VEOLIA

PHARMACEUTICAL MANUFACTURING

Wastewater Treatment Guide

WATER TECHNOLOGIES

This guide offers an expert overview of the challenges posed in treating wastewaters from Pharmaceuticals manufacturing facilities and the processes employed to manage them.

Veolia Water Technologies has been meeting industries' water and wastewater needs for over 160 years. Within the Pharmaceutical industry it has over 100 wastewater reference projects throughout the world; many of them with industry leaders. This guide draws upon Veolia's experience in helping Pharmaceutical Manufacturers comply with legislation, meet sustainability objectives, reduce risk and optimize costs.

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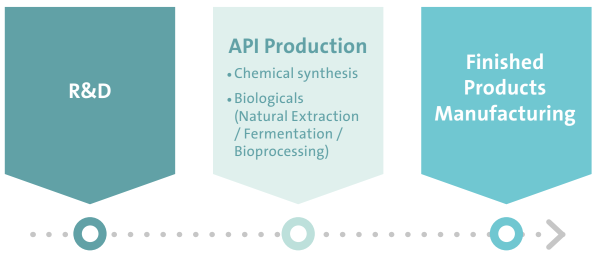
1. INTRODUCTION

In today's Pharmaceutical manufacturing facilities, an effective wastewater treatment is essential. The production of chemically synthesized and biological drugs uses large quantities of water and a variety of compounds that inevitably find their way into the plants' effluents in varying concentrations. Implementing an efficient wastewater treatment is often a legal obligation for Pharmaceutical Manufacturers; increasingly, sustainable development and cost control are also key drivers. This guide aims to give an overview of the treatment processes applicable to this industry.

A. DEFINITION & CLASSIFICATION OF PHARMACEUTICAL MANUFACTURING

Pharmaceuticals are produced in a number of ways. Large volume pharmaceutical manufacturing can be broadly broken down into two stages: the production of active pharmaceutical ingredients (APIs) and finished products manufacturing, with the former feeding into the latter. APIs are produced as a result of chemical synthesis or biological processing.



Chemical Synthesis API (also referred to as Small Molecules)

- Chemicals and solvents are combined in reaction tanks to produce the API. This batch process may require multiple reactions. The final version of the API is produced as a result of various extraction and purification processes.
- API products are typically produced in large batches and campaigns.
- The equipment may be used to manufacture many types of APIs, which can result in large variations in wastewater over time.
- Wastewaters from chemical synthesis operations are diverse due to many operations and reactions taking place in the reactor as well as at different stages.
- Plants have relatively high flows of wastewater with inconsistency in flow rates and loads.
- More recent plants are adopting continuous manufacturing, which results in smaller volumes of wastewater with greater consistency than batch production.

Biological API (also referred to as Large Molecules)

- Bioprocessing plants use natural sources and scaling technologies to manufacture products such as antibodies, therapeutic proteins, gene therapies, insulin, vaccines, etc.
- The manufacturing process is often unique to the product. Single-use equipment is increasingly employed for flexibility and also results in reduced demand for water.
- Fermentation is susceptible to contamination by viruses; in such situations whole batches may be rejected.
- Plants have relatively large flows of wastewater (especially where single-use is not used.)

Finished Products (also referred to as Fill & Finish)

- Chemical Synthesis
  > Plants convert bulk APIs into dosage form products for consumers. These come in different forms: solid, semisolid and liquid.
  > The process uses steps such as milling, mixing, grinding, compression, and packaging. Many types of fillers, binders, flavoring agents, preservatives and antioxidants are added during the process.
  > The process equipment is common to almost all drug manufacturing processes meaning that plants can adapt to market demand over time (resulting in a change in wastewaters).
- Biological Processing
  > In the fill-and-finish stage the protein (API) is formulated into a final product by combining it with WFI (Water For Injection), salts, sugars, alcohols, etc. and contained within its packaging (bags, vials, etc.)
  > The fill-and-finish process often takes place at the same location as the production of the biological API.
- Batch production is still the dominant approach to manufacturing.

B. CHARACTERIZATION OF PHARMACEUTICAL MANUFACTURERS' WASTEWATERS

Pharmaceutical manufacturing wastewaters are known for their inconsistency; even between facilities manufacturing the same product, one can find variations in the wastewaters' characteristics. Typical challenges:

- Products are often produced in batches, which result in variable flows, different pollutants and changing concentrations.
- There is a risk of toxic and persistent substances in wastewaters, which can pose a challenge for some types of biological wastewater plants.
- The presence of high organic content, typically solvents like alcohols, glycols, etc. may further complicate treatment.

Moreover, clients often have concerns about intellectual property or public image that discourages them from sharing essential information on wastewater pollutants. An understanding of the potential sources of wastewater can encourage discussion and avoid issues with the wastewater treatment plant.

B1. Sources and substances present

WASTEWATER SOURCES	DETAILS	SUBSTANCES PRESENT IN WASTEWATER	TREATMENT IMPACTS	TYPE OF PLANT
Chemical reactors	Wastewater is produced with each chemical modification as reactors are emptied, cleaned and refilled.	**Presence of reaction residues** - unreacted reactants, products and by-products: acids, bases, metals, halides, nitrates, cyanides, sulfates and API traces. **Water temperature** may be warm depending on washing needs.	➲ High variability and interactivity of chemical compounds: analyses always required for successful characterization and treatment line selection. ➲ API traces: specific treatment to be considered if they are to be reduced. ➲ Temperature needs to be regulated if outside of biomass and membrane tolerances.	Chemical APIs
Fermentation and purification processes	Some raw materials from media and buffers used during fermentation (broth) and isolation remain in streams discharged to the wastewater plant.	**Biologically active substances (e.g enzymes), nutrients** (starch, sugars, polyols), trace elements, vitamins, amino acids, inorganic and organic salts, surface active agents, or complex (undefined) ingredients.	➲ Biologically active substances potentially need to be deactivated. ➲ Nutrients are very biodegradable, favoring biological treatment. ➲ High salinity is an issue for biomass development and increases corrosion. ➲ Surface active agents: encourage foaming.	Biological APIs
Extraction processes	Solvents from the mother liquor are recovered but as recovery efficiency is not 100%, a portion is present in plants' wastewaters.	**Over 30 solvents are regularly used** within this industry including ethanol, methanol, acetone, isopropanol, acetic acid, etc.	➲ Solvents are organic compounds, which result in high concentrations of COD in the wastewater. ➲ Solvents can be toxic for biomass in biological treatment. ➲ Some solvents are more volatile than water (Low Boiling Point solvents) meaning that evapoconcentration is not a treatment option as they will be evaporated and found in the distillate.	Chemical APIs Biological APIs
Mixing and granulation processes	Rinsing of equipment following mixing of APIs and excipients.	**Presence of mixing residues of excipients and APIs:** waste starches, sugars, API traces, detergents, etc.	➲ Waste starches and sugars are biodegradable ➲ API traces: see comments in row on 'Chemical Reactors.' ➲ The presence of detergents is the main cause of foam issues in wastewater treatment plants.	Finished products

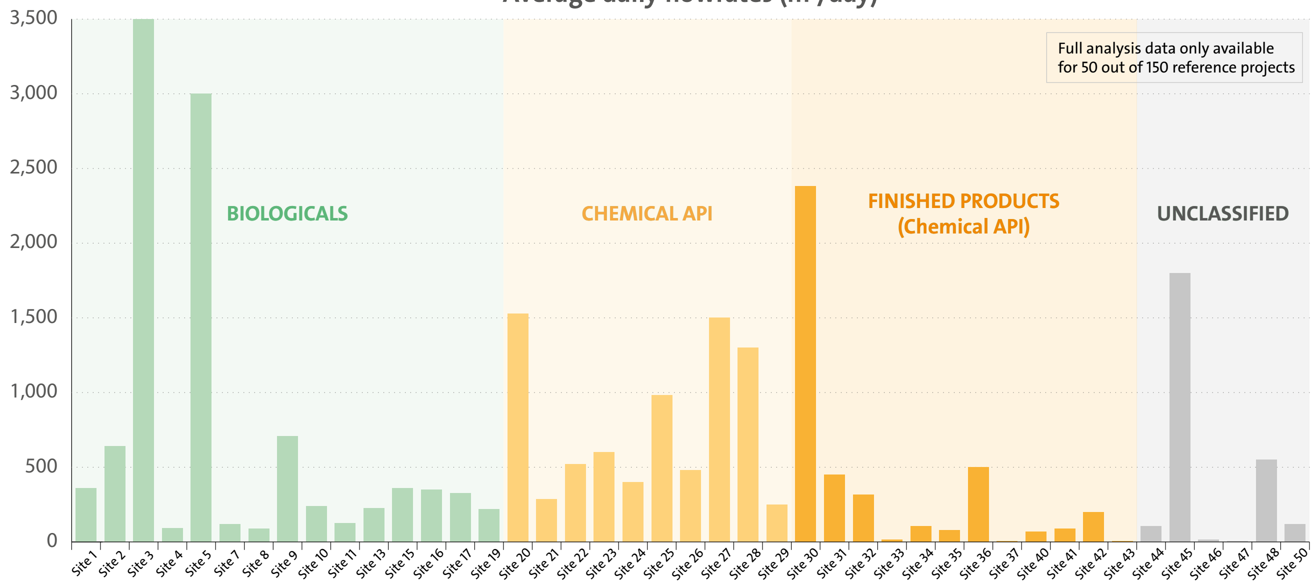
WASTEWATER SOURCES	DETAILS	SUBSTANCES PRESENT IN WASTEWATER	TREATMENT IMPACTS	TYPE OF PLANT
Equipment and floor cleaning	Equipment and floors are regularly cleaned, spillages may create peaks in volume/ load.	**Detergents and trace pollutants related to the equipment's usage.**	➲ Detergents: see comments in previous row.	Chemical APIs Biological APIs Finished Product
Scrubber blowdown	Solvent vapors are treated using scrubbers, scrubber blowdown is sent to wastewater.	**Presence of soluble and insoluble organic compounds and absorbed chemicals (acid/ bases).**	➲ Organic compounds: contribute to the wastewater's COD. ➲ Acid/bases: pH needs to be regulated for optimized process performance.	Chemical APIs Biological APIs Finished Products
Laboratory facilities		**Potential presence of toxic compounds and API traces.**	➲ May be toxic for biomass in biological treatment. ➲ API traces: see comments in row on 'Chemical Reactors.'	Chemical APIs Biological APIs Finished Products
Production of compendial waters and utility waters	Reverse osmosis concentrates, cooling tower and boiler blowdowns, etc.	**Dissolved salts, Alkalinity, Cleaning In Place (CIP) chemicals, Total Suspended Solids.**	Salts: see comments in 'Fermentation & Purification Processes' row.	Chemical APIs Biological APIs Finished Products
Sanitary wastewater	When not segregated, the sanitary wastewater is combined with the plant's other wastewaters.	**Presence of organic pollution, suspended solids, Fat, Oil & Grease (FOG), microorganisms, etc.**	No specific issue for wastewater treatment but should be segregated if reuse is considered.	Chemical APIs Biological APIs Finished Products

B2. Wastewater characteristics

"Each manufacturing or formulation plant is special, differing from other similar pharmaceutical plants in size, types of intermediates, bulk substances, or products produced, amounts and types of solvents used, and thus, in the raw materials used and wastes/emissions generated."
US EPA Notebook(1)

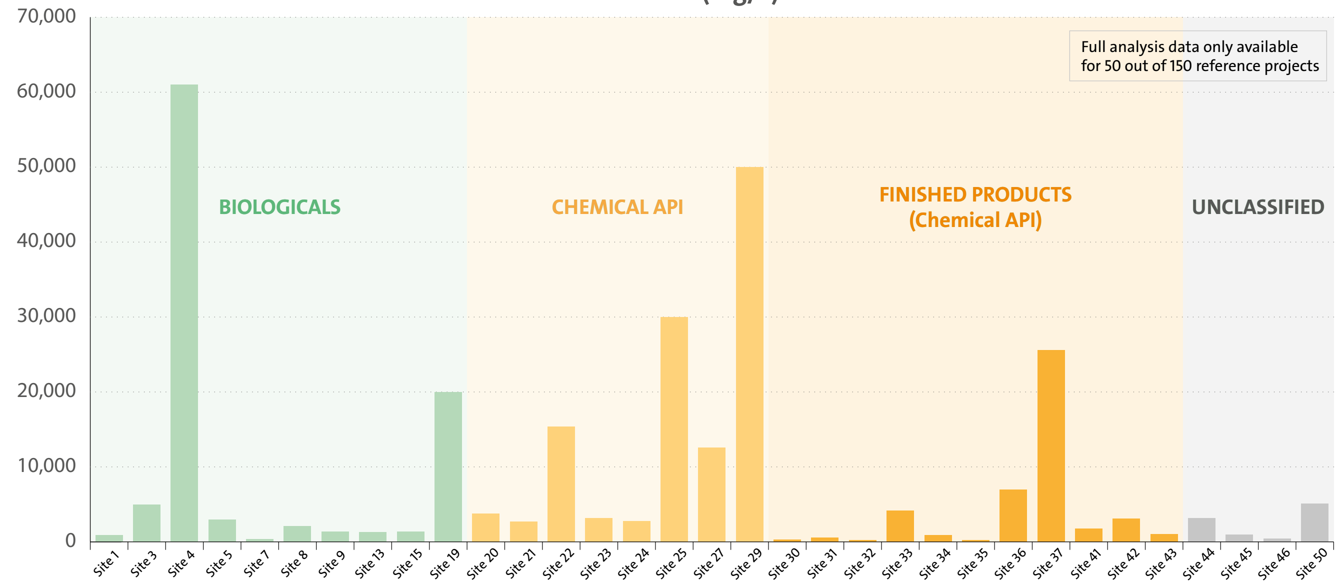
Research conducted by Veolia on 50 plants manufacturing pharmaceuticals confirms that wastewaters in this industry are highly variable. Veolia looked at flow rate, COD and COD/BOD$_5$ ratios in the research. The results are summarized in the following graphs.

PHARMACEUTICAL WASTEWATER INFLUENT
Average daily flowrates (m³/day)

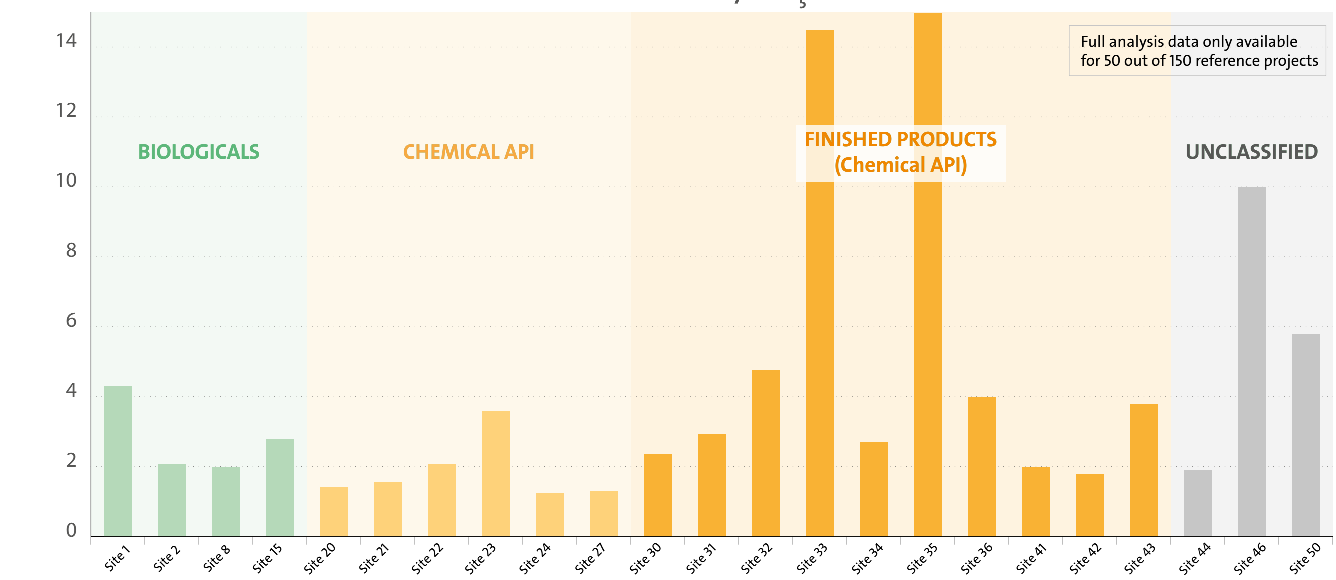


(1) *US EPA sector notebook - Profile of the Pharmaceutical manufacturing Industry - Report #EPA/310-R-97-005.*

PHARMACEUTICAL WASTEWATER INFLUENT
COD (mg/L)



PHARMACEUTICAL WASTEWATER INFLUENT
Ratio COD/BOD$_5$



Wastewater volumes

Daily flow rates are extremely different from one manufacturing site to another and logically depend on the size of each site. Typically API production sites produce larger quantities of wastewater relative to finished goods plants, but there are always exceptions to the rule. Common values of daily volumes are between 30 and 600 m^3/d.

Within production sites, and due to batch production techniques, there are often fluctuations in volume and quality of wastewaters.

Chemical Oxygen Demand (COD)

There is a large range of COD values, ranging from 400 mg/l to 62,000 mg/l, with API production (chemical & biological) plants usually producing the most concentrated waters. Outside of this research, Veolia has also seen a plant with a COD value of 300,000 mg/l.

COD/BOD$_5$ Ratio

The first step to assess the biodegradability of any effluent is the COD/BOD$_5$ ratio, for which the following limits have been established by Veolia:

- COD/BOD$_5$ < 2: effluent is easily biodegradable
- COD/BOD$_5$ 2-3: effluent is biodegradable
- COD/BOD$_5$ > 3: effluent may not be biodegradable

In the pharmaceutical industry values range from 1 to 15, showing the extreme variation of the ability of the wastewater to be biologically degraded.

It should be noted that this ratio does not provide information on the fraction of COD that is non-biodegradable or very difficult to degrade biologically, called Refractory COD.

Refractory COD/Non-biodegradable dissolved COD

Refractory COD is principally due to the presence of organic molecules, which are difficult to degrade. These substances are often derived from chemical synthesis. Refractory COD is also generated by the presence of substances and compounds that inhibit the metabolic functions of microorganisms. This inhibition can be induced by heavy metals but also organic substances such as active biocides (bactericides, etc.).

Depending on the effluent, refractory COD may vary widely.

Refractory COD is a critical factor as it limits the ability to reach low COD discharge limits through biological treatment only. Refractory COD is also referred to as "hard COD", "ultimate COD", "persistent COD" or "inert COD".

Total Suspended Solids (TSS)

TSS is the total amount of suspended solids in the wastewater (suspended organic solids + suspended mineral matter). Values observed vary greatly between sites: from 10 to 4,500 mg/l.

Total Kjeldahl Nitrogen (TKN)

TKN is made up of ammonia (N-NH_4^+) and organic nitrogen. Values observed are between 0 and 300 mg/l. Part of TKN can be soluble non-biodegradable organic nitrogen which can be an issue in case of low total nitrogen limit (TN).

Total Phosphorus (TP)

TP values are rarely communicated in tender documents. Values observed are between 0 mg/l and 50 mg/l.

Fat, Oil and Grease (FOG)

FOGs are present in wastewaters from manufacturing sites producing creams, lotions or ointments. For example, a concentration of 2,500 mg/l has been reported on a concentrated "fat" stream.

The presence of FOG in high concentration has an impact on the efficiency of the biological treatment stage as it can be adsorbed on the surface of the biomass, which may limit the transfer of soluble substrates and oxygen to it. In such circumstances, their removal prior to biological treatment is key.

Temperature

Temperature at the entry point of a wastewater treatment plant: from 5°C to 70°C. It is an important parameter as some treatment processes, such as biological treatment, are temperature sensitive. Membrane processes are also sensitive with most membranes damaged at temperatures exceeding 35°C (hollow fiber membranes at 38°C).

pH

pH values at the entry point of a wastewater treatment plant vary from 3 to 12. pH should be corrected in order to ensure efficiency at each stage of treatment and to ensure that the treated water meets regulatory requirements, usually between 6.5 and 8.5.

Salts

Salts are likely to be present: chlorides whose concentration might be over 1 g/l, but also sulfates and bromates.

Microbiological parameters

If sanitary effluents are mixed with industrial wastewater, microorganisms will be present in the wastewater (bacteria, etc.).

2. TREATED WATER QUALITY

Treated water may be discharged to the natural environment (river, lake or sea), sent to the municipal water treatment plant or to a centralized industrial water treatment plant. Treated water may also be reused (reclaimed). The discharge quality required depends on the destination and the local legislation.

Guaranteed parameters are usually: COD, BOD_5, TSS, TKN (or $N\text{-}NH4^+$), TN, TP, pH and Temperature. Total Nitrogen (TN) is the sum of TKN, nitrates and nitrites.

For a treatment line with reuse, guaranteed parameters are dependent on the reuse application. In most cases, the applications are for low grade water requirements such as make up water for cooling tower, boiler, floor washing or irrigation. Water parameters will be for example Total Dissolved Solids (TDS), conductivity, hardness, etc.

In the last few years, requirements on API concentrations in the treated water have appeared on projects located in developed countries like France, the Netherlands, Switzerland and the USA. These requests often come from pharmaceutical companies with strong Corporate Social Responsibility (CSR) policies who wish to reach higher standards than the local regulatory requirements.

A. DISCHARGE WATER QUALITY

EXAMPLES	UNIT	EXAMPLE 1	EXAMPLE 2	EXAMPLE 3	EXAMPLE 4	EXAMPLE 5
Discharge		To municipal sewer (Europe)	To municipal sewer (Europe)	To river (Europe)	To industrial park WWTP (Asia)	To reuse on site (Middle-East)
pH		5.5-8.5	6-10	5.5-8.5	-	6-7
Temperature	**°C**	30	42	30	-	25-37
COD	**mg/l**	2,000	800	90	800	50-100
BOD_5	**mg/l**	800	400	25	500	<2
TSS	**mg/l**	600	400	30	400	-
$N\text{-}NH4^+$	**mg/l**	-	-	-	10	-
TKN	**mg/l**	-	-	10	-	-
TN	**mg/l**	150	-	-	-	-
TP	**mg/l**	50	10 (Phosphates)	2	-	0.1
FOG	**mg/l**	-	100	-	-	-
TDS	**mg/l**	-	-	-	-	250
Other parameters		AOX < 1 mg/l Zn < 2 mg/l Cu < 0.5 mg/l	Detergents < 100 mg/l	-	-	Hardness < 1°F SiO_2 < 1 mg/l Cl^- < 70 mg/l

Expert Guidance from Veolia

If you are facing an issue with your wastewater treatment plant, planning an expansion or upgrade, or building a new facility, then request guidance from Veolia, the market leader in pharmaceutical wastewater treatment.

Complete this online questionnaire or contact your local Veolia expert:
www.pharmaceuticals-manufacturing-wastewater.com

B. QUESTIONNAIRE/LABORATORY TESTS/BENCH TESTS/PILOT TESTS/AUDITS

Pharmaceutical wastewaters are unique and complex. It is thus important to obtain a maximum amount of details about the production site and the nature of its effluent in order to design an efficient treatment line.

> Questionnaire

A detailed questionnaire can help with this and is essential for defining an effective water treatment system. Using the data collected from the questionnaire, an experienced supplier can advise on possible treatment options or identify parameters that may require further investigation.

Below is an extract of Veolia's questionnaire for wastewater projects in this industry.

PARAMETERS	UNITS	COMPOSITION OF WASTEWATER TO BE TREATED			TREATED EFFLUENT DISCHARGE REQUIREMENTS
		MINIMUM	AVERAGE	MAXIMUM	
Waste water discharge (from production process)	-	Continuous /discontinuous			river/sewer/re-use/...
Volume of effluents to be treated	m³/d				
Maximum flow rate (peak value)	m³/h	/	/		
pH	-				
Temperature	°C				
Total COD	mgO_2/l				
Soluble COD	mgO_2/l				
BOD_5	mgO_2/l				
Total Suspended Solids TSS	mg/l				
Total Kjeldahl Nitrogen TKN	mg/l as N				
Ammonia $N\text{-}NH_4^+$	mg/l as N				
Total Phosphorus TP	mg/l as P				
Fat, Oil and Grease	mg/l				

Extract from Veolia's questionnaire.

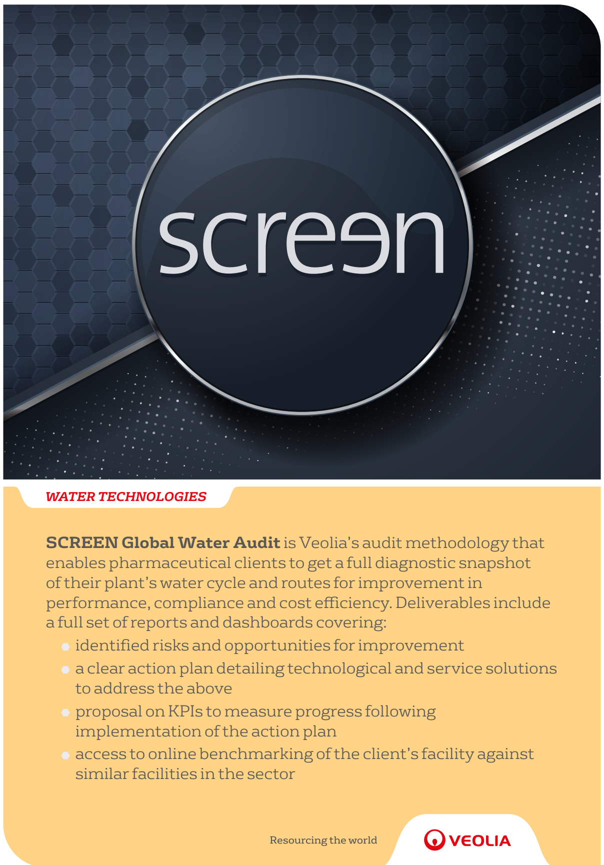
> Lab tests

Once the treatment line is drafted, it is strongly recommended to perform lab tests in order to check the wastewater degradability

Bench-scale tests are essential to evaluate the wastewater's biodegradability when: the COD/BOD_5 ratio looks unfavorable, the effluent contains potentially toxic pollutants, or if the wastewater looks in other ways challenging for biological treatment.

For a treatment line using evapoconcentration, bench-scale testing is systematic. The tests are used to assess concentration rates and distillate quality.

Bench-Scale testing on an AnoxKaldnes™ Moving Bed Biofilm Reactor (MBBR)



> Pilot-scale testing

In some cases, pilot tests may be proposed. Their objectives depend on the nature of the project but they can give data for optimizing the size of the treatment works, the consumption of chemicals, the stability and efficiency of various solutions, etc.

> Audits

Audits provide complementary information to data gathered via questionnaires. They are a particularly useful tool for upgrade projects as a means of identifying options for optimization and repurposing of existing equipment within improved process lines.

3. KEY PROCESSES IN PHARMACEUTICAL MANUFACTURING WASTEWATER TREATMENT

A. TYPE OF POLLUTION AND PROCESSES TO REMOVE IT

The table below presents the key processes for reducing the global pollution parameters in pharmaceutical wastewaters. Water treatment experts combine these processes to form a treatment line that meets removal objectives and inline with the safety protocols, the budget and the available space.

pH	Temperature	TSS & Colloids	FOG	Biodegradable COD (BOD_5) API
Neutralization	**Cooling**	**Coagulation-Flocculation + Flotation** **Coagulation-Flocculation + Sedimentation** **Filtration**	Grease & Oil removal **Coagulation-Flocculation + Flotation**	**Biological Treatment** **Evapoconcentration** Membrane filtration AOP (Advanced Oxidation Process)

Refractory COD API	TKN TN	TP	TDS	Microbial parameters
Evapoconcentration **Activated carbon adsorption** Membrane Filtration AOP (Advanced Oxidation Process)	Biological Treatment Stripping	**Biological Treatment** Chemical Precipitation	**Evaporation** Reverse Osmosis	**Membrane Filtration** Disinfection

The key processes in bold letters above are described in more detail within this technical guide.

Modern wastewater treatment is no longer just about focusing on the end-of-the-pipe. Actions are increasingly taken upstream to deal with more challenging issues at their source.

Segregation of specific wastewater streams

In certain circumstances it may be prudent to segregate specific wastewater streams:

- Highly concentrated or toxic streams may be singled out for a specific treatment to reduce their toxicity or volume. For example, evapoconcentration is often employed in such circumstances with the reduced volume of concentrate disposed of off-site and the permeate continuing on for treatment in the main wastewater plant.
- Some API containing streams may be better handled separately from the main wastewater treatment plant. This is of interest particularly for sites where the bulk of the wastewater does not contain APIs as it avoids the cost of treating the full volume of wastewater with API reduction/removal technologies.

Deactivation of biological API wastewater

In biological API manufacturing, it is often necessary to deactivate streams containing biologically active ingredients. It concerns the production of vaccines, recombinant proteins, gene therapy, viral vectors, somatic cell therapy, drugs derived from human blood and plasma. The wastewater streams containing substances to be deactivated are mostly treated by thermal decontamination but chemical deactivation is also applied in some cases. Some decontamination criteria depend on the BioSafety level of the site (BSL). BioSafety levels, which are ranked from one to four, are selected based on the agents or organisms that are being researched or worked on in the pharmaceutical site. They are individual safeguards designed to protect personnel, as well as the surrounding environment and community.

Thermal deactivation is a specialized activity and usually outside of the scope of wastewater treatment projects.

Once the stream is deactivated, it is usually mixed with other wastewater streams and ready for wastewater treatment itself.

B. KEY PROCESSES

B1. Equalization

What is an equalization tank?

An equalization tank is a tank installed at the head of the wastewater treatment plant (WWTP) where the wastewater is stored during a certain period prior to the treatment.

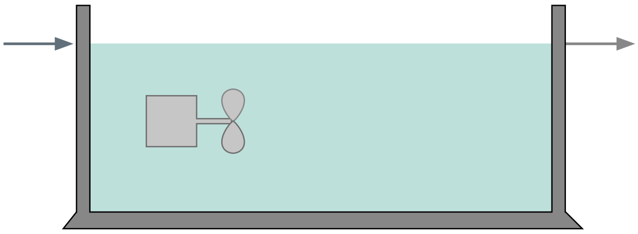


Diagram of an equalization tank

Why install an equalization step in a Pharmaceutical manufacturing wastewater treatment plant (WWTP)?

Pharmaceutical manufacturing wastewaters come primarily from the cleaning and rinsing of the mixing tanks after or between production runs of different products. This batch processing leads to high variability in the wastewater quality. The aim of the equalization step is to buffer the wastewater.

What are the results of the equalization step?

- It smooths peaks of flow and pollution: equalizes the flow rate, balances the pollution, evens out temperature fluctuations.
- It minimizes chemical usage (e.g. downstream pH adjustment): optimizes downstream design and operating costs.
- It improves the reliability of the WWTP: reducing the downstream impact from inhibitory compounds.

B2. Pretreatment

What is pretreatment?

Pretreatment is a preliminary treatment of the wastewater, usually a physical treatment. For Pharmaceutical manufacturing wastewaters the pretreatment is typically screening. Different types of screening can be used: coarse screening (10 to 25 mm), fine screening (<10 mm), rotary screening, etc. The screens remove matters such as paper, plastics and fibers.

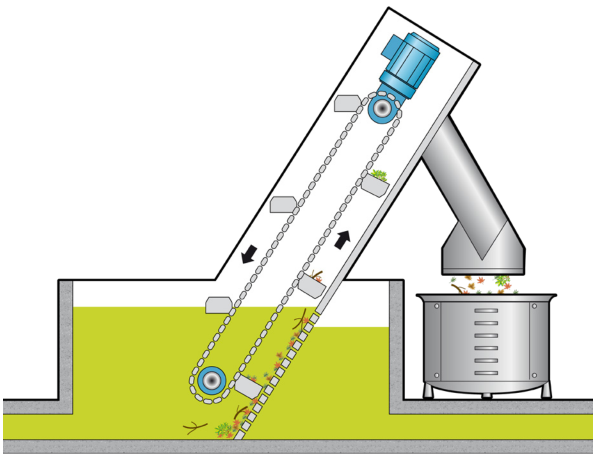


Diagram of screening

Why install pretreatment for Pharmaceutical manufacturing wastewaters?

The pretreatment prevents damage and clogging of the downstream equipment, piping, valves, etc. The choice of the pretreatment step is made according to the needs of the downstream treatment stages.

What are the results of the pretreatment step?

Issues with downstream treatment processes may be avoided: for example, clogging of the membrane if an MBR is chosen, clogging of the outlet sieves if MBBR is selected, etc.

Consequence of poor screening prior to an MBBR process: clogging of outlet sieves.

B3. Neutralization

What is neutralization?

Neutralization is the process of adjusting the pH of water through the addition of an acid (sulfuric acid, for example) or a base (caustic soda, for example), depending on the target pH and process requirements.

Why install neutralization in Pharmaceutical manufacturing wastewater treatment plants?

A pH neutralization stage is used to ensure that the pH value is within a suitable range for downstream treatment stages.

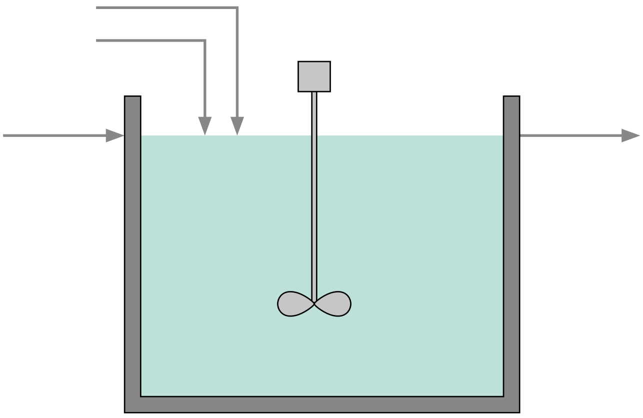


Diagram of a neutralization tank

What are the results of the neutralization step?

Processes like coagulation are pH dependent so the pH has to be adjusted to achieve maximum process efficiency. Also optimal pH for any biological treatment is around neutrality (6.5-7.5).

B4. Primary separation

In primary separation, the total suspended solids (TSS) that can settle and float are removed from the wastewater. This step is not necessary for most pharmaceutical wastewaters where the TSS content is low. However, when TSS and FOG are significantly present in the influent, they must be removed prior to the biological treatment.

B4.1 Dissolved Air Flotation (DAF)

What is DAF?

Dissolved Air Flotation (DAF) is a primary separation process where solid contaminants are removed through the use of an air-in-water solution (called "whitewater") produced by injecting air under pressure into the raw water (direct flotation) or a recycle stream of clarified DAF effluent (indirect flotation). The bubbles attach themselves to particulate matter in the wastewater and cause them to rise to the surface where the sludge formed is removed by scrapers into a sludge holding tank. It is also necessary to collect and discharge the settled matter at the bottom of the DAF.

Why install DAF in a Pharmaceutical manufacturing wastewater treatment plant?

DAF is ideally suited to particles that are slow settling, of neutral density or buoyant. This is particularly applicable to some kinds of pharmaceutical wastewaters where FOG content is very high, in cream and ointments manufacturing for example.

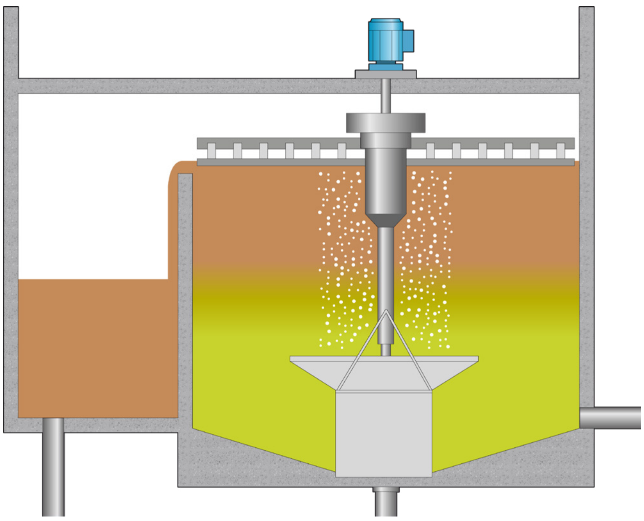


Diagram of a Dissolved Air Flotation tank (DAF)

Due to the presence of surfactants, some FOGs will not be in free phase but rather dissolved in water as an emulsion. The addition of metallic salt will break the link between them and the surfactants (in the coagulation tank). The addition of flocculant (in the subsequent flocculation tank) will promote floc formation and improve the recovery of small flocs.

Best Practice: *In traditional or circular flotation units with traditional saturation systems, small flocs (having a very low ascent speed according to Stokes law) have a tendency to come out with the treated effluent. Therefore designs with corrugated plate lamellar packs are preferred today. The lamellae encourage the aggregation of small flocs, increasing their size and the speed of separation.*

What are the results of the DAF step?

- A chemically enhanced DAF will remove most FOGs, TSS and some COD, thus reducing the load on the downstream treatment stages.
- A DAF will remove the majority of surfactants responsible for foaming in biological treatment
- The sludge produced at that stage is quite concentrated, around 4 to 8% Dry Solids (DS).

B4.2 Sedimentation

What is sedimentation?

Sedimentation is a physical water treatment process using gravity to remove suspended solids and particulate matters from wastewater. It is usually combined with flocculation and coagulation for better removal results. A layer of accumulated solids, called sludge, forms at the bottom of the tank and is periodically removed.

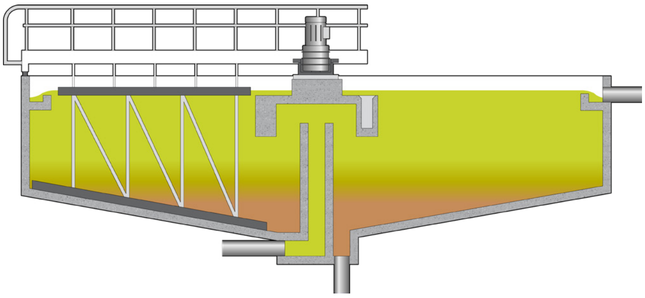


Diagram of a sedimentation tank.

Best practice: *Many advanced sedimentation technologies exist on the market. Some of them use lamella and thus extend considerably the surface area available for sedimentation. Other technologies accelerate the sedimentation process by using microsand, which acts as a ballast for the flocculated particles and accelerates their settling. Veolia has developed the Multiflo™ technology, sedimentation with lamella settling and the Actiflo® technology, combining microsand ballasted flocculation with lamella settling.*

What are the results of the sedimentation step?

A chemically enhanced sedimentation will remove most TSS and some COD, thus reducing the load on the downstream treatment stages.

B5. Cooling

What is cooling?

The objective is to reduce the wastewater temperature. The wastewater passes through a heat exchanger so that the outlet temperature does not exceed a set limit.

Why install a cooling step in a Pharmaceutical manufacturing wastewater treatment plant?

Temperature restrictions on biological treatment dictate that streams with a temperature higher than the permitted level need to pass through a cooling system to reduce the effluent temperature. Indeed the degradation of the organic matter for high COD loads can lead to a non-negligible temperature rise in the biomass.

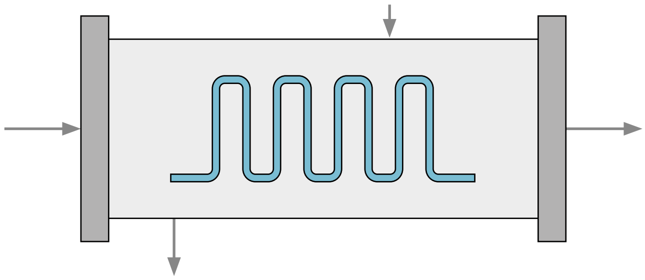


Diagram of a heat exchanger

What are the results of the cooling step?

Cooling allows for correct and efficient operation of downstream processes.

B6. Biological treatment

What is biological treatment?

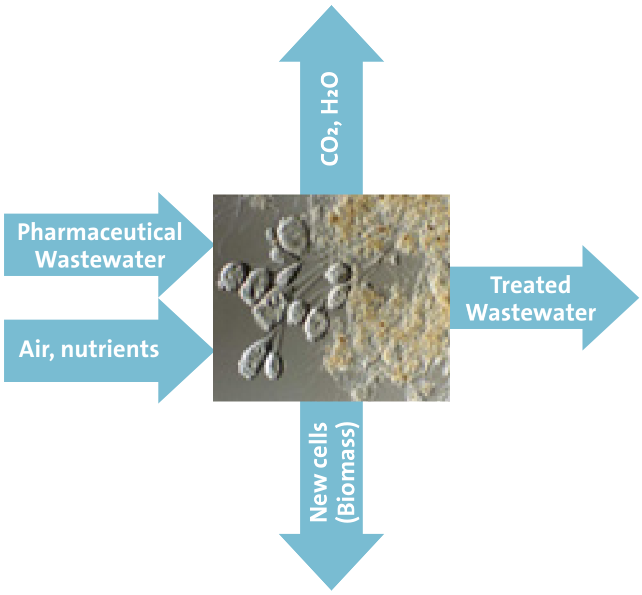
Biological treatment uses bacteria to convert biodegradable organic matter contained in wastewater into simple substances and additional biomass. There are two types of biological treatment: aerobic and anaerobic.

Why install biological treatment in a Pharmaceutical manufacturing wastewater treatment plant?

In most cases, Pharmaceutical manufacturing wastewaters are concentrated waters with medium to high COD concentration. When this organic pollution is biodegradable, biological treatment is the least expensive method for COD removal.

What is aerobic treatment?

In aerobic treatment, aggregates or flocs of bacteria (biomass) form when the tank containing the wastewater is aerated: microbial colonies and oxygen combine to breakdown the organic matter present in the wastewater. The resulting bacteria aggregates are then separated from the treated water.



In a conventional activated sludge process, the biomass is free floating and a clarifier is employed to separate the biomass from the treated water.

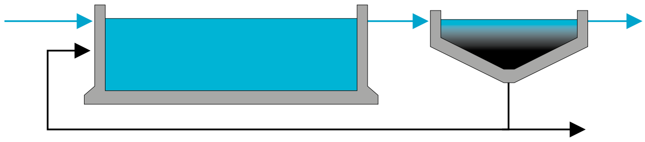


Diagram of a Conventional Activated Sludge (CAS)

What are the results of the aerobic treatment?

The aerobic treatment removes:

- BOD_5 and most COD, down to refractory COD
- Reduces TSS in the separation stage
- Reduces nitrogen (TN) if required

B7. Advanced aerobic treatment

Conventional activated sludge is one of the oldest processes that exists for the treatment of carbonaceous or nitrogenous pollution. It is widely used, but it is also limited in terms of water quality, modularity, integration and ease of operation. To overcome these limitations the industry has developed other aerobic treatments, as detailed below.

B7.1 Membrane Bio-Reactor (MBR)

What is MBR?

MBR is an aerobic biological treatment where the clarifier is replaced by a selective barrier that retains the biomass (suspended matter and bacteria) while allowing dissolved matter to pass through. This membrane also retains colloidal matter, organic macromolecules, microorganisms, etc. The implementation of an MBR process consists of one or more activated sludge basins and membrane modules.

Why install an MBR in a Pharmaceutical manufacturing wastewater treatment plant?

Sometimes with a traditional activated sludge process problems occur in sludge separation during the final clarification stage. The presence of the membrane avoids all of these problems and also makes the treatment line more compact. The use of a membrane changes the definition of the soluble part of the pollution since - depending on the membrane retention threshold - most colloids cannot go through the membrane walls. This leads to a significant increase in COD removal compared to conventional activated sludge system (CAS). MBRs are therefore very competitive for treating highly concentrated wastewaters and they produce the highest quality treated water of any of the biological processes.

The treatment fields and applications of the MBR process for Pharmaceutical manufacturing wastewaters are:

APPLICATION	TYPICAL SCENARIO
Treatment of carbon pollution	> Highly concentrated influents > Tight layout requirement > Stringent discharge requirements > Refurbishment of existing plants
Treatment of nitrogen pollution	
Simultaneous treatment of carbon, nitrogen and phosphorus	
Physical disinfection (especially with respect to bacteria)	> Need for a high water quality: recycling of water treated on site, reuse of water for irrigation or industrial needs, stringent discharge requirements > Pretreatment for reverse osmosis

What are the results?

The performance of the MBR treatment:

- 95% reduction of COD, down to refractory COD
- 99% reduction of BOD_5
- 99% reduction of TSS
- Reduces N if required, to TN concentration comparable to CAS effluent
- Reduction of 4-5 log of Total Coliforms

B7.2. Moving Bed Biofilm Reactor (MBBR)

What is an MBBR?

An MBBR is a biological process based on the biofilm principle. It consists of an aeration tank with special plastic carriers that provide a surface where a biofilm can grow. A biofilm is a group of microorganisms and their extracellular polymeric substances (EPS) attached to a surface. The microorganisms that develop on the carrier surface are essentially from the same group as those found in conventional activated sludge.

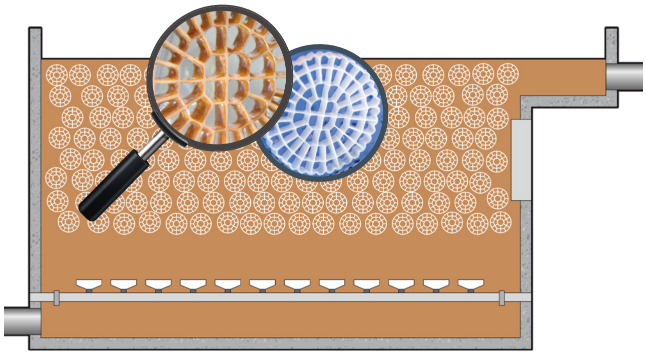


Diagram of a Moving Bed Biofilm Reactor (MBBR)

Why install an MBBR in a Pharmaceutical manufacturing wastewater treatment plant?

Due to the prevalence of batch production in Pharmaceutical manufacturing facilities, variations in load and composition of wastewaters are common. Furthermore, there is always a risk of toxic compounds reaching the wastewater plant. The biofilm within MBBR plants results in a robust process that can handle variations in load and composition. For example, during a toxic episode, because of diffusion limitation, the toxic compounds will only "kill" the outer part of the biofilm while the internal biomass will be protected and continue to treat the inflowing wastewater. This is a key advantage over conventional activated sludge (CAS) and MBR systems.

MBBR is also more compact than a CAS system, making it a good choice where lack of space is an issue. In addition, the compactness of MBBR tanks makes it possible to create multi-stage systems. For example, Veolia has exploited this feature to create a patented MBBR technology (eXeno™) with specialized microorganisms at each stage, resulting in a system capable of reducing concentrations of certain APIs.

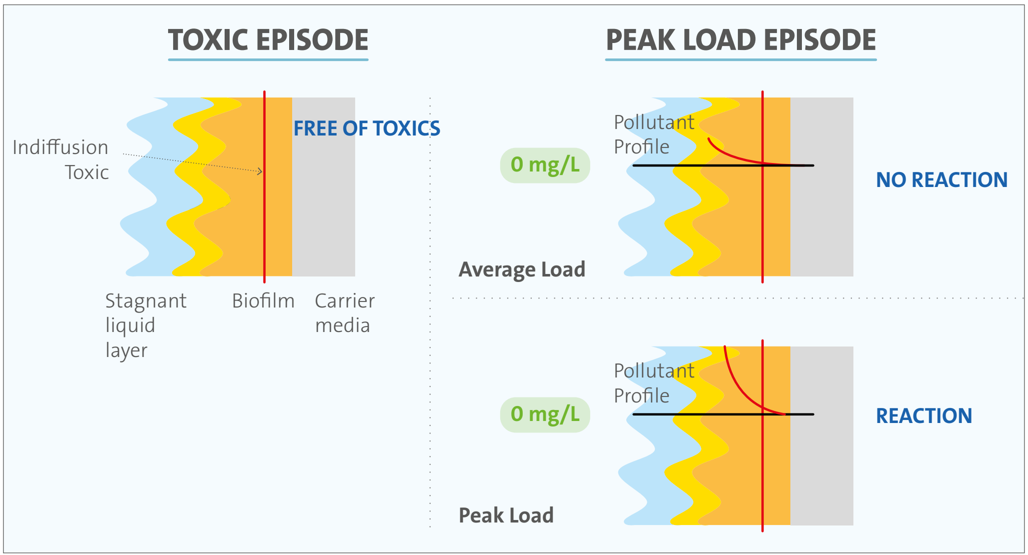


Diagram showing the Biofilm robustness

The general MBBR process can be applied to most carbon and/or nitrogen removal applications:

APPLICATION	TYPICAL SCENARIO
Treatment of carbon pollution	For new plants, especially those requiring a small footprint and easy operation
Treatment of nitrogen pollution	
Simultaneous treatment of carbon and nitrogen	For upgrading an existing activated sludge (by adding carriers to the existing tank.)
Simultaneous treatment of carbon, nitrogen and micropollutants	For new plants
Pretreatment as a roughing reactor (high load systems.)	For existing plants in front of a biological treatment stage
Post-treatment for process improvements and/or micropollutants reduction.	For existing plants after a biological stage
Post-treatment for removing the by-products formed during chemical oxidation processes	For plants using ozonation for micropollutant reduction

What are the results of the MBBR?

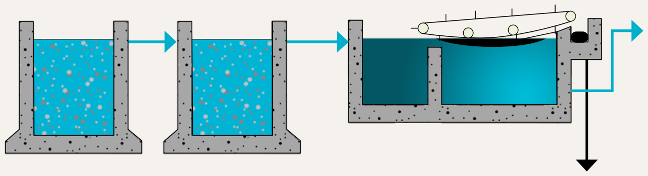
With regards to COD and Nitrogen, the removal efficiencies achieved are comparable to those obtained in a conventional activated sludge system, however, due to higher activity in the biofilm, the volume of the MBBR reactor is greatly reduced. A key differentiator for a certain configuration of this technology (eXeno™) for Pharmaceuticals Manufacturers is its superior performance in reducing concentrations of micropollutants, such as APIs.

As with other biological processes, the amount of refractory COD in wastewater limits the possibilities of reaching a certain discharge limit for COD by biological treatment only. The minimum discharge limit for total COD that is possible to achieve will thus be determined by the degradability of the wastewater and the efficiency of the applied clarification.

There are several configurations of MBBR that may be considered. The choice of the most suitable option depends on the type of effluent, the requirements on treated water quality, the existing treatment and the available tanks, if any. Based on Veolia's experience in treating Pharmaceutical manufacturing wastewaters, the three options on the next page are most suitable.

Configuration MBBR+Sludge separation system

This combination (AnoxKaldnes™ pure MBBR for Veolia) consists of one or more MBBR tanks followed by sludge separation system, commonly a DAF.

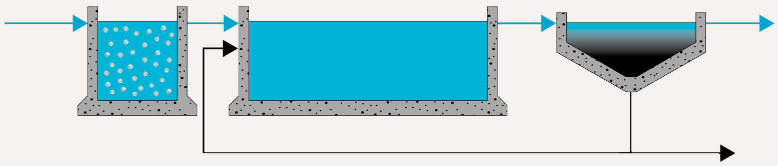


THIS CONFIGURATION IS THE FIRST CHOICE WHEN:	WHY?
Partial organic matter removal is required	Biodegradable compounds which are slow to degrade will not be degraded within the process due to the short retention time
There are large variations of load and composition	Insensitive to temporary limitations such as pH, temperature or toxicity
For toxic wastewaters	Simple to create multi-stage system with specialized microorganisms to handle particular compounds
Compact plant is needed	Small footprint
Robustness is needed	No sludge bulking
Easy operation is an important parameter	Self-controlling biomass

Performance of the MBBR + DAF configuration: 80-90% removal of COD

Configuration: MBBR + Activated sludge

This combination (BAS™ for Veolia) consists of one or more MBBR tanks followed by an activated sludge system. In this system a large part of the readily biodegradable organic pollution is removed in the MBBR tank while the slowly biodegradable COD will be removed in the activated sludge tank. The volumes of both biological steps will be reduced. A useful configuration when there is a lack of space.



THIS CONFIGURATION IS THE FIRST CHOICE WHEN:	WHY?
An existing activated sludge plant needs upgrading	The existing activated sludge tank can be used either as an MBBR tank or remains as an activated sludge tank
Maximum biological organic removal is needed One or more specific compounds which are not readily biodegradable need to be removed	The two (or multiple) stage biological treatment allows for the removal of the slowly biodegradable COD
There are variations in load and composition Robustness is needed Low effluent TSS concentration is required without addition of chemicals	The process is stable and robust; the start-up and restart after disturbance is faster than a CAS. Bulking risk is limited due to the quality of sludge
Low sludge production is important	Sludge production yield is lower than in CAS, especially in nutrient limited operation

Performance of the MBBR + AS configuration: >95% removal of COD

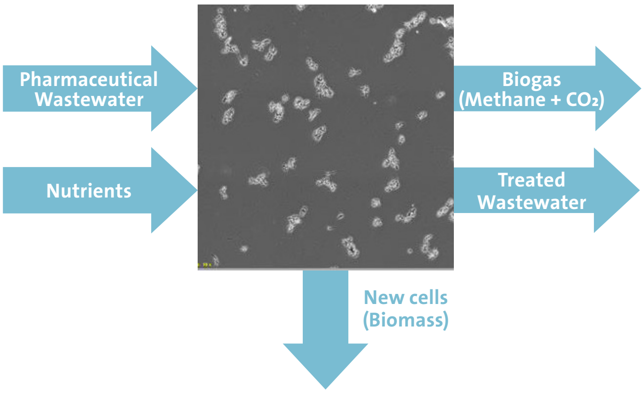
Configuration multi-stage MBBR (eXeno™) for API reduction: **see special section on page 25**

B8. Anaerobic treatment

What is anaerobic treatment?

Anaerobic treatment or "methanization" is a biochemical process carried out by several types of microorganisms in an oxygen-free environment.

Anaerobic treatment can be applied wherever the wastewater is biodegradable, but is most suitable for high concentrations of COD (more than 3 g/l).



Why install anaerobic treatment in a Pharmaceutical manufacturing wastewater treatment plant?

It is a very interesting process in terms of operating costs as no aeration is required. In addition, organic pollution is partly converted into biogas that may be used in several ways (burned in boilers for instance). The biogas is principally made up of methane and carbon dioxide.

Another advantage of anaerobic treatment in comparison with aerobic treatment is lower sludge production. On the other hand, its limits are a lower removal rate of COD and no removal of TN.

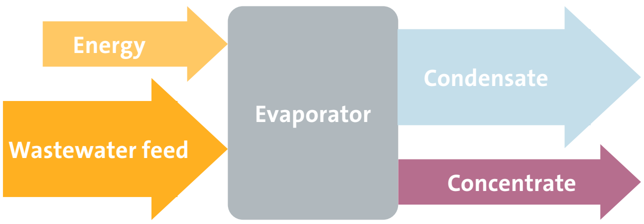
What are the applications for anaerobic treatment of Pharmaceutical manufacturing wastewaters?

Anaerobic treatment is mostly applied to manufacturing sites using biological processes (antibiotic production for example) as wastewaters are usually highly biodegradable. Another condition is the economical feasibility, which usually means plants with large daily wastewater volumes.

B9. Evapoconcentration

What is evapoconcentration?

Evapoconcentration (or evapocondensation) is a method of concentrating a solution by boiling the more volatile solvent, typically water. This process consists of evaporation (passage from liquid phase to vapor phase) followed by condensation of the vapor (passage of gas phase to liquid phase).



Why install evapoconcentration in a Pharmaceutical manufacturing wastewater treatment plant?

This process is used to reduce the volume of wastewater prior to disposal (the concentrate) while producing a high-quality condensate, which in some cases may be recycled or reused, contributing to Zero Liquid Discharge objectives. Evapoconcentration may also be used to recover by-products from the effluent.

Applications for pharmaceutical manufacturing wastewaters:

FOR WASTEWATERS WITH
• Extremely high COD (> 30-50,000 mg/l) • Non-biodegradable and toxic wastewaters • Presence of surfactants in high concentration
Presence of metals, ions, hardness
Presence of APIs and micropollutants
For relatively low daily flow rates, • usually around 5-50 m^3/d • maximum 200 m^3/d

Evapoconcentration comes into its own when it can be used to replace an off-site disposal solution; resulting in cost savings and reducing health and safety risks of handling and transporting wastes. When energy is available on site - hot water or low pressure steam- it is even more cost-effective.

What are the results of evapoconcentration?

Evapoconcentration will separate the wastewater into 5-10% of concentrate and 95-90% of condensate. The concentrate contains the pollutants having a boiling temperature higher than water (metals, ions, oils) while the condensate contains mostly water and products having a boiling temperature lower than water.

Expected pollution reduction in the condensate

- If the organic compounds are less volatile than water, very good reduction of COD and BOD_5
- Almost total elimination of minerals and metals: range 90-98%
- Micropollutants/APIs: Reduction according to micropollutants/API molecular weight and applied temperature

B10. Tertiary treatment and emerging pollutants

B10.1. Tertiary treatment

What is tertiary treatment?

Tertiary treatment is one (or several) additional treatment step(s) after the biological treatment (secondary treatment). It improves wastewater quality before it is reused, recycled or discharged to the environment.

A variety of processes exist:

- Polishing: microfiltration, ultrafiltration (UF), multi-media filtration (MMF)
- Micropollutants removal: adsorption, oxidation, filtration and concentration processes
- Disinfection tools: ultraviolet, oxidation (by chlorine)

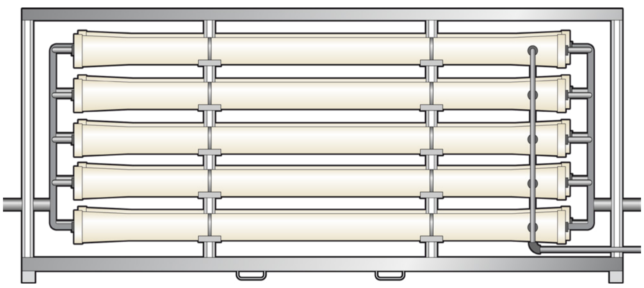


Diagram of a Reverse Osmosis skid

Why install tertiary treatment in a Pharmaceutical wastewater treatment plant?

The objective of a tertiary treatment may vary from case to case.

Strict discharge requirements

In the case of treated wastewater discharge to sensitive areas, the requirements are very stringent. A polishing step will achieve an additional reduction of the residual TSS and associated COD.

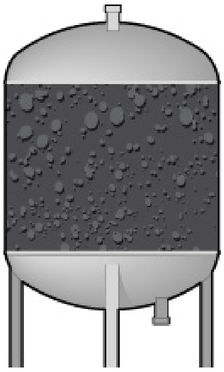


Diagram of an activated carbon filter

Tertiary treatment is also employed to meet water quality expectations in the case of water containing difficult-to-treat pollutants such as APIs in pharmaceutical manufacturing wastewaters.

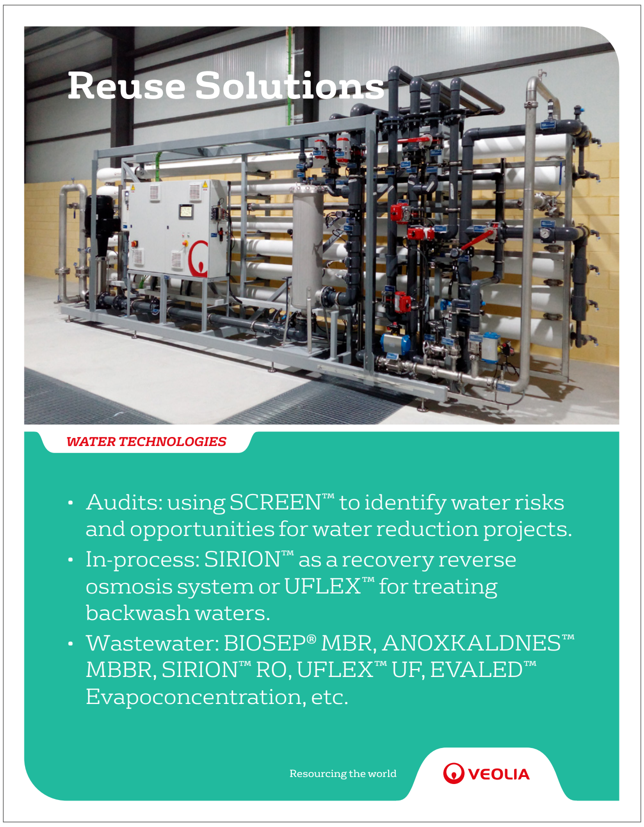
Sustainability objectives

Many companies today have sustainability targets for water. Water treatment specialists work to reduce water usage by optimizing applications, reusing in-process waters and applying appropriate tertiary treatment to allow for the reuse of wastewater where possible. Some examples of where treated wastewater may be reused:

- within the wastewater treatment plant for the preparation/dilution of water treatment chemicals,
- within the production facility in non-GMP applications such as cooling tower make-up, boiler feed make-up, rinsing, cleaning or use in and around the site for irrigation.

The choice of treatment line will depend on the objective, the incoming water quality, the site configuration and the local legislation.

UV water treatment unit for disinfection



B10.2. Emerging pollutants

UNESCO defines **emerging pollutants** in a broad sense as any synthetic or naturally-occurring chemical or any microorganism that is not commonly monitored or regulated in the environment with potentially known or suspected adverse ecological and human health effects. These contaminants include chemicals found in pharmaceuticals, personal care products, pesticides, industrial and household products, metals, surfactants, industrial additives and solvents. Many of them are used and released continuously into the environment even in very low quantities and some may cause chronic toxicity, endocrine disruption in humans and aquatic wildlife and the development of bacterial pathogen resistance[2].

Emerging pollutants are often substances, not necessarily new on the market, but newly identified as potentially harmful and for which data concerning their presence, fate in the environment and their potential impacts on health or the environment are insufficient to justify regulatory measures.

Micropollutants

A micropollutant is a substance (i.e. mineral, organic, biological or radioactive) that can cause undesirable effects on living organisms at very low levels (e.g. from ng/l to µg/l). Adverse effects range from temporary alterations of biological functions to death of individuals,

[2] *Emerging Pollutants in Water and Wastewater – UNESCO.*

but can also disrupt the renewal of generations and the dynamic equilibrium of ecosystems.

Micropollutants cover a great diversity of chemical families (e.g. heavy metals, PAHs (Polycyclic aromatic hydrocarbons), PCBs (polychlorinated biphenyls), chlorinated solvents, etc.) and are usually grouped according to their uses (e.g. biocidal products, agricultural pesticides, pharmaceuticals, etc.). They are present in many products that we consume daily (pharmaceuticals, cosmetics, phytosanitary products, insecticides, etc.) at home or in industry.

Endocrine disruptor / Endocrine Disrupting Chemical (EDC)
"An endocrine disruptor is an exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub)populations."[3]

EDCs are suspected of having negative effects in humans at very low doses sometimes even though they may have been considered safe according to conventional toxicology methods.

EDCs are found among many classes of chemicals, including current-use pesticides, phytoestrogens, metals, active ingredients in pharmaceuticals, and additives or contaminants in food, personal care products, cosmetics, plastics, textiles and construction materials.

Legislation on emerging pollutants
The lack of scientific data about health effects today means that few emerging pollutants are regulated anywhere in the world.

In 2008, the European Union developed a mechanism which aims to support the identification of priority substances for regulation under the Water Framework Directive. The watch list is a list of potential priority substances that need to be monitored to determine their environmental risk.

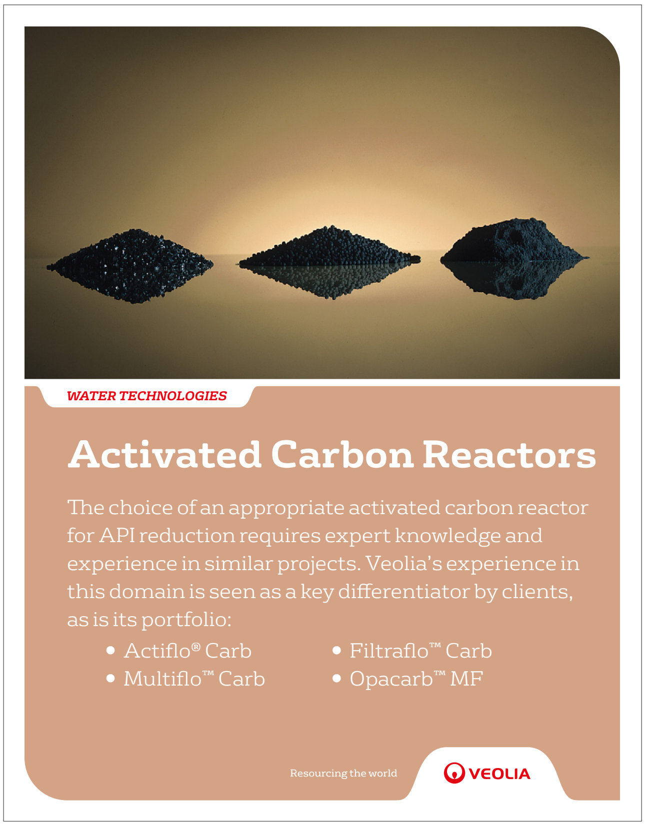
The watch list was reviewed in 2018 and includes hormones (17-Alpha-ethinylestradiol (EE2), 17-Beta-estradiol (E2), Estrone (E1)), macrolide antibiotics (Erythromycin, Clarithromycin, Azithromycin), antibiotics (Amoxicillin, Ciprofloxacin), neonicotinoids and pesticides.

Similar schemes are present elsewhere, in particular within developed economies.

[3] *Global assessment of the state-of-the-science of endocrine disruptors- International Programme on Chemical Safety, WHO, 2002.*

Treatment of Emerging Pollutants
There are many processes that exist for micropollutant reduction. According to the removal mechanism, they can be categorized as following:

- adsorption processes,
  - > adsorption on activated carbon, using Powdered Activated Carbon (PAC) or Granular Activated Carbon (GAC)
  - > adsorption on specific media as used for example within Macro-Porous Polymer Extraction (MPPE)
- oxidation processes,
  - > biological oxidation, i.e biological treatment using microorganisms
  - > chemical oxidation using ozone, UV, hydrogen peroxide or a combination (collectively referred to as Advanced Oxidation Processes (AOP))
  - > electrochemical oxidation, using electrodes
- filtration processes,
  - > high-pressure filtration such as Nanofiltration (NF) and Reverse Osmosis (RO) membranes
- concentration processes,
  - > Evapoconcentration for example.



It is critical to understand that there is not a universal solution to handle all micropollutants. The treatment options available all have pros and cons.

- Some treatment processes show limited removal of micropollutants but may suffice in certain situations;

- Processes such as activated carbon adsorption, AOPs, RO may be more effective but have higher operating costs;
- And other treatment processes that concentrate the target compounds into a residual such as sludge, exhausted GAC/PAC, concentrate, or brine will require further handling.

Another point of increasing interest is the fate of the micropollutants. Biological treatment in many cases can reach the mineralization of the targeted micropollutants, while chemical oxidation may transform the target molecule into another compound that may be less or more toxic than the parent compound (by-products).

The choice of the solution will depend on many parameters: the nature and physical-chemical properties of the micropollutant, the biodegradability of the wastewater, the daily volume to treat, the existing treatment facilities, the requirements and destination of the treated wastewater. A multi-barrier approach based on a treatment line combining different processes should be adopted to address a broad range of micropollutants. This is a complicated topic and it is strongly advised to work with an experienced supplier. The supplier should have appropriate laboratory facilities for analysing the suitability of treatment lines for challenging micropollutants.

Adsorption on activated carbon

Adsorption is the physical phenomenon in which molecules of a liquid (or a gas) adhere to an external or internal surface of a solid substance. Activated carbon is a media with a porous structure and a very large internal surface area (up to 1,500 m^2/g), which makes it highly suitable for adsorption.

Activated carbon is commonly used in the adsorption of micropollutants. This material is usually in granular form inside a filter (GAC) or in powder form (PAC), generally in an activated carbon contactor.

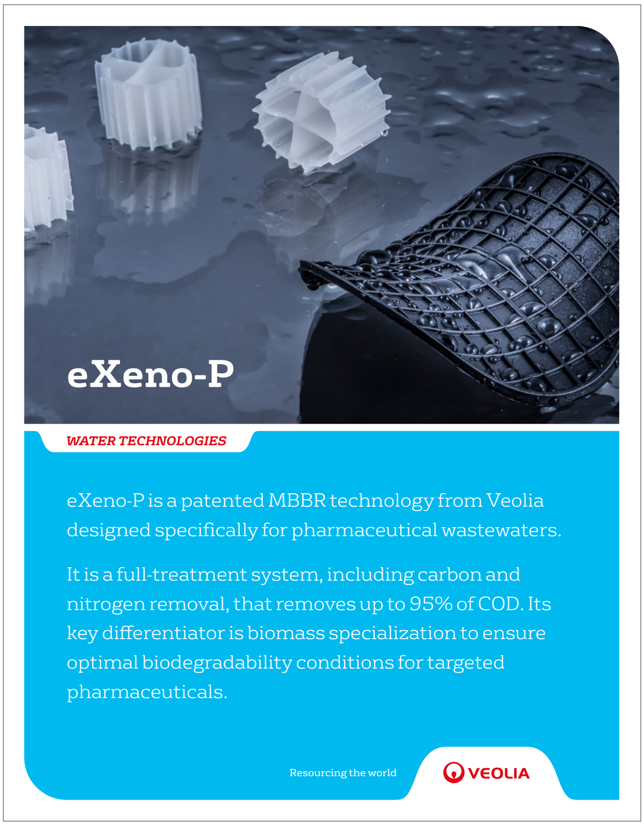
There are different technologies using activated carbon. All of these technologies are broadly used for drinking water treatment and their use in wastewater is now growing due to micropollutant reduction targets.

For pharmaceutical wastewater treatment, the activated carbon solution is a good choice when there is already an existing biological treatment so it can be used as tertiary treatment. Activated carbon adsorption can be combined with ozonation (Actiflo® Carb from Veolia for example) with the objective to increase the micropollutant reduction performance.

Biological oxidation: advanced biological treatments

Conventional activated sludge (CAS) systems are effective in reducing some micropollutants, mostly the easily degradable compounds. However advanced biological treatments generally achieve higher reduction rates than CAS.

- Membrane BioReactor (MBR): the combination of activated sludge and ultrafiltration membranes gives good reduction rates on a reasonable spectrum of micropollutants. In the activated sludge tank, the easily degradable compounds are oxidized by the biomass, then the membrane acts as a selective barrier and retains some organic molecules (macro-molecules with size between 0.1 and 0.01 µm) which would not be retained on a clarifier in a CAS system. *The MBR solution is notably interesting in applications where there is a need for a high water quality: recycling of the water treated on site or stringent discharge requirements.*
- Moving Bed Biofilm Reactor: eXeno™, this patented Veolia technology typically involves multiple MBBR reactors in series with conditions to encourage the development of specialized microorganisms in each reactor tank to target a variety of complex compounds. In the first stage, more easily degradable compounds are removed while the more difficult compounds are removed in the succeeding reactors. The low load conditions in late stages allow for the development of specific microorganisms capable of degrading the more complex compounds.



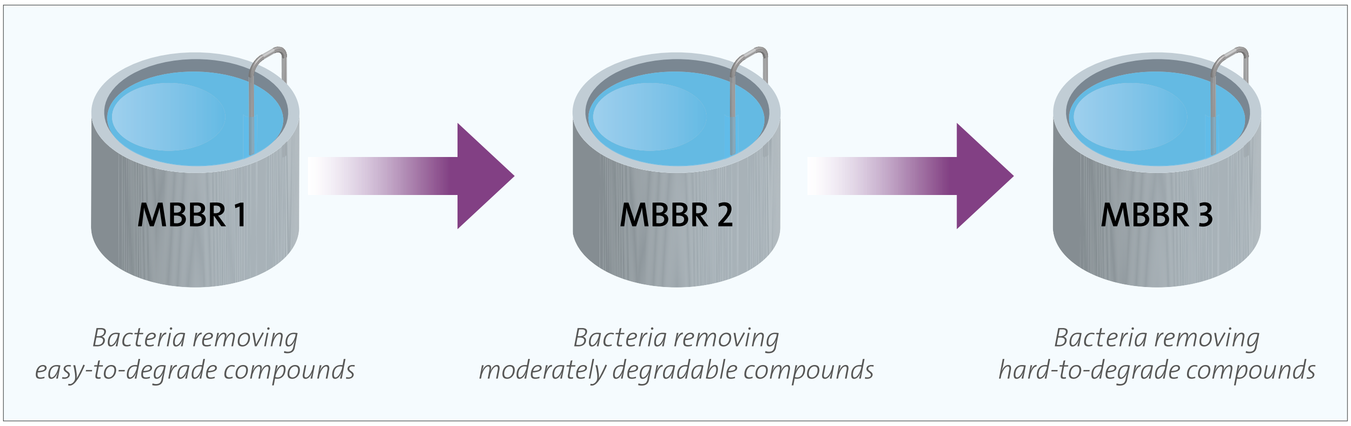


Diagram of a staged MBBR for micropollutant reduction

Chemical oxidation

- Ozone is a powerful oxidant that can destroy or break down many organic pollutants and inorganic pollutants into smaller molecules that are more easily biodegradable. Oxidation with ozone is generally effective for the removal of a broad spectrum of APIs.

  The expected reduction of micropollutants is within a range of 80-90%. One of the main drawbacks of oxidation with ozone is the potential formation of by-products whose environmental fate is unknown and might be worse than the API's themselves. For this reason, the use of ozonation followed by a biological or activated carbon step is considered a better solution than ozone alone because biodegradable organic compounds including by-products formed by ozonation can be removed by microorganisms and adsorbed.

- Advanced oxidation processes (AOP): These processes involve the production of a more powerful secondary oxidant from a primary oxidant. They implement a chemical activation to activate ozone, hydrogen peroxide and oxygen, and to produce highly reactive hydroxyl radicals. To date these technologies have been rarely employed for the treatment of pharmaceutical wastewaters.

Membrane Filtration

The ability of a membrane to remove a micropollutant depends on the pollutant's size, charge and hydrophobicity. Pressure is required to separate micropollutants from water via membranes. Nanofiltration can remove most organic pollutants and reverse osmosis removes all the smallest molecules.

Membrane technologies are optimized solutions when other compounds are to be removed from wastewater, such as salts, microorganisms, refractory COD. They are also a good choice for recycling applications.

Concentration

The evapoconcentration process produces a concentrate where the compounds less volatile than the water will stay. Thus some of the micropollutants are separated depending on their molecular weight and applied temperature.

The evapoconcentration solution is a good match for relatively low daily flow rates and highly concentrated or poorly biodegradable wastewaters.

B11. Sludge treatment, waste and by-product disposal

What is sludge treatment?

Sludge refers to the residual, semi-solid material that is produced as a by-product of wastewater treatment.
In most cases, sludge originates from:

- The primary separation (if one exists)
- The biological treatment, e.g. directly from the MBR or from the secondary separation in the case of MBBR
- The tertiary treatment, if one exists

Why install sludge treatment in a Pharmaceutical manufacturing wastewater treatment plant?

Sludge treatment technologies aim to:

- Minimize the volume to be discharged by removing water
- Facilitate transportation, handling and storage by improving the texture of the sludge

What types of treatment are suitable for Pharmaceutical manufacturing sludges and what are the results?

The technologies used for sludge treatment include: centrifuge decanter, screw press, volute dewatering press or filter press.
Conditioning of the sludge prior to dewatering is required.

Centrifuge decanter

A centrifuge decanter is often proposed because of low capital expenditure compared to other technologies. A centrifuge decanter aims to obtain the pasty state of sludge (a sort of "cake") in a short space of time. Using centrifuge decanter technology, the expected dryness of the cake is within the range of 15 to 25% dry solids (DS).

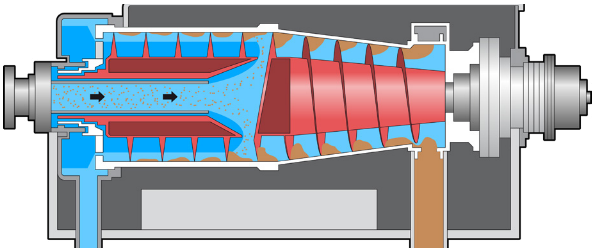


Diagram of a centrifuge decanter

Volute dewatering press

It is another dewatering technology which gives good results. It is structured with a filter element that consists of two types of rings: a fixed ring and a moving ring - a screw that thrusts the filter element, transfers and pressurizes the sludge. The gaps between the rings and the screw pitch get narrower towards the sludge cake outlet, which thickens and dewaters the sludge.

Using this technology on a mix of sludges coming from DAF (oily) and biological sludge, the expected dryness of the cake is within the range of 20 to 25% dry solids (DS).

Due to the principle of separation (no centrifuge force), no issue with foaming has been observed. The technology is reliable, easy to operate and low energy.

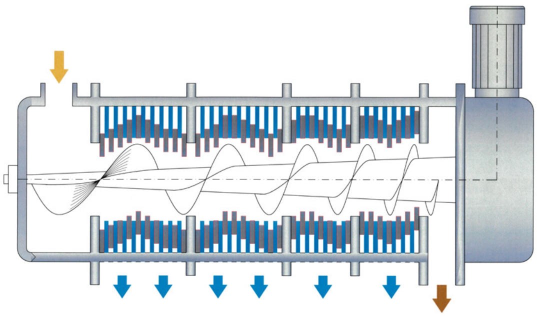


Diagram of a volute dewatering press

Screw press

A screw press comprises a screw rotating at low speed inside a cylindrical cage. The sludge is fed between the screw and the cage and is transported by the rotating screw in a direction parallel to the axis. The sludge is progressively compressed as it moves towards the discharge outlet. The gradual increase of the pressure is used to extract the water flowing out the press at the periphery of the cage, while the cake moves along the axis of the barrel to the discharge gate at the other end of the machine.

Depending on sludge origin, the expected dryness of the cake will be within the range of 15-25% dry solids (DS).
Due to the principle of separation (no centrifuge force), no issue with foaming has been observed. The technology is reliable, easy to operate, low energy and low noise. However capital expenditure is usually higher than the centrifuge decanter solution.

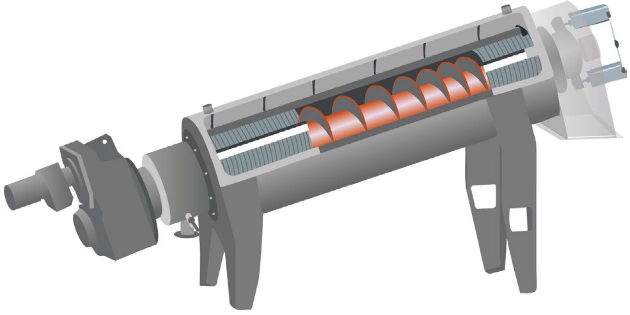


Diagram of a screw press

Filter press

The filter press is a machine used to filter liquids loaded with solid matter in suspension under pressure. It is composed of 3 main parts: the frame, the filter part and the hydraulic power unit. Its operation is discontinuous. The filtration cycle can be broken down into four phases (a filling phase – a pressing phase – a compaction phase – a demounting phase) and can vary from less than half an hour to more than half a day depending on the type of sludge. A backwash cycle using pressurized water is activated every 10 to 30 pressings in order to maintain the filtration capacity.

The filter cake is expected to be between 30-35% DS.

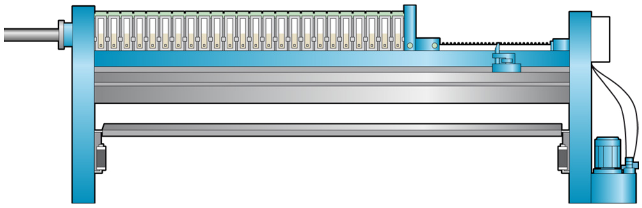


Diagram of a filter-press

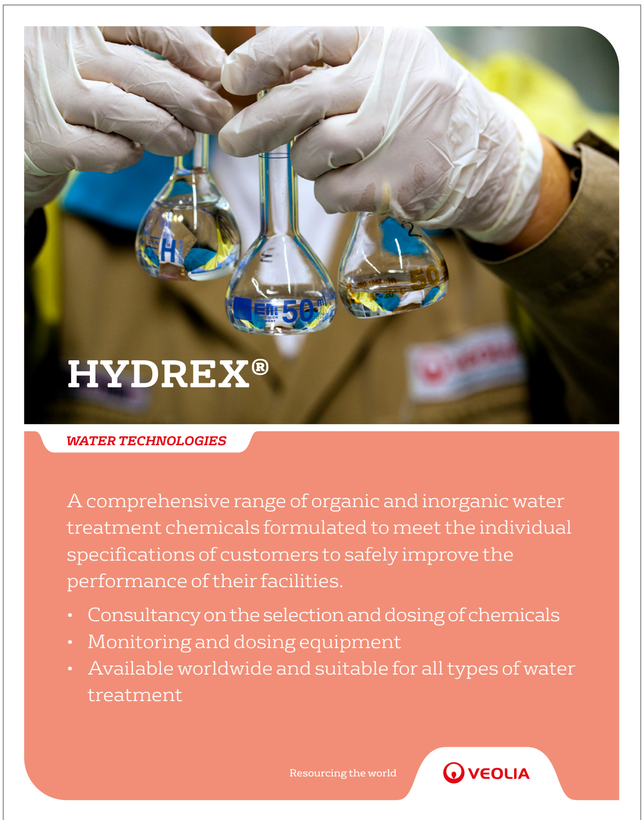
4. SERVICES

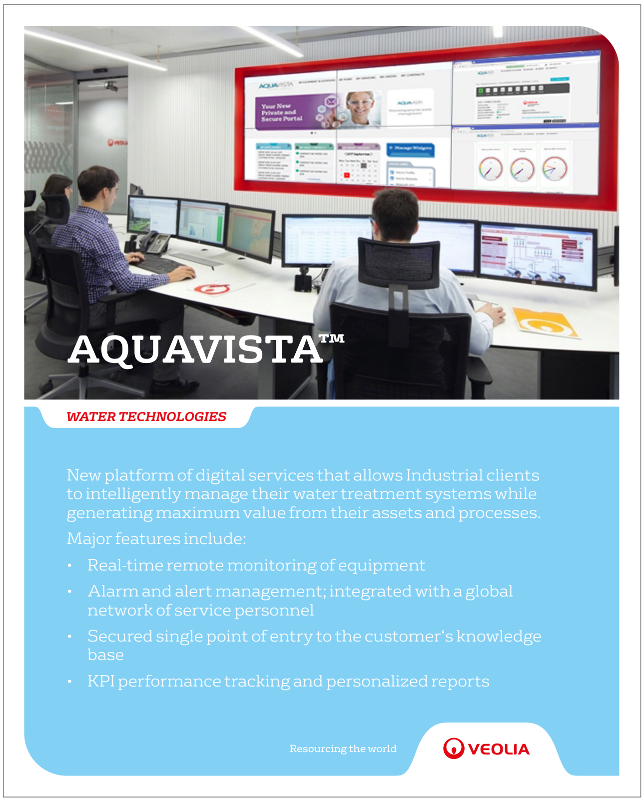
A- Maintenance Services

Once installed a plant must be maintained in order to ensure that it continues to treat water to the discharge requirements for compliance. Maintenance services may be responsive, preventive or predictive. Preventative and predictive maintenance are most frequently used to ensure plant uptime, compliance and operational efficiency objectives are met. Predictive maintenance plans use real-time data from the plant and compare it to historic data (for the plant or similar plants) in an attempt to foresee potential issues.

B- Water Treatment Chemicals

Water treatment chemicals are an essential element of an effective operating and maintenance routine. Wastewater qualities and volumes from Pharmaceutical manufacturing plants vary with the production of batches. It is therefore important to ensure that the appropriate formula and dosage are being used at the appropriate moment. The latter requires an experienced consultant or in some cases may be better managed through outsourced operation of the plant.





C- Digital Services

Operating wastewater treatment plants can be a challenge in any industry. Pharmaceutical manufacturing plants, with their variability of production, can be particularly difficult. In this situation it can be useful to implement Internet of Things technologies. These allow external suppliers and specialists to monitor and advise on how best to manage the plant under current conditions; ensuring uptime, compliance and efficiency.

D- Mobile Wastewater Services

Mobile treatment solutions are principally of interest to Pharmaceutical manufacturing facilities for treatment of APIs or toxic compounds upstream of the main wastewater treatment plant. A mobile solution may be preferred due to the temporary nature of the pollution (e.g. seasonal production, temporary production for clinical trials, batch issues, etc.) or due to difficulties in securing capital for long term infrastructure investments.

Secondary drivers for mobile wastewater treatment plants are maintenance and operation of the main wastewater plant.

Production variations over time may also pose a challenge to the wastewater treatment plants' operators who may call upon mobile solutions for additional temporary treatment capacity.

5. EXAMPLES OF TREATMENT LINES

A. EQUALIZATION > MBBR > DAF > COOLING

Manufactured products

Finished Products

Products for Human Health: syrups, dermatologic soaps, suppositories.

Design capacity

Average capacity: 100 m^3/d
Future capacity: 130 m^3/d - 2.1 T/d COD
COD: 1,700 to 6,600 mg/l
COD/BOD_5: 2
Refractory COD: 300 mg/l
TSS: 200 mg/l
Zn: 13 mg/l
AOX: 8.4 mg/l
Temperature: 25-34 °C

Treated water requirements

COD < 2,000 mg/l
BOD_5 < 800 mg/l
TSS < 600 mg/l
Zn < 2 mg/l
AOX < 1 mg/l
Temperature < 30 °C

Discharge

To municipal wastewater treatment.

Challenge

The challenge was to treat different pollution parameters within a restrained number of processes with the option to extend the plant for future growth of the production site.

Solution

With a COD/BOD_5 ratio of 2, the biodegradability of the wastewater favored the selection of an MBBR following equalization. The biologically treated effluent is separated from the biological sludge with a coagulation-flocculation step followed by a DAF. In this last step, Zn precipitates and is removed from the wastewater. Some Powdered Activated Carbon is added in the DAF to ensure the additional removal of AOX. A final cooling step reduces the treated water temperature to the required target.

Treatment Line

EQUALIZATION TANK → MBBR → DAF → COOLING

Veolia technologies

AnoxKaldnes™ pure MBBR.

Performance

88 to 90% COD reduction.

B. EQUALIZATION > EVAPOCONCENTRATION > MBBR > HYDROSTATIC FILTRATION > GAC FILTRATION

Manufactured products

Finished Products
Products for Animal Health: Antiparasitic pipettes for cats and dogs, dewormers, anti-ticks and fleas for livestock.

Design capacity

Average capacity: 15 m^3/d
with 3 different wastewater streams.
COD: 900 to 9,000 mg/l
COD/BOD_5: 14,5
TSS: 170 mg/l
TP: 3.5 mg/l

Treated water requirements

COD < 90 mg/l
TSS < 30 mg/l
TKN < 10 mg/l
TP < 2 mg/l
Zn < 1 mg/l

Discharge

To river.

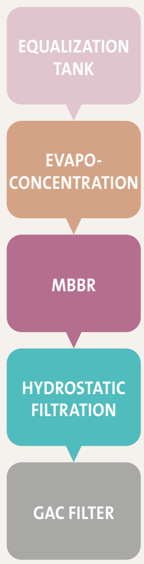
Challenge

The challenge was to treat this highly variable and not biodegradable wastewater to a very stringent quality requirement.

Solution

Following equalization, evapoconcentration was the preferred technology due to the unfavorable COD/BOD_5 ratio for biodegradability, the variability of the wastewater characteristics and the small daily flow rate. The condensate is biologically treated in two MBBR tanks arranged in series, with the addition of nutrients, alkalinity and salinity. A tertiary treatment using a Granular Activated Carbon filter removes a part of the hard COD and completes the treatment line.

Treatment Line



Veolia technologies

Evaled™ Evaporator.
AnoxKaldnes™ pure MBBR.

Performance

95 to 99% COD reduction.

C. EQUALIZATION > EVAPOCONCENTRATION

Manufactured products

Biological API + Finished Products
Products for Human Health: Plasma-based products.

Design capacity

Treatment of a segregated wastewater containing several solvents, mainly Polyethylene Glycol (PEG) diluted in water and mixed with acetic acid, sorbitol and ethanol.
Average capacity: 80 m^3/d
COD: 100,000 - 300,000 mg/l
pH: 3-5

Treated water requirements

COD < 2,000 mg/l
PEG reuse

Discharge

To the existing wastewater treatment plant on site.

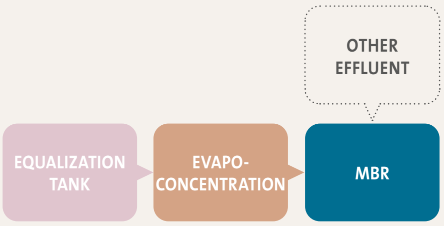
Challenge

The challenge was to treat the extremely concentrated wastewater on site rather than sending it for costly off-site disposal.

Solution

Evapoconcentration was the technology of choice for this project. It produced a condensate with a low COD concentration compatible with biological treatment and as such is combined with the site's other wastewater streams for treatment in the existing MBR. The concentrate from the evapoconcentration process containing 40% PEG is distributed to a third party for use as an additive in cement production.

Treatment Line



Veolia technologies

Evaled™ Evaporator.

Performance

99% of COD reduction.
PEG reuse off site.

D. NEUTRALIZATION > EQUALIZATION > COOLING > MBBR > SAND BALLASTED LAMELLAE SETTLING

Manufactured products

Biological API + Finished Products
Products for Human Health: Plasma-based and recombinant proteins used to treat hemophilia.

Design capacity

Average capacity: 485 m^3/d
Maximum capacity: 700 m^3/d - 0.485 T/d BOD_5
BOD_5: 680 mg/l
COD/BOD_5: 2.8
TSS: 300 mg/l
Temperature: 20-70 °C
pH: 4-12

Treated water requirements

COD < 600 mg/l
BOD_5 < 400 mg/l
TSS < 400 mg/l
Temperature < 40°C
pH: 6-9

Discharge

To sewer.

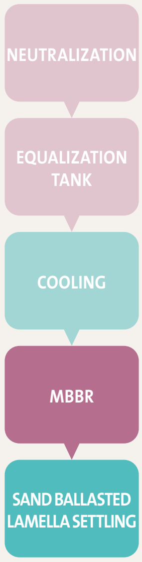
Challenge

The main challenge was the limited space available for the wastewater treatment plant. In addition, due to future growth in production at the site, its design needed to handle two construction phases and a limited construction period.

Solution

After the neutralization and equalization steps, the wastewater is cooled to a temperature suitable for optimized development of the biomass on the MBBR carriers. After biological treatment in four MBBR tanks arranged in series, the biological sludge is separated from the treated effluent in a sand ballasted lamella settler. The MBBR and sand-ballasted lamella settler are both compact processes with small footprints and fast project execution.

Treatment Line



Veolia technologies

AnoxKaldnes™ pure MBBR.
Actiflo® sand ballasted lamella settling.

Performance

COD reduction > 70%.
BOD_5 reduction > 70%.

E. EQUALIZATION > ANAEROBIC REACTOR > MBR

Manufactured products

Biological API + Finished products

Design capacity

> Whole plant:
Average capacity: 3,000 m^3/d
Maximum capacity: 3,500 m^3/d
COD: 3,000 - 5,000 mg/l

> Including a highly concentrated wastewater stream from process manufacturing and aqueous solvents:
Average capacity: 92 m^3/d - 5.6 T/d
Average COD: 61,000 mg/l

Treated water requirements

COD < 80 mg/L
TN < 25 mg/l
TP < 2 mg/l

Discharge

To river.

Challenge

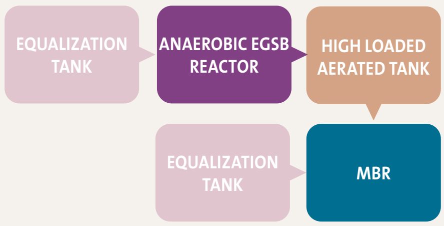
Due to the client's commitment towards sustainable development, the objective was to minimize the impact on the environment by drastically reducing the energy consumption of the existing treatment process used for the highly concentrated wastewater stream.

Solution

In the upgraded configuration, the highly concentrated wastewater stream is treated using an anaerobic Expanded Granular Sludge Blanket reactor (EGSB). The effluent from the former is then combined with the main stream and treated in an MBR system with 5-steps of cascading aerated tanks followed by ultrafiltration membranes. The EGSB produces biogas that is collected and processed. The gas is used in a Combined Heat and Power plant (CHP). The electricity generated covers 90% of the wastewater treatment plant's requirements. The thermal energy is used to heat water which feeds a district heating grid.

Furthermore, the membrane performance for bacteria and particle reduction ensure that the treated wastewater complies with stringent discharge requirements, e.g "bathing water quality".

Treatment Line



Veolia technologies

Biobed® EGSB reactor.
Biosep® MBR.

Performance

> 99% of COD reduction.

F. EQUALIZATION > MBBR > DAF > MBBR > ACTIVATED CARBON > SAND FILTRATION

Manufactured products

Chemical API and Finished Products
Products for Human Health: 120 drugs.

Design capacity

Average capacity: 1,800 m^3/d
Total Organic Carbon (TOC): 250-1,000 mg/l
Presence of highly toxic compounds and API

Treated water requirements

95% TOC reduction
Free of toxic compounds

Discharge

To a lake serving as a drinking water resource for a capital city.

Challenge

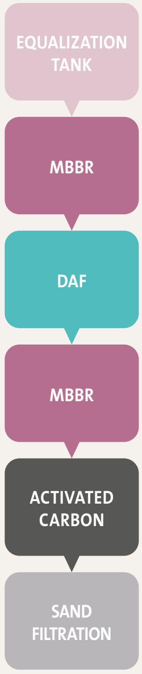
The main challenge was that the wastewater was toxic for the bacteria used in the biological treatment processes. In addition the wastewater contained many difficult to degrade organic compounds.

Solution

After intensive lab and pilot trials, it was demonstrated that only certain microfungi could resist and break down the toxic compounds. A tailor-made treatment process in six MBBR stages was developed.

In the first three MBBR reactors, fungal growth was promoted by lowering the pH to 4. In the following three stages, after the wastewater “detoxification”, pH was adjusted to 7 to promote bacteria for the reduction of residual organic compounds. The biological treatment process is complemented by chemical phosphorus precipitation as well as polishing with activated carbon and a sand filter to take care of any residual toxicity and suspended solids.

Treatment Line



Veolia technologies

eXeno-P staged MBBR.

Performance

97% TOC reduction.
99% reduction for 5 APIs.
80% TN reduction.
99% TP reduction.

G. EQUALIZATION > MBR

Manufactured products

Finished products
Cough syrups, mouth washes, toothpastes.

Design capacity

Average capacity: 350 m^3/d - COD: 2.5 T/d
COD: 3,500 - 7,000 mg/l
COD/BOD_5: 2.4

Treated water requirements

COD < 125 mg/L
BOD_5 < 30 mg/L
TSS < 35 mg/l
TKN < 10 mg/l
TP< 2 mg/l

Discharge

To river.

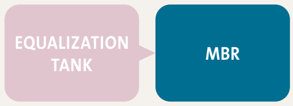
Challenge

Due to the requirements for discharge to sensitive areas, the client needed to obtain a very high quality of treated water based not only on COD, BOD_5 and TSS parameters but also on TN and TP parameters, all while ensuring a compact footprint.

Solution

After an equalization step, MBR provides advanced biological treatment for the elimination of COD, BOD_5 and TSS, and obtains significant microbial reduction. Due to its compact size, the installation has a small footprint.

Treatment Line



Veolia technologies

Biosep® MBR.

Performance

98% COD reduction.
99% BOD_5 reduction.

6. GLOSSARY

AOP	Advanced Oxidation Process: process which removes organic materials by oxidation through reactions with hydroxyl radicals (OH).
AOX	AOX is the abbreviation of the parameter for water soluble "adsorbable organic halogens" in which 'A' stands for adsorbable, 'O' for organic and 'X' for the halogens chlorine, bromine and iodine.
BOD_5	Biochemical (or biological) Oxygen Demand in 5 days (mg/l). BOD_5 is the amount of oxygen necessary for degradation of organic materials present in the effluent by the action of microorganisms. BOD_5 is expressed in milligrams of oxygen consumed per liter of sample during 5 days of incubation at 20°C.
CAS	Conventional Activated Sludge (including clarifier).
Cl^-	Chlorides.
COD	Chemical Oxygen Demand. COD is an index of the pollution, mainly organic, in an effluent. It evaluates the amount of oxygen needed to oxidize the pollutant load.
Cu	Copper.
DAF	Dissolved Air Flotation.
EPS	Extracellular Polymeric Substance: EPS are natural polymers secreted by microorganisms into their environment. These compounds are important in biofilm formation and cell attachment to surfaces.
EQ	Equalization (tank or key process).
Exogenous	An exogenous substance is present and active in an organism but originated outside that organism.
Fenton	Fenton reagent process is one of the AOP, used for refractory COD removal. It is based on a reaction with hydrogen peroxide catalyzed by iron Fe^{2+}.
Hardness	Total hardness (TH) is the sum of the ions calcium [Ca^{2+}] and magnesium [Mg^{2+}] expressed as equivalent of calcium carbonate ($CaCO_3$).
HRT	Hydraulic Retention Time is a measure of the average length of time that the compound remains in a tank.
LBP solvent	Low Boiling Point solvent.
Mother Liquor	A residual liquid resulting from crystallization and remaining after the substances that readily or regularly crystallize have been removed.
SiO_2	Silica.
TDS	Total Dissolved Solids.
TOC	Total Organic Carbon.
Zn	Zinc.

About Veolia Water Technologies

Veolia Water Technologies provides the complete range of services required to design, deliver, maintain, and upgrade water and wastewater treatment facilities and systems for industrial clients and public authorities.

The company's extensive portfolio of technologies features everything from online diagnostic solutions to evaporation and crystallization, energy-producing sludge treatment, state-of-the-art desalination, laboratory-grade water and mobile water services. By optimizing both processes and monitoring, Veolia Water Technologies helps clients reduce their water footprint while generating considerable savings in energy and chemical consumption.

The production of purified water, highly purified water, pyrogen free water and water for injection to international pharmaceutical standards is recognized as a critical process. Veolia Water Technologies' experts develop solutions for pharmaceutical clients that meet and exceed these standards by focusing on the clients' key requirements. The company also focuses on providing total water management of the facilities, including wastewater treatment and reuse and recycling to utilities or other applications.

www.veoliawatertechnologies.com

About Veolia

Veolia group is the global leader in optimized resource management. With over 171,000 employees worldwide, the Group designs and provides water, waste and energy management solutions which contribute to the sustainable development of communities and industries. Through its three complementary business activities, Veolia helps to develop access to resources, preserve available resources, and to replenish them.

With its expertise in infrastructure design and construction, Veolia provides businesses in the pharmaceutical industry with turnkey water treatment (purified water, injection water, wastewater) and energy production facilities (biomass, cogeneration, biogas). These units meet the strict standards imposed by supranational and national authorities.

www.veolia.com

This guide has been written by the experts of Veolia Water Technologies.

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Your regional contact

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