Measurement of Chlorine/Chloramine Levels in Feed Water Used in Dialysis Water Systems:
Effect of pH and Choice of Reference Standard on Test Values

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Discussion

To protect dialysis patients from hemolysis and other potential medical issues, a 0.1 mg/L (ppm) maximum allowable safe level of chloramines in water used for dialysis is well documented in the dialysis standards (AAMI/ISO). Historically, the level of chloramines in feed water used in dialysis water systems has been measured between the dialysis clinic's worker and polisher carbon tanks using total chlorine analytical methods (i.e. "tests"). Per page 10 of the AAMI RD62:2006 Standard (for dialysis water treatment), these total chlorine tests can be traced back to the American Public Health Association and EPA specifications for the use of the 4500-Cl G method, the Amperometric Titration Standard Method 4500-C1 D and ASTM Method D 1253-86 "and/or other equivalent analytical methods". The 4500-Cl G analytical method refers to the DPD colorimetric method. Within the past ten years, AAMI/ISO has added the MTK/TMK colorimetric method as a specific acceptable total chlorine analytical test method for measuring low levels (less than 0.1mg/l) of chloramines in water to be used for dialysis. The K100-0118/F Ultra-Low™ Total Chlorine Test Strip from RPC uses the TMK (Thio-Michler's Ketone) colorimetric method with a patented aperture reagent pad mount which greatly increases sensitivity, precision, and resolution when compared with other total chlorine test / test strip methods.

Total chlorine tests measure the total of the amount of free chlorine and combined chlorine/chloramines in the water under test. Consequently, total chlorine tests do not measure chloramines separately. Per the AAMI RD62 Standard, free chlorine in dialysis feed water at levels above 0.5 mg/l (ppm) may also cause hemolysis and other serious issues for the patient. A total chlorine test, will read positive with a free chorine level or chloramines level of 0.1 mg/l (ppm); for that reason, only a single total chlorine test is required to determine if the level of free chlorine and chloramines in the feed water is below their respective maximum allowable limits.

Because there are no easy to use and cost effective tests for use in the dialysis clinic to specifically determine chloramines only – and it is impractical…as a free chlorine test would still be required – the dialysis industry standards/regulatory bodies (e.g. AAMI/ISO/CMS) years ago moved to acceptance of the total chlorine test – with a maximum allowable limit of 0.1 mg/l (ppm) total chlorine - to replace the separate tests / listed maximum allowable limit values for free chlorine and chloramines.

When measuring chloramines in water (as a subset of total chlorine) - due to inversely decreasing hypochlorous acid (HOCl) as pH levels exceed ~6.0[1,2] (*figure 1*) - all of these total chlorine analytical methods are affected in a false negative direction at some level of pH… as the pH of the water increases.

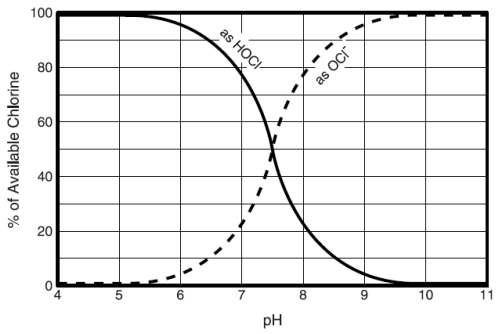

Fig. 1: Relationship Between HOCl and OCl^- at Various pH Values

Some basic chemistry references[1,2] state that “It may be concluded that in free residual chlorination, the higher the pH value the less active is the residual because of its lower proportion of hypochlorous acid.” Whether or not this “concluded” reduction in residual activity (mainly monochloramine) at high pH levels reduces the risk to dialysis patients has not been well studied.

Therefore, there are important details that must be considered with regard to the pH of the dialysis feed water and ultimately the dialysis product water when using any total chlorine test.

These questions should be asked and answered:

1) What is the measured pH value of the water to be tested?
   a. Is that value within the acceptable range recommended by AAMI (et al) for dialysis feed water?
   b. If the water pH value is outside the AAMI recommendation - beyond a possible effect on the total chlorine test - are there other possible issues generated?
2) Does the total chlorine test method being used have a built in buffer to compensate for higher pH levels?
   a. If so, at what measured pH level is the test negatively impacted at the dialysis maximum allowable level for chloramines (0.1 mg/l)?
   b. Is that measured value within or outside the AAMI recommended range for feed water pH?
   c. Is there an easy to use method for “testing the test” or adjusting the test for high pH water?
3) When quantifying / measuring a specific amount of chloramines in water at a specific pH level of that water, what reference method for analysis is being used and how do the various reference methods differ and/or potentially impact the test result?

At the time of this writing, the RPC K100-0118/F Ultra-Low™ Total Chlorine Test Strip is by far the most often used test – by nearly all dialysis providers in the USA - to measure total chlorine (chlorine/chloramines) in water intended for use in dialysis. For that reason, it’s very important that questions 1-3 above be answered relative to the RPC K100-0118/F Ultra-Low™ Total Chlorine Test Strip and to determine how the RPC Ultra-Low™ test compares against other test methods such as 4500-Cl G (DPD).

<u>RPC K100-0118/F Ultra-Low™ Total Chlorine Test Strip Relative to Questions 1-3 Above</u>

1) In regard to question number one (1) above, AAMI - per its’ TIR58[3] “Water Testing Methodologies” document - and the TIR58 reference documents - recommends that dialysis source or feed water pH be within a range of 6.0 to 8.0.
   a. From TIR 58: *“The rate of the oxidation-reduction reaction responsible for the removal of chlorine and chloramines slows as pH increases. The pH of the water can interfere with RO membrane performance as well. Generally low pH water corrodes plumbing fixtures and faucets. Basic (pH>7) water can cause incrustation and scaling problems. High pH water could cause bicarbonate concentrates and dialysate to precipitate as well.”*
      i. A slowing of the oxidation-reduction reaction at higher pH levels may result in insufficient carbon to remove monochloramine to less than the 0.1 mg/l level…and a reduction of RO performance can result in a host of other issues. To reduce the pH of high pH water to within the AAMI recommended range a pretreatment side dealkalizer tank(s) or an acid injection pump should be employed. Due to possible day to day changes in the acid injection pump output, the dealkalizer tanks(s) would be preferable in most cases.

2) In regard to question number two (2) above, the RPC Ultra-Low™ Total Chlorine Test Strip does have a buffer built into the reagent that is integrated within the test strip test pad.

   a. RPC test data shows that - when used with the 20 second dip time and standard 100 ml sample size[4] – the test will accurately read/detect a 0.1 mg/L (ppm) chloramine standard reference solution within a pH range of 5.5 to 8.0. At a pH level of between 8.0 and 8.5, the test begins to be slightly affected (negatively) by the higher pH.

   b. RPC test data shows that - when used with the typical 60 second dip time and standard 100 ml sample size[4] – the test will accurately read / detect a 0.1 mg/L (ppm) chloramine standard reference solution within a pH range of 5.5 to 8.5. At a pH level of between 8.6 and 9.0, the test began to be affected negatively by the higher pH.

   c. Neither Ultra-Low™ test procedure (dip time) is impacted negatively within the AAMI recommended pH range.

   d. In the event the dialysis system feed water is outside the AAMI recommended pH range, there are two procedures that can be followed when using the K100-0118/F Ultra-Low™ Total Chlorine Test Strip.

      i. Using an RPC K100-0104 or K100-0104.5 pH test strip, monitor the feed water pH daily. If at any time the pH is greater than the AAMI recommended maximum of 8.0, use the K100-0118/F Ultra-Low™ 60 second dip time - and install a dealkalizer tank(s) to reduce the pH level to below 8.0. **This is the procedure recommended by RPC.**

      ii. To troubleshoot / determine whether or not the K100-0118/F Ultra-Low™ is accurately reading / detecting a level of 0.1 mg/l (ppm) chloramines in the subject water, use the RPC K100-0118QC Test Kit to test the test strip. This kit makes up an easy to use on-site 0.1 mg/l chloramine standard reference solution. If the test strip reads less than 0.1 mg/l in the reference solution (using the subject feed water), then it is likely the pH was high enough to affect the test strip. A second K100-0118QC kit can be used to test the test strip with the RO product water…as the RO process will reduce the pH when delivered as product water.

3) In regard to question number three (3) above, every lot of the RPC Ultra-Low™ Total Chlorine Test Strip is validated against two reference standards, the DPD 4500-Cl-G method, and a Chloramine-T 0.1 mg/l (ppm) reference standard solution.

   a. Both of these standard methods have been qualified against the amperometric titration analytic method (4500-Cl D) for total chlorine. Amperometric titration[5] is considered to be the “method of choice” and most accurate method for measuring total chlorine in interference free water.

   b. The Chloramine-T reference standard solution was created by the renowned PhD scientists at the Merck Group as the “Merck Chloramine-T Trihydrate Total Chlorine QA Analytical Method”.

      i. The Merck Group is headquartered in Darmstadt, Germany, with approximately 50,000 employees in around 70 countries. Merck was founded in 1668 and is the world's oldest operating chemical and pharmaceutical company, as well as one of the largest pharmaceutical companies in the world. Merck is a pioneer in testing chemistries.

      ii. Merck uses this Chloramine-T reference standard solution to validate its’ own total chlorine test strips.

      iii. RPC uses the exact same Merck Chloramine-T reference standard solution to validate every lot of its’ K100-0118/F Ultra-Low™ Total Chlorine Test Strips and its’ K100-0106 E-Z Chek® Sensitive Total Chlorine Test Strips.

c. How does the Chloramine-T reference standard compare against the use of a spectrophotometer for measuring the amount of monochloramine in a solution?

   i. Make-up of the Chloramine-T reference solution - **exactly at the critical value of interest for dialysis (0.1 mg/l)** - involves only the use of Chloramine-T powder mixed and serially diluted with purified water. Because there are only a few steps to make up this reference solution, the potential for error is minimized and serial precision (repeatability) in making up the solution is maximized.

   ii. A spectrophotometer does not discriminate between the sample of interest and interfering substances that absorb at or very near the same wavelength. Interfering substances can add to the actual monochloramine value which will result in a false high value.

   The detectors used in spectrophotometers are broadband, meaning they respond to all the light that reaches them. If there are impurities in the sample that reflect light, an erroneous reading may be recorded. Stray light also causes a decrease in absorbance and reduces the linearity range of the instrument.

   Absorption results can be influenced by temperature, pH, impurities and contaminants. All of these factors can change the absorption properties of the sample, leading to inaccurate readings.

   iii. Spectrophotometers require many procedural steps to complete each test[6].

   iv. The specified make up of a monochloramine reference standard solution used for calibration of the spectrophotometers typically requires multiple solutions / reagents[4]. It is step intensive to complete and as such introduces a high probability of error in the reference standard solution.

   In addition, if a lab technician were to carry out - without error - the make-up of the Hach specific monochloramine reference solution, the resultant reference value produced is 4.5 mg/l (ppm). This Hach specific “reference standard” value is 45 times greater than that of the critical dialysis value of 0.1 mg/l (ppm). Use of this extremely high reference value to calibrate the spectrophotometer would certainly introduce error when measuring a value that is 45 times less (i.e. 0.1 mg/l)

Summary

Many years ago, RPC recognized the need for an ultra-sensitive test capable of repeatedly delivering accurate results at levels of total chlorine less than 0.1 mg/l (ppm) in feed water for use in dialysis. An RPC exclusive partner test strip manufacturer had a unique patented test strip that looked promising for this application. Vern Taaffe of RPC worked directly with their Chief Technical Officer - an accomplished analytical chemist - to develop an RPC specific test strip for use in dialysis. After extensive research, testing, and RPC dialysis specific collaboration, RPC completed this project and released this unique test strip within the dialysis industry. This RPC product was developed specifically for use in testing water intended for use in dialysis.

That product is the K100-0118/F Ultra-Low™ Total Chorine Test Strips. One of the elements of the RPC Ultra-Low™ that differs from other total chlorine test strips is that the standard tolerance of the RPC Ultra-Low™ at 0.1 mg/l is designed to be entirely on the plus side of 0.1 mg/l. This is intended to prevent a false negative due to the test strip production tolerance.

In regard to choosing a reference standard for total chlorine measurement validation, RPC, chose Merck's credibility, knowledge, experience and track record - combined with RPC's own dialysis specific experience - over that of Hach and others. This RPC dialysis experience includes the clear understanding that AAMI/ISO/CMS standards do not call out or recognize the use of spectrophotometers for reference analysis of chlorine/chloramines residuals in water intended for use in dialysis. In addition, RPC recognizes that while each analytical reference method for chlorine/chloramines has its' own disadvantages, the "Merck Chloramine-T Trihydrate Total Chlorine QA Analytical Method" is best suited for use in this dialysis specific application.

Hach and others have had recalls of their chorine testing devices used in the dialysis industry, whereas in 30 years to date RPC has had no recalls of its chlorine testing devices. In addition, RPC has had three FDA inspections in the past ten years…resulting in zero citations. One of these FDA inspections focused on the K100-0118/F Ultra-Low™ Total Chlorine Test Strips.

RPC empirical data is evidence of the K100-0118/F Ultra-Low™ Total Chlorine Test Strips superior performance, validity, and success - in that minimal field complaints - including no false negatives and no dialysis patient issues – have been reported for approximately 100 million tests over the past ten (10) years.

Conversely, and prior to the RPC Ultra-Low™ gaining nearly the entire USA dialysis market for feed water total chlorine testing, the RenalWeb technician discussion forum[7] had nearly constant reports of issues with the Hach DPD tests (and DPD tests from other manufacturers). As a result of the Ultra-Low™ replacing the DPD tests, RenalWeb reports of problems with feed water chlorine testing have disappeared.

With a history / database of approximately 100 million tests over the past ten (10) years – and the disappearance of constant reports of DPD related chlorine test issues - it's clear that the RPC K100-0118/F Ultra-Low™ Total Chlorine Test Strips have been the answer – not the problem – for testing chlorine in dialysis system feed water (of all types) and for ensuring patient safety.

References

[1] USDA, Agricultural Marketing Service, Agricultural Analytics Division, Technical Evaluation Report, Hypochlorous acid, August 2015

[2] Hydro Instruments, Basic Chemistry of Chlorination, BCOC Rev. 7/10 Page 2

[3]Association for the Advancement of Medical Instrumentation (AAMI), Technical Information Report: TIR58:2014 Water Testing Methodologies

[4] RPC, K100-0118/F, Ultra-Low™ Total Chlorine Test Strips Instructions for Use, document number 072505S

[5] American Public Health Association, Standard Methods for the Examination of Water and Wastewater, 4-56, Chorine Residual Testing

[6] Hach Document DOC316.53.01015 Indophenol Method monochloramines / spectrophotometers

[7] RenalWeb, Technician Discussion Forum, chlorine testing blog, August 2009 – June 2010 (available from RPC)