# HOUSEHOLD WATER TREATMENT USING SODIUM DICHLOROISOCYANURATE (NaDCC) TABLETS: A RANDOMIZED, CONTROLLED TRIAL TO ASSESS MICROBIOLOGICAL EFFECTIVENESS IN BANGLADESH

## THOMAS CLASEN,\* TANVEER F. SAEED, SOPHIE BOISSON, PAUL EDMONDSON, AND OLEG SHIPIN

Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, United Kingdom; School of Environment, Resources and Development, Asian Institute of Technology, Bangkok, Thailand; International Health Research Associates, Milwaukee, Wisconsin; Medentech, Wexford, Ireland

Abstract. We assessed the microbiologic effectiveness of sodium dichloroisocyanurate (NaDCC) tablets used on a routine basis at the household level by a vulnerable population. In a 4-month trial in Dhaka, Bangladesh, one half of the 100 participating households received NaDCC tablets and instructions on how to use the same; the other one half received a placebo and the same instructions. Monthly samples of stored drinking water from intervention households were significantly lower in thermotolerant coliforms (TTCs) than those of control households (geometric mean, 2.8 [95% CI: 2.2, 3.6] versus 604.1 [95% CI: 463.2, 787.9]; P < 0.0001). While 61.7% (116/188) of samples from the intervention households met World Health Organization (WHO) guidelines for 0 TTCs in drinking water, none of the 191 samples from control households met such a benchmark. Residual free chlorine in water samples suggested that householders consistently used the intervention, but 11.7% of samples exceeded the WHO guideline value of 5.0 mg/L, underscoring the need to ensure that tablet dose and vessel size are compatible.

## INTRODUCTION

Unsafe drinking water, along with poor sanitation and hygiene, are the main contributors to an estimated 4 billion cases of diarrhea disease annually, causing 1.8 million deaths, mostly among children < 5 years of age.<sup>1</sup> Contaminated water is also an important contributor to other potentially waterborne diseases, including typhoid, hepatitis A and E, and poliomyelitis. An estimated 1.1 billion people lack access to improved water supplies; many more are forced to rely on water that is microbiologically unsafe.<sup>2</sup>

Bangladesh has made remarkable progress in extending coverage of improved water supplies both in urban and rural settings.<sup>3</sup> In the urban slums of Dhaka, however, inadequately treated water, poorly maintained distribution systems, low coverage of sanitation facilities, and poor hygiene and water handling practices conspire to cause high levels of acute diarrhea among residents forced to rely on water supplies that are highly contaminated with fecal pathogens.<sup>4</sup> While the delivery of safe, piped-in water is an important goal, the World Health Organization (WHO) has begun to promote household water treatment as a means of achieving the health gains associated with safe drinking water (http:// www.who.int/household\_water/en/). Recent reviews have found such household treatment to be significantly more effective in preventing diarrhea than interventions at the source or point of distribution.5,6

Simple chlorination with sodium hypochlorite (NaOCl) has been shown to be among the most effective<sup>7</sup> and costeffective<sup>8</sup> approaches for treating water in the home. In randomized controlled trials, it has also been repeatedly shown to reduce episodes of diarrhea.<sup>9–11</sup> Nevertheless, the consistent and correct use of sodium hypochlorite has proved challenging in many settings. Sodium dichloroisocyanurate (NaDCC) tablets, long used in emergencies and recently approved by the WHO and US Environmental Protection Agency for the routine treatment of drinking water, may have certain advantages over sodium hypochlorite in terms of convenience and affordability that could overcome some of these challenges.<sup>12</sup> We undertook this study to assess the microbiologic performance of NaDCC tablets when distributed for use by a vulnerable population for treating water at the household level in a routine (non-emergency) context.

## MATERIALS AND METHODS

Study site and recruitment. The trial was conducted in the Geneva camp, an informal settlement of ~4,000 families in the Mohammadpur area of Dhaka. The camp is characterized by severe overcrowding and minimal services. One hundred households were selected to participate in the study from volunteers in an accessible series of blocks after a meeting in which full details were provided. Investigators explained that one half of the participating households would be randomly selected to receive an intervention designed to improve microbial water quality, and the other one half would receive a placebo that would have no effect on their water quality. To avoid any increased risk, all participants were encouraged to continue following their customary practices for collecting, treating, and storing water, even though they would also be adding the tablets to their water. A baseline survey was conducted to collect certain demographic data and information on water management, sanitation facilities, and hygiene practices. During the baseline survey, an investigator procured a pre-intervention sample of drinking water stored in the home to assess it for turbidity (in nephelometric turbidity units [NTUs]) and for residual free chlorine (RFC) and thermotolerant coliforms (TTCs). Thereafter, participating households were randomly allocated to either the intervention or control groups and followed up over 4 months from September to December 2005.

**Intervention.** The intervention consisted of Aquatabs brand water purification tablets manufactured by Medentech (Wexford, Ireland). The tablets combine solid NaDCC with a pharmaceutical/food-grade effervescent base that allows the tablets to dissolve rapidly when introduced into water, thus

<sup>\*</sup> Address correspondence to Thomas Clasen, Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK. E-mail: thomas.clasen@lshtm.ac.uk

creating a visual clue of its activity for users. Like other forms of chlorine, NaDCC produces hypochlorous acid, a wellknown oxidizing agent. Its chemistry, toxicity, and microbial effectiveness have recently been reviewed.<sup>12</sup> Tablets can be sized to treat specific volumes of water, typically 1, 5, 10, and 20 L. Based on a pilot study in a similar area of Dhaka,<sup>13</sup> we used a 67-mg NaDCC tablet designed to treat 20-25 L of water, producing a dose of free available chlorine (FAC) of 2 mg/L. Intervention households received foil-wrapped strip packs of 10 NaDCC tablets. Control households received a placebo consisting of tablets of the same color, size, and packaging but consisting solely of the effervescent base used in producing Aquatabs with no NaDCC. The active tablet and the placebo were only distinguishable by the lot number on the packaging, which was known only to the field investigator who distributed tablets to each householder on a weekly basis. Because householders lived in close proximity and often shared water, it was determined that a single-blind trial design would improve the validity of a comparison between intervention and control groups by ensuring that all participating households had their own tablets. Because of limited field personnel, however, it was not possible to blind the trial at the investigator level. The female head of each participating household attended a meeting during which the investigator showed how to treat their water using the tablets. Participants were instructed to use a vessel containing 20-25 L of clear water (examples of such vessels were shown) and to add one tablet to the water and wait at least 30 minutes before drinking the treated water. After the demonstration, the investigator answered any questions about the tablets and their use, and each attendee demonstrated to the investigator that she had mastered them. It is noted that the intervention consisted solely of the distribution of tablets and instructions on how to use the same for the treatment of water and no further information or instruction on water treatment or handling practices, hygiene, or any other behavior that may affect their exposure to diarrheagenic pathogens. Neither did they receive a vessel or any other hardware for use in treating water or storing treated water.

Water sampling and analysis. Starting in the second week after distribution of the tablets and continuing once each month for the ensuing 4 months, an investigator made unannounced visits at each participating household and procured a 125-mL sample of stored water that the head of household identified to be drinking water. The households sampled on any given day were determined by the investigator, but on each day, the investigator sampled an equal number of intervention and control households. If, without prompting from the investigator, the householder reported that the water had been treated but that the 30-minute contact time had not yet elapsed, the investigator returned to the household to collect the sample after such 30-minute period. The water was first assessed on site for RFC using DPD1 reagent (Palintest Limited, Tyne & Wear, UK) and a color comparator. The scale of the comparator allowed for readings by 0.1mg/L from 0.1 to 1.0 plus eight readings between 0.5 and 6.0 mg/L. The water sample for microbial assay was collected in sterile Whirl-Pack bags containing a tablet of sodium thiosulfate to neutralize any RFC. All samples were preserved between 4°C and 10°C and analyzed within 4 hours, following the membrane filter technique using the Oxfam Delagua portable incubator (Robens Institute, University of Surrey, Gilford, Surrey, UK). Sample water was passed through a 0.45-µm membrane filter (Millipore, Bedford, MA) and incubated on membrane lauryl sulphate media (Oxoid Limited, Basingstoke, Hampshire, UK) at 44 ± 0.5°C for 18 hours. The number of yellow colonies were counted and recorded as individual TTCs. When a volume of 100 mL produced a number of yellow colonies that were too numerous to count, the count was assigned a value for purposes of statistical analysis of 300 TTCs per 100 mL.

**Data collection and analysis.** Data were recorded on Excel spreadsheets (Microsoft, Redmond, WA) and analyzed using Stata 8 (Stata Statistical Software: Release 8.0; Stata Corp., College Station, TX). Student *t* test was used to compare intervention and control groups at baseline and for each follow-up visit. Geometric means for the overall follow-up period were calculated using summary measures (four values) for each household. Because bacterial counts in water samples tend to be distributed according to the log scale, we assessed such distribution and analyzed TTC counts after log<sub>10</sub> transformation to satisfy the assumption of normality. For such purposes, 1 was substituted for any values equal to 0. Generalized estimating equations (GEEs) were used for the analysis of repeated observations at the same household.

Ethics. Written, informed consent was obtained from the male or female head of each participating household at the beginning of the study. The study expectations and obligations by both the participants and investigators were explained and all questions were answered. Because participants were advised that the intervention had not been assessed in field settings for its microbial effectiveness and that in any event, one half would receive an indistinguishable, non-effective placebo, they were all encouraged to continue to follow their normal practices for collecting, treating, and storing water and not to rely on the tablets to provide safe drinking water. In this way, the study was not expected to increase any risk to participants. The study was reviewed and approved by the ethics committees of the London School of Hygiene and Tropical Medicine and the Asian Institute of Technology. Medentech agreed to endeavor to make Aquatabs available at the study site through local nongovernmental organizations (NGOs) or distributors after completion of the study if the intervention proved effective in improving water quality.

#### RESULTS

Baseline. Baseline demographic and other characteristics for the study population and for the control and intervention groups are shown in Table 1. A total of 100 households with 555 persons were recruited into the study (mean, 5.5 persons per household; range, 1-7). Of study participants, 10.6% were < 5 years of age at the start of the study, and 40% were between 5 and 18 years; only 25% were > 30 years of age. Most female heads of household were older than 30 (74%), and only 4% were < 20. Sixty percent of such female heads of household had no formal education and were illiterate, and an additional 22% had some primary education only. The homes of all study participants consist of single rooms and were constructed of brick with metal roofs. Householders procured their water either from their own (34%) or communal tube wells (66%). None of the household had their own sanitation facilities. All householders reported using communal latrines (located adjacent to the communal tube wells), although young children were observed to practice open def-

| Baseline characteristics       | Total      | Control     | Intervention | Difference |
|--------------------------------|------------|-------------|--------------|------------|
| Demographics                   |            |             |              |            |
| Total number of persons        | 555 (100%) | 276 (49.7%) | 279 (51.3%)  | NS         |
| Age group of mothers           |            | ~ /         |              | NS         |
| 15–30 tears                    | 4 (4%)     | 3 (6%)      | 1 (2%)       |            |
| 21-30 years                    | 22 (22%)   | 10 (20%)    | 12 (24%)     |            |
| 31–40 years                    | 44 (44%)   | 23 (46%)    | 21 (42%)     |            |
| > 40 years                     | 30 (30%)   | 14 (28%)    | 16 (32%)     |            |
| Household size                 | × ,        |             |              | 0 < 0.001  |
| 1–3 occupants                  | 9 (9%)     | 3 (6%)      | 6 (12%)      |            |
| 4–7 occupants                  | 54 (54%)   | 19 (38%)    | 35 (70%)     |            |
| > 7 occupants                  | 37 (37%)   | 28 (56%)    | 9 (18%)      |            |
| Sanitation and hygiene         |            | · · · · · · | × ,          |            |
| Type of sanitation             |            |             |              |            |
| Communal latrine               | 100 (100%) | 50 (50%)    | 50 (50%)     | NS         |
| Hand washing events            |            | · · · · · · | × ,          |            |
| After defecating               | 100 (100%) | 50 (50%)    | 50 (50%)     | NS         |
| Before eating                  | 100 (100%) | 50 (50%)    | 50 (50%)     | NS         |
| After cleaning the child       | 0(0%)      | 0 (0%)      | 0 (0%)       | NS         |
| Water handling practices       |            | ( )         | × ,          |            |
| Type of water source           |            |             |              |            |
| Household tubewell             | 34 (34%)   | 19 (38%)    | 15 (30%)     | NS         |
| Communal tubewell              | 66 (66%)   | 31 (62%)    | 35 (70%)     | NS         |
| Claim to treat water (boiling) | 5 (5%)     | 3 (6%)      | 2 (4%)       | NS         |
| Water storage                  |            | ( )         | ~ /          |            |
| Kalshi                         | 76 (76%)   | 40 (80%)    | 36 (72%)     | NS         |
| Other                          | 24 (24%)   | 10 (20%)    | 14 (28%)     | NS         |
| Access water by                | × /        | × /         | × /          |            |
| Pouring                        | 98 (98%)   | 50 (100%)   | 48 (96%)     | NS         |
| Dipping utensil                | 2(2%)      | 0(0%)       | 2 (4%)       | NS         |

 TABLE 1

 Baseline data for control and intervention groups\*

\* Demographic data are by individual; remaining data is by household

NS, not significant

ecation around the home. All female heads of household reported washing their hands with soap after defecating and before preparing or eating food; none reported washing hands after cleaning a child after defecation. Most (76%) reported using a "kalshi," a metal, vase-shaped vessel with wide brim and an open mouth shown in Figure 1, to collect

FIGURE 1. A "kalshi" vessel used to collect, treat, and store drinking water in the home (illustration by Michael Dillon).

and store water. Significantly, these were generally ~12-14 L in capacity rather than the 20-25 L volume that the 67-mg NaDCC tablet was intended to treat. Virtually all female heads of household (98%) reported accessing stored water by pouring it from the vessel into a glass or cup. Just 5% of households reported treating their drinking water, all by boiling. The mean cost for oil estimated by these householders for boiling was BDT 44.2 (US\$0.65) per day. Other householders reported that they did not treat their water, most because they could not afford fuel for boiling. Turbidity of pre-intervention water samples was low, with 94% of baseline samples having < 5 NTUs, and the maximum turbidity from any samples was 12 NTU. None of the pre-intervention samples contained detectible RFC. Except for household size shown in Table 1, there were no statistically significant differences between control and intervention groups with respect to baseline data.

**Microbial water quality.** Figure 2 shows the geometric mean TTC levels (and 95% confidence intervals [CIs]) for control and intervention households at baseline and at each sampling point. At baseline, there was no statistically significant difference between the geometric mean TTC counts between control (750.6; 95% CI: 602.2, 935.7) and intervention (922.4; 95% CI: 741.0, 1,148.1) groups (P = 0.1858). At each sampling point thereafter, water samples from the intervention group were substantially lower in TTC counts than samples from the control group. For the entire 4-month intervention period, the geometric mean TTC count was 2.80 (95% CI: 2.21, 3.56) for the intervention group and 604.12 (95% CI: 463.21, 787.91) for the control group, a difference that was highly significant (P < 0.0001).

The microbiologic performance of the NaDCC tablets can

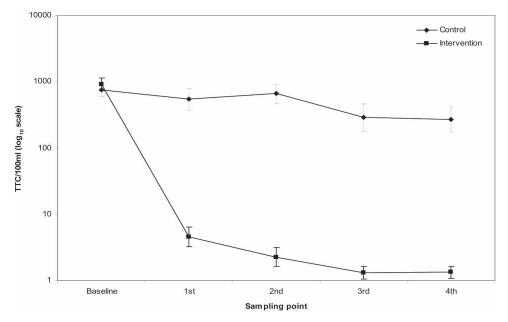


FIGURE 2. Geometric mean TTC counts (95% CI) by study group at baseline and each sampling point.

also be evaluated based on their capacity to reduce the portion of water samples presenting higher levels of fecal contamination. Table 2 sets forth the percentage of samples taken that fall into the various WHO risk categories for fecal contamination: 0 (in compliance), 1-10 (low risk), 11-100 (intermediate risk), 101-1,000 (high risk), and > 1,000 TTC/100 mL (very high risk). The intervention was associated with a statistically significant improvement in the percentage of samples meeting lower risk categories. While none of the 191 samples from the control group met WHO guidelines for 0 TTC/100 mL, 61.7% samples from the intervention households met such a benchmark. Conversely, 81.2% of samples from control households fell into the high risk or very high risk categories compared with none for the intervention group. The highest TTC count in drinking water samples from the intervention group was 26 TTC/100 mL.

**Free chlorine residual.** None of the samples from the control group were positive for RFC. Table 3 shows the distribution of RFC levels for intervention households at each sampling point and for all sampling points taken as a whole. None of the samples taken from this group had RFC levels < 0.1 mg/L. Of the 188 samples analyzed, 88 (46.8%) had an RFC of 0.1 to 2.0 and 166 (88.3%) had an RFC between 0.1 and 5.0 mg/L.

Table 4 shows the level of RFC against TTC/100 mL classified by risk category. GEEs were used to study the relationship between RFC concentration and TTC levels among the intervention group. The analysis yielded no statistically significant association between the two variables (P = 0.3185).

#### TABLE 2

Number (and percentage) of samples by WHO risk category (in TTC/100 mL)

| TTC/100 mL (WHO risk category) | Control    | Intervention | Р       |
|--------------------------------|------------|--------------|---------|
| 0 (conforming)                 | 0 (0%)     | 116 (61.7%)  | < 0.001 |
| 1–10 (low risk)                | 2 (1.0%)   | 44 (23.4%)   | < 0.001 |
| 11–100 (intermediate risk)     | 34 (17.8%) | 28 (14.9%)   | 0.496   |
| 101–1,000 (high risk)          | 89 (46.6%) | 0 (0%)       | < 0.001 |
| > 1,000 (very high risk)       | 66 (34.6%) | 0 (0%)       | < 0.001 |

### DISCUSSION

During a 4-month blinded, randomized, controlled trial in a slum in Dhaka, the use of NaDCC tablets at the household level was associated with a substantial decrease in the number of thermotolerant (fecal) bacteria in stored drinking water. The intervention also significantly increased the portion of stored drinking water that conformed to WHO guidelines for safe or low risk drinking water. The fact that 100% of water samples from the intervention households were positive for RFC also suggests that the intervention had strong uptake and compliance despite minimal programmatic support. While NaDCC tablets have been used widely in emergency applications, this is believed to be the first trial to assess the potential of the disinfectant for improving the microbial quality of drinking water when used by a vulnerable population on a routine basis. In light of the increasing body of evidence showing the health impact of household water treatment,<sup>5,6</sup> these results suggest that NaDCC tablets may be an effective intervention for preventing waterborne disease among a population treating their water at home on a regular basis.

While the intervention was microbiologically effective, the level of RFC in the treated water is potentially a concern. According to the manufacturer, the target level for effective disinfection with NaDCC tablets is 2 mg of FAC per liter, or 4 mg/L for highly turbid (> 100 NTUs) water. While some microbial pathogens (notably, Cryptosporidium sp., Mycobacterium sp., and certain viruses) exhibit greater resistance to chlorine, a few micrograms per liter of free chlorine kills or inactivates most waterborne pathogens.14 The WHO Guidelines for Drinking Water Quality establishes a guideline value-the concentration that does not result in any significant risk to health over a lifetime of consumption-for chlorine in drinking water of 5 mg/L, although the Guidelines note that this value is conservative and that no adverse effect level was identified in the critical study.<sup>15</sup> Results from this study show that 11.7% of samples (22 of 188) contained RFC in excess of this 5 mg/L guideline value. All of these were re-

|            |            | Sampling point |           |           |            |
|------------|------------|----------------|-----------|-----------|------------|
| RFC (mg/L) | 1          | 2              | 3         | 4         | Total      |
| 0.1-1      | 4 (7.8%)   | 4 (8.3%)       | 4 (8.9%)  | 6 (13.6%) | 18 (9.6%)  |
| 1.5        | 4 (7.8%)   | 9 (18.7%)      | 9 (20.0%) | 8 (18.2%) | 30 (16.0%) |
| 2.0        | 9 (17.6%)  | 13 (27.1%)     | 9 (20.0%) | 9 (20.4%) | 40 (21.3%) |
| 3.0        | 6 (11.8%)  | 7 (14.6%)      | 9 (20.0%) | 9 (20.4%) | 31 (16.5%) |
| 4.0        | 10 (19.6%) | 7 (14.6%)      | 5 (11.1%) | 7 (15.9%) | 29 (15.4%) |
| 5.0        | 10 (19.6%) | 3 (6.2%)       | 2 (4.4%)  | 3 (6.8%)  | 18 (9.6%)  |
| 6.0        | 8 (15.7%)  | 5 (10.4%)      | 7 (15.6%) | 2 (4.5%)  | 22 (11.7%) |
| Total      | 51 (100%)  | 48 (100%)      | 45 (100%) | 44 (100%) | 188 (100%) |

 TABLE 3

 Residual free chlorine (RFC) concentration (mg/l) in household stored water samples of intervention group

corded at 6 mg/L, the upper detection limit of the apparatus; thus, it is not clear how high the RFC may have reached in some cases. Exceeding this level with such frequency may be regarded as a potential health concern. The *Guidelines* also note that the taste and odor thresholds for chlorine are 5 and 2 mg/L, respectively, and that there is increasing likelihood that some consumers may object to the taste of water with RFC concentrations of between 0.6 and 1.0 mg/L. Further studies should evaluate the impact of various levels of RFC on uptake (i.e., acquisition, correct use, consistent use) of the intervention.

Excess dosing in this case seems to have been caused by a miscalculation of the size of the vessels that householders would use to treat their drinking water. In a 1-month pilot study in the Lalbagh area of Dhaka, the same 67-mg tablet used in the present study was used because all householders collected and stored their water in vessels (mainly kalshis) with a capacity of 20-25 L.13 In that study, none of the 132 samples had a RFC in excess of 3.0 mg/L. In this case, the kalshis used to treat water were consistently smaller than in the pilot study-averaging 12-14 L. It seems that these smaller-sized vessels led to higher concentrations of RFC here. Recognizing the potential problem, investigators considered changing the dose of NaDCC by encouraging householders to use only half a tablet. In this case, they elected not to do so because some householders did use larger containers, and it was agreed that the risk of underdosing was greater than the risk of overdosing. In the future, it will be important for implementers to correctly size the tablet for the population or, if necessary, distribute standard-sized vessels with the tablets to increase the likelihood of optimal dosing.

A second issue concerns the presence of TTCs even from water samples containing higher levels of RFC. While this might raise questions about the biocidal efficacy of the intervention, the susceptibility of TTC (> 99% of which are *E. coli*) to hypochlorous acid, the active agent produced by NaDCC and other chlorine disinfectants, is well documented.<sup>16</sup> A small portion of these positive samples may have been collected before the required contact time with the dis-

| TABLE | 4 |
|-------|---|
|-------|---|

Residual free chlorine (RFC) concentration against thermotolerant coliform (TTC) risk category in household stored water samples of intervention group

|                       |                                      | TTC/100 mL                          |                                     |  |
|-----------------------|--------------------------------------|-------------------------------------|-------------------------------------|--|
| RFC (mg/L)            | 0                                    | 1–10                                | 11-30                               | Total                                  |
| < 0.5<br>0.5–5<br>> 5 | 8 (6.9%)<br>96 (82.8%)<br>12 (10.3%) | 2 (4.5%)<br>37 (84.1%)<br>5 (11.4%) | 1 (3.6%)<br>22 (78.6%)<br>5 (17.8%) | 11 (5.8%)<br>155 (82.4%)<br>22 (11.7%) |
| Total                 | 12(10.5%)<br>116(100%)               | 44 (100%)                           | 3(17.8%)<br>28 (100%)               | 188 (100%)                             |

infectant. Because the sample bag contains sodium thiosulfate to immediately neutralize the chlorine, such samples would contain culturable TTCs even in the presence of higher levels of RFC. The more likely explanation is that samples were contaminated during collection. Samples from household stored water were not drawn aseptically from the vessels but poured out of the vessel to duplicate the method used by householders when drawing a drink of water. Because kalshi and similar vessels have wide brims that are frequently touched by hand or otherwise exposed to contamination, it is likely that water poured over such brim could have washed some of these contaminants into the sample bag where they would have survived because of the immediate neutralization of the chlorine. Both of these explanations are compatible with the finding that there was no relationship between the levels of RFC and TTC in the product water. Further studies should investigate these and other possible explanations for the observation here of TTCs in water samples recorded to contain RFC. Such studies should also include steps to minimize this contamination.

Certain aspects of this study limit its generalizability to other populations and settings. First, as with most trials, participants were self-selected and may have been more motivated to use the intervention than might be expected by a general population targeted for intervention. Second, the source water available to householders in the study setting, although of poor microbial quality, was readily accessible in sufficient quantities to meet household needs. In settings where water supplies are inadequate, conventional improvements in such supplies (protected wells, boreholes, piped-in supplies) may take priority over point-of-use water treatment. Third, during the study period, the water in the study community was consistently of low turbidity (< 5 NTUs). High or variable turbidity (such as during monsoons), if it consists of organics that increase chlorine demand, will require corresponding changes in the amount of NaDCC necessary to ensure proper disinfection. This may require added programmatic support and could increase the risk of insufficient dosing by householders seeking to conserve tablets.

Because the intervention has shown microbiologic effectiveness in the field when used by the target population, it is now appropriate to assess its health impact in a rigorous field trial. A recent systematic review of water quality interventions to prevent diarrhea identified some of the methodologic shortcomings of such health impact evaluations.<sup>6</sup> Among other things, it was recommended that such assessments be blinded, be reasonably long in duration, and be conducted in a programmatic rather than research context. Because there is increasing evidence that the health gains from water quality interventions depend on correct and consistent use by the target population,<sup>6,17</sup> it is also important that such an evaluation carefully measure compliance. Finally, because the ultimate impact of such an intervention will depend on its ability to be scaled up on a sustainable basis, it is important to study factors associated with uptake by an at-risk population and models for its dissemination.

#### Received July 21, 2006. Accepted for publication September 6, 2006.

Acknowledgments: The authors thank the residents of the Geneva camp who generously participated in this study and Dushtha Shasthya Kendra, Neelima Afroz Molla, and Dr Akram Hossain for assistance.

Disclosure: T. Clasen provides consulting services to Medentech, a manufacturer of NaDCC tablets. P. Edmonson is technical director at Medentech. These statements are made in the interest of full disclosure and not because the authors consider this to be a conflict of interest.

Financial support: Medentech, a manufacturer of NaDCC tablets, donated the tablets and placebos used in this trial and covered the cost of consumables used in the water analyses.

Authors' addresses: Thomas Clasen, Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK, E-mail: thomas.clasen@ lshtm.ac.uk. Tanveer F. Saeed, School of Environment, Resources and Development, Asian Institute of Technology, PO Box 4, Klong Luang, Pathumthani 12120, Thailand, E-mail: onindo26@yahoo.com. Sophie Boisson, International Health Research Associates, 2501 E. Beverly Road, Milwaukee, WI 53211, E-mail: sophie.boisson@ gmail.com. Paul Edmondson, Medentech, Whitemill Industrial Estate, Clonard Road, Wexford, Ireland, E-mail: pedmondson@ medentech.com. Oleg V. Shipin, School of Environment, Resources and Development, Asian Institute of Technology, PO Box 4, Klong Luang, Pathumthani 12120, Thailand, E-mail: oshipin@ait.ac.th.

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