DISINFECTION

ENHANCED TOC REDUCTION IN PHARMACEUTICAL WATER SYSTEMS USING HIGHLY REFLECTIVE UV DISINFECTION REACTORS

Ultraviolet (UV) systems are commonly used to provide disinfection in high-purity water systems used in pharmaceutical, biotech and diagnostic facilities, and research laboratories. The requirements for high-purity water used in pharmaceutical systems are governed by the U.S. Pharmacopeial Convention (USP) and enforced by the U.S. Food and Drug Administration (FDA). The requirements for Clinical Lab Reagent Water (CLRW), used in diagnostic facilities, is regulated by the Clinical Lab Standards Institute.

With a liberal USP and CLRW TOC specification of ≤ 500 parts per billion (ppb), the UV reactors in these high-purity water systems normally use "ozone-free" UV lamps that do not generate any UV wavelengths below 200 nanometer (nm), which means that they are usually assumed to have little effect on organic contaminants and are mainly intended for bacterial control. It has been observed, however, that high-purity water systems incorporating highly reflective UV reactors with ozone-free lamps are showing a significant reduction in total organic carbon (TOC) levels, compared to conventional UV systems.

The presence of TOCs in the water may have a negative effect on the performance of downstream processes, depending on the water's purpose, or the type of TOC, and may also require additional processing downstream. Additionally, there is some evidence that a correlation exists between TOC concentrations and the level of bacteria, endotoxin, and development or proliferation of biofilm within Purified Water systems. Dissolved organics, and the addition of UV systems to recirculating Purified Water loops, has shown an impact on the water's conductivity. While conductivity is one measure of water purity, it does not account for neutrally charged organics in the water. Municipal water supplies can often contain several hundred different organic species. UV is capable of breaking up these organics, thereby ionizing them with the production of carbonic acid, and subsequently reducing the water's conductivity.

In this study, TOC data was collected from 12 separate sampling sites of similar construction, using Purified Water from a recirculating loop: one site used no UV, four employed conventional UV reactors, and seven employed highly reflective UV reactors.

All used ozone-free (254 nm only) low-pressure mercury UV lamps, with the exception of two of each reactor type utilized lamps that produced both 254-nm and 185-nm UV light. The data show conclusively that, even when the reactor was fitted with "ozone-free" lamps that supposedly have no effect on TOC levels, the use of a highly reflective UV reactor in a UPW system designed for pharmaceutical production or biotech lab applications reduce the measured TOC levels from on the order of 30 ppb to about 3 ppb.

Meeting Specifications

In the past, achieving the guidelines laid down by USP or CLSI (Table A), or surpassing them, often required more expensive systems with multiple UV lamps, producing both 254 nm for disinfection, and 185 nm for TOC removal. New installations with highly reflective UV technology are obtaining high-purity water that has TOC levels of as much as an order of magnitude lower than that for similar systems with conventional UV reactors, at costs competitive with those systems, and are achieving this with "ozone-free" (254 nm only) low-pressure mercury UV lamps. Lower TOC levels can reduce microbial proliferation, biofilm formation, and system component fouling, thereby improving system performance, water quality consistency, reliability and maintenance cost.

Some of the distinctive characteristics of newer high-purity water systems include infrared machine welded high-purity piping and connections/materi-

TABLE A
Requirements for High-Purity Water found in the USP and CLRW Guidelines

	USP	*CLRW*
Specification	*Tolerance*	*Tolerance*
Added substances	none	N/A
Conductivity	≤ 1.3 µS/cm[1]	≤ 0.1 µS/cm
TOC[2]	≤ 500 ppb	≤ 500 ppb
cfu (mL)[3]	≤ 100 cfu/mL	≤ 10 cfu/mL

Notes:
[1] *microsiemens per centimeter at a temperature of 25°C*
[2] *Total Organic Carbon in parts per billion*
[3] *Colony-Forming Units per milliliter*

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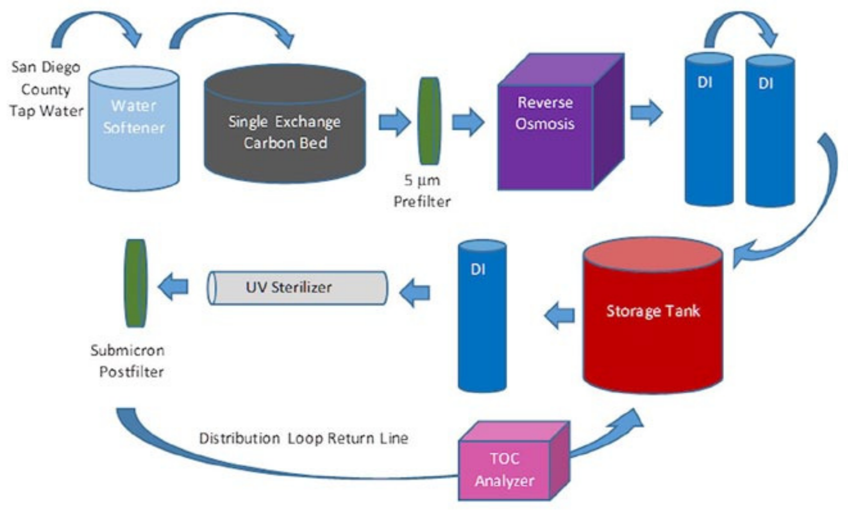

Figure 1. Basic diagram of high-purity water treatment system used in study.

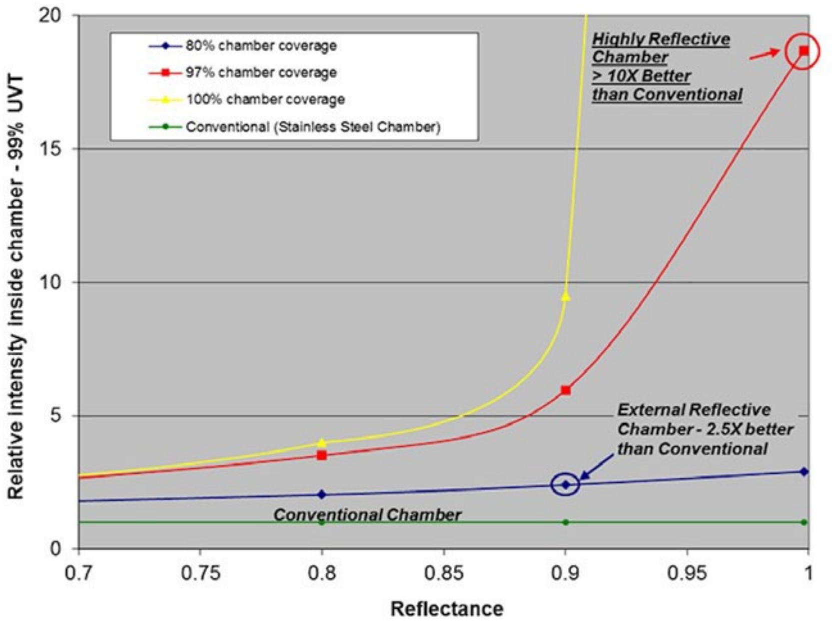

Figure 2. Relative intensity inside a UV chamber at 99% UVT.

als with low extractable water contact materials throughout. Minimization of airborne and gas contaminants is also important to maintaining high-purity water. Higher recirculation rates assuring a "clean" flow path with minimal dead space of less than 6 diameters (< 6D) as according to Genova (1) is a key design parameter. These parts all fit in with sanitary design considerations to use compatible materials, minimize deadlegs, and optimize pipe velocity. Higher quality ion exchange (IX) resins or electrodeionization (EDI) is useful for keeping the high-purity water in a highly polished condition.

Possible TOC leaching and potential upsets to a high-purity water system can consist of exposing the system to atmospheric contaminants during maintenance, including filter changes, consumables replacement, and RO membrane replacement. Spraying down connections or gaskets with isopropyl alcohol, changing out piping or point-of-use (POU) modifications (especially polyvinyl chloride [PVC]) are also potentially problematic, as are changes in the system vacuum or process water intrusions (fermentation connections).

As stated, there is a greater likelihood of higher TOC values in new high-purity water systems and from newer system parts because of their leaching of organic extractables. In this case study, which employed the TOC measurements of UPW systems that ranged from 1 week old to 11 years old, there were no discernable differences in TOC levels because of the system age. This is attributed to the TOC reduction because of the inclusion of HRC's overcoming any high leaching rates associated with new parts in the system.

Test Systems

This study focused on the quality of loop water systems at life sciences facilities. These test sites, located in San Diego County, CA, used local, municipally treated water as the feedwater source, which generally has a TOC level of 2-4 parts per million (ppm). Figure 1 shows the typical elements of the system.

First the source water is pretreated, often using IX softening to remove hardness, followed by granular activated carbon for chlorine removal. All the systems employed 5-micron (µm) prefiltration prior to single-pass reverse osmosis (RO) and subsequent mixed-bed deionization (DI) to remove most of the remaining dissolved solids prior to filling a reservoir storage tank. High-purity water pumped from the storage tank flows through additional mixed-bed DI, the UV reactor(s), and downstream submicron final filters for additional purification and polishing before the UPW is distributed to the POU located on the recirculating loop.

High-purity water that is not used at the POU is recirculated back to the storage tank and downstream polishing system. The TOC analyzer used in this study was located on the distribution loop return, just prior to the storage tank and downstream processing through the DI polishing system. This location would be indicative of a worst-case analysis position for any contaminants picked up from the recirculation loop and POU. Leaching of organics from filters, plastic loop piping, storage tanks, faucets, tubing, seals, and gaskets will increase this level without remediation.

A general rule of thumb is that newer system parts will leach more organics into the system than old, potentially contributing another 200 to 1,000 ppb of organics into the recirculating loop. Depending upon the organic species, flowrate, temperature, pH, water conductivity, it may take several weeks and many rinses of the entire loop and storage tank to rinse or process these elements out.

UV System

An important aspect of TOC reduction is the need for a higher clarity of USP water. This not only contributes to the overall sanitary conditions of the system itself, but also promotes the further TOC reduction ability through the availability of UV light transmission. UV treatment relies on the ability of the light to transmit through the water column, this characteristic is known as UV transmittance (UVT). High-purity water used in pharmaceutical process water, post RO, usually transmits more than 98% of the UV light through 1 cm of water, which is defined as 98% UVT. For comparison, tap water is typically between 92% and 94% UVT. Impurities such as chlorine and other total dissolved solids (TDS) absorb the UV, reducing the transmittance of tap water.

UV reactors are typically one of three designs; conventional chambers, external reflective chambers (ERC), and highly reflective chambers (HRC). Figure 2 shows the calculated relative UV intensity inside each of these designs as a function of both water UVT and reflectivity of the reflector, with conventional chambers used as a reference. These data are based on published performance specifications for each of these reactors.

The key issue when designing or sizing a UV system is to achieve the required dose within the treatment chamber. In a conventional chamber, this is achieved through the use of larger chambers with more lamps, since only 20% to 30% of the light will reflect off the stainless steel chamber. In the ERC designs, the lamps are external to the water tube and positioned so that aluminum reflectors allow for multiple passes of the UV through the water, but most of the UV is external to the water column. The result is a reduction in the number of lamps required, but there may be limits on the flow, and hence the dose, that can be achieved in a single chamber.

In the HRC design, the use of a reflector around the water column captures the UV rays and reflects them back into the water, with the illuminated volume matching the water volume as closely as possible. As seen in Figure 2, this is the most efficient use of the UV light radiating from the lamp since almost all of the illumination is in the water versus in the air gap between the reflector as with the ERC design in Figure 2. Figure 3 highlights the design configurations of the three methods, and Figure 4 shows a cut-away view of the HRC flowtube.

The Study

TOC measurements were taken at 12 different locations with high-purity water systems in the San Diego area. All used local tap water as their source. With the exception of sample location I1, which is a conventional dual reactor setup with 254-nm and 185-nm UV where TOC analysis was performed at the loop supply, the TOC sampling for the other 11 sample locations was performed at the return loop of each high-purity water system. Sample point "A" (see Table B below) was chosen as the control as it did not employ a UV reactor in the loop water system.

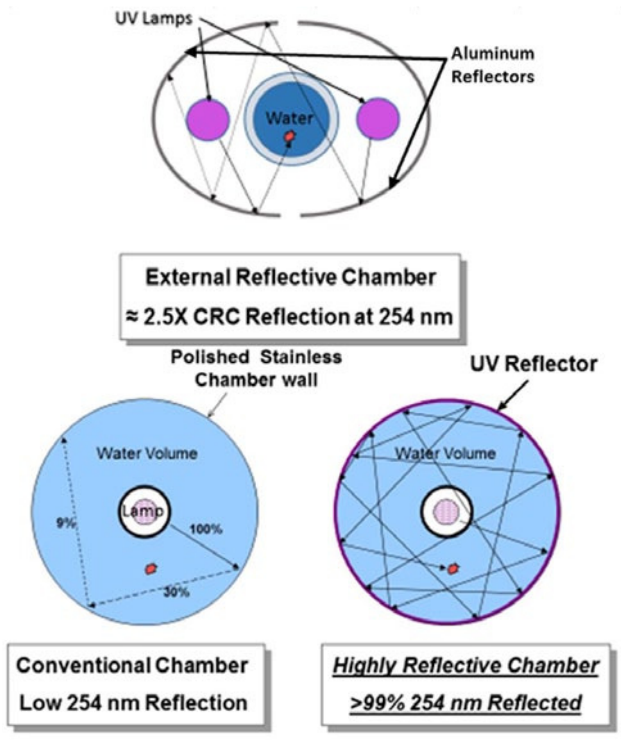

Figure 3. The reflectivity of an ERC, CRC, and a HRC. The HRC reflects >99% of the 245-nm light (photons), allowing for greater destruction of bacterial and organic contaminants in the water.

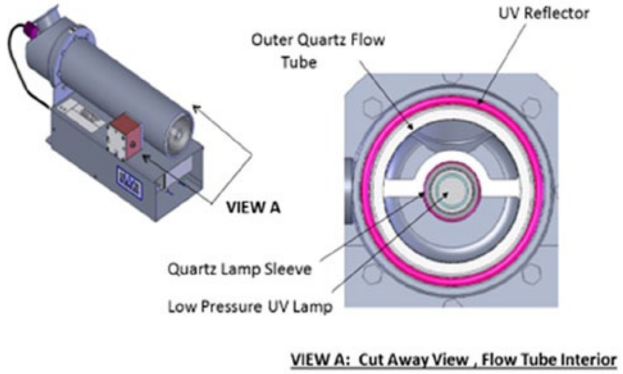

Figure 4. Cut away view of the flow tube interior for the HRC used in this study.

Process Description

A model example of the specifics of the systems used in this study is shown in Figure 1. System configuration, materials of construction, and system operational parameters can all have an effect on TOC reduction performance. All of the systems selected and tested in this study adhered to this configuration in an effort to minimize extraneous variables associated with TOC reduction. The following paragraphs provide a process and system component description, along with general operational and performance parameters.

For all of the systems tested, San Diego municipally treated water is first pretreated with ion exchange softening to remove hardness ions and prevent scaling of downstream RO membranes. Softened water is then fed to a granular activated carbon bed to remove oxidizing compounds along with some minimal organic removal. Softened, dechlorinated water is then fed to

TABLE B
Comparison of Cases

Location	*UV Type*	*Power [W]*	*TOC (ppb)*	*Specific En. [kW-h/kgal]*	*Log TOC Reduction (30 ppb base)*	*EE/O [kW-h/kgal/log]*
A	none	--	30	--	--	--
B1	conv. 254	190	35	0.075	none	--
B2	conv. 254/185	540	5	0.300	0.778	0.386
C1	conv. 254	265	23	0.164	0.115	1.426
C2	HR 254	85	5	0.018	0.632	0.028
D	HR 254	85	7	0.089	0.778	0.114
E	HR 254/185	85	2	0.202	1.176	0.172
F	HR 254	85	5	0.030	0.778	0.038
G	HR 254	85	5	0.118	0.778	0.152
H	HR 254	85	3	0.202	1.000	0.202
I1	conv. 254/185	122	21	0.239	0.155	1.542
I2	HR 254	85	6	0.118	0.699	0.169

a 5-µm prefilter to remove particulate prior to a single-pass RO system. The single-pass RO system is designed to remove 95% to 99% of source water ions as well as most of the source water organics larger than 10 angstroms.

Most of the RO systems used in this study used the latest ultra-low-pressure RO membranes, operating -at feed pressures below 100 pounds per square inch gauge (psig), and performing at an average ion rejection of 98%. Four of the 12 test locations that had conventional UV reactors (B1, B2, C1 and I1) used higher pressure RO membranes operating at 140 to 180 psig and an average ion rejection of 98% to 99%. Higher pressure RO is typically indicative of increased ionic and organic rejection.

Since all of the RO systems tested were fairly small systems supporting life science lab facilities, recoveries for all of the RO systems tested was 35% to 65%. RO permeate was further deionized with semiconductor grade mixed-bed DI resin, followed by 0.2-µm filtration prior to filling a conical polyethylene storage tank.

High-purity water measuring 17.5 to 18.2 megohm-cm resistivity is pumped from the storage tank to the recirculating/polishing distribution loop. Prior to distribution to the POU, the high-purity water is further polished. Except for the conventional UV reactor systems, which included additional UV reactors, all of the systems had semiconductor-grade mixed-bed resin, followed by a UV reactor and submicron filtration prior to distribution to the POU. The polishing systems with conventional UV reactors included a 185-nm UV reactor before the polishing mixed bed, and a 254-nm reactor after the polishing mixed bed.

Figure 5. System I1 with conventional 254-nm and 185-nm UV reactors.

Conductivity or resistivity along with temperature is monitored online at the loop supply. Except for location I1, TOC was monitored online at the loop return. Location I1 included on-line TOC measurement at the loop supply immediately downstream of the polishing equipment.

All of the systems tested were designed as USP PW, or Clinical Lab Reagent Water systems, and included heat-fused polypropylene distribution piping operating at recirculation velocities of 4 to 6 feet per second. Routine maintenance was performed on all of the systems, including annual system sanitization using Minncare cold sterilant. Routine microbial testing is performed on each system to maintain typical cfu counts of < 10 cfu/mL, and continuous resistivity measurements of 17.5 to 18.2 megohm-cm at ambient temperatures (22 to 28°C).

Results and Discussion

In this study, 12 USP water systems were used to measure TOC after treatment with UV sterilization at 254 nm or 254/185 nm in conventional or HRC units. The log TOC reduction was calculated using 30 ppb output from the RO-only system from location A (see Table B) as the baseline.

Of particular note are the last two locations tested, I1 and I2 (Figures 5 and 6). Both of these systems are located side-by-side, serving different labs on identically constructed distribution loops in the same building. Both systems use the exact same feedwater source, same model Sievers 500RL on-line TOC analyzer and, except for the use of conventional versus HRC UV reactors, both systems utilize equivalent purification processes and system configurations.

Key differences between these test locations are that I2 was only 1-week old at the time of testing and had received only 700 gallons of rinsing compared to I1 which is 3 years old and received 493,000 gallons of rinsing. I2 TOC was measured on the loop return, whereas I1 TOC was measured on the loop supply. These key differences would normally indicate a worst case TOC measurement condition for I2 versus a best-case TOC measurement condition for I1, further emphasizing the significant performance difference between conventional and HRC reactors.

In addition to the TOC level, the power consumption was also measured in Watts (W) for each UV unit. Specific Energy was then calculated in kilowatt hours per thousand gallons (kW-h/kgal), which enabled the calculation of Electrical Energy per Order (EE/O). The conventional chambers used power in a range from 190 to 540 W, while all of the HRCs used only 85 W. The largest difference in EE/O was between the conventional reactors I1 at 1.542 kW-h/kgal/log EE/O, achieving a level of 21 ppb TOC, and HRC C2 at 0.028 kW-h/kgal/log EE/O, achieving a level of 5 ppb TOC.

The results presented in Table B show that systems employing HRCs have significantly lower TOC levels and a lower EE/O to achieve those lower levels. Note in particular that every system with 254-nm-only lamps in a conventional reactor has a TOC level above 23 ppb, while every system with 254-nm-only lamps in HRC reactors has a TOC level below 7 ppb. Also, the better TOC levels in the HRC systems were achieved with lower power requirements than that for systems with conventional reactors. In addition, the conventional reactors all used more EE/O of TOC reduction, even when the system was fitted with individual 254-nm and 185-nm reactors.

The mechanism behind these improvements is being studied but is not yet well understood. It is suspected that the 254-nm light is dissociating some of the TOC components that can absorb photons at that wavelength. The higher efficiency of the HRCs as compared to that in conventional chambers leads to more photons available to interact with those particular TOC molecules. This in turn leads to more TOC molecules being converted into molecules that can be removed by the IX resins, leaving fewer TOCs in the water. The future plans section discusses the approach to verify and quantify this hypothesis.

Conclusions

High-purity water systems using 254-nm-only highly reflective UV reactors have significantly lower TOC levels than those using 254-nm-only conventional UV reactors. This phenomenon can also be seen in newly constructed systems with typically higher organic leachable contaminants. These reactors are therefore achieving TOC levels equivalent to those employing dual 254/185-nm conventional UV reactors, while using much less energy and with lower capital outlay. High-purity water systems using 254/185-nm highly reflective UV reactors have even lower TOC levels than those employing 254/185-nm conventional UV reactors, also with much less energy and less capital outlay. 254-nm-only conventional reactors appear to have no effect on TOC levels.

Figure 6. System I2 with single HRC UV reactor.

As mentioned previously, lower TOC levels in high-purity water systems can be beneficial for the continued well-being of the system, by reducing biofilms and other fouling. Given our constantly changing water supply because of scarcity, flooding, changes in sources, seasonality, and increasing population demand, organic contaminant profiles will change, placing additional demand on purification and control procedures.

USP and CLRW water specifications allow for up to 500 ppb TOC. The reduction accomplished by the RO/DI system to 30 ppb, accompanied by the further reduction of TOC to levels down around 2 ppb, can be an added bonus to companies that have the need for water with significantly low TOC such as high performance liquid chromatography (HPLC). High TOC levels can interfere with life science experiments and analyses, creating the need without HRC reactors to buy expensive HPLC water.

Planned Future Work

Speciation of the TOCs flowing into and out of high-purity water systems is always an ideal goal. Furthermore, being able to speciate the TOCs to identify those susceptible to dissociation in the 254-nm-only reactors would help with a better understanding to the mechanism of the TOC reduction observed. However, as every water system and the water itself at different locations are all unique, this is a costly and time consuming undertaking.

This was a relatively small sample set, even though the results are very clear cut, that highly reflective UV can effectively reduce TOCs in high-purity water. It would be beneficial to collect data from other sites to further verify the observed effects.

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