Clinical Study Protocol

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
Name of Finished Product:	AMIA APD Solution Generation System; AMIA APD Generated Solution
Name of Active Ingredients: **Investigational Product:**	Dextrose Concentrate Electrolyte Concentrate AMIA APD Solution Generation System
IND Number:	141130
Indication:	End stage renal disease (ESRD) requiring peritoneal dialysis (PD)
Investigators:	Multi-center
Sponsor:	Baxter Healthcare Corporation One Baxter Parkway Deerfield, IL 60015 USA
Sponsor Contact:	[redacted] Global Clinical Operations Baxter Healthcare Corporation One Baxter Parkway, Deerfield, IL 60015 Email: [redacted]
Medical Monitor:	[redacted], MD, MS, FAAP [redacted], Renal Care Baxter Healthcare Corporation One Baxter Parkway, Deerfield, IL 60015 Mobile: [redacted] Email: [redacted]

	Date
Original Protocol:	2018 JUN 15
Amendment 1:	2018 OCT 16
Amendment 2:	2018 DEC 13
Amendment 3:	2019 FEB 28
Amendment 4:	2019 APR 30
Amendment 5:	2019 JUL 09
Amendment 6:	2019 NOV 01

Table of Contents

SYNOPSIS 7

LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS 12

1. INTRODUCTION 14
   1.1 Background 14
   1.2 Benefits and Risks for the Study Population 17
   1.3 Study Sponsor 18

2. STUDY OBJECTIVES 19
   2.1 Primary Objectives 19
   2.2 Secondary Objectives 19

3. INVESTIGATIONAL PLAN 19
   3.1 Overall Study Design and Plan 19
   3.2 Study Endpoints 20
      3.2.1 Primary Endpoints 20
      3.2.2 Secondary Endpoints 21
   3.3 Rationale for Study Design and Control Group 21
   3.4 Study Duration and Dates 22
   3.5 Study Intervention Discontinuation and Patient Discontinuation/Withdrawal 22
      3.5.1 Removal of Patients from Therapy, Assessment, or Study 22
      3.5.2 Discontinuation of the Study 24

4. STUDY POPULATION SELECTION 24
   4.1 Study Population 24
   4.2 Inclusion Criteria 24
   4.3 Exclusion Criteria 26
   4.4 Home Assessment and Installation 27
   4.5 Recruitment 27

5. STUDY TREATMENT(S) 28
   5.1 Description of Treatment(s) 28
      5.1.1 Study Product: AMIA APD Solution Generation System 28
   5.2 Enrollment, Randomization, and Assignment to Treatment Group 30
   5.3 Treatment Duration and Study Visits 30
   5.4 Selection and Timing for Each Patient 31
      5.4.1 Care Partner 32

5.5 Method of Assigning Patients to Treatment Groups 32
5.6 Blinding 33
5.7 Concomitant Therapy 33
5.8 Prohibitions and Restrictions 33
5.9 Treatment Compliance 33
5.10 Packaging and Labeling 34
5.11 Accessibility and Control of Study Participant Data 34
5.12 Storage and Accountability 35
5.13 Investigational Product Retention 36

6. STUDY PROCEDURES 36

6.1 Informed Consent 36
6.2 Medical History 37
6.3 Physical Examination 37
6.4 Vital Signs 37
6.5 Clinical Laboratory Tests 37
6.5.1 Laboratory Parameters 37
6.5.2 Blood collection 38
6.5.3 24-Hour Urine Collection 39
6.5.4 Peritoneal Kt/V_{urea}, Renal Kt/V_{urea} and Total Kt/V_{urea} 39
6.5.5 White Cell Count and Cell Culture 39
6.5.6 Sample Collection, Storage, and Shipping 40
6.5.7 Simulated Treatments 40
6.5.8 Water and Dialysate Sampling Analysis 40
6.5.8.1 Chemical Contaminants 41
6.5.8.2 Microbiological Cultures and Endotoxin – Product Water and Water from Holding Bag 41
6.5.8.3 Dialysate Composition Testing 42
6.5.8.4 Additional Sampling Procedures 42
6.5.8.5 Process for Responding to Out-of-Specification Results 42
6.5.8.6 Chlorine and Conductivity Testing 43
6.6 Power Outage 44
6.7 Boil Water Advisory Procedure 44
6.8 Removal of Patients from the Study 44
6.9 Other Study Procedures 45
6.10 Appropriateness of Measurements 45

7. DATA COLLECTION FOR SAFETY ASSESSMENTS AND REPORTING 45

7.1 Definition of Adverse Events and Device Deficiencies 45
7.2 Safety Reporting 47
7.2.1 Adverse Event of Special Interest 50
7.2.2 Medical Events Commonly Associated with Peritoneal Dialysis 51
7.2.3 Adverse Events Reporting 51
7.3 Product Complaints 51

7.4 Medical Monitor 52
7.5 Safety Reporting to Authorities and Institutional Review Board 52
7.6 Pregnancy Reporting 52

8. STUDY ACTIVITIES 52

8.1 Schedule of Evaluations and Procedures 52
8.2 Screening Period (approximately 3 weeks) 53
8.3 Training for PD Home Solution Generation System 54
8.4 Baseline Period (In-center Training Period) 54
8.5 Each Treatment Day 55
8.6 Simulated Treatment Visit 1 (Before 1st Treatment in the Home, Study Visit 1) 56
8.7 Study Visits 2, 3 and 4 (Study Treatment Weeks 4, 8 and 12) 57
8.8 Total Kt/V_{urea} Visit 57
8.9 Follow-up Period 58
8.10 End of Study Visit or Early Termination Procedures 58

9. DATA MANAGEMENT, QUALITY CONTROL AND QUALITY ASSURANCE 59

9.1 Auditing 59
9.2 Non-compliance with the Protocol 59

10. PLANNED STATISTICAL METHODS 60

10.1 General Considerations 60
10.2 Determination of Sample Size 60
10.3 Analysis Populations 60
10.4 Demographics and Baseline Characteristics 60
10.5 Primary Analysis 61
10.6 Secondary Analysis 61
10.7 Sensitivity Analysis 62
10.8 Interim Analysis 62

11. ADMINISTRATIVE CONSIDERATIONS 62

11.1 Investigators and Study Administrative Structure 62
11.2 Institutional Review Board Approval 62
11.3 Food and Drug Administration 63
11.4 Ethical Conduct of the Study 63
11.5 Patient Information and Consent 64
11.6 Patient Confidentiality 64
11.6.1 Health Insurance Portability and Accountability Act Authorization Procedures 64
11.7 Study Monitoring 65

11.8 Case Report Forms and Study Records....65
11.9 Access to Source Documentation....65
11.10 Data Generation and Analysis....66
11.11 Retention of Data....66
11.12 Financial Disclosure....67
11.13 Publication and Disclosure Policy....67

12. REFERENCE LIST....68

List of In-Text Tables

Table 1. Composition of Dextrose Concentrate....16
Table 2. Composition of Electrolyte Concentrate....16
Table 3. Composition of the AMIA APD Generated Solution (mmol/L)....17
Table 4. List of Laboratory Tests[a]....38
Table 5. Adverse Event Term Definition....45
Table 6. Definition of Terms....47
Table 7. Causality Assessments....49
Table 8. Severity Assessments....50
Table 9. Outcome Conclusion Criteria....50

List of In-Text Figures

Figure 1. General Arrangement of the AMIA APD Solution Generation System....15
Figure 2. Overview of Study Assessments....20

List of Appendices

Appendix 1 Schedule of Events....69
Appendix 2 Schedule of Clinical Laboratory Evaluations....75
Appendix 3 Dianeal Low Calcium (2.5 mEq/L) Peritoneal Dialysis Solution Formulations....77
Appendix 4 Formulas....78
Appendix 5 Definitions of Adverse Events of Special Interest Terms....79
Appendix 6 Medical Events Commonly Associated with Peritoneal Dialysis....80
Appendix 7 New York Heart Association Functional Classification....81
Appendix 8 Sponsor Signatures....82
Appendix 9 Investigator's Signature....84

SYNOPSIS

Name of Finished Product:

AMIA Automated Peritoneal Dialysis (APD) Solution Generation System

AMIA APD Generated Solution

Name of Active Ingredient:

Dextrose Concentrate

Electrolyte Concentrate

Investigational Product:

AMIA APD Solution Generation System

Indication:

End stage renal disease (ESRD) requiring peritoneal dialysis (PD).

Study Title:

Performance evaluation of the AMIA APD Solution Generation System in patients using the AMIA APD Cycler.

Study Number:
BXU011787

Primary Objective:

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 Water Device (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.

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}.

Overall Study Design and Plan:

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 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.

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.

Study Population:

The study population consists of patients with ESRD treated with PD using the AMIA APD Solution Generation System. Up to 50 patients receiving a regimen of PD with the AMIA or HomeChoice APD Cycler for at least 12 weeks 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.

Inclusion Criteria:

Each patient must meet ALL of the following criteria to be enrolled in this study:

1. Patient is 18 years or older.
2. Patient with ESRD receiving PD, and who is already trained and regularly using the AMIA or HomeChoice APD Cycler with Dianeal PD Solution for at least 12 weeks.
3. Patient is receiving or willing and able to use Dianeal Low Calcium (2.5 mEq/L) PD prescriptive regimen at study treatment initiation per Investigator's assessment.
4. Patient demonstrates adequate PD therapy with clinical euvolemia as assessed by the Investigator with a total Kt/V_{urea} of a minimum of 1.7 within 45 days of Screening.[2] If a total Kt/V_{urea} is not available within 45 days of Screening, it will be measured at Screening.
5. Investigator assesses that, with appropriate training, the patient will be able to successfully manage his/her dialysis treatments with the AMIA APD Solution Generation System.
6. Patient is available and is willing to complete training on the AMIA APD Solution Generation System.
7. Patient and home environment are deemed suitable for treatment with the AMIA APD Solution Generation System, while in the home.
8. Home electrical and water assessments meet suitability criteria for the AMIA APD Solution Generation System.
9. The patient's home has suitable wireless connection or patient is willing to allow installation of suitable wireless connection.
10. Patient and/or care partner (if participating, see Section 5.4.1) is able to read and understand English, and provide informed consent after an explanation of the proposed study. If the patient does not read and understand English, patient may still participate if he/she has a co-residing care partner who reads and understands English, assessed as adequate by the PI.
11. Women of childbearing potential (not menopausal or surgically sterile) must not be pregnant. Serum qualitative and quantitative pregnancy test will be done within 14 days prior to initiation of study product.
    - If qualitative serum β-hCG results are positive, repeat quantitative serum pregnancy test within 48 hours.
    - If quantitative serum β-hCG levels show clinically significant rise within 48 hours, serum progesterone level should be taken. Serum progesterone > 5 ng/mL will exclude a patient from the study.
12. Sexually active males and females agree to use a reliable means of contraception during the study and for 30 days afterwards (e.g., oral contraceptive and condom, intrauterine device and condom, or diaphragm with spermicide and condom).

Exclusion Criteria:

Patient who meets ANY of the following criteria will be excluded from the study:

1. Patient with a history of PD catheter dysfunction within 12 weeks prior to study enrollment, as evaluated by the Investigator.
2. Patient who had episodes of peritonitis or exit site infection within 12 weeks prior to study enrollment.
3. Patient who has signs of impending or current infection including a cloudy dialysis effluent or dialysis white cell count > 100/µL or > 0.1 x 10^9/L (after a dwell time of at least 2 hours), with > 50% polymorphonuclear cells, and/or positive dialysis effluent culture.
4. Patient who has a severe primary immunodeficiency disorder or other condition that may mask clinical signs of peritonitis, as evaluated by the Investigator.
5. Patient with a history of repeated non-compliance with PD therapy (e.g., a substantial number of missed clinic visits, missed treatments or a history of mismanagement of diet or medications), as evaluated by the Investigator.
6. Patient who has acute renal failure with the chance for recovery.
7. Patient who is pre-scheduled for a living donor kidney transplant within the next 6 months.
8. Patient who is not expected to live at least 6 months while maintaining PD treatment.
9. Patient who had major abdominal surgery within 6 months prior to study enrollment.
10. Patient with current abdominal hernia, as evaluated by the Investigator.
11. Patient with advanced liver or pulmonary disease as evaluated by the Investigator.
12. Positive serology test for Hepatitis B Virus or Hepatitis C Virus infection, or aspartate transaminase or alanine aminotransferase > 3 x upper limit of normal at Screening.[3]
13. Patient with diagnosed stage III or IV New York Heart Association (NYHA) heart failure. (Appendix 7)
14. Patient who has an active malignancy.[a]
15. History of a clinically significant illness and/or clinically significant surgery within the past 14 days preceding the Screening Visit as determined by the Investigator.
16. Patient who is enrolled in another interventional clinical study.

Test Product, Dose, and Mode of Administration:

AMIA APD Solution Generation System, Dextrose Concentrate and Electrolyte Concentrate.

To be used in patients currently receiving PD with the AMIA or HomeChoice PD System and Dianeal PD Solution.

Duration of Treatment:

Each patient will participate in the study for approximately 18 weeks. The Study Periods are as follows:

- Screening Period including home suitability assessment, feed water testing, and home installation, when suitable – approximately 3 weeks.
- Baseline Period (In-center Training Period) – approximately 2 weeks.
- Study Treatment Period - 12 weeks.
- Follow-up Period – 5-10 days following the last treatment with the AMIA APD Solution Generation System.
- End of Study/ Early Termination Visit (occurring on the last day of the Follow-up Period [day 5-10]).

[a] Please note, cancers determined to be cured or in remission for ≥ 1 years, curatively resected basal cell or squamous cell skin cancers, cervical cancer in situ, or resected colonic polyps are acceptable diagnosis.

Study Endpoints:

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.

Secondary Endpoints:

- Safety profile of the AMIA APD Solution Generation System used to treat patients with PD by collecting AEs, SAEs, 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 one time during Week 5, 6, 7 or 8 of the Study Treatment Period.

Statistical Methods:

General Considerations:

Further details of the planned statistical methods will be provided in the study statistical analysis plan (SAP). The SAP will be finalized prior to database lock. Any changes to the statistical methods described in the protocol will be documented in the SAP.

Unless otherwise noted, all analyses will be performed using SAS/GRAPH® 9.4 software, SAS/STAT® 14.1 software and Base SAS® 9.4. Copyright© 2002-2012, SAS Institute Inc. SAS and all other SAS Institute Inc. product or service names are registered trademarks or trademarks of SAS Institute Inc., Cary, NC, USA. All Rights Reserved.[4]

Summary statistics will be presented with mean, standard deviation, median, minimum and maximum for continuous variables and frequency count and percentage based on study population will be used to summarize categorical variables. Prior to analysis, data will be reviewed for consistency. Missing data values will not be imputed and all non-missing values will be used.

Determination of 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.

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).

Demographics and Baseline Characteristics:

Demographic data include age, gender, race, height, weight, body mass index calculated as weight (kg)/height^2 (m), and ethnicity.

Other baseline/ demographic data will include total Kt/V_{urea} which will be summarized by sample size, mean, standard deviation, median, minimum and maximum.

Demographic and baseline characteristics will be summarized on the Safety Set.

Primary Analysis:

Primary Efficacy:

AMIA APD Generated Solution specifications will be collected from the final dialysis solution generated by the patient using the AMIA APD Solution Generation System, during simulated treatment.

The chemical composition measurements taken from the final PD solution will be summarized by count and percentage for those that meet specification vs those that do not. Summary statistics including sample size, mean, standard deviation, median, minimum and maximum will also be presented for the chemical composition measures of the solution. These summaries will be provided on the Safety Set.

Primary Safety:

Product water from the WD (pre-sterilizing filters) and water in the holding bag (post-sterilizing filters), generated during simulated treatments will be sampled. The measurements of product water will be summarized by count and percentage for those that meet ISO Standard 13959[1] for microbiological (including endotoxin) and chemical contamination vs those that do not, and the measurements from the holding bag will be summarized by count and percentage for those that achieve 0 CFU/mL (no growth) and <0.03 EU/mL vs those that do not. Both measures will also be summarized by sample size, mean, standard deviation, median, minimum and maximum. These summaries will be provided on the Safety Set.

Secondary Analysis:

Adverse events will be mapped to a Primary System Organ Class and Preferred Terms according to MedDRA Version 21.0 or higher and summarized using frequencies and percentages. In addition, AEs will be summarized by seriousness, severity, and relationship to study product or typical PD therapy. Device alarms and their relation to AEs or SAEs will be summarized using frequency counts and percentages. Vital Signs (BP, pulse, temperature) will be summarized by mean, standard deviation, median, minimum and maximum for all recorded timepoints and also for change from pre-to post treatment for all post Baseline timepoints. These summaries will be conducted on the Safety Set.

Total Kt/V_{urea} will be summarized using descriptive statistics at all collection timepoints and change from Baseline will also be summarized. This summary will be performed on the Safety Set.

Interim Analysis:

An interim analysis is not planned for this study.

Date of Original Approved Protocol:

2018 JUN 15

Date of Most Recent Protocol Amendment:

2019 NOV 01

LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

AE	Adverse Event
ADE	Adverse Device Effect
ADR	Adverse Drug Reaction
AESI	Adverse Event of Special Interest
APD	Automated Peritoneal Dialysis
AR	Adverse Reaction
BAD	Baxter Awareness Date
β-hCG	Beta Serum Human Chorionic Gonadotropin
BP	Blood Pressure
CBC	Complete Blood Count
CFR	Code of Federal Regulations
CFU	Colony Forming Units
DD	Device Deficiency
EDC	Electronic Data Capture
eDiary	Electronic Diary
ESRD	End Stage Renal Disease
eCRF	Electronic Case Report Form
EP	European Pharmacopoeia
EU	Endotoxin Units
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HBsAg	Hepatitis B Surface Antigen
HCV	Hepatitis C Virus
HIPAA	Health Information Portability and Accountability Act
ICF	Informed Consent Form
ICH	International Conference on Harmonization
IIPV	Increased Intraperitoneal Volume
IND	Investigational New Drug Application
IP	Intraperitoneal
IRB	Institutional Review Board
Kt/V_{urea}	Dimensionless Number Used to Quantify Hemodialysis and Peritoneal Dialysis Adequacy
NAT	Nucleic Acid Testing
NF	National Formulary
NYHA	New York Heart Association

PC	Product Complaint
PD	Peritoneal Dialysis
PI	Principal Investigator
QS	Quantity Sufficient
RO	Reverse Osmosis
SADE	Serious Adverse Device Effect
SADR	Serious Adverse Drug Reaction
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SAR	Serious Adverse Reaction
SUSAR	Suspected Unexpected Serious Adverse Reaction
UADR	Unexpected Adverse Drug Reaction
UF	Ultrafiltration
USP	United States Pharmacopoeia
WCC	White Cell Count
WD	Water Device

1. INTRODUCTION

1.1 Background

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.

Peritoneal dialysis, as discussed by Popovich in 1976[5] is now an established form of therapy to manage patients with ESRD. This therapy is integrated with other modalities such as hemodialysis and transplantation, with approximately 11% of all dialysis patients globally currently being treated with PD.[6]

Complementary therapies offer longer-term survival for patients with ESRD. However, none of them are devoid of side effects and today their limitations are better understood by the nephrologist.

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 [redacted] and a Water Device (WD). [redacted]

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). Table 1 lists the composition of the Dextrose Concentrate, Table 2 lists the composition of the Electrolyte Concentrate, and Table 3 lists the composition of the AMIA APD Generated Solution. 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%) (See 0). The use of Dianeal low calcium solution is supported by ISPD guidelines suggesting a low calcium (2.5 mEq/L) PD solution to avoid positive calcium balance or hypercalcemia.[7] Consistent with the ISPD guidelines, Dianeal Low Calcium constituted approximately 92% of total Dianeal used in 2017 in the US.

Table 1. Composition of Dextrose Concentrate

Component	Component Quantity	
	Quality Standard	g/L (nominal)
Dextrose Hydrous	USP	550.0
Hydrochloric Acid	NF	pH adjuster
Water for Injection	USP/EP	QS

USP = United States Pharmacopeia; NF = National Formulary; EP = European Pharmacopoeia; QS = Quantity sufficient

Table 2. Composition of Electrolyte Concentrate

Component	Component Quantity	
	Quality Standard	g/L (nominal)
Calcium Chloride, Dihydrate	USP	3.675
Magnesium Chloride, Hexahydrate	USP	1.017
Sodium Chloride	USP	107.5
Sodium Lactate Solution	USP	89.65
Water for Injection	USP/EP	QS

USP = United States Pharmacopeia; EP = European Pharmacopoeia; QS = Quantity sufficient

Table 3. Composition of the AMIA APD Generated Solution (mmol/L)

Component	1.5% Dextrose	2.5% Dextrose	4.25% Dextrose
Dextrose	75.5	126	214
Sodium	132	132	132
Calcium	1.25	1.25	1.25
Magnesium	0.25	0.25	0.25
Chloride	95	95	95
Lactate	40	40	40
pH	~ 6	~ 6	~ 6

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.

1.2 Benefits and Risks for the Study Population

Peritoneal dialysis is a well-established life-sustaining medical renal replacement therapy for individuals with ESRD. Dextrose-based dialysis solutions, such as AMIA APD Generated Solution, produced by the AMIA APD Solution Generation System, continue to be the fundamental basis of PD therapy. The AMIA APD Solution Generation System can produce AMIA APD Generated Solution in three standard dextrose concentrations (1.5%, 2.5% and 4.25%).

When prepared as part of the AMIA APD Solution Generation System, the AMIA APD Generated Solution is a pharmacologically inactive, hypertonic PD solution containing dextrose, a monosaccharide, as the primary osmotic agent. An osmotic gradient must be created between the peritoneal membrane and the dialysis solution for ultrafiltration (UF)

to occur. The hypertonic concentration of dextrose in the AMIA APD Generated Solution exerts an osmotic pressure across the peritoneal membrane resulting in transcapillary UF. Like other PD solutions, the AMIA APD Generated Solution contains electrolytes to facilitate the correction of electrolyte abnormalities. The AMIA APD Generated Solution contains a buffer, lactate, to help normalize acid-base abnormalities.

Patients treated with the AMIA APD Solution Generation System will also benefit from reduced physical strain due to less weight in solution bags, reduction in storage space required for solutions, and less packaging waste (e.g., empty solution containers and cardboard shipping containers) to manage.

During the study, patient or care partner (if participating) will be required to document treatment information in the electronic diary (eDiary), as instructed by the Investigator. Patient will be expected to comply with study treatment instructions, conduct simulated treatments and attend Study Visits.

There are inherent risks to PD therapy. Similar to PD therapies with other dextrose-based solutions, such as Dianeal, there are potential risks associated with the use of the AMIA APD Solution Generation System. AMIA APD Generated Solution is expected to have the same safety profile as Dianeal PD Solution. Important identified risks with Dianeal and other dextrose-based solutions that will be applicable to the AMIA APD Generated Solution include: aseptic peritonitis, hypovolemia, hypokalemia, hyponatremia, encapsulating peritoneal sclerosis, and medication error - administration of incorrect glucose concentration. Important potential risks include lactic acidosis, hyperglycemia, and hypocalcemia.

Overall, the benefits outweigh the potential adverse effects of using AMIA APD Generated Solution in patients with ESRD for which PD therapy is indicated. Therefore, the benefit-risk balance is positive for AMIA APD Generated Solution. Participation of PD patients in this prospective study may support future opportunity of PD patients to benefit from a potential access to this approach to PD treatment.

1.3 Study Sponsor

Baxter Healthcare Corporation
One Baxter Parkway
Deerfield, IL 60015 USA

2. STUDY OBJECTIVES

2.1 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.

2.2 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}.

3. INVESTIGATIONAL PLAN

3.1 Overall Study Design and Plan

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 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.

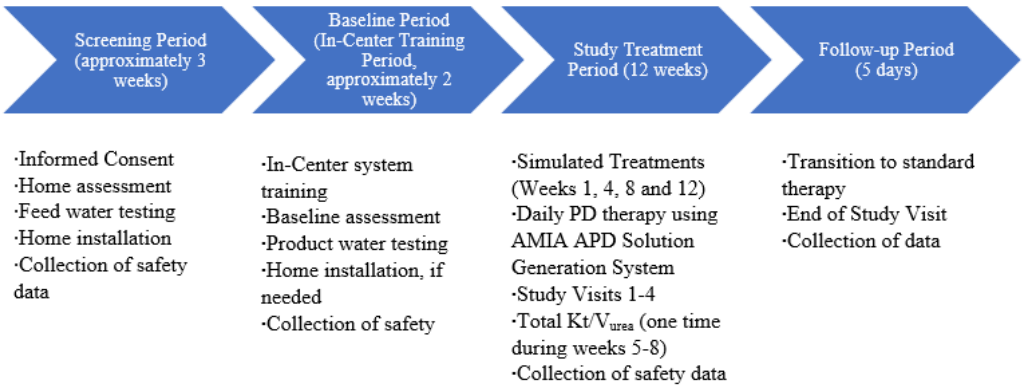
During the Screening Period, all consenting patients will have a home assessment, including feed (tap) water analysis, to confirm their home environment is suitable for this study. Eligible patients will be followed for data collection regarding dialysate solution composition and safety while using the 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 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 and Appendix 2. A trial scheme for the study is shown in Figure 2 below.

Figure 2. Overview of Study Assessments



3.2 Study Endpoints

3.2.1 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.

3.2.2 Secondary Endpoints

- Safety profile of the AMIA APD Solution Generation System used to treat patients with PD by collecting AEs, SAEs, 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 one time during weeks 5, 6, 7 or 8 of the Study Treatment Period.

3.3 Rationale for Study Design and Control Group

The rationale for using an open-label, single arm, prospective, descriptive study design without a control group is that it allows Baxter to generate clinical use system performance and safety data on the AMIA APD Solution Generation System therapy when used by patients within the current population of patients performing APD therapy using the AMIA APD Cycler. The primary endpoints in this study, involve testing of the final dialysis solution, product water (pre-sterilizing filters) and water in the holding bag (post-sterilizing filters) produced by the patients using the AMIA APD Solution Generation System during a simulated treatment. The chemical composition of the final dialysis solution will be compared to the specifications of Baxter's approved Dianeal Low Calcium (2.5 mEq/L) PD Solution.

The product water from the WD (pre-sterilizing filters) will be collected and tested against ISO Standard 13959[1] for microbiological (including endotoxin) and chemical contamination. The water in the holding bag (post-sterilizing filters) will be collected and tested to confirm that 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. As such, the goal of this clinical study is to demonstrate that the AMIA APD Solution Generation

System generates a dialysis solution equivalent to Baxter's approved Dianeal Low Calcium (2.5 mEq/L) PD Solution. (See 0).

3.4 Study Duration and Dates

Each patient will participate in the study for approximately 18 weeks. The Study Periods are as follows:

- Screening Period including home suitability assessment, feed water testing, and home installation when suitable – approximately 3 weeks.
- Baseline Period (In-center Training Period) – approximately 2 weeks.
- Study Treatment Period - 12 weeks.
- Follow-up Period – 5-10 days following the last treatment with the AMIA APD Solution Generation System.
- End of Study/ Early Termination Visit (occurring on the last day of the Follow-up Period [day 5-10]).

3.5 Study Intervention Discontinuation and Patient Discontinuation/Withdrawal

3.5.1 Removal of Patients from Therapy, Assessment, or Study

A patient is considered withdrawn/prematurely discontinued from the study if his/her participation is discontinued before completion of the required evaluations as specified in the protocol. Patient is free to withdraw from participation in the study at any time upon request. An Investigator may discontinue or withdraw a patient from the study for the following reasons:

1. If any clinical AE, laboratory abnormality, or other medical condition or situation occurs such that continued participation in the study would not be in the best interest of the patient.
2. Inadequate dialysis, based on PI judgement.
3. Protocol violation (e.g., the patient failed to meet protocol entry criteria or did not adhere to the protocol requirements).
4. Disease progression which requires discontinuation of the study intervention.
5. If the participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation.
6. Pregnancy.

7. Renal transplant.
8. Death.
9. Changes to another dialysis center.
10. Home feed water affected by “boil water advisory”.
11. Lost to follow-up (i.e., patient fails to return for the End of Study Visit).
12. Voluntary withdrawal (i.e., patient’s request).
13. Termination of the study.
14. Investigator’s discretion.
15. Patient misses more than 4 consecutive days of prescribed therapy with the AMIA APD Solution Generation System (including hospitalizations and device issues). If a patient misses 4 consecutive days of prescribed therapy with AMIA APD Solution Generation System then the total Kt/V_{urea} assessment (between Weeks 5 - 8) should be deferred by 1 week to allow a full week of prescribed treatment using the AMIA APD Solution Generation System. Note: after patients have completed the total Kt/V_{urea} assessment required during Week 5, 6, 7 or 8 of the Study Treatment Period, in order to accommodate potential vacation/travel, patients 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.
16. Patients who withdraw from study due to missed therapy due to AMIA APD water device replacement may be allowed to rescreen to re-enroll up to 1 time, as assessed by Investigator and Sponsor.
17. Patient consistently misses more than 1 prescribed treatment per week, as assessed by the Investigator, over the course of the 12-week Study Treatment Period.
18. Other reason (with reason noted on the electronic case report form [eCRF]).

The reason for patient discontinuation or withdrawal from the study will be recorded on the appropriate page of the eCRF. A patient who signs the ICF but does not receive the

study treatment may be replaced. Patient who signs the ICF and receives the study treatment, and subsequently withdraws, or is withdrawn or discontinued from the study, will not be replaced.

3.5.2 Discontinuation of the Study

If a clinically significant finding is identified (including, but not limited to changes from Baseline) during the clinical investigation, the Sponsor, Investigator, the Institutional Review Board (IRB) or regulatory authorities will determine if any change in patient management is needed. Any new clinically relevant finding will be reported as an AE. Risks to a patient that may warrant discontinuation of the study include but are not limited to:

- Device malfunction, considered by the Investigator and/or Baxter Healthcare Corporation as possibly leading to a deficiency in the patient's treatment.
- Unexpected/Unanticipated AE or ADE.

The Sponsor shall review untoward events and assess risks during the conduct of the clinical investigation. The Sponsor shall terminate the clinical investigation if an unacceptable risk is confirmed. Decision to restart the study will be made jointly by Baxter Healthcare Corporation, the regulatory authority, the site-specific IRB and the PI following evaluation of the problems encountered.

4. STUDY POPULATION SELECTION

4.1 Study Population

The study population consists of patients with ESRD treated with PD using the AMIA APD Solution Generation System. Up to 50 patients receiving a regimen of PD with the AMIA or HomeChoice APD Cycler for at least 12 weeks 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.

4.2 Inclusion Criteria

Each patient must meet ALL of the following criteria to be enrolled in this study:

1. Patient is 18 years or older.
2. Patient with ESRD receiving PD therapy, and who is already trained and regularly using the AMIA or HomeChoice APD Cycler with Dianeal PD Solution for at least 12 weeks.

3. Patient is receiving or willing and able to use Dianeal Low Calcium (2.5 mEq/L) PD prescriptive regimen at study treatment initiation per Investigator's assessment.
4. Patient demonstrates adequate PD therapy with clinical euvolemia as assessed by the Investigator with a total Kt/V_{urea} of a minimum of 1.7 within 45 days of Screening[2], or measured at Screening. If a total Kt/V_{urea} is not available within 45 days of Screening, it will be measured at Screening.
5. Investigator assesses that, with appropriate training, the patient will be able to successfully manage his/her dialysis treatments with the AMIA APD Solution Generation System.
6. Patient is available and is willing to complete training on the AMIA APD Solution Generation System.
7. Patient and home environment are deemed suitable for treatment with the AMIA APD Solution Generation System, while in the home.
8. Home electrical and water assessments meet suitability criteria for the AMIA APD Solution Generation System.
9. The patient's home has suitable wireless connection or patient is willing to allow installation of suitable wireless connection.
10. Patient and/or care partner (if participating) (See Section 5.4.1) is able to read and understand English, and provide informed consent after an explanation of the proposed study. If the patient does not read and understand English, patient may still participate if he/she has a co-residing care partner who reads and understands English, assessed as adequate by the PI.
11. Women of childbearing potential (not menopausal or surgically sterile) must not be pregnant. Serum qualitative and quantitative pregnancy test will be done within 14 days prior to initiation of study product.
    - If qualitative serum β-hCG results are positive, repeat quantitative serum pregnancy test in 48 hours.
    - If quantitative serum β-hCG levels show clinically significant rise within 48 hours, serum progesterone level should be taken. Serum progesterone > 5 ng/mL will exclude a patient from the study.

12. Sexually active males and females agree to use a reliable means of contraception during the study and for 30 days afterwards (e.g., oral contraceptive and condom, intrauterine device and condom, or diaphragm with spermicide and condom).

4.3 Exclusion Criteria

Patient who meets ANY of the following criteria will be excluded from the study:

1. Patient with a history of PD catheter dysfunction within 12 weeks prior to study enrollment, as evaluated by the Investigator.
2. Patient who had episodes of peritonitis or exit site infection within 12 weeks prior to study enrollment.
3. Patient who has signs of impending or current infection including a cloudy dialysis effluent or dialysis white cell count > 100/ μL or > 0.1 x 10^9/ L (after a dwell time of at least 2 hours), with > 50% polymorphonuclear cells, and/or positive dialysis effluent culture.
4. Patient who has a severe primary immune deficiency or other condition that may mask clinical signs of peritonitis, as evaluated by the Investigator.
5. Patient with a history of repeated non-compliance with PD, therapy (e.g., a substantial number of missed clinic visits, missed treatments or a history of mismanagement of diet or medications), as evaluated by the Investigator.
6. Patient who has acute renal failure with the chance for recovery.
7. Patient who is pre-scheduled for a living donor kidney transplant within the next 6 months.
8. Patient who is not expected to live at least 6 months while maintaining PD treatment.
9. Patient who had major abdominal surgery within 6 months prior to study enrollment.
10. Patient with current abdominal hernia, as evaluated by the Investigator.
11. Patient with advanced liver or pulmonary disease, as evaluated by the Investigator.
12. Positive serology test for Hepatitis B Virus or Hepatitis C Virus infection, or aspartate transaminase or alanine aminotransferase > 3 x upper limit of normal at Screening.[3]

13. Patient with diagnosed stage III or IV New York Heart Association (NYHA) heart failure. (Appendix 7)
14. Patient who has an active malignancy.[b]
15. History of a clinically significant illness and/or clinically significant surgery within the past 14 days preceding the Screening Visit as determined by the Investigator.
16. Patient who is enrolled in another interventional clinical study.

4.4 Home Assessment and Installation

During the Screening Period, all consented patients will have a home assessment to confirm the patient's home environment is suitable for the study. The patient's home environment must meet the AMIA APD Solution Generation System requirements to be eligible for enrollment (Refer to AMIA APD Solution Generation System Patient Guide for details of the system requirements).[8] 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 his/her required in-center training on the AMIA APD Solution Generation System.

4.5 Recruitment

Once the Food and Drug Administration (FDA) has reviewed and accepted the Investigational New Drug (IND) Application and a site's IRB has also reviewed and approved the study for its respective study center, Baxter will review the site's documentation and then notify the site once it is approved to recruit and screen study patients. Sites must wait until they receive confirmation from Baxter that they are "approved to screen" before recruiting patients.

[b] Please note, cancers determined to be cured or in remission for ≥ 1 years, curatively resected basal cell or squamous cell skin cancers, cervical cancer in situ, or resected colonic polyps are acceptable diagnosis.

5. STUDY TREATMENT(S)

5.1 Description of Treatment(s)

5.1.1 Study Product: AMIA APD Solution Generation System

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

All therapies using the AMIA APD Solution Generation System are to be prescribed and performed under the supervision of a study physician who is well informed about PD and the study system. AMIA APD Generated Solution is to be administered intraperitoneally.

The AMIA APD Solution Generation System is a drug-device combination product. The AMIA APD Solution Generation System includes the AMIA APD Cycler, the WD, Sharesource Platform, the AMIA APD Concentrates, a disposable set, and a bag tray. The bag tray is a platform for the AMIA APD Cycler to be placed on, and to hold the concentrate and holding bags.

The AMIA APD Cycler consists of:

- AMIA APD Cycler.
- Solution Generation System Link Module with Bluetooth technology for wireless communication with the WD.

The WD consists of:

- Pre-treatment filter pack.
- Reverse osmosis membrane.
- Heater.
- Conductivity and temperature sensors.
- Ports for patient connection (product water and drain line).
- Water Softener (this is an accessory to the WD).

The disposable set consists of:

- Cassette.
- Holding bag.

- Heater bag.
- Two inline sterilizing grade filters.
- Patient line.
- Dextrose line.
- Electrolyte line.
- Last fill solution line.
- Drain line.

AMIA APD Concentrates include:

- An Electrolyte Concentrate.
- A Dextrose Concentrate.

The AMIA APD Solution Generation System mixes dialysis solution generated from the AMIA APD Concentrates and sterile, non-pyrogenic water (post-sterilizing filters). The AMIA APD Cycler requests the volume of water needed to generate enough solution for the next patient fill. While delivering appropriate volumes of water and concentrates to the heater bag, the AMIA APD Cycler mixes the solution. Once the solution is mixed, the AMIA APD Cycler sends a small volume of solution from the heater bag to the WD to perform a conductivity check prior to delivering the solution to the patient.

The WD generates dialysis quality water (sterile non-pyrogenic water) from feed water using the Water Softener, a pre-treatment filter pack, and a RO membrane.

The Water Softener removes impurities and hardness. The feed water enters the Water Softener and passes through three different resins with diverged qualities to remove impurities from the feed water.

Pre-treatment is a process for removing total chlorine. The feed water enters the replaceable filter pack and flows through the mechanical filter and activated carbon for purification.

Reverse osmosis is a membrane process and the most widely used technique for purification of water for dialysis. When the feed water is in contact with the semipermeable membrane, the most vital part of the system, and a high pressure is applied, water will flow through the membrane to the permeate water side. Most of the

other constituents, such as dissolved salts, particles, bacteria and pyrogens, will remain on the feed water side of the membrane and be flushed to the drain as components of the reject water.

5.2 Enrollment, Randomization, and Assignment to Treatment Group

This is an open-label, single-arm study, and patients will not be randomized. Only patients who have signed the ICF and have met the entry criteria will be allowed to continue their participation in the study. Following signing the ICF, the patients will also undergo a Screening Visit and a home suitability assessment. (Please refer to the Point of Care APD Clinic and Home Assessment Guide for the procedures involved in the home suitability assessment.)[9]

Up to 50 patients receiving a regimen of PD with the AMIA or HomeChoice APD Cycler for at least 12 weeks 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. At the discretion of the Sponsor, continued enrollment or initiation of treatment with the AMIA APD Solution Generation System may be discontinued once the Sponsor reaches a sufficient number of patients enrolled to achieve a target goal of 30 patients completing the 12-week Study Treatment Period and the Follow-up Period. All patients will be treated with the AMIA APD Solution Generation System.

5.3 Treatment Duration and Study Visits

The treatment duration will be 12 weeks. Patients will receive PD treatment, as prescribed, in their home throughout the duration of the study. 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. If required, per patient prescription and if the patient has been treating with premixed Extraneal prior to study enrollment, premixed Extraneal may be used for the last fill.

Baseline assessments will occur during the Baseline Period (In-Center Training Period) before patients initiate treatment with the AMIA APD Solution Generation System (See Section 8.4 for details of assessments occurring at Baseline).

Simulated treatments will occur in addition to the patient's normal therapy regimen. The simulated treatment will take place before the patient receives study treatment. The initial simulated treatment will occur before the first treatment in the home with the AMIA APD Solution Generation System, Study Treatment Week 1 (Study Visit 1). Simulated treatments will continue during Study Treatment Weeks 4 (Study Visit 2), 8 (Study Visit 3) and 12 (Study Visit 4). Patients will be required to use new AMIA APD Concentrates and disposable sets for their treatment, following a simulated treatment.

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 produced by patients using the AMIA APD Solution Generation System, compared to the specifications of Baxter's approved Dianeal Low Calcium (2.5 mEq/L) PD Solution.

The product water from the WD (pre-sterilizing filters) will be collected and tested against ISO standard 13959 for microbiological (including endotoxin) and chemical contamination.[1] The water in the holding bag (post-sterilizing filters) 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.

Study Visits 2, 3 and 4 will occur during Study Treatment Weeks 4, 8 and 12, respectively. Refer to Section 8.7 for details of assessments occurring at each Study Visit.

5.4 Selection and Timing for Each Patient

Home suitability assessment and feed water testing will occur during the Screening Period. Home installation and product water testing are to occur during the Screening and/or the Baseline Period (In-center Training Period) to provide the most flexibility in patient's schedule. Patient will receive in-center training on the use of the system, which is to last approximately 2 weeks and is to begin after the Screening Period. Patient will continue to treat with standard AMIA or HomeChoice APD Cycler with Baxter's approved Dianeal Low Calcium (2.5 mEq/L) PD Solution during the Baseline Period (In-center Training Period). Baseline assessments are to occur during the Baseline Period (In-center Training Period) before the first treatment with the AMIA APD Solution Generation System. Patient will receive instructions on how to record his/her daily PD treatment and how to collect 24-hour peritoneal effluent and urine.

Following completion of the Baseline Period (In-center Training Period), the 12-week Study Treatment Period of in-home PD treatments using the AMIA APD Solution Generation System, will begin. The initial simulated treatment is to occur before the

patient administers his/her first PD treatment using AMIA APD Solution Generation System at home (Study Visit 1). Simulated treatments will continue during weeks 4 (Study Visit 2), 8 (Study Visit 3) and 12 (Study Visit 4) of the Study Treatment Period.

After the last treatment with the AMIA APD Solution Generation System, patient is to transition back to Standard AMIA or HomeChoice treatment with Baxter's approved Dianeal Low Calcium (2.5 mEq/L) PD Solution and enter a Follow-up Period of 5-10 days. Return of all investigational products and study related supplies will be scheduled during this time. The End-of-Study Visit is to occur on day 5-10 of the Follow-up Period.

The dialysis prescription for daytime exchanges should be kept consistent with the patient's pre-study prescription. The prescription of daytime dwells will not be modified unless determined to be clinically necessary by the Investigator. If a change in prescription occurs, it will be recorded in the patient's source data and accurately reflected in the eCRF.

5.4.1 Care Partner

Patient may have a care partner in the home to assist with his/her therapy. If participating, the care partner must sign the ICF, receive and complete In-center training on the study activities and other study procedures to be performed. The care partner's presence and role during the Study Treatment Period will be determined based upon his/her responsibilities identified during the consent process. If the care partner is trained and solely responsible for a treatment activity (e.g., connecting and disconnecting the patient) and/or if the patient does not read and understand English, the care partner will need to reside in the home with the patient and be present to facilitate that activity during all treatments within the Study Treatment Period using the AMIA APD Solution Generation System. Outside of these requirements, the care partner's presence will be at the discretion of the Investigator.

5.5 Method of Assigning Patients to Treatment Groups

All patients who sign the ICF will be assigned a unique patient number. This is a single-arm study where all patients will be treated with the AMIA APD Solution Generation System. The patient IDs generated at Screening shall be the patient's ID for the course of the study. If a patient is withdrawn or fails Screening and they are later screened to re-enroll, they will be assigned a new patient ID and must sign a new informed consent. The statistical analysis plan (SAP) will indicate how these data will be handled. Data from all patient IDs will be retained.

5.6 Blinding

This is an open-label study that will not utilize blinding of the investigational product. All patients will be treated with the AMIA APD Solution Generation System. The study site team will be instructed to follow their local procedure(s) to ensure the study patients receive their appropriate treatment.

5.7 Concomitant Therapy

The PI should review any additions or changes in concomitant therapy. Medications should be recorded in the source documents or equivalent. Prior medications that are still active, defined as those taken during the 30-day window prior to Screening, will be recorded on the eCRF. Concomitant medications, including dose, frequency, start and stop dates and indication for use, will be recorded on the eCRF throughout the study.

5.8 Prohibitions and Restrictions

There are no activity or diet restrictions specific to the study. Patient should discuss his/her daily diet and activities with his/her physician. Patient should only be using AMIA APD Generated Solution for treatments, unless he/she has been instructed not to use the system by his/her study physician/ nurse (Refer to Section 3.5.2).

5.9 Treatment Compliance

Compliance will be assessed regularly by the Investigator by reviewing the patient's Sharesource Platform data and eDiary entries. The patient (with assistance from the care partner if the patient does not read and understand English) will be instructed to complete the eDiary daily to document treatment activities including, but not limited to, the following:

- Patient status/ condition updates – potential AEs experienced.
- 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 and the estimated duration of sleep.
- Treatment outcome (i.e., complete treatment, incomplete treatment) and reasons for incomplete treatment.
- Confirmation if the patient altered their treatment parameters within the range(s) allowed by the Investigator.

- Investigational product usage and supply requirements.
- Document completion of study requirements.

Patients' responses will be reported electronically to the PI and designees. The site staff will use the eDiary data along with the Sharesource Platform machine log data to monitor and track the patient following local regulations. This eDiary data will serve as supplemental source documentation for the sites to support consistent data collection during the Study Treatment Period.

5.10 Packaging and Labeling

All investigational products will be manufactured, handled, stored, and provided to patients in accordance with good manufacturing practice regulations and guidance, and International Conference on Harmonization (ICH) guidelines for good clinical practice (GCP).

All investigational products or their immediate package will bear a label with the following information:

1. The name and place of business of the manufacturer, packer, or distributor (in accordance with Part 801.1 of Title 21 of the CFR).
2. The name of the investigational product.
3. The following statement "Investigational Device" or "New Drug"
4. The following statement "Limited by Federal law to investigational use."

The investigational product label and/ or other labelling will describe all relevant contraindications, hazards, AEs, interfering substances or devices, warnings, and precautions.

5.11 Accessibility and Control of Study Participant Data

In order to ship investigational product and service investigational products to/ at patients' homes, a subset of Baxter personnel and designees will need access to shipping addresses/ contact information. A study-specific procedure will be created and implemented by Baxter Clinical Services to document how Baxter Service and Baxter Clinical Services will collect, control, and secure patients' contact information and addresses. Access to the collected data will be restricted to the teams/ team members who need the information to appropriately conduct this study. Study patients will have direct

communication with Baxter Service personnel and designees to ensure timely installation/ service of the investigational product and supply delivery. Baxter personnel or designees will service devices directly in patients' homes, collect samples, and designated couriers will deliver specified investigational products (e.g., AMIA APD Concentrates) directly into patients' homes. These groups will communicate through the study sites to minimize direct patient interaction where appropriate. The Sponsor will ultimately redact all collected confidential information from study documentation when patients end their study participation and all investigational products are removed from the patients' homes.

5.12 Storage and Accountability

The study products are to be stored according to label specifications.

The sites and patients will be required to maintain accurate records of the disposition of the investigational products (study devices [serial numbers] and drugs [batch numbers]), including dates, quantities, serial/ batch/ lot numbers, expiration dates as applicable and use in the study. Importantly, the following requirements must be noted:

- The date of receipt at home and/or site.
- Identification of each investigational drug (batch number) and device (serial number).
- The date of use.
- Patient identification.
- The date of return of used and unused, expired or malfunctioning investigational drugs and devices, if applicable.

The Investigator is ultimately responsible for the accountability of all investigational products at the site. All used disposable investigational products must be disposed of per each site's SOP. Patients are to follow site-provided waste removal instructions for all disposable investigational products used in a patient's home. Baxter will be accountable for coordinating the return of supplies (all unused disposables and devices) to the depot once the study is complete.

It is prohibited by law to use investigational products outside the intent of this protocol in accordance with 21 CFR 312 and 21 CFR 812.

5.13 Investigational Product Retention

At the end of the study, all devices and unused disposable investigational products at investigational sites and patient homes will be returned to Baxter. If needed, the Sponsor may authorize an alternative disposition of unused products. However, disposition can only occur after the Sponsor has been notified and given written authorization. The Sponsor will maintain a written record of any authorized disposition of the investigational products.

6. STUDY PROCEDURES

6.1 Informed Consent

Prior to collecting any study data, each patient being considered for the study, as well as his/her care partners (if participating, see Section 5.4.1), will be provided the most recent IRB-approved ICF for review. The PI must ensure that the patient has received all relevant information, orally and in writing, relating to the type, objective and possible risks and benefits of the study. Patient must also be informed that he/she is free to withdraw from the study at any time.

All questions must be answered, and patient must be given enough time to review the ICF before signing it. The informed consent statement(s) will be reviewed, signed and dated by the patient and care partner (if participating) and the person who administered the informed consent(s). A copy of the signed ICF will be given to the patient and care partner (if participating) and the original will be placed in the patient's medical record. Confirmation of a patient's informed consent must also be documented in the patient's medical records prior to any data collection under this protocol. An IRB approved patient ICF will be provided to the PI. The ICF must not be altered without the prior agreement of the relevant IRB and Baxter.

Upon signature of the ICF, the study patient will be screened to verify eligibility (see Inclusion and Exclusion Criteria in Sections 4.2 and 4.3, respectively). Consented patients who have met the study entry criteria will be allowed to continue their participation in the study.

If modifications are needed according to local regulations, or if new information becomes available (e.g., from Baxter) that can significantly affect a patient's health and medical care, a new version of the patient information and ICF will be prepared in cooperation with the PI(s), the IRB and Baxter. Patient and care partner (if participating, see Section 5.4.1), if still participating in the study must provide written informed consent by signing the new ICF and will receive a copy of the signed form and the patient information. A

copy of the new version of the form and patient information shall be given to each previously enrolled patient for information.

In addition to the ICF (discussed above), each Patient will also be required to consent to the Sharesource Patient Notice and Declaration of Consent upon starting-up their AMIA APD Solution Generation System.

6.2 Medical History

A complete medical history will include a review of all major body systems and renal history (primary etiology of renal disease and PD history including the APD prescription per day, history of peritonitis and other disorders or diagnosis). Medication history will include all medications being taken 30 days prior to Screening, with each medication having a corresponding indication recorded in the Medication History eCRF.

6.3 Physical Examination

A physical examination will be performed at Screening and at the End-of-Study Visit. Any change will be noted and recorded on the appropriate eCRF page. These physical examinations should not differ from the patient's usual medical care. An attempt should be made to perform a final physical examination on patients who terminate the study early, particularly if they are terminating due to an AE.

6.4 Vital Signs

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 is to be measured with an appropriate cuff size after the patient has been sitting for at least 5 minutes.

6.5 Clinical Laboratory Tests

6.5.1 Laboratory Parameters

Laboratory assessments will occur at Screening and after the patient has been dialyzing for at least 4 weeks (occurring one time during Week 5, 6, 7 or 8 of the Study Treatment Period), as outlined in Appendix 2. If a patient misses 4 consecutive days of prescribed therapy with AMIA APD Solution Generation System then the total Kt/V_{urea} assessment (between Weeks 5-8) should be deferred by 1 week to allow a full week of prescribed treatment using the AMIA APD Solution Generation System.

Should a medical emergency arise, a local laboratory may be utilized; however, a copy of the laboratory certification, laboratory normal ranges and methodologies will be required. A list of laboratory tests is provided in Table 4.

Because of the potential for false-positive beta serum human chorionic gonadotropin (β- hCG) test results in females with chronic kidney disease and end stage renal disease, both qualitative and quantitative serum pregnancy tests should be taken.

Table 4. List of Laboratory Tests[a]

Blood	Peritoneal	Urine
β-hCG Hepatitis B and Hepatitis C[b] CBC with differential Chemistry Profile[c]	PD effluent: WCC with differential Cell culture 24-hour PD effluent: [d] Total Volume Creatinine Urea nitrogen	24-hour urine collection[d] Total volume Creatinine Urea nitrogen

β-hCG = beta serum human chorionic gonadotropin; CBC = complete blood count; PD = peritoneal dialysis; WCC = white cell count

[a] At Screening, chemistry, serology, and hematology tests are completed at a central laboratory. At other time points, they are completed at a local laboratory.

[b] Patients will be screened (those without a history of positive Hepatitis B or Hepatitis C serology) for both infections at the Screening Visit.
-Hepatitis B: Hepatitis B surface antigen (HBsAg) in acute and chronic infection;
-Hepatitis C: Screening assay (EIA or CIA) for anti-Hepatitis C virus (HCV).
If positive, automatic verification of positive Screening results by an additional, more specific assay (e.g., nucleic acid testing [NAT] for HCV RNA) will be done.

[c] The chemistry profile includes glucose, calcium, albumin, total protein, sodium, potassium, bicarbonate, chloride, creatinine, blood urea nitrogen, alkaline phosphatase, alanine aminotransferase, aspartate amino transferase, bilirubin, and phosphorus.

[d] 24-hour urine (if not anuric) and 24-hour peritoneal effluent collection for total Kt/V_{urea} will occur one time during Week 5, 6, 7 or 8 of the Study Treatment Period.

6.5.2 Blood collection

Each patient is to have blood collected at Screening and after he/she has been dialyzing with the AMIA APD Solution Generation System for at least 4 weeks (occurring one time during Week 5, 6, 7 or 8 of the Study Treatment Period).

6.5.3 24-Hour Urine Collection

Patients who are not anuric[c] are to collect their 24-hour urine output during the 24 hours preceding Screening (if Kt/V_{urea} assessment is not available) and after they have been dialyzing with the AMIA APD Solution Generation System for at least 4 weeks (assessment done one time during Week 5, 6, 7 or 8 of the Study Treatment Period). If a total Kt/V_{urea} is available from within 45 days of Screening, then it will be used as the Screening/Baseline value (i.e., no urine and peritoneal effluent samples will be collected for the Kt/V_{urea} calculation).

Patients will be provided with instructions on how to properly collect the sample. They will be asked to void and discard their urine prior to the 24-hour urine sample collection. All urine voided after this time until the following morning at the same time (the exact time will be recorded) is to be saved and refrigerated.

6.5.4 Peritoneal Kt/V_{urea}, Renal Kt/V_{urea} and Total Kt/V_{urea}

A total Kt/V_{urea} assessment is required at Screening and will also serve as the Baseline value. However, if a total Kt/V_{urea} is available from within 45 days of Screening, then it will be used as the Screening/Baseline value (i.e., no urine and peritoneal effluent samples will be collected at Screening for the Kt/V_{urea} calculation). Weekly Peritoneal Kt/V_{urea} will be calculated from blood and 24-hour PD effluent samples collected and renal Kt/V_{urea} will be calculated from 24-hour collection of urine samples (if applicable) and blood samples after the patient has been dialyzing with the AMIA APD Solution Generation System for at least 4 weeks (assessment done one time during Week 5, 6, 7 or 8 of the Study Treatment Period). Total Kt/V_{urea} is the sum of peritoneal Kt/V_{urea} and renal Kt/V_{urea}. Formulas to calculate Total Kt/V_{urea} are provided in Appendix 4.

6.5.5 White Cell Count and Cell Culture

Peritoneal effluent must be obtained at Screening to assess WCC with differential and cell culture. If PD effluent is collected at Screening to calculate Weekly Peritoneal Kt/V_{urea} then the same effluent may be used for assessing WCC with differential and cell culture.

[c] Anuria is defined in the adult population as a passage of <50 mL of urine per day.

6.5.6 Sample Collection, Storage, and Shipping

A study specific Laboratory Manual will be provided from each of the central laboratories to the PI and will include detailed instructions on the collection, preparation, storage, and shipping procedures for study samples and the appropriate laboratory ranges. Collection of 24-hour PD effluent samples will be made using the batch method. All laboratory samples will be collected, stored, shipped and processed by the laboratories according to each central lab's procedures.

6.5.7 Simulated Treatments

For simulated treatments, patients will set up the system as they would for a study treatment, but will not connect the patient line or use the generated solution for treatment. During the monthly simulated treatment, the prescriptions will be manipulated to ensure that the patient produce all three glucose concentrations of the Dianeal Low Calcium PD solutions at different time points for testing. Samples will be collected by the clinic nurse or designee and the disposable set will no longer be usable. The simulated treatment will be ended with no treatment performed on the patient and the patient will then remove the remaining components of the disposable set from the system.

6.5.8 Water and Dialysate Sampling Analysis

Feed water used to supply the WD will be collected by Baxter personnel and sent for analysis during the home assessment process and again at the de-installation visit. Feed water shall not exceed the chemical or biological contaminant levels as stated in the AMIA APD Solution Generation System feed water specification and Feed Water Sampling at Installation for PoC APD.[10,11] The product water from the WD (pre-sterilizing filters) shall conform to ISO 13959[1] for microbiological (including endotoxin) and chemical contamination, and the water in the holding bag (post-sterilizing filters) shall not exceed 0 CFU/mL for bacteria (no growth) and be < 0.03 EU/mL for endotoxins, consistent with Dianeal specifications for sterility. Product water shall not exceed the nitrate contamination limit of 2 mg/L. Sampling for product water testing for microbiological and chemical contamination may be done on different days within the allocated window.

The Sponsor or its designee will train the site nurses responsible for collecting the water and dialysate samples during the study. Instructions will be provided in the study training materials. Standardized recovery methods and controls will be incorporated into the testing protocol(s). Central laboratories will be used for all water and dialysate testing.

Sample results will be sent to the study sites and Sponsor for real time review and action (if appropriate). Observations and decisions regarding corrective measures (e.g., re-culture and/or disinfection of the WD) will be based on the organism growing and on whether bacterial or endotoxin levels exceed the specified guidelines. An internal Sponsor Committee will also review study wide results on a bi-weekly basis, at a minimum, to search for trends and to action appropriately.

Analysis of water will be performed on samples obtained as follows.

6.5.8.1 Chemical Contaminants

Feed Water

Samples of feed water will be collected by Baxter personnel or designees and tested for chemical contaminants from each study site during site feasibility, prior to AMIA APD Solution Generation System installations at the site, according to limits stated in the AMIA APD Solution Generation System feed water specification.[10] Samples will also be collected from feed water at patients' homes during home assessments while consented patients are in the Screening Period and at de-installation.

AMIA APD Solution Generation System Product Water

Samples of product water from the WD (pre-sterilizing filters) will be collected from each device by Baxter personnel or designees at installation at the patients' homes, and tested for chemical contaminants. Product water will be tested according to ISO 13959 which includes testing for nitrate contamination, and the <2 mg/L limit of nitrates will be confirmed. These samples from the AMIA APD Solution Generation System will be collected at the water line port. Patients cannot treat on the AMIA APD Solution Generation System in the home until the post-installation product water results are received and reviewed by the study site and Sponsor per the AMIA APD Solution Generation System Patient Guide. The sample will be collected in conjunction with Study Visit 1 and during Study Treatment Weeks 4, 8 and 12.

6.5.8.2 Microbiological Cultures and Endotoxin – Product Water and Water from Holding Bag

Samples of AMIA APD Solution Generation System water (product water) will be collected from the system by Baxter personnel or designees at installation at the patients' homes and at timepoints designated in the protocol (Study Treatment Weeks 1 [Study Visit 1], 4 [Study Visit 2], 8 [Study Visit 3] and 12 [Study Visit 4]). Product water from

the WD (pre-sterilizing filters) will be collected and tested for microbiological (including endotoxin) contamination per USP <61> and USP <85>.

Patients will generate water in the holding bag using the AMIA APD Solution Generation System during a simulated treatment in their home at timepoints designated in the protocol (Study Treatment Weeks 1 [Study Visit 1], 4 [Study Visit 2], 8 [Study Visit 3] and 12 [Study Visit 4]). Water in the holding bag will be collected and tested for microbiological contamination and endotoxin levels per USP <71> and USP <85>. Water in the holding bag (post-sterilizing filters) shall not exceed 0 CFU/mL for bacteria (no growth) and shall be < 0.03 EU/mL for endotoxins, consistent with Dianeal specifications for sterility.

All samples will be collected and packaged using aseptic techniques and sent to the central lab for analysis. Patients cannot treat on the AMIA APD Solution Generation System in the home until the post-installation product water results are received and reviewed by the study site and Sponsor per the AMIA APD Solution Generation System Patient Guide.

6.5.8.3 Dialysate Composition Testing

Patients will generate dialysis solution using the AMIA APD Solution Generation System during a simulated treatment in their home at timepoints designated in the protocol (Study Treatment Weeks 1 [Study Visit 1], 4 [Study Visit 2], 8 [Study Visit 3] and 12 [Study Visit 4]). The heater bag containing the dialysis solution generated by the simulated treatment will be collected by Baxter personnel or designee and shipped to a central laboratory for analysis of chemical composition.

6.5.8.4 Additional Sampling Procedures

The dual in-line sterilizing grade filters will be collected during sample collection procedures at each simulated treatment. The filters will be returned to Baxter R&D for possible investigation and used as an investigatory tool in the event of a positive finding from endotoxin or microbiological contamination in the holding bag.

6.5.8.5 Process for Responding to Out-of-Specification Results

6.5.8.5.1 Decision Trees

Clinical study decision trees for feed water[12], product water (pre-sterilizing filters)[13], water from the holding bag (post-sterilizing filters)[14], and dialysis solution samples[15] have been developed and will be included in training materials and provided to study sites. These decision trees provide guidance to the clinical site and the Baxter team on

appropriate actions to be taken in situations where out of specification (OOS) results are received from the samples. Decision trees are structured to ensure patient safety. If test results are out of specification, the decision trees provide a mechanism for removing affected patient(s) from therapy if any safety concerns arise as determined by a clinician and/or the study team.

Upon confirmation of an OOS value for endotoxin or bacteria, a root cause investigation will be initiated, specific components of the AMIA APD Solution Generation System may be changed, and the replaced components may be sent to Baxter for functional assessment.

Additional actions may include:

- Resample.
- All device logs evaluated for anomalies.
- Aseptic procedure checklists recorded during sample collection and processing reviewed for anomalies.
- The Contract Laboratory will conduct an independent investigation of their procedures and processes for any OOS endotoxin or micro-organism result.

Consideration for additional actions such as retrieval and analysis of hardware and/or disposables, on site investigation for additional machine and environmental cultures.

6.5.8.6 Chlorine and Conductivity Testing

Chlorine testing of the water will be performed prior to each dialysis treatment. Water for chlorine testing is collected from the Water Sample Outlet and tested as specified in the AMIA APD Solution Generation System Patient Guide.[16] Stricter local regulations for testing will be utilized if required.

Conductivity testing of the dialysate is performed by the AMIA APD Solution Generation System after each heater bag replenish prior to delivering fluid from that replenish to the patient without input from the user. If the conductivity test shows the dialysate is not within specification, the AMIA Solution Generation System will empty the heater bag and perform a new replenish. The system will warn the user if a conductivity issue is noted and user action is required.

Chlorine and conductivity testing are conducted as part of normal operation of the system to ensure device reliability. These results are captured in device logs and are not included

in study endpoints or any planned statistical analysis. Independent chlorine testing is included in the monthly product water testing and compliance of the conductivity of the solution is monitored through the heater bag dialysis solution testing.

6.6 Power Outage

If the WD is off due to a power outage for more than 3 consecutive days during the use of the AMIA APD Solution Generation System, Baxter Technical Services must restore the WD to operating conditions before the patient can use the AMIA APD Solution Generation System for treatment. When not in use, the WD must be plugged in and turned on. The water supply to the WD and the patient's home must remain on and connected to the drain.

6.7 Boil Water Advisory Procedure

If a municipal water supplier issues a "boil water advisory" for the feed water at a patient's location, the patient should discontinue use of the study generated PD solution and commence APD therapy using approved Dianeal Low Calcium (2.5 mEq/L) PD Solution bags or prior solution as assessed by the Investigator. Patients will be discontinued from the study following a boil water advisory affecting the feed water in their home.

6.8 Removal of Patients from the Study

Patients are considered withdrawn / prematurely discontinued from the study if their participation is stopped before completion of the required evaluations as described in this protocol (see Section 3.5.1). If a patient is prematurely removed from the study, all data prior to discontinuation should be recorded in the eCRF and all available data will be included in all analyses.

The Investigator may terminate a patient's study participation at any time during the study if he/ she judges it to be in the patient's best interest. If a patient is withdrawn from the study, the Clinical Study Manager or Monitors should be informed at the earliest possible opportunity, regardless of the reason(s) for withdrawal. In addition, a patient may discontinue his or her participation at any time during the study without having to justify the decision. If a patient's participation is discontinued, the reason(s) must be recorded in the source documents and on the eCRF. If a patient discontinues for any reason, every effort should be made to perform all of the procedures that are scheduled for the End-of-Study/ Early Termination Visit. In addition, SAEs, related or not and ADEs, will be followed post-study according to the safety plan.

6.9 Other Study Procedures

- Comprehension and retention testing (materials provided by Baxter) for patient and/or care partner (if participating) will occur at the end of the Baseline Period (In-center Training Period). If the patient does not read and understand English, the care partner will assist the patient with comprehension and retention testing. The Investigator or a designee must also 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 his/her PD prescription is stable, then the patient can begin treatment in the home.
- Home installation will occur during the Screening or the Baseline Period (In-center Training Period).
- The patient will conduct chlorine testing prior to every treatment.
- Additional testing and procedures will be performed per local standard of care.

6.10 Appropriateness of Measurements

Measurements for the primary and secondary endpoints are well accepted. Other chemistry and hematology measurements to evaluate safety are standard for the indication or patient population being studied.

7. DATA COLLECTION FOR SAFETY ASSESSMENTS AND REPORTING

7.1 Definition of Adverse Events and Device Deficiencies

Table 5. Adverse Event Term Definition

Term	Definition
Adverse Event (AE)	Any untoward medical occurrence in a patient or clinical investigation subject administered a product which does not necessarily have a causal relationship with this treatment.
Adverse Drug Reaction (ADR) or Adverse Reaction (AR) /Adverse Device Effect (ADE)	Adverse event related to the use of study product.
Suspected Adverse Reaction (SAR)	Any AE for which there is a reasonable possibility that the product caused the AE. For the purposes of IND safety reporting “reasonable possibility” means there is evidence to suggest a causal relationship between the product and the AE.
Unexpected Adverse Drug Reaction (UADR)	An adverse reaction in which the nature or severity is not consistent with the applicable product information (e.g., Investigator’s Brochure for unapproved

Table 5. Adverse Event Term Definition

Term	Definition
	investigational product or package insert/summary of product characteristics for an approved product). (ICH E6 (R2)) The Adverse reaction may not be listed at the specificity or severity that has been observed; or if an investigator brochure is not required or available, is not consistent with the risk information described in the general investigational plan or elsewhere in the current application, as amended. (21 CFR 312.32)
Adverse Event of Special Interest (AESI)	An adverse event of special interest (serious or non-serious) is one of scientific and medical concern specific to the Sponsor's product or program, for which ongoing monitoring and rapid communication by the investigator to the Sponsor can be appropriate. Such an event might warrant further investigation in order to characterize and understand it. Depending on the nature of the event, rapid communication by the study Sponsor to other parties (e.g., regulators) might also be warranted. (FDA Guidance for Industry E2F).
Serious Adverse Event (SAE) or Serious Adverse Drug Reaction (SADR) or Serious Adverse Device Effect (SADE)	Any untoward medical occurrence that at any dose: • Results in death (including fetal death). • Is life-threatening. • Requires inpatient hospitalization or results in prolongation of existing hospitalization. • Results in persistent or significant disability/incapacity. • Is a congenital anomaly/birth defect (ICH E6 (R2)). • Is a medically important event or reaction that may not be immediately life-threatening or result in death or hospitalization, but may jeopardize the patient or requires intervention to prevent one of the other outcomes listed above.
Device Deficiency (DD)	Inadequacy of an (investigational) medical device related to its identity, quality, durability, reliability, safety or performance, such as malfunction, misuse or use error and inadequate labeling. This includes DDs that might have led to an SAE if: • Suitable action had not been taken or • Intervention had not been made or • If circumstances had been less fortunate.
Suspected Unexpected Serious Adverse Reaction (SUSAR) /Unanticipated Adverse Device Effect (UADE)	An AE that in the view of the Investigator or Sponsor, meets the definition of serious, unexpected, and is suspected to have a causal relationship to study product. Suspected Unexpected Serious Adverse Reactions are also reportable for active comparator products, placebo, or the clinical study protocol itself (i.e., events due to study procedures). Any SADE on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of patients.

Table 6. Definition of Terms

Term	Definition
Awareness Date or Baxter Awareness Date (BAD)	The date on which any Baxter employee or their agent becomes aware of an adverse event (AE). This date is considered Day 0 on the regulatory reporting time clock.
Date of Onset	The date when the signs and symptoms of the AE begin.
Investigational Product (IP)	Experimental product under study or development. This term is more specific than investigational medicinal product, which includes comparators and placebos. For this protocol, the term "investigational drug" is synonymous with "investigational product". For this protocol, the term "investigational product" is synonymous with AMIA APD Solution Generation System.
Diagnosis vs Complications	A patient experiences not only a diagnosis, but also additionally a complication of the diagnosis (i.e., myocardial infarction with congestive heart failure); both the diagnosis and the medical complication should be collected and recorded as separate AEs.

7.2 Safety Reporting

All AEs, PCs and 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 ICF through the End-of-Study/ Early Termination Visit.

Any medical condition, that is present at the time that the participant is screened, will be considered medical history and not reported as an AE (see Appendix 6). Any medical event that is commonly associated with a study participant's PD therapy will be considered medical history and not reported as an AE (see Appendix 6). However, if the study patient's condition/event worsens (change in severity or frequency) at any time during the study, it will be recorded as an AE.

If a definitive diagnosis has been medically established by the physician caring for the patient or by the Investigator, this diagnosis should then be recorded as the AE on the eCRF and the signs and symptoms removed. If a definitive diagnosis has not been medically established, the signs and symptoms should then be recorded as the AEs.

Adverse events that change in severity will be reported at each incidence, but documented only once in the eCRF with the highest degree of severity.

An elective procedure/ surgery that occurs during the course of a study, but is being performed for a documented pre-existing condition and was pre-planned prior to study entry will not qualify as an AE. If, however, the pre-existing condition unexpectedly deteriorates during the study requiring the procedure/ surgery to be performed earlier than planned, the condition for which the procedure/ surgery is being performed will qualify as an AE.

Laboratory and vital sign abnormalities qualify as AEs if medical intervention is required to treat or address the abnormality, if the patient must be discontinued from the study due to the abnormality, or if the Investigator determines the value is clinically significant.

An AE can result from the use of the study product in accordance with the protocol, as well as from an accidental or intentional misuse of the study product or any other treatment error such as unintentional administration or use of another product during the course of the study.

If an AE or DD occurs, a full description of the event should be recorded including the date and time of onset, as well as outcome, seriousness, severity, event description, actions taken, and causal relationship of the AE. Investigators should review and reference the causality (see Table 7) and severity definitions (see Table 8) when determining relationship of the AE to the study product or typical PD therapy. The Investigators may also discuss the event(s) with the Baxter Medical Monitor or designee.

All AEs should be actively solicited and documented in the eCRFs, no matter how common they are for a particular patient and regardless of the causality assigned by the Investigator. Additionally, any AE voluntarily reported by the patient should be recorded and verified by the Investigator or a designee with the relevant source documents and eCRF. Each SAE will be documented on a separate SAE report form.

The outcome/ resolution of all AEs will be determined by the Investigator and documented in the AE eCRF. Investigators will be instructed to follow all treatment emergent AEs as follows: Adverse device effects (related AEs) and all SAEs (related or not) will be followed until resolution or stable, including following the patient after the end of the study if necessary.

For the outcome conclusions that can be used on the eCRF by the Investigator, refer to Table 9.

If a patient in this study also receives a Baxter medicinal/ drug product which is part of a patient's normal treatment (not an investigational product or comparator), any AE which is considered causally related to the medicinal/ drug product by either the Investigator or the medical monitor shall be forwarded by the Investigator or a designee within 24 hours of becoming aware of the AE to Baxter Global Patient Safety ([redacted] for assessment as per Baxter's process for case processing of spontaneous reports.

Causality is a determination of whether there is a reasonable possibility that the study product is etiologically related to/ associated with an AE. Causality assessment includes, for example, assessment of temporal relationships, dechallenge/rechallenge information, association (or lack thereof) with underlying disease, presence (or absence) of a more likely cause, and physiologic plausibility.

Table 7. Causality Assessments

Classification	Causality Criteria	Causal Association
Probably Associated	• An AE that follows a strong temporal relationship to the administration/use of the study product and/or recurs on rechallenge. • Results in a positive sensitivity test. • Unlikely to be attributed to disease, procedure or other drugs/devices. • An AE improves with withdrawal of the product.	Yes
Possibly Associated	• An AE follows a reasonable temporal relationship to the administration/use of the study product. • An alternative etiology is equal or less likely.	Yes
Unlikely Associated	• An AE has little or no temporal relationship to the administration/use of the study product. • An alternative etiology is more likely.	No
Not Associated	• An AE that is due to underlying or concurrent illness, complications, concurrent treatments or effect of another concurrent device/drug and is not associated to the device/drug, that is, does not follow a reasonable temporal relationship to administration/use of the study product. • Has a much more likely alternative etiology.	No

Table 8. Severity Assessments

Criterion	Definition
Mild	Is a transient discomfort and does not interfere in a significant manner with the patient's normal functioning level. The AE resolves spontaneously or may require minimal therapeutic intervention.
Moderate	Produces limited impairment of function and can require therapeutic intervention, but produces no sequelae.
Severe	Results in a marked impairment of function and can lead to temporary inability to resume usual life pattern. The AE produces sequelae requiring (prolonged) therapeutic intervention.

Table 9. Outcome Conclusion Criteria

Fatal
Not recovered/Not resolved/Permanent: This outcome is reached for AEs which are ongoing when the patient's end of study is due to death related to another AE
Recovering/Resolving: This outcome is reached for AEs which are ongoing at the patient's end of study
Recovered/Resolved with Sequelae: If there are some residual effects caused by the event
Recovered/Resolved
Unknown

7.2.1 Adverse Event of Special Interest

Adverse events of special interest are listed below. The adverse events within this section represent those that are thought to have an association with the use of the AMIA APD Solution Generation System or in conjunction with performing the peritoneal dialysis procedure.

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

- Hyperglycemia
- Hypocalcemia

The definitions of AESIs are provided in Appendix 5.

7.2.2 Medical Events Commonly Associated with Peritoneal Dialysis

The medical events and their definitions, that have been commonly reported as possibly related to PD therapy in general, are provided in Appendix 6. This list has been provided to ensure these events are captured in the patients' medical history, when appropriate. If an event is part of the patient's medical history, it will not be considered as an AE for the study unless the frequency increases or the severity worsens.

7.2.3 Adverse Events Reporting

The PI shall:

- Record every AE with a full description.
- Follow-up or new information about an SAE should be provided by the Investigator or a designee using the SAE form within 24 hours of becoming aware of the new information.
- All non-serious AEs that are upgraded to an SAE should be forwarded to Baxter or designee within 24 hours.
- Supply Baxter or designee, upon Baxter's or designee's request, with any additional information related to the safety reporting of a particular event.
- Report any SAE if becoming aware after study completion has occurred in a patient during their participation in the study, the SAE must be reported on the SAE Form within 24 hours of awareness.
- If an event is part of the patient's medical history, it will not be considered as an AE for the study unless the frequency increases or the severity worsens.

7.3 Product Complaints

A product complaint is any written, electronic, or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, usability, safety, effectiveness, or performance of a product after it is released for distribution or related to a service that affects the performance of such product. A complaint may involve the possible failure of the product itself, its packaging, or its labeling (i.e., product label,

package insert, or any instructions for use). The complaint need not be confirmed by the manufacturer to be considered a complaint. Any product complaints identified by the investigator will be reported to Baxter using a paper Product Complaint/Non-Medical Complaint Form.

7.4 Medical Monitor

The medical monitor will regularly review data collected from eCRFs, and laboratory data for potential safety concerns. This review plan will be documented in a study Safety Management Plan.

Periodic review of reported AEs will be completed by Baxter or designee. At the site level the Investigator must assess risk and clinical significance of events to each individual study patient, including removing the patient from the study if necessary.

7.5 Safety Reporting to Authorities and Institutional Review Board

It is the responsibility of the Investigator to report any SAEs to IRB according to local regulatory requirements

Baxter or designee will assess each SAE reported by the Investigator to determine if the event qualifies as an Expedited Report according to local regulations. Expedited reports will be submitted to the appropriate Authority by Baxter or designee. Per regulations, Investigators will receive a letter from Baxter or designee describing the expedited SAE. The Investigator should file this letter within their Investigator Site File. Additionally, the Expedited Report letter may need to be submitted by the Investigator to their IRB, as appropriate per local regulations.

7.6 Pregnancy Reporting

If a female study patient or a study patient's partner becomes pregnant during the study patient's participation in the trial, the pregnancy must be reported to the Sponsor by providing a completed Pregnancy Report Form and Pregnancy Follow-up Form to Baxter Global Patient Safety ([redacted].

8. STUDY ACTIVITIES

8.1 Schedule of Evaluations and Procedures

All clinical study evaluations will be performed according to Appendix 1 and the instructions listed below. If a patient discontinues from the study prematurely, every attempt will be made to perform all of the procedures and evaluations that are scheduled for the final visit (i.e., End-of-Study/ Early Termination Visit).

8.2 Screening Period (approximately 3 weeks)

Consented patients who have met the study entry criteria will be allowed to continue their participation in the study and will undergo the Screening assessments and home evaluation.

The following procedures should be completed during the Screening Period:

1. Patients and care partners (if participating) (See Section 5.4.1) sign the ICF on the first day of the Screening Period.
2. Record patient medical history (PD history including the APD prescription per day, history of peritonitis and other disorders or diagnosis). Medical history will also include demographics (age, gender, race, height, weight, body mass index calculated as weight (kg)/height2 (m), and ethnicity) and prior medications (all medications being taken at the time of Screening and 30 days prior to Screening, with each medication having a corresponding indication recorded on the Medical History eCRF form).
3. Physical examination including weight and height.
4. The date of the last total Kt/V_{urea} calculation should be noted (if a total Kt/V_{urea} is available from within 45 days of Screening, then it will be used as the Screening/Baseline value [i.e., no urine and peritoneal effluent samples will be collected for total Kt/V_{urea}]).
5. Clinical laboratory evaluations as outlined in Appendix 2.
6. Vital signs including BP, pulse rate and temperature.
7. Home suitability assessment.
8. Feed water analysis for the home.
9. Home Installation, when suitable.
10. The PI or designee 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 BP, pulse rate, weight, fluid status and dialysis prescription.
11. Collection of concomitant medication information.
12. Collection of AEs/ SAEs.
13. The Investigator must assess the stability of the patient (Clinical and prescription stability).

14. If the patient is a screen failure, the reason for their failure must be recorded. Any patient who withdraws from the study before installation of the device is considered a screen failure. In addition, any patient who withdraws from the study after the installation but before confirming that all the inclusion criteria and none of the exclusion criteria are met, and withdraws due to a non-device related issue, is also considered a screen failure.

8.3 Training for PD Home Solution Generation System

Study personnel performing training with the AMIA APD Solution Generation System for this clinical study will be comprised of physicians, PD nurses and other clinicians. Study staff will be trained on the use of the AMIA APD Solution Generation System by the Sponsor's representative prior to patient enrollment. Training dates and training material, provided by Baxter, will be documented and filed in the Investigator Site File.

8.4 Baseline Period (In-center Training Period)

The Baseline Period (In-center Training Period) will begin immediately following the Screening Period, will include in-center training, and will last for approximately 2 weeks. The following information will be collected and procedures or evaluations will be performed:

1. Baseline Assessments
   - Assessment by an Investigator or a designee. At a minimum, this assessment will include evaluation of BP, pulse rate, weight, fluid status and dialysis prescription.
   - Collection of concomitant medication information.
   - Collection of AEs/ SAEs.
2. Installation of the AMIA APD Solution Generation System in the patient's home (if not yet performed).
3. AMIA APD Solution Generation System specific device training and general therapy training for the patient and care partner (if participating) (See Section 5.4.1).
4. Machine information including 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.

5. Baseline Period (In-center Training Period) will conclude with:
    - Successful comprehension and retention testing, provided by Baxter, for the patient and/or care partner (if participating). If the patient does not read and understand English, the care partner will assist the patient with comprehension and retention testing.
    - 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.
    - Written confirmation of independent care by patient and care partner (if participating).

8.5 Each Treatment Day

Patients will set up and complete a treatment using the AMIA APD Solution Generation System according to their prescribed dialysis regimen.

The following assessments will be completed each day throughout the Study Treatment Period.

1. Collection of concomitant medication information.
2. Weight pre- and post-dialysis.
3. Vital signs, before and after each treatment, including seated BP, pulse rate and temperature.
4. Collection of AEs/ SAEs.
5. Collection of ADEs and SADEs once the patient is connected to the AMIA APD Solution Generation System.
6. Collection of AMIA APD Solution Generation System-related PCs/ DDs, 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 Treatment Period.
7. Collection of machine information.
8. Collection of machine observations.
9. Chlorine testing performed by patients before each treatment.

10. Collection of diary source data (eDiary).

8.6 Simulated Treatment Visit 1 (Before 1st Treatment in the Home, Study Visit 1)

The following assessments will be completed during Simulated Treatment Visit 1, Study Visit 1.

1. A simulated treatment will be set up by the patient. The dialysis solution generated during simulated treatment will be collected by the clinic nurse or designee from the system in the heater bag and used to evaluate the chemical composition of the final dialysis solution produced by patients using the AMIA APD Solution Generation System compared to the specifications of Baxter's approved Dianeal Low Calcium (2.5 mEq/L) PD Solution.
2. Product water from the WD (pre-sterilizing filters) will also be collected by a clinic nurse or designee and will be tested to confirm that it conforms to ISO standard 13959[1] for microbiological (including endotoxin) and chemical contamination. Collecting a product water sample involves connecting a container and/ or tubing to the WD and obtaining a sample volume of water from the WD for microbiological and chemical testing. This procedure cannot be performed using the disposable set required for actual treatment setup, since the sterilizing-grade filters will remove additional microbial contamination. The purpose of this procedure is to demonstrate that the WD is functioning appropriately in the patient's home, and since sampling is not dependent upon the user performing the procedure, patients do not have to perform it for the study (decreasing the impact on patients/ nurses).
3. 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. Simulated treatment is prepared by the patient, in the same manner in which actual treatment is prepared (using the disposable set, filters, etc.) Due to the risk of contamination, the holding bag cannot be compromised, particularly since the water needs to be sterile. The purpose of this procedure is to demonstrate that the system functions as intended when used by patients under real-world conditions.
4. Assessment by an Investigator or a designee.

5. Collection of AEs/ SAEs.
6. Collection of AMIA APD Solution Generation System-related PCs and DDs.

8.7 Study Visits 2, 3 and 4 (Study Treatment Weeks 4, 8 and 12)

Study Visits 2, 3 and 4 will occur during Study Treatment Weeks 4, 8 and 12 of the Study Treatment Period, respectively. In addition to the assessments included in Section 8.5, the following assessments will be completed during Study Visits 2, 3 and 4.

1. A simulated treatment will be set up by the patient. The dialysis solution generated during simulated treatment will be collected by the clinic nurse or designee from the system in the heater bag and used to evaluate the chemical composition of the final dialysis solution produced by patients using the AMIA APD Solution Generation System compared to the specifications of Baxter's approved Dianeal Low Calcium (2.5 mEq/L) PD Solution.
2. Product water from the WD (pre-sterilizing filters) will be also be collected by a clinic nurse or designee and tested to confirm that it conforms to ISO standard 13959[1] 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. For more information regarding the differences in simulated treatment testing for product water from the WD and for product water from the holding bag, refer to points 2 and 3 in Section 8.6.
3. Assessment by an Investigator or a designee.

After the final Study Treatment Visit, patients are to transition back to treatments with AMIA 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.

8.8 Total Kt/V_{urea} Visit

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 Week 5, 6, 7 or 8 of the Study Treatment Period). The patient will collect 24-hr

PD effluent and 24-hr urine prior to the visit by a clinic nurse or designee who will then collect these samples and a blood sample for analysis.

Refer to Sections 6.5.2, 6.5.3, and 6.5.4 for instructions for this assessment.

Clinical laboratory evaluations as outlined in Appendix 2.

8.9 Follow-up Period

After the last study treatment with AMIA APD Solution Generation System, patients will transition back to Standard AMIA treatment with Baxter's approved Dianeal Low Calcium (2.5 mEq/L) PD Solution and enter a Follow-up Period of 5-10 days. During this time, an assessment by an Investigator or a designee will occur. At a minimum, this assessment will include evaluation of BP, pulse rate, weight, fluid status and dialysis prescription. Adverse events, SAEs, ADEs and SADEs will be collected throughout the Follow-up Period and through the End-of-Study/ Early Termination Visit.

8.10 End of Study Visit or Early Termination Procedures

The End of Study assessments will be performed 5-10 days after the last treatment with the AMIA APD Solution Generation System (i.e., at week 13 for patients who completed the 12 weeks of treatment). If a patient discontinues from the study prematurely, every attempt should be made to perform all procedures and evaluations that are scheduled for the End of Study/ Early Termination Visit. A patient who withdraws from the study after installation and after meeting all the inclusion criteria and none of the exclusion criteria is considered an Early Termination patient. In addition, a patient who withdraws from the study after installation but before confirming that all the inclusion criteria and none of exclusion criteria are met and withdraws due to a device-related issue (e.g., leaking, alarms, etc.), is also considered an Early Termination patient.

The following data will be collected:

1. Collection of AEs/ SAEs.
2. Adverse events of special interest (Refer to Section 7.2.1 for the full list of AESIs).
3. Physical examination including weight.
4. Assessment by an Investigator or a designee.
5. Vital Signs.

9. DATA MANAGEMENT, QUALITY CONTROL AND QUALITY ASSURANCE

The Sponsor is responsible for implementing and maintaining quality assurance and quality control systems with written SOPs to ensure that studies are conducted and that the data are generated, documented and reported in compliance with the protocol and applicable regulatory requirements. Quality control will be applied to all stages of data handling to ensure reliability and correct processing. The Sponsor is responsible for securing agreement from all involved parties to ensure direct access to all study related centers, source documents and reports for the purpose of monitoring and auditing. Agreements made with the Investigator/ institution will be in writing.

9.1 Auditing

The Sponsor and/ or Sponsor's representatives may conduct audits to evaluate study conduct and compliance with the protocol, standard operating procedures, other written instructions/agreements, ICH GCP, the IRB and applicable regulatory guidelines/ requirements. The Investigator will permit auditors to visit the study site, as described in the Clinical Study Agreement. Auditing processes specific to the study will be described in the auditing plan.

9.2 Non-compliance with the Protocol

The Investigator will not deviate from this protocol without prior documented approval from the Sponsor and the IRB, except in cases of medical emergency. The Investigator may deviate from the protocol without prior approval only when the change is necessary to eliminate an apparent immediate hazard to the patient. In that event, the Investigator will notify the Sponsor immediately by phone, notify the IRB and confirm notification to the Sponsor in writing as soon as possible, but within five (5) working days after the change is implemented.

A protocol deviation is any noncompliance with the clinical study protocol, study-related procedures, or ICH GCP requirements. The noncompliance may be either on the part of the participant, the Investigator, or the study site staff. As a result of deviations, corrective actions are to be developed by the site and implemented promptly.

Protocol violations/ deviations will be documented in source documents and in the Investigator's research study files as applicable. Protocol violations/ deviation waivers will not be issued. The clinical team will review deviations at a study level on a regular basis, as detailed in the Clinical Operations/Monitoring Plans.

10. PLANNED STATISTICAL METHODS

10.1 General Considerations

Further details of the planned statistical methods will be provided in the study SAP. The SAP will be finalized prior to database lock. Any changes to the statistical methods described in the protocol will be documented in the SAP.

Unless otherwise noted, all analyses will be performed using SAS/GRAPH® 9.4 software, SAS/STAT® 14.1 software and Base SAS® 9.4. Copyright© 2002-2012, SAS Institute Inc. SAS and all other SAS Institute Inc. product or service names are registered trademarks or trademarks of SAS Institute Inc., Cary, NC, USA. All Rights Reserved.[4]

Summary statistics will be presented with mean, standard deviation, median, minimum and maximum for continuous variables and frequency count and percentage based on study population will be used to summarize categorical variables. Prior to analysis, data will be reviewed for consistency. Missing data values will not be imputed and all non-missing values will be used. To determine patients who had been re-enrolled in the study, there will be a question on the eCRF indicating whether the patient has been enrolled in the trial previously and the number the patient was previously enrolled under. The details on how data from these patients will be analyzed will be described in the SAP.

10.2 Determination of 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.

10.3 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).

10.4 Demographics and Baseline Characteristics

Demographic data include age, gender, race, height, weight, body mass index calculated as weight (kg)/height^2 (m), and ethnicity.

Other baseline/ demographic data will include total Kt/V_{urea} which will be summarized by sample size, mean, standard deviation, median, minimum and maximum.

Demographic and baseline characteristics will be summarized on the Safety Set.

10.5 Primary Analysis

Primary Efficacy:

AMIA APD Generated Solution specifications will be collected from the dialysis solution generated by the patient using the AMIA APD Solution Generation System, during simulated treatments. The chemical composition measurements taken from the dialysis solution will be summarized by count and percentage for those that meet specification vs those that do not. There will be three summaries of these data based on initial test values, based on retest values, and based on the most recent test values. Summary statistics including sample size, mean, standard deviation, median, minimum and maximum will also be presented for the chemical composition measures of the solution. These summaries will be provided on the Safety Set.

Primary Safety:

Product water from the WD (pre-sterilizing filters) and water in the holding bag (post-sterilizing filters), generated during simulated treatments will be sampled. The measurements of product water will be summarized by count and percentage for those that meet ISO Standard 13959[1] for microbiological (including endotoxin) and chemical contamination vs those that do not, and the measurements from the holding bag will be summarized by count and percentage for those that achieve 0 CFU/mL (no growth) and <0.03 EU/mL vs those that do not. There will be three summaries of these data: based on initial test values, based on retest values, and based on the most recent test values. All measures will also be summarized by sample size, mean, standard deviation, median, minimum and maximum. These summaries will be provided on the Safety Set.

10.6 Secondary Analysis

Adverse events will be mapped to a Primary System Organ Class and Preferred Terms according to MedDRA Version 21.0 or higher and summarized using frequencies and percentages. In addition, AEs will be summarized by seriousness, severity, and relationship to study product or typical PD therapy. Device alarms and their relation to AEs or SAEs will be summarized using frequency counts and percentages. Vital Signs (BP, pulse, temperature) will be summarized by mean, standard deviation, median, minimum and maximum for all recorded timepoints and also for change from pre-to post treatment for all post Baseline timepoints. These summaries will be conducted on the Safety Set.

Total Kt/V_{urea} will be summarized using descriptive statistics at all collection timepoints and change from Baseline will also be summarized. This summary will be performed on the Safety Set.

10.7 Sensitivity Analysis

A sensitivity analysis of the primary safety endpoint of product water from the water device may be performed using the results of the home installation test in lieu of missing Simulated Treatment Visit 1 data.

10.8 Interim Analysis

An interim analysis is not planned for this study.

11. ADMINISTRATIVE CONSIDERATIONS

11.1 Investigators and Study Administrative Structure

The investigator will comply with the protocol (which has been approved/given favorable opinion by the IRB/EC/NCA), ICH GCP, the ethical principles of the Declaration of Helsinki, and applicable regulatory requirements as described in the Clinical Study Agreement. The investigator is ultimately responsible for the conduct of all aspects of the study at the study site and verifies by signature the integrity of all data transmitted to the sponsor. Whenever the term 'investigator' is noted in the protocol text, it may refer to either the PI at the site, or an appropriately qualified, trained and delegated individual of the investigational site. Sub-investigators or other authorized study personnel are eligible to sign for the investigator, except where the investigator's signature is specifically required.

11.2 Institutional Review Board Approval

The responsible IRB must be constituted according to the applicable local and national requirements of each participating location. The Sponsor or its designee will require documentation noting all names and titles of members who compose the respective IRB. If any member of the IRB has direct participation in this study, written notification regarding his or her abstinence from voting must also be obtained.

The Sponsor or its designee will supply relevant documents for PIs to submit to their respective IRB for review and approval of the protocol. The Investigator will not enroll patients into the study until the Investigator has received written approval for, or written favorable opinion on, the protocol, the informed consent document(s), and any patient-facing materials from their IRB. The IRB approval must refer to the study by exact protocol title, number, and version date; identify version of other documents (e.g., patient

or care partner ICFs) reviewed; and state the approval date. The Investigator will make all required progress reports to their IRB in writing in a timely manner and will obtain all required approvals in writing (at least annually in all cases) to continue to participate in the study.

The Investigator will promptly report to their IRB any unanticipated problems associated with the study product involving risks to patients or others, whether encountered at their site or provided as a safety report by Baxter.

The Investigator will promptly notify their IRB of any planned protocol amendment and will not implement any protocol amendment until the IRB has provided written approval of, or written favorable opinion on, the amendment.

11.3 Food and Drug Administration

The Sponsor is responsible for submissions to the FDA.

Food and Drug Administration will notify the Sponsor in writing of the date it receives the IND.

The Baxter Project Manager may send investigational products to study sites and/or include patients in the study:

- 30 days after FDA receives the IND, unless FDA notifies the Sponsor that the investigations described in the IND are subject to a clinical hold; or
- On notification by FDA that the clinical investigations in the IND may begin.

11.4 Ethical Conduct of the Study

This study will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, the ethical and quality standards of GCP (ICH E6) and all applicable regulatory requirements and laws.

The PI will provide all necessary information on the protocol and the study product to all physicians, nurses, and other personnel who participate in this study under the PI's supervision and will discuss this material with them as needed, to ensure that they are fully informed regarding the conduct of the study and the potential effects of the study product.

11.5 Patient Information and Consent

The Investigator will not enroll patients into the study until the Investigator has received written approval for, or written favorable opinion on, the protocol and the informed consent documents(s), from their IRB. Prior to obtaining patient consent, the PI or designee will explain to the patient the nature and purpose of the study and the data to be provided to Baxter. The applicable ICF or authorization will be obtained from the patient before any study data is collected. After the ICF is signed, it will be placed in the patient's medical record and a signed copy will be given to the patient. The time and date of informed consent should be documented in the patient's medical records.

11.6 Patient Confidentiality

The Investigator must ensure that the patient's confidentiality is maintained. Patient medical information obtained for the purposes of this study is confidential and disclosure to third parties, other than Health Authority representatives, Baxter representatives, or the site's IRB, is prohibited. Patients should not be identified by name or medical record number on any documents or materials (samples, slides) sent to Baxter or its representatives or during verbal communications. Patients should be identified only by the protocol-assigned unique patient identification number.

To help maintain patient confidentiality, each patient will be assigned a unique patient identification number. The site Investigator, designated site staff, and a limited number of Baxter personnel or designees will have access to patient identifying information. (Please refer to Section 5.11 for a full list of people with access to patient identifying information). All data will be compiled to construct a dataset comprising unique patient identification numbers in lieu of specific patient identifying data; all study datasets will be password-protected. While there is always a risk of loss of privacy when participating in a research program, reasonable efforts will be made to ensure the confidentiality of patient data. Under no circumstances shall any patient identifying information be shared with or disclosed to a third party for promotional uses. As stated above, the patient must be informed that his/ her personal study-related data will be used by Baxter and its representatives in accordance with country law or local IRB data protection directives.

11.6.1 Health Insurance Portability and Accountability Act Authorization Procedures

Preparation of the Health Insurance Portability and Accountability Act (HIPAA) authorization form is the responsibility of the PI and must include all elements required by the Department of Health and Human Service's Privacy Rule. Prior to the beginning of the study, the PI must have the IRB or the appropriate institution privacy board's

written approval/favorable opinion of the HIPAA authorization form. The PI must provide the patient or legally-authorized representative with a copy of the HIPAA authorization form in the language in which the patient is most proficient. The language must be nontechnical and easily understood. The PI should allow the time necessary for the patient or the patient's legally-authorized representative to inquire about the details of the authorization. The HIPAA authorization must be signed and personally dated by the patient or by the patient's legally-authorized representative and by the person who obtained the authorization. The patient or legally-authorized representative should receive a copy of the HIPAA authorization form prior to the patient's participation in the study.

11.7 Study Monitoring

The Sponsor team or designee will monitor the study data on site and remotely as part of safety management and clinical monitoring. Monitoring will occur at regularly scheduled intervals at the study site to allow for verification by sampling of source documents and comparing these with information recorded on the eCRFs. In addition, eCRFs may also be monitored remotely during the course of study participation. Full details on eCRF monitoring will be specified in the Clinical Operations/ Monitoring Plan.

The PI or a designated member of the PI's staff must be available during monitoring visits to review data and resolve any queries and to allow direct access to the patient's records (e.g., medical records, office charts, hospital charts and study-related charts) for source data verification. The eCRFs must be completed prior to each visit and be made available to the monitor so that their accuracy and completeness may be checked.

11.8 Case Report Forms and Study Records

All clinical data associated with this study will be collected and reported electronically via a web address and secure password. The database will be housed on a physically and logically secure computer server maintained in accordance with written security policies. The electronic data capture (EDC) system meets approved established standards for the security of health information and is validated per 21 CFR Part 11. The system also meets the ICH guideline E6R1 regarding electronic study data handling and is available for audit upon request. Patient confidentiality will be strictly maintained. Patient identifying information will not be included in the database, but must be maintained in a secure fashion at the Investigator site.

11.9 Access to Source Documentation

Representatives of the Sponsor, or its designee, must be allowed to visit the study site regularly to assess the data quality and the integrity of the study. These representatives

will review study records on site and directly compare these with the source documents, discuss the conduct of the study with the PI and verify that the facilities remain acceptable. In addition, the study may be evaluated by the Sponsor's internal auditors or a designee and/or by government inspectors, who must be allowed access to eCRFs, source documents and other study files.

11.10 Data Generation and Analysis

Web-based electronic data entry must be completed for all patients enrolled in the study. The electronic data entry will be the responsibility of the Investigator. The database will be maintained by Baxter or designee.

Electronic Investigator signatures will be used to attest to the accuracy of data entered into the EDC system. The Study Monitor, in collaboration with the Investigators, must ensure that data entered into the EDC system are correct. Computerized data checks will be used to supplement manual review to check for data omissions, inconsistencies and out of range values. An electronic audit trail system will be used to track all changes in the database. Data editing for correction or clarification purposes must be done before the eCRFs have been transmitted for data processing and analysis.

Data management will be carried out by Baxter Global Clinical Development, Data Sciences and Reporting department or assigned designee.

Baxter or their assigned designee is responsible for the creation of the study eCRF and the associated electronic study database.

11.11 Retention of Data

The Institution/PI will retain all study records in compliance with applicable regulatory requirements and in any event a minimum of fifteen (15) years following the termination or completion of the study, whichever is later or as outlined in your clinical study agreement. The Institution/PI must contact the Sponsor before destroying any records associated with the study. The Sponsor or its designee will notify the Institution/PI in writing when the study records can be destroyed. If the PI withdrawals from the study (e.g., relocation, retirement), the study records shall be transferred to a mutually agreed upon designee (e.g., another PI), Baxter will be notified in writing of any such transfer. When required, Institution/PI shall make the Study records available for inspection by Sponsor and/or regulatory authority.

11.12 Financial Disclosure

The financial aspects of the study will be documented in an agreement between the Sponsor and the Investigator.

11.13 Publication and Disclosure Policy

Any information shared by the Sponsor regarding this study, including this protocol, is considered proprietary information and should be kept confidential.

The data generated by this clinical study are the property of the Sponsor. This data may be used by the Sponsor, now and in the future, for presentation or publication at the Sponsor's discretion or for submission to regulatory agencies. In addition, the Sponsor reserves the right of prior review and approval of data from this study relative to the potential release of proprietary information to any publication or for any presentation.

12. REFERENCE LIST

1. International Organization for Standardization. 13959:2014. Water for haemodialysis and related therapies. Geneva, Switzerland: International Organization for Standardization.; 2014.
2. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis*. 2002;39(2 Suppl 1):S1-266.
3. National guideline for the management of the viral hepatitides A, B, and C. Clinical Effectiveness Group (Association of Genitourinary Medicine and the Medical Society for the Study of Venereal Diseases). *Sex Transm Infect*. 1999;75 Suppl 1:S57-64.
4. SAS Institute Inc. SAS OnlineDoc Version 9.2 - Product Documentation. Vol. 2012. Cary, NC USA; 2008.
5. Popovich R, Moncrief J, Decherd J, Bomar J, Pyle W. The definition of a novel portable/wearable equilibrium dialysis technique. Vol. 5: Trans Am Soc Artif Intern Organs; 1976:64.
6. Fresenius Medical Care. Fresenius Medical Care 2015 Annual Report: ESRD patients in 2015: A global perspective; FMC 2015.
7. Wang AY, Brimble KS, Brunier G, et al. ISPD Cardiovascular and Metabolic Guidelines in Adult Peritoneal Dialysis Patients Part I - Assessment and Management of Various Cardiovascular Risk Factors. *Perit Dial Int*. 2015;35(4):379-387.
8. Baxter Healthcare Corporation. Amia APD Solution Generation System Patient Guide. Document #BXU522141. Effective Date 15 March 2018.
9. Baxter Healthcare Corporation. Point of Care APD Clinic and Home Assessment Guide. Document #BXU517247. Current Issue.
10. Baxter Healthcare Corporation. PoC APD Feed Water Specification. Document #BXU009418. Current Issue.
11. Baxter Healthcare Corporation. Feed Water Sampling at Installation for Point of Care (PoC) Automated Peritoneal Dialysis. Document #BXU526052. Current Issue.
12. Baxter Healthcare Corporation. BXU011787 Amia APD SGS Feed Water Sample Testing Results Decision Tree, Document No BXU011787-SSP-CO-019, Current Issue.
13. Baxter Healthcare Corporation. BXU011787 Amia APD SGS Water Device Product Water Sample Results Decision Tree, Document No BXU011787-SSP-CO-020, Current Issue.
14. Baxter Healthcare Corporation. BXU011787 Amia APD SGS Water Device Holding Bag Water Sample Results Decision Tree, Document No BXU011787-SSP-CO-021, Current Issue.
15. Baxter Healthcare Corporation. BXU011787 Amia APD SGS Sample Results Dialysis Solution Decision Tree, Document No BXU011787-SSP-CO-022, Current Issue.
16. Baxter Healthcare Corporation. Amia APD Solution Generation System Patient Guide. Document #BXU522141. Current Issue.
17. The Criteria Committee of the New York Heart Association. *Nomenclature and Criteria for Diagnosis of Diseases of the Heart and Great Vessels*. Boston: Mass: Little, Brown & Co; 1994:253-256.

Appendix 1 Schedule of Events

Observation	Screening (approx. 3 weeks)	Baseline Period (In-center Training, approx. 2 weeks)[a]	Simulated Treatment Visit 1[b]	Each Treatment Day[c]	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]

Observation	Screening (approx. 3 weeks)	Baseline Period (In-center Training, approx. 2 weeks)[a]	Simulated Treatment Visit 1[b]	Each Treatment Day[c]	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]
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				
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				

Observation	Screening (approx. 3 weeks)	Baseline Period (In-center Training, approx. 2 weeks)[a]	Simulated Treatment Visit 1[b]	Each Treatment Day[c]	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]
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			
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				

Observation	Screening (approx. 3 weeks)	Baseline Period (In-center Training, approx. 2 weeks)[a]	Simulated Treatment Visit 1[b]	Each Treatment Day[c]	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]
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 for details of care partner's responsibilities.

Observation	Screening (approx. 3 weeks)	Baseline Period (In-center Training, approx. 2 weeks)[a]	Simulated Treatment Visit 1[b]	Each Treatment Day[c]	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]

[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.

Observation	Screening (approx. 3 weeks)	Baseline Period (In-center Training, approx. 2 weeks)[a]	Simulated Treatment Visit 1[b]	Each Treatment Day[c]	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]

[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.

Appendix 2 Schedule of Clinical Laboratory Evaluations

Observation	Screening	Total Kt/V_{urea} Visit
Blood Draw:		
Serum β-hCG[a]	X	
Hepatitis B[b]	X	
Hepatitis C[b]	X	
CBC with differential	X	
Chemistry Profile[c]	X	
Creatinine[d]		X
Urea Nitrogen[d]		X
PD Effluent:		
White Cell Count with differential	X	
Cell Culture	X	
Total Kt/V_{urea}[d]	X	X
24-hour PD Effluent Collection:		
Total Volume	X	X
Creatinine	X	X
Urea Nitrogen	X	X
24-hour Urine Collection:		
Total Volume	X	X
Creatinine	X	X

Observation	Screening	Total Kt/V_{urea} Visit
Urea Nitrogen	X	X

[a] Women of childbearing potential (not menopausal or surgically sterile) must have a negative serum pregnancy test result within 14 days prior to initiation of study product.
-If qualitative serum β-hCG results are positive, repeat quantitative serum pregnancy test within 48 hours.
-If quantitative serum β-hCG levels show clinically significant rise, within 48 hours, serum progesterone level should be taken. Serum progesterone > 5 ng/mL will exclude a patient from the study.

[b] Patients will be screened (those without a history of positive Hepatitis B or Hepatitis C serology) for both infections at the Screening Visit.
-Hepatitis B: Hepatitis B surface antigen (HBsAg) in acute and chronic infection;
-Hepatitis C: Screening assay (EIA or CIA) for anti-Hepatitis C virus (HCV). Automatic verification of positive Screening results by an additional, more specific assay (e.g., nucleic acid testing [NAT] for HCV RNA).

[c] The chemistry profile includes glucose, calcium, albumin, total protein, sodium, potassium, bicarbonate, chloride, creatinine, blood urea nitrogen, alkaline phosphatase, alanine aminotransferase, aspartate amino transferase, bilirubin, and phosphorous.

[d] To assess total Kt/V_{urea}, 24-hour urine (if not anuric), 24-hour PD effluent, and serum will be collected at Screening. However, if a total Kt/V_{urea} is available from within 45 days of Screening, then it will be used as the Screening/Baseline value (i.e., no urine and peritoneal effluent samples will be collected to calculate Kt/V_{urea}). Total Kt/V_{urea} assessment will also occur after the patient has been dialyzing for at least 4 weeks with the AMIA APD Solution Generation System, (assessment done one time during Week 5, 6, 7 or 8 of the Study Treatment Period.)

Appendix 3 Dianeal Low Calcium (2.5 mEq/L) Peritoneal Dialysis Solution Formulations

Component	Dianeal Low Calcium (2.5 mEq/L) PD Solution Formulation (g/L)		
	1.5% Dextrose	2.5% Dextrose	4.25% Dextrose
Dextrose, hydrous	15.0	25.0	42.5
Sodium chloride	5.38	5.38	5.38
Magnesium chloride hexahydrate	0.051	0.051	0.051
Calcium chloride dihydrate	0.183	0.183	0.183
Sodium lactate	4.48	4.48	4.48
Water for injection	qs to 1000 mL	qs to 1000 mL	qs to 1000 mL
Component	**Dianeal Low Calcium (2.5 mEq/L) Ionic Composition (mmol/L)**		
Sodium	132		
Calcium	1.25		
Magnesium	0.25		
Chloride	95		
Lactate	40		
pH at 25°C	4.0 - 6.5		

Appendix 4 Formulas

The following equations [d] [e] [f] will be used to calculate total Kt/V_{urea}:

$$Peritoneal\ \frac{Kt}{V_{urea}} = \frac{\left(\frac{Dialysate\ urea\ \left(\frac{mmol}{L}\right)}{Serum\ urea\ \left(\frac{mmol}{L}\right)} \times Total\ Drainage\ volume\ of\ 24-h\ (L) \times 7d\right)}{V_{urea}}$$

$$Renal\ \frac{Kt}{V_{urea}} = \frac{\left(\frac{24hr\ urine\ urea\ \left(\frac{mmol}{L}\right)}{Serum\ urea\ \left(\frac{mmol}{L}\right)}\ x\ 24-h\ urine\ (L)\ x\ 7d\right)}{V_{urea}}$$

Total Kt/V_{urea}= Peritoneal Kt/V_{urea} + Renal Kt/V_{urea}

[d] Szeto C., Wong T., Leung C., et al. Importance of dialysis adequacy in mortality and morbidity of Chinese CAPD patients, 2000. *Kidney International*. 2000; 58: 400-407

[e] Nolph K.D., Moore H.L., Twardowski Z.J., et al. Cross-sectional Assessment of Weekly Urea and Creatinine Clearances in Patients on Continuous Ambulatory Peritoneal Dialysis, 1992. *Asaio Journal.* 1992.

[f] Keshaviah P.R., Nolph K.D., Prowant B. et al. Defining Adequacy of CAPD with Urea Kinetics. *Baxter Health Corp., University of Missouri, Columbia, and Dialysis Clinic, Inc, Columbia.*

Appendix 5 Definitions of Adverse Events of Special Interest Terms

Aseptic Peritonitis	Inflammation of the peritoneum lining the abdominal cavity as the result of infectious, autoimmune, or chemical processes.
Encapsulating Peritoneal Sclerosis	A devastating but rare complication of long-term PD. The disease is associated with extensive thickening and fibrosis of the peritoneum resulting in the formation of a fibrous cocoon encapsulating the bowel leading to intestinal obstruction.
Hypovolemia	An abnormal decrease in fluid volume or rapid shift from one compartment of body fluid to another.
Hyperglycemia	An abnormally high level of glucose in the blood.
Hypocalcemia	A low blood calcium level, occurs when the concentration of free calcium ions in the blood falls below 2.1 mmol/L.
Hypokalemia	A low blood potassium level, occurs when the concentration of potassium in the blood falls below 3.5 mmol/L.
Hyponatremia	A low blood sodium level, occurs when the concentration of sodium in the blood falls below 135 mmol/L.
Lactic Acidosis	Acidosis due to the buildup of lactic acid in the body.
Medication Error	Errors in prescribing, dispensing, or administering medication with the result that the patient fails to receive the correct drug or the indicated proper drug dosage.

Appendix 6 Medical Events Commonly Associated with Peritoneal Dialysis

The following are medical events that have been commonly reported as possibly related to PD therapy in general:

Abdominal pain:	A generic term for focal or general discomfort localized to the abdominal region.
Back pain:	Pain felt in or along the spine or musculature of the posterior thorax.
Bleeding:	The escape of blood from an injured vessel.
Chest pain:	A general term for any dull, aching pain in the thorax, usually referring to that of acute onset, which is often regarded as being myocardial in origin unless proven otherwise.
Drain pain (outflow pain):	A sense of abdominal discomfort; pain or crampy discomfort arising during the drain phase of a peritoneal dialysis exchange that may occur during a manual or automated peritoneal dialysis exchanges.
Edema (Peripheral and/or facial; Scrotal):	An abnormal accumulation of fluid in intercellular spaces of the body.
Fever:	A fever is any body temperature elevation over 100 °F (37.8 °C).
Headache:	Pain in the head which can arise from many disorders or may be a disorder in and of itself.
Hematuria:	Presence of blood or red blood cells in the urine.
Hernia:	Protrusion of a part or structure through the tissues normally containing it.
Hydrothorax:	Accumulation of serous fluid in one or both pleural cavities.
Hypertension:	Persistently high arterial blood pressure.
Hypoglycemia:	An abnormally low level of glucose in the blood.
Hypotension:	Persistently low arterial blood pressure.
Itching:	An uncomfortable sensation of irritation of the skin or mucous membranes that causes scratching or rubbing of the affected parts.
Chills:	A sensation of cold, with convulsive shaking of the body.
Muscle cramps:	A sudden and involuntary contraction of one or more muscles
Nausea:	An unpleasant sensation vaguely referred to the epigastrium and abdomen, with a tendency to vomit.
PD catheter leak:	An appearance of any moisture around the PD catheter identified as dialysate.
Vomiting:	The ejection of matter from the stomach in retrograde fashion through the esophagus and mouth.

This list does not include medical events that are part of the exclusion criteria and/or should always be considered an AE regardless of medical history, severity or frequency.

Appendix 7 New York Heart Association Functional Classification

NYHA Functional Classification[17]	
NYHA Class	**Patients with Cardiac Disease (Description of HF Related Symptoms)**
Class I (Mild)	Patients with cardiac disease but without resulting in limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation (rapid or pounding heart beat), dyspnea (shortness of breath), or anginal pain (chest pain).
Class II (Mild)	Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain
Class III (Moderate)	Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain.
Class IV (Severe)	Patients with cardiac disease resulting in the inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

Appendix 8 Sponsor Signatures

Study Title:	Performance evaluation of the AMIA Automated Peritoneal Dialysis (APD) Solution Generation System in patients using the AMIA APD Cycler
Study Number:	BXU011787
Original Protocol:	2018 JUN 15
Amendment 1:	2018 OCT 16
Amendment 2:	2018 DEC 13
Amendment 3:	2019 FEB 28
Amendment 4:	2019 APR 30
Amendment 5:	2019 JUL 09
Amendment 6:	2019 NOV 01

This clinical study protocol was subject to critical review and has been approved by the Sponsor. The following personnel contributed to writing and/or approving this protocol:

Signed:_____ Date:_____

[redacted], MD, MS, FAAP
[redacted], Renal Care
Baxter Healthcare Corporation

Signed:_____ Date:_____

[redacted], Global Regulatory Affairs
Baxter Healthcare Corporation

Signed:_____ Date:_____

[redacted], Statistics, Global Clinical Development
Baxter Healthcare Corporation

Signed:_____ Date:_____

[redacted], MD
[redacted], Device Vigilance, Global Patient Safety
Baxter Healthcare Corporation

Signed:_____ Date:_____

[redacted], MD
[redacted], Global Therapy Lead, Clinical/Medical Affairs
Baxter Healthcare Corporation

Signed:_____ Date:_____

[redacted], MD
[redacted], Global Patient Safety,
Baxter Healthcare Corporation

Signed:_____ Date:_____

[redacted]
, Global Clinical Development
Baxter Healthcare Corporation

Appendix 9 Investigator's Signature

Study Title:	Performance evaluation of the AMIA Automated Peritoneal Dialysis (APD) Solution Generation System in patients using the AMIA APD Cycler.
Study Number:	BXU011787
Original Protocol:	2018 JUN 15
Amendment 1:	2018 OCT 16
Amendment 2:	2018 DEC 13
Amendment 3:	2019 FEB 28
Amendment 4:	2019 APR 30
Amendment 5:	2019 JUL 09
Amendment 6:	2019 NOV 01

I have read the protocol described above. I agree to comply with all applicable regulations and to conduct the study as described in the protocol.

Signed:_____ Date:_____

<enter name and credentials>
<enter title>
<enter affiliation>
<enter address>
<enter phone number>