

# State of the Art Sanitisation of Purified Water (PFW) UV

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## ■ ABSTRACT

This report focuses on sources, proliferation and control of microbiological growth inside a purified water (PFW) tank. The most widely used practice in the industry for controlling microbiological growth inside tanks and pipework is to operate the PFW system with frequent hot water sanitisation and regular microbiological monitoring to ensure the water being of an appropriate microbiological quality at the points of use. Worldwide, the majority of PFW tanks are operated at room temperature, and throughout normal operation these tanks store the bulk of the water whilst a small amount is in circulation. It is a well-known fact that PFW tanks working above a certain room temperature present conditions which assist significant microbial growth. However, there is no specific microbial control system functioning for the bulk water stored inside the tank. As a result, microbial growth accelerates thus necessitating hot water cleaning of the PFW tank at regular intervals (typically once a week). By utilising advanced tank disinfection technology, the microbial growth is inhibited inside the PFW tank. This enables PFW tank operators to achieve longer intervals between sanitisations and as a result plant productivity increases and operating costs can be expected to reduce.

## ■ KEY WORDS

- Pharmaceutical industry
- Purified water
- Microbiological contamination
- UV disinfection of tanks
- Quality control
- Microfloat

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## ■ ZUSAMMENFASSUNG

### Desinfektion von Pharmawasser nach dem Stand der Technik

Dieser Bericht konzentriert sich auf die Ursachen, Ausbreitung und Kontrolle der Verkeimung von Pharmawasser in Pharmawassertanks.

Die übliche Vorgehensweise in der Pharmazeutischen Industrie zur Desinfektion/Keimkontrolle von Pharmawasser in Lager- und Verteilungssystemen ist die regelmäßige Behandlung mit heißem Wasser. Damit soll sichergestellt werden, dass das Pharmawasser eine angemessene mikrobiologische Qualität an den Entnahmestellen aufweist.

Weltweit wird die Mehrheit der Pharmawassertanks bei Raumtemperatur betrieben und bei normalem Betrieb befindet sich der Großteil des Wassers im Tank während nur ein kleiner Teil des Volumens im System zirkuliert. Es ist bekannt, dass Pharmawassertanks, die eine längere Zeit oberhalb einer bestimmten Raumtemperatur betrieben werden Bedingungen bieten, die ein signifikantes mikrobiologisches Wachstum unterstützen; gleichzeitig ist im Pharmawassertank jedoch keine permanente Senke für die Verkeimung vorhanden, womit dem Betreiber die dauerhafte Kontrolle über das System fehlt. Die regelmäßige Reinigung und Keimabtötung durch eine thermische Behandlung des Pharmawassertanks (üblicherweise einmal pro Woche) mit Heißwasser ist die derzeit anerkannte beste Lösung.

Mit der integrierten in-situ Tankdesinfektion kann das mikrobiologische Wachstum innerhalb des Pharmawassertanks permanent und zuverlässig unterbunden werden. Dies ermöglicht es Betreibern von Pharmawassertanks längere Intervalle zwischen den Reinigungen zu erreichen, wodurch die Produktivität erhöht und eine Reduzierung der Betriebskosten erreicht wird.

## 1. Introduction

This report considers the modern room temperature operated purified water (PFW) Generation and Distribution system in relation to issues due to microbial growth [1]. It also highlights the use of advanced tank disinfection technology which addresses most of the issues faced by today's room temperature operated PFW tanks.

Water is widely used in the pharmaceutical industry, especially in the processing, formulation, and manufacture of pharmaceutical products, active pharmaceutical

**Table 1**

USP specification according to USP 24–28.

United States Pharmacopeia 24–28 (USP 24–28)	
Test	PFW (PFW)
Conductivity	< 1.3 $\mu\text{S}/\text{cm}$ at 25 °C
pH	5.0–7.0
Total Organic Carbon(TOC)	< 500 ppb
Total Bio burden	< 10,000 CFU/100 ml
Endotoxin	N/A
Coliform Level	0/100 ml
Source water – U.S EPA National Primary Drinking water Regulations	

**Table 2**

European Specification according to EP (2005).

European Pharmacopeia ( 2005)	
Test	PFW (PFW)
Total Organic Carbon (TOC)	NMT 0.5 mg/l
Conductivity (20 °C/25 °C)	4.3/5.1 $\mu\text{S}\cdot\text{cm}^{-1}$
Aluminium	NMT 10 ppb*
Heavy metals	NMT 0.1 ppm
Nitrates	NMT 0.2 ppm
Total Variable aerobic count	100 micro/100 ml
Bacterial Endotoxin	< 0.25 IU/ml
Source water – U.S EPA National Primary Drinking water Regulations	

\* If intended for use in the manufacture of dialysis solution

ingredients (APIs), intermediates and the analytical reagents. Water used – PFW and Water For Injection (WFI) – is vital to the manufacture of drug products. Water should be considered as a raw material which must, at a minimum, comply with specifications set out in Pharmacopeia and as guided by USA [2, 3] and International GMP issues, engineering guides or regulatory bodies (FDA, EUP or WHO) and individual national and regional authorities' guidance [4].

The majority of feed water for PFW production is drinking water from municipal or ground water sources. The treatment begins by purifying the source water using a number of treatment systems and operations including softening, filtration, ion exchange, reverse osmosis, deionization and/or other suitable purification procedures including microbiological growth prevention [5–7].

PFW systems must be monitored in order to reliably and consistently produce and distribute water of acceptable chemical and microbiological quality. PFW systems operating above certain ambient temperature conditions are particularly susceptible to the formation of persistent biofilms of microorganisms, which can be the source of

undesirable levels of microorganisms and/or endotoxins in the water.

## 2. PFW international specification

Table 1 and 2 show the international specifications of PFW according to regulations in the USA and Europe [2–4].

## 3. Water Treatment today – PFW generation and distribution (embedded issues)

In this section, the weak points of the water purification, storage and distribution of today are considered. All systems which have been visited by the authors included, to varying degrees, the following:

- PFW Generation – source water purification, softening, polishing and bacterial control up to PFW tank inlet
- PFW Storage and Distribution – microbiological control in the distribution loop and delivery at the point of use

PFW generation systems and processes vary from site to site and region to region. Therefore, it is difficult to generalise the PFW system operation. Hence, in this paper the authors' solution is focused on the most widely and commonly used room temperature operated PFW generation and distribution system.

### 3.1 PFW Generation – Typical schematic and the existing issues

As shown in Fig. 1, PFW generation usually is from operations at ambient room temperature and the quality of water produced varies according to the operating conditions:

- 1) Quality of feed water may vary (e.g. due to seasonal changes).
- 2) The reliability and robustness of the water treatment equipment.
- 3) Ambient temperature PFW systems are especially susceptible to microbiological contamination; particularly when the equipment is static during periods of no or low demand for water.
- 4) Reverse Osmosis system membranes are "bacterial fermenters".
- 5) Efficiency, effectiveness of the in line UV-system; in order to maintain a high Reynolds number (turbulent flow), a very high capacity discharge pump is used at the tank outlet. This significantly reduces the residence time of water inside the in line UV-system.
- 6) There are a number of intermediate storage tanks in the system typically after UF/RO. The construction and operation of these tanks are very different to PFW tank and the water stored in these tanks is not subjected to any treatment.

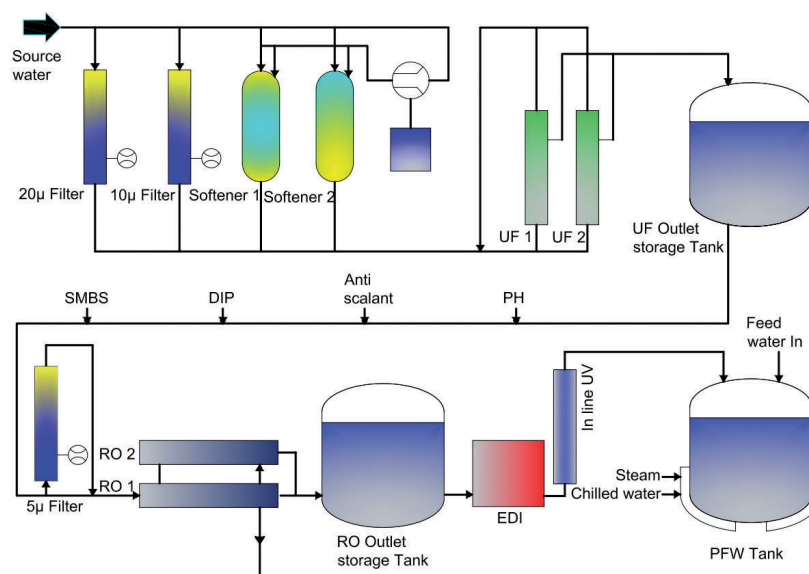


Figure 1: Typical schematic of installations to generate PFW (Source of all figures: Enviolet GmbH).

- 7) Frequent sanitisation is required for all water treatment equipment.
- 8) Cost of power and chemicals consumed by water treatment equipment compound the cost of PFW generation.

### 3.2 PFW tank storage and distribution systems – schematic and existing issues

An alternate PFW Storage and Distribution system is shown in Fig. 2 below. The generated PFW is fed into the PFW tank which is required to provide an adequate volume of PFW for peak-consumption and circulated for permanent availability to the production process. The storage and distribution system is a key part of the whole system. Once water has been purified using an appropriate method, it can either be used directly or, more fre-

quently, fed into a storage tank for subsequent distribution to user points. PFW stored in this way will have to meet manufacturing needs in terms of quality and quantity.

Any storage and distribution system should be designed and built to prevent recontamination of the water after treatment. However, this is the area where the current advanced purified systems lack appropriate additional controls to reduce significant microbial growth and ensure the quality of PFW is maintained [7, 8].

Usually the *PFW tank storage systems* as shown in Fig. 2 operate at ambient room temperature and depending on status and operation the following issues can be observed:

- 1) PFW tanks store typically over 90 % of water volume with the remainder in circulation in the pipework. A huge volume of water is not treated inside the storage tank (5)–(8) refer systems according to chapter 5, Alternative 1).
- 2) There is virtually no control of microbial growth inside the storage tank where over 90 % water is kept at any given point in time.
- 3) In order to prevent or minimize the development of biofilm, regular hot water sanitisation is necessary, typically once a week.
- 4) Hot water sanitisation, which takes typically 6–8 h, causes interruption in the plant operation, non-utilisation of man power and loss of production capacity.
- 5) Storage tanks require venting to compensate for the dynamics of changing water levels:
  - Such vents are a potential source of untreated air entry.
  - Mechanical integrity of vent filters is an area of concern.

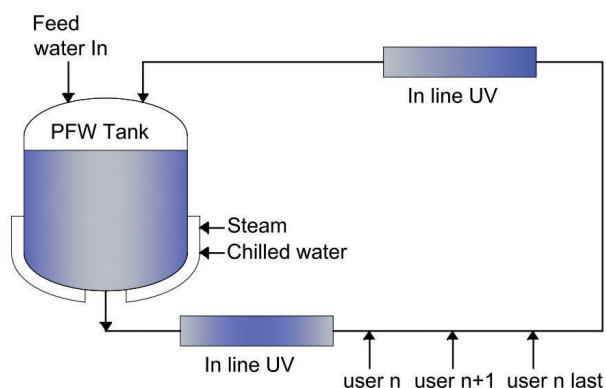


Figure 2: Typical schematic of PFW storage and distribution without advanced tank sanitisation.

- Heated vented filters require frequent inspection for heat tracing.
  - Condensation within the filter matrix might lead to filter blockage and to microbial growth which could contaminate the storage tank.
- 6) Unalarmed pressure relief valves or busting disks are meant to protect the tank from over pressurisation.
    - Disk failures may be caused by equipment blocked by condensate which is a source of microbial contamination.
    - Any mechanical failure which remains unchecked will result in huge bio burden increase in the PFW.
    - Test results are genuinely not available until 5 days after bio count checking.
  - 7) The space above the water inside the tank is a potential area for bacterial growth.
    - Bacteria which enter the tank find themselves a safe haven in this zone (i.e. above certain temperatures the spray ball water droplets and air encourage rapid bacterial multiplication since the conditions inside the tank are very favourable for bacterial growth. Bacterial contamination of the PFW is inevitable).
  - 8) Nozzles within the storage tank with dead zones (spare nozzles and nozzle height) harbour microbial contamination.
  - 9) Similarly, a hairline scratch of 0.3 microns or more in the tank's inner walls can also harbour bacteria and help them to multiply and contaminate the PFW.
  - 10) If the water inside the tank is infected then contaminated water is delivered to production. Often companies establish SOPs based on their experience. The PFW tank SOP relating to sanitisation is mostly driven by the bacterial counts. The typical values are 40 CFU/ml as an alarm limit and 50–60 CFU/ml as action limit. Frequent cleaning affects productivity and increases the cost of PFW.
  - 11) Residence time of water within the tank – this depends on the tank size, the actual volume of water stored inside the tank, recirculation rate and the length and size of the distribution pipework. The higher the residence time inside the tank, the higher the chances of bacterial divide.
  - 12) Use of sanitising agents (chemicals) can increase the length of the cleaning process. Plant operators have to spend extra time and effort to ensure that all the sanitising chemicals (ozone) are completely removed prior to the distribution of water to user points.
  - 13) Practical issues relating to safe handling of chemicals used for regeneration and sanitisation.
  - 14) Vast consumption of both chemicals and energy for sanitisation of PFW tanks operating at room temperature.
  - 15) The cost of this consumption of chemicals and energy is compounded in the case of PFW tanks operating with:

- Direct addition of oxidants such as ozone into the tank.
- Continuous indirect heating of the PFW by applying steam in the outer jacket of the PFW tank.
- Continuous cooling of PFW by circulating chilled water in the outer jacket of the PFW tank.

The *distribution system* of PFW usually shows issues at several points:

- 1) Circulation pump dead zones trapped within the system are a source of microbial contamination (especially at the time of start up after hot water sanitisation).
- 2) While circulating in pipework, there are chances for increase in CFU counts/ml of the PFW. This would depend on the piping length, route, the bends, 2D piping guidelines, recirculation rate, temperature to which the piping is exposed etc.
- 3) There are in line UV systems at the tank outlet and or at the return line to prevent microbial growth.
- 4) In many cases, the sampling point is after the in line UV system in the return line (in this case the actual CFU/ml counts at the distribution points are different from the ones at the sampling points).
- 5) PFW from the tank is subjected to the in line UV treatment system prior to its delivery to production. Areas of concern can include adequate UV intensity and residence time, gradual loss of UV emissivity with bulb age, gradual formation of UV-absorbing film at the water contact surface and unapparent UV bulb failure.
- 6) Sometimes, the return water from the production blocks is also subjected to in line UV treatment prior to returning to the PFW tank via a spray valve assembly. Areas of concern here include adequate UV intensity and residence time, gradual loss of UV emissivity with bulb age, gradual formation of UV-absorbing film at the water contact surface and unapparent UV bulb failure.
- 7) Occasionally, in line ultra-filtration is used to remove bacteria from the circulating water – here the known issues of ultra-filtration apply.
- 8) Endotoxin concerns usually employ an in line ultra-filtration or charge modified filters – here the known issues of ultra-filtration apply.
- 9) If in line UV-systems are switched off during sanitisation, there is a period of time after being switch on again when the in line UV system is not effectively engaged in fighting bacteria because it takes a while for a UV lamp to reach full power after being re-started.
- 10) Components and distribution lines should be sloped and fitted with drain points so that the system can be completely drained. Drained but moist surfaces will still support microbial growth and proliferation. The initial water returning to the tank, without a fully functional in line UV system can pass water with



bacterial contamination into the tank. Thus, the bacteria which enter into the tank may multiply/divide inside the tank.

#### 4. Supplementary techniques adopted to limit microbial growth and its proliferation

It can be necessary to carry out additional operations to limit microbial growth and to ensure stable and optimal operating conditions:

##### *Alternative 1*

The bactericidal treatment of water by directly injecting a small quantity of ozone into the PFW tank is a technologically sound option. Residual ozone, if not eliminated, may cause considerable stress on the downstream usage and processes. The removal of residual ozone prior to use can result in additional costs and usually produces H<sub>2</sub>O<sub>2</sub> as by-product if UV-irradiation is used to eliminate ozone. Although residual ozone is supposedly eliminated by in line UV treatment systems, in reality plants struggle to achieve ozone free water. As a general rule a UV dosage of 90,000 (J/m<sup>2</sup>) is required to completely destroy 1 ppm (1 mg/l) of residual ozone but in line UV systems are rarely capable of delivering such a high UV dosage. Besides the UV exposure time for fast transient water inside the in line UV reactors is of concern. Therefore plant operators face a very serious challenge with a direct ozone dosing system as it is essential to remove the chemical agent (ozone) prior to supplying the water to the user points. They also encounter issues as a result of the slower rate of ozone destruction due to higher half-life time of ozone in the PFW; contaminated waters show shorter half-life times for the decomposition of ozone to oxygen.

##### *Alternative 2*

Another approach is to control bacterial growth by the continuous application of steam in the outer shell of the tank and heating the entire volume of PFW to 65 °C to prevent bacterial growth. Technically this is an acceptable and a practically feasible solution. However, this method of operating the PFW tank to limit the bacterial growth prevention is expensive.

##### *Alternative 3*

A third option to inhibit the bacterial divide is to continuously circulate chilled water in the outer shell of the tank to maintain the entire volume of PFW at temperatures below 20 °C to prevent bacterial division. Technically this solution is an acceptable and practically feasible solution. However, this method of operating the PFW tank to limit the bacterial growth prevention is very expensive.

Even by utilising the above listed supplementary alternatives, users continue to perform hot water tank sanitisation, albeit with a longer period between the sanitisa-

tions (typically once every 3–4 weeks), as this method is part of the validation.

#### 5. Advanced Tank Disinfection Technology by disinfection in place

In applications in which microorganisms contaminate process water and potentially lead to an unacceptable level of rejects and interruptions to the production schedule, the best solution is to integrate UV disinfection into the production process [9].

An Advanced Tank Disinfection System consists of floating and immersed active UV disinfection devices, with various property rights hold by a.c.k. aqua concept (Germany). Microfloat<sup>®</sup> – a floating UV disinfection device irradiates both the air above and the water inside the PFW storage tank, as well as the tank walls above and below water surface. Bacterial elimination from air and water inside the tank as well as sanitisation of tank walls above and below water surface are secured by this device. Microspear<sup>®</sup> – an immersed UV disinfection device which is designed to be fully or partially submerged in water and also in direct contact with the air inside the tank irradiates the water and helps to eliminate bacteria from water and tank walls below water surface.

Based on the tank size, volume of water, recirculation rate and other parameters, the number of Microfloats and Microspears required are engineered to fit in a particular tank. In short, the tank itself is converted into a large UV reactor by combining these 2 UV devices. This method not only enables total disinfection but also builds up a complete germ barrier inside the tank. The result is that more than 98 % of the PFW is permanently under UV-irradiation and the build-up of biological growth is prevented.

It is evident that existing PFW systems are operated with excessive reliance on frequent hot water sanitisation of the PFW system components (a) chemically at generation stage before the water enters the tank and (b) thermally in the tank and the distribution lines.

In most cases, current PFW treatment methods affect production schedules, as there will be no PFW available at point of use during hot water sanitisation. The cleaning process varies from plant to plant and lasts typically 4–8 h. This can significantly reduce the available production time and capacity.

The Advanced Tank Disinfection System as shown in Fig. 3 is designed to:

- 1) Eliminate bacteria which have entered the tank in the source water.
- 2) Eliminate bacteria which have entered the tank through the vent filter.
- 3) Eliminate bacterial growth inside the tank head space, tank water and moist tank inner wall surfaces.

4) Act as an insurance system to compensate for any mechanical/process failure in any of the water treatment modules that are used in the water generation system that are actually designed to prevent the microbial contamination/proliferation.

5) Ensure that bacteria cannot survive inside the tank. Table 3 shows a calculation for the UV dose in conventional through-flow reactors and inside a tank equipped with the advanced tank disinfection devices; the data is derived from a pharmaceutical manufacturing plant.

The calculation is based on the following conditions and a mathematical program based on a symmetric model was used, which was specially designed for the layout of UV disinfection reactors and equipment:

- Spectral Absorption Coefficient at irradiation wavelength of 254 nm to be 1/m; in PFW values for SAC(254) between 0,1/m and 1/m are typical, so calculation with 1 is under worst conditions.
- Average lamp live at 90 % dose of a new UV-lamp.
- UV-light assumed as central light source within water body.
- UV-power of floating device available for water sanitisation to be 60 % only.
- Flow rate is same as water replacement/consumption

- No reflection of UV-light from the reactor jacket (= PFW tank walls).

This data shows that the advanced disinfection system produces a UV-dose more than 10 times higher than a conventional system, even at lower power consumption. The main advantage is that this extreme dose is not applied to a small volume of water passing a sanitisation device for some seconds per h. The advance disinfection system keeps more than 98 % of the PFW inside the system comprising PFW storage tank and distribution system permanently sanitized, whilst the conventional system only keeps approximately 1 % of the PFW sterile.

## 6. Example of Advanced Tank Disinfection Technology in an API manufacturing unit

### 6.1 Background

A company is engaged in manufacturing API for in house, export and domestic consumption. They operate a 3 KL PFW tank. The PFW system feeds 3 production blocks spread over 3 floors with a number of user points and the average water consumption over a year of production is max. 1,2 m<sup>3</sup>/h.

### 6.2 The issues of PFW prior to installing the Advanced Tank Disinfection System

- 1) Microbial control was possible by weekly sanitisation.
- 2) Occasional water failure due to excessive microbial counts.
- 3) Unscheduled sanitisation required due to excessive bio burden in the PFW and therefore disruption in the production schedule.
- 4) During the long rainy season experienced by this site, the quality of the incoming water is far lower than in other seasons with respect to chemical and microbial parameters. This increased the load on the water generation system and repeated independent sanitisation of PFW modules. They also experienced reaching the alert/action limit faster for PFW due to higher microbial counts in the PFW tank.
- 5) During summer, the incoming water quality is better than in the rainy season. However, due to the higher atmospheric temperatures, the microbial counts in the PFW tank reach the alert/action limit in a shorter amount of time.

■ Table 3

UV dose comparison, conventional through-flow reactors and advanced tank disinfection devices.

UV-system	Through-flow system	Advanced Tank Disinfection System
Electrical power of UV lamps	200 W	120 W
Rate of water replacement	0.5–max.1.2 m <sup>3</sup> /h	
Recirculation rate	4.2 m <sup>3</sup> /h	
Volume of unit	15 l	3 m <sup>3</sup> (normal operation)
Material	SS 316 L	SS 316 L
Dimension	1,225 (l) x 106 mm (dia)	1,345 mm (dia) x 1,950 mm (H)
Dose	4,720 J/m <sup>2</sup>	48,400 J/m <sup>2</sup>

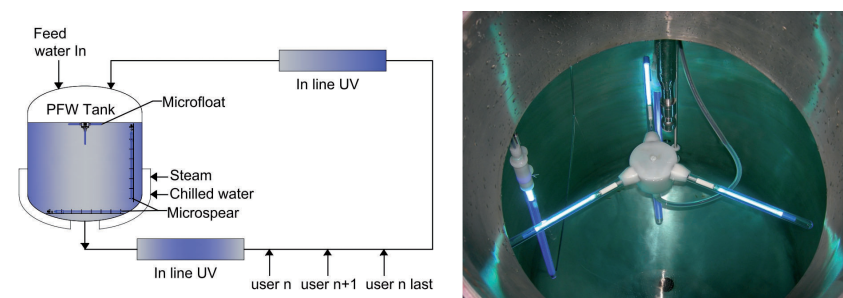


Figure 3: Schematic of PFW storage and distribution with advanced tank sanitisation (left) and photo of site installation with proven concept for disinfection in place on a PFW storage tank (right).

- 6) The operating cost of this PFW tank was higher than that of other tanks.

### 6.3 Site installation drawing / photos

Figure 3 shows the setup in the described show case.

### 6.4 The comparison of results

Table 4a and 4b show data of average microbial results before (4a) and after (4b) the installation of an Advanced Tank Disinfection System. The supply water from the purified water generation always showed an acceptable microbial quality.

■ Table 4a

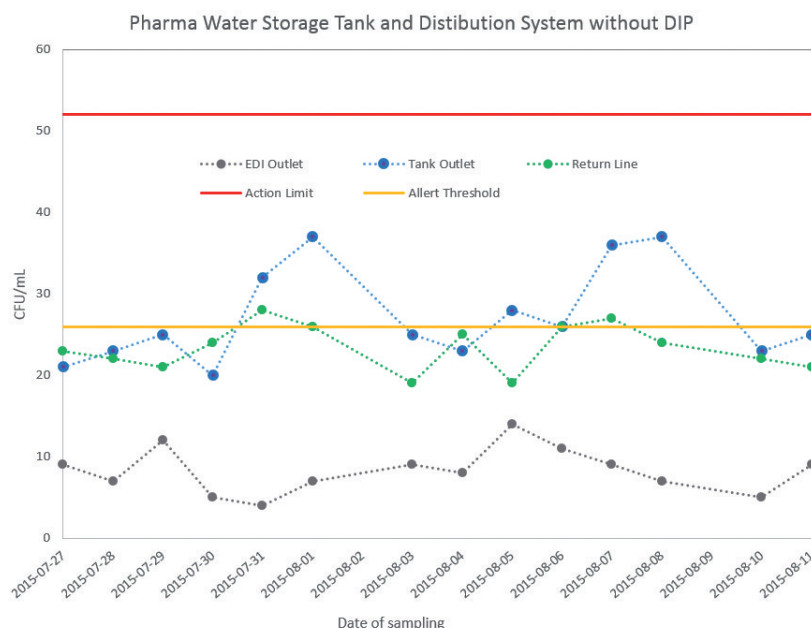
Data of Total Viable Counts prior to the installation of the advanced tank sanitisation system.

#	Date	Total Viable Count in CFU/ml		
		EDI Outlet	Tank Outlet	Return line
1	27.07.2015	9	21	23
2	28.07.2015	7	23	22
3	29.07.2015	12	25	21
4	30.07.2015	5	20	24
5	31.07.2015	4	32	28
6	01.08.2015	7	37	26
7	03.08.2015	9	25	19
8	04.08.2015	8	23	25
9	05.08.2015	14	28	19
10	06.08.2015	11	26	26
11	07.08.2015	9	36	27
12	08.08.2015	7	37	24
13	10.08.2015	5	23	22
14	11.08.2015	9	25	21

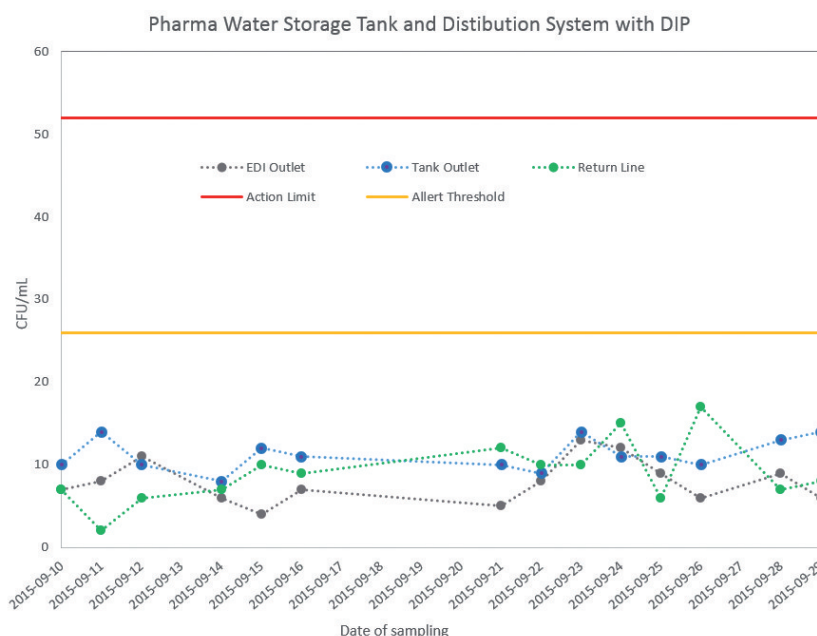
■ Table 4b

Results for operation with new disinfection system in place.

#	Date	Total Viable Count in CFU/ml		
		EDI Outlet	Tank Outlet	Return line
1	10.09.2015	7	10	7
2	11.09.2015	8	14	2
3	12.09.2015	11	10	6
4	14.09.2015	6	8	7
5	15.09.2015	4	12	10
6	16.09.2015	7	11	9
7	21.09.2015	5	10	12
8	22.09.2015	8	9	10
9	23.09.2015	13	14	10
10	24.09.2015	12	11	15
11	25.09.2015	9	11	6
12	26.09.2015	6	10	17
13	28.09.2015	9	13	7
14	29.09.2015	6	14	8



**Figure 4a:** Viable counts in the pharma water storage tank and distribution system as operated for many years.



**Figure 4b:** Viable counts in the pharma water storage tank and distribution system as operated after installing the advanced tank sanitisation system as DIP (Disinfection In Place).

The maximum value allowed in the PFW loop would be 50 viable counts. Normally with values of 30 and more, a tank sanitisation with hot water treatment is performed as the alert limit is set to 26 viable counts. In the conventional system, it could be observed that that once a week a hot water clean was required to get back the microbial results to an acceptable level.

Figures 4a and 4b show very clearly the huge improvement which installing the advanced disinfection system in the pharma water storage tank can bring. After installing the Advanced Tank Disinfection System, the germ counts consistently showed an acceptable level of microorganisms during a longer period. Although the sample results did not require a hot water sanitisation every



30 days, the customer decided to carry it out in order to comply with regulations from the FDA.

## 6.5 Advanced Tank Disinfection System benefits

### 6.5.1 System Benefits

- Chemical free (oxidants) and safe disinfection system.
- Total volume of the water inside the tank is continuously UV disinfected/treated.
- The system acts against germs 24/7 inside the tank.
- The system can also deal with the failures of the existing water/air feed systems (i.e. bacteria entry into the tank).
- In conventional PFW generation systems, water is treated upstream prior to entering into the tank for chemical, physical and microbiological parameters. Similarly, in the distribution loop, the water is treated again for microbial elimination and endotoxins removal. There is no control inside the tank where over 90 % of the PFW is stored. This system treats the water inside the PFW tank for microbial elimination.
- The existing tank is converted into a UV reactor using Microfloat and Microspear.

### 6.5.2 Operational Benefits

- Pharmaceutical grade API water is not wasted.
- Reduction in steam consumption.
- Simplification of tank operation and maintenance.
- Reduction in the frequency/number of hot water sanitisations.
- Any seasonal water quality variations will not affect the PFW system's performance.
- No special treatment process is required during summer weather conditions.
- High efficiency.
- Less significant endotoxin levels in the water.

### 6.5.3 Cost Benefits

- Power and chemicals to treat R/O, Nano, ACF, Anion, and Cation are saved.
- Pharmaceutical API grade water is no longer directly pumped to the effluent treatment plant/CT due to microbial contamination.
- Steam cost is saved.
- Higher productivity due to increased system availability because of reduced sanitisations.

## 7. WFI Feed Water

WFI feed water generally comes from the PFW tank. Better quality PFW enhances the WFI production. Fur-

thermore, reduced PFW sanitisation time helps to ensure the uninterrupted operation of the WFI plant.

## 8. Conclusion

The Advanced Tank Disinfection System is used both for biological inhibition inside the PFW tank and as an insurance against the failure of the microbial control system in the water generation circuit.

The Advanced Tank Disinfection System can easily be applied to new and existing tanks in a short time. This system is proven to be highly and quickly effective against germs growing inside the PFW tank. It effectively reduces the sanitisation frequency and increases productivity. This system is effective 24/7 inside the tank whether the tank is filled with water or air. Multiple installations have demonstrated the overall effectiveness of the Advanced Tank Disinfection System and results prove this as shown by the above quantifiable data of a real world pharmaceutical facility.

The use of a well-designed Advanced Tank Disinfection System provides steady, measureable low concentrations of bio burden. Thereby this technology's effectiveness is confirmed and ultimately its value in mitigating the bio burden and other potential biological water system contaminants. This conclusion is unsurprising as similar results in other industrial equipment were the underlying reason for applying this technology to pharma water applications.

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