ORIGINAL RESEARCH

Remote Site Production of Sterile Purified Water from Available Surface Water

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Abrreviations:
CDC = Centers for Disease Control
CW = challenge water
EFA = effective filter area
EPA = Environmental Protection Agency
EU = Endotoxin Units
LRV = log reduction value
PW = product water
SPW = Sterile Purified Water, USP
SWFI = Sterile Water for Injection, USP
WPD = Water Purification Device
WPP = Water Purification Pack
US = United States
USP = United States Pharmacopeia

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Abstract

A water purification and sterilization device was tested for its functional capabilities. Challenge water consisting of potable water augmented with bacteria, endotoxin, virus, suspended solids, and dissociable ions (sodium chloride, lead or arsenic salts) was passed through the device. The product water quality attributes were analyzed. The device demonstrated reduction in bacteria of >7 logs, endotoxin was reduced by >4 logs, virus was reduced by >4 logs, and dissociable ions were reduced by >3 logs. The product water of the device met the limits for a range of chemical entities specified by the United States Pharmacopeia and Association for the Advancement of Medical Instrumentation. The product water met the quality attributes of Sterile Water for Injection, USP, Sterile Purified Water, USP, and the Water for Dialysis. The device provides a logistical advantage in reducing the weight of transport of packaged water by 83% and the cube by 67%. It operates manually by gravity and is disposable after a single use. The device provides an effective alternative to the transport and use of packaged sterile water in remote locations by production of sterile water at the point-of-need using available water. It also is capable of producing safe drinking water following the production of clinical waters. This device has been cleared by the US Food and Drug Administration for production of three liters Sterile Purified Water, USP from Environmental Protection Agency (EPA) grade drinking water.

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Introduction

Sterile Purified Water can provide a safe and effective means of wound cleansing. Wound cleansing is an important part of the wound healing process as the presence of debris, necrotic tissue, excess wound exudate, dressing residue, and metabolic waste on the surface of the wound can impede healing and increase the potential for infection.[1–3]

Infection control via cleaning of equipment used in medical procedures and of medical personnel's hands is considered the single most important procedure for preventing nosocomial infections,[4] according to the Center for Disease Control (CDC) guideline for hand washing and hospital environmental control. In spite of this, there is poor compliance with hand-washing protocols by physicians caused by lack of motivation, lack of facilities, understaffing, and unacceptable hand-washing products.[4] Guidelines for replacement of soiled wound dressings and proper wound irrigation requires use of sterile water.[5]

Sterile water also is important for equipment cleaning for a wide range of clinical applications, such as intubation, nasogastric tubes. Surgical and dental instrument sterilization with "sterilant/disinfectant" requires that the process be followed by aseptic rinsing with sterile water, drying, and placement in a sterile container.[6] The CDC also recommends that sterile saline or sterile water should be used as a coolant/irrigator when surgical procedures involving the cutting of bone are performed.[6]

Sterile and/or purified water is recommended for use as a diluent for enteral, nutritional, oral vaccine, oral drug preparations, or infant formula. Use of sterile or purified water is recommended or required for numerous medications and oral vaccines.[7] The most efficient means of large-scale therapy for acute epidemic gastrointestinal diseases like cholera is oral rehydration with electrolyte formulations.[8] However, diluent water for oral rehydration solutions (ORS) is commonly available drinking water containing the pathogen causing the original infection.

Immunocompromised individuals susceptible to infection by opportunistic agents or having chemical sensitivities or environmental illnesses would benefit from a "medical-grade" of water, free of offending organisms or contaminating chemicals.[9]

Availability of sterile and/or purified water in remote locations is limited by the logistics associated with transport of this water to the point-of-need. The remoteness of many locations makes the cost of this transport prohibitively expensive. The alternative to transportation of sterile water to the remote settings is purification at the point-of-need using drinking water.

The cost of transportation of any material commonly is based upon the cost per pound. Commercial transportation costs vary tremendously based upon distance. Military logistics costs commonly are based upon rate per hour for a given aircraft platform. For example, the C-141B hourly cost of operation is [US]$46,000 for priority cargo flights.[10]

By increasing the number of delivered liters produced per pound of cargo, the cost per liter is reduced. It is not possible to reduce the volume of packaged water. However, water purification devices capable of producing multiple liters of product water can accomplish such a reduction in transport costs.

The MainStream™ device (PRISMEDICAL Corporation, American Canyon, CA) provides a means of producing Sterile Purified Water, US Pharmacopeia (USP) in remote locations from EPA grade drinking water. (The PRISMEDICAL Triton™ Water Purification Unit can produce EPA grade water from available fresh water [not described here].) It consists of a reservoir bag, a purification pack, and a collection bag. The device is terminally sterilized by exposure to a validated dose of gamma irradiation. It produces three liters of sterile water in approximately 45 minutes using only gravity, without other external power. External pressurization of the source water, reservoir bag using a weight can decrease the production time to 15 minutes.

The object of this investigation was to test the capacity of a device designed for remote site purification of drinking water to meet the water quality attributes of Sterile Water for Injection, USP[11] (SWFI) and Sterile Purified Water, USP[12] (SPW). These attributes pertain to the critical purity measures for waters used in clinical settings; including sterility, concentration of dissociable ions present (conductivity), pH, endotoxin concentration, particulate concentration, and chemical composition (aluminum, calcium, carbon dioxide, chloride, sulfate, and oxidizable substances.[11–12] The AAMI RD5[13] and RD62[14] include acceptable chemical concentration of waters intended for use in production of hemodialysis solutions. The chemicals included in the RD62 have contaminant maximum concentrations (mg/L) of calcium 2 (0.1 mEq/L), magnesium 4 (0.3 mEq/L), potassium 8 (0.2 mEq/L), sodium 70 (3.0 mEq/L), antimony 0.006, arsenic 0.005, barium 0.10, beryllium 0.0004, cadmium 0.001, chromium 0.014, cyanide 0.02, lead 0.005, mercury 0.0002, selenium 0.09, silver 0.005, aluminum 0.01, chloramines 0.10, free chlorine 0.50, copper 0.10, fluoride 0.20, nitrate (as N) 2.0, sulfate 100, thallium 0.002, and zinc 0.10.[14]

Methods

Available Surface Water Quality Analysis

A database of water quality information consisting of >40 years of testing over a wide portion of the globe was compiled.[15] This database contains more than 27 million lines of data. Statistical analysis of the data provided the frequency of observation and concentration likely to be encountered in the environment for a wide range of contaminants. The box plot ranking of the contaminant concentrations provided the probability for encountering any given concentration of the contaminant. For chemical contaminants analysis of the toxicity associated with specific concentrations of contaminant defines the relative hazard represented by that contaminant.

Challenge Water Preparation

To adequately test the capabilities of a water purification device (WPD), a standardized challenge water (CW) was developed. This water consisted of municipally treated water meeting Environmental Protection Agency (EPA) Primary Drinking Water Standards that was augmented with bacteria, endotoxin, and dissociable ions. After passing the CW through the WPD the product water (PW) was recovered and tested for the water quality attributes of the USP monograph for Sterile Purified Water,[11] additional USP tests and the Association for the Advancement of Medical Instrumentation (AAMI) RD5[13] and RD62[14] tests for water for dialysis. Additional testing included challenge with suspended solids and chemical challenge with chlorine, arsenic, and lead.

Product Water Preparation

Three liters of CW were added to the fill bag of the MainStream™ device. Product Water was collected by gravity flow through the purification pack and into the collection bag.

Bacterial Preparation and Enumeration

To adequately challenge the system with bacteria, a modified microfilter validation method of ADVAMED (formerly Health Industry Manufacturers Association [HIMA])[16] was utilized. Briefly, *Brevundimonas diminuta* (ATCC No. 19146) was grown in tryptic soy broth for 24 hours at 37°C. The culture was pelleted by centrifugation at 1,000 g for 20 minutes. The pellet was re-suspended in saline lactose broth and incubated for 24 hours at 37°C. *B. diminuta*

grown for 24 hours under these restricted growth conditions results in reduced bacterial diameter of 0.3 microns.[17] The culture was pelleted by centrifugation at 1,000 g for 20 minutes and resuspended in water.

A sufficient amount of bacterial concentrate was added to the CW to achieve $2.5x10^5$ colony forming units (cfu)/mL. Bacteria were enumerated by culturing serial (1:2) dilutions of the CW on paired TSA plates. Bacteria were enumerated after incubation for 48 hours at 37°C. Bacterial concentration was expressed as the average cfu/mL. Product water bacterial concentration was determined by filtration of 1 liter of PW through a sterile filter under vacuum. The filter was then cultured for 48 hours at 37°C. This volume of PW was sufficient to achieve $>1x10^7$ cfu/volume of cultured PW/cm^2 of effective filter area (EFA) or a >7 log reduction value (LRV). The LRV was calculated by the following:

1. Calculation of the effective filter area (EFA) = the area of effective filter expressed in cm^2
2. Calculation of the number of organisms required for $>10^7$ organisms/cm^2 of EFA
3. Calculation of the log reduction value/cm^2 = $\log_{10}$ number of organisms in the challenge/ number of organisms in the filtrate*

*Where no colonies were observed the number of organisms in the filtrate is expressed as one (1), and the resulting LRV is expressed as > the calculated LRV.

Endotoxin Augmentation and Quantification

Endotoxin was obtained from Charles River or Associates of Cape Cod Indicator Endotoxin. A sufficient amount of endotoxin concentrate was added to the CW to achieve 200 Endotoxin Units ±100 EU/mL. The concentration of endotoxin recovered was determined by turbidimetric analysis[18] using the Endosafe Endotoxin Analyzer (Model Number: ELx808, Charles River Laboratories).

Virus Augmentation and Quantification

The bacteriophage, ΦX174, was selected as a representative virus challenge based upon discussions with the FDA (Personal Communication, C.D. Lytle, March 1999) and use of this virus in analogous testing.[19] The virus was propagated in *Escherichia coli* (ATCC No. 13706-B1) per ATCC procedures.[20] The CW was augmented with a $1x10^6$ plaque forming units (pfu)/mL. The CW was passed through the WPD and collected as PW. A 1 mL sample of product water was plated with a lawn of *Escherichia coli*. Plaques were measured after 24 hours incubation at 37°C.

Dissociable Ion Augmentation and Quantification

The level of conductivity of the CW was augmented with sodium chloride to bring the conductivity to 2.0 ±0.1 mS/cm or a total dissolved solids TDS concentration of 1,000 ppm (mg/L). The concentration of TDS in the CW was determined by measurement of the conductivity[21] with a conductivity meter (Cole Palmer, Accumet, Model 20).

Particulate Matter Determination

Particulate matter test method was adapted from the USP method.[22] Product water was analyzed by passage of PW through a microfilter followed by visual enumeration of particles. The counts were expressed as number of particles of >10 micron or >25 micron/mL of the PW. The limits for these particles per volume of fluid analyzed was <12.0 particles/mL for particles >10 microns and <2.0 particles/mL for particles >25 microns.

Particulate Matter Challenge

The insoluble portion of AC Fine Test Dust (Part No. 415, Duke Scientific, CA) was used to simulate the levels of suspended particles in surface waters. The 90th percentile of suspended solids within the database was 159 mg/L; the 97.5th percentile was 552 mg/L.[15] These concentrations of particulates were suspended in CW. Flow rates were monitored during the challenge.

SPW, USP Chemical Testing

Chemistry tests listed in the USP Monograph for SPW[12] were performed on the PW. The pH was measured[23] using a pH meter (Cole Palmer, Accumet, Model No. 20). For measurement of PW with conductivity levels <10.0 µS/cm, the PW was augmented with 0.3 mL of saturated potassium chloride/100 mL of water.

Ammonia concentration in the PW was determined. A 100 mL sample of PW was mixed with alkaline mercuric-potassium iodide (Nessler's Reagent).[24] The concentration limit was less color in the test sample than a positive control containing 30g of ammonia.

Calcium concentration in the PW was determined.[12] Two mL of 3.5% ammonium oxalate was added to a 100 mL of PW. The acceptance limit was no turbidity in the test sample.

Carbon dioxide concentration in the PW was determined.[12] A 25 mL sample of PW was mixed with 25 mL of 0.3% calcium hydroxide solution. Acceptable PW test samples remained clear.

Chloride concentration in the PW was determined.[12] Five drops of nitric acid in 1 mL of 0.1 N silver nitrate was added to a 20 mL sample of PW. Acceptance was based upon less turbidity in the test sample than a positive control containing 0.5 mg/L Cl.

Sulfate concentration in the PW was determined.[12] One mL of barium chloride test solution (12 g barium chloride/100 mL) was added to 100 mL of PW test sample. Acceptable PW test samples did not develop turbidity.

Oxidizable substances concentration in the PW was determined.[12] A 100 mL PW sample was mixed with 10 mL of 2 N sulfuric acid and heated to boiling, followed by addition of 0.2 mL of 0.1 N potassium permanganate. In acceptable PW test samples, the pink color does not disappear.

AAMI Chemistry Testing

The Association for the Advancement of Medical Instrumentation RD5[13] and RD62[14] chemistry tests were performed after one hour and 24 hours of incubation in a collection bag using inductively coupled plasma spectrophotometry (Spectra Laboratories, Hayward, CA). These tests

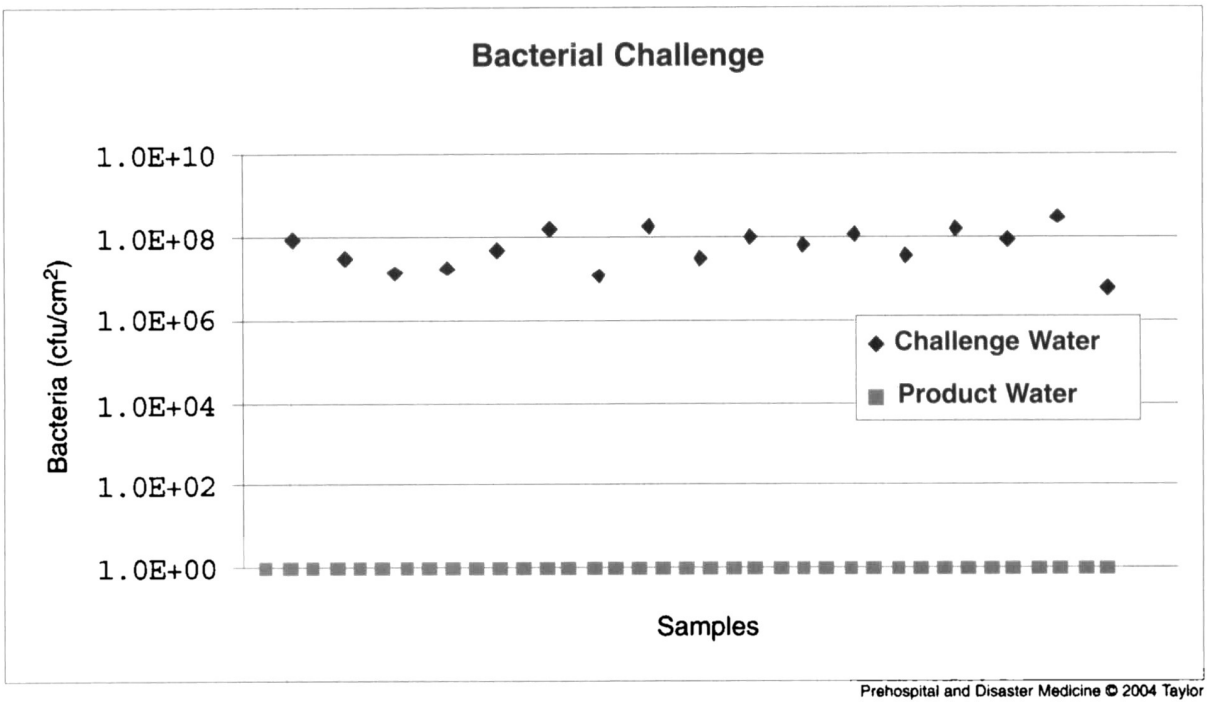

Figure 1—Bacterial challenge (Challenge Water containing >1 x 107 cfu/cm^2 of effective filter area (EFA) of *B. diminuta* grown for 24 hours under restricted growth conditions was passed through the Water Purification Device. The Product Water (PW) bacterial content was determined by passage of PW through a sterile filter, which was then cultured for 48 hours. Where no colonies were observed in the PW, the bacterial concentration was expressed as <1 cfu/cm^2 of EFA.)

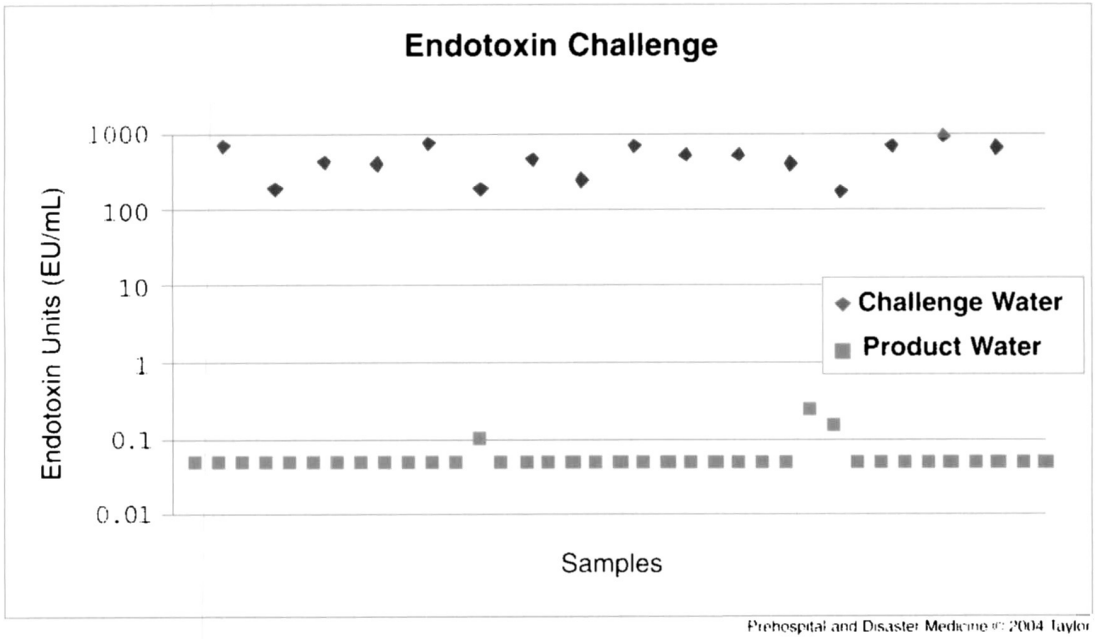

Figure 2—Endotoxin challenge (Challenge Water containing standardized endotoxin at 200 EU/mL + 100 EU was passed through the Water Purification Device. The endotoxin concentration of the Product Water was determined turbidometrically.)

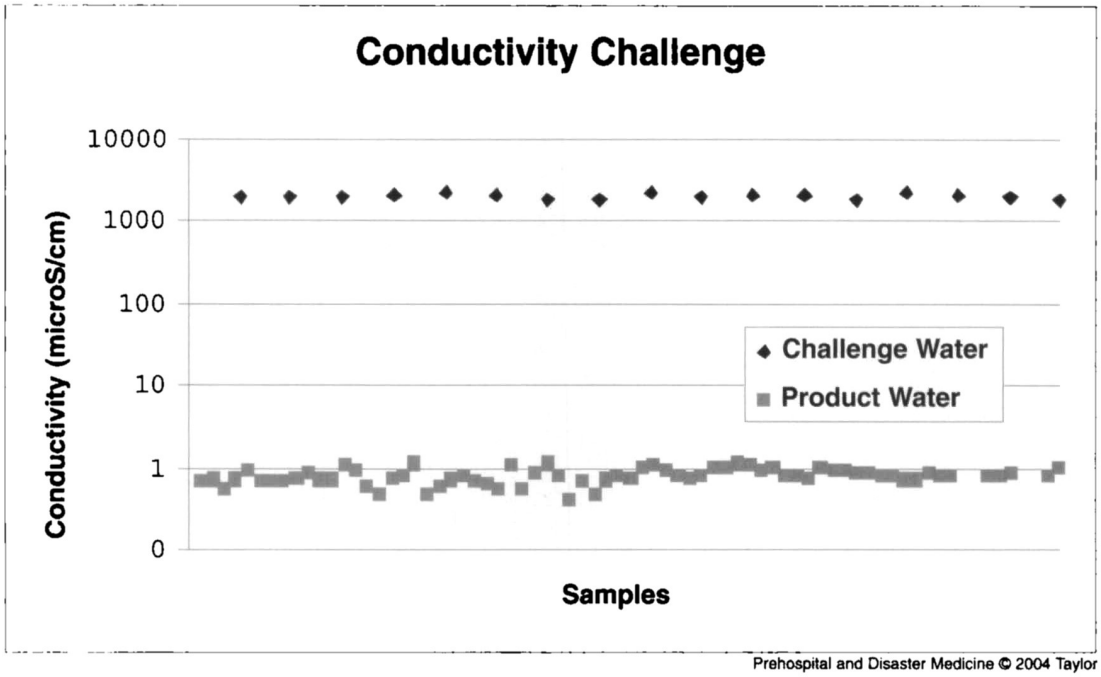

Figure 3—Conductivity challenge (Challenge Water was augmented with dissociable ions (sodium chloride) to a conductivity level of 2,000 S/cm + 0.1 S/cm, then passed thorough the Water Purification Device. The conductivity of the Product Water was determined.)

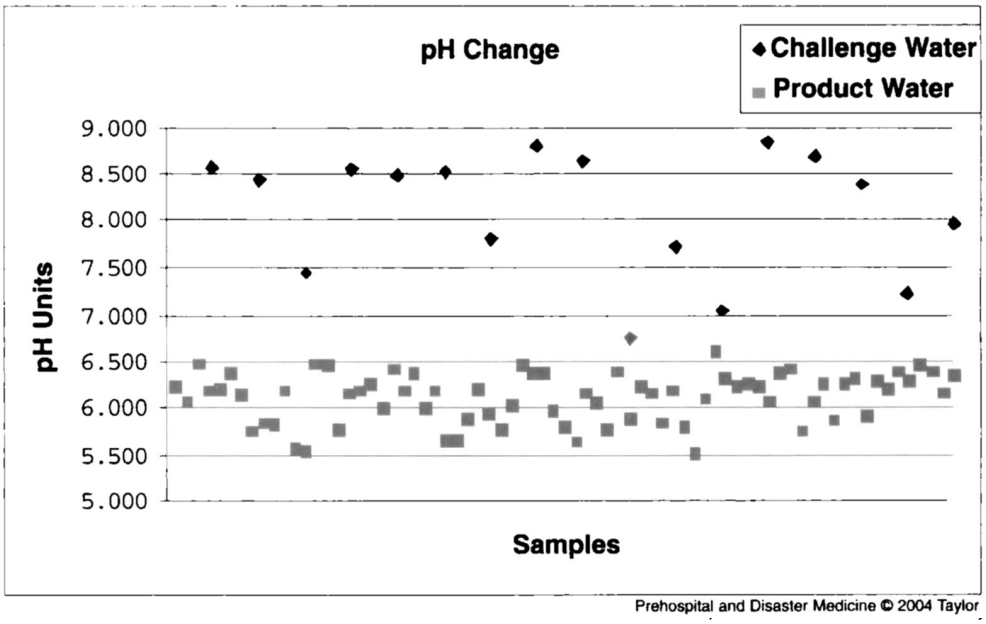

Figure 4—Change in pH (The pH of the Challenge Water was analyzed prior to passage through the Water Purification Device. Following collection of the PW the pH was determined.)

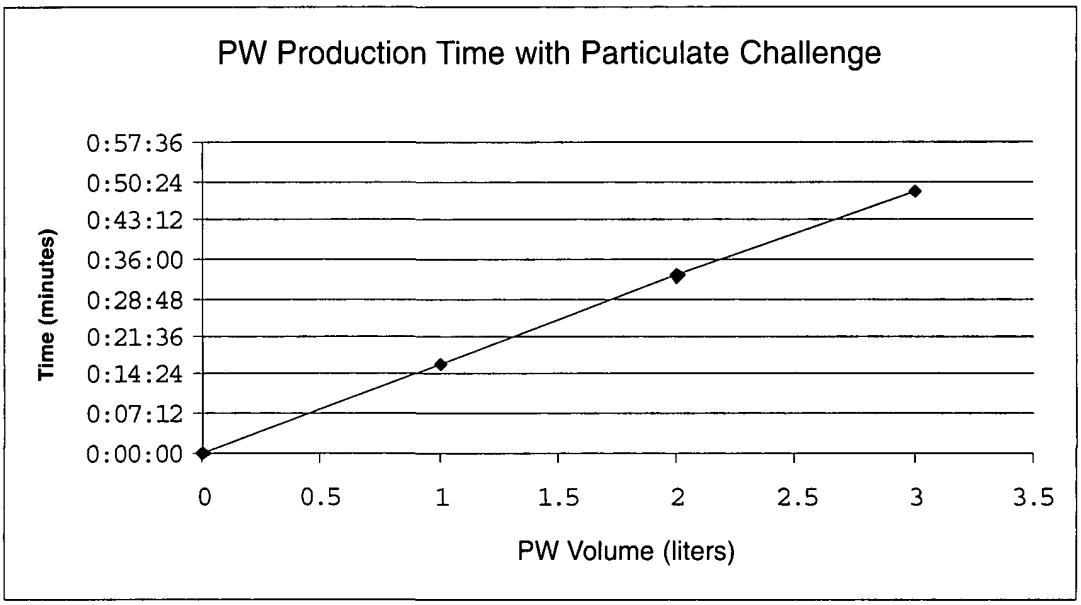

Figure 5—Particulate challenge (Challenge Water containing suspended solids equivalent to the 90th percentile of solids in the database were used to challenge the Water Purification Pack. Product Water production time per delivered volume was monitored.)

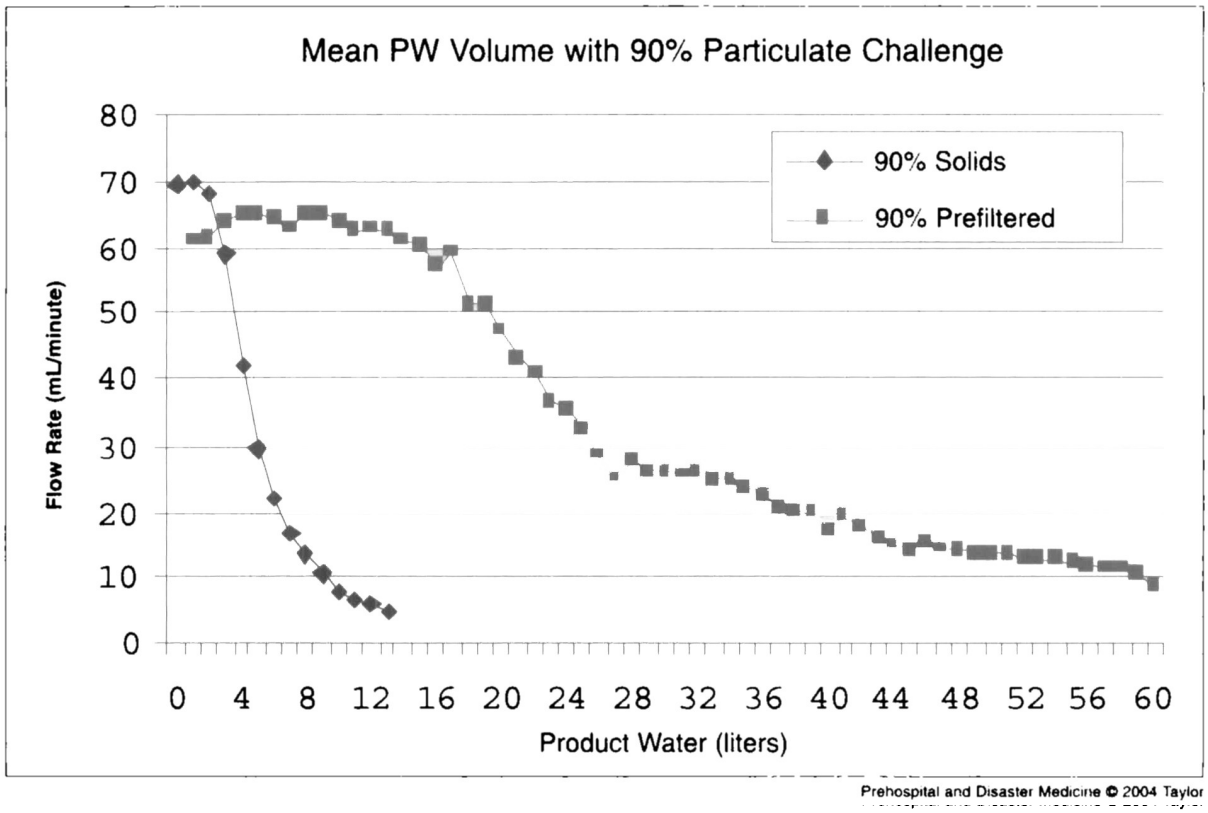

Figure 6—Product Water (PW) volume production from 90th percentile particulate challenge (Particulate containing CW equivalent to the 90th percentile of suspended solids in surface Waters[15] was used to challenge Water Purification Pack. Flow rates were monitored per delivered PW volume.)

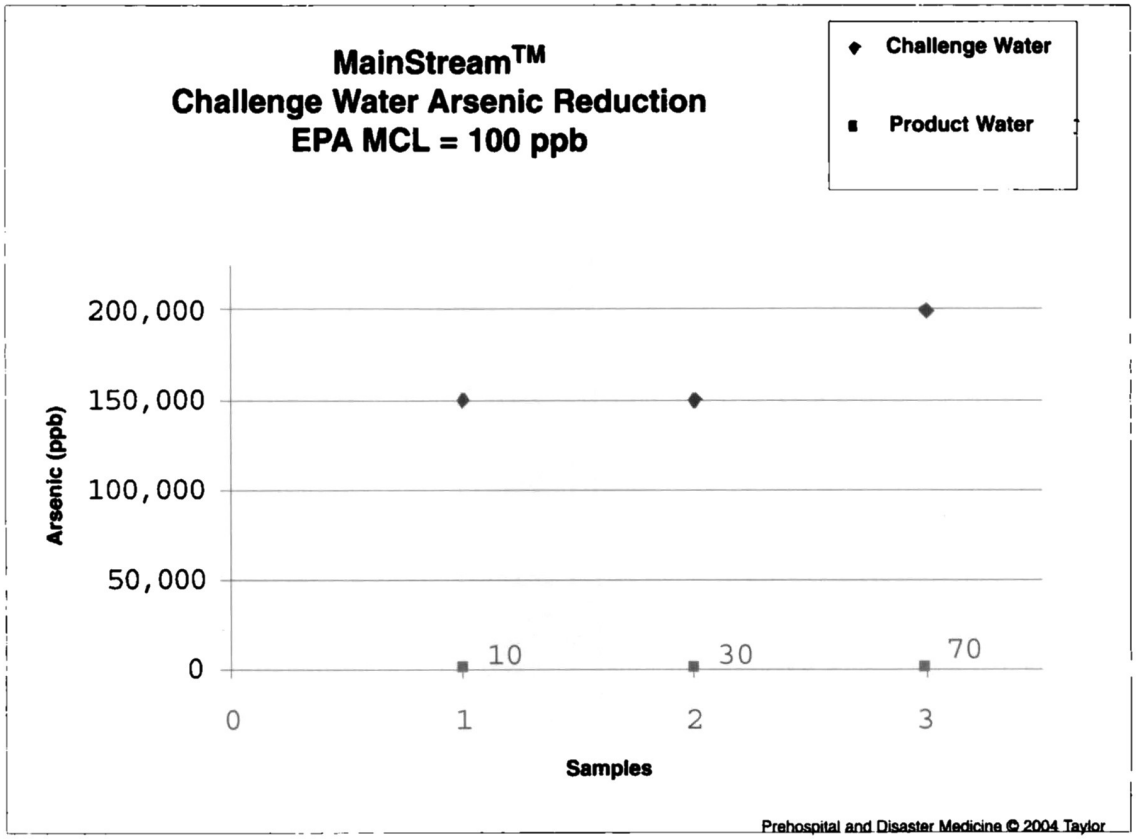

Figure 7—Arsenic Reduction (A mean Challenge Water concentration of 167,000 g/L (ppb) was used to challenge Water Purification Pack. The arsenic concentration in Product Water was measured. (ppb = parts per billion))

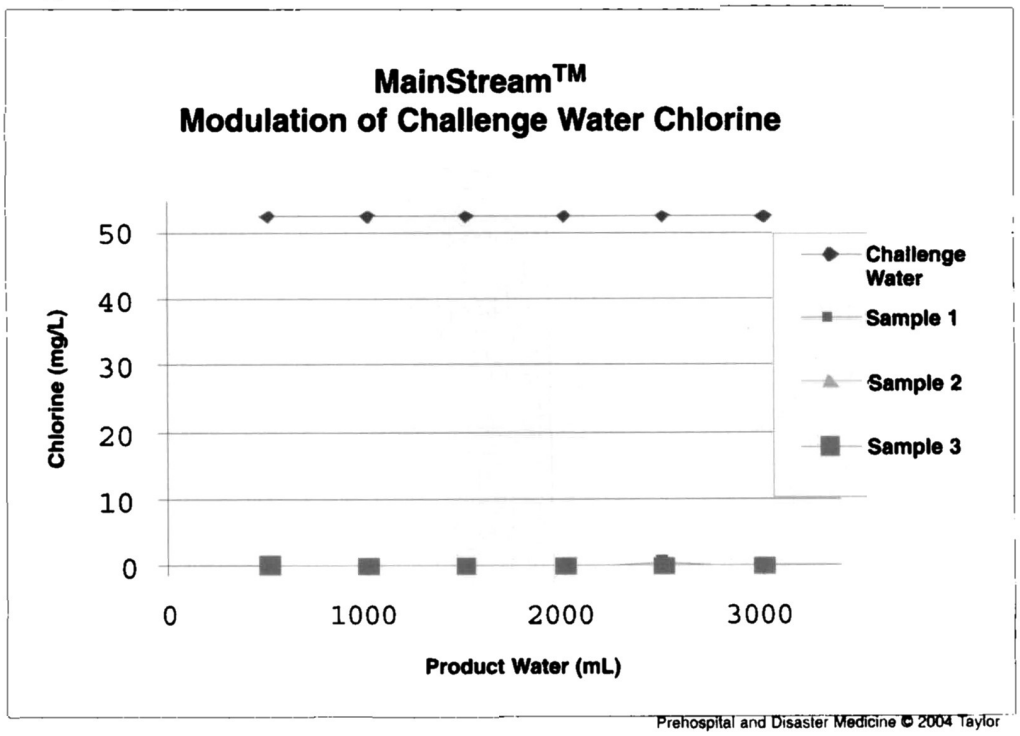

Figure 8—Modulation of challenge water chlorine reduction (Challenge Water containing 53 mg/L of chlorine was passed through Water Purification Pack (MainStream™). The Product Water was analyzed for chlorine concentration.)

included: sodium, potassium, aluminum, calcium, copper, magnesium, selenium, zinc, chromium, lead, arsenic, mercury, cadmium, beryllium, antimony, thallium, silver, barium, fluoride, nitrate, and sulfate.

Additional Chemical Challenge Testing

Arsenic challenge testing utilized arsenic trioxide (Sigma, arsenic trioxide, 31,138-3). Arsenic concentrations were determined by spectrophotometry, using HACH Method 8013, Silver Diethyldithiocarbamate Method.[25]

Lead challenge testing utilized lead acetate (Sigma, lead (II) acetate trihydrate, 215902). Lead concentrations in CW and PW were determined by inductively coupled plasma using EPA Method 200.7.[26]

Chlorine challenge testing utilized Clorox added to CW. Chlorine concentration in CW and PW was determined spectrophotometrictially using HACH Method 8167, DPD Method.[27]

Logistical Cost Analysis

A fictitious relief mission from the United States (US) to Ashgabat, Turkmenistan was used for purposes of comparative logistic cost analysis. For analysis of commercial transportation costs, the United Parcel Service (UPS) Express services were used with a 150 pound standard shipping weight. Military transportation analysis utilized the hourly operational costs of the C-141B cargo airplane. For the proposed relief mission, the Command Center of the US Air Force Air Mobility Command at McGuire Air Force Base in New Jersey was selected as the point of origin. For comparative purposes, the MainStream^{TM} was compared to commercially available 1L packaged water.

Results

The CW was passed through the device by the force of gravity. The PW was collected in the collection bag or an appropriate collection vessel. The PW was analyzed for bacterial concentration, endotoxin concentration, conductivity, pH, virus concentration, particulate matter, ammonia, calcium, carbon dioxide, chloride, sulfate, oxidizable substances, and a battery of chemical analysis (RD5 and RD62) for Water for Dialysis.

Bacterial Challenge

The bacterial concentration data are listed in Table 1 and Figure 1. The mean cfu of *B. diminuta* volume of PW cultured/cm^2 of effective filter area in the 17 CW was 7.9x10^7. The 95% confidence limit of the means was between 1.1x10^8 and 4.4x10^7 cfu/filtered volume/cm^2 of EFA. Challenge bacteria were not observed in any of the 37 PW cultures tested. The mean LRV from the CW to the PW was >7.6. The limit specified by HIMA for fluid sterilization is >7.0 LRV.[16]

Endotoxin Challenge

The endotoxin concentration data are listed in Table 1 and Figure 2. The mean concentration of endotoxin in the 17 CW was 499.53 ±233.57 EU/mL. The upper and lower 95% confidence limit of the means were 608 and 391 EU/mL, respectively. The mean value for the concentrations of the endotoxin in the 37 PW was 0.06 ±0.03 EU/mL. Only three of the PW samples were above the detection limit of 0.05 EU/mL. The limit of endotoxin for SWFI is 0.25 EU/mL.[18]

Virus Challenge

The virus concentration data are listed in Table 1. Three devices were challenged with >3 liters of 3x10^6 pfu/mL of ΦX174 bacteriophage. The PW from these samples did not contain detectable virus particles.

Conductivity Challenge

The conductivity data are listed in Table 1 and Figure 3. The mean value for the conductivity of the 17 CW samples analyzed was 2,033 ±135 µS/cm. The 95% confidence level of the mean was between 2098 and 1968 µS/cm. The mean conductivity of the 73 PW samples was 0.96 ±0.57 µS/cm. The upper and lower 95% confidence limit of the means were 1.10 and 0.82 µS/cm, respectively. The limit of conductivity (Stage I) specified by the USP21 is 1.3 µS/cm.

pH

The pH data are listed in Table 1 and Figure 4. The mean pH values of the 17 CW was 8.1 ±0.7 units, with the upper and lower 95% confidence limit of the means of 8.4 and 7.8, respectively. The mean pH of the 73 PW samples was 6.2 ±0.3 units with the upper and lower 95% confidence limit of the means of 6.2 and 6.1 units, respectively. The pH limit specified by the USP23 for SWFI and SPW are between 5.0 and 7.0 pH units.

Particulate Matter

The results of the particulate matter tests are listed in Table 1. The mean value for the particulate matter of >10 microns of the 37 PW samples tested was 0.25 ±0.19 particles/mL. The upper and lower 95% confidence limit of the mean values were 0.31 and 0.19 particles/mL, respectively. The limit of >10 micron particles specified by the USP21 is 25 particles/mL. The mean particulate matter of >25 microns of the 37 PW samples tested was 0.12 ±0.08 particles/mL. The upper and lower 95% confidence limit of the mean values were 0.15 and 0.10 particles/mL, respectively. The limit of >25 micron particles specified by the USP22 is 3 particles/mL.

Thirty-seven PW samples were tested for appearance (solution and device characteristics) and the chemical analyses described in the Sterile Purified Water, USP Monograph. These data are in Table 2. All PW samples were clear and colorless. All PW samples were within the USP limits for ammonia, calcium, chloride, carbon dioxide, and sulfate and did not contain detectable levels of oxidizable substances.

AAMI/RD5 Testing

The PW of six devices were tested for the AAMI RD5 chemistry battery for Water for Dialysis. These data are in Table 3. The CW exceeded RD5 limits for sodium, aluminum, calcium, copper, and magnesium. The PW of the

three tests samples were within the RD5 limits for all of the test parameters.

AAMI/RD62 Testing

The PW of three devices were tested for the AAMI RD62 chemistry battery for Water for Dialysis after the water was incubated in the collection bag for 24 hours. These data are in Table 4. The CW exceeded RD62 limits for sodium, aluminum, calcium, copper, and magnesium. The PW of the three tests samples were within the RD62 limits for all of the test parameters.

Particulate Challenge Testing

It was previously determined that 93% of the TD was insoluble in water. Therefore, for challenge testing with suspended solids, the mg/L of TD added per liter of CW was 107.5% of the desired measured amount. The 90th and 97.5th percentile concentrations of suspended solids observed in the database in mg/L were used as CW concentrations.[15] The mean time for production of three liters of PW from the MainStream^{TM} device was 43.5 minutes from the 90th percentile of suspended solids CW (Figure 5). The mean volume of PW produced from the 90th percentile CW was 10 liters with flow rates >10 mL/min. With the introduction of a prefilter, the mean PW volume at >10 mL/min was 58 liters (Figure 6).

Chemical Challenge Testing

Arsenic

The 99.5th percentile of arsenic concentration in surface water from the database was determined to be 180 µg/L.[15] Challenge testing was performed with a mean CW concentration of 167,000 µg/L (Figure 7). The mean calue for the concentration of arsenic in the PW was 36.7 µg/L (Figure 7).

Lead

Challenge water containing lead at a concentration of 220 µg/L was mixed with 150 mg/L of dissociable ions, to mimic water quality typically observed in municipally treated water (Table 5). The mean lead concentration at the 50th liter of PW was <0.003 µg/L. The mean lead concentration at the 60th liter of PW was 0.005 µg/L. The limit of detection of lead by this assay (inductively couple plasma) was 0.003 µg/L.

Chlorine

The typical disinfecting concentration of chlorine in water using Clorox as the disinfecting agent is 5 ppm (mg/L). For challenge testing, the CW concentration was 53,000 µg/L (Figure 8). The mean value for the PW concentration of chlorine was 50 µg/L (Figure 8).

Cost Comparison

A fictitious relief mission from the United States (US) to Ashgabat, Turkmenistan was used for purposes of comparative logistic cost analysis. For analysis of commercial transportation costs, the UPS Express services were utilized using a 150 pound (lbs) standard weight. Analysis of commercial transportation costs is provided in Table 6. Turkmenistan is in the UPS zone 907.[27] The cost of transporting this weight from the US to Ashgabat is US$1,665.25.[27] The standard weight selected would be equivalent to approximately 63 liters of packaged sterile water based upon a measured weight of 2.38 lbs/L (1,081 g/L). This would result in a transport cost per liter of US$26.42 for packaged sterile water. The same standard transport weight would enable the transport of 136 MainStream^{TM} devices. Since each device has an approved capacity of three liters of product water, there would be a total of 409 liters of product sterile water from transport of 150 lbs of MainStream^{TM} devices. The cost per liter of the delivered product water from the MainStream^{TM} devices would be US$4.07.

Military transportation costs are based upon hourly operational rates. For the C-141B cargo airplane, the hourly operational cost is roughly US$46,000.[10] For the proposed relief mission, the Command Center of the US Air Force Air Mobility Command at McGuire Air Force Base in New Jersey was selected as the point of origin. The distance between McGuire and Ashgabat is 6,299 miles. The Speed of the C-141B is 500 miles per hour.[28] Therefore, the transport time for this relief flight would be 12.6 hours. The cost of such a mission would be US$579,508. The capacity of the C-141B is 68,725 lbs.[28] Analysis of military transportation costs is provided in Table 7. This capacity would enable delivery of 28,876 liters of packaged water. The cost per liter of packaged water would be US$20.07. The C-141B capacity would enable delivery of 62,477 MainStream^{TM} devices. With a three liter per unit capacity for MainStream^{TM} devices, the delivered volume of product water would be 187,432 liters. The cost per liter of delivered product water from MainStream^{TM} devices would be US$3.09. It is estimated that the residual capacity of the MainStream^{TM} device for production of safe drinking water would be 22 liters, depending upon the quality of the available water. The delivered cost per liter of the additional drinking water would be US$0.42. The combined cost per liter for the "dual-use" of production of sterile water and safe drinking water would be US$0.76.

Discussion

Sterile, purified water can provide a wide range of therapeutic benefits in remote locations. The greatest hindrance to the remote site availability of sterile water is the logistics associated with transportation to the point-of-need. This is due to the weight and cube (inherent volume) of packaged water. An alternative to transportation to the remote point-of-need would be point-of-use purification of available water to produce sterile, purified water in the remote location.

To meet this need, a water purification device was developed by PRISMEDICAL Corporation. The device (Water Purification Device [WPD]) consists of a bag to hold source water (Fill Bag), a purification component (Water Purification Pack [WPP]), and a bag to aseptically contain the sterile water (collection bag). Selected purifica-

Test Parameter	Challenge Water (Mean ±SD)	n	USP PW Specifications (Mean ±SD)	Δ
Conductivity Challenge (S/cm)	2,033 ±135	73	0.96 ±0.57	-99.95%
pH	8.1 ±0.7	73	6.2 ±0.3	-24.09%
Endotoxin Challenge (EU/mL)	499.5 ±223.5	37	0.06 ±0.03	-99.99%
Bacterial Challenge (cfu/cm^2 of EFA)	7.9x10^7 ±7.2x10^7	37	<1	>7.569 LRV
Particulate Materials (≥10 M/mL) (≥25 M/mL)	ND ND	37 37	0.25 ±0.19 0.12 ±0.08	NA NA
Virus (pfu/mL)	3x10^6	3	0	>6 LRV

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Table 1—Functional purification tests (LRV = Log Reduction Value; M/ML = micron/mL; ND = Not Done; NA = Not Applicable)

Chemical	Limit	CW	Unit 87	Unit 88	Unit 89
Sodium	70.0	318.402	<0.050	<0.050	<0.050
Potassium	8.0	1.836	<1.000	<1.000	<1.000
Aluminum	0.01	0.014	<0.008	<0.008	<0.008
Calcium	2.0	16.260	<0.050	<0.050	<0.050
Copper	0.1	0.150	<0.005	<0.005	<0.005
Magnesium	4.0	17.64	<0.050	<0.050	<0.050
Selenium	0.9	<0.005	<0.005	<0.005	<0.005
Zinc	0.1	<0.005	0.009	0.006	0.007
Chromium	0.014	<0.005	<0.005	<0.005	<0.005
Lead	0.005	<0.002	<0.002	<0.002	<0.002
Arsenic	0.005	<0.002	<0.002	<0.002	<0.002
Mercury	0.0002	<0.0002	<0.0002	<0.0002	<0.0002
Cadmium	0.001	<0.0010	<0.0010	<0.0010	<0.0010
Fluoride	0.2	<0.10	<0.10	<0.10	<0.10
Nitrate	2.0	<0.2	<0.2	<0.2	<0.2
Sulfate	100.0	21.2	<1.0	<1.0	<1.0
Silver	0.005	<0.003	<0.003	<0.003	<0.003
Barium	0.1	0.035	<0.001	<0.001	<0.001

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Table 3—Association for the Advancement of Medical Instrumentation RD5 test for water for dialysis. (CW = challenge water)

Test Parameter	Limit (SPW)	Result
Appearance Solution Device Pouch	 N/A N/A N/A	 Clear, Colorless Pass Pass
Ammonia	<0.3	<0.3
Calcium	Negative	Negative
Chloride	Negative	Negative
Carbon Dioxide	<0.5	<0.5
Sulfate	Negative	Negative
Oxidizable Substances	Negative	Negative

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Table 2—Appearance and sterile purified water USP (SPW) monograph tests (n = 37; Pass = no damage)

Chemical	Limit	CW	Unit 77	Unit 79	Unit 80
Sodium	70.0	361.600	<0.050	<0.050	<0.050
Potassium	8.0	1.923	<1.000	<1.000	<1.000
Aluminum	0.01	0.026	<0.008	<0.008	<0.008
Calcium	2.0	19.810	<0.050	<0.050	<0.050
Copper	0.1	0.232	<0.005	<0.005	<0.005
Magnesium	4.0	22.320	<0.050	<0.050	<0.050
Selenium	0.9	<0.005	<0.005	<0.005	<0.005
Zinc	0.1	0.048	0.010	0.015	0.013
Chromium	0.014	<0.005	<0.005	<0.005	<0.005
Lead	0.005	0.002	<0.002	<0.002	<0.002
Arsenic	0.005	<0.002	<0.002	<0.002	<0.002
Mercury	0.0002	<0.0002	<0.0002	<0.0002	<0.0002
Cadmium	0.001	<0.0010	<0.0010	<0.0010	<0.0010
Beryllium	0.001	<0.0004	<0.0004	<0.0004	<0.0004
Antimony	0.006	<0.006	<0.006	<0.006	<0.006
Thallium	0.002	<0.002	<0.002	<0.002	<0.002
Silver	0.005	<0.003	<0.003	<0.003	<0.003
Barium	0.1	0.040	<0.001	<0.001	<0.001
Fluoride	0.2	0.13	<0.10	<0.10	<0.10
Nitrate	2.0	<0.2	<0.2	<0.2	<0.2
Sulfate	100.0	35.8	<1.0	<1.0	<1.0

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Table 4—Association for the Advancement of Medical Instrumentation RD62 test for water for dialysis. (CW = challenge water)

Sample	1	2	3	Mean	Standard Deviation
CW (mg/L)	0.220	0.220	0.220	0.220	0
50 liters PW (mg/L)	<0.003	<0.003	0.003	<0.003	0
60 liters PW (mg/L)	0.004	0.005	0.005	0.005	0.001

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Table 5—Lead reduction per product water (PW) volume (mg/L = milligrams/liters)

Commercial Transportation Costs

Relief Mission

Origin	Destination	Shipper	Zone[a]	Weight (lbs)[a]	Cost/weight[a]
USA	Ashgabat, Turkmenistan	UPS Express[1]	907	150	$1,665

Mission Deliverables Cost Analysis

Packaged Water			MainStream™ (3L@)[b]		
Units/weight	Delivered liters/weight	Cost/liter (US$)	Units/ weight[c]	Delivered liters/weight[b]	Cost/liter (US$)
63	63	26.42	136	409	4.07

Military Transportation Costs

Relief Mission

Origin	Destination	Shipper	Miles	Speed (mph)[d]	Mission hour	Rate/Hour (US$)[e]	Cost/Mission (US$)	Weight (lbs)[d]
McGuire AFB, NJ	Ashgabat, Turkmenistan	USAF C-141B	6,299	500	12.6	46,000	579,508	68,725

Mission Deliverables Cost Analysis

Packaged Water			MainStream™ (3L@)[b]			Dual-Use (Combined Use 25L@)		
Units/weight	Delivered liters/weight	Cost/liter (US$)	Units/ weight[c]	Delivered liters/weight[b]	Cost/liter (US$)	Units/ weight[c]	Delivered DW liters/weight[f]	Cost/liter (US$)
31,239	31,239	18.55	62,477	187,432	3.09	62,477	1,374,494	0.74

Table 6—Analysis of Transportation Costs (A fictitious relief mission from the US to Ashgabat, Turkmenistan was analyzed for commercial and military logistics costs. ([a]The UPS Express service was used for commercial transportation comparison;[27] [b]The MainStream™ has been cleared for production of 3 liters of Sterile Purified Water, USP; [c]The weight of the MainStream™ is 1.1 pounds per unit; [d]Capacity of the C-141B;[28] [e]Hourly operational rate based upon prior disaster relief mission costs.[10]; [f]Capacity of drinking water production depends upon the available water quality. For this analysis a 22 liters capacity of DW per MainStream™ device is assumed beyond the 3 liter SPW capacity.))

tion components contained within the housing were intended to retain inorganic chemicals (including heavy metals), organic chemicals, particulate matter, dissociable ions, microbes and microbial by-products (including endotoxins), and viruses.

A design feature of this device was that it be small and lightweight for ease of transport to remote locations. It weighs 1.1 pounds (500 grams). It is operated manually and requires no external power for ease of use in remote locations. The device operates at low pressures (<5 psi), meaning pressures that could be generated by hand without external power. The primary mode of use is by gravity. Additionally, it is provided sterile.

The design is a single-use, disposable device, thus eliminating the logistics associated with replacement of components and the requirement for revalidation of sterility in remote settings.

The objective of this study was to verify the purification capabilities of this device and demonstrate the MainStream™ PW quality attributes.

To ensure that the solutions produced by the device met the quality attributes of Sterile Water for Injection, USP and Sterile Purified Water, USP, the PW was tested according to the USP monographs for these packaged waters.[11–12] The USP tests included: tests for ammonia, calcium, carbon dioxide, chloride, sulfate, oxidizable substances, endotoxin, particulate matter, and pH.

The USP tests do not address the purification requirements necessary to achieve water purification of available water. Therefore, additional tests were developed to adequately challenge the device. These included testing to demonstrate retention of bacteria, endotoxin, and viruses. Testing also included removal of dissociable ions. These tests were derived from the passage of a CW through the device as would be performed in the field, followed by analysis of the PW quality attributes. To adequately challenge the WPD, the CW was augmented with bacteria, endotoxin, virus, and dissociable ions.

The MainStream™ demonstrated a >7 LRV of bacterial test organisms for a >99.99% reduction in endotoxin, a

4 log reduction in virus, and a >99.9% reduction in dissociable ions. Particulate matter and pH were within USP limits. The PW was within USP and AAMI limits for the chemical tests for ammonia, calcium, carbon dioxide, chloride, oxidizable substances, sodium, potassium, aluminum, calcium, copper, magnesium, selenium, zinc, chromium, lead, arsenic, mercury, cadmium, beryllium, antimony, thallium, silver, barium, fluoride, nitrate, and sulfate. In brief, the MainStream™ PW met the quality attribute requirements for Sterile Water for Injection, USP, Sterile Purified Water, USP and AAMI Water for Dialysis based upon RD5 and RD62 testing.[13-14]

Various forms of challenge testing outside of USP requirements were performed to expand the understanding of the PW characteristics. Particulate challenge testing demonstrated that the WPP could produce an average of 58 liters of PW with flow rates >10 mL/min (Figure 6). This PW was not tested for USP quality requirements. Chemical challenge test demonstrated that the WPP could markedly reduce the concentration of arsenic, lead, and chlorine in CW from toxic concentrations to non-toxic concentrations in PW. The concentration of chloride was the limit of detection for the analytical method used, therefore does not represent a true end point for chlorine retention capacity.

The MainStream™ provides significant logistical advantages in getting sterile water to remote settings by reduction of the weight and cube. The short duration exposure of the PW to the collection container provides additional patient safety by avoiding long-term exposure to the pliable packaging, thus reducing exposure to the associated leachable agents derived from that packaging.

An additional benefit of the MainStream™ device is the direct production of the packaged water, eliminating the intermediate, bulk water production step required for conventional medical packaged waters. This non-sterile intermediate step in packaged waters represents the potential for formation of biofilm, thus representing a potential patient hazard.

The logistics costs associated with transport of water can be based upon military or commercial transportation costs. For comparative purposes, a fictitious relief mission from the United States to Ashgabat, Turkmenistan was utilized. Analysis of the logistic costs for this mission demonstrated that the cost of transportation of packaged water is very expensive. By expanding the volume of sterile water production per pound of cargo, the amount of delivered water can be increased by roughly 550%, thus reducing the cost per liter by 85%. Although the costs described do not take into consideration the purchase cost of the packaged water versus the MainStream™ devices, it is anticipated that mass production costs of the MainStream™ device will provide a significant reduction over the delivered cost of packaged sterile water. Incorporation of a dual-use capability will extend the reduction of a delivered cost per liter.

Conclusion

The MainStream™ fills an unmet need in providing sterile water availability at the point-of-need in situations not addressed by conventional means. The residual purification capacity of the device can provide a means of production of a considerable volume of decontaminated, sterile drinking water.

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