SCOPE
These guidelines apply to the control, and monitoring, of:

• Water intended for use in the preparation of dialysis fluid in all settings, including patients’ homes and acute care units.
• Water used for in-house production of liquid concentrates.
• Water used for reprocessing dialysers.

These guidelines should be taken into consideration when designing and modifying water treatment systems. The suppliers of all components should ensure that their products are compatible with these guidelines. Where the complete installation is assembled using components from different suppliers, the renal unit staff must take overall responsibility for implementing the guidelines. Although day-to-day management of the quality of the water used for dialysis is normally delegated to technical staff, ultimate responsibility for water quality may lie with the physician or pharmacist in charge of the dialysis service, or with a designated team, according to national regulations. To reflect this multidisciplinary process, a comparison between this document and the guidelines on dialysis fluid purity issued by the European Renal Association/European Dialysis and Transplant Association (ERA-EDTA) has been carried out and this document has been approved by ERA-EDTA.

2 APPLICABLE STANDARDS AND GUIDELINES


3 GLOSSARY

For the purpose of these guidelines, the following definitions apply:

Activated Carbon Filter (ACF): A device containing chemically/thermally treated carbon material, through which the water to be treated is perfused. The adsorptive properties of the carbon remove certain solutes.
Breakthrough: The moment when the output of a certain substance from an ACF exceeds a predetermined level.
Cartridge filter: A disposable filter, containing either granular activated carbon (GAC) or a porous block of carbon material that is housed within a reusable vessel.
Chloramine: An oxidant formed by the combination of chlorine and ammonia. This can be present in three forms, monochloramine, dichloramine and trichloramine, depending on the solution pH and chlorine to ammonia ratio. A fourth form, organic chloramine is produced when free chlorine reacts with organic nitrogen compounds.
Chlorine: An oxidising agent, Cl₂ is a gas at normal temperature and pressure. When in solution chlorine forms the hypochlorite anion and hypochlorous acid, the proportions being dependent upon the pH. These are expressed as the free chlorine component of the total available chlorine.
Dialysis fluid: A solution, which is intended to exchange solutes and/or water with blood during haemodialysis or haemodiafiltration (IEC 60601-2-16 2.107). Dialysate is commonly used in place of dialysis fluid, although this term should be reserved for contaminated fluid leaving the dialyser.
**Distribution system:** The pipe-work used to transport treated water to the dialysis machine, together with any associated tanks, pumps, filters, irradiation units etc. The connections to the dialysis machines also form a part of the distribution system.

**DPD test:** Diethylphenylenediamine test method. This is a chemical reaction in which free chlorine causes formation of a pink colour in the test solution. The addition of Potassium Iodide will liberate bound chlorine to give a measurement of total chlorine.

**Empty Bed Contact Time (EBCT):** A theoretical value indicating the amount of time that water is in contact with the carbon material. This is derived from the volume of carbon material and the flow rate through the carbon. This is only relevant for GAC filters.

\[
\text{GAC volume (litres) / flow rate (litres minute}^{-1} \rightleftharpoons \text{EBCT (minutes)}
\]

NB. The GAC volume is not the volume of the GAC filter vessel, as this will not be full of GAC material. The calculation gives a value assuming the carbon occupies ‘zero volume’. The flow rate is the maximum through the vessel at any time, e.g. if one RO is flushing while another is producing water for dialysis.

**Granular Activated Carbon (GAC):** A type of carbon that is in the form of granules.

**Fines:** Small particles produced by mechanical attrition of a material, such as the carbon granules in a GAC filter.

**Iodine Number:** The capacity for a carbon to adsorb iodine expressed as mg g\(^{-1}\).

**Organic chloramines:** Organic chloramines cannot be distinguished from mono and dichloramines by the DPD test method. There are few references to their toxicity compared to the other forms of chloramine.

**Redundancy:** A design concept where there is more than one similar device, each capable of performing the required function on its own.

**Total available chlorine (total chlorine):** The sum of free chlorine and combined chlorine (chloramine).

**Water treatment system:** The entire system, including purification devices, pumps, monitoring systems and distribution system, from the incoming water supply to the point of use.

4 **Introduction**

The ERA/EDTA Best Practice Guidelines for Dialysis Fluid Purity specify that water for dialysis should comply with the requirements of the European Pharmacopoeia monograph for water used for diluting concentrated haemodialysis solutions (EP Monograph 1167). References 1 to 3 review the clinical arguments for lowering the chlorine content of dialysis fluid. EP 1167 requires that water used for diluting concentrated haemodialysis solutions should contain total available chlorine of no more than 0.1 ppm (milligrams/litre).

Published standards and guidelines on carbon filtration of water for dialysis are limited to the use of GAC material. Porous block carbon filters may provide a viable alternative, but to date there is very limited data regarding their use for treating water to be used for haemodialysis. The performance of new devices such as block carbon filters, particularly in larger installations processing large volumes of water for dialysis, should be monitored closely to ensure compliance with the requirements for control of total chlorine levels.

5 **Guidelines**

5.1 **Design**

Water treatment systems should be designed to be capable of producing water that meets the requirements for dialysis with a realistic level of maintenance.

The GAC filter should be positioned up-stream of the reverse osmosis (RO) device with a 5-micrometer particle filter placed between the GAC filter and the RO. The GAC filter can be positioned either before or after any ion exchange resin devices (water softeners etc.), except where the incoming water chlorine level exceeds the maximum level specified by the resin manufacturer. In these circumstances the GAC filter should be positioned before the ion exchange resin devices. The GAC filter should consist of two devices in series, with a total EBCT of 10 minutes unless a risk assessment has been carried out to justify the use of a lower contact time. An acid washed carbon with a maximum ash content of 3% and a minimum iodine number of 1000 should be used as the filter material.

Isolation and bypass devices should be fitted to allow for maintenance. These bypass devices should be designed to prevent unintentional use during dialysis treatment. When a GAC filter is bypassed, additional chlorine/chloramine reduction devices may need to be installed.

These guidelines do not recommend omitting a carbon filter from the water treatment system. If dialysis facilities choose not to install a carbon filter this should be substantiated with a documented risk assessment.

**RATIONALE**

Without long-term data analysis it is difficult to estimate...
Guidelines for the control of chlorine and chloramine in water for haemodialysis using activated carbon filtration

the EBCT for a particular feed water. The AAMI RD62:2001 standard EBCT of 10 minutes has been used consistently to produce water with a maximum chloramine level of 0.1 milligrams per litre. [Evidence] If a lower EBCT is to be used it should be substantiated using local historical total chlorine data, as the adsorptive properties of carbon may vary with time, temperature and pH [4]. [Opinion]

Whilst the AAMI RD62:2001 standard advocates a total EBCT of 10 minutes, the breakthrough level is measured after the first GAC filter, suggesting that an EBCT of 5 minutes is capable of reducing the feed water level to ≤ 0.1 milligrams per litre of chloramine. However a single GAC filter with an EBCT of 5 minutes would not have the redundancy to cope with elevated feed water levels. [Opinion]

As GAC material is porous it provides an ideal environment for the growth of water borne micro-organisms; it must therefore be placed before any RO device so as not to compromise the final water quality and the RO membrane must be protected from fouling with carbon fines by using particle filtration. Increasing GAC filter size does not however cause an increase in bacteriological activity [5]. [Evidence]

The AAMI RD62:2001 standard recommends using a carbon with a minimum Iodine Number of 900. However as many carbons are now available with an Iodine Number in excess of 1000, this should be the minimum value used when designing a filter. [Opinion]

An unwashed carbon may have a high ash content that when first used will elute aluminium and other alkaline salts. This could compromise the final water quality and cause a reduction in the volume of the carbon material. The use of acid washed carbon is recommended to reduce these undesirable effects [6]. [Evidence]

By installing two GAC filters in series with suitable bypass and isolation valves it will be possible to replace exhausted GAC material whilst continuing to provide filtered water to the downstream RO device. [Opinion]

5.2 Frequency of Total Chlorine Measurement

Water used for haemodialysis should be tested daily to verify the GAC filter is operating correctly, and to ensure that the water meets the requirements of the European Pharmacopoeia (total chlorine level ≤ 0.1 mg/L) or the local specifications for purity.

The test advocated by the EP is the DPD test method for Total Chlorine, and this should be employed to ensure the efficacy of the carbon filtration. Testing should be done on a daily basis and the results recorded for trend analysis. Continuous automatic total chlorine monitoring equipment may also be used to perform this task.

If chlorine disinfectants are not added routinely to the water supply, or if the total chlorine level in the water supplied to the dialysis facility is known to be acceptably low and stable, a longer testing interval may be used.

In the home dialysis environment the testing interval may be increased. Where this is practised the GAC filter should be ‘over-sized’. An EBCT of 20 minutes should be considered. More frequent testing, i.e. at the start of every patient shift should be implemented when the first GAC filter total chlorine level exceeds the EP limit. This test sample should be taken after the second GAC filter. This should continue until the exhausted GAC filter has been replaced.

The feed water from the water supplier should be tested on a weekly basis to determine the feed water characteristics. If chlorine disinfectants are not routinely added to the water supply to ensure that abnormal changes in the water quality are reported to a designated hospital representative. This arrangement should also ensure that the hospital representative is informed of planned changes in the source and/or treatment of water supplied to any dialysis location.

RATIONALE

Good manufacturing, laboratory and clinical practices separate monitoring from control methods. In this case, the installation of an adequately sized GAC filter is the control. Total chlorine testing is the independent monitoring method. [Opinion]

The DPD test is inexpensive and widely used. It can be carried out at the point of sampling. Automated readers are available to reduce inter-operator errors. Continuous automatic total chlorine monitors can also be used.

Where a test method other than the DPD test is used, it should be validated to ensure correlation with the DPD test. If samples are tested in an external laboratory, the transit time should be minimised.

The monitoring of total chlorine level after the second GAC filter needs to be more frequent once the first GAC filter has ‘broken through’ as there is no redundancy in the system. The break-through may be due to GAC material becoming exhausted over time, any increase in flow rate, or to an unusually high level of chlorine disinfectant in the feed water. Recording of the feed water characteristics enables the reason for breakthrough to be determined. [Opinion]

If chlorine disinfectants are not routinely added to the water supply, the testing frequency may be extended provided that...
an adequate reporting procedure is in place with the water supplier. This would involve the supplier notifying the dialysis facility of their intention to add chlorine disinfectant to the water supply. This would only be a satisfactory arrangement if the notice given, provided the facility with time to make carbon filtration arrangements. If chlorine disinfectants are routinely added, the supplier should inform the facility of any abnormal increase in level, 50% or 1.0 mg/L, which ever is the lesser amount. [Opinion]
Where chlorine disinfectants are added locally to the water supply at the hospital/clinic, the responsible authority should be made aware of the above requirements.

5.3 Sampling location and techniques

When two GAC filters are in series, the sample should be taken after the first GAC filter, and tested immediately on-site.
When the first GAC filter has broken through, the sample should be taken after the second GAC filter.
Feed water samples should be taken where the water enters the water treatment system.

The EBCT will vary with water consumption. The sample should therefore be taken during times of maximum flow. This may be when a redundant RO device is in ‘flush’ mode and/or when the dialysis machine flow rates are set to their maximum.
The sample tap should be flushed to expel stagnant water from the dead space before the sample is collected.
Ideally the samples should be tested on-site with a DPD test kit (or other suitable method), by staff who have been trained in the appropriate use of the kit.
Rationale: The adsorption of chlorine and chloramine by GAC relies on contact of the solute with the adsorption sites within the carbon material. As this contact time decreases with increased flow through the GAC, the sample should be taken when this flow rate is at its maximum [4]. [Evidence]
Chlorine based disinfectants are volatile and should therefore be tested as soon as the sample is taken. [Opinion]
Although the Chlorine/Chloramine test methods are quick and simple, they require interpretation of a colour change. The chemicals used may also pose a health and safety risk. Therefore training for testers is to be advised. [Opinion]
The feed water sample should be taken before any treatment process, as ion exchange devices may have an effect on the total chlorine level. [Evidence]

5.4 GAC filter maintenance

A maintenance programme should be adopted that ensures the GAC filter continues to produce water with a total chlorine level ≤ 0.1 mg/L.

By sampling the water from the locations and at the frequency previously specified it will be possible to determine when the GAC material in a filter has become exhausted. Total chlorine levels consistently above 0.1 mg/L will indicate this. The feed water should also be monitored to determine if this is the cause of the elevated post GAC filter level. Consultation with the water supplier will determine when the feed may return to the previous level and therefore if GAC filter breakthrough is likely to be long term.
The maintenance programme should include a protocol for the replacement of exhausted GAC material. This should indicate who is responsible for instigating and overseeing the operation, who will supply and install the GAC material, who will monitor the total chlorine level whilst the exhausted GAC filter is being serviced, and finally who determines that the operation is complete.
Apart from replacing the GAC material when breakthrough occurs the GAC filters will also need to be serviced according to the manufacturers’ or suppliers’ recommendation. This may include routine replacement of the carbon before breakthrough has occurred to control microbiological contamination.
If only one GAC filter is installed it should be replaced on a timed basis. If monitoring indicates chlorine breakthrough, the filter should be replaced immediately and the replacement interval reduced.
The GAC filters will require back flushing to prevent compacting of the GAC material, leading to poor perfusion of the GAC.
This should occur when dialysis is not being performed, as the GAC filter may not supply water during parts of this cycle.
The manufacturers’ or suppliers’ recommendations should be followed to determine how often back flushing is required. The flow through the GAC filter during back flushing should meet the manufacturers’ minimum requirement to ensure adequate redistribution of the GAC material.
Disinfecting of GAC material is not advised, as it may be ineffective [7,8].

RATIONALE

Good equipment maintenance practice requires that preventive action be taken before deterioration in performance occurs. [Opinion]
When only one GAC filter is installed, breakthrough should
be avoided, as there is no redundancy. The installation should be monitored for rising total chlorine level after the filter to estimate the normal life expectancy of the filter. The maintenance programme should ensure that the GAC filter is routinely replaced well before its normal life expectancy is reached.

5.5 Adverse Total Chlorine Level

A protocol for dealing with total chlorine levels in excess of 0.1 mg/L after the final GAC filter should be in place.

This protocol should outline who is responsible for instigating and overseeing the operation, what action should be taken to reduce the total chlorine level, what is the maximum acceptable level in the dialysis fluid and who decides when it is not safe to continue with dialysis.

If the second GAC filter outlet total chlorine level is above 0.1 mg/L, the level of the RO product water should be monitored very frequently. The ‘permeate’ conductivity of the RO should also be monitored to indicate if the membrane is experiencing damage.

The following actions should be considered when the GAC filters fail to produce acceptable water:

- Increase EBCT by reducing flow. This may include switching off redundant RO devices, and reducing dialysis fluid flow rates.
- Installing extra carbon filters. It may be possible to install disposable GAC filters, or replace particle filter cartridges with disposable carbon filter cartridges.

Should the RO product water contain an unacceptable level of total chlorine, dialysis should be discontinued and alternative arrangements made. The level at which dialysis must be stopped should be agreed with the Clinical Director of the dialysis unit.

Rationale

Even if the second GAC filter cannot produce acceptable water, the reverse osmosis device may achieve some reduction in total chlorine. Extreme care should be taken in these circumstances as the RO membrane may be damaged by exposure to chlorine compounds. This further reduces the RO system’s ability to filter the water. [Opinion]

As acute haemolysis has been shown to occur at levels above 0.5 mg/L, a limit should be set at which it is no longer desirable to dialyse the patients. [1,9,10]

5.6 Disposable Filters

A protocol for dealing with total chlorine levels in excess of 0.1 mg/L after the final GAC filter should be in place.

The use of a permanently installed GAC filter may not always be practical, for example home dialysis and small clinics. In these circumstances disposable ACF’s may be used. A disposable ACF may either be a small GAC filter that is returned to the manufacturer following breakthrough, or a cartridge filter installed in a reusable housing. A cartridge ACF may be constructed using GAC or a porous block of carbon material.

Most of the design consideration applied to a permanent GAC filter should be applied to the disposable type with the following exceptions:

- A disposable ACF may not need to be followed by particle filtration, however pre-filtration may be required.
- An EBCT may not be applicable for disposable ACF’s.

However the selected filter should be validated using the expected operating conditions if suitable performance data is not available from the manufacturer.

- An iodine number may not be applicable for disposable ACF’s.
- The sampling locations may need to be limited in situations where many disposable ACF’s are used in one treatment area.
- Disposable ACF’s do not require back flushing.

Rationale

The design criteria used for permanent GAC filters cannot always be applied to disposable filters. Some cartridge GAC filters have particle filtration included in the design, and some carbon block filters do not release fines, making the need for post ACF filtration unnecessary. The manufacturer’s advice should be followed when using these filters. [Opinion]

As an iodine number is only applicable for GAC it cannot be applied to carbon block filters. There are however carbon block filters that the manufacturers’ claim have an enhanced affinity for chloramine. Reference to the specific manufacturer’s data is required to access the effectiveness of this GAC. [Opinion]

Where many disposable ACF’s are used to treat water from the same source it may not be practical to test every filter. Providing all the filters are identical, water could be tested from a representative number to verify their operation. [Opinion]
6 Outcome measures

The implementation of this guideline should be audited by reviewing the record of total chlorine levels over time. The record should show post ACF and feed water total chlorine levels. Adherence to planned preventive maintenance, including filter replacement should be audited.

If routine measurements of haemoglobin are available, these should be audited periodically to look for trends that may be related to water quality. The dose of erythropoetin should also be audited as high dose levels may also indicate poor dialysis water quality.

A mechanism should be established for informing the physician in charge of the dialysis unit of the water quality on a routine basis and when the water fails to comply with the requirements of the European Pharmacopoeia or the local specification.

7 Appendix: Comparison with the recommendations in the ERA-EDTA Best Practice Guidelines for Haemodialysis: Section IV.

This appendix compares the guidance provided in this document (EDTNA/ERCA) with the relevant sections of the ERA-EDTA guidelines for dialysis fluid purity. In general, the recommendations are identical, but the EDTNA/ERCA document goes into greater detail of the implementation and the handling of exceptional situations.

Allowed levels of chlorine and chloramine

Both documents state that water for dialysis should comply with the requirements of the European Pharmacopoeia monograph for water used for diluting concentrated haemodialysis solutions (i.e. the total chlorine level should be less than 0.1 mg/l) and recommend the use of activated carbon filters to remove chlorine and chloramines. The EDTNA/ERCA guidelines also include advice on the quality of carbon and the configuration and location of carbon filters for multi-user systems, and on the use of carbon filters for home haemodialysis and temporary stations (e.g. intensive care).

Monitoring

Both documents recommend testing the water for chlorine and chloramines on a daily basis. The EDTNA/ERCA guidelines allow dialysis units to extend the interval between testing in locations supplied with water that has low, stable levels of chlorine provided they have carried out a risk assessment based on historical data and provided they have established a formal relationship with the water supplier to ensure that they are informed of any changes in the municipal water treatment procedures. Testing intervals may also be extended for home haemodialysis facilities provided an over-sized carbon filter is installed. More frequent testing, i.e. before every shift, is recommended if there is any indication that the carbon filter is no longer functioning adequately.

The EDTNA/ERCA document also describes the test procedure and the requirement for staff to be properly trained.

Maintenance

Both documents recommend regular backwashing to ensure that the filter continues to offer a large surface area for adsorbing contaminants. The ERA-EDTA guidelines recommend disinfecting and changing the components of the water treatment system in accordance with the manufacturer’s instructions and any microbiological records. The EDTNA/ERCA document does not recommend disinfecting the carbon filter as this does not seem to be effective, but it does recommend changing the filter medium in accordance with the manufacturer’s instructions even if there has been no breakthrough of chlorine or chloramines.

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REFERENCES


