Guideline on water treatment facilities and water quality for haemodialysis and related therapies

Clinical Practice Guideline by the

UK Renal Association and Association of Renal Technologists

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Contents

Introduction

Water of the appropriate quality used in the preparation of dialysis fluid is an essential requirement of haemodialysis and related therapies. International standards have been developed to promote the installation of fit for purpose water treatment facilities for haemodialysis and to safeguard the routine production of treated water suitable for use for haemodialysis and haemodiafiltration.

Quality requirements for the water and concentrates used to prepare dialysis fluid, and for dialysis fluid, are provided in BS ISO 13959;2009: *Water for haemodialysis and related therapies*, BS ISO 13958;2009: *Concentrates for haemodialysis and related therapies*, and BS ISO 11663;2009, *Quality of dialysis fluid for haemodialysis and related therapies*. In addition the requirements for water treatment equipment are provided in BS ISO 26722; 2009: *Water treatment equipment for haemodialysis and related therapies*. BS ISO 23500; 2011: *Guidance for the preparation and quality management of fluids for haemodialysis* addresses the quality management of the water treatment system and distribution loop within the renal unit [(1-4)]. The rationale for the development of these standards is to protect haemodialysis patients from adverse effects arising from known chemical and microbiological contaminants found in water and improperly prepared dialysis fluid. However, in spite of the availability of standards, there have been instances of failure to achieve the requirements of the standards, particularly in new build renal units, where the responsibility for the water treatment plant operation and monitoring lies outside NHS remit and is provided either by external contractors under a private finance initiative (PFI) or by an equivalent scheme which transfers responsibility for the delivery of infrastructure and services such as maintenance to third parties on behalf of the public sector.

This guideline incorporates and updates the section on water quality and water treatment for haemodialysis in the haemodialysis module of the 5th edition of the Renal Association Clinical Practice Guidelines [(5)]. The main purpose of this interpretive guidance is to assist all involved in water treatment provision in minimization of adverse events which may cause risks to patients. It is NOT intended to replace the national standards and the interpretive guidance MUST be read in conjunction with the standards [(1-4)].

References

1. BS ISO 13959; 2009: *Water for haemodialysis and related therapies*,
2. BS ISO 11663; 2009: *Quality of dialysis fluid for haemodialysis and related therapies*
3. BS ISO 13958; 2009: *Concentrates for haemodialysis and related therapies*,
4. BS ISO 26722; 2009: *Water treatment equipment for haemodialysis and related therapies*
5. Nephron Clin Pract 2011;118 (Suppl.1):c1-c390 http://content.karger.com/ProdukteDB/produkte.asp?Aktion=Ausgabe&Ausgabe=255298&ProduktNr=228539

Summary of clinical practice guideline on water treatment facilities and water quality for haemodialysis and related therapies

1. Clinical governance of water treatment facilities for haemodialysis

Guideline 1.1 – Designation of water treatment facilities as patient equipment

We recommend that water treatment facilities for haemodialysis are designated as patient equipment. (not graded)

Guideline 1.2 – Responsibility for clinical governance

We recommend that the senior clinician in charge of the renal unit (or designated deputy) has responsibility for the overall clinical governance of the water treatment facility. (1C)

Guideline 1.3 – Responsibility for planning of new or replacement water treatment facilities

We recommend that the clinician (or designated deputy) with responsibility for clinical governance is involved throughout the planning, designation and installation of a new or replacement water treatment facility for haemodialysis. (1C)

2. Planning and commissioning of water treatment facilities for haemodialysis

2.1 Source and supply of raw water for haemodialysis

Guideline 2.1 - Specification of the water supply for haemodialysis

We recommend that new build renal units should have a direct feed (drinking or potable) water supply separate from that of the hospital water supply. If existing water treatment systems use a hospital water supply there should be awareness of the potential risks that may arise from the introduction of chemicals into the hospital water supply by either the renal unit or hospital engineering staff. In this setting addition of chemicals into the hospital water supply should not be undertaken without prior consultation with renal services. (1C)

2.2 Setting the design specification for the water treatment infrastructure

Guideline 2.2 - Design specification of the water treatment system for haemodialysis

We recommend that the complete water treatment, storage and distribution system should meet the requirements of all of the following standards: (1B)

BS ISO 13959; 2009: *Water for haemodialysis and related therapies*,

BS ISO 11663; 2009: *Quality of dialysis fluid for haemodialysis and related therapies*,

BS ISO 26722; 2009: *Water treatment equipment for haemodialysis and related therapies*.

Guideline 2.3 – Haemodialysis facilities

We recommend that the specification of new or refurbished HD facilities should adhere to the guidelines that are described in the NHS Estates Health Building Notes 07-01 Satellite Dialysis Unit and 07-02 Main Renal Unit. (1C)

3. Installation and validation of water treatment facilities for haemodialysis

Guideline 3.1 – Installation and validation of a water treatment facility for haemodialysis

We recommend that each stage of the installation, performance validation and initial, performance and operational qualification should be agreed and documented in advance and signed off by the

manufacturer and the senior clinician in charge of the renal unit (or designated deputy) who has responsibility for the overall clinical governance of the water treatment facility. (1C)

4. Operation and maintenance of water treatment facilities for haemodialysis

Guideline 4.1 – Routine maintenance and monitoring

We recommend that maintenance and monitoring plans for the water treatment plant are established using the knowledge acquired during the complete validation process for the water treatment system which are in accordance with BS ISO 23500; 2011: *Guidance for the preparation and quality management of fluids for haemodialysis*. Policies and procedures are mandatory and should be set up and implemented at the earliest opportunity. (1B)

Guideline 4.2 – Training of operators of the water treatment facility

We recommend that operators should be trained in the use of the equipment by the manufacturer or be trained using materials provided by the manufacturer. The training should be specific to the functions performed. Periodic audits of the operators' compliance with procedures should be undertaken and documented and there should be an ongoing training programme to maintain the operator's knowledge and skills. (1C)

Guideline 4.3 - Monitoring of feed, treated and dialysis water for haemodialysis
We recommend that a routine testing procedure for water for dialysis should form part of the renal unit policy. Each unit should have standard operating procedures in place for sampling, monitoring and recording of feed and product water quality. The minimum frequency of monitoring of water for dialysis is as follows:

Contaminant	Frequency of testing
Chlorine	At least weekly
Total viable counts	At least monthly
Endotoxin	At least monthly
Chemical contaminants other than chlorine	At least every 3 months

If the interval between sample testing exceeds those indicated in the Table, documentation should be in place to demonstrate that the sampling schedule used has been based on trend analysis. The operating procedures should include details of the procedures to be followed if the prescribed limits are exceeded. (1C)

5. Monitoring the quality of treated water and dialysis fluid for haemodialysis

Guideline 5.1: Chemical contaminants in water used for the preparation of dialysis fluid

We recommend that the concentrations of chemical contaminants in water used to prepare dialysis fluid should not exceed the limits stated either in BS ISO 13959; 2009: *Water for haemodialysis and related therapies* or in the European Pharmacopoeia (6th edition, 2007). A programme of improvement should begin immediately if routine monitoring demonstrates that concentrations of chemical contaminants exceed the maximum allowable limits. (1B)

Guideline 5.2 - Microbiological contaminants in water used for the preparation of dialysis fluid in <u>new</u> water treatment plants

We recommend that all new water treatment plants should be capable of producing water suitable for the production of "ultrapure dialysis fluid". The microbiological contaminant levels of ultrapure dialysis fluid should be < 0.1 CFU/mL and < 0.03EU/mL. (1B)

Guideline 5.3 - HD: Microbiological contaminants in water used for the preparation of dialysis fluid in <u>existing</u> water treatment plants

The microbiological quality of the dialysis fluid in existing water treatment plants should not exceed the limits specified in BS ISO 11663; 2009*: Quality of dialysis fluid for haemodialysis and related therapies* (100 CFU/ml for bacteria and 0.25 EU/ml for endotoxin). If routine monitoring demonstrates microbiological contaminant levels in excess of 50 CFU/ml and 0.125 EU/ml for bacteria and endotoxin (50% of the maximum permitted levels) a programme of corrective measures should be commenced immediately. (1B)

Guideline 5.4 - Bicarbonate dialysis fluid for haemodialysis

We recommend that the dialysis fluid should contain bicarbonate as the buffer. (1B)

Guideline 5.5 – Preparation of dialysis fluid

We recommend that dialysis fluid is produced by the mixing of treated water, acid and bicarbonate concentrates. The microbiological contaminant levels for acid and bicarbonate concentrates are defined in BS ISO 13958; 2009: *Concentrates for haemodialysis and related therapies.* (1B)

Guideline 5.6 – Quality of dialysis fluid

We recommend concordance with BS ISO 11663; 2009: *Quality of dialysis fluid for haemodialysis and related therapies*: standard dialysis fluid is considered as the minimum quality, ultrapure dialysis fluid is recommended for routine haemodialysis and ultrapure dialysis fluid is mandatory for creating on-line prepared substitution fluid used in convective therapies such as on-line haemodiafiltration. (1B)

6. Water treatment facilities for home haemodialysis

Guideline 6.1 – Maintenance of the water and power supply

We recommend that the utility companies providing both water and power to the patient's home be notified that home dialysis is being performed at that location and that restoring service after any interruption should be a priority. (not graded)

Guideline 6.2 – Training of the patient and/or helper

We recommend that the patient and/or helper in the home should be formally trained in the proper operation and maintenance of the water treatment equipment by the renal technicians. The patient and /or helper should keep a log of the maintenance and monitoring procedures. (not graded)

Guideline 6.3 – Frequency of monitoring water used for home haemodialysis

We recommend that the chemical and microbial quality of the water used for the preparation of dialysis fluid for home haemodialysis should be monitored at least annually and every 3 months respectively. (1C)

Rationale of clinical practice guideline on water treatment facilities and water quality for haemodialysis and related therapies

1. Clinical governance of water treatment facilities for haemodialysis

Guideline 1.1 – Designation of water treatment facilities as patient equipment

We recommend that water treatment facilities for haemodialysis are designated as patient equipment (not graded)

Guideline 1.2 – Responsibility for clinical governance

We recommend that the senior clinician in charge of the renal unit (or designated deputy) has responsibility for the overall clinical governance of the water treatment facility. (1C)

Guideline 1.3 – Responsibility for planning of new or replacement water treatment facilities

We recommend that the clinician (or designated deputy) with responsibility for clinical governance is involved throughout the planning, designation and installation of a new or replacement water treatment facility for haemodialysis. (1C)

Rationale for 1.1-1.3

The water treatment facilities for haemodialysis and related therapies should be designated as patient equipment to ensure compliance with the regulations and standards which have been established for such equipment. This safeguard also highlights that the ultimate responsibility for clinical governance for the water treatment facility should rest with the clinical director of the renal unit or a designated deputy, since they are responsible for the clinical care of the patient [(1)]. The clinician in charge of the renal unit may appoint a deputy, who may be a senior renal technology specialist or a consultant renal specialist, to take responsibility for the water treatment facility and act as line manager for clinical governance.

In the modern era the users and operators of water treatment facilities for haemodialysis may not be the same, for example in a renal unit funded through PFI or an equivalent scheme the operator of the water treatment plant may be an external contractor whilst the user is the renal service. In other instances, the operation of the water plant may be by members of the renal services technical staff or NHS estates staff. Irrespective of the structure, there should be clear lines of communication established between the nephrologist who is ultimately responsible for the clinical care of the patient and internal or external staff responsible for the operation and maintenance of the equipment. Good record keeping in association with robust lines of communication should be established between senior renal unit personnel and those who undertake the monitoring and maintenance of the water equipment plant to ensure that there is a timely transfer of information. The MHRA has produced guidance on managing medical devices to outline a systematic approach to the purchasing, deployment, maintenance, repair and disposal of medical devices[2] and this guideline should ensure that the maintenance and monitoring of water treatment facilities for haemodialysis are performed by the equivalent of NHS Renal Technologists staff who have a full understanding of theory/maintenance of water treatment for haemodialysis.

Given that the senior clinician and/or technologist will have responsibility for clinical governance of the water treatment facility it is essential that they are closely involved at each stage of the planning, designation, installation and validation of new or replacement water treatment facilities for haemodialysis [(1)].

Reference

1. ISO 23500; 2011: *Guidance for the preparation and quality management of fluids for haemodialysis and related therapies*
2. Managing Medical Devices. Guidance for healthcare and social services organisations. MHRA DB2006(05) November 2006

2. Planning and commissioning of water treatment facilities for haemodialysis

2.1 Source and supply of raw water for haemodialysis

Guideline 2.1 - Specification of the water supply for haemodialysis

We recommend that new build renal units should have a direct feed (drinking or potable) water supply separate from that of the hospital water supply. If existing water treatment systems use a hospital water supply there should be awareness of the potential risks that may arise from the introduction of chemicals into the hospital water supply by either the renal unit or hospital engineering staff. In this setting addition of chemicals into the hospital water supply should not be undertaken without prior consultation with renal services. (1C)

Rationale

Individual components used in the water treatment infrastructure can vary due to feed water quality and product water requirements. The technical features of the water treatment component of that system should be based on the criteria detailed in ISO 26722. In addition to the general specifications outlined the system design should also comply with local building and water regulations. If the feed water is from a private well, an annual analysis of the quality of the product water may not be sufficient to ensure that the treatment system will remove contaminants present and a more frequent analysis may be needed if the well is subject to seasonal changes or contamination from sources such as septic tanks, underground fuel storage tanks, or agricultural waste and chemicals. Such monitoring might not need to be the full chemical analysis if only certain contaminants are known to be of concern.

Recently there have been incidents of contamination of water used for haemodialysis arising from the chemical sterilisation of hospital water supplies to minimize the presence of Legionella as the chemicals used are not effectively removed by the water treatment plants in renal units. A separate water supply to the renal unit is preferred as this will minimize the risk of adverse events from inadvertent contamination of the hospital water supply by such chemicals.

2.2 Setting the design specification for the water treatment infrastructure

Guideline 2.2 - Design specification of the water treatment system for haemodialysis

We recommend that the complete water treatment, storage and distribution system should meet the requirements of all of the following standards: (1B)

BS ISO 13959; 2009: *Water for haemodialysis and related therapies*,

BS ISO 11663; 2009: *Quality of dialysis fluid for haemodialysis and related therapies*

BS ISO 26722; 2009: *Water treatment equipment for haemodialysis and related therapies*.

Rationale

In drawing up the initial design specification providers and users are encouraged to obtain detailed descriptions of all purification processes used by the water utility, together with the operating manuals and maintenance procedures from the manufacturer or the vendor providing the water purification and distribution system to permit informed decisions to be made.

The design specification of new water treatment facilities for haemodialysis should refer to and meet all of the BS ISO standards [1-4]

At the planning stage, the following should also be considered:

- *Treated water capacity during sanitization*
  If heat sanitization is planned for the system, the distribution loop is sanitized along with the links from the distribution loop to the dialysis machines. The demand for water during such sanitization is higher than required by the dialysis machines during operation.

- *Treated water capacity during the winter months*.
  Commonly, RO systems capacity is rated at a specified incoming water temperature. There should be awareness that such temperatures may not be achieved during the winter months, and the efficiency of the system will fall. To meet the required water demand there may be a need to pre heat the feed water or to install a plant with increased capacity to compensate for the fall in RO efficiency during the winter months.

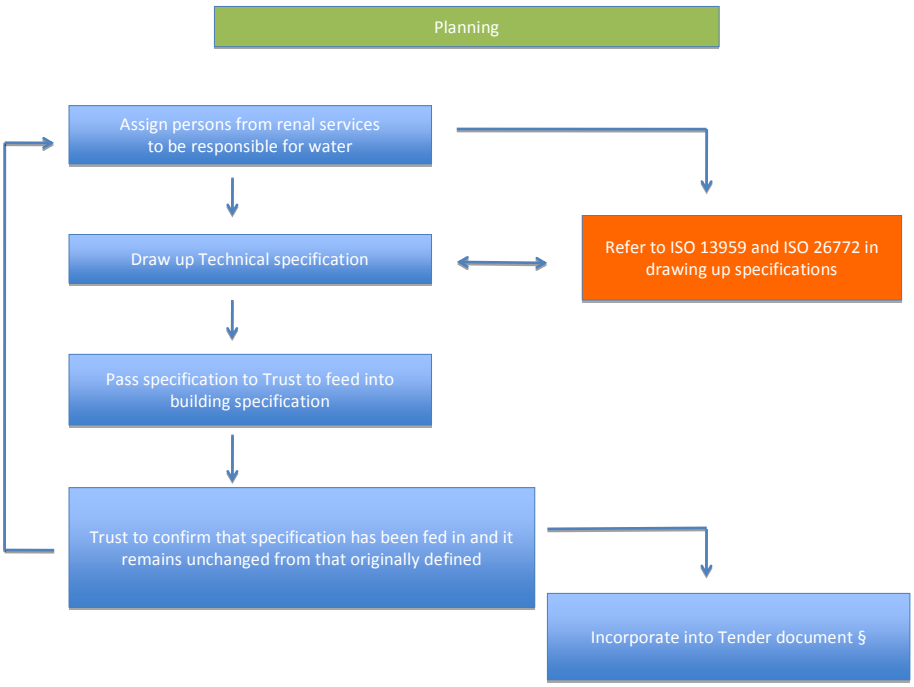
- *Sanitization of the system*
  If chemical sanitization is to be used, the period of down time should be sufficient to enable the chemicals to be rinsed completely from the system prior to the commencement of the next dialysis shift.

- *Compliance with* BS ISO 13958; 2009: *Concentrates for haemodialysis and related therapies*
  This is only necessary if the hospital/renal unit is producing its own dialysis fluid. If the concentrate is purchased from a commercial supplier they will have already complied with this requirement.

- *Contingency plans in the event of system failure or malfunction*.
  Contingency plans should describe how to deal with events that completely prevent dialysis from being performed, such as failure of the facility's municipal water supply or electrical service following a natural disaster or water main break. Planning should also address how to deal with sudden changes in municipal water quality.

The layout of the water treatment system should provide easy access to all components of the system, including all meters, gauges, and sampling ports used for monitoring system performance. Critical alarms, such as those associated with deionizer exhaustion or low water levels in a storage tank, should be configured to sound in the patient treatment area as well as in the water treatment room.

Figure 1 summarises the planning of the design specification of a new water treatment facility for haemodialysis.



References

1. BS ISO 13959; 2009: *Water for haemodialysis and related therapies*,
2. BS ISO 11663; 2009: *Quality of dialysis fluid for haemodialysis and related therapies*
3. BS ISO 26722; 2009: *Water treatment equipment for haemodialysis and related therapies*

Guideline 2.3 – Haemodialysis facilities

We recommend that the specification of new or refurbished HD facilities should adhere to the guidelines that are described in the NHS Estates Health Building Notes 07-01 Satellite Dialysis Unit and 07-02 Main Renal Unit. (1C)

Rationale

The need for high quality water treatment facilities for haemodialysis is highlighted in the recent WHO guidance on water safety in buildings. [1] The water treatment facility should be integrated within the specification that is required for a modern HD unit which has been detailed by NHS Estates. This should be followed in all new and refurbished satellite and main renal unit HD facilities. [2,3]

References

1. Water safety in buildings. WHO Press, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland, March 2011. http://whqlibdoc.who.int/publications/2011/9789241548106_eng.pdf
2. The National Service Framework for Renal Services Part 1: Dialysis and Transplantation, Department of Health, London, UK, January 2004. (www.doh.gov.uk/nsf/renal/index.htm)
3. NHS Estates, Facilities for Renal Services, Health Building Note 53: Volume 1, Satellite dialysis unit & Volume 2, Main renal unit

3. Installation and validation of water treatment facilities for haemodialysis

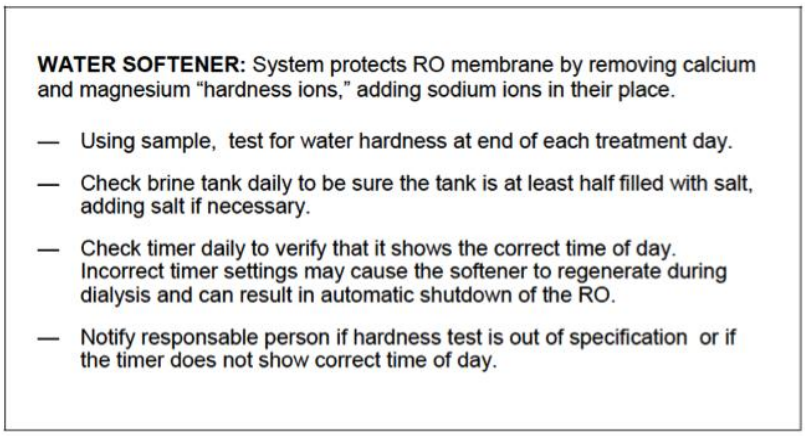
Guideline 3.1 – installation and validation of a water treatment facility for haemodialysis

We recommend that each stage of the installation, performance validation and initial, performance and operational qualification should be agreed and documented in advance and signed off by the manufacturer and the senior clinician in charge of the renal unit (or designated deputy) who has responsibility for the overall clinical governance of the water treatment facility. (1C)

3.1 Installation

The installation of the water treatment infrastructure should be by qualified personnel in line with the manufacturer's recommendations. On completion schematic diagrams that identify components, valves, sample ports, and flow direction should be available and the system appropriately marked. Major water system components should be marked in a manner that not only identifies a device but also describes its function, how performance is verified, and what actions to take in the event performance is not within an acceptable range.

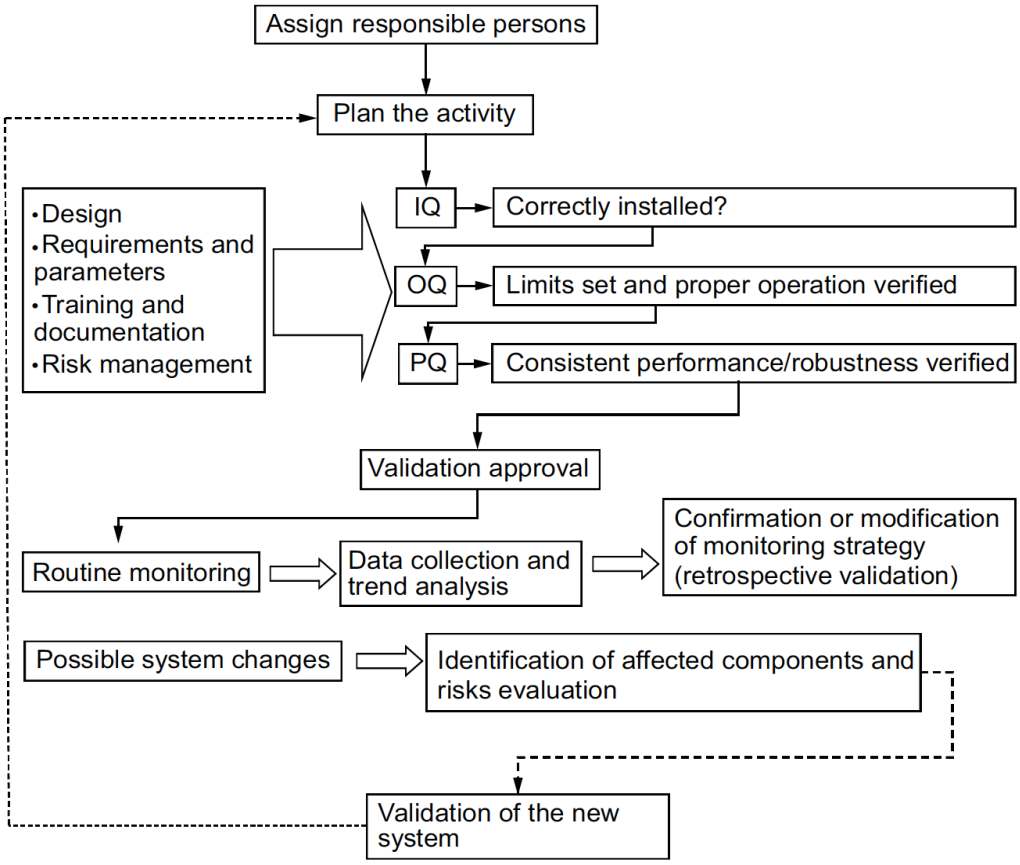
Figure 2 shows the type of labelling which is required for each component of the water treatment system to describe how each component is tested and its action limits. The example below is for an automatically regenerated softener.



3.2 Performance validation

The validation process should provide documentary evidence that the system will consistently produce water, dialysis fluid, or substitution fluid meeting the quality requirements of ISO 13959 or ISO 11663. The contractor or supplier of the water treatment system should draw up the validation plan, which must be submitted to and approved by a member of the renal services with responsibility for clinical care of the patient. It is recognised that not all nephrologists will have sufficient background knowledge for such approval and a designated technical expert may deputise on their behalf. If such a designated person is not part of the renal team, this should be clearly indicated on the documentation together with signed approval from a member of the renal team.

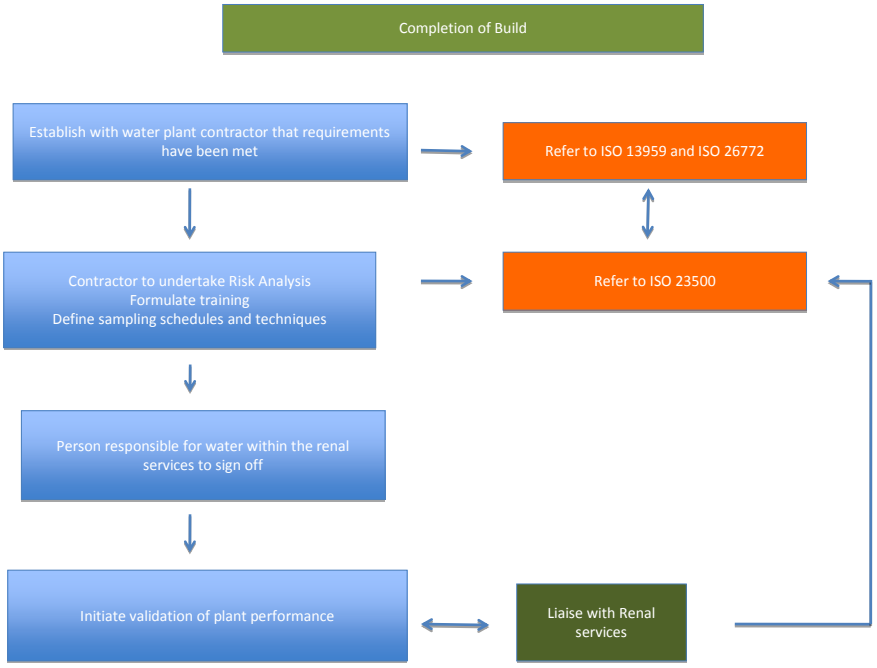
Figure 3 shows an example of a validation process (IQ = Initial or Installation Qualification**,** OQ = Operational Qualification, PQ = Performance Qualification).



3.3 Completion of installation of water treatment facility

The water treatment facility when completed should be confirmed to have met all aspects of the design specification. This needs to be agreed and signed off by the manufacturer/installer, commissioning team and by the person within the renal service with responsibility for clinical governance of the water treatment facility (Guidelines 1.2 and 1.3).

Figure 4 shows the essential action required on completion of building of the water treatment facility.



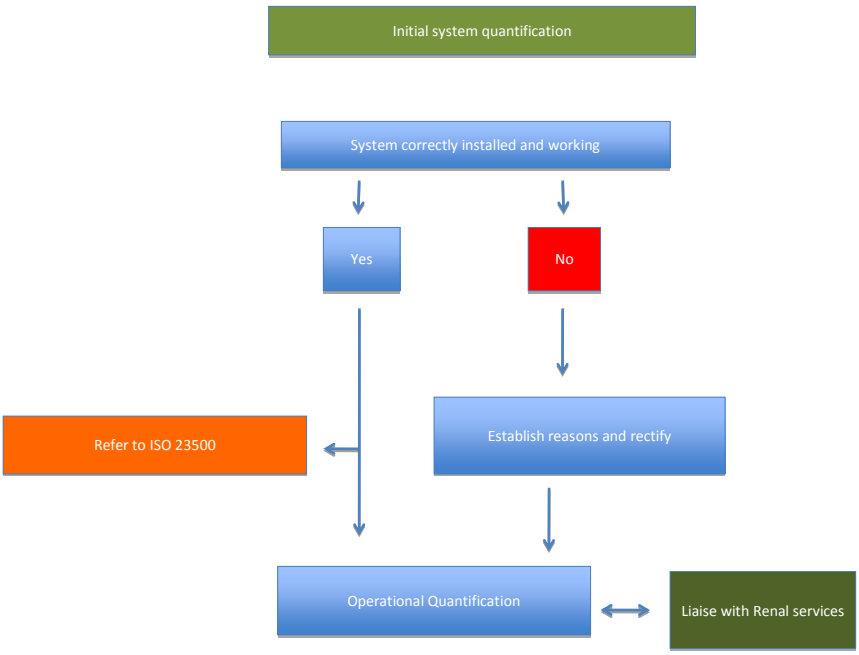
3.4 Initial qualification

On completion of installation, full system documentation should be available including system flow diagrams, layout, log books and operator's manuals. Following completion of the installation, an installation qualification is performed. The purpose of this is to define and provide documented proof that the system has been installed in accordance with the approved plans and the manufacturer's technical requirements and specifications.

Problems have arisen from a lag between completion of the installation process and the commencement of the validation process. To avoid such problems, it is imperative that the water treatment plant and distribution system are not left for any period during which there is fluid present in the system but there is no flow through the system.

Furthermore, it is highly desirable that the entire system is run for short periods on a daily basis. If this is not possible then suitable alternate approaches will need to be established and discussed with a designated technical expert. If the designated technical expert is part of the renal team, this should be clearly indicated on the documentation together with signed approval from a member of the renal team.

Figure 5 summarises the initial system qualification process.

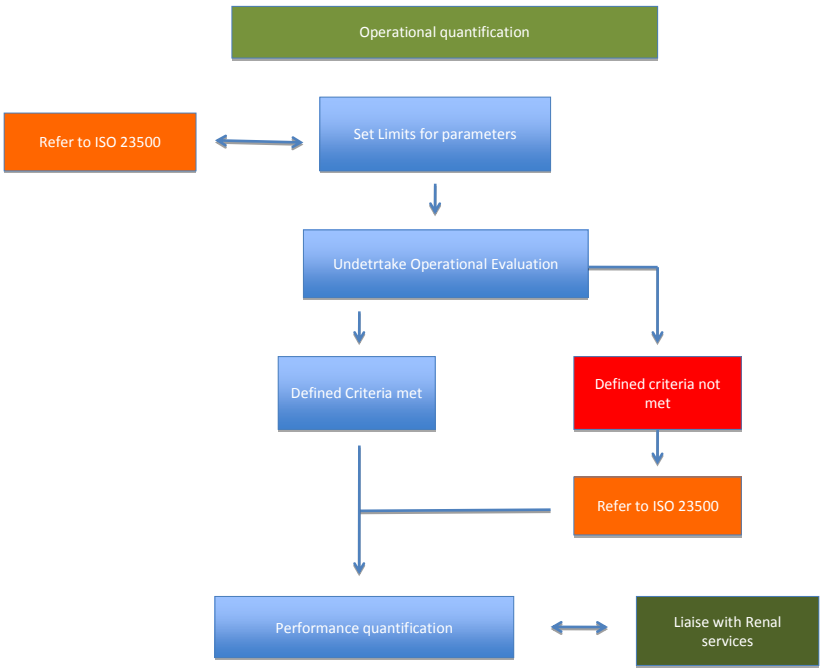


3.5 Operational qualification

The initial qualification of the water treatment system is followed by an operational qualification, the purpose of which is to verify the proper operation of the system, including operating range, set point, interlock and functional testing. On completion the following information should be available:

- test records;
- set up record;
- calibration schedule;
- sampling procedures;
- maintenance plans (e.g. disinfection, filter changes, etc.) and monitoring plans (e.g. conductivity, microbiological analysis);
- record of operator(s) training.

Figure 6 summarises the operational qualification process.



3.6 Performance qualification

Performance qualification generally follows a successful completion of the validation plan. The purpose of the performance qualification is:

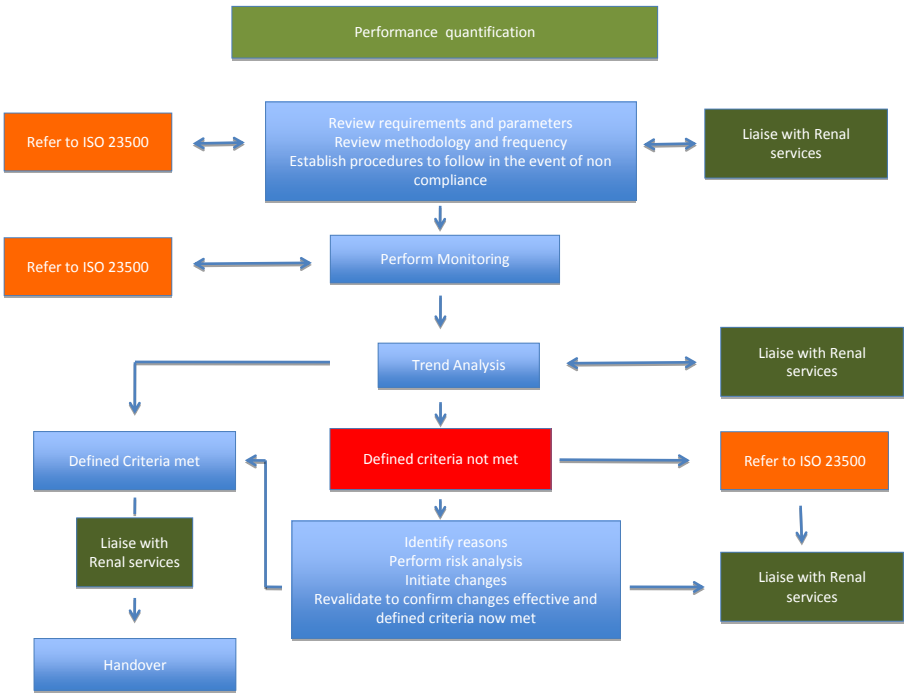
- a demonstration that the plant has been installed in accordance with the design plans and following the manufacturer's procedures for installation (i.e. Installation Qualification);
- a demonstration that the system performs all the required actions and can be operated in accordance to relevant technical manuals (i.e. Operational Qualification).

The Performance Qualification includes periodic assessment of a set of physical, chemical and microbiological parameters to demonstrate that a consistent performance pattern can be achieved for the specific system design and performance requirements. The sampling and testing pattern can be relaxed during the monitoring phase (normal operation) provided it can be demonstrated that the system consistently yields high quality results over an extended period and that continuously monitored parameters provide full surveillance of the system performance. Under these assumptions, the following scheme may be adopted:

The first phase requires a full chemical and microbiological analysis of the dialysis water, followed by weekly microbiological analyses during the first month, to demonstrate consistent quality in the interval between disinfections. During this period all the information about the system behaviour should be collected and fine-tuning of the action levels performed. In this phase the testing frequency of the microbiological parameters is kept at a higher level to create a 'trend analysis' and identify any deviations to ensure the patients' safety.

The achievement of at least three consecutive results, consistently below the action level allows the start of the second phase where the final testing of microbiological parameters and the disinfection plan are implemented. Attainment of results within the action level for two consecutive months allows the successful completion of the Performance Qualification and the start of routine monitoring operations.

Figure 7 summarises the performance qualification process.



4. Operation and maintenance of water treatment facilities for haemodialysis

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We recommend that maintenance and monitoring plans for the water treatment plant are established using the knowledge acquired during the complete validation process for the water treatment system which are in accordance with BS ISO 23500; 2011: *Guidance for the preparation and quality management of fluids for haemodialysis*. Policies and procedures are mandatory and should be set up and implemented at the earliest opportunity. (1B)

Guideline 4.2 – Training of operators of the water treatment plant

We recommend that operators should be trained in the use of the equipment by the manufacturer or be trained using materials provided by the manufacturer. The training should be specific to the functions performed. Periodic audits of the operators' compliance with procedures should be undertaken and documented and there should be an ongoing training programme to maintain the operator's knowledge and skills. (1C)

Guideline 4.3 - Monitoring of feed, treated and dialysis water for haemodialysis

We recommend that a routine testing procedure for water for dialysis should form part of the renal unit policy. Each unit should have standard operating procedures in place for sampling, monitoring and recording of feed and product water quality. The minimum frequency of monitoring of water for dialysis is as follows:

Contaminant	Frequency of testing
Chlorine	At least weekly
Total viable counts	At least monthly
Endotoxin	At least monthly
Chemical contaminants other than chlorine	At least every 3 months

If the interval between sample testing exceeds those indicated in the Table, documentation should be in place to demonstrate that the sampling schedule used has been based on trend analysis. The operating

procedures should include details of the procedures to be followed if the prescribed limits are exceeded. (1C)

Rationale for 4.1-4.3

The manufacturer of the water treatment plant and distribution system should demonstrate that the requirements for microbial contamination are met throughout the complete system at the time of installation [(1)]. No specific recommendations regarding the frequency of monitoring are made but it should be performed at least monthly in respect of the product water and after any maintenance work on the water treatment system. The frequency of monitoring of the feed (or raw water) quality may be performed less frequently. For home installations it may be impractical to maintain a monthly testing programme and to ensure adequate patient safety the dialysis machine should be fitted with point of use filtration.

The laboratory tests required to demonstrate compliance with the recommendations for monitoring of chemical contamination of dialysis water should be carried out during commissioning and thereafter monthly or following alterations to the water treatment plant. The frequency of testing may be modified once local trends have been established, but should not fall below annually. An initial full test on the supply water may be advisable and regular monitoring of water quality data from the supplier is essential when tests are omitted based on low levels of contamination in the water supply.

The absence of any type of bacteriostat in the water following treatment makes it susceptible to bacterial contamination downstream of the water treatment plant. Microbial contamination may be enhanced by stagnant areas within the distribution network or irregular cleaning. The presence of microbial contamination contributes to the development of biofilm which may also be found in the dialysate pathway of the proportionating system, particularly when non-sterile liquid bicarbonate concentrate is used. Such biofilm is difficult to remove and results in the release of bacteria and bacterial fragments (endotoxins, muramylpeptides, and polysaccharides). The dialysis membrane prevents transmembrane passage of intact bacteria but bacterial fragments have molecular weights that allow them to pass across the membrane into the bloodstream. Considerable differences exist in the adsorption capacity of such membranes, which may permit the passage of short bacterial DNA fragments [(2-4)]. Current proportionating systems incorporate filters for the removal of such fragments on the basis of size exclusion and hydrophobic interaction. The aim of implementing a disinfection programme is to prevent formation rather than elimination of biofilm and a routine testing procedure for microbiological contaminants in dialysate, dialysis water and feed water should form part of the renal unit policy. It is unnecesary to perform microbiological monitoring of dialysate or substitution fluid if production paths are fitted with validated microbiological filters operated and monitored within the manufacture's instructions.

Testing for chemical contaminants will normally include continuous conductivity monitoring of the water leaving the reverse osmosis system, and regular in-house checks of hardness and total chlorine [(5)]. There is increasing use of chlorine dioxide to prevent growth of Legionella bacteria in hospital water systems. There is currently no guidance on the control and monitoring of chlorine dioxide in water for dialysis. Confirmation that the standard DPD test used to monitor chlorine and chloramines gives an accurate measure of the levels of chlorine dioxide and its breakdown products (chlorite and chlorates) is needed as is data on the carbon filter empty bed contact time that is required for the effective removal of these compounds.

Records should be kept of all chemical and microbiological test results and remedial actions [(1)].

References

1. ISO 23500; 2011: Guidance for the preparation and quality management of fluids for haemodialysis and related therapies
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5. Monitoring the quality of treated water and dialysis fluid for haemodialysis

Guideline 5.1: Chemical contaminants in water used for the preparation of dialysis fluid

We recommend that the concentrations of chemical contaminants in water used to prepare dialysis fluid should not exceed the limits stated either in BS ISO 13959; 2009: *Water for haemodialysis and related therapies* or in the European Pharmacopoeia (6th edition, 2007). A programme of improvement should begin immediately if routine monitoring demonstrates that concentrations of chemical contaminants exceed the maximum allowable limits. (1B)

Rationale

Knowledge of the potentially harmful effects of trace elements and chemicals continues to expand and techniques of water treatment are continuously being modified. Recommendations for the maximum allowable concentrations of chemical contaminants have been prepared by a variety of standard developing organisations, professional societies and pharmacopoeias, such as AAMI [(1)], International Standards Organisation [(2)] and the European Pharmacopoeia [(3)]. While there is general agreement concerning the maximum allowable levels of inorganic chemicals with documented toxicity in haemodialysis patients (aluminium, chloramines, copper, fluoride, lead, nitrate, sulphate, and zinc) there are some exceptions e.g. the current edition of the European Pharmacopoeia does not explicitly specify maximum allowable levels for copper or chloramines. Of note none of the standards and recommendations includes limits for specific organic chemical contaminants. The rationale for this omission is that organic chemicals with specific toxicity in haemodialysis patients have not been identified and that carbon adsorption and reverse osmosis removes most organic compounds. However, there has been a recent report of patient exposure following inadequate removal of organic chemicals in the preparation of dialysis water [(4)].

Tables 1-3 list all the contaminants for which a maximum allowable limit is defined for water for dialysis in one or more of the standards. With the exception of nitrate, where the standards differ in their recommendations, the most stringent limit has been adopted. An exception has been made in the case of nitrate, for which the European Pharmacopoeia (EP) specifies a maximum of 2 mg/l nitrate whereas the AAMI and ISO 13959 standards recommend a limit of 2 mg/l of nitrate as nitrogen (N), equating to approximately 9 mg/l of nitrate. The more stringent limits may only be met using a double pass reverse osmosis water treatment system which is not universally used and, in view of this, the less stringent recommendation has been adopted for nitrate.

Table 1: Maximum allowable concentrations of chemical contaminants in dialysis water for which monitoring is mandatory (reproduced from ISO 13959 and EP)

Chemical contaminant	Maximum recommended concentration (mg/l=ppm)
Aluminium	0.01
Calcium	2 (0.05mmol/l)
Total chlorine*	0.1
Copper	0.1
Fluoride	0.2
Magnesium	2 (0.08 mmol/l)
Nitrate (as N)	2 (equates to 9 mg/l NO_3)
Potassium	2 (0.05 mmol/l)
Sodium	50 (2.2 mmol/l

* All of the above should be tested initially every 3 months apart from total chlorine concentrations which should be tested at least weekly.

Table 2 defines a group of contaminants for which the drinking water limit is 2 to 5 times the recommended limit for dialysis [5]. In water treated by reverse osmosis, these contaminants will only exceed the limits in Table 2 if they occur at relatively high levels in the water supplied to the unit. These contaminants can be omitted from routine tests if data is available to show that the levels in the water supplied to the unit rarely exceed the limit in the table. These data should be obtained from the municipal water supplier or from tests on the raw water if it is obtained from a private source.

Table 2: Maximum allowable concentrations of chemical contaminants in dialysis water which may be omitted from routine monitoring (reproduced from ISO 13959 and EP)

Chemical contaminant	Maximum recommended concentration (mg/l=ppm)
Ammonium	0.2
Arsenic	0.005
Cadmium	0.001
Chloride	50
Chromium	0.014
Lead	0.005
Mercury	0.0002
Sulphate	50

The final group of contaminants (barium, beryllium, silver, thallium, tin and zinc) are those for which a limit has been defined for water for dialysis and there is no limit specified for drinking water in the UK. These trace elements are not considered to occur in levels that give cause for concern and, if low levels are present, they are removed effectively by reverse osmosis. Testing is only required if there is evidence of high levels in the local water supply (zinc, for example, can be introduced in the pipework). Antimony (AAMI limit 0.006 mg/l) and selenium (AAMI and ISO limit 0.09 mg/l) have been excluded from the requirements for monitoring as the limits for drinking water in the UK are lower than the limit for water for dialysis.

Table 3: Maximum allowable concentrations of chemical contaminants in dialysis water which only require monitoring when indicated.

Chemical contaminant	Maximum recommended concentration (mg/l = ppm)
Barium	0.1
Beryllium	0.0004
Silver	0.005
Thallium	0.002
Zinc	0.1

Although standard laboratory test methods may be specified to be used to measure chemical contaminants e.g. for chloride, any test method validated by the United Kingdom Accreditation Service is acceptable provided the detection limit is not less than 50% of the limits given in Tables 1-3.

The manufacturer or supplier of a complete water treatment system should recommend a system that is capable of meeting the above requirements based on a feed water analysis and allowing for seasonal variation in feed water quality. The complete water treatment, storage and distribution system should meet the requirements of ISO 26722 [6] and be shown to be capable of meeting the requirements of ISO 13959 [2] at the time of installation [7].

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6. BS ISO 26722; 2009: *Water treatment equipment for haemodialysis and related therapies*
7. BS ISO 23500; 2011: *Guidance for the preparation and quality management of fluids for haemodialysis and related therapies*

Guideline 5.2 - Microbiological contaminants in water used for the preparation of dialysis fluid in new water treatment plants

We recommend that all new water treatment plants should be capable of producing water suitable for the production of "ultrapure dialysis fluid". The microbiological contaminant levels of ultrapure dialysis fluid should be < 0.1 CFU/mL and < 0.03EU/mL. (1B)

Guideline 5.3 - HD: Microbiological contaminants in water used for the preparation of dialysis fluid in existing water treatment plants

The microbiological quality of the dialysis fluid in existing water treatment plants should not exceed the limits specified in BS ISO 11663; 2009: *Quality of dialysis fluid for haemodialysis and related therapies* (100 CFU/ml for bacteria and 0.25 EU/ml for endotoxin). If routine monitoring demonstrates microbiological contaminant levels in excess of 50 CFU/ml and 0.125 EU/ml for bacteria and endotoxin (50% of the maximum permitted levels) a programme of corrective measures should be commenced immediately. (1B)

Rationale for 5.2 – 5.3

The dialysis membrane was regarded as an effective barrier against the passage of bacteria and endotoxin (potent pyrogenic materials arising from the outer layers of bacterial cells) from dialysis fluid to blood. This produced a complacent attitude towards the purity of dialysis fluid. About 10 years ago, several in vitro studies showed that intact membranes used in dialysers are permeable to bacterial contaminants [1-3].

The pore size of the membrane appears to be less important than the thickness and the capacity of the membrane to adsorb bacterial products. Consequently low flux (standard) dialysis does not necessarily translate into higher microbiological safety than high flux dialysis or haemodiafiltration. Patients receiving standard dialysis treatment with low flux cellulose-based membranes (thickness 6–8 microns), may therefore be at greater risk of pyrogenic reactions (see below) than those treated using thicker synthetic membranes which have the capacity to adsorb bacterial endotoxin.

In patients treated with high flux membranes, a risk of pyrogen transfer due to backfiltration (a movement of dialysis fluid into the blood pathway of the device due to an inverted pressure gradient rather than the diffusion gradient discussed above) may exist. Lonneman et al, however, concluded that diffusion rather than convection is the predominant mechanism of transmembrane transport of pyrogens, and backfiltration across pyrogen adsorbing membranes does not necessarily increase their passage [4]. It should be emphasised that the adsorption capacity of the synthetic membranes is not infinite and that a breakthrough of pyrogenic substances can occur in the event of excessive water contamination.

A raised C-reactive protein (a sensitive marker of activation of the acute phase response) is associated with a significantly increased risk of death [5,6] and has led to speculation that micro-inflammation associated with transmembrane transfer of endotoxins and bacterial fragments may contribute to raised

serum levels of CRP in patients undergoing regular haemodialysis. Impure dialysis fluid has also been implicated in the pathogenesis of dialysis-related amyloidosis and an increased rate of loss of residual renal function. Ultrapure dialysis fluid is produced by ultrafiltration of dialysis fluid in dialysis machines and is used as an on-line substitution fluid in convective therapies such as haemodiafiltration or haemofiltration. It may also be used in high flux haemodialysis. A number of clinical studies have shown that the use of ultrapure dialysis fluid is associated with a range of clinical benefits [7-10]. Its use for haemodialysis has been associated in the short term with lower indices of inflammatory response (serum CRP and IL-6), in the medium term with better preservation of residual renal function, nutritional status and correction of anaemia and in the longer term may reduce the risk of complications due to dialysis-related amyloidosis. In a prospective 30 month observational study patients with combined high levels of CRP and pro-inflammatory cytokines showed an increase in all-cause mortality (RR =2.57, $p < 0.001$) and cardiovascular death (RR = 1.9, $p < 0.001$) [9]. Although the clinical benefit of ultrapure dialysis fluid has not been established in a large scale randomized trial it would seem prudent to ensure that water is as pure as reasonably possible and the European Best Practice Guidelines recommend the use of ultrapure water for all dialysis treatments [11].

New water treatment systems have the capability of producing water suitable for the production of ultrapure dialysis fluid but the fluid requires further treatment if it is to be used as infusion fluid in convective therapies. In some dialysis units up to 100% of treatments are performed with such techniques. Modern dialysis machines permit the production of substitution fluid on site and on-line allowing large reinfusion volumes to be used. Prior to the introduction of on-line production of reinfusion fluid, the permitted endotoxin level was relatively high (0.25 EU/ml). However current standards specify much lower levels although variability among recommendations exists [12]. Reinfusion fluid used in haemofiltration and haemodiafiltration must be sterile and non-pyrogenic; a final filter is used to achieve this and the line downstream of the filter must be sterile [13].

The tests used for monitoring microbial contamination of water for dialysis should be appropriate to the type of organisms found in water. A low nutrient agar, such as Tryptone Glucose Extract Agar or Reasoner's 2A, should be used [14-16] and samples should be incubated for at least 7 days at 20-22ºC [17]. These conditions have been shown to give good recovery for most environmental bacteria found in purified water. Some species are better adapted for growth at a higher temperature and/or on richer media, but the long incubation time will allow most of these to grow. Details of methods for sampling and culturing of water for dialysis are available in the Appendix of European Best Practice Guidelines for Haemodialysis Part 1 [11] and in the EDTNA/ERCA Guidelines on Control and Monitoring of Microbiological Contamination in Water for Dialysis [18], which also gives specific test conditions for fungi.

Detailed procedures for the collection and analysis of samples of water and dialysis solution for microbiological analysis also form part of ISO 23500 [19].

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19. BS ISO 23500; 2011: *Guidance for the preparation and quality management of fluids for haemodialysis and related therapies*

Guideline 5.4 - Bicarbonate dialysis fluid for haemodialysis

We recommend that the dialysis fluid should contain bicarbonate as the buffer. (1B)

Guideline 5.5 – Preparation of dialysis fluid

We recommend that dialysis fluid is produced by the mixing of treated water, acid and bicarbonate concentrates. The microbiological contaminant levels for acid and bicarbonate concentrates are defined in BS ISO 13958; 2009: *Concentrates for haemodialysis and related therapies.* (1B)

Rationale for 5.4-5.5

One of the critical functions of dialysis is the correction of the metabolic acidosis caused by the failure of the diseased kidneys to excrete non-volatile acids and to regenerate bicarbonate. Bicarbonate is the natural buffer normally regenerated by the kidneys and was the initial choice as dialysate buffer. If, however, sodium bicarbonate is added to a calcium- or magnesium-containing dialysate, their respective carbonate salts will precipitate unless the dialysate is maintained at a low pH level. Since it does not precipitate calcium or magnesium, acetate was used as an alternative buffer [(1)] because of its rapid conversion to bicarbonate in the liver. In the late 1970s and early 1980s, a number of studies suggested that some of the morbidity associated with haemodialysis could be attributed to the acetate component of the dialysate [(2,3)]. This appears to have been unmasked by the introduction of high-efficiency and short-duration dialysis, using membranes with large surface areas. Acetate intolerance led to the reappraisal of bicarbonate as a dialysis buffer in the early 1980s and, following the solving of the issue of precipitation, to its reintroduction. A systematic review of 18 randomised trials indicated a reduction in the number of treatments complicated by headaches, nausea/vomiting and symptomatic hypotension when bicarbonate was used [(4)]. Economic evaluations showed the cost of self-mix bicarbonate buffer to be similar to that of acetate. It should be noted, however, that even 'bicarbonate' dialysate contains moderate amounts of acetate [(5)]. Increased interest in the UK is being shown in the NxStage machine which uses lactate as a buffer and cannot be used with bicarbonate.

It is not possible to set evidence-based standards for other components of the dialysate. However there is recent evidence that non-diabetic haemodialysis patients using glucose-free dialysate have a surprisingly high rate of asymptomatic hypoglycaemia without an associated counter-regulatory response [(6, 7)]. The long-term effects of repeated dialysis-induced hypoglycaemia are uncertain. Hypoglycaemia is not observed if the dialysate contains glucose, but glucose-containing dialysate is slightly more expensive. Currently many dialysis units retain the dialysate glucose concentration at 200

mg/L. In elderly and diabetic patients higher insulin levels coupled with the higher glucose levels impair potassium removal during haemodialysis. Hyperglycaemia also activates inflammatory pathways and contributes to the pro-inflammatory state of haemodialysis patients. For these reasons a reduction in the dialysate glucose concentration may be useful. A recent study by Burgmeister et al suggested that a level of around 100 mg/L would be appropriate for both diabetic and non-diabetic patients [(8)].

Individualisation of dialysate potassium may be required in patients with hypokalaemia and adjustment of dialysate sodium concentrations during haemodialysis (sodium profiling) may be beneficial in some patients with haemodynamic instability.

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Guideline 5.6 – Quality of dialysis fluid

We recommend concordance with BS ISO 11663; 2009: *Quality of dialysis fluid for haemodialysis and related therapies*: standard dialysis fluid is considered as the minimum quality, ultrapure dialysis fluid is recommended for routine haemodialysis and ultrapure dialysis fluid is mandatory for creating on-line prepared substitution fluid used in convective therapies such as on-line haemodiafiltration.

Rationale

Haemodialysis patients are directly exposed to large volumes of dialysis fluid, with the dialyser membrane being the only barrier against transfer of hazardous contaminants from the dialysis fluid to the patient. To minimize this hazard, BS ISO 13958; 2009: *Concentrates for haemodialysis and related therapies* and BS ISO 13959; 2009: *Water for haemodialysis and related therapies*, set out the quality requirements for the water and concentrates used to prepare dialysis fluid [(1,2)]. However, dialysis fluid could contain unacceptable levels of contaminants even though it is prepared from water and concentrates meeting the requirements of the above standards. Furthermore, the dialysis fluid might be used as the starting material for the online preparation of fluids intended for infusion into the patient, for example, in therapies such as online haemodiafiltration. For these reasons, BS ISO 11663; 2009: *Quality of dialysis fluid for haemodialysis and related therapies* outlines the acceptable limits for microbiological contaminants of the dialysis fluid. BS ISO 11663; 2009: *Quality of dialysis fluid for haemodialysis and related therapies* defines three levels of quality of dialysis fluid: standard dialysis fluid, ultrapure dialysis fluid, and online prepared substitution fluid [(3)].

a) Standard dialysis fluid shall contain a total viable microbial count of less than 100 CFU/ml and an endotoxin concentration of less than 0.5 EU/ml. The action level for the total viable microbial count in dialysis fluid should be 50 CFU/ml. If microbial counts exceeding the action levels are observed in the dialysis fluid, corrective measures, such as disinfection and retesting, should be taken promptly to reduce the levels.

b) Ultrapure dialysis fluid shall contain a total viable microbial count of less than 0.1 CFU/ml and an endotoxin concentration less than 0.03 EU/ml. As for standard dialysis fluid, if the limits are exceeded corrective measures should be taken to reduce the levels to an acceptable range.

c) Microbiological requirements for on-line prepared substitution fluid

Substitution fluid for convective therapies, such as haemodiafiltration and haemofiltration, may be produced online by a process of ultrafiltration with bacteria and endotoxin retentive filters. This on-line process shall be validated to produce fluid that is sterile and non-pyrogenic. Compliance of on-line produced fluid with the requirements of BS ISO 11663;2009: *Quality of dialysis fluid for haemodialysis and related therapies* cannot be demonstrated with traditional test procedures. For this reason, compliance with BS ISO 11663;2009: *Quality of dialysis fluid for haemodialysis and related therapies* shall be ensured by proper operation of a validated system, verified according to the manufacturer's instructions on installation, and confirmed by a regular monitoring and maintenance schedule.

1. BS ISO 13958; 2009: *Concentrates for haemodialysis and related therapies*
2. BS ISO 13959; 2009: *Water for haemodialysis and related therapies*
3. BS ISO 11663; 2009: *Quality of dialysis fluid for haemodialysis and related therapies*

7. Water treatment facilities for home haemodialysis

Guideline 6.1 – Maintenance of the water and power supply

We recommend that the utility companies providing both water and power to the patient's home be notified that home dialysis is being performed at that location and that restoring service after any interruption should be a priority. (not graded))

Guideline 6.2 – Training of the patient and/or helper

We recommend that the patient and/or helper in the home should be formally trained in the proper operation and maintenance of the water treatment equipment by the renal technicians. The patient and /or helper should keep a log of the maintenance and monitoring procedures. (not graded)

Guideline 6.3

We recommend that the chemical and microbial quality of the water used for the preparation of dialysis fluid for home haemodialysis should be monitored at least annually and every 3 months respectively. (1C)

Rationale for 6.1-6.3

The general considerations described in the previous sections of this document are equally applicable to home haemodialysis installations. To incorporate a haemodialysis machine in a home, the home will need a water supply, a drain connection, and a power source.

If the feed water to the home is from a private well, an annual analysis of the quality of the product water may not be sufficient to ensure that the treatment system installed will remove contaminants present and a more frequent analysis may be needed, particularly if the well is subject to seasonal changes or liable to contamination from sources such as septic tanks, underground fuel storage tanks, or agricultural waste and chemicals.

The equipment selected for home haemodialysis should be simple to operate. As in the hospital the final configuration of the water treatment system will depend on the quality of the feed water and the water produced should comply with the requirements of BS ISO 26722; 2009: *Water treatment equipment for haemodialysis and related therapies*. Any alarm associated with a component of the water treatment system should be audible and visible in the patient treatment area.

There are a number of specific points pertinent to home installations:

- Carbon beds/filters

These are used to effect removal of chlorine/chloramine from the feed water and if the water is derived from a well, to also remove organic contaminants from ground water. Two carbon beds (with backwashing facilities) connected in series and sampled from a port located between the two is desirable and provides a degree of safety over a single carbon bed / filter. If two filters in series are used or chloramines are not detected in the raw water the equivalent total empty bed contact time of 10 minutes could be sufficient. If carbon filters are used in preference to beds, a well defined schedule of replacement should be in place.

- The distribution system for the treated water at home.

Because systems used for home haemodialysis operate intermittently, the distribution system should be designed and maintained to minimize bacterial proliferation. An integrated heat sanitization is preferable since this will sanitize the line supplying the water to the dialysis machine. Consideration should also be given to installing a point-of-use ultrafilter in either the dialysis water or dialysis fluid path. If installed, the ultrafilter should be maintained and replaced according to the manufacturer's instructions.

Monitoring of water and dialysis fluid quality

Routine monitoring of each treatment

A log sheet should be provided by the renal unit and used to record all measures of water treatment system performance. Measurements should be made at least 15 minutes after the water treatment system has been set in operation and before dialysis is initiated. To ensure that dialysis is not undertaken with suboptimal water quality, prior to each treatment, the performance of the reverse osmosis system should be monitored and recorded by checking the product water conductivity and percent rejection. If the reverse osmosis system is found to be outside its acceptable range, the renal unit responsible for the patient should be notified. If the water treatment includes a stand alone softener, the water hardness should be monitored prior to each treatment using a sample obtained through a labelled sample port located between the softener and the reverse osmosis system. For hardness tests requiring colour differentiation, the person performing the analysis should be able to distinguish between the colours of blue, purple, and red. If the person cannot differentiate these colours, an automated meter should be used. The results obtained should be recorded on the log sheet.

Monitoring for chemical and microbiological quality

The chemical quality of the treated water used for dialysis should be analyzed at least once a year to ensure it meets the requirements of BS ISO 13959; 2009: *Water for haemodialysis and related therapies*. A more frequent analysis may be needed if there are seasonal variations in source water quality or if the source water is supplied from a well. When any repairs or component replacements are made to water treatment equipment, the impact on water quality should be evaluated and a chemical analysis performed if indicated.

To meet the requirements of BS ISO 11663; 2009: *Quality of dialysis fluid for haemodialysis and related therapies* the microbiological quality of the dialysis fluid should be analyzed at least quarterly using the appropriate techniques, however if daily dialysis schedules are being practiced, this frequency may be insufficient.

Sampling should be prior to any disinfection of the water treatment system and dialysis machine and a system should be in place to ensure proper collection of the samples and their timely submission to the testing laboratory. If patients or helpers are expected to perform sampling, they should have received adequate training to do so, and this training should be appropriately documented.

Reference

1. Dialysate for haemodialysis, Amendment 1 – Annex C: Special considerations for home haemodialysis. AAMI (in press)

Addendum

A summary of recent installations of water treatment facilities in the UK which demonstrate inadequate planning and/or problems with installation and validation is in preparation by Maurice Harrington as supporting evidence for the need for this guideline.