal field staff				*29,718*

Operating expenses		Rate $		
Lab supplies				250
Lab supplies water collection		0.1	400	40
Lab supplies urine collection		0.1	600	60
Lab As total in urine and speciation		25	600	15,000
As in water		10	460	4,600
Microbiology, total coliform, fecal coliform, fecal streptococci		8	400	3,200
Subtotal operating expenses				*23,150*

Travel and transport				
Travel and transport,				4000
Subtotal travel				*4000*

Capital expenditure				
Computer and printer		2500		2,500
Freezer for samples -20 degree C		600	2	1,200
Subtotal capital expenditure				*3,700*

Other expenditures				
Printing, photocopies				1,000
Training and dissemination				1,000
Communication (e mail fax phone)				650
Office supplies				500
Unforeseen expenditures				500
Subtotal other expenditure				*3,650*

Total direct cost				**79,177**
Level of institutional overhead				25%
Institutional overhead cost				19,794
Total				**98,971**

28/11/02

Md. Bozlur Rahman
Manager, Budget & Costing
ICDDR,B: Centre for
Health & Population Research
Mohakhali, Dhaka-1212
Bangladesh

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.

Staff: ICDDR, B is comprised of field staff, public health specialists, epidemiologists, biostatisticians, social scientists, laboratory scientists, and clinicians. These personnel are funded by individual research projects based upon time allocated to the projects. In this study, Dr. Mahfuzar Rahman will serve as the Principal Investigator (40% time commitment, 20% salary for 6 months). He will coordinate project implementation and will provide scientific expertise to the collaborative team. Drs. Md. Yunus, and (25% time commitment, 16% salary for 6 months each) will serve as co-investigators and will provide scientific consultation. In this budget, funds are not requested for Drs Rob Brieman, but funds are requested for Drs Khalequzaman, Sirajul Islam, Abbas Bahuya and MA Wahed (10% commitment, 6% effort) who will provide consultation in epidemiology, and will provide technical consultation on arsenic assessment in biological and water samples.

Fieldwork: Field activities will be performed in Matlab, where a research infrastructure is established. Only direct field costs relating to this study are included in the budget.

Intervention: Procter & Gamble Company will provide the intervention flocculent-chlorination project for this efficacy study.

Laboratory analyses: The Environmental Microbiology and Nutritional Biochemistry Section at ICDDR,B/Intronic laboratory, Dhaka will provide laboratory services including AAS.

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.

Initially, the proposed study activities will be explained to community leaders. Many families will hear about the study from these community discussions and from relatives or neighbors who attended. Next, when going house to house for recruitment, project workers will specifically explain the project to all adults who are available in the household at the time of the visit. Members of the household will discuss them amongst themselves, and with others in the community. They will be free to withdraw from the study at any point without consequence.
Accepting family consent from a head of household departs from standard U.S. guidelines for informed consent.

Regulation 45 CFR 46.116 notes that an IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in 45 CFR 46.116, or waive the requirements to obtain informed consent provided the IRB finds and documents that:

1. The research involves no more than minimal risk to the subjects;
2. The waiver or alteration will not adversely affect the rights and welfare of the subjects;
3. The research could not practicably be carried out without the waiver or alteration; and
4. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

This project involves no more than minimal risk to the subjects. Consent is voluntary; potential subjects will be fully informed, and the process of deciding whether or not to be in the study is a process appropriate to the local culture and process of decision making. Because of the work schedule of the extended families living in these villages it is not practical to secure individual written consent from each adult in the family and assent from each child. Should any additional pertinent information become available after enrollment, for example from the study itself or other study of the product, this information will be shared with study subjects

APPENDIX 1A:
International Centre for Diarrhoeal Disease Research, Bangladesh: General Voluntary Consent Form for Adult Household Members

Title of the Research Project: Efficacy Flocculent Technology as an Arsenic Mitigation Strategy
Principal Investigator: Mahfuzar Raman, MBBS, PhD

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.

Hello, my name is _____. I (we) work with ICDDR,B / BRAC. We are working with ICDDR,B/ BRAC, and the Centers for Disease Control and Prevention in the United States, and the Procter & Gamble Company on a research project. The purpose of our study is to see if a new product can reduce the amount of arsenic in drinking water.
The study will last for four months. Each household in the study will receive packets of a new powder to add to all of their tubewell water. We will ask that all water used for drinking and cooking is treated.

If you want to join the study, we will ask you to do these things: First, we will ask you questions about your family, your water, and your health. It will take about 20 minutes to answer our questions. Second, we will come back and tell you how to use the product to make your water safer. This visit will take between 30 and 60 minutes. Third, someone from the project will come once a week for about 10 minutes. They will ask if anyone in your household has had diarrhea in the last week. They will answer any questions that you have about the product that you are using to make your water safer. Fourth, someone from the project will come by at an unannounced time to take a sample of the water that your household uses for drinking and cooking. This will help us to see how often the product is being used. It will take us several months to understand the results of the study. But when we do we will explain the results of the study to the community.

The choice to take part in this project is completely up to you. If you choose to be a part of this study, it may help you and your family. The drinking and cooking water resulting from the different treatment methods used in this study might lower the amount of arsenic that your family consumes. There are some minor risks with the study. If a child eats the contents of the packet of powder given to one group, there is the possibility that the child could become sick from the amount of iron in the product. To prevent this, the product is in a sealed packet that can only be opened with a pair of scissors and we suggest that the packets be kept out of the reach of children.

All results will be kept private to the extent allowed by the law. We will keep the records in locked rooms and only study staff will be allowed to look at them. Your name and other private facts will not appear when we discuss this study publicly or when we publish the results. The tests we do for this study, the products, the supplies needed to use the products will be provided at no cost to you.

We will leave a copy of the consent form with you. If you have questions for me (us) during the interview, ask them at any time. Also, if you want to stop the interview at any time, just let me (us) know. You do not have to answer any questions that you do not want to answer. You may decide not to join the study or you may decide to stop part way through the study. If you decide not to be in the study or decide to leave the study, you will not receive the benefits of being in the study, but you will not be penalized in any other way or lose any other benefits or services.

If you have more questions about the study, you may contact Dr. Mahfuzar Rahman, ICDDR,B, Dhaka (phone: 8811751-60 ext. 2236) or Dr Md Yunus, ICDDR,B, Matlab. If you have other questions related to your rights as a subject in the study, you may contact the ICDDR,B Secretariat, Mr. Bejoy Saha (phone: 8810117).

If you are willing to be in the study, please sign your name or give left thumb impression below.

Signature/Thumb impression of participant	**Signature of Interviewer**	**Signature of witness**
Date:	**Date:**	**Date:**

Appendix- 1A

আর্ন্তজাতিক উদারাময় গবেষনা কেন্দ্র , বাংলদেশ

সম্মতি পত্র

প্রধান গবেষক ঃ ডা: ম্াহফুজার রহমান

সূচনা উদ্দেশ্যঃ

আস্সালামু আলাইকুম, আমি..... । আমি (আমরা) আই,সি,ডি,ডি,আর,বি / ব্র্যাক এ চাকরী করি। আমার এই কাজে আই,সি,ডি,ডি,আর,বি / ব্র্যাক দ্য সেন্টার ফর ডিজিজ কন্টোল এন্ড প্রিভেনস্ন ইন দ্য ইউনাইটেড স্টেটস এবং দ্য প্রক্টর এন্ড গ্যাম্বল কোম্পানী যৌথ উদ্যোগে এই রিসার্চ করছি। এই প্রজেক্ট এর উদ্দেশ্য হল একটি নতুন প্রজেক্ট এর মাধ্যমে পানিতে আর্সেনিক এর পরিমান কমানো যায় কিনা তা পরীক্ষা করা।

এই গবেষনা কাজটি চলবে চার মাস। প্রতিটি ঘরকেই একটি নতুন পাউডারের প্যাকেট দেয়া হবে তদের টিউবওয়েলের পানিতে মেশানোর জন্য.এবং আমরা আপনার রান্না ও খাওয়ার পানি ব্যবহারের জন্য বলব এবং আমরা বলব যে, ব্যবহাব এর সব পানিই যেন এই পদ্ধতির অর্ন্তভূক্ত হয়।

আপনারা যদি এই গবেষনা কাজে যোগ দিতে সম্মত হন তাহলে আপনাদেরকে নিম্নে বর্নিত কাজ গুলো করতে বলা হবেঃ

প্রথমত, আমরা আপনার পরিবার স্বাস্থ্য এবং পানি সর্ম্পকে প্রশ্ন করবো। আমাদের প্রশ্নের উত্তর দিতে ২০ মিনিটের মত সময় লাগবে।। দ্বিতীয়ত, আমরা লটারীর মাধ্যমে নির্বাচন করব যে আপনার বাড়ী কোন গ্রুপে পড়বে। এরপর আমরা আবার এসে এই দ্রব্য কি করে ব্যবহার করতে হয় তা শিখিয়ে দিয়ে যাবো। এতে প্রায় ৩০ মিনিট থেকে ১ ঘন্টার মত সময় লাগবে। তৃতীয়ত, এই প্রজেক্টের যে কেউ প্রতি সপ্তাহে ১০ মিনিটের জন্য আপনাদের বাড়ী আসবেন। তারা আপনাকে জিজ্ঞেস করবেন যে বিগত সাপ্তাহে আপনাদের বাড়ীর কারোর ডায়রিয়া হয়েছিল কিনা, তারা এই নতুন প্রোডাক্ট যা আপনারা আপনাদের পানিকে আরও নিরাপদ করার জন্য ব্যবহার করছেন, সে সংক্রান্ত যেকোন প্রশ্নের জবাব দেবেন। । চতুর্থত, এই প্রজেক্ট এর যে কেউ যেকোন সময় এসে বাড়ীতে রান্না ও খাওয়ার জন্য ব্যবহৃত পানির নমুনা নিয়ে যাবেন। এটা আমাদের বুঝতে সাহয্য করবে যে এই প্রোডাক্টি কত ঘন ঘন ব্যবহার করা হয়েছিল।এই গবেষণার ফলাফল বিশ্লেষণ করতে আমাদের কয়েক মাস সময় লাগবে। কিন্তু বিশ্লেষণ এর পর আমরা আপনাদের কাছে এসে তা ব্যাখা করে যাবো।

এই প্রজেক্ট এ অংশগ্রহনের সিদ্ধান্ত সম্পূর্ণ আপনার উপর নির্ভর করে। যদি আপনি এই গবেষণায় অংশ নিতে আগ্রহী / ইচ্ছুক হন তাহলে তা আপনার ও আপনার পরিবারের কাজে আসতে পারে। এই গবেষণার জন্য ব্যবহৃত পদ্ধতির দ্বারা এবং আপনার পরিবারের রান্না এবং খাবারের জন্য যে পানি ব্যবহার করেন তাতে আর্সেনিক গ্রহন এর মাত্রা কমিয়ে আনতে পারে। এই গবেষণায় সামান্য ঝুঁকির সম্ভাবনা রয়েছে।যদি কোন বাচ্চা এই পাউডারের প্যাকেট থেকে কিছু খেয়ে ফেলে তাহলে এই দ্রব্য এর আয়রন এর মাত্রার জন্য সে বাচ্চা অসুস্থ্য হয়ে পড়তে পারে। এই ঝুঁকি এড়ানোর জন্য এই নমুনাটি একটি প্যাকেটে রয়েছে যা কাঁচি বা আন্যান্য ধারালো জিনিরেস সাহায্যে খোলা যায় এবং আমাদের পরামর্শ হল যে এই প্যাকেটগুলো বাচ্চাদের নাগালের বাইরে রাখা ভালো।

আইন অনুযায়ী আপনাদের পরীক্ষা সমূহের ফলাফল গোপন রাখা হবে। আমরা ফলাফল সমূহ একটি বন্ধ রুমে রাখব। এবং শুধু মাত্র গবেষণা কাজের কর্মীগণ এই গবেষণার ফলাফল দেখতে পাবেন। আপনি / আপনাদের নাম ও অন্যান্য ব্যক্তিগত তথ্যসমূহ কখনই জনসম্মুখে উপস্থাপন করা হবেনা। এই গবেষণার জন্য করা পরীক্ষা সমূহের প্রোডাক্ট, এবং এই প্রোডাক্ট ব্যবহারের জন্য উপকরন সমূহ সম্পূর্ণ বিনামূল্যে আপনাদের সরবরাহ করা হবে।

আমরা আপনাকে একটি সম্মতি পত্র দেব। ইন্টারভিউর সময়ে আপনার আমার / আমাদের প্রতি যদি কোন প্রশ্ন াকে তাহলে তা যেকোন সময়ে করতে পারেন। আপনার যদি ইচ্ছা না করে তহলে আপনি যেকোন প্রশ্নের উত্তর দিতে অস্বীকৃতি জানাতে পারেন। এই গবেষণা কার্যে অংশগ্রহণ না করার সিদ্ধান্ত সম্পূর্ণ আপনার অথবা এই কাজের মাঝামাঝি সময়ে চাইলেও অংগ্রহন করা বাদ দিতে পারেন। আপনি যদি এই গবেষণার অংশ নিতে না চান তাহলে এই কাজে অংশগ্রণের সুযোগ সুবিধা থেকে বঞ্চিত হবেন। কিন্তু এর জন্য আপনারা অপরাপর সুযোগ সুবিধা বা সাহায্য থেকে বঞ্চিত হবেন না

এই গবেষণা প্রসঙ্গে আপনার যদি আর কোন প্রশ্ন থাকে তাহলে আপনি ডঃ মাহ্ফুর রহমান, টেলিঃ ৮৮১১৭৫১- ৬০, এক্স - ২২৩৬ এর সাথে যোগাযোগা করতে পারেন। এই গবেষণার গবেষিত জনগন হিসাবে যদি আপনার আর কোন প্রশ্ন থাকে তাহলে আপনি ডা ঃ মো ঃ ইউনুস এর সংগে যোগাযোগা করতে পারেন।

আপনি যদি এই গবেষণায় সম্মত হন তাহলে দয়া করে আপনার নাম সই করুন বা বাম হাতের বৃদ্ধাঙ্গুলির ছাপ দিন।

অংশগ্রহনকারীর স্বাক্ষার	ইনটারভিয়ার স্বাক্ষর	স্বাক্ষীর স্বাক্ষর
নাম ঃ ----------	নাম ঃ ----------	নাম ঃ ----------
তাং ----------	তাং ----------	তাং ----------

APPENDIX 1B:
International Centre for Diarrhoeal Disease Research, Bangladesh: Head of the Household Voluntary Consent Form

Title of the Research Project: Efficacy Flocculent Technology as an Arsenic Mitigation Strategy
Principal Investigator: Mahfuzar Raman, MBBS, PhD

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.

Hello, my name is _____. I (we) work with ICDDR,B / BRAC. We are working with ICDDR,B/ BRAC, and the Centers for Disease Control and Prevention in the United States, and the Procter & Gamble Company on a research project. The purpose of our study is to see if a new product can reduce the amount of arsenic in drinking water.
The study will last for four months. You will receive packets of a new powder to add to all of your tubewell water. We will ask that all water used for drinking and cooking is treated.

If you want to join the study, we will ask you to do these things: First, we will ask you questions about your family, your water, and your health. It will take about 20 minutes to answer our questions. Second, we will come back and tell you how to use the product to make your water safer. This visit will take between 30 and 60 minutes. Third, someone from the project will come once a week for about 10 minutes. They will ask if anyone in your household has had diarrhea in the last week. They will answer any questions that you have about the product that you are using to make your water safer. Fourth, someone from the project will come by at an unannounced time to take a sample of the water that your household uses for drinking and cooking. This will help us to see how often the product is being used.

The choice to take part in this project is completely up to you. If you choose to be a part of this study, it may help you and your family. The drinking and cooking water resulting from the different treatment methods used in this study might lower the amount of arsenic that your family consumes. There are some minor risks with the study. If a child eats the contents of the packet of powder given to one group, there is the possibility that the child could become sick from the amount of iron in the product. To prevent this, the product is in a sealed packet that can only be opened with a pair of scissors and we suggest that the packets be kept out of the reach of children.

All results will be kept private to the extent allowed by the law. We will keep the records in locked rooms and only study staff will be allowed to look at them. Your name and other private facts will not appear when we discuss this study publicly or when we publish the results. The tests we do for this study, the products, the supplies needed to use the products will be provided at no cost to you.

We will leave a copy of the consent form with you. If you have questions for me (us) during the interview, ask them at any time. Also, if you want to stop the interview at any time, just let me (us) know. You do not have to answer any questions that you do not want to answer. You may decide not to join the study or you may decide to stop part way through the study. If you decide not to be in the study or decide to leave the study, you will not receive the benefits of being in the study, but you will not be penalized in any other way or lose any other benefits or services.

If you have more questions about the study, you may contact Dr. Mahfuzar Rahman, ICDDR,B, Dhaka (phone: 8811751-60 ext. 2236) or Dr Md Yunus, ICDDR,B, Matlab. If you have other questions related to your rights as a subject in the study, you may contact the ICDDR,B Secretariat, Mr. Bejoy Saha (phone: 8810117).

If you allow your child and other family members to participate in the study, please sign your name or give left thumb impression below.

Signature of the Guardian/ Thumb impression of participant	**Signature of Interviewer**	**Signature of witness**
Date:	**Date:**	**Date:**

Appendix- 1B

আর্ন্তজাতিক উদারাময় গবেষনা কেন্দ্র , বাংলদেশ

সম্মতি পত্র

প্রধান গবেষক ঃ ডা: ম্াহফুজার রহমান

সুচনা উদ্দেশ্যঃ

আস্সালামু আলাইকুম, আমি..... । আমি (আমরা) আই,সি,ডি,ডি,আর,বি / ব্র্যাক এ চাকরী করি। আমার এই কাজে আই,সি,ডি,ডি,আর,বি / ব্র্যাক দ্য সেন্টার ফর ডিজিজ কন্টোল এন্ড প্রিভেনসন্ ইন দ্য ইউনাইটেড স্টেটস এবং দ্য প্রক্টর এন্ড গ্যাম্বল কোম্পানী যৌথ উদ্যোগে এই রিসার্চ করছি। এই প্রজেক্ট এর উদ্দেশ্য হল একটি নতুন প্রজেক্ট এর মাধ্যমে পানিতে আর্সেনিক এর পরিমান কমানো যায় কিনা তা পরীক্ষা করা।

এই গবেষনা কাজটি চলবে চার মাস। প্রতিটি ঘরকেই একটি নতুন পাউডারের প্যাকেট দেয়া হবে তদের টিউবওয়েলের পানিতে মেশানোর জন্য.এবং আমরা আপনার রান্না ও খাওয়ার পানি ব্যবহারের জন্য বলব এবং আমরা বলব যে, ব্যবহাব এর সব পানিই যেন এই পদ্ধতির অর্ন্তভূক্ত হয়।

আপনারা যদি এই গবেষনা কাজে যোগ দিতে সম্মত হন তাহলে আপনাদেরকে নিম্নে বর্নিত কাজ গুলো করতে বলা হবেঃ
প্রথমত, আমরা আপনার পরিবার স্বাস্থ্য এবং পানি সর্ম্পকে প্রশ্ন করবো। আমাদের প্রশ্নের উত্তর দিতে ২০ মিনিটের মত সময় লাগবে। দ্বিতীয়ত, আমরা লটারীর মাধ্যমে নির্বাচন করব যে আপনার বাড়ী কোন গ্রুপে পড়বে। এরপর আমরা আবার এসে এই দ্রব্য কি করে ব্যবহার করতে হয় তা শিখিয়ে দিয়ে যাবো। এতে প্রায় ৩০ মিনিট থেকে ১ ঘন্টার মত সময় লাগবে। তৃতীয়ত, এই প্রজেক্ট যে কেউ প্রতি সপ্তাহে ১০ মিনিটের জন্য আপনাদের বাড়ী আসবেন। তারা আপনাকে জিজ্ঞেস করবেন যে বিগত সাপ্তাহে আপনাদের বাড়ীর কারোর ডায়রিয়া হয়েছিল কিনা, তারা এই নতুন প্রোডাক্ট যা আপনারা আপনাদের পানিকে আরও নিরাপদ করার জন্য ব্যবহার করছেন, সে সংক্রান্ত যেকোন প্রশ্নের জবাব দেবেন। । চতুর্থত, এই প্রজেক্ট এর যে কেউ যেকোন সময় এসে বাড়ীতে রান্না ও খাওয়ার জন্য ব্যবহৃত পানির নমুনা নিয়ে যাবেন। এটা আমাদের বুঝতে সাহয্য করবে যে এই প্রোডাক্টি কত ঘন ঘন ব্যবহার করা হয়েছিল।

এই প্রজেক্ট এ অংশগ্রহনের সিদ্ধান্ত সম্পূর্ণ আপনার উপর নির্ভর করে। যদি আপনি এই গবেষণায় অংশ নিতে আগ্রহী / ইচ্ছুক হন তাহলে তা আপনার ও আপনার পরিবারের কাজে আসতে পারে। এই গবেষণার জন্য ব্যবহৃত পদ্ধতির দ্বারা এবং আপনার পরিবারের রান্না এবং খাবারের জন্য যে পানি ব্যবহার করেন তাতে আর্সেনিক গ্রহন এর মাত্রা কমিয়ে আনতে পারে। এই গবেষণায় সামান্য ঝুঁকির সম্ভাবনা রয়েছে।যদি কোন বাচ্চা এই পাউডারের প্যাকেট থেকে কিছু খেয়ে ফেলে তাহলে এই দ্রব্য এর আয়রন এর মাত্রার জন্য সে বাচ্চা অসুস্থ্য হয়ে পড়তে পারে। এই ঝুঁকি এড়ানোর জন্য এই নমুনাটি একটি প্যাকেটে রয়েছে যা কাঁচি বা আন্যান্য ধারালো জিনিরেস সাহায্যে খোলা যায় এবং আমাদের পরামর্শ হল যে এই প্যাকেটগুলো বাচ্চাদের নাগালের বাইরে রাখা ভালো।

আইন অনুযায়ী আপনাদের পরীক্ষা সমূহের ফলাফল গোপন রাখা হবে। আমরা ফলাফল সমূহ একটি বন্ধ রুমে রাখব। এবং শুধু মাত্র গবেষণা কাজের কর্মীগণ এই গবেষণার ফলাফল দেখতে পাবেন। আপনি / আপনাদের নাম ও অন্যান্য ব্যক্তিগত তথ্যসমূহ কখনই জনসম্মুখে উপস্থাপন করা হবেনা। এই গবেষণার জন্য করা পরীক্ষা সমূহের প্রোডাক্ট, এবং এই প্রোডাক্ট ব্যবহারের জন্য উপকরন সমূহ সম্পূর্ণ বিনামূল্যে আপনাদের সরবরাহ করা হবে।

আমরা আপনাকে একটি সম্মতি পত্র দেব। ইন্টারভিউর সময়ে আপনার আমার / আমাদের প্রতি যদি কোন প্রশ্ন াকে তাহলে তা যেকোন সময়ে করতে পারেন। আপনার যদি ইচ্ছা না করে তহলে আপনি যেকোন প্রশ্নের উত্তর দিতে অস্বীকৃতি জানাতে পারেন। এই গবেষণা কার্যে অংশগ্রহণ না করার সিদ্ধান্ত সম্পূর্ণ আপনার অথবা এই কাজের মাঝামাঝি সময়ে চাইলেও অংগ্রহন করা বাদ দিতে পারেন। আপনি যদি এই গবেষণার অংশ নিতে না চান তাহলে এই কাজে অংশগ্রণের সুযোগ সুবিধা থেকে বঞ্চিত হবেন। কিন্তু এর জন্য আপনারা অপরাপর সুযোগ সুবিধা বা সাহায্য থেকে বঞ্চিত হবেন না

এই গবেষণা প্রসঙ্গে আপনার যদি আর কোন প্রশ্ন থাকে তাহলে আপনি ডঃ মাহ্ফুর রহমান, টেলিঃ ৮৮১১৭৫১- ৬০, এক্স - ২২৩৬ এর সাথে যোগাযোগা করতে পারেন। এই গবেষণার গবেষিত জনগন হিসাবে যদি আপনার আর কোন প্রশ্ন থাকে তাহলে আপনি ডা ঃ মো ঃ ইউনুস এর সংগে যোগাযোগা করতে পারেন।

আপনি যদি আপনার শিশু ও পরিবারের অন্যান্য সদস্যদের এই গবেষণায় অংশগ্রহনে সম্মত হন তাহলে দয়া করে আপনার নাম সই করুন বা বাম হাতের বৃদ্ধাঙ্গুলির ছাপ দিন।

অভিভাবকের স্বাক্ষার	ইনটারভিয়ার স্বাক্ষর	স্বাক্ষীর স্বাক্ষর
নাম ঃ ----------	নাম ঃ ----------	নাম ঃ ----------
তাং ----------	তাং ----------	তাং ----------

APPENDIX 1C:
International Centre for Diarrhoeal Disease Research, Bangladesh: Voluntary Consent Form for Sentinel Mother

Title of the Research Project: Efficacy Flocculent Technology as an Arsenic Mitigation Strategy
Principal Investigator: Mahfuzar Raman, MBBS, PhD

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.

Introduction and Purpose:
Hello, my name is _____. I (we) work with ICDDR,B / BRAC. We are working with ICDDR,B/ BRAC, and the Centers for Disease Control and Prevention in the United States, and the Procter & Gamble Company on a research project. The purpose of our study is to see if a new product can reduce the amount of arsenic in drinking water.
The study will last for four months. Each house in the study will receive packets of a new powder to add to all of their tubewell water. We will ask that all water used for drinking and cooking is treated.
First, we will ask questions about your family, your water, and your health. Second, we will give the person who prepares the drinking and cooking water, a specimen cup to collect a urine sample. It will take about 20 minutes to answer our questions and give us the samples. Third, we will come back and tell you how to use the product to make your drinking and cooking water safer. This visit will take between 30 and 60 minutes. Fourth, someone from the project will come once a week for about 10 minutes. They will ask if anyone in your household has had diarrhea in the last week. They will answer any questions that you have about the product that you are using. Every fourth visit, or once a month, for three months, they will give the person who prepares the drinking and cooking water a specimen cup for the collection of an urine sample. Fifth, someone from the project will come by at an unannounced time to take a sample of the water that your household uses for drinking and cooking. This will help us to see how often the product is being used.

The choice to take part in this project is completely up to you. If you choose to be a part of this study, it may help you and your family. The drinking and cooking water resulting from the different treatment methods used in this study might lower the amount of arsenic that your family consumes. There are some minor risks with the study. If a child eats the contents of the packet of powder given to one group, there is the possibility that the child could become sick from the amount of iron in the product. To prevent this, the product is in a sealed packet that can only be opened with a pair of scissors or other sharp object and we suggest that the packets be kept out of the reach of children.

We will keep the records in locked rooms and only study staff will be allowed to look at them. The tests we do for this study, the products, the supplies needed to use the products will be provided at no cost.

If you have more questions about the study, you may contact Dr. Mahfuzar Rahman, ICDDR,B, Dhaka (phone: 8811751-60 ext. 2236) or Dr Md Yunus, ICDDR,B, Matlab. If you have other questions related to your rights as a subject in the study, you may contact the ICDDR,B Secretariat, Mr. Bejoy Saha (phone: 8810117).

If you are willing to have the person who prepares the drinking and cooking water provide urine samples to us and to be in the study, please sign your name or give left thumb impression below.

Signature/Thumb impression of participant	**Signature of Interviewer**	**Signature of witness**
Date:	**Date:**	**Date:**

Appendix- 1C

আর্ন্তজাতিক উদারাময় গবেষনা কেন্দ্র , বাংলদেশ

সম্মতি পত্র

প্রধান গবেষক ঃ ডা: মাহফুজার রহমান

সূচনা উদ্দেশ্যঃ

আস্সালামু আলাইকুম, আমি..... । আমি (আমরা) আই,সি,ডি,ডি,আর,বি / ব্র্যাক এ চাকরী করি। আমার এই কাজে আই,সি,ডি,ডি,আর,বি / ব্র্যাক দ্য সেন্টার ফর ডিজিজ কন্টোল এন্ড প্রিভেনস্ন ইন দ্য ইউনাইটেড স্টেটস এবং দ্য প্রক্টর এন্ড গ্যাম্বল কোম্পানী যৌথ উদ্যোগে এই রিসার্চ করছি। এই প্রজেক্ট এর উদ্দেশ্য হল একটি নতুন প্রজেক্ট এর মাধ্যমে পানিতে আর্সেনিক এর পরিমান কমানো যায় কিনা তা পরীক্ষা করা।

এই গবেষনা কাজটি চলবে চার মাস। প্রতিটি ঘরকেই একটি নতুন পাউডারের প্যাকেট দেয়া হবে তদের টিউবওয়েলের পানিতে মেশানোর জন্য.এবং আমরা আপনার রান্না ও খাওয়ার পানি ব্যবহারের জন্য বলব এবং আমরা বলব যে, ব্যবহাব এর সব পানিই যেন এই পদ্ধতির অর্ন্তভূক্ত হয়।

প্রথমত, আমরা আপনার পরিবার স্বাস্থ্য এবং পানি সর্ম্পকে প্রশ্ন করবো। মূত্র গ্রহন করার জন্য আমরা একটি নমুনা পাত্র দিব। এই প্রশ্নোত্তর পর্ব ও মূত্র গ্রহনের জন্য ২০ মিনিটের মত সময় লাগবে। দ্বিতীয়ত, আমরা লটারীর মাধ্যমে নির্বাচন করব যে আপনার বাড়ী কোন গ্রুপে পড়বে। এরপর আমরা আবার এসে এই দ্রব্য কি করে ব্যবহার করতে হয় তা শিখিয়ে দিয়ে যাবো। এতে প্রায় ৩০ মিনিট থেকে ১ ঘন্টার মত সময় লাগবে। তৃতীয়ত, এই প্রজেক্ট যে কেউ প্রতি সপ্তাহে ১০ মিনিটের জন্য আপনাদের বাড়ী আসবেন। তারা আপনাকে জিজ্ঞেস করবেন যে বিগত সাপ্তাহে আপনাদের বাড়ীর কারোর ডায়রিয়া হয়েছিল কিনা, তারা এই নতুন প্রোডাক্ট যা আপনারা আপনাদের পানিকে আরও নিরাপদ করার জন্য ব্যবহার করছেন, সে সংক্রান্ত যেকোন প্রশ্নের জবাব দেবেন। প্রতি চতুর্থ ভিজিটে বা মাসে একবার করে তিন মাসের জন্য যারা এই পানি ব্যবহার করেন, প্রজেক্ট কর্মীগণ তাদের মূত্র সংগ্রহের জন্য একটি নমুনা কাপ দেবেন । চতুর্থত, এই প্রজেক্ট এর যে কেউ যেকোন সময় এসে বাড়ীতে রান্না ও খাওয়ার জন্য ব্যবহৃত পানির নমুনা নিয়ে যাবেন। এটা আমাদের বুঝতে সাহয্য করবে যে এই প্রোডাক্টি কত ঘন ঘন ব্যবহার করা হয়েছিল।এই গবেষণার ফলাফল বিশ্লেষণ করতে আমাদের কয়েক মাস সময় লাগবে। কিন্তু বিশ্লেষণ এর পর আমরা আপনাদের কাছে এসে তা ব্যাখা করে যাবো।

এই প্রজেক্ট এ অংশগ্রহনের সিদ্ধান্ত সম্পূর্ণ আপনার উপর নির্ভর করে। যদি আপনি এই গবেষণায় অংশ নিতে আগ্রহী / ইচ্ছুক হন তাহলে তা আপনার ও আপনার পরিবারের কাজে আসতে পারে। এই গবেষণার জন্য ব্যবহৃত পদ্ধতির দ্বারা এবং আপনার পরিবারের রান্না এবং খাবারের জন্য যে পানি ব্যবহার করেন তাতে আর্সেনিক গ্রহন এর মাত্রা কমিয়ে আনতে পারে।

এই গবেষণায় সামান্য ঝুঁকির সম্ভাবনা রয়েছে।যদি কোন বাচ্চা এই পাউডারের প্যাকেট থেকে কিছু খেয়ে ফেলে তাহলে এই দ্রব্য এর আয়রন এর মাত্রার জন্য সে বাচ্চা অসুস্থ্য হয়ে পড়তে পারে। এই ঝুঁকি এড়ানোর জন্য এই নমুনাটি একটি প্যাকেটে রয়েছে যা কাঁচি বা আন্যান্য ধারালো জিনিরেস সাহায্যে খোলা যায় এবং আমাদের পরামর্শ হল যে এই প্যাকেটগুলো বাচ্চাদের নাগালের বাইরে রাখা ভালো।

আমরা রেকর্ড সমুহ বন্ধ ঘরে রাখব এবং শুধু মাত্র গবেষণা কাজের কর্মীগণ তা দেখতে পাবেন।

এই গবেষণার জন্য করা পরীক্ষা সমূহের দ্রব্য, এবং এই দ্রব্য ব্যবহারের জন্য উপকরন সমূহ সর্ম্পূণ বিনামূল্যে আপনাদের সরবরাহ করা হবে।

এই গবেষণা প্রসঙ্গে আপনার যদি আর কোন প্রশ্ন থাকে তাহলে আপনি ডঃ মাহ্ফুর রহমান, টেলিঃ ৮৮১১৭৫১- ৬০, এক্স - ২২৩৬ এর সাথে যোগাযোগা করতে পারেন। এই গবেষণার গবেষিত জনগন হিসাবে যদি আপনার আর কোন প্রশ্ন থাকে তাহলে আপনি ডা ঃ মো ঃ ইউনুস এর সংগে যোগাযোগা করতে পারেন।

আপনি যদি এই গবেষণায় আপনার মূত্র নমুনা দিতে সম্মত হন তাহলে দয়া করে আপনার নাম সই করুন বা বাম হাতের বৃদ্ধাঙ্গুলির ছাপ দিন।

অংশগ্রহনকারীর স্বাক্ষার	ইনটারভিয়ার স্বাক্ষর	স্বাক্ষীর স্বাক্ষর
নাম ঃ ----------	**নাম ঃ** ----------	**নাম ঃ** ----------
তাং ----------	তাং ----------	তাং ----------

Appendix- 1D

আর্ন্তজাতিক উদারাময় গবেষনা কেন্দ্র , বাংলদেশ

সম্মতি পত্র

APPENDIX 1D:
International Centre for Diarrhoeal Disease Research, Bangladesh: Voluntary Consent Form for Environmental Testing of Discarded Flocculent

Title of the Research Project: Efficacy Flocculent Technology as an Arsenic Mitigation Strategy
Principal Investigator: Mahfuzar Raman, MBBS, PhD

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.

Hello, my name is _____. I (we) work with ICDDR,B / BRAC. We are working with ICDDR,B/ BRAC, and the Centers for Disease Control and Prevention in the United States, and the Procter & Gamble Company on a research project. The purpose of our study is to see if a new product can reduce the amount of arsenic in drinking water. The study will last for four months. Your house has been chosen to receive packets of a new powder to add to all of your tubewell water. We will ask that all water used for drinking and cooking is treated.

Procedures:
If you will use the packets of powder to treat your water, we will ask you to do these things:
Dispose of all of your used flocculent in a container that you will locate out of the reach of children and animals.
Only dispose of the used flocculent in this container.
Add equal amounts of soil collected from your household to the container where you will add the used flocculent.
It will take us several months to understand the results of this study. But when we do, we will explain the results to you.

Risks and Benefits:
The choice to dispose of the flocculent in a designated container is completely up to you. If you choose to dispose of the flocculent in a designated container with soil, it will help us to understand what happens to the flocculent after it is discarded. This will help us to know if this product would be a good choice to help lower the amount of arsenic that your family consumes.
We do not know if there are risks to disposing of the flocculent in a designated container.

Confidentiality:
The results from the samples will be kept private to the extent allowed by law. We will keep the records in locked rooms and only study staff will be allowed to look at them. Your name and other private facts will not appear when we discuss this study publicly or when we publish the results.

Cost/ Payment:
The tests we do for this study, the products, the supplies needed to use the products will be provided at no cost.

Right to Refuse or Withdraw:
We will leave a copy of the consent form with you. If you have questions for me (us), ask them at any time. Also, if you do not want to participate by disposing of your discarded flocculent and soil samples in a designated container, just let me (us) know. You may decide not to dispose of your used flocculent in a designated container or you may decide stop disposing of your used flocculent in a designated container, part way through the study. If you decide not to dispose of your used flocculent in a designated container, you will still receive the benefits of being in the study, and you will not be penalized in any other way or lose any other benefits or services.

Persons to Contact:
If you have more questions about the study, you may contact Dr. Mahfuzar Rahman, ICDDR,B, Dhaka (phone: 8811751-60 ext. 2236) or Dr Md Yunus, ICDDR,B, Matlab. If you have other questions related to your rights as a subject in the study, you may contact the ICDDR,B Secretariat, Mr. Bejoy Saha (phone: 8810117).

Agreement to Participate:
If you are willing to dispose of the flocculent in a designated container with soil and have samples collected, please sign your name or give left thumb impression below.

Signature/Thumb impression of participant	**Signature of Interviewer**	**Signature of witness**
Date:	**Date:**	**Date:**

প্রধান গবেষক ঃ ডাঃ মাহফুজার রহমান

সূচনা উদ্দেশ্যঃ

আস্সালামু আলাইকুম, আমি..... । আমি (আমরা) আই,সি,ডি,ডি,আর,বি / ব্র্যাক এ চাকরী করি। আমার এই কাজে আই,সি,ডি,ডি,আর,বি / ব্র্যাক দ্য সেন্টার ফর ডিজিজ কন্টোল এন্ড প্রিভেনস্ন ইন দ্য ইউনাইটেড স্টেটস এবং দ্য প্রক্টর এন্ড গ্যাম্বল কোম্পানী যৌথ উদ্যোগে এই রিসার্চ করছি। এই প্রজেক্ট এর উদ্দেশ্য হল একটি নতুন প্রজেক্ট এর মাধ্যমে পানিতে আর্সেনিক এর পরিমান কমানো যায় কিনা তা পরীক্ষা করা।

এই গবেষনা কাজটি চলবে চার মাস ।প্রতিটি ঘরকেই একটি নতুন পাউডারের প্যাকেট দেয়া হবে তদের টিউবওয়েলের পানিতে মেশানোর জন্য.এবং আমরা আপনার রান্না ও খাওয়ার পানি ব্যবহারের জন্য বলব এবং আমরা বলব যে, ব্যবহাব এর সব পানিই যেন এই পদ্ধতির অর্ন্তভূক্ত হয়।

আপনার বাড়ী নির্বাচিত হয়েছে সেই গ্রুপে যে আপনারা আপনাদের ব্যবহৃত টিউবওয়েলের পানিতে প্যাকেট করা নতুন পাউডার ব্যবহার করবেন। আমরা খাবার এবং রান্না করার সকল পানি এই পাউডার দিয়ে পরিশোধন করার জন্য বলব।

কার্যপ্রনালী:

আপনি যদি পানি পরিশোধনের জন্য প্যাকেটের পাউডার ব্যবহার করেন তাহলে আপনাকে নিম্নলিখিত কাজগুলো করার জন্য বলা হবে ঃ

আপনার বাড়ীর নিকটে একটি গর্ত করে তাতে ব্যবহারকৃত ফ্লকুলেন্ট ফেলুন।

কেবলমাত্র ব্যবহারকৃত ফ্লকুলেন্টই উক্ত গর্তে ফেলুন।

গবেষনার ফলাফলের জন্য আমাদের কয়েক মাস সময় লাগবে। কিন্তু যখনই ফলাফল পাওয়া যাবে তখনই আপনাদের তা জানান হবে।

ঝুঁকি এবং উপকারিতাসমুহ:

ব্যবহৃত ফ্লকুলেন্ট আলাদা গর্তে ফেলানো সম্পূর্ণ আপনার উপর নির্ভর করছে। আপনি যদি ব্যবহৃত ফ্লকুলেন্ট আলাদা গর্তে ফেলান তাহলে পরিত্যক্ত ফ্লকুলেন্ট শেষ পর্যায়ে কি অবস্থায় পরিনত হয় তা আমাদের বুঝতে সাহায্য করবে। এই সামগ্রীটি আর্সেনিকের পরিমান কমানোর ব্যাপারে কতটুকু কার্যকরী এই প্রক্রিয়ার মাধ্যমে আমরা তা জানতে পারবো।

গর্তে ব্যবহারকৃত ফ্লকুলেন্ট ফেলানো ঝুঁকিপূর্ণ কিনা আমরা তা জানি না।

গোপনীয়তা:

আইন অনুযায়ী গর্ত থেকে নেয়া উপকরনের পরীক্ষা সমূহের ফলাফল গোপন রাখা হবে। আমরা ফলাফল সমূহ একটি বন্ধ রুমে রাখব। এবং শুধু মাত্র গবেষণা কাজের কর্মীগণ এই গবেষণার ফলাফল দেখতে পাবেন। গবেষনাটি জনসম্মুখে আলোচনার সময় অথবা ফলাফল প্রকাশের সময় আপনি / আপনাদের নাম ও অন্যান্য ব্যক্তিগত তথ্যসমূহ কখনই জনসম্মুখে উপস্থাপন করা হবেনা।

খরচ/মুল্য পরিশোধ:

এই গবেষণার জন্য করা পরীক্ষা সমূহের প্রোডাক্ট, এবং এই প্রোডাক্ট ব্যবহারের জন্য উপকরন সমূহ সর্ম্পূণ বিনামূল্যে আপনাদের সরবরাহ করা হবে।

না করার/ ত্যাগ করার অধিকার:

আমরা আপনাকে একটি সম্মতি পত্র দেব। ইন্টারভিউর সময়ে আপনার আমার / আমাদের প্রতি যদি কোন প্রশ্ন াকে তাহলে তা যেকোন সময়ে করতে পারেন। আপনার যদি ইচ্ছা না করে তহলে আপনি যেকোন প্রশ্নের উত্তর দিতে অস্বীকৃতি জানাতে পারেন। এই গবেষণা কার্যে অংশগ্রহণ না করার সিদ্ধান্ত সম্পূর্ণ আপনার অথবা এই কাজের মাঝামাঝি সময়ে চাইলেও অংগ্রহন করা বাদ দিতে পারেন। আপনি যদি এই গবেষণার অংশ নিতে না চান তাহলে এই কাজে অংশগ্রণের সুযোগ সুবিধা থেকে বঞ্চিত হবেন। কিন্তু এর জন্য আপনারা অপরাপর সুযোগ সুবিধা বা সাহায্য থেকে বঞ্চিত হবেন না

এই গবেষণা প্রসঙ্গে আপনার যদি আর কোন প্রশ্ন *াকে তাহলে আপনি ডঃ মাহফুর রহমান, টেলিঃ ৮৮১১৭৫১- ৬০, এক্স* - ২২৩৬ অথবা ডা ঃ মো ঃ ইউনুস, মতলব এর সাথে যোগাযোগা করতে পারেন। এই গবেষণার গবেষিত জনগন হিসাবে আপনার অধিকার সম্পর্কিত যদি কোন প্রশ্ন থাকে তাহলে আপনি আই,সি,ডি,ডি,আর,বি সেক্রেটারী, মিঃ বিজয় সাহা (ফোনঃ ৮৮১০১১৭)এর সংগে যোগাযোগা করতে পারেন।

আপনি যদি আলাদা গর্তে ব্যবহারকৃত ফ্লকুলেন্ট ফেলতে এবং তা হতে নমুনা দিতে সম্মত হন তাহলে দয়া করে আপনার নাম সই করুন বা বাম হাতের বৃদ্ধাঙ্গুলির ছাপ দিন।

অংশগ্রহনকারীর স্বাক্ষার	ইনটারভিয়ার স্বাক্ষর	স্বাক্ষীর স্বাক্ষর
নাম ঃ ----------	**নাম ঃ** ----------	**নাম ঃ** ----------
তাং ----------	তাং ----------	তাং ----------

Appendix 2

Baseline Questionnaire

Efficacy Flocculent Technology as an Arsenic Mitigation Strategy

Household ID _____ Date of interview _____ Interviewer _____

Name of mother _____ Name of father _____

Address _____ Tubewell that supplies water _____

1.1 How many people are currently living in the household? _____

1.2 How many children under the age of 5 years? _____

1.3 How many children under the age of 1 year? _____

1.4 What language is spoken in the home? _____

1.5 How many people obtain their water from the same tubewell? _____

1.6 How long has the family been drinking water from this tubewell? _____

1.7 List the source(s) of water for the following:

1.7a Drinking: ____ *(1=tubewell only, 2=surface water only, 3=both, 4=neither)*

1.7b Cooking: ____ *(1=tubewell only, 2=surface water only, 3=both, 4=neither)*

1.7c Bathing: ____ *(1=tubewell only, 2=surface water only, 3=both, 4=neither)*

1.8 Does the household currently store water? _____(*1=yes, 2=no, 3=don't know*)

1.8a *If yes*, what is used to store water?

☐ plastic container, uncovered ☐ plastic container, covered
☐ aluminum container, uncovered ☐ aluminum container, covered
☐ clay container, uncovered ☐ clay container, covered
☐ other _____ (describe)

1.9 Is anything done to treat the water used for drinking and cooking before it is drunk or used to cook?

_____ (*1=yes, 2=no, 3=don't know*)

1.9a *If yes*, what is done to the water before it is used for drinking or cooking?

☐ water is boiled
☐ chlorine is added to water
☐ water is filtered through structural filtering system
☐ water is filtered through cloth
☐ alum is added
☐ flocculent product is added
☐ other _____*(describe)*

1.10 How is drinking water dispensed from the vessel?

☐ scooped out with a glass or cup
☐ poured from the top
☐ poured through a tap or spigot
☐ other _____*(specify)*

Appendix 2: Baseline Questionnaire (continued)

1.11 List all of the people who live in this household (share a common cooking pot):

ID Number	Name	Sex	Age	Birth date	Does this person leave the home during the day? 1=yes, 2=no, 3=don't know

Appendix 2: Baseline Questionnaire (continued)

1.12 Can the mother of the youngest child in the household read?
1. yes
2. no
3. don't know

1.13 Can the mother of the youngest child in the household write?
1. yes
2. no
4. don't know

1.14 What is the highest level of education obtained by the mother of the youngest child?
1. no schooling
2. some primary education
3. finished primary school
4. some secondary school
5. finished secondary school

1.15 Which of the following describes the occupation of the father of the youngest child?
1. unemployed
1. employed on daily wages
2. salaried employee
3. shopkeeper
4. other (*please specify*) _____

1.16 Considering all of the earning members of the household, in which of the following groups would you place your household's monthly income?
1. < 2000 Tk
2. 2001-3000 Tk
3. 3001-4000 Tk
4. 4001-5000 Tk
5. 5001-10,000 Tk
6. >10,000 Tk
7. refused to respond

1.17 What kind of toilet facilities does your household use?
1. flush toilet
2. toilet without flush tank
3. pit latrine
4. none
5. other (*specify*) _____

1.18 Where do most members of your household bathe?
1. running stream
2. still pond/ lake
3. other (*specify*) _____

1.19 Do you use soap?
1. yes
2. no
3. don't know

1.19a *If yes*, when do you use soap?_____*(record response)*

Appendix 2: Baseline Questionnaire (continued)

Observations:

2.0 Is the water storage container same as described?	1. Y	2. N	3. N/A
2.1 Is there water available for handwashing?	1. Y	2. N	3. N/A
2.2 Is there soap available for handwashing?	1. Y	2. N	3. N/A
2.3 Are there areas of visible animal and human feces?	1. Y	2. N	3. N/A

2.4 Describe the general sanitary condition of the household: (*check appropriate box*)

□ very clean □ clean □ dirty □ very dirty

Appendix 3: **Weekly Data Collection Form**

Efficacy of Flocculent Technology as an Arsenic Mitigation Strategy

Household ID _____ Date of interview _____ Interviewer _____

Name of mother _____ Name of father _____

Address _____ Tubewell that supplies water _____

1. In the last 7 days, has anyone in the household had diarrhea? *(3 or more loose stools in 24 hrs)*

   1) Y 2) N 3) N/A

   (If no, end questionnaire here)

2. Was this a new episode of diarrhea? (*circle N if this episode was previously reported*)

   1) Y 2) N 3) N/A

3. During how many days since our last visit has a member of the household had diarrhea?

   _____ days

4. Did the person lose noticeable weight during the episode of diarrhea?

   1) Y 2) N 3) N/A

5. Did you take the person/ did the person go to a healthcare provider for the diarrheal illness?

   1) Y 2) N 3) N/A

6. Did the person stay in a hospital for the diarrheal illness?

   1) Y 2) N 3) N/A

7. Did the person take any medicine for the diarrheal illness?

   1) Y 2) N 3) N/A

8. How many days of school/ work did the person miss during the last week due to the diarrheal illness? _____ days missed

Appendix 4: Assessment and Acceptability of Intervention Product Data Collection Form
Efficacy of Flocculent Technology as an Arsenic Mitigation Strategy

Household ID _____ Date of interview ___/___/___
Interviewer_____

Name of mother _____ Name of father _____

Address _____ Tubewell that supplies water _____

Interviewee:
☐ father ☐ mother ☐ daughter/ son ☐ other
(*specify*)_____

1. What do members of your family say about the product(s) that you are using to make your drinking water safer?

_____

_____

_____

_____

2. What do members of your family say about the purified water?

_____

_____

_____

_____

_____

3. How much water did your family use for drinking yesterday?
☐ less than 1water vessel
☐ 1 water vessel
☐ more than 1 water vessel, but less than 2 water vessels
☐ 2 water vessels
☐ more than 2 water vessels, but less than 3 water vessels
☐ 3 water vessels
☐ more than 3 water vessels
☐ don't know

4. Size of water vessel:
☐ small (7L)
☐ medium (10 L)
☐ large (15 L)
☐ 20 L
☐ 35 L
☐ unknown

Appendix 4: Assessment and Acceptability of Intervention Product (continued)

5. How much water did your family use for cooking yesterday?
   - ☐ less than 1water vessel
   - ☐ 1 water vessel
   - ☐ more than 1 water vessel, but less than 2 water vessels
   - ☐ 2 water vessels
   - ☐ more than 2 water vessels, but less than 3 water vessels
   - ☐ 3 water vessels
   - ☐ more than 3 water vessels
   - ☐ unknown

6. Did you treat any of your drinking water with the product that we gave you?
   - ☐ yes
   - ☐ no

   6.a. *If yes*, how much of your drinking water in the last week did you treat?
   - ☐ all of it
   - ☐ some of it
   - ☐ none of it
   - ☐ don't know
   - ☐ not applicable

7. Did you treat your cooking water?
   - ☐ yes
   - ☐ no

   7.a. *If yes*, how much of your water used for cooking did you treat in the last week?
   - ☐ all of it
   - ☐ some of it
   - ☐ none of it
   - ☐ don't know
   - ☐ not applicable

8. When did you last treat your water with the product?
   - ☐ this morning
   - ☐ yesterday afternoon
   - ☐ yesterday morning
   - ☐ day before yesterday
   - ☐ other (*specify*) _____

9. Who treated the last vessel of drinking water for the house?
   - ☐ mother
   - ☐ other adult
   - ☐ child
   - ☐ don't know
   - ☐ not applicable

10. *If a child* treated the last vessel of drinking water, how many years old is the child? _____

11. In what vessel do you store treated water? (*describe*)

_____

Appendix 4: Assessment and Acceptability of Intervention Product (continued)

12. Is storage vessel for treated water covered when not in use?
- ☐ always covered
- ☐ sometimes covered
- ☐ never covered
- ☐ don't know
- ☐ not applicable

13. *If covered*, with what is vessel covered? (*describe*) _____

Now we will ask what your husband, your children, and you think about the product that we gave you to treat your water:

14a. Does your husband prefer drinking treated water or untreated water?
- ☐ Treated
- ☐ Untreated
- ☐ Unsure

14b. Do your children prefer drinking treated water or untreated water?
- ☐ Treated
- ☐ Untreated
- ☐ Unsure

14c. Do you prefer drinking treated water or untreated water?
- ☐ Treated
- ☐ Untreated
- ☐ Unsure

15a. What does your husband think about the appearance of treated water compared to untreated water?
- ☐ Treated water looks better
- ☐ Treated and untreated water look about the same
- ☐ Treated water looks worse
- ☐ Unsure

15b. What do your children think about the appearance of treated water compared to untreated water?
- ☐ Treated water looks better
- ☐ Treated and untreated water look about the same
- ☐ Treated water looks worse
- ☐ Unsure

15c. What do you think about the appearance of treated water compared to untreated water?
- ☐ Treated water looks better
- ☐ Treated and untreated water look about the same
- ☐ Treated water looks worse
- ☐ Unsure

16a. What does your husband think about the taste of treated water compared to untreated water?
- ☐ Treated water tastes better
- ☐ Treated and untreated water taste about the same
- ☐ Treated water tastes worse
- ☐ Unsure

Appendix 4: Assessment and Acceptability of Intervention Product (continued)

16b. What do your children think about the taste of treated water compared to untreated water?

- ☐ Treated water tastes better
- ☐ Treated and untreated water taste about the same
- ☐ Treated water tastes worse
- ☐ Unsure

16c. What do you think about the taste of treated water compared to untreated water?

- ☐ Treated water tastes better
- ☐ Treated and untreated water taste about the same
- ☐ Treated water tastes worse
- ☐ Unsure

17a. What does your husband think about the smell of treated water compared to untreated water?

- ☐ Treated water smells better
- ☐ Treated and untreated water smells about the same
- ☐ Treated water smells worse
- ☐ Unsure

17b. What do your children think about the smell of treated water compared to untreated water?

- ☐ Treated water smells better
- ☐ Treated and untreated water smells about the same
- ☐ Treated water smells worse
- ☐ Unsure

17c. What do you think about the smell of treated water compared to untreated water?

- ☐ Treated water smells better
- ☐ Treated and untreated water smells about the same
- ☐ Treated water smells worse
- ☐ Unsure

18a. Does your husband think that treated water is healthier than untreated water?

- ☐ yes
- ☐ no
- ☐ there is no difference
- ☐ unsure

18b. Do you think that treated water is healthier than untreated water?

- ☐ yes
- ☐ no
- ☐ there is no difference
- ☐ unsure

19. Additional comments about the water treatment process:

_____

_____

_____

_____

_____

Thank you very much for your time and comments

Appendix 5: Drinking Water Sample Collection Form
Efficacy Flocculent Technology as an Arsenic Mitigation Strategy

Household ID _____ Date of collection___/___/___ Time of collection: __:__am/pm

Name of mother _____ Name of father _____

Address _____ Tubewell that supplies water _____

Name _____ Household ID _____

Village _____ Volume of water collected:_____ml

Did you treat this water?

☐ Yes
☐ No
☐ Don't know

If yes, how was water treated?
☐ added intervention combination chlorination-flocculent product
☐ boiled
☐ filtered
☐ traditional arsenic mitigation strategy (*describe*)_____

Check List

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

Face Sheet Included ☐

1. Approval of the Division Director on Face Sheet ☐

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

4. Table of Contents ☐

5. Project Summary ☐

6. Literature Cited ☐

7. Biography of Investigators ☐

8. Ethical Assurance ☐

9. Consent Forms ☐

10. Detailed Budget ☐

Procter&Gamble
Product Safety & Regulatory Affairs
Central Product Safety, ETC

Sylvia Gimeno - Diederik Schowanek
May 30, 2002

Environmental Research Program for PŪR powder

Drinking Water Preparation Technology for Developing Countries

1. Summary

- An initial environmental ('Tier 0') assessment for PUR powder suggests that the technology will be environmentally acceptable, and that no significant environmental issues are to be expected.

The use of the product for local *test markets* in developing countries can be approved from an environmental point of view.. The current generic assessment (Sections 1-5) is based on available literature/MSDS data and data estimated from mathematical models, assuming river water is purified and no abnormally high levels of Arsenic are present in this source water. It also assumes that after the use of PUR powder, the resulting waste flocculent (floc) will be disposed and that it will end up mostly reaching the surrounding soil. Arsenic-contining well water is considered in Section 6.

For *national expansion* of the PUR technology in developing countries a more detailed and quantitative test program on the waste flocculent is recommended, as outlined in this memo. The objective of this testing program will be to derive a realistic PNEC for soil and septic tanks/latrines, which will be used to assess the environmental safety of the floc. In order to reduce environmental impact by the non-biodegradable/non recyclable sachet, it is recommended to install a collection system for the (refundable) sachets.

- In combination with realistic usage habits, to be gathered from consumer tests, a truly quantitative risk assessment ('Tier 1') can then be performed.

- The results of the Tier 1 assessment will define eventual additional testing needs ('Tier 2') (not presented) to refine the risk assessment if necessary.

The floc is expected to reach as 'indirect discharge' the soil and the water, since the floc is recommended to be disposed into the latrine or toilet. Possible 'direct discharge' into the soil and in the waters surfaces, which may be a common habit in some geographies are also considered

2. Background

2.1 Product use and functioning

The consumer mixes the content of one PUR sachet with 10 liter of water, stirs for 30 seconds and applies intermittent stirring for 15 minutes. This last is repeated three times. After settling, a waste flocculent (floc) is filtered over a cloth, and discarded. The water is then suitable for human consumption after 30 minutes.

2.2 PUR powder formulation

Each PUR sachet contains approximately 5.4 g powder (dose for purifying 10 liter source water) with the following components (Table 1).

Table 1

Chemical	Typical Level of use in DW[1] (mg/L)[2]
Iron (III) sulphate (i.e. ferric)	100-600
Sodium carbonate	50-150
Bentonite	200
Chitosan*	-
Polyacrylamide	1/4[3]
Calcium hypochlorite	10[2], 0.5-5[4]
Potassium permanganate	15

[1]-DW - drinking water, [2]-see NSF documentation- Drinking Water Treatment Chemicals - Health Effects, ANSI/NSF Standard 60-2001. Publ. NSF International, Ann Arbor, MI, USA. [3]-Depending on use and monomer content. [4]-EPA Guidance Manual, Alternative Disinfectants and Oxidants, USEPA, April 1999.

* expected is that Chitosan will be removed from the final formulation and that the concentrations of all other chemicals will decrease by at least 10-40%.

2.3 Sachet composition

The sachets containing the powder are layered (and child resistant) and consist of the following materials PET23/PE17/AL9/Coex21/LLDPE38 (PET=polyethylene terephthalate, PE=polyethylene, AL=aluminum foil, Coex, LLDPE=linear low density polythylene, the numbers refer to the thickness in microns of each layer). The theoretical empty sachet weight is 1.24 grams per sachet based on target weight and size.

2.4 Waste flocculent (floc) composition

The floc contains the potential organic, inorganic, and biological contaminants entrapped from the starting water, and the precipitated flocculent/coagulant/disinfectant. Each floc will have a variable volume of approximately 50 mL, depending on the water content of each floc. The composition of a typical floc is given in Annex 1. Note that this is based on an earlier formulation which did not contain potassium permanganate, therefore the actual levels of Mn may not be reflected in Annex 1.

Annex 2 gives the typical composition of sludge issued from waste water treatment plants. Sewage contains approximately 1000 mg l^{-1} of impurities of which about 2/3 are organic, thus the sewage consists of 99 % of H_2O and 0.1% total solids upon evaporation. The composition of sludge varies considerably depending on the source of sewage. Where industrial sewage contributes and mixes with the domestic sewage at water treatment works, higher concentrations of heavy metals such as Pb, Zn, and Cu are expected in the sludge. Thus the produced sludge requires safe and economical disposal (1). As for industrial and domestic sludge produced in the waste water treatment plants, the (long term) environmental impacts of the floc produced by using PUR, should be considered as well.

The levels of heavy metals in the floc will depend on the source water used. In order to represent a generic situation, river water will be used to produce the floc test material.

3. Disposal scenarios/ recommendations

3.1 Routes of disposal of the waste flocculent (floc)

When accessible, the recommended disposal route for the waste flocculent is via septic tank (or latrine, available to up to 70% of the population in Guatemala), or toilet.. It should also be stressed that the floc should not be buried in a plastic bag, nor in the sachet, since these materials are non biodegradable and the process of biodegradation of the PUR sludge would be extremely slowed down.

The environmental risk assessment will focus on ensuring product safety under those disposal scenarios. Box 1 (section 5) gives the estimated percentages of each envisaged disposal routes. Realistic disposal scenarios should be provided in order to refine the risk assessment.

3.2 Disposal of the sachet - Recommendation

Most of the components of the sachet are recyclable, but only when considered separately. Therefore, due to its multilayer structure, the PUR sachet is not recyclable. It is recommended that the sachet is disposed via the municipal solid waste and not disposed in the environment, since it will not biodegrade. Volume forecasts for 2003 (B. Ellis, Feb 4, 2002) envisage 38.000.000 sachets used by 2,000,000 households. This will generate 46,12 tons of non-recyclable, non-biodegradable solid waste. Since Guatemala lacks adequate system for the collection and disposal of solid wastes, especially in the rural areas where PUR powder is expected to be most used, the sachets are suspected to be lost in the environment.

For perspective, the solid waste generated by Guatemala is estimated to be 1,260,000 tons per year (278,000 t in the urban area, 608,000 tons in the rural area and 374,000 tons in the metropolitan area) [#]. The solid waste generated by the PUR sachet will contribute to 0.007% of the total solid waste. Guatemala City has a single point of recycling soild waste, called "El trebol", and is able to recycle 1200 tons of solid waste per day. The rest is burnt in the open air or deposited in one of the 500 illegal landfills located around the city [#].

[#] http://www.ecouncil.ac.cr/centroam/conama/conam.htm

4. Tier O assessment of PUR ingredients

4.1 Amount of floc produced

For perspective, the United States and the European Union (15 countries) produce each yearly an amount of sludge from waste water treatment plants of about 6.5 million tons (dry solids). In the UK, it is estimated that 1.5 million tons of sludge are produced annually. In Europe, at least, the production of sewage sludge is expected to increase as a greater proportion of sewage is treated and as higher treatment standards are applied under the phased implementation of the European Community Urban Wastewater Treatment Directive and other related Directives[#].

4.2 Estimation of environmental exposure - Worst case calculation for Tier 0

The Tier 0 risk assessment is principally based on the assessment of calcium hypochlorite, since it is the most toxic chemical. Some initial realistic worst case calculations were performed in the absence of precise user-data; the estimated maximum use of 2 sachets per person/day. A house hold is assumed to be composed of 5 people.

Septic tanks: The tank/latrine volume is assumed to be of 1 m3. This results in a spent flocculent loading rate of max. 55 g/m3.day, of which up to 2% is calcium hypochlorite, i.e. 1.1 mg/l.d (assuming no decay).

Soil and agricultural land: The average soil around a house is assumed to be 100 m2, with a bulk density 1.5 kg/l and a depth of 10 cm. This gives a loading rate of ~ 20 kg spent flocculent/15000 kg soil.year = ~ 1.3 g/kg soil.year of which up to 2% is calcium hypochlorite, i.e. 0.03 g/kg soil.year (assuming no decay).

4.3 Ecotoxicity data summary

Table 2. Overview of acute ecotoxicity data for PUR ingredient used for Tier 0 assessment.

Component (CAS #)	Bio/degradability/ Chemical reaction	EC50 algae (mg/L)	LC50 invertebrates (mg/L)	LC50 FISH (mg/L)	Bioaccumulation potential
Iron (III) sulphate (10028-22-5)	n.a.	n.d.	n.d.	n.d.	n.d.
Sodium carbonate (144-55-8)	n.a.	> 250 (3)	2350-4200 (7)	7700 (7)	*VERY LOW (6,8)*
Bentonite (1302-78-9)	n.a.	*30 (8)*	*22 (8)*	*> 100 (8)*	*VERY LOW (6,8)*
Chitosan* (9012-76-4)	Moderately T0.5 soil > 60 days*	> 100 ?	> 100 ?	> 100 ?	
Polyacrylamide (monomer:	Moderately (5) *(monomer FAST 4)*	> 100 ?	> 100 ?	> 100 (5)	*Monomer: VERY LOW (6,8)*
Calcium Hypochlorite (7778-54-3)	immediate chemical reaction (2)	0.2 (9)	0.005 (9)	0.05 (2)	*VERY LOW (6,8)*
Potassium permanganate	*FAST (4)*	*602 (8)*	*1020 (8)*	0.75-5 (1)	*0.9, BCF 8 (6)*

n.a.: not applicable, n.d : no data found (for Fe(III)sulfate toxicity will be low due to low solubility)
* : estimated value based on data for similar materials
References: italics: predicted/modeled result.
1. MSDS Fischer, 2. Hypochlorite Scientific Support Dossier, AISE, 3. EU Ecolabel DID list, 4. SRC Biowin v3.67 Biodegradation model, 5. Data for acrylamide (CAS 79-06-1) in MSDS J.T. Baker, 6. SRC BCF v2.13, 7. Fischer MSDS , 8. ECOSAR log KOW ECOSAR v0.99e 9. ERA report for sodium hypochlorite

THE INGREDIENTS FE(III)SULFATE (FLOCCULENT), SODIUM CARBONATE (CORROSION INHIBITOR), BENTONITE AND CHITOSAN (FOOD ADDITIVE AND ANTIMICROBIAL AGENT) HAVE A HISTORY OF SAFE USE IN DRINKING WATER/FOOD PREPARATION. THEY HAVE A LOW ORDER OF TOXICITY, AND ARE NOT EXPECTED TO POSE ANY PARTICULAR ECOTOXICITY CONCERN. POTASSIUM PERMANGANATE AND CALCIUM HYPOCHLORITE ARE BOTH HARMFUL TO AQUATIC LIFE IN VERY LOW CONCENTRATIONS.

HTTP://OURWORLD.COMPUSERVE.COM/HOMEPAGES/JMPETT/SLUDGEAN.HTM

An initial environmental ('Tier 0') assessment for PUR powder suggests that the technology will be environmentally acceptable, and that no significant environmental issues are to be expected.

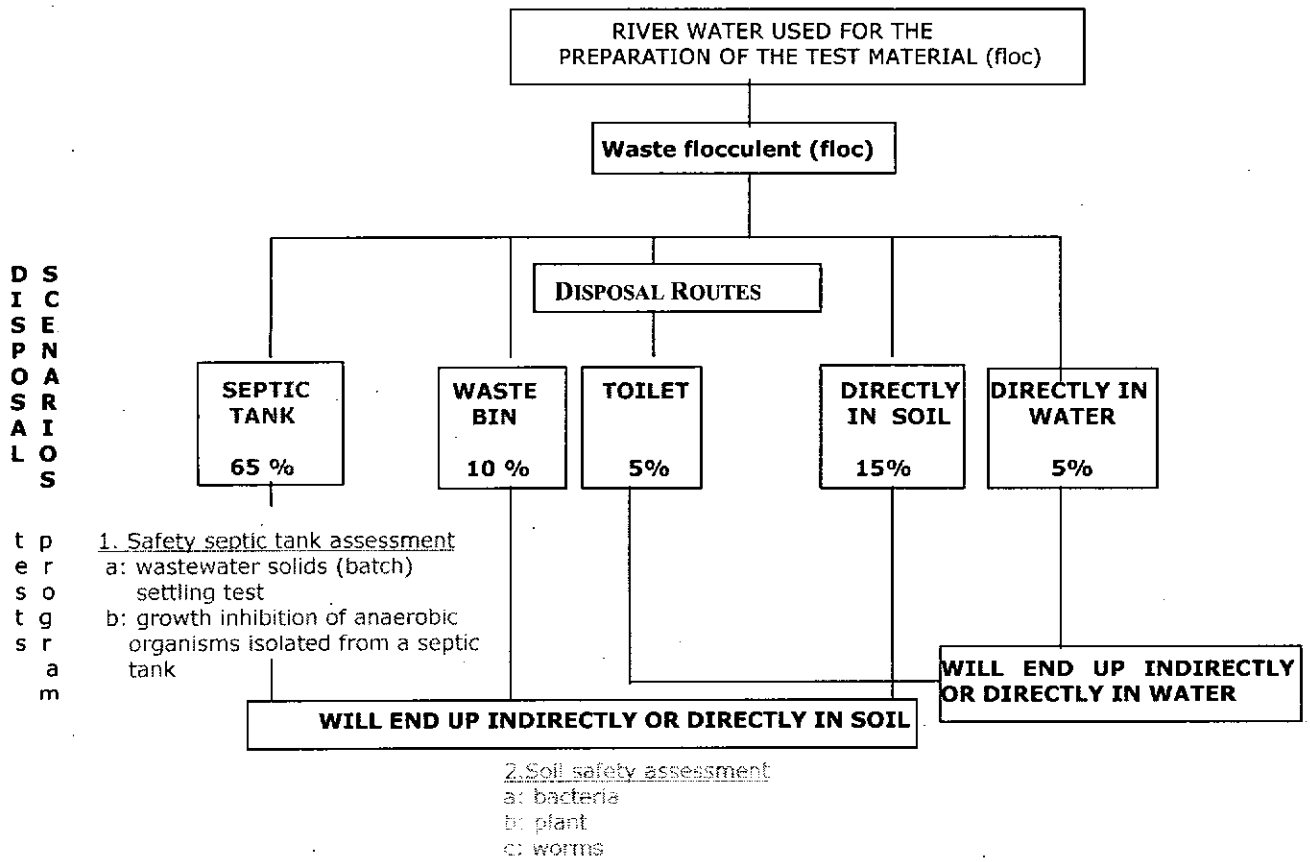
5. Generic Tier 1 Risk assessment

5.1 Ecotoxicity test designs for Tier 1

The next assessment tier (Tier 1) will require testing on the flocculent to include the probable effect of interactions between the PUR ingredients (Table 2). However, to better understand the effects of active chlorine in the tests, fresh and aged flocculent should be used at least in the short term tests.

Box 1 identifies the tests that could be conducted to initially ensure the environmental safety of the floc. A range finding procedure will be used prior to each definitive tests, if necessary. Dosage levels for the testing will be determined based on estimated realistic use scenarios and effects in the range finding tests as to derive a reliable PNEC.

Box 1



1. For the septic tank safety testing two functional endpoints will be assessed: effect on flocculation/settling and effect on glucose uptake. The levels of sulphide ions should be monitored during the duration of the test.

2. Assessment of the effects of flocs in soil organisms is suggested, since most of the floc will be ending up in the soil (in)directly. For the soil safety testing The use of 3 test levels (microorganisms, worms, plants) will allow to derive a reliable estimate of $PNEC_{soil}$.

   In order to evaluate the *fertilizing value* of PUR sludge (spent flocculent), a study was commissioned to Rainbow Associates (horticultural product consultants in the UK, A. Rainbow, Report No. RRP20101, Feb 14, 2001). Detailed results on chemical composition are shown in Annex 1. This shows that the flocculent (as prepared with tap water to which 5 ppm humic acid was added to form a crude model surface water) had no particular fertilizer quality. It was therefore concluded that the floc could not stand as a fertilizer alone. The chemical analysis also shows that the floc contains nothing that would be obviously harmful/phytotoxic, since most potentially toxic elements were undetectable.

Table 3 inventories the tests that could be conducted and. It must be stressed that actual costs may be ca. 20% higher since additional handlings may be required for the generation of the test material. Prices indicated in Table 3 do not include analytical measurements for (in)organics in source, purified water and floc .

Table 3. Summary of 'Tier 1' tests for waste flocculent of PUR powder.

Type of test	1. Septic tank safety	2a. EC50 soil microbiology	2b. EC50 Plant germination	2c. LC50 Earth-worm toxicity
Contract lab	TNO *	TNO	TNO	TNO
Protocol	a. Standard methods 2710C & 2710E, NEN 6233; Activated sludge volume and settling rate b. ISO 13641-1 Toxicity to anaerobic bacteria, at high biomass concentrations**	OECD 216 & 217: Soil Microorganisms, Carbon and Nitrogen Transformation Tests (1 type of soil, nitrate analysis)	OECD 208: Terrestrial Plants (3 plants), Growth Test	OECD 207 Earthworm: Acute Toxicity Tests
	48 hours	28 days	14 days	14 days
Dosing range (t.b.d.)	0 – 1000 mg/l	0 – 5000 mg/kg	0 – 5000 mg/kg	0 – 5000 mg/kg
Cost in USD (ex vat)				
Timeline****	15 weeks	15 weeks	18 weeks	14 weeks
Possible starting period	Within 2 months but preferably July 2002	May 2002	April 2002	April 2002

* TNO Netherlands Organisation for Applied Scientific Research.
** including sulfide monitoring
*** The effect of active chlorine in the short microbial assays should be investigated, therefore both fresh and spent flocculent will need to be tested separately
**** Time between signature of contract and reporting.

The following procedure is proposed for the preparation of representative test material (exact procedure to be agreed with the contract lab). Results from the four Hydropure focus groups in rural Guatemala (San Juan Sacatepequez, June 29, 2000) reveal that water is mainly collected from their roofs or mountain streams, or from a well supplemented with spring water. These waters are generally considered drinkable but not really clean (K.B. Baier). For practical reasons and for being conservative it is recommended that the water used for the preparation of the floc to be tested in the contract laboratory should be collected from a river which is believed to be in someway contaminated with various (in)organic pollutants. The levels of the pollutants might be measured in the river water, in the purified water and in the floc. Sufficient PUR sachets should be provided to the contact lab for them to generate test material.

- Mix 1 sachet/10 liter river water, apply as recommended on sachet
- Filter flocculent over cloth or vacuum filter – collect flocculent
- Use directly or allow 24 h aging
- Dose according to original sachet dry weight (flocculent will take water during use, which will result in a higher wet weight after preparation)

5.2 Tier 1 Environmental risk assessment

To be completed based on Tier 1 test results. If refined assessment is required, additional testing may be required (eg. chronic test of 8 weeks on earthworm reproduction: and continuation of an acute test to 100d of the soil microbiology for 2 concentrations:).

6. Specific Environment Risk Assessment for PŪR applied to Arsenic containing well water

The above risk assessment relates to a generic situation. However, contamination of tube wells with Arsenic (As) is not uncommon (e.g. situation in Bangladesh), and can lead to significant adverse health effects in the population from drinking water exposure. The efficiency of PUR to reduce As levels in the drinking water is high (> 95 % removal from water containing 50 – 500 ppb As). As a consequence, the As ends up in the waste flocculent, and should be included in the environmental risk assessment.

The environmental chemistry of As is very complex, but it can be assumed that in ground water As is initially present as the As(V) anion, or as As(III) under mildly reducing conditions. Under strong reducing conditions As will occur as the insoluble As_2S_3. When aerated, or in the presence of hypochlorite the As(V) will prevail. Anionic arsenic (arsenate, AsO_4^{3-}) will precipitate and strongly adsorb to Fe(III)oxyhydroxides under acidic to neutral conditions. This high affinity for Fe(III) colloids explains the excellent removal of the As from the raw water.

In soils, As(V) compounds are bound on Fe(III), Al(III), clays and carbonates and are rather immobile, i.e. they will not leach out significantly under oxic conditions. Their mobility under reducing conditions is higher. Bioconcentration of As occurs in aquatic organisms, but biomagnification is not significant. Terrestrial plants may accumulate As by root uptake from soil, and some species do so considerably (ref. EPA). This also depends on the soil texture, pH, etc.

As exposure calculation (realistic worst case):

Assume 10 L water with 500 ppb As (an extremely high level of As contamination) is flocculated with a PUR sachet (5.4 g). This will lead to ~5 mg As/5 g waste flocculent (DM), or ~1 g As/kg sludge DM. The As-rich floc can be blended into stable solid materials (glass, brick or cement). Analyses of an As-rich sludge in cement (30% by weight) by the lab procedure called the toxicity characteristic leaching procedure (TCLP) revealed that the leachate had negligible As levels and were below the limit of acceptability (5 mg As /L leachate) (Gupta et , 2000 in Johnston et al, 2001). Studies mentioned in this report also suggest that when hydrous ferric are used to remove arsenic from water, the resulting sludge does not require any special disposal.

In practice, it is likely that some of the waste flocculent will be disposed of in the soil. The normal background values for As in soils are < 30 mg/kg (Ide & Ectors), although some natural soils of specific geological origins can contain higher levels. The soil levels are to be compared to the soil clean-up standards based on risk assessment, as applied e.g. in Belgium or The Netherlands. The Belgian guidance ('A') value, for example, is 20 mg As/kg soil, and the 'C' value (maximum acceptable) in the order of 50 – 80 mg/kg according to the soil use (excluding industrial soil). Assuming an As background of 10 mg/kg, critical As levels may be reached in the immediate vicinity of the house after 1 - 2 generations of assumed continuous use and disposal of PUR. Given the conservative nature of this assessment this is likely not of real environmental relevance, but could be refined with real data.

Another aspect of this environmental assessment would be indirect exposure of humans via crops grown near the house and that may have accumulated As. It is therefore recommended as a precautionary measure not to apply the sludge to cropland, but to a) collect & treat it (cities) or disperse and dilute it over a wider area (rural societies). This is unlikely to lead to any adverse environmental effect (but need further assessment of attractiveness and effects on domestic and wild animals).

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*http://www.ce.vt.edu/program_areas/environmental/teach/gwprimer/landappl/sewer.html
**http://www.dep.state.pa.us/dep/biosolids/training/sewagesludge/1_1_0.htm

Annex 1 : Chemical Analysis of Spent Flocculent (floc)- January 2001

% m/m sample	4.5	Whole Sample	95.5	Whole Sample	100	
	% m/m	% m/m	WS mg/l	% m/m	% m/m	ppm
Nitrogen as N	0.2	0.009090	3.1	0.000296	0.009386	93.9
Phosphorus as P	0.1	0.004545	< 2	0.000191	< 0.004736	< 47.4
Potassium as K	0.02	0.000909	3	0.000286	0.001195	12.0
Magnesium as Mg	0.43	0.019544	15	0.001432	0.020975	209.8
Sodium as Na	0.06	0.002727	76	0.007255	0.009982	99.8
Calcium as Ca	1.2	0.054540	104	0.009927	0.064467	644.7
Sulphur as S	0.14	0.006363	68	0.006491	0.012854	128.5
Iron as Fe	11.8	0.536310	< 0.5	0.000048	< 0.536358	< 5364
Copper as Cu	0.02	0.000909	< 0.1	0.000010	< 0.000919	< 9.19
Zinc as Zn	0.01	0.000455	< 0.1	0.000010	< 0.000464	< 4.64
Manganese as Mn	0.02	0.000909	0.5	0.000048	0.000957	9.57
Boron as B	< 0.001	0.000045	< 0.1	0.000010	< 0.000055	< 0.55
Chloride as Cl	0.004	0.000182	44	0.004200	0.004382	43.8
Chromium as Cr	< 0.01	0.000455	< 1	0.000095	< 0.000550	< 5.50
Cadmium as Cd	0.0009	0.000041	< 0.02	0.000002	< 0.000043	< 0.43
Lead as Pb	0.0031	0.000141	< 0.1	0.000010	< 0.000150	< 1.50
Nickel as Ni	0.002	0.000091	< 0.1	0.000010	< 0.000100	< 1.00
Mercury as Hg	< 0.0001	0.000005	< 0.01	0.000001	< 0.000005	< 0.05
Aluminium as Al	0.68	0.030906	0.00	0.000000	0.030906	309.1
Insoluble in hot, 10% HCl	35	1.590750	0.00	0.000000	1.590750	15908
TOTAL	**49.70**	**2.258915**	**317.63**	**0.030319**	**2.289234**	**22892**

* air dried

Moisture content = 31.4%

Therefore, dry matter content of whole sample = 3.12%

Solid fraction	Total	Concentrated acid soluble		Water soluble	
	% m/m	% m/m	%CA/T	% m/m	%W/T
Nitrogen as N	0.2	ND	NA	0.001	0.50
Phosphorus as P	0.1	0.02	20.00	< 0.02	< 20.00
Potassium as K	0.02	0.02	100.00	< 0.01	< 50.00
Magnesium as Mg	0.43	0.1	23.26	< 0.02	< 4.65
Sodium as Na	0.06	0.05	83.33	0.05	83.33
Calcium as Ca	1.2	0.75	62.50	0.09	7.50
Sulphur as S	0.14	0.07	50.00	0.082	58.57
Iron as Fe	11.8	3.27	27.71	< 0.005	< 0.04
Copper as Cu	0.02	0.01	50.00	< 0.001	< 5.00
Zinc as Zn	0.01	0.003	30.00	< 0.001	< 10.00
Manganese as Mn	0.02	0.007	35.00	< 0.001	< 5.00
Boron as B	< 0.001	< 0.001	NA	< 0.001	NA
Chloride as Cl	0.004	0.004	100.00	0.004	100.00
Chromium as Cr	< 0.01	< 0.01	NA	< 0.01	NA
Cadmium as Cd	0.0009	0.0002	22.22	< 0.0002	< 22.22
Lead as Pb	0.0031	< 0.001	< 32.26	< 0.001	< 32.26
Nickel as Ni	0.002	< 0.001	< 50.00	< 0.001	< 50.00
Mercury as Hg	< 0.0001	< 0.0001	NA	< 0.0001	NA
Aluminium as Al	0.68	0.00	0.00	0.00	0.00
Insoluble in hot, 10% HCl	35	NA	NA	NA	NA

Annex 2: Typical Sludge composition

Constituent	Concentration
Organic matter	65 - 75 % dry solids
Nitrogen	4%
Phosphorous	3 – 4%
Zinc	1600 mg/kg ds
Copper	700
Lead	400
Chromium	300
Nickel	150
Cadmium	15
Arsenic	5
Mercury	10

http://ourworld.compuserve.com/homepages/jmpett/SludgeAN.htm

Annex 3: Maximum allowed concentrations of pollutant in sewage sludge to be applied to the land

Pollutant	Ceiling Concentrations (mg/kg of sewage sludge on a dry weight basis).
Arsenic	75
Cadmium	85
Copper	4,300
Lead	840
Mercury	57
Molybdenum	75
Nickel	420
Selenium	100
Zinc	7,500
Poly-Chlorinated Biphenyls (PCB's)	8.6

http://www.dep.state.pa.us/dep/biosolids/training/sewagesludge/1_1_0.htm

Annex 4: Maximum allowed concentrations of pollutant in sewage sludge to be applied to a lawn or a home garden

Pollutant	Monthly Average Concentrations (mg/kg of sewage sludge on a dry weight basis).
Arsenic	41
Cadmium	39
Copper	1,500
Lead	300
Mercury	17
Molybdenum	(N/A)
Nickel	420
Selenium	100
Zinc	2,800
Poly-Chlorinated Biphenyls (PCB's)	4

http://www.dep.state.pa.us/dep/biosolids/training/sewagesludge/1_1_0.htm

CONFIDENTIAL Document

Human Safety Assessment for PŪR – Purifier of Water

Procter & Gamble
Personal Health Care

Product Safety & Regulatory Affairs

May 30, 2002

B. D. Ellis,PhD

Global Human Safety

PŪR Brand

SAFETY ASSESSMENT FOR PŪR-Purifier of Water

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PŪR Human Safety Assessment

Background

The PŪR product was developed to "help purify drinking and cooking water" from sources that people are currently using for drinking and cooking purposes. The PŪR product can improve the quality of the water that a consumer uses for drinking and cooking, including most surface or well water sources, previously treated or not. This product combines coagulation and flocculation technologies to reduce the levels of suspended solids, bacteria, viruses, parasites, heavy metals and organics, while also supplying disinfectant technology to further reduce sensitive microbiological contaminants

Safety Assessment

This Safety Assessment for the PŪR product is subdivided into two components:

1) Formulation Safety during storage and use – ingestion of sachet contents, ingestion of the floc resulting from water treatment.
2) Finished water safety – microbiological and chemical reduction efficacy, disinfection by-products.

Chemical composition and formulation assessment

PŪR has been formulated as a flocculent/coagulant/disinfectant that precipitates out of solution, adsorbing and entrapping potential organic, inorganic, and biological contaminants. The treated water is filtered through a cloth for sludge removal and the disinfectant remains in solution, providing disinfectant efficacy after 30 minutes contact time. As a treatment process, this sequesters the added flocculent and floc building components into a precipitate of approximately 50 mL volume along with contaminants that were present in the starting water. Thus, both flocculents/flocculation aids and contaminants are removed from the water and are concentrated in the floc. Table 1 presents the current PŪR formulation.

Table 1. PŪR formulation.

Chemical	Typical Level of use in DW[1] (mg/L)[2]
Iron (III) sulphate (i.e. ferric)	100-600
Sodium carbonate	50-150
Bentonite	200
Chitosan	-
Polyacrylamide	1/4[3]
Calcium hypochlorite	10[2], 0.5-5[4]
Potassium permanganate	15

[1]–DW – drinking water, [2]–see NSF documentation- Drinking Water Treatment Chemicals – Health Effects, ANSI/NSF Standard 60-2001. Publ. NSF International, Ann Arbor, MI, USA. [3]-Depending on use and monomer content. [4]-EPA Guidance Manual, Alternative Disinfectants and Oxidants, USEPA, April 1999.

Table 2 provides a brief functional explanation of each ingredient in the PŪR formulation along with any Regulatory and/or Safety Standards that apply to these chemicals when used in food or for drinking water treatment.

Table 2. Brief functional explanation for PŪR ingredients and other relevant uses in the food or water treatment industries.

Component	Function	Other Relevant Uses
Iron (III) sulphate (i.e. ferric sulphate)	Used as a coagulant in water treatment	Generally recognized as safe (GRAS) by the USFDA when used as a flavoring agent in food under conditions of GMP.
Sodium carbonate	Used for pH control	Used for corrosion control and softening in water treatment plants and may be certified as a drinking water additive according to NSF Standard 60 (Drinking Water Additives – Health Effects). GRAS when used as a flavoring agent and

		antioxidant in foods (21 CFR 184.1742) under conditions of GMP. It meets the requirements of the Food Chemical Codex and is a permitted food additive under the current UK legislation "Miscellaneous Additives in Food Regulations"
Bentonite	Used as a coagulant aide for removing turbidity associated with water and wastewater	Commonly used in dental materials, cosmetics and in pharmaceuticals as a binding or suspending agent. It is GRAS according to the USFDA when used as a processing aid (apple juice, wines) under GMP
Chitosan	Used as a flocculent aide and a metal binding agent in the PŪR formula.	It is used as a processing agent and thickener/stabilizer in Japan (Japan, Food Sanitation Law, 1996-Food Additives of Natural Origin) and is sold as a dietary supplement in the United States.
Polyacrylamide	Used as a coagulant and flocculation aid	Routinely used in commercial water treatment systems for improving the efficiency of coagulation and is certified as a drinking water additive according to NSF Standard 60 (Drinking Water Additives – Health Effects)
Calcium hypochlorite	Used for the disinfection of drinking water	Approved for such use by EPA and WHO, and is certified as a drinking water additive according to NSF Standard 60 (Drinking Water Additives – Health Effects)
Potassium permanganate	Used to oxidize metals such as Mn^{2+} and Fe^{2+} in addition to alleviating aesthetic problems resulting from the presence of organic odor and color causing compounds in water	A commonly used oxidant for water treatment and is certified as a drinking water additive according to NSF Standard 60 (Drinking Water Additives – Health Effects)

Table 3 provides relevant toxicological information for each of the ingredients in PŪR. The PŪR formula is composed of traditional chemicals used in potable water treatment with the exception of chitosan. Under conditions of intended use, the concentration of individual chemicals in the PŪR formulation do not pose a significant safety concern and inherently exhibit a low order of acute and/or chronic toxicity at current formulation concentrations. For example, special consideration and additional discussion is provided for certain specific components: iron, polyacrylamide, potassium permanganate, chitosan, and calcium hypochlorite. Although PŪR is not intended for consumption, accidental ingestion of the contents of a sachet of PŪR powder should it occur could result in an adverse reaction due to the 460 mg of iron. Due to the polymerization process used in the production of polyacrylamide, there is a residual amount of acrylamide monomer remaining in the final product.

Table 3. Toxicological information for PŪR components (Safety Data Summary).

Iron (III) sulphate exsiccated (ferric sulphate)	• Ferrous sulphate is an approved vitamin supplement. • Sulfate has an EPA secondary maximum contaminant level goal of 250 mg/L based on aesthetic effects (taste and odor, when sodium is the counter-ion). No health based guideline for sulphate in drinking water, however, health authorities should be notified if the level in drinking water exceeds 500 mg/L. Cathartic effects have been reported in humans drinking water with a sulfate content exceeding 600 mg/L. • EPA suggests a level of 0.3 mg/L as a secondary (aesthetic) standard for iron. WHO states that levels as high as 2 mg/L do not pose a health hazard • **HIGHLY VARIABLE LD50S FOR DIFFERENT SALTS AND ANIMAL SPECIES REPORTED (300-600 MG/KG IN MOUSE, 800-2000 MG/KG IN RATS).** • Not teratogenic in chicken embryo test. No maternal toxicity nor teratogenic effects found for iron (III) sulphate in mice or rats. An 8-generation reproduction study in rats showed no evidence for toxicity due to iron oxide (est. intake was 25 mg./day). • A variety of iron salts were inactive in mutagenicity studies in *Saccharomyces cerevisiae* strain D-4 and *Salmonella typhimurium* strains TA1535, TA1537, TA1538 with and without metabolic inactivation. Iron (II) sulphate was active in suspension tests with activation. • Iron is toxic at doses ranging from 20 to 60 mg/kg. Average lethal dose in humans is 200-250 mg/kg, but death has occurred with doses as low as 60 mg/kg.
Chitosan (de-acetylated chitin)	• (RTECS[2]) orl-rat TDLo: 957 gm/kg/58D-C • Exposure estimates range from 7 to 21 grams per day (Primex GRAS application, National Cancer Institute literature review submitted to National Toxicology Program, USA). • Exposure to chitosan from PŪR is likely to be less than 5 –10 µg/L
Calcium hypochlorite ($Ca(OCl)_2$)	• Oral LD50 in rats = 850 mg/kg. Acute pulmonary edema, nausea, vomiting and other GI changes. • **USING AN NOAEL OF 15 MG/KG BODY WEIGHT/DAY A TOLERABLE DAILY INTAKE (TDI) OF 150 MG/KG BODY WEIGHT IS CALCULATED WHEN APPLYING AN UNCERTAINTY FACTOR OF 100. ALLOCATING 100% OF THE TDI TO DRINKING WATER, THE GUIDELINE VALUE IS 5 MG RESIDUAL CHLORINE/LITER. NO ADVERSE EFFECT LEVEL WAS IDENTIFIED IN THE STUDY USED TO DEVELOP THIS VALUE BY WHO.**
Potassium permanganate	• Topical antiseptic, astringent, deodorant • Oral LD50 in guinea pigs is 810 mg/kg, in mice 750 mg/kg, in rats 750 mg/kg (RTECS) • Fatal dose is estimated at 10 grams, kidney and liver toxin, corrosive to GI tract. Human oral LDLo is 143 mg/kg.
Bentonite	• A form of bentonite (BH 20 grout) is certified to ANSI/NSF Standard 60 (Drinking water treatment chemicals – Health Effects). Biologically inert when ingested (Hazardous Substances Database).
Sodium Carbonate	• LD50: mouse (oral) 6600mg/kg, rat (oral) 4090 mg/kg • Approved for use in foods, Food Chemical Codex.
Polyacrylamide	• Polyacrylamide is approved for use and complies with 40 CFR 141.111 (USEPA) requirements for percent monomer (acrylamide) and dose. • Monomer (acrylamide) maximum contaminant level (USEPA primary drinking water standard, MCL) is equivalent to 0.5 µg/L and the MCL is treatment technique based. At 0.05% monomer, the dose may not exceed 1 mg/L, or equivalent. EPA and WHO have same criteria for the upper limit in drinking water. • Monomer (acrylamide) is controlled at or below WHO accepted drinking water levels (0.5 ppb). • LD50s are >1 gm/kg (rat), 12950 mg/kg (mouse), and 11250 mg/kg (rabbit), data from RTECS, Registry of Toxic Effects of Chemical Substances

Guidelines for drinking-water quality. 2nd Ed. Vol.2. Health Criteria and other supporting information. International Programme on Chemical Safety. World Health Organization. Geneva. 1996. [2] Registry of Toxic Effects of Chemicals.

Ingestion of Sachet Contents

Polyacrylamide

Polyacrylamide is a polymeric chemical coagulant used for increasing the efficiency of removal of a variety of contaminants in drinking water. There are no regulations associated with polyacrylamide due to the inert nature of the polymer. USEPA and WHO have set a health based maximum contaminant level of 0.5 ppb in drinking water. Controlling the polymer dose and percent contaminating monomer attains control of monomer content. Five lots used to produce PŪR over the last year have averaged 0.0014% ± 0.0009% (standard deviation) with a minimum of 0.001% and a maximum of 0.003% (i.e monomer content <0.015 ppb). See Appendix 1 for more information on acrylamide monomer.

Ferric Sulphate

The sachet contains 460 mg of ferric iron. This amount of iron, if accidentally ingested by a young child has the potential to cause iron toxicity. Literature data indicates mild to moderate/severe toxicity can occur at 20-60 mg/kg (see Table 4). Therefore, ingestion by a child <20 kg (approximate age range is < 8 years) would result in this range of exposure.

Table 4. Dose dependent outcomes resulting from ingestion of iron at 460 mg $Fe3^{+}$.

Body Weight (kg)	Exposure Level (mg/kg)	Outcome
<≈ 2	>≈ 230	likely fatal
>≈2 & <≈7.5	<≈230 - >≈61	highly toxic
>≈7.5 & <≈15	<≈ 61 ->≈ 31	moderately toxic to toxic
>≈ 15	<≈31	toxic to no toxicity

Iron Poisoning

Iron overdose was the leading cause of death due to toxicological agents in children under 6 years in the United States (1995). Iron is used as a pediatric or prenatal vitamin supplement and for treatment of anemia. With ingestions greater than 20 mg/kg but less than or equal to 40 mg/kg, patients may show signs of GI toxicity. As the ingestion of elemental iron exceeds 40 mg/kg, patients are more likely to show signs of toxicity. Ingestions exceeding 250 mg/kg are likely to be fatal while adverse responses increase when doses above 60 mg/kg are attained. Iron poisoning is almost always acute and for practical purposes is mainly limited to toddlers who accidentally ingest iron-supplement pills. Acute iron toxicity causes diarrhea, abdominal pain, gastric bleeding, lethargy and seizures. If untreated, the condition can lead to coma and death.

Exposure Assessment for Iron

To minimize exposure, PŪR is packaged in sealed single use sachets. To communicate the potential hazard from ingestion, adults should receive verbal instructions to keep the sachets away from young children and to dispose of the flocculated material away from children. The packages should contain a warning similar to "KEEP OUT OF REACH OF CHILDREN".

There are significant issues associated with the use of Ipecac and potential iron poisoning and these are addressed in Appendix 2. Appendix 3 contains information on symptoms, pathophysiology, and outcomes resulting poisoning by iron.

Potassium permanganate

Potassium permanganate is added because of the formation of a perceptible yellow coloration in some treated waters. This discoloration arises from source water manganese and contaminant manganese in the ferric sulphate. The yellow color is due to the slow oxidation of manganese (Mn^{2+}) to manganese dioxide (MnO_2), forming a colloid at the concentrations found after treatment. The level of manganese that apparently causes this can be very low and in the range of 50 to 100 micrograms/L. These levels are not a safety issue (WHO provisional health-based guideline value for manganese is 500 micrograms/L) but they do raise aesthetic issues such as taste and staining. Manganese can be found in many source waters (especially ground waters) worldwide and water utilities have successfully addressed high levels with the addition of potassium permanganate ($KMnO_4$).

See Appendix 4 (USEPA Guidance Manual – Alternative Disinfectants and Oxidants, April 1999) for more information related to potassium permanganate and water treatment. Appendix 5 presents information related to permanganate levels in PŪR treated water in addition to toxicological data for permanganate and manganese in water.

Calcium Hypochlorite

Hypochlorite is well understood with respect to its action as a disinfectant for the control of waterborne microbial pathogens. In their book, Guidelines for Drinking Water Quality (2nd ed., Vol. 1, Recommendations, 1993) the WHO states (pg. 135) that:

Normal conditions of chlorination (i.e., a free residual chlorine of >=0.5 mg per litre, at least 30 minutes contact time, pH less than 8.0, and water turbidity of less than 1 NTU) can bring about over 99% reductions of E. coli and certain viruses but not of the cysts or oocsyts of parasitic protozoa.

This view is reiterated in the 1996 WHO Guidelines for Drinking-Water Quality: Health Criteria and Other Supporting Information Vol. 2 supplement. The 1993 and 1996 WHO guideline publications explicitly support a maximum free chlorine level of 5 mg/L so that adequate disinfection is never compromised in the delivery of microbiologically safe drinking water. A reduction of 99% in the concentration of viruses or bacteria may not be sufficiently protective of public health. The infectious dose associated with a number of viruses of concern (e.g. rotavirus) can be very low. Depending on the level of contamination, raw source water may contain greater than 1000 cultivable viruses/L (Safety of Water Disinfection: Balancing Chemical and Microbial Risks, Ed. Gunther F. Craun, ILSI Press, Washington DC, USA, 1993). A 99% reduction in this level still leaves 10 cultivable viruses/L, a sufficiently high dose for infection since, on average, a person consumes approximately 2 liters of water per day. While bacteria are more susceptible to chlorination they are present at higher concentrations and in the presence of particulate material can escape the effects of disinfection at low chlorine dosing levels.
Table 5 below provides values for recommended maximum and minimum chlorine residual levels that are protective of human health in drinking water as recommended by the World Health Organization and the United States Environmental Protection Agency. Appendix 6 contains information on chlorine extracted from the WHO publication Guidelines for Drinking Water Quality: Health Criteria and Other Supporting Information. Vol. 2. Supplement. 1996).

Table 5. Compilation of guideline values for chlorine developed worldwide.

Organization	Country	Maximum Residual (health based)	Minimum Residual
WHO	International	5.0 mg/L[1]	0.5 mg/L[2]
USEPA	United States	4 mg/L[3]	0.2 mg/L[4]

[1] Based on an NOAEL of 15 mg/kg body weight/day. Tolerable daily intake (TDI) of 150 mg/kg body weight is calculated when applying an uncertainty factor of 100. Allocating 100% of the TDI to drinking water, the guideline value is 5 mg residual chlorine/liter. It is noted, however, that this value is conservative, as no adverse effect level was identified in the study used to develop this value.

[2] For effective disinfection there should be a residual concentration of free chlorine of ≥0.5 mg/L after 30 minuntes contact time at pH<8.0. Recommended median turbidity before disinfection should not exceed 1 NTU and it should not exceed 5 NTU in any one sample.

[3] Maximum residual disinfectant level goal (MRDLG = 4) and the maximum residual disinfectant level (MRDL = 4.0 mg/L) are similar. The MRDLG is established at the level at which no known or anticipated adverse effects on the health of persons occur and which allows for control of waterborne microbial contaminants. MRDLG was based on an NOAEL of 14 mg/kg/day and application of a 100 fold uncertainty factor and a source contribution of 80%. USEPA created the terms MRDLG and MRDL, during the regulatory negotiations to distinguish disinfectants (because of their beneficial use) from contaminants.

[4] Surface water treatment rule: The disinfection process must demonstrate by continuous monitoring and recording that the disinfectant residual in the water entering the distribution system is never less than 0.2 mg/L for more than 4 hours. It is recommended that a residual level be maintained at the end (or in dead ends) of the distribution system.

Chitosan

Structure

Chitosan is derived from chitin, which is found indigenously in the cell walls of various fungi, crustaceans, and insects. Chemically chitosan, a cationic polysaccharide, is the N-deacetylated product of chitin. The structure of chitosan is mainly that of a polymer of D-glucosamine and N-acetyl-D-glucosamine. Both chitin and chitosan are considered to be nitrogenous polysaccharides. Chitosan can be chemically derived by deacetylating its raw material, chitin. Commercially, chitin is obtained from the cuticles of sea animals, which are a waster product of the food industry. The term chitosan refers to a family of polymers whose members differ in their degree of deacetylation and molecular weight. These two characteristics are fundamental to the physicochemical properties of the chitosans and therefore have considerable influence on their biological activities.

Uses

Among other uses, chitosan functions as a flocculating agent for water (Norway) and wastewater treatment and a chelating agent for removal of trace heavy metal contamination from aqueous solutions. Chitosan is also used as an excipient for oral drug formulations. Cationic chitosan forms polyelectrolyte complexes with polyanionic polymers and the chelate complexes with metal ions resulting in precipitation. These reactions have been used for the clarification of polluted wastewater.

Exposure Assessment for Chitosan

Estimates of the mean and 90th percentile exposure to chitosan (7.97 and 15.94 grams respectively) remains lower than the recommended levels of intake for dietary fiber (25-30 grams per day) in the United States. The National Cancer Institute estimated that exposure through multiple sources can amount to a daily consumption of 10 to 20 grams of chitosan. It was estimated that 0.1 to 0.05% of the chitosan may be present in the diet when it is used as a food processing aid (i.e. protein coagulating agent) (Dietrich Knorr. 1994. Use of Chitinous Polymers in Food: A Challenge for Food Research and Development. Food Technology v. 38(1) p. 85-89, 92-97. .pp 85-97). Therefore, exposure to chitosan from PŪR is likely to be less than 5 –10 µg/L (10 mg/L x percent remaining).

Safety Assessment for Chitosan

There is an application before the USFDA requesting that chitosan be considered as GRAS (Generally Recognized As Safe - this is usually associated with a petition to use the component as a food additive). Technical effects ascribed to chitosan fall under FDA 21 CFR 170.3 (o) and include the following; antioxidants, curing and pickling agents, dough strengtheners, emulsifiers and emulsifier salts, formulation aids, humectants, nutrient supplements, processing aids, stabilizers and thickeners, surface-active agents, synergists, and texturizers. The safe use of chitosan has been based on decades of human experience with chitosan consumption in Japan, China, and other Pacific Rim nations.

As of 1995, EPA has no reports involving adverse events associated with the use of chitosan by workers involved in its use as a pesticide ingredient. The FDA had 2 reported matches on a search of the 1998 SN/AEMS database

(Special Nutritional/Adverse Events Monitoring System, 1998 was the latest year available). One involved a report of "very constipated, stool was very hard and dry" where the only ingredient was chitosan and the other was "premature ventricular contractions" where the ingredients included chitosan, erythorbic acid, citric acid, cruciferous concentrate. No reports were found in the literature involving potential immunological responses associated with persons allergic to crustacean protein (databases searched included HSDB, IRIS, AGRICOLA, RTECS, BIOSIS, MEDLINE, CSA Biological and Medical Sciences Area, TOXLINE, Food and Human Nutrition).
Chitosan was nominated to the National Toxicology Program (NTP) for study by the National Cancer Institute based on significant human exposure through use as a dietary supplement and other commercial applications and potential for toxicity from interference with dietary fat absorption. The ICCEC (Interagency Committee for Chemical Evaluation and Coordination) recommended that mechanistic studies be performed to evaluate vitamin E and mineral depletion.

Other Toxicological Considerations

PŪR Eye Irritation Toxicity

In a Low Volume Eye Test (LVET) study, 100% concentration (dry powder), no rinse, the Mean Average Score (MAS) for PŪR was 4.6 over all animals (in triplicate) and all animals cleared within three days. For comparison, calcium hypochlorite (powder) scores a 66.7 under these conditions. This data indicates that PŪR would be placed in the slight to moderate eye irritant category. This study was performed on the non permanganate containing formulation, but based on the low amount of potassium permanganate in the PŪR formulation, similar results would be expected.

PŪR Dermal Toxicity

Based on the ingredients used to formulate PŪR, overall dermal irritation would be expected to be mild to moderate, as indicated by the eye irritation test. Ferric sulphate, sodium carbonate, and bentonite represent a significant percentage (95.78% wt/wt) of the formulation and are all skin irritants. Calcium hypochlorite and potassium permanganate are strong oxidants in concentrated form and polyacrylamide is a skin irritant. The amount of each chemical in PŪR is low and would not be expected to contribute significantly to dermal irritation, which is indicated by the low score in the eye irritation study.
A skin sensitization study was used to assess the possible allergenic potential of chitosan when administered topically to albino guinea pigs. A modified Buhler Test was used (Ritz, H.L. and Buhler, E.V.: Planning, conduct and interpretation of guinea pig sensitization patch tests: in Drill, Lazar, Current Concepts Cutaneous Toxicity. Academic Press, 1980. pp.25-40). Twenty male animals of the test group were treated topically with 7.5% of the chitosan preparation once a week for a 3 week induction phase. Two weeks after the final induction application the animals were challenged with the same test article preparation used for induction but at a concentration of 1.875%. The ten animals of the control group were not treated during the induction but were treated once at challenge with 1.875% of the chitosan preparation. None of the control and test animals were observed with skin reactions after the challenge with chitosan at the concentration of 1.875%. Based on these results, chitosan was considered not to be a skin sensitizer.

PŪR Inhalation Toxicity

Similar to dermal toxicity and eye toxicity, PŪR is expected to be a potential lung irritant according to the individual ingredients. The 3 major components comprising 95.67% wt/wt would tend to dominate the potential lung and mucous membrane irritation. Sodium carbonate, at high concentrations can be destructive to tissues of the mucous membranes and upper respiratory tract. Ferric sulphate may cause irritation to the upper respiratory tract. Bentonite can be irritating to the respiratory system. Calcium hypochlorite can be irritating in high concentrations, however, at the low concentration found in PŪR, it is not expected to be any more irritating than the any other powdered components in PŪR.

Labeling Recommendations

Based on the information in the preceding paragraphs, the following labeling recommendations are suggested from a human safety perspective:

1) DO NOT INGEST POWDER.
2) KEEP OUT OF REACH OF CHILDREN
3) The powder contains calcium hypochlorite and flocculants, including on average 460 mg of iron (III) as $Fe_2(SO_4)_3$. If ingested seek medical attention immediately.
4) Statement of irritation to skin and eyes:
    a. Rinse eyes and skin thoroughly with water if contacted by powder.

Packaging Recommendations

Based on the potential for iron poisoning as outlined previously, child resistant packaging is recommended. The current packaging has been tested by a US standard, described in detail in US Code of Federal Regulations Title 16, Part 1700. This test report is appended as Appendix 7.

Floc Ingestion and other Misuse Scenarios

Ingestion of the floc has the same toxicological issues as for ingestion of the sachet and therefore it is recommended that the floc be disposed of in a manner whereby children and animals would not be expected to come in contact with a significant amount. Table 6 provides an overview of potential misuse scenarios and the current strategy for risk minimization (also see section on Protozoan removal).

Efficacy & Finished Water Safety

Table 7 provides concentrations of ingredients remaining in the water after the PŪR process has been completed, guideline values that the World Health Organization suggests are protective of human health, and concentrations typically found in source waters.

Table 6. Misuse Scenarios associated with PUR use (NOTE: "**Process**" = flocculation/coagulation/precipitation/disinfection).

Misuse Scenario	Result	Risk Management	Final water quality
Ingest whole sachet: • 460 mg Ferric ion • 80 mg Ca Hypochlorite	**Iron ingestion**: Dependent on body weight • <≈ 2 kg –likely fatal • >≈2 kg & <≈7.5 kg –highly toxic • >≈7.5 kg & <≈15 kg moderately toxic to toxic • >≈ 15 kg toxic to no toxicity **Chlorine Ingestion**: • Practically non-hazardous (TDLo in man =143 mg/kg)	• Child Resistant Package • Use Instructions • Label • Nature of product (hygroscopic, unpalatable)	Not applicable
Floc ingestion: • **ALL** floc material resulting from treating 10 L (≈50 mL of floc) • Concentration of source water contaminants	• Iron ingestion is tabulated above (99.99% of iron is in the floc) • Availability of iron in floc – not known, assume same as sachet (worse case) • Floc aesthetics (color and texture) are extremely negative • Effects of floc ingestion and contaminants are dependent on starting water quality • Consuming 20% of floc (≈10 mL) would be equivalent to drinking 2L of beginning water	• Use Instructions • Label • Nature of floc (unpalatable aesthetics)	• Not applicable for floc ingestion • Improved due to contaminant sequestration into floc and effective disinfection.
Sachet use in small water volume (e.g. 500 mL)	• Floc formation as intended, Fe sequestered in floc. • If ingested, same health related scenario as floc/sachet ingestion (floc volume is proportional to amount of sachet used) • Water in small volume would be highly unpalatable due to high chlorine content (100 ppm hypochlorite in 500 mL, bleach is 55,000 ppm), additional aesthetic negatives (yellowing due to high chlorine/Mn content) • Floc ingestion has same caveats as above • Volume of floc can be one-half volume of water at low volumes of water (floc will slowly dewater and sediment out as smaller volume of sludge)	• Use Instructions • Label Nature of floc (unpalatable aesthetics)	High chlorine content, otherwise, improved water quality.
Fraction of sachet in fraction of water	• **"Process"** would be as intended for first use but chlorine would dissipate in open sachet over time. • **"Process"** would still be effective (assuming a homogeneous mixture), however, as less powder is used, the likelihood of effective disinfection decreases due to the statistical distribution of hypochlorite crystals in the sachet	• Use Instructions Label	Improved by all processes initially, but an effective disinfectant dose would drop below 0.5 mg/Liter at ≈100 liters (residual chlorine still depends on source water quality)
Sachet use in excess volume (>10L)	• **"Process"** would occur as intended up to ≈300 L. Process efficiency decreases as starting turbidity increases.	• Use Instructions	Improved over initial water quality, however, chlorine dose is ≈30 times lower (<0.2 mg/L), insufficient for effective disinfection
Source water quality and effectiveness	• Effective in all known drinking water sources to date • Effectiveness would vary according to degree of source water contamination if the product is misused on non-drinking source waters (e.g. raw sewage, gross fecal contamination, minor fecal contamination)	• Use Instructions • Education	Robust formulation indicates that the final water quality would still be improved over initial water quality although potability[1] may be questionable

[1] Potability –defined as safe to drink – microbiological, chemical, and physical parameters meet WHO standards.

Table 7. Post-treatment concentration of chemicals found in PUR treated waters and those found in "typical" waters.

Chemical	Concentration due to PUR[a]	Typical Source Water or Drinking Water Concentrations
Sulfate[c]	100-200 mg/L	Typically 20 mg/l but range from 0 to 630 mg/l in rivers. Drinking water treatment usually increases the concentration. Concentrations ranging from 97 mg/L (Saskatchewan, Canada), 30-40 mg/L in W. Canadian rivers and 250mg/L in Mexican lakes have been measured. **WHO aesthetic guideline set at 500 mg/L.** ***No health based Guideline.***
Iron[c]	0.15-0.3 mg/L	Median river concentrations reported at 0.7 mg/L, in drinking water iron is normally less than 0.3 mg/L but may be present at higher concentrations in countries where iron salts are used as coagulating agents and where cast, steel, and galvanized iron pipes are used in water distribution. **Up to 2 mg/L is non-hazardous to health (WHO).**
Carbonate[b]	50-100 mg/L	Component of buffering system in most freshwater and drinking water. $CaCO_3$ typically in the range of 10-500 mg/L. **No health based guideline (WHO).**
Sodium[c]	20-100 mg/L	Most waters are <20mg/L but some countries can exceed 250 mg/L. High concentrations can be due to minerals, salt intrusion, and addition of drinking water treatment chemicals such as sodium salts of fluoride, bicarbonate, and hypochlorite. **WHO – no health based value.**
Bentonite[b] (clay)	100-200 mg/L	Clay particles suspended in water cause turbidity. Bentonite (clay) is designed to be removed during PUR treatment. <5 NTU rarely objectionable, interferes with disinfection, therefore keep as low as possible. **No WHO standard.**
Chitosan[b]	2-20 mg/L	Binds metals, designed to be removed during PUR treatment. Typically less than 0.05 to 0.1% of applied dose remains in wastewater treatment.
Polyacrylamide[b]	1-5 mg/L	Polyacrylamide is removed during treatment. Maximum monomer concentration is 0.01%, average of five lots has been 0.0014%. **WHO guideline value for acrylamide is 0.5 ppb.** See Appendix 1 for more information.
Total Organic Carbon[c]	≈1.6 mg/L	Highly variable with ranges from <1 ppm to >10 ppm. PUR treatment would typically lower TOC concentrations to <7 ppm. **No WHO health based guideline value.**
Hypochlorite (as Free Chlorine)[c]	0.5 to 5 mg/L (residual after 30 minutes.)	Concentrations in drinking water (at the tap) are highly variable but if chlorine is used in the distribution system, concentrations could range from 0 to >5ppm but are typically 0.2 to 1 mg/L. WHO states that for effective disinfection, the chlorine concentration should be >0.5 ppm after 30 minutes in water with a median turbidity of not >1.0 NTU and pH <8.0. Doses are highly variable and dependent on chlorine demand. **WHO Health based maximum guideline value is 5 mg/L.**
Potassium[b]	0.02-0.1 mg/L	**No WHO health based guideline value.**
Permanganate[b]	0.1-0.5 mg/L	Not found in source waters and unlikely to be found in PUR treated waters due to high chemical reactivity. Less than 0.03 mg/L (detection limit) detected in PUR treated waters.
Calcium[b]	1-5 mg/L	Present at 10 – 500 ppm. Ca^{2+} up to 100 mg/L is common. **No WHO health based guideline value.**
pH[c]	No effect on initial water pH	Depends on buffering capacity of the water, but most raw waters are in the range of 6.5 to 8.5. **WHO guideline value set to <8.0 for purposes of effective disinfection.** PUR treated waters generally in the range of 6.5-7.5.

Reference: (1) Guidelines for drinking-water quality. 2nd Ed. Vol.2. Health Criteria and other supporting information. International Programme on Chemical Safety. World Health Organization. Geneva. 1996. [a] These concentrations are within drinking water guidelines established by the World Health Organization and the United States Environmental Protection Agency. Measured concentrations may vary due to wide ranging raw water conditions. Values represent residual levels in PUR treated deionised water. [b]- calculated from formulation. [c] – measured.

Disinfection By-products

In 1974, scientists discovered that during the water treatment process, chlorine reacts with organic matter in raw water to form disinfection by-products (DBPs). Other disinfectants such as ozone, chloramines, and chlorine dioxide also form DBPs. Concerns that the presence of these compounds in drinking water may present potential health risks led the U.S. Environmental Protection Agency to propose regulations to control DBPs. Current regulations suggest that when total trihalomethanes (TTHM), those DBPs most often identified in the presence of chlorine present minimal risk to human health when controlled to levels below 80 µg/L. The trihalomethanes (THM) generally act as an indicator of the presence of other chlorination by-products and control of the four compounds listed in Table 8 should help to reduce levels of other uncharacterized chlorination by-products. The WHO has set a guideline value for each of the four chemicals listed in Table 8, however, other regulatory agencies such as the EPA have developed a drinking water standard based on the sum of the four individual chemicals (e.g. EPA Primary Drinking Water Regulation for Total THMs is 80 µg/L). In controlling THMs, a multistep treatment system such as is used by PŪR is consistent with accepted methods for reducing precursors (i.e. flocculation and coagulation).

Table 8. Disinfection by-products as total trihalomethanes and values associated with

Chemical Class	Disinfection by-product	WHO Guideline Value (µg/L)
Total Trihalomethanes	Chloroform	(2000, 200, 20)[1]
	Bromoform	100
	Bromodichloromethane	(600, 60, 6)[1]
	dibromochloromethane	100

[1] Both compounds were evaluated on the basis of cancer formation in laboratory animals and the risk assessment represents a lifetime of consumption (70 years, 2 liters of water per day, 70 kg body weight) using the most protective value. A linearized multistage model was used and values correspond to an excess risk of 10^{-4} (1in 10,000), 10^{-5} (1 in 100,000), and 10^{-6} (1 in 1,000,000), respectively.

PŪR flocculation and coagulation are important for removing organic disinfectant by-product precursor material as shown in laboratory experiments. PŪR reduced the organic humic acids present in model EPA waters from >25 mg/L to less than 1 mg/L within the 15 minute period required for the PŪR physical process to come to completion. DBP formation in these model waters is indicated in Table 9 below. Background concentration in starting water was 3 ppb as chloroform. A number of factors impact DBP formation including pH, temperature, source water, time, and chlorine dose. Additional information on real waters from Guatemala using a no-permanganate containing formulation indicates that low levels of total THMs were formed (<30 ppb).

Table 9. DBP formation over time due to PŪR treatment in different water types.

Time/ hour	TTHMs/ppb versus Water Type			
	Deionised	Deionised	Deionised[1]	Highly contaminated model surface
3	4 (3)[2]	5 (5)[2]	6 (5)[2]	25 (3, 3, 5, 14)[3]
24	6 (5)[2]	10 (9)[2]	10 (9)[2]	35 (3, 4, 7, 21)[3]
48	8 (7)[2]	15 (14)[2]	15 (14)[2]	38 (3, 4, 7, 23)[3]

[1] THIS WATER HAD BEEN TREATED WITH DOUBLE DOSE OF FORMULATION.
[2] TTHMS QUOTED WITH $CHCl_3$ CONCENTRATION/PPB QUOTED IN BRACKETS.
[3] TTHMs quoted with $CHCl_3$, $CHBrCl_2$, $CHBr_2Cl$ and $CHBr_3$ concentrations/ppb quoted in brackets.

PŪR Functionality – Safety/Efficacy Related Conclusions

The PŪR product is intended to improve the quality of water that a consumer uses for drinking, it was not developed to produce potable water from every possible source water. PŪR employs use of multiple treatment barriers including flocculation/coagulation, sedimentation/filtration, and disinfection. Flocculation and coagulation are designed to remove particulate matter including contaminants, turbidity, and microorganisms (see Table 10). During this process, organic material that creates a disinfectant demand is removed, therefore decreasing the disinfection by-product formation potential of the source water in addition to permitting a lower dose of chlorine to be applied to achieve sufficient disinfection. As a generally accepted guideline (USEPA), Table 10 provides some general conclusions regarding the level of reduction feasible for the 3 classes of organisms relevant to the non-disinfectant

drinking water technology related to PŪR. Practically, in the presence of chlorine, bacterial inactivation and removal efficacy has been very good, providing 6-log reductions in bacterial colony forming units in post treatment water (after 30 minutes). Reductions in viral plaque forming units in cell-culture based assays indicate that the product efficaciously inactivates the model viruses poliovirus and rotavirus. Protozoan cyst reduction, as indicated by the removal of *Cryptosporidium parvum* oocysts is in the range of 2 to 4 logs.

Table 10. Waterborne pathogens, disinfectant susceptibility, and levels of reduction achievable by use of typical water treatment procedures.

Organism	Resistance to Disinfection	Removal by sedimentation, coagulation, filtration[1]
Bacteria	Type specific, generally low except for spores	Good, 2 to 3 log removal
Viruses	Generally more resistant than bacteria	Poor, 1 to 3 log removal
Protozoa	More resistant than bacteria or viruses	Good, 2 to 3 log removal

[1]-EPA Guidance Manual: Alternative Disinfectants and Oxidants, April 1999.

PŪR has been formulated as a disinfectant/flocculent/coagulant that precipitates out of solution, adsorbing and entrapping potential organic, inorganic, and biological contaminants. Treated water is then filtered through a cloth for sludge removal and hypochlorite remains in solution, providing disinfectant efficacy after 30 minutes contact time for up to 24 hours. As a treatment process, this sequesters the added iron, bentonite, chitosan, and Magnafloc into a precipitate of approximately 50 mL volume along with contaminants that were present in the starting water. Therefore, from an ingestion perspective, consumption of floc has the same implications as consumption of the powder. Additionally, contaminants that were originally dispersed in 10 liters of water are now concentrated in 50 mL of floc (concentrated approximately 500 times). This sludge should be disposed of with normal household trash and kept out of contact of people and animals. Table 7, noted previously, provides concentrations of component ingredients in the water after the PŪR process has been completed along with published guideline values that the World Health Organization suggests are protective of human health.

Microbiological Efficacy

The applicable WHO guideline used for evaluating PŪR is the following:

- **Effective terminal disinfection can be carried out by maintaining a chlorine residual of at least 0.5 ppm for 30 minutes in water with a median turbidity of less than 1 NTU (maximum of 5 NTU) at a pH of less than 8.0.**

Bacterial efficacy is correlated with the concentration of residual disinfectant in the post PŪR treated water. Chlorine (hypochlorite) has a long history of efficacious and effective use as a water disinfectant. Laboratory data using EPA model waters developed for evaluating the ability of devices to produce microbiologically pure ("microbiological purifier") water were used in the development stage of PŪR. Field-testing in a variety of countries with highly variable raw drinking water quality has shown the effectiveness of PŪR to produce water that is microbiologically safer than the starting water and meets the WHO guideline noted above. The product has been tested for chemical or biological efficacy on waters from Guatemala, Indonesia, Philippines, Bangladesh, Morocco, Kenya, and South Africa. The production of microbiologically safe drinking water depends on the total process associated with PŪR treatment. Turbidity removal is important in the PŪR process and other water treatment processes because it removes material that creates a chlorine demand in addition to providing surfaces upon which bacteria can escape the disinfection process.

WHO guidelines for drinking water quality recommend that indicators of fecal contamination (*Escherichia coli* or thermotolerant coliform bacteria) should not be detectable in any 100 mL sample of any water intended for drinking. While not totally applicable in the case of PŪR, WHO guidelines for centrally treated and distributed water indicate the following:

1) Neither fecal indicators nor total coliform bacteria should be detectable in any 100 mL sample of treated water entering the distribution system.
2) For water within the distribution system, the recommendation is again that no fecal indicators should be detectable in any 100 mL sample. The same applies to total coliforms, although the guideline does make

allowances in the case of larger supplies where an increased number of samples are examined. In this case total coliforms should not be present in 95 percent of the samples taken throughout any 12-month period.

Turbidity Removal

Tests performed on a variety of source waters (surface water, well water, collected rain water, model waters) with a wide range of starting turbidities (from <1 to >1000 NTU) indicate that on average PŪR treatment reduces final water turbidity to values of less than 1 NTU. This turbidity reduction helps to ensure chlorine is in fact disinfecting the water. Efficacy of any disinfection process is determined by the purity achieved by any prior treatment process. Physical processes such as flocculation and coagulation remove organic material and turbidity that interfere with the disinfection process. Aggregated and adsorbed microorganisms can be physically removed on coagulated particles at levels indicated in Table 10 and those remaining in solution are disinfected with the residual chlorine released in the PŪR process.

Biological Reduction (Bacteria, Viruses, and Protozoan oocysts)

Both water quality and analytical difficulty introduce variability in viral reduction numbers resulting in a large range of detected reductions. *C•t* values (concentration•time) are the product of the concentration and time required to bring about a 99% (2-log) reduction of a given agent. Concentration is measured in mg/L (parts per million) and time is measured in minutes. Table 11 provides *C•t* values for a number of common infectious waterborne organisms or model microorganisms. PŪR provides a *C•t* value of approximately 144 mg•min/L after 30 minutes at a dose of 4.8 mg•free chlorine/L (target dose for PŪR) and 288 mg•min/L after 1 hour. In practice, chlorine residuals are likely to be lower due to chlorine demand in the pre-treated and post-treated water. Thus, *C•t* values of 90 mg•min/L and 180 mg•min/L after 30 and 60 minutes respectively are much more realistic. The value attained after 30 minutes indicates that PŪR should be sufficient for the inactivation of a significant proportion (>99%) of contaminating microorganisms (bacteria and viruses). Both laboratory and field data indicate that this effectiveness is attained in real life conditions.

Table 11[1]. *C•t* values (mg•min/L) required for 99% inactivation of various agents by chlorine at 5°C.

Agent	*C•t* value (mg•min/L)
Escherichia coli	0.034 – 0.05
Poliovirus type 1	1.1 – 2.8
Hepatitis A (virus)	1.8
Rotavirus	0.01 – 0.05
Giardia lamblia cysts	47 - >150
Giardia muris cysts	30 – 630
Cryptosporidium parvum oocysts from human feces	$7.7 \times 10^6 - 8.7 \times 10^6$

[1] – Table from Guidelines for Drinking-Water Quality. Second Edition. Vol. 2. Health criteria and other supporting information. WHO, Geneva. Pg. 113. 1996.

PŪR was evaluated and qualified by field and laboratory testing. Test data consistently show a >6 log reduction in bacterial counts for representative waterborne disease causing organisms. Efficacy against parasites, as determined with *Cryptosporidium parvum* produced log reductions in the range of 1.7 to >4-logs. Data are not available to assess the virus removal efficacy of PŪR in field samples, however, laboratory tests show efficacy against model viruses. For perspective, the contact times required for 99% inactivation of poliovirus 1 are 1.1-2.8 mg•min/L and for rotavirus they are 0.01-0.05 mg•min/L. Actual reduction values in laboratory tests were 1.3-6.0 logs for poliovirus 1, 3->5.7 logs for rotavirus, and 3.3 to 6.0 log reduction for a mixed culture of poliovirus and rotavirus under varying conditions of temperature, pH, and organic load. Low log reduction values were associated with low temperature, high turbidity, high TOC and calcium hypochlorite levels that were 50% lower than that used in the final formulation of PŪR (i.e. highly stressed water conditions and low hypochlorite levels).

Floc Concentration Effects and Protozoan Cyst Removal

Chlorine disinfection is well known to be ineffective at inactivating *Cryptosporidium* oocysts whereas flocculation/coagulation can be effective at reducing the concentration of cysts and other particulate matter found in water. Cysts (and other contaminants) that were in the water prior to treatment become entrapped in the sludge that is filtered out and this sludge could potentially be ingested. Laboratory measurements on the flocculation efficiency associated with PŪR and resultant *Cryptosporidium parvum* oocyst removal indicate that approximately 20% of the floc (volume is approx. 50 mL from treating 10 liters) would need to be ingested for a person to be exposed to the same number of oocysts that were found in the original source water (see Table 12).

Assumptions:

1) Typical floc volume from treating 10 liters of water is approximately 50 mL,
2) Concentration of oocysts in source water is 10 oocysts/L, and
3) Water consumption = 2 liters per day.

Therefore, theoretical oocyst exposure = 20 oocysts/day/person.

Table 12. PŪR removal efficiency, floc fractional volume ingested and contaminant exposure in PŪR treated water vs. untreated waters. The numbers in the lightly shaded area are the number of oocysts ingested at the indicated removal efficiency and fraction of floc ingested.

Fraction of floc ingested	Removal Efficiency (% removal, #oocysts/mL floc)			
	1 log (90%, 1.80)	2 logs (99%, 1.98)	3 logs (99.9%, 1.998)	4 logs (99.99%, 1.9998)
0.10	9	9.9	9.99	9.999
0.20	18	19.8	19.98	19.998
0.50	45	49.5	49.95	49.995
1.00	90	99	99.9	99.99

Appendices

Appendix 1

Polyacrylamide and Acrylamide Monomer

Appendix 1

Appendix 2

American Academy of Clinical Toxicology; European Association of Poisons Centres and Clinical Toxicologists: Position Statement on the use of Syrup of Ipecac (Part1) and Drug and Poison Control Center Information: Statement on Iron Poisoning (Part 2)

Appendix 2-Part 1

Appendix 2- Part 2

Appendix 3

Iron Poisoning

Appendix 3

Appendix 4

Alternative Disinfectants and Oxidants Guidance Manual. Chapter 5 - Potassium Permanganate. EPA Document #815-R-99-014

Appendix 4

Appendix 5

Permanganate formulation information and residual permanganate levels

Appendix 5

Appendix 6

Chlorine Information - Guidelines for drinking-water quality, 2nd ed. Vol. 2. Health criteria and other supporting information.

Appendix 6

Geneva, World Health Organization, 1996. pp. 796-803.

Appendix 7

Report: Evaluation of the Sachet "L' Blue, F=1 For Child-Resistant Effectiveness for Procter & Gamble

Appendix 7

Abstract Summary, Ethics Review Committee

Protocol 2002-17: Efficacy of Flocculent Technology as an Arsenic Mitigation Strategy

This proposed study is designed to evaluate the effectiveness of a point-of-use combined chlorination-flocculent water treatment method to improve the microbiological and chemical composition of water used for drinking and other household purposes. The investigation will be undertaken in two phases; an initial stage that will consist of the collection of baseline data followed by an intervention stage that will evaluate the efficacy, the acceptance and use pattern of chlorination-flocculent product as a means of improving drinking water quality and will be conducted in the Matlab area. Following the identification of communities with arsenic contamination of their drinking water supply (>50μg/L), baseline data will be collected in the selected communities. This will include information pertaining to the demographics of households, diarrhea incidence, healthcare utilization, assessment of water use in the household, laboratory evaluation of water sources, and measurement of biological parameters for arsenic content. During the intervention phase of twelve-week duration, a total of 100 tubewells and one associated household per tubewell will be identified. One hundred households deriving their water from arsenic-contaminated tubewells will be randomly assigned to receive the point-of-use intervention chlorination-flocculent product and necessary supplies for its use. Baseline and follow-up measurements of biological parameters and of water composition will be obtained in both study groups. Weekly evaluation of intervention households' drinking water for residual chlorine levels and the incidence of diarrheal episodes will complement the monthly measurements of urine arsenic content in the mother of the household and measurements of the arsenic content of household drinking water. Measurements of the microbiological contamination of household water will be conducted at baseline, at mid-study, and at the conclusion of the intervention phase. Individual discussions with households using the flocculent product will assess use (problems & advantages) and the acceptability at the conclusion of the intervention phase. If less than half of the intervention households are using the product at 2 weeks following introduction of the intervention, the rationale for non-use will be explored, and additional activities to promote use will be undertaken before collecting subsequent urine samples. An assessment of the potential consequence of exposure to used, discarded flocculent product will be undertaken in 10 randomly selected households receiving the intervention product. Samples of discarded flocculent will be collected in a designated container with soil. This soil-flocculent mixture will be evaluated for arsenic content at mid-study and at conclusion of the intervention period. An additional 10 households who will not receive the intervention product will similarly collect soil from areas where they might dispose of flocculent, in designated containers. This soil will be evaluated at mid-study and at conclusion of the study period for arsenic content as a comparison to the discarded flocculent-soil mixture collected by the intervention group. The principal analysis of this study will be a comparison in individual women of their pre-treatment level of urinary arsenic compared to their level of urinary arsenic after 12 weeks of use of the intervention chlorination-flocculent product. Appropriate statistical methods will be applied to account for repeated observations of a single individual over time and clustering within communities.

1. The population included in this proposed study will be comprised of Bangladeshi residents of the Matlab DSS area and will include persons of both genders and all ages. As the intervention product will be added to the household water consumed by all members of the household, there is the potential that special population groups

will participate in the study. The intervention proposed in this protocol presents a minimal risk to participants, including children and pregnant women. Consent is voluntary; potential subjects will be fully informed, and the process of deciding whether or not to be in the study is a process appropriate to the local culture and process of decision-making.

2. The studies and interventions proposed in this protocol present minimal risk to participants, including children and pregnant women. The combination flocculent-chlorination product is composed of traditional chemicals used in drinking water treatment. Sodium carbonate is used as a flavorant and antioxidant in foods. Bentonite is used in dental materials, cosmetics and in pharmaceuticals as a binding or suspending agent. Magnafloc is routinely used in commercial water treatment systems. The World Health Organization recognizes calcium hypochlorite as equivalent to sodium hypochlorite and as an effective and safe drinking water disinfectant. Chitosan is derived from chitin, a polysaccharide found in the exoskeleton of shellfish such as shrimp, lobster, and or crabs. Chitosan is currently being sold as a "fat absorber" through various nutrition outlets. Clinical studies have shown no adverse health effects from ingestion of chitosan. At the dosage in the individual sachets, the chemicals are generally safe and inherently exhibit a low order of acute and chronic toxicity, except for iron sulfate. The sachet contains 425 mg of ferric iron. This amount of iron if accidentally ingested by a young child has the potential to cause iron toxicity. Ingestion of 30 mg/kg elemental iron is usually required to cause toxicity. A fatal dose is usually >250 mg/kg; however, deaths have occurred from ingestion of as little as 60 mg/kg. In the United States, child resistant packaging has markedly decreased accidental iron ingestions in children. The treated water does not have excessive iron concentration (0.1- 0.3 mg/liter) because the hydrous oxide form of iron precipitates out of solution. The used flocculent looks like mud and will likely be discarded on the ground with other refuse. After water treatment, the vast majority of the iron in the intervention product is converted from the more soluble ferric sulfate to the much less soluble and less bioavailable ferric oxide and ferric hydroxide. Thus, the predominant hazardous material in the discarded flocculent will be the hazardous material that was previously in the water; in this study, arsenic. Moving the materials from drinking water to refuse would be expected to markedly decrease the exposure of family members to arsenic. During previous studies in Guatemala, the used flocculent was consistently discarded far away from children and no accidental ingestions have occurred. The standard arsenic mitigation strategies that are currently in use in Bangladeshi communities have been evaluated for safety and as most are structural interventions, do not present a risk to human health. Moreover, the advocacy of the practices themselves, are part of the routine public health response to arsenic contamination in Bangladesh. They would occur whether or not this study is conducted. The activity that the study adds in these arms is increased surveillance.

3. Iron supplementation is commonly given to women during pregnancy and post-partum in Bangladesh. Thus, similar concentrations of iron as would be found in the intervention chlorination-flocculent product are already present in many Bangladeshi households. The treatment for acute iron ingestion is immediate medical attention. Instructions will be provided to households receiving the intervention flocculent-chlorination product to proceed immediately to the nearest health clinic for evaluation in the event of

suspected or actual ingestion of the product. Mothers will be provided with the location of the nearest health clinic or medical facility to the household receiving the intervention product by the village health worker responsible for that household. To minimize the possibility of accidental ingestion, the intervention flocculent product will be packaged in sealed single use sachets that are difficult for young children to open. To communicate the potential hazard from ingestion, adults will receive verbal instructions to keep the sachets away from young children and to dispose of the sludge away from children. The printing on the sachets will clearly communicate that the contents are not to be ingested directly. No ingestions have occurred in the Guatemala field study where packets have been supplied to 200 households for 8 months.

4. Each participating household and members within each household will be assigned unique identification numbers. These household and member identifiers will be collected on assessments to be used during the project during repeat visitations. These alphanumeric identifiers are needed to ensure accurate linkage of data. Personal identifiers will be removed from all computer files and only the identification number will be included in data analyses. A list linking the identification codes to the households and household members will be stored with restricted access at ICDDR,B offices. Professionals on the study team who require the information for assessing data validity will be provided with access. The list will be destroyed once data analysis is complete.

5. Initially, the proposed study activities will be explained to community leaders. Many families will hear about the study from these community discussions and from relatives or neighbors. Next, when going house to house for recruitment, project workers will specifically explain the project to all adults who are available in the household at the time of the visit. Members of the household will discuss participation amongst themselves, and with others in the community. They will be free to withdraw from the study at any point without consequence.
Accepting family consent from a head of household departs from standard U.S. guidelines for informed consent. Regulation 45 CFR 46.116 notes that an IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in 45 CFR 46.116, or waive the requirements to obtain informed consent provided the IRB finds and documents that:
    - The research involves no more than minimal risk to the subjects;
    - The waiver or alteration will not adversely affect the rights and welfare of the subjects;
    - The research could not practicably be carried out without the waiver or alteration; and
    - Whenever appropriate, the subjects will be provided with additional pertinent information after participation

    a) *Please refer to above explanation.*

    b) The results of the study will be shared with the participating institutions and the communities who participated in the study.

    c) There is no potential risk to the subject or privacy of the individual and compensation therefore will not be necessary.

6. A village health worker will administer the baseline assessment questionnaire to the mother or head of household in a 20-minute face-to-face interview held at the interviewee's home. Additional weekly assessments will involve verbal face-to-face interviews of less than 5 minutes duration. An acceptability assessment conducted as a 20-minute face-to-face interview at the conclusion of the intervention period will be administered by village health workers to the mothers of the households whom received the intervention product.

7. The study participants will benefit from receiving an intervention to reduce the arsenic content of their drinking water. Additionally, all study participants will benefit from improved surveillance of diarrhea that according to verbal autopsy reports is the leading cause of death among children less than five years of age in rural Bangladesh. Community health workers will act as a resource, providing educational interventions during regular visits to study families. If children are identified who have diarrhea, oral rehydration solution and instructions for its use will be provided. Benefits to households assigned to the intervention product include the possibility of a lower incidence of diarrhea and gastrointestinal illness as the intervention product contains a chlorine derivative that reduces the microbiological contamination of water. Households in the intervention product study arm will also receive materials required for the treatment of water with the product including 10 litre buckets, suitable stirring utensils, scissors, filtering cloths, and a supply of the intervention product that will be replenished during the intervention phase of the study. The supplies and training are necessary to insure proper use of the intervention product and are not considered a payment for participation. Households assigned to the standard arsenic mitigation strategies arm of the study will be offered one of the standard interventions appropriate for their community in accordance with the government of Bangladesh arsenic mitigation strategy and the policies of the Bangladesh Rural Assistance Committee (BRAC). Additionally, they will receive education regarding the health effects of arsenic contamination of their tubewell water supply and will be provided with instruction on how to use their standard intervention.

8. The proposed study does not require the use of records, organs, tissues, the fetus, or the abortus. The study will involve the voluntary collection of urine specimens from sentinel mothers of each intervention household that will undergo analysis for inorganic arsenic content. Confidentiality will be maintained regarding the urine arsenic test results and any remaining urine will be discarded and will not be subjected to additional testing. The statement to the subject should include information specified in item 2,3,4,5(c) and 7 as well as indicating the approximate time required for participation in the activity.

   The consent form reflects the above items.

Response to the Reviews (Reviewers 1 and 2) ICDDR,B RRC

Proposal: "Efficacy of Flocculent Technology as an Arsenic Mitigation Strategy"

Reviewer 1:

1. Selection of participants:
   a. We appreciate the suggestion to confine the study to a few adjacent villages, followed by the random selection of 200 tubewells for implementation. This was our original objective and plan for this efficacy study.
   b. We appreciate the comment regarding a concern about the variation in the number of households per tubewell. As our level of randomization will be the tubewell, this is not a prominent concern for us. As we will be analyzing the arsenic levels inform a sentinel mother chosen from 1 household per tubewell, there will be an equal number of intervention and control subjects analyzed. The only problem with having more households per tubewell is that it will require that we use more products, but we have planned for this additional requirement.

2. Scheduled activities for enrolled households: We will provide training sessions to an adult, female household member prior to the implementation of both the intervention and control measures.

3. Variables: primary outcome measurement
   We agree. The new equipment at ICDDRB/Intronics lab, Dhaka will permit us to speciation the urinary arsenic into inorganic and organic components and we will do so for the study.

4. Laboratory methods: We appreciate the comments that the sample collection methodology is vital to insuring accurate results and will review these aspects in detail with those responsible for collecting the urine and water samples.

5. Interventions: We appreciate the comments pertaining to the arsenic mitigation options that may be available to those households randomly assigned to the control groups. For our study, the most important comparison will be the change in arsenic levels from baseline.
   Furthermore, our comparison is not against another specific technology, but will be against the standard habits and practices.

6. Staff provision: We would welcome a review of the protocol by a water engineer. If a series of tasks that were felt to be an important contribution to the protocol would require an ongoing professional contribution are identified, we would approach the funding agency to consider adding a water engineer to the study team.

Reviewer 2:

1. Feasibility:
   We appreciate the comments regarding the assessment of the environmental impact of the discarded flocculent. The period of evaluation will actually span the **12 weeks** of the intervention period. Baseline measurements will be assessed during the 2-week baseline period and environmental samples will be obtained during the subsequent 12-week intervention period. Although the results obtained from this 12-week period would likely reflect the short-term

environmental impact, a more extensive environmental assessment could be conducted with a future implementation study. We realize that even 12 weeks is a relatively short time period, but there is little reason to believe that the strength of binding between arsenic and iron would vary much by season. Furthermore, we are cognizant that a process cannot be proven safe. There is always a risk that another scenario, with more time, or different assumptions could provide additional risks. We can, within the limitations of the study design, attempt to model the environmental impact of this intervention product.

The stability data compiled by Procter & Gamble support a 2-year shelf life of the flocculent-chlorination product.

International Centre for Diarrhoeal Disease Research, Bangladesh
CENTRE FOR HEALTH AND POPULATION RESEARCH
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Memorandum

17 November 2002

To : Dr. Mahfuzar Rahman
Principal Investigator of protocol # 2002-017
Public Health Sciences Division

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

Sub : **Protocol # 2002-017**

Thank you for your memo dated 3rd November 2002 with the modified version of your protocol # 2002-017 entitled "Efficacy of flocculent technology as an arsenic mitigation strategy". Your response and the modified version of the protocol were placed before the ERC in its meeting held on 13th November 2002. After review and discussion in the meeting, the Committee found that you have not satisfactorily addressed the issues raised by the Committee in its earlier meetings; and made the following observations on the modified version of the protocol:

a. The Committee felt that that efficacy of a particular technology and its promotion in the community (before efficacy and safety are established) should not ethically be studied simultaneously.

b. All households adjacent to an arsenic contaminated tubewell should not be encouraged to drink arsenic contaminated water even with an arsenic mitigation strategy nor should be followed up for safety or adverse effects, education or promotion unless each of the households are included in the study for complete evaluation, with informed consent of each member of the households. Therefore, only one representative household per tubewell should be included for this efficacy study. That should satisfy the study objective.

c. The PI should specifically mention the control arsenic mitigation strategy with its efficacy and safety data.

You are, therefore, advised to address the above issues and submit the modified version of the protocol for consideration of the Chair.

Thank you.

copy: Associate Director
Public Health Sciences Division