# Statistical Analysis Plan: BXU011787

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|---|---|
| **Study Title:** | Performance evaluation of the AMIA Automated Peritoneal Dialysis (APD) Solution Generation System in patients using the AMIA APD Cycler |
| **Study Number:** | BXU011787 |
| **Study Phase:** | N/A |
| **Study Design** | This is an open-label, single arm, prospective, descriptive study in up to 50 peritoneal dialysis (PD) patients who are stable on in-home APD using the AMIA APD Cycler such that a total target of 30 evaluable patients complete the 12-week Study Treatment Period and the Follow-up Period. The study will be conducted at up to 15 sites in the United States. |
| **Product Name:** | AMIA APD Solution Generation System;<br>AMIA APD Generated Solution |
| **Name of Active Ingredients:** | Dextrose Concentrate |
| **Investigational Product:** | Electrolyte Concentrate<br>AMIA APD Solution Generation System |
| **Indication:** | End stage renal disease (ESRD) requiring PD |
| **Statistician:** | [redacted] |
| **Sponsor:** | Baxter Healthcare Corporation<br>One Baxter Parkway<br>Deerfield, Illinois 60015, USA |
| **Responsible Medical Officer:** | [redacted] MD<br>[redacted] Renal Care<br>Baxter Healthcare Corporation<br>One Baxter Parkway<br>Deerfield, IL 60015 USA |
| **Final Date:** | 04MAR2020 |

[redacted]

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|---|---|
| **Study Title:** | Performance evaluation of the AMIA Automated Peritoneal Dialysis (APD) Solution Generation System in patients using the AMIA APD Cycler |
| **Study Number:** | BXU011787 |
| **Statistician:** | [redacted] |

I have read this report and confirm that to the best of my knowledge it accurately describes the conduct and results of the study.

Prepared by: [redacted], MS
[redacted], Statistics
Baxter Healthcare

Date: [redacted]

Approved by: [redacted], MS
[redacted]
Baxter Healthcare

Date: [redacted]

Approved by: [redacted], MD
[redacted] Renal Care
Baxter Healthcare

Date: [redacted]

## 2. LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

| | |
|---|---|
| ADE | Adverse Device Effect |
| AE | Adverse Event |
| AESI | Adverse Event of Special Interest |
| APD | Automated Peritoneal Dialysis |
| BMI | Body Mass Index |
| BP | Blood Pressure |
| CFU | Colony Forming Units |
| DD | Device Deficiency |
| eCRF | Electronic Case Report Form |
| ESRD | End Stage Renal Disease |
| EU | Endotoxin Units |
| ICF | Informed Consent Form |
| MedDRA | Medical Dictionary for Regulatory Activities |
| PC | Product Complaint |
| PD | Peritoneal Dialysis |
| PI | Principal Investigator |
| PT | Preferred Term |
| RO | Reverse Osmosis |
| SADE | Serious Adverse Device Effect |
| SAE | Serious Adverse Event |
| SAP | Statistical Analysis Plan |
| SGS | Solution Generation System |
| SOC | System Organ Class |
| TAMC | Total Aerobic Microbial Count |
| TEAE | Treatment-Emergent Adverse Event |
| TYMC | Total Combined Yeast and Mold Count |
| WD | Water Device |

## 3. INTRODUCTION

This statistical analysis plan (SAP) is provided to describe the framework for the reporting, summarization, and statistical analysis methodology of the safety and efficacy parameters measured throughout the study. It is based on clinical trial protocol BXU011787 Amendment 6, dated 01NOV2019.

Peritoneal dialysis (PD) is a well-established treatment for renal failure including long-term management of end stage renal disease (ESRD) by continuous ambulatory peritoneal dialysis or automated peritoneal dialysis (APD). It is a procedure for removal of uremic toxins which are normally excreted by the kidneys, and for aiding the regulation of fluid and serum electrolytes as well as acid-base balance. In patients with renal failure, during PD, uremic toxins, present in high concentrations in the blood, cross the peritoneal membrane into the dialyzing fluid, according to the principles of osmosis and diffusion. Peritoneal dialysis solutions contain variable amounts of glucose, all of them being hyperosmolar to the plasma, creating an osmotic gradient which facilitates fluid removal from the plasma to the solution.

The AMIA APD Solution Generation System consists of the AMIA APD Cycler, Sharesource Platform, AMIA APD Concentrates (a Dextrose Concentrate and an Electrolyte Concentrate), a disposable set (containing a cassette, a water line with holding bag and two sterilizing grade filters, a heater bag, a patient line, a dextrose concentrate line, a last fill solution line, an electrolyte concentrate line, and a drain line), a bag tray, a Water Softener (also referred to as the Ion Exchanger), and a Water Device (WD). The WD consists of a pre-treatment filter pack, reverse osmosis (RO) membrane, heater, conductivity and temperature sensors, and ports for a patient connection. The Water Softener is an accessory to the WD.

The AMIA APD Solution Generation System combines an updated AMIA APD Cycler with Sharesource Platform (previously cleared under K151525) with an in-home water system technology and leverages newly developed AMIA APD Concentrates.

The AMIA APD Solution Generation System is intended for automatic control of dialysis solution exchanges in the treatment of adult renal failure patients undergoing PD in home or clinic environments.

The AMIA APD Solution Generation System is a drug-device combination product. All therapies using the AMIA APD Solutions Generation System must be prescribed and performed under the responsibility of a physician who is well informed about PD and the study system.

The system is designed to produce dialysis solution as prescribed by the clinician. The resulting AMIA APD Generated Solution will be mixed from the sterile AMIA APD Concentrates (a Dextrose Concentrate and an Electrolyte Concentrate) and sterile, non-pyrogenic water (post-sterilizing filters). AMIA APD Generated Solution is formulated to have a nominal solution chemistry that is equivalent to the labeled composition of Dianeal Low Calcium (2.5 mEq/L), in three standard dextrose strengths (1.5%, 2.5% and 4.25%).

The AMIA APD Concentrates, after dilution by the AMIA APD Solution Generation System, are indicated for adult patients in acute or chronic renal failure when non-dialytic medical therapy is judged to be inadequate.

- The AMIA APD Concentrates are only intended to be used together, and only as a part of the AMIA APD Solution Generation System.
- The Dextrose Concentrate is a sterile, non-pyrogenic product used in the preparation of the AMIA APD Generated Solution when using the AMIA APD Solution Generation System.
- The Electrolyte Concentrate is a sterile, non-pyrogenic product containing the electrolytes and buffer used in the preparation of the AMIA APD Generated Solution when using the AMIA APD Solution Generation System.

## 4. TRIAL OBJECTIVES

### 4.1 Primary Objectives

**Efficacy**

To evaluate the chemical composition of the final dialysis solution produced by patients using the AMIA APD Solution Generation System during simulated treatment, compared to the specifications of Baxter's approved Dianeal Low Calcium (2.5 mEq/L) PD Solution.

**Safety**

To evaluate the product water from the WD (pre-sterilizing filters) as meeting ISO standard 13959[1] for microbiological (including endotoxin) and chemical contamination, and water in the holding bag (post-sterilizing filters) as meeting system microbiological requirements, when produced in patients' homes using the AMIA APD Solution Generation System, during a simulated treatment.

### 4.2 Secondary Objectives

- To evaluate the safety of the AMIA APD Solution Generation System, used to treat patients with ESRD, by collecting adverse events (AEs), serious adverse events (SAEs), adverse device effects (ADEs), serious adverse device effects (SADEs), incidence of device alarms and vital signs.
- To assess PD adequacy by calculation of total $Kt/V_{urea}$.

## 5. STUDY DESIGN

### 5.1 Study Design

This is an open-label, single arm, prospective, descriptive study. Up to 50 PD patients, who are stable on in-home APD using the AMIA APD Cycler or HomeChoice APD Cycler, will be enrolled in this study such that a total target of 30 evaluable patients complete the 12-week Study Treatment Period and the Follow-up Period.

The group of patients who withdrew prior to the completion of the treatment period and corresponding follow-up visits will be considered as *early terminated*, and the corresponding reason for termination will be recorded. The complimentary group of patients who complete the full study period (treatment + follow-up) will be considered as *completed*.

### 5.2 Sample Size

A formal sample size calculation was not performed. Up to 50 patients will be enrolled such that a total target of 30 evaluable patients complete the 12-week Study Treatment Period and the Follow-up Period.

### 5.3 Randomization Procedure

Not applicable, as this is a single arm study.

### 5.4 Schedule of Visits and Procedures

During the Screening Period, all consenting patients will have a home assessment, including feed (tap) water analysis, to confirm their home environment is suitable for this study. Eligible patients will be followed for data collection regarding dialysate solution composition and safety while using the AMIA APD Solution Generation System.

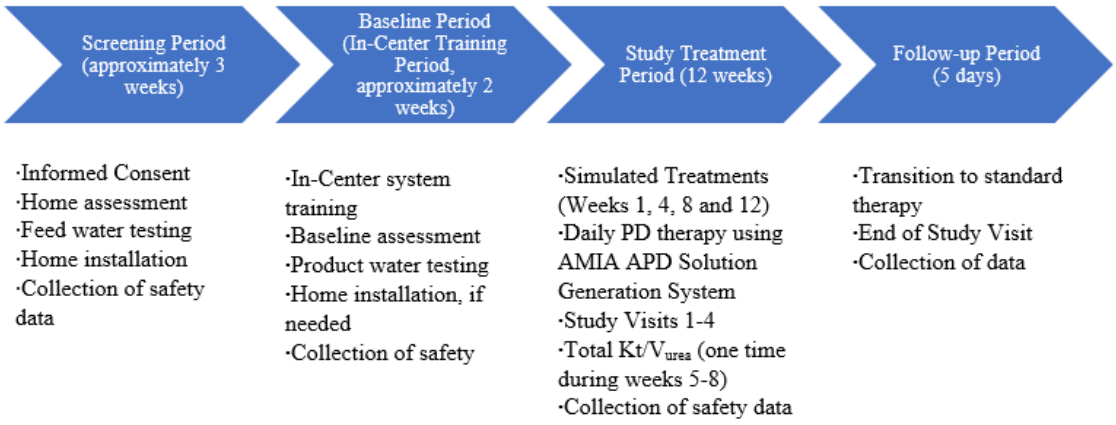
Data will be collected throughout the duration of the study (approximately 18 weeks), including the Screening Period, Baseline Period (In-center Training Period), Study Treatment Period, Follow-up Period and the End-of-Study Visit/ Early Termination Visit.

All AEs (not reported as medical history), product complaints (PCs) and device deficiencies (DDs) observed by the study personnel or reported by the patient during the course of the study will be documented from the time of signing the informed consent form (ICF) through the End-of-Study/ Early Termination Visit. The Principal Investigator (PI) or designee (e.g., sub-investigator) will assess each patient at the Screening Visit and on a weekly basis, according to standard of care. At a minimum, this assessment will include evaluation of blood pressure (BP), pulse rate, weight, fluid status and dialysis prescription.

Laboratory data will be collected at screening and during the use of the AMIA APD Solution Generation System.

Evaluations will be taken as illustrated in Appendix 1. A trial scheme for the study is shown in Figure 1 below.

**Figure 1. Overview of Study Assessments**




## 5.5 Efficacy Measures

### 5.5.1 Primary Endpoints

Primary efficacy endpoint is:

- Testing of the chemical composition of the final dialysis solution produced by patients using the AMIA APD Solution Generation System, during simulated treatment, compared to the specifications of Baxter's approved Dianeal Low Calcium (2.5 mEq/L) PD Solution.

Primary safety endpoints are:

- Microbiological (including endotoxin) and chemical testing of product water from the WD (pre-sterilizing filters) per ISO Standard 13959.[1]
- Microbiological testing of water in the holding bag (post-sterilizing filters) to confirm that the water does not exceed 0 colony forming units (CFU) /mL for bacteria (no growth) and is <0.03 endotoxin units (EU)/ mL for endotoxins, consistent with Dianeal specifications for sterility.

### 5.5.2 Secondary Endpoint(s)

- Safety profile of the AMIA APD Solution Generation System used to treat patients with PD by collecting AEs, SAEs, adverse device effects (ADEs), SADEs, incidence of device alarms and vital signs.
- Peritoneal dialysis adequacy will be measured by sample collection and calculation of total $Kt/V_{urea,}$ occurring once at any time during weeks 5, 6, 7 or 8 of the Study Treatment Period.

## 6. GENERAL STATISTICAL CONSIDERATIONS

Unless otherwise specified, summary statistics (n, arithmetic mean, standard deviation [SD], median, minimum, and maximum values) will be presented for continuous variables. Counts and, if relevant, percentages will be presented for categorical variables.

Unless otherwise specified, all data tables, listings, and figures will be on all patients in the Safety Set (as defined in section 7.2)

Unless otherwise specified, data listings will include site ID, patient ID, sex, age at screening (rounded down to the nearest whole number), race, and baseline weight.

Unless otherwise specified, the estimated mean and median for a set of values will be displayed to 1 more significant digit than the original values, standard deviations will be displayed to 2 more significant digits, and minimum and maximum values will be displayed with the same number of significant digits as the original values. All percentages will be displayed out to 1 decimal places.

Unless otherwise noted, all analyses will be performed using SAS/Graph® 9.4 software, SAS/STAT® 15.1 software, and BaseSAS® 9.4. 

# 7. DISPOSITION

## 7.1 Patient Disposition

Patient disposition will be summarized and will include:

- Number of patients who signed informed consent
- Number of patients enrolled (defined as having a home installation and meeting all eligibility criteria)
- Number of patients treated
- Number of patients in the Safety Set
- Number of patients who completed the study
- Number of patients who discontinued (withdrew early) from the study and subsequently re-enrolled. These patients will also be summarized by primary reason for withdrawal from the study. The percentages associated with each reason for early withdrawal will have the total number of patients who withdrew early and re-enrolled as the denominator
- Number of patients who discontinued and did not subsequently re-enroll. The percentage associated with this will be the number of patients who withdrew and did not re-enroll.

Patients who withdrew early from the study will be listed, and the listing will include the number of days that the patient remained in the study, the primary reason from withdrawal, and whether the patient re-enrolled.

All disposition tables and listings will be based on the set of all patients who signed informed consent.

## 7.2 Analysis Populations

The Safety Set is based on the intent-to-treat principle and will include all patients who have received at least one treatment with the AMIA APD Solution Generation System and who have at least one measurement for the primary endpoint (either primary efficacy or primary safety).

## 7.3 Completion and Discontinuation

A patient who withdraws from the study prior to meeting all eligibility criteria or prior to having the device installed in their home will be considered a screen failure. All withdrawals past this point will be considered a withdrawal and be counted as a

discontinuation. In the event that a patient has a home installation and has not yet met all eligibility criteria but decides to withdraw from the study due to a device issue (i.e. leaking, alarms, etc.), then the patient will be considered as discontinued and NOT as a screen failure.

A patient is considered to have completed the study when he/she ceases active participation in the study because the patient has, or is presumed to have, completed all study procedures according with the protocol (with or without protocol deviations). Any other cases are classified as discontinuation.

Reasons for completion/discontinuation will be reported on the Completion/Discontinuation electronic case report form (eCRF), including:

- Adverse event
- Change to another dialysis center
- Death
- Disease progression
- Home feed water affected by boil water advisory
- Inadequate dialysis
- Investigator discretion
- Lost to follow-up
- Met an exclusion criteria
- Missed more than 4 consecutive days of therapy
- Consistently missed more than 1 prescribed treatment per week
- Pregnancy
- Protocol violation
- Renal transplant
- Termination of the study
- Voluntary withdrawal
- Water device replacement
- Other

Regardless of the reason, all data available for the patient up to the time of completion/discontinuation should be recorded on the appropriate eCRF.

Every effort will be made to have discontinued patients complete the study completion/termination visit. If the completion/termination visit is done as an additional, unscheduled visit, the assessment results shall be recorded with the completion/termination visit. If a patient terminates participation in the study and does not return for the completion/termination visit, his/her last recorded assessments shall remain recorded with his/her last visit. The reason for discontinuation will be recorded and the data collected up to the time of discontinuation will be used in the analysis and included in the clinical study report.

Patients who discontinue may be allowed to reenroll in the study. These patients will have separate but linked patient IDs (one for each enrollment in the study); this will be captured in the eCRF. These patients will be assigned one unique USUBJID during SDTM creation. Unless otherwise specified, for all patient-related analyses (e.g. demographics and baseline characteristics), these data will be summarized only once in tables, and all data will be listed next to their corresponding USUBJID in listings. For all device-related analyses (e.g. chemical composition testing of dialysis solution, microbiological testing of product water), all data gathered will be summarized and listed.

## 8. DEMOGRAPHICS AND BASELINE CHARACTERISTICS

Demographics (age, sex, race, ethnicity), baseline characteristics (height, weight, body mass index [BMI]), primary renal diagnosis etiology, whether the patient had a caretaker, and baseline $Kt/V_{urea}$ will be summarized descriptively. A listing for this data will also be generated. For patients who have re-enrolled, demographics and baseline characteristics will be summarized once using the information from their most recent enrollment. If values are different for subsequent enrollments, they will be listed only.

## 9. MEDICAL HISTORY AND CONCOMITANT MEDICATION

Medical history and non-drug therapies will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) and listed. Concomitant medications will be coded using the WHO Drug Dictionary.

Medical history, concurrent medical conditions, renal medical history, and concomitant medications will be listed. Concurrent medical conditions and concomitant medications will be classified as “Prior” and “Concurrent”, depending on when the start date and end date is with respect to the date of first treatment. All medications that start and end prior to the date of first treatment will be classified as “Prior”, and those that have any amount taken after the date of first treatment will be classified as “Concurrent”. The date of first

treatment will be defined as the first day the patient had ever received treatment from the Point of Care device. If they stopped treatment and re-enrolled, the date of first treatment from the first enrollment will be used to determine Prior or Concomitant medications.

For patients who have re-enrolled, data will be pooled, and all unique medical history, concurrent medical conditions, renal medical history, and concomitant medications will be listed.

## 10. IN-CENTER TRAINING PERIOD

The following data is collected in regards to the in-center training:

- Whether the patient completed device specific training
- Whether the patient completed comprehension and retention testing
- Date of testing
- Reason if they did not complete testing
- Whether the care partner completed device specific training (if applicable)
- Whether the care partner completed comprehension and retention testing (if applicable)
- Date of care partner's training (if applicable)
- Whether PI concluded patient's PD prescription is stable and can begin treatment at home

All of the above will be listed only. For patients who have re-enrolled, data will be listed for each instance of training.

## 11. TREATMENT COMPLIANCE AND EXPOSURE

### 11.1 Treatment Compliance

Compliance will be assessed regularly by the Investigator by reviewing the patient's Sharesource Platform data and eDiary entries. The patient will be instructed to complete the eDiary daily to document treatment activities including, but not limited to, the following:

- Treatment interruptions
- Confirmation if the patient contacted dialysis center for support with a product or health-related issue
- Confirmation if the patient was able to sleep during treatment

- Treatment outcome (i.e., complete treatment, incomplete treatment) and reasons for incomplete treatment
- Confirmation if the patient altered their treatment parameters
- Investigational product supply requirements

The above eDiary data (with the exception of the investigational product supply requirements) will be summarized using frequencies and percentages for the number of patients experiencing at least one event and the total number of events per total treatments, and it will be summarized continuously using mean, standard deviation, minimum, median, and maximum for the total number of occurrences per patient. These data will also be listed.

For patients who have re-enrolled, the eDiary data will be pooled together.

Interruptions to therapy will be summarized using frequencies and percentages of the following:

- Number of interruptions per patient
- Reason for interruption
- Whether the patient was on standard of care PD therapy

The length of treatment interruption for all interruptions as well as per patient will be summarized for all interruptions using n, mean, median, standard deviation, minimum, and maximum.

The length of treatment interruptions for all interruptions will be calculated as follows:

$$\frac{\sum_{i=1}^{t}(Treatment\ restart\ date - Date\ of\ interruption)}{t},$$

where i is each interruption and t is the total number of interruptions.

The length of total treatment interruptions per patient will be calculated as follows:

$$\frac{\sum_{i=1}^{n}\sum_{j=1}^{m}(Treatment\ restart\ date - Date\ of\ interruption)}{n},$$

where j is each interruption per patient, m is the total number of interruptions per patient, i is each patient, and n is the total number of patients with an interruption.

### 11.2 Protocol Deviations

Protocol deviations will be summarized for all patients. Patient counts will be presented for minor protocol deviations, major protocol deviations, and for each category of major protocol deviation.

Protocol deviations will also be listed. The listing will include site ID, patient ID, age, sex, race, weight at baseline (kg), verbatim description of the protocol deviation, date the protocol deviation occurred, the version of the protocol that the deviation occurred under, the assigned classification of protocol deviation, and whether the protocol deviation was determined to be major or minor (grade).

## 12. CHANGES IN PLANNED ANALYSES FROM THE PROTOCOL

There have been no changes from the planned analyses in the protocol.

## 13. EFFICACY PARAMETERS

### 13.1 General Considerations

Unless otherwise specified, only data required per protocol (specified visits and retests per decision trees) will be displayed in summary tables. All data (including unscheduled visits, non-protocol mandated samples, etc.) will be displayed in listings.

For all device related endpoints, the results at each visit will be representative of the number of weeks the water device has been in use (i.e. visit 2 represents 8 weeks of use for that specific water device). Therefore, if a patient received a new water device midway through the study, the number of weeks in use would restart from 1.

### 13.2 Primary Efficacy Analysis

The primary efficacy endpoint of the study, chemical composition of the dialysis solution from the simulated treatment, will be analyzed descriptively using frequencies and percentages of those that meet specifications vs those that do not.

The dialysis solution will be considered as meeting specifications if all of the below parameters are within the specified limits:

| **Parameter** | **Limits** |
|---|---|
| pH at 25°C | 4.0 to 6.5 |
| Color | ≤ 15 |
| 5-HMF | ≤ 0.25 |

| | |
|---|---|
| Dextrose Hydrous Assay:<br>1.5% Dextrose, Hydrous<br>2.5% Dextrose, Hydrous<br>4.25% Dextrose, Hydrous | <br>1.40 to 1.60<br>2.38 to 2.62<br>4.00 to 4.50 |
| Sodium Lactate (g/L) | 4.23 to 4.73 |
| Sodium (mEq/L) | 125 to 139 |
| Chloride (g/L) | 5.28 to 5.83 |
| $MgCl_2$ $6H_2O$ (g/L) | 0.041 to 0.061 |
| $CaCl_2$ $2H_2O$ (g/L) | 0.157 to 0.210 |

If any one of the above parameters tested fall outside of the limits given, then the particular test is considered not meeting specifications. If any of the above parameters were not tested, then the particular test is considered missing. All testing for dialysis solution will be completed at the Baxter Round Lake laboratory facility.

The testing of the dialysis solution occurs four times throughout the trial: once at simulated treatment (week 1), and once at each of the treatment visits (weeks 4, 8, and 12). The Dextrose Hydrous % will be set to the following for each of the weeks: 1.5% at weeks 1 and 12, 2.5% at week 4, and 4.25% at week 8.

There will be three summaries of these data: one based on initial values, one based on retest values (as mandated per decision tree), and one based on the most recent test values. These three summaries will be done on a combination of all visits and individually for each of the visits.

In addition to the above, there will be two additional tables detailing the chemical composition of the dialysis solution. The first will show the test results (met vs did not meet specifications) for each of the individual parameters, and the second will be a descriptive summary (n, mean, standard deviation, minimum, median, and maximum) of the results of each of the individual parameters.

If a patient had been re-enrolled in the study, all data will be gathered and summarized for this analysis.

The test results will also be listed. Patient's age, sex, race, and weight at baseline will not be shown for this listing. This listing will include all enrolled patients.

### 13.3 Secondary Efficacy Analysis

Total $Kt/V_{urea}$ will be summarized descriptively for baseline and the Total $Kt/V_{urea}$ visit (occurring one time during week 5, 6, 7 or 8 of the Study Treatment Period). Change from baseline will also be summarized. For patients who re-enroll, if the baseline value is the same for each enrollment instance, then the baseline value will be summarized only once. If the baseline value is different, then each baseline value will be summarized. All available mid-treatment values and corresponding changes from baseline will be analyzed. A listing with these values will also be created.

## 14. SAFETY AND TOLERABILITY

### 14.1 Primary Safety Analysis

#### 14.1.1 General Considerations

Unless otherwise specified, only data required per protocol (specified visits and retests per decision trees) will be displayed in summary tables. All data (including unscheduled visits, non-protocol mandated samples, etc.) will be displayed in listings.

For all device related endpoints, the results at each visit will be representative of the number of weeks the water device has been in use (i.e. visit 2 represents 8 weeks of use for that specific water device). Therefore, if a patient received a new water device midway through the study, the number of weeks in use would restart from 1.

#### 14.1.2 Microbiological and chemical contamination testing of the product water from the WD (pre-sterilizing filter)

The results of the microbiological and chemical contamination testing of the product water from the WD will be analyzed descriptively using frequencies and percentages of those that meet specifications vs those that do not. A test will be considered meeting specifications if all of the following parameters fall within the specified limits:

| Parameter | Limits |
|---|---|
| TAMC (CFU/mL) | ≤ 100 |
| TYMC (CFU/mL) | ≤ 100 |
| Endotoxins (EU/mL) | ≤ 0.25 |
| Aluminum (mg/L) | ≤0.01 |
| Copper (mg/L) | ≤0.1 |
| Fluoride (mg/L) | ≤0.2 |
| Lead (mg/L) | ≤0.005 |
| Nitrate (as N) (mg/L) | ≤2 |

| | |
|---|---|
| Sulphate (mg/L) | ≤100 |
| Zinc (mg/L) | ≤0.1 |
| Calcium (mg/L) | ≤2 |
| Magnesium (mg/L) | ≤4 |
| Potassium (mg/L) | ≤8 |
| Sodium (mg/L) | ≤70 |
| Antimony (mg/L) | ≤0.006 |
| Arsenic (mg/L) | ≤0.005 |
| Barium (mg/L) | ≤0.1 |
| Beryllium (mg/L) | ≤0.0004 |
| Cadmium (mg/L) | ≤0.001 |
| Chromium (total) (mg/L) | ≤0.014 |
| Mercury (mg/L) | ≤0.0002 |
| Selenium (mg/L) | ≤0.09 |
| Silver (mg/L) | ≤0.005 |
| Thallium (mg/L) | ≤0.002 |
| Nickel (mg/L) | ≤0.010 |
| Cobalt (mg/L) | ≤0.0025 |
| Total Chlorine (mg/L) | ≤0.1 |

If any of the above parameters fall outside the limits, then the test is considered not meeting specifications. If any of the above parameters were not tested, then the particular test is considered missing. The microbiological tests are performed at [redacted], and the chemical contamination tests are performed at [redacted].

There will be three summaries of these data: one based on initial values, one based on retest values (as mandated per decision tree), and one based on the most recent test values. These three summaries will be done on a combination of all visits and individually for each of the visits.

In addition to the above, there will be two additional tables detailing the microbiological and chemical contamination testing of the product water from the water device. The first will show the test results (met vs did not meet specifications) for each of the individual parameters, and the second will be a descriptive summary (n, mean, standard deviation, minimum, median, and maximum) of the results of each of the individual parameters.

If a patient had re-enrolled, all data will be used in this analysis.

The test results will also be listed. Patient's age, sex, race, and weight at baseline will not be shown for this listing. This listing will include all enrolled patients.

A sensitivity analysis will be conducted for this endpoint using the results of the home installation visit in cases where the simulation visit 1 data is missing. The sensitivity analysis will include all of the above tables only.

### 14.1.3 Microbiological testing of the water from the holding bag

The results of the microbiological testing of the product water from the holding bag will be analyzed descriptively using frequencies and percentages of those that meet specifications vs those that do not. A test will be considered meeting specifications if all of the following parameters fall within the specified limits:

| **Parameter** | **Limits** |
|---|---|
| Tryptic Soy Broth Growth | No growth |
| Fluid Thioglycolate Growth | No growth |
| Endotoxins (EU/mL) | ≤ 0.03 |

If any of the above parameters fall outside the limits, then the particular test is considered not meeting specifications. If any of the above parameters were not tested, then the particular test is considered missing. These tests will be performed at [redacted].

There will be three summaries of these data: one based on initial values, one based on retest values (as mandated per decision trees), and one based on the most recent test values. These three summaries will be done on a combination of all visits and individually for each of the visits.

In addition to the above, there will be two additional tables detailing the microbiological testing of the product water from the holding bag. The first will show the test results (met vs did not meet specifications) for each of the individual parameters, and the second will be a descriptive summary (n, mean, standard deviation, minimum, median, and maximum) of the results of each of the individual parameters.

If a patient had re-enrolled, all data will be used in this analysis.

The test results will also be listed. Patient's age, sex, race, and weight at baseline will not be shown for this listing. This listing will include all enrolled patients.

## 14.2 Adverse Events (AEs)

### 14.2.1 General

Summaries of AEs will be presented using counts and percentages for the safety set.

Tables by preferred term and tables by system organ class (SOC) and preferred term will be sorted in descending order by the percentage of patients.

For all adverse event analyses, the date of first treatment will refer to the first date the patient ever received treatment with the Point of Care device. If a patient had stopped treatment then re-started, the date that they first started (including prior enrollments) will be used as the date of first treatment.

Unless otherwise specified, the summaries of adverse events will include the total number of patients experiencing the adverse event, the total number of events, and the adverse event rate (number of events per patient year). The total number of patient years will be calculated as follows for all adverse events (including pretreatment AEs):

$$\frac{\sum_{i=1}^{n}(Date\ of\ Study\ Completion/Withdrawal - Informed\ Consent\ Date) + 1}{365.25},$$

where n represents all patients in the Safety Set.

The total number of patient years will be calculated as follows for all treatment-emergent adverse events:

$$\frac{\sum_{i=1}^{n}(Date\ of\ Study\ Completion\ or\ Withdrawal - Date\ of\ first\ treatment) + 1}{365.25},$$

where n represents all patients in the Safety Set.

The adverse event rate will be calculated as:

$$\frac{Total\ Number\ of\ Events}{Total\ patient\ years}$$

For summaries of AEs presented by severity, the maximum severity will be presented if patients have multiple AEs within a SOC and preferred term (PT) with varying severity. If the severity of an adverse event is missing, then that adverse event will be classified as *severe*.

For summaries of AEs presented by relationship, the most conservative relationship will be presented if patients have multiple AEs within a SOC and PT with different relationships to either study product or typical PD therapy.

For patients who had re-enrolled, all adverse events will be listed and summarized.

Adverse event listings will be sorted by site ID, patient ID, and adverse event start date. They will include verbatim term, system organ class, preferred term, adverse event start date, adverse event end date, treatment start date, date of death (if relevant), causality, severity, action taken, seriousness, outcome, relationship to study device, relationship to typical PD therapy, relationship to another Baxter product, alternate causality, whether a treatment was provided, if it resulted in a change in concomitant medication, if it led to a SUSAR or UADE, and whether AE led to discontinuation from study. If an adverse event changes in severity, then each severity will be listed.

### 14.2.2 Classification of Adverse Events

*Pre-treatment adverse event* – An adverse event that starts between the date of signing the informed consent form (ICF) and the start of the first treatment.

*Treatment-emergent adverse event (TEAE)* – An adverse event that starts on or after the start of the first treatment.

In case of incomplete information on study treatment or AE onset, events will be classified as treatment-emergent unless there is sufficient data to rule out the possibility that the event started after the start of study treatment application.

### 14.2.3 Adverse Events of Special Interest (AESI)

In this study, AESIs are defined as any of the following events:

- Aseptic Peritonitis
- Hypovolemia
- Hypokalemia
- Hyponatremia
- Encapsulating Peritoneal Sclerosis
- Medication Error:  administration of incorrect glucose concentration
- Lactic Acidosis
- Hyperglycemia

- Hypocalcemia

### 14.2.4 Presentation of Adverse Events

An AE overview summary table will be prepared to include the number of patients reporting an AE, the percentage of patients (%) with an AE, the number of events reported, for the following categories:

1. Any treatment emergent adverse event
2. Treatment-emergent SAEs.
3. Treatment-emergent pre-defined AEs of special interest
4. Treatment-emergent study device-related AEs.
5. Treatment-emergent typical PD-related AEs
6. Treatment-emergent study device-related SAEs
7. Treatment-emergent typical PD-related SAEs
8. Treatment-emergent AEs leading to withdrawal.
9. Treatment-emergent AEs leading to death.

Adverse events will be further tabulated by body system using the MedDRA coded values. The table will display the total number of patients reporting an AE, the percentage of patients (%) with an AE, and the number of events reported by overall, system organ class (SOC), and preferred term. Table summaries will be produced for:

- All treatment-emergent AEs
- Treatment-emergent AEs leading to withdrawal
- Treatment-emergent SAEs
- Treatment-emergent AEs leading to death
- Treatment-emergent pre-defined AEs of special interest
- Treatment-emergent pre-defined SAEs of special interest
- Treatment-emergent AEs by severity
- Treatment-emergent SAEs by severity

- Treatment-emergent AEs by relationship to study product
- Treatment-emergent SAEs by relationship to study product
- Treatment-emergent AEs by relationship to typical PD therapy
- Treatment-emergent SAEs by relationship to typical PD therapy
- Treatment-emergent adverse events in ≥5% of patients

Adverse events occurring between informed consent and treatment start (pre-treatment AEs), treatment-emergent adverse events, treatment-emergent SAEs, treatment-emergent adverse events leading to withdrawal, treatment-emergent adverse events related to study device, typical PD therapy, or another Baxter product, and adverse events for patients who died will be listed.

For the SAE listing, the seriousness criteria will also be included in the listing.

If there are less than 5 adverse events in one of the bulleted categories above, then a listing may be created instead of a table for those AEs.

## 14.3 Other Safety Data

### 14.3.1 General

Unless otherwise specified, tables, listings, and figures will be based on the Safety Set.

### 14.3.2 Device Alarms and Device Deficiencies/Product issues (DDs)

All device deficiency tables and listings will be done on the Safety Set. The number of device alarms and their relation to AEs will be summarized using frequency counts and percentages. The number of patients experiencing at least one device alarm and at least one device alarm due to an AE will also be summarized. Included in this summary will also be the number of patients experiencing at least one DD/product issue and at least one DD/product issue resulting in an AE, suspected unexpected serious adverse reaction (SUSAR), or unexpected adverse drug reaction (UADE). All of the above will also be summarized as a rate of events per total device installation days. This rate will be calculated by taking the number of events and dividing it by the total number of days the device is installed at a patient's home across all patients. The total number of device days will be calculated as follows:

$$\sum_{i=1}^{n}(Date\ of\ last\ treatment - Date\ of\ home\ installation) + 1,$$

where i is each patient and n is the total number of patients in the Safety Set.

All device deficiencies and product issues will be summarized by frequencies and percentages of both patients and total events, and by a rate of events per total number of device installation days for the following:

- Product causing DD
- Type of deficiency/product issue
- Occurrence of DD
- Whether the device gave an alert, alarm, or error message
- If there was a safety concern
- If the DD resulted in an AE or SUSAR/UADE

A listing will also be provided for all device deficiencies/product issues sorted by site ID, patient ID, and DD date. It will provide the product affected, date of onset, type, description, occurrence, whether a message was given (alert, alarm, error, or none), message description, if/what is a potential safety concern, and if/what AE resulted because of this DD.

For patients who had re-enrolled, all DDs will be listed and summarized.

### 14.3.3 Vital Signs

Vital signs (systolic blood pressure, diastolic blood pressure, pulse rate, and temperature) will be summarized descriptively at each time-point using both absolute values and change from baseline for all post-baseline timepoints. The baseline value will be any measurements taken during the Baseline Period. If the Baseline Period measurements are missing, then measurements taken at screening will be used as baseline. If a patient had re-enrolled, all data gathered will be summarized (using baseline values as determined in section 16.1).

### 14.3.4 Laboratory Results

The following laboratory results (and corresponding changes from baseline, if applicable) will be summarized descriptively using n, mean, standard deviation, minimum, median, and maximum for all timepoints taken:

- Hematology:
  - Complete blood count with differential from serum blood draw
  - White cell count with differential from PD Effluent
  - Cell culture from PD Effluent

- Chemistry:
  - Chemistry profile from blood draw consisting of:
    - Glucose
    - Calcium
    - Albumin
    - Total protein
    - Sodium
    - Potassium
    - Bicarbonate
    - Chloride
    - Creatinine
    - Blood urea nitrogen
    - Alkaline phosphatase
    - Alanine aminotransferase
    - Aspartate amino transferase
    - Bilirubin
    - Phosphorus
  - Creatinine from 24-hour PD Effluent collection
  - Urea Nitrogen from 24-hour PD Effluent collection
  - Creatinine from 24-hour urine collection
  - Urea Nitrogen from 24-hour urine collection

If a patient had re-enrolled, all data gathered from all laboratory tests will be summarized.

For all laboratory values, the measurement taken at screening is considered baseline except for the Creatinine and Urea Nitrogen from Blood Draw; these two parameters will use their measurements taken during the Baseline Period as baseline.

### 14.3.5 Feed Water Analysis

The results of the feed water analysis from the patients' home will be analyzed descriptively using frequencies and percentages of those that meet specifications vs those that do not. A test will be considered meeting specifications if all of the following parameters fall within the specified limits:

| Parameter | Maximum Limit |
|---|---|
| Aluminum | 0.3 mg/L |
| Antimony | 0.006 mg/L |
| Arsenic | 0.01 mg/L |
| Barium | 2 mg/L |
| Beryllium | 0.004 mg/L |
| Cadmium | 0.005 mg/L |
| Chromium | 0.1 mg/L |
| Cobalt | 0.025 mg/L |
| Copper | 1.3 mg/L |
| E. Coli Units | <1 CFU/mL |
| Fluoride | 2 mg/L |
| Heterotrophic Plate Count | <500 CFU/mL |
| Lead | 0.015 mg/L |
| Mercury | 0.002 mg/L |
| Nickel | 0.02 mg/L |
| Nitrate (measured as Nitrogen) | 10 mg/L |
| Selenium | 0.05 mg/L |
| Silver | 0.1 mg/L |
| Thallium | 0.002 mg/L |
| Total Coliform Unit | <1 CFU/mL |
| Turbidity | 3 NTU |
| Zinc | 5 mg/L |

If any of the above parameters fall outside the limits, then the particular test is considered not meeting specifications. If any of the above parameters were not tested, then the particular test is considered missing. These tests will be performed at [redacted].

There will be three summaries of these data: one based on initial values, one based on retest values (as mandated per decision trees), and one based on the most recent test values. These three summaries will be done on a combination of all visits and individually for each of the visits.

In addition to the above, there will be two additional tables detailing the feed water analysis. The first will show the test results (met vs did not meet specifications) for each of the individual parameters, and the second will be a descriptive summary (n, mean,

standard deviation, minimum, median, and maximum) of the results of each of the individual parameters.

If a patient had re-enrolled, all data will be used in this analysis. The test results will also be listed. Patient's age, sex, race, and weight at baseline will not be shown for this listing. This listing will include all enrolled patients.

## 15. INTERIM ANALYSIS

An interim analysis has not been planned for this study.

## 16. DETAILS ON DATA HANDLING

### 16.1 Baseline definition

Unless otherwise specified, baseline is defined as the values collected during the baseline visit, which is to occur during the in-center training. If multiple values are available, the value closest to the start of treatment will be used for baseline.

If a patient had re-enrolled and collected separate baseline data for their latter enrollments, then the baseline value collected with each corresponding enrollment should be used as baseline. For example, if patient X enrolled once under X.1 and again under X.2 and collected baseline data for both, then all data associated with X.1 should use the values collected at baseline for X.1, and those data associated with X.2 should use the values collected at baseline for X.2. If a patient re-enrolled and did not re-collect baseline values, then the data taken at their first baseline visit will be counted as baseline. If baseline data is missing, then data from screening may be used as baseline.

For Total $KT/V_{urea}$, if a value is available within 45 days of screening, then this value will serve as the baseline. If a value is not available, a new value will be taken during the screening period to use as baseline.

Any medical condition that is present at the time that a participant is screened will be considered baseline medical history and is not reported as an adverse event.

### 16.2 Handling of Missing or Incomplete Dates/Times

Unless otherwise specified, missing dates and times will not be imputed.

#### 16.2.1 Treatment Start and Stop Dates

No imputation will be done if the treatment start/stop dates are missing.

### 16.2.2 Concomitant Medication Start and Stop Dates

If medication start date is unknown but the stop date is prior to the start of the study treatment, then the medication will be classified as "Prior". If medication start date is unknown and stop date is also unknown, then the medication will be classified as "Concurrent".

### 16.2.3 Adverse Event Start and Stop Dates

If the start date/time of an adverse event is missing and the stop date/time is prior to the date of first treatment, then the adverse event will be classified as a pre-treatment adverse event. If the start date/time is missing and the stop date/time is either missing or after the date of first treatment, then the adverse event will be classified as treatment-emergent.

Start and stop dates for adverse events will not be imputed.

## 16.3 Visit Windows/Unscheduled Visits

The visit windows are defined below:

**Table 1: Visit Windows**

| Time-point/Visit | Time Window |
|---|---|
| **Screening** | Approximately 3 weeks |
| **Baseline period** | Approximately 2 weeks after Screening |
| **Simulated Treatment (Visit 1)** | Up to 7 days prior to Day 1 of Study Treatment period |
| **Visit 2** | Any time during week 4 of treatment |
| **Total $Kt/V_{urea}$ visit** | Any time between week 5 thru 8 of study treatment |
| **Visit 3** | Any time during week 8 of study treatment |
| **Visit 4** | Any time during week 12 of study treatment |
| **End of Study Visit or Early Termination visit** | 5 days after last treatment with AMIA APD Solution Generation System |

In the instance that multiple results are collected at the baseline visit, the last available result will be used in the analyses. For assessments collected post-baseline, the first available result will be used, or the assessment from the withdrawal visit will be used if the nominal visit result is unavailable. All re-tests will be presented in safety listings.

Results from unscheduled visits will not be included in the table summaries. These values will only be presented in the listings.

### 16.4 Pooling Strategy for Study Sites

Data will be pooled across all study sites.

## 17. LIST OF TABLES, FIGURES AND LISTINGS

| Table Number | Table Name |
|---|---|
| 14.1.1 | Patient Overview |
| 14.1.2 | Patient Disposition |
| 14.1.3 | Protocol Deviations Summary |
| 14.1.4 | Categorical Demographic and Baseline Characteristics |
| 14.1.5 | Continuous Demographic and Baseline Characteristics |
| 14.2.1 | Overall Testing of the Chemical Composition of the Dialysis Solution (Primary Efficacy Endpoint) |
| 14.2.2 | Individual Parameter Testing of the Chemical Composition of the Dialysis Solution |
| 14.2.3 | Individual Parameter Summary of the Chemical Composition of the Dialysis Solution |
| 14.2.4 | Total $Kt/V_{urea}$ Summary (Secondary Efficacy Endpoint) |
| 14.2.5.1 | eDiary Treatment Summary |
| 14.2.5.2 | Treatment Interruptions Summary |
| 14.3.1.1.1 | Summary of Adverse Events |
| 14.3.1.1.2 | Treatment-Emergent Adverse Events by SOC and Preferred Term |
| 14.3.1.1.3 | Serious Treatment-Emergent Adverse Events by SOC and Preferred Term |
| 14.3.1.1.4 | Treatment-Emergent Adverse Events Related to Study Device by SOC and Preferred Term |
| 14.3.1.1.5 | Treatment-Emergent Adverse Events Related to Typical PD Therapy by SOC and Preferred Term |
| 14.3.1.1.6 | Treatment Emergent Adverse Events Related to Another Baxter Product by SOC and Preferred Term |
| 14.3.1.1.7 | Serious Treatment-Emergent Adverse Events Related to Study Device by SOC and Preferred Term |
| 14.3.1.1.8 | Serious Treatment-Emergent Adverse Events Related to Typical PD Therapy by SOC and Preferred Term |
| 14.3.1.1.9 | Serious Treatment-Emergent Adverse Events Related to Another Baxter Product by SOC and Preferred Term |
| 14.3.1.1.10 | Treatment-Emergent Adverse Events Leading to Withdrawal by SOC and Preferred Term |
| 14.3.1.1.11 | Treatment-Emergent Adverse Events Leading to Death by SOC and Preferred Term |

| | |
|---|---|
| 14.3.1.1.12 | Treatment-Emergent Adverse Events of Special Interest by SOC and Preferred Term |
| 14.3.1.1.13 | Treatment-Emergent Adverse Events in ≥5% of Patients by SOC and Preferred Term |
| 14.3.1.3.1 | Treatment-Emergent Adverse Events by SOC, Preferred Term, and Severity |
| 14.3.1.3.2 | Treatment-Emergent Adverse Events by SOC, Preferred Term, and Relationship with Study Device |
| 14.3.1.3.3 | Treatment-Emergent Adverse Events by SOC, Preferred Term, and Relationship with Typical PD Therapy |
| 14.3.1.3.4 | Treatment-Emergent Adverse Events by SOC, Preferred Term, and Relationship with Another Baxter Product |
| 14.3.4.1 | Hematology Laboratory Summary at Baseline |
| 14.3.4.2 | Chemistry Laboratory Summary at Baseline |
| 14.3.5.1 | Vital Signs Summary and Change from Baseline |
| 14.3.6.1 | Summary of Device Deficiencies |
| 14.3.6.2 | Summary of Device Deficiency Characteristics |
| 14.3.7.1 | Microbiological and Chemical Testing of the Product Water from the Water Device (pre-sterilizing filter) (Primary Safety Endpoint) |
| 14.3.7.2 | Individual Parameter Microbiological and Chemical Testing of the Product Water from the Water Device (pre-sterilizing filter) |
| 14.3.7.3 | Individual Parameter Summary of Microbiological and Chemical Testing of the Product Water from the Water Device (pre-sterilizing filter) |
| 14.3.7.4 | Microbiological Testing of the Water from the Holding Bag (Primary Safety Endpoint) |
| 14.3.7.5 | Individual Parameter Microbiological Testing of the Water from the Holding Bag |
| 14.3.7.6 | Individual Parameter Summary of Microbiological Testing of the Water from the Holding Bag |
| 14.3.7.7 | Testing of the Feed Water |
| 14.3.7.8 | Individual Parameter Testing of the Feed Water |
| 14.3.7.9 | Individual Parameter Summary of Feed Water |
| **Listing Number** | **Listing Name** |
| 16.2.1 | Patient Disposition |
| 16.2.2 | Protocol Deviations |
| 16.2.3 | Patient Overview |
| 16.2.4.1 | Demographic and Baseline Characteristics |
| 16.2.4.2 | Concomitant Medications by Coded Drug Term |
| 16.2.4.3 | Non-Drug Therapies by Coded Term |

| | |
|---|---|
| 16.2.4.4 | Medical History |
| 16.2.4.5 | Renal Medical History |
| 16.2.4.6 | In-Center Training Log |
| 16.2.6.1 | Chemical Composition of Dialysis Solution |
| 16.2.6.2 | Total $Kt/V_{urea}$ Measurements |
| 16.2.6.3 | eDiary Treatment Information |
| 16.2.6.4 | Treatment Interruptions Information |
| 16.2.7.1.1 | Treatment-Emergent Adverse Events |
| 16.2.7.1.2 | Pre-Treatment Adverse Events |
| 16.2.7.1.3 | Treatment-Emergent Adverse Events Leading to Withdrawal |
| 16.2.7.1.4 | Treatment-Emergent Adverse Events Leading to Death |
| 16.2.7.1.5 | Treatment-Emergent Adverse Events Related to Study Device |
| 16.2.7.1.6 | Treatment-Emergent Adverse Events Related to Typical PD Therapy |
| 16.2.7.1.7 | Treatment-Emergent Adverse Events Related to Another Baxter Product |
| 16.2.7.1.8 | Treatment-Emergent Adverse Events of Special Interest |
| 16.2.7.1.9 | Serious Treatment-Emergent Adverse Events |
| 16.2.7.1.10 | Serious Pre-Treatment Adverse Events |
| 16.2.7.1.11 | Serious Treatment-Emergent Adverse Events Leading to Withdrawal |
| 16.2.7.1.12 | Serious Treatment-Emergent Adverse Events Leading to Death |
| 16.2.7.1.13 | Serious Treatment-Emergent Adverse Events Related to Study Device |
| 16.2.7.1.14 | Serious Treatment-Emergent Adverse Events Related to Typical PD Therapy |
| 16.2.7.1.15 | Serious Treatment-Emergent Adverse Events Related to Another Baxter Product |
| 16.2.7.1.16 | Treatment-Emergent Suspected Unexpected Serious Adverse Reactions or Unexpected Adverse Device Effects |
| 16.2.7.2 | Patient Deaths |
| 16.2.8.1 | Laboratory Measurements |
| 16.2.8.2 | Abnormal Laboratory Measurements |
| 16.2.9.1 | Vital Signs |
| 16.2.11.1 | Microbiological and Chemical Contamination Testing of the Product Water from the Water Device (Pre-Sterilizing Filter) |
| 16.2.11.2 | Microbiological Testing of the Water from the Holding Bag |
| 16.2.11.3 | Testing of the Feed Water |
| 16.2.12.1 | Device Deficiencies and Product Issues |

| | |
|---|---|
| 16.2.12.2 | Device Deficiencies Resulting in an Alarm |
| 16.2.12.3 | Device Deficiencies Leading to AEs |
| 16.2.12.4 | Device Deficiencies Leading to SUSARs |
| 16.2.12.5 | Device Deficiencies Leading to UADEs |

## Appendix 1 Schedule of Events

| Observation | Screening (approx. 3 weeks) | Baseline Period (In-center Training, approx. 2 weeks)[a] | Simulated Treatment Visit 1 | Each Treatment Day[bc] | Treatment Visits 2, 3 and 4 (Treatment weeks 4, 8 and 12, respectively)[d] | Total $Kt/V_{urea}$ Visit[e] | Follow-up Period (5-10 days) | End of Study/ Early Termination Visit[f] |
|---|---|---|---|---|---|---|---|---|
| Informed Consent of patient and care partner (if participating)[g] | X | | | | | | | |
| Demographics[h] | X | | | | | | | |
| Medication histories (within 30 days of Screening)[i] | X | | | | | | | |
| Physical examination including weight and height | X | | | | | | | X |
| Daily weight (pre- and post-dialysis) | | X | | X | | | | |
| Vital signs[j] | X | | | | X | | | X |
| Home suitability assessment[k] | X | | | | | | | |
| Feed water analysis for the home | X | | | | | | | X[aa] |
| Assessment by an Investigator or a designee[l] | X | X | X | | X | | X | X |
| Adverse Event assessments[m] | X | X | X | X | X | | X | X |
| Concomitant medications[n] | X | X | | X | | | | |

| Observation | Screening (approx. 3 weeks) | Baseline Period (In-center Training, approx. 2 weeks)[a] | Simulated Treatment Visit 1 | Each Treatment Day[bc] | Treatment Visits 2, 3 and 4 (Treatment weeks 4, 8 and 12, respectively)[d] | Total $Kt/V_{urea}$ Visit[e] | Follow-up Period (5-10 days) | End of Study/ Early Termination Visit[f] |
|---|---|---|---|---|---|---|---|---|
| Clinical laboratory evaluations | X | | | | | X | | |
| AMIA APD System specific training[o] | | X | | | | | | |
| Comprehension and retention assessment[p] | | X | | | | | | |
| Investigator confirmation of prescription stability[q] | X | X | | | | | | |
| Written confirmation for independent care[r] | | X | | | | | | |
| Machine information[s] | | X | | X | | | | |
| Machine observations[t] | | | | X | | | | |
| Product Water Microbiological Test sampling (Simulation)[u] | X[v] | | X | | X | | | |
| Product Water Chemical Contamination Test sampling (Simulation)[u] | X[v] | | X | | X | | | |

| Observation | Screening (approx. 3 weeks) | Baseline Period (In-center Training, approx. 2 weeks)[a] | Simulated Treatment Visit 1 | Each Treatment Day[bc] | Treatment Visits 2, 3 and 4 (Treatment weeks 4, 8 and 12, respectively)[d] | Total $Kt/V_{urea}$ Visit[e] | Follow-up Period (5-10 days) | End of Study/ Early Termination Visit[f] |
|---|---|---|---|---|---|---|---|---|
| Microbiological testing of water from holding bag[u] | | | X | | X | | | |
| Testing of chemical composition of the final dialysis solution[u] | | | X | | X | | | |
| AMIA APD Solution Generation System-related Product Complaints and Device Deficiencies[w] | | | X | X | | | | |
| Chlorine Testing[x] | | X | | X | | | | |
| Home installation[y] | X | X | | | | | | |
| Collection of diary source data (eDiary)[z] | | | | X | | | | |
| Transition to conventional PD therapy | | | | | | | X[bb] | |

[a] Baseline measurements will be taken during the Baseline Period (In-Center Training Period) before the patient starts treatment with AMIA APD Solution Generation System.

[b] The Simulated Treatment Visit 1 assessments will occur before the first treatment with AMIA APD Solution Generation System in the patient's home. The Simulated Treatment Visit 1 can be conducted -7 days from first actual treatment..

[c] Assessments under Each Treatment Day column will occur every day from the first actual treatment with the AMIA APD Solution Generation System in the patient's home until the last day of the 12 week Study Treatment Period

[d] After patients have completed the $Kt/V_{urea}$ assessment required during Week 5, 6, 7 or 8 of the Study Treatment Period, in order to accommodate potential vacation/travel, they may voluntarily interrupt investigational AMIA APD Solution Generation System treatment and perform standard of care PD therapy using the marketed AMIA or HomeChoice APD Cycler with currently available PD solution (e.g. Dianeal) up to 2 separate times with prior approval from the Investigator for up to 14 days in total; however, patients must complete a total of 12 weeks of cumulative therapy using the AMIA APD Solution Generation System.

[e] A visit to assess Total $Kt/V_{urea}$ will occur after the patient has been dialyzing with the AMIA APD Solution Generation System for at least 4 weeks (assessment done one time during weeks 5, 6, 7 or 8 of the Study Treatment Period). Patients who have missed 4 consecutive days of prescribed therapy with AMIA APD Solution Generation System should defer their $Kt/V_{urea}$ assessment by 1 week to allow a full week of prescribed treatment using the AMIA APD Solution Generation System.

[f] The End of Study assessments will be performed 5-10 days after the last treatment with AMIA APD Solution Generation System, i.e., at Week 13 for patients who completed the 12 weeks of treatment.

[g] Patient may have a care partner to assist with performing study procedures. Refer to Section 5.4.1 of the protocol for details of care partner's responsibilities.

[h] Demographic data include age, gender, race, ethnicity, height, weight, body mass index = $kg/m^2$, where kg is a person's weight in kilograms and $m^2$ is their height in meters squared.

[i] Medication history will include all medications that are still active, taken within the 30 days prior to Screening, with each medication having a corresponding indication recorded in the Medication and Medical History eCRFs.

[j] Vital signs (BP and pulse rate) will be recorded on the eCRF at Screening, Study Visit 2, Study Visit 3, Study Visit 4, and at the End-of-Study Visit. Weight will be recorded at Screening and at the End-of-Study Visit. Blood pressure will be measured with an appropriate cuff size after the patient has been sitting for at least 5 minutes.

[k] Please refer to the Point of Care APD Clinic and Home Assessment Guide for the procedures involved in the home suitability assessment.[9]

[l] The Principal Investigator or a designee (e.g., sub-investigator) will assess each patient at the Screening Visit and on a weekly basis. At a minimum, this assessment will include evaluation of BP, pulse rate, weight, fluid status and dialysis prescription.

[m] AEs and SAEs will be collected after the informed consent is signed and will continue to be collected throughout the Study Treatment Period and during the follow-up period of 5-10 days after the last study treatment. Adverse device events and SADEs will be collected from the time of signing informed consent.

[n] Medications taken during the study will be documented throughout the study and will include a review of all major body systems and renal history (primary etiology of renal disease and current PD prescription).

[o] Patients will receive device-specific training which will last up to 2 weeks.

[p] Comprehension and retention testing will occur at the end of the Baseline Period (In-center Training Period) for patients and care partners (if participating). If the patient does not read and understand English, the care partner will assist the patient with comprehension and retention testing.

[q] The Investigator must reassess the stability of the patient during the Baseline Period (In-center Training Period). Once the clinician concludes that the patient is clinically stable and their PD prescription is stable, then the patient can begin treatment in the home.

[r] Written confirmation of independent care by patient and care partner (if participating).

[s] Machine information will include the available code number(s) and a lot/serial number(s) at initial installation and if the device or any of the disposables are changed.

[t] Machine observations with each treatment will include the following: duration of PD treatments, start and stop times, total UF volume programmed and removed as obtained from machine log, and technical treatment interruptions – machine alarms.

[u] Microbiological (including endotoxin) and chemical testing of product water produced in the home will occur after the installation of the AMIA APD Solution Generation System. Simulated treatments will occur during week 1, before the first treatment in the home with the AMIA APD Solution Generation System, and during Study Treatment Weeks 4, 8 and 12. The dialysis solution generated by the simulated treatment will be collected from the system in the heater bag and used to evaluate the chemical composition of the final dialysis solution. Product water from the WD (pre-sterilizing filters) will be collected and tested to confirm that it conforms to ISO standard 13959 for microbiological (including endotoxin) and chemical contamination, and water from the holding bag (post-sterilizing filters), generated during a simulated treatment, will be collected and tested to confirm it does not exceed 0 CFU/mL for bacteria (no growth) and is < 0.03 EU/mL for endotoxins, consistent with Dianeal specifications for sterility. The simulated treatment will occur in addition to the patient's normal therapy regimen (except at the last Simulated Treatment Visit, which is conducted after the last treatment). Patients will be required to use new AMIA APD Concentrates and disposable sets for their PD treatment. The chemical collection test sampling may occur on a different day than the product water microbiological test sampling.

[v] Tests carried out during Screening are for safety checks prior to therapy and will not be used in the analysis.

[w] Collection of AMIA APD Solution Generation System-related product complaints and device deficiencies, which would include functional characteristics (e.g., particulate matter, PD fluid discoloration, leaks, tubing separations), will begin from the time of signing informed consent and will continue throughout the entire Study Period.

[x] Chlorine testing will occur prior to every treatment on the AMIA APD Solution Generation System.

[y] To provide schedule flexibility for the consented patient, Baxter Service or its designee may begin the home installation process during the Screening Period. System installation and product water from the WD (pre-sterilizing filters) testing are expected to take approximately two weeks. This will ensure the system is ready for activation after the patient completes their required training on the AMIA APD Solution Generation System.

[z] eDiary source data will include data not limited to treatment activities listed in section 5.9 of the protocol. If the patient does not speak English, the care partner will assist the patient with completion of the eDiary.

[aa] Feed water analysis for the home may take place at de-commissioning.

[bb] After the final Study Treatment Visit, patients are to transition back to treatments with AMIA or HomeChoice with Baxter's approved Dianeal Low Calcium (2.5 mEq/L) PD Solution in their home environment and enter a 5-10 day Follow-up Period. Return of all investigational products and study related supplies will be scheduled during this time.