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Innovative technologies and environmental sustainability in the pharmaceutical wastewater treatment at Ascoli Piceno Pfizer plant

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Abstract

This paper is based on an internship experience lasting 450 hours at the Pfizer company in Ascoli Piceno and focuses on sustainability and the treatment of pharmaceutical wastewater produced by the plant itself.

A first part is dedicated to the description of the plant and its functionality, highlighting the results obtained from the pilot test and the fundamental processes of the real wastewater treatment plant.

A second part, the focus of this paper, concerns the reuse of treated water considering different possible options and evaluating the economic and environmental sustainability of each of them.

According to these parameters and comparing the different alternatives, the option that seems to be the best is defined.

The aim of treated water recovery is to reduce the consumption of groundwater, of which Pfizer makes great use, that is influenced by the climate changes and the precipitation scarcity with consequences on the functionality of the systems and their reliability.

Introduction

Pharmaceutical companies participate considerably in the well-being of people and in the treatment of health problems.
Despite this, during the production and packaging of these drugs there is a significant impact on the environment due to the use of water which is then introduced into the surface bodies that can be rich in organic and inorganic substances, exhausted solvents, reagents, active pharmaceuticals ingredients (API) and a high content of BOD, TSS and COD.
These waters contribute to the processes of eutrophication, oxygen depletion, bioaccumulation, loss in biodiversity and therefore to a reduction in the body receptors quality. For this reason, this wastewater must undergo treatment before being discharged.
To this end, Pfizer takes care of minimizing the impact of its activities and products on the environment, providing a precious good for humans but at the same time preserving the environment and our ecosystem.

Particular attention is to be paid to the emission of active pharmaceutical ingredients (API) through the water produced in the plant since antibiotic resistance (AMR) is currently a widespread problem globally.

Antibiotic resistance (AMR) represents an alarming public health priority, both for the important clinical implications (increased morbidity, lethality, duration of the disease, development of complications, epidemics), and for the economic consequences that derive from it in healthcare field. The emergence and spread of multi-antibiotic-resistant bacteria drastically limits therapeutic options.

To deal with this increasingly emerging problem, in Italy, the Ministry of Health has issued the National Plan to Combat Antibiotic Resistance (PNCAR) 2017-2020, which underlines the important role of epidemiological surveillance and whose effects can be evaluated in time.

Wastewater treatment (or wastewater purification), in environmental and chemical engineering, indicates the process of removing contaminants from a wastewater of urban or industrial origin, i.e. an effluent that has been contaminated by organic pollutants and /or inorganic.

The sewage purification treatment consists of a succession of several phases (or processes) during which unwanted substances are removed from the waste water, which are concentrated in the form of sludge, giving rise to a final effluent of such quality as to be compatible with the self-purifying capacity of the receiving body (land, lake, river or sea through an underwater pipeline or on the shoreline) chosen for the spill, without it being damaged (for example from the point of view of the ecosystem associated with it).

The purification cycle is made up of a combination of several chemical, physical and biological processes. The sludge coming from the purification cycle is often contaminated with toxic substances and therefore must also undergo a series of treatments necessary to make it suitable for disposal, for example, in special landfills or for reuse in agriculture as is or after composting. Usually in a wastewater treatment plant two specific lines are distinguished:

• the water line;
• the sludge line.

The raw sewage coming from the sewers is treated in the water line and generally includes three stages, called: pre-treatment, biological oxidative treatment and further treatments.

In the sludge line, the sludge is treated (separated from the clarified wastewater) during the sedimentation phases foreseen in the water line. The purpose of this line is to eliminate the high quantity of water contained in the sludge and to reduce its volume, as well as to stabilize (make rot-proof) the organic material and to destroy the pathogenic organisms present, in such a way as to make the final disposal less expensive and less harmful to the environment.
The final treated effluent or clarified wastewater is conveyed into a pipeline called an emissary, with final delivery of surface waters (watercourses, sea, etc.), incisions or the surface layer of the soil (e.g. drainage trenches). If the final effluent has certain characteristics, it can also be used for irrigation or in industry.

The treatments that are carried out within a treatment plant can be classified into:

- <u>mechanical treatments</u>: they are based on the action of purely physical or mechanical principles; preliminary operations to remove undissolved solids are part of this typology;
- <u>chemical treatments</u>: they are based on the addition of specific chemical substances; neutralization reactions belong to this category (used to adjust the pH of the water), to facilitate precipitation and for disinfection;

- biological treatments: they are based on biological processes carried out by microorganisms present in the water; the treatments carried out for the separation of solids dissolved in water belong to this category.

Through this paper we want to pay particular attention to the reuse of the water treated by the purification plant of the Pfizer plant by evaluating different possible quality scenarios of the water leaving the plant and an evaluation, in terms of costs and environmental sustainability, of the effects that this recovery has on water taken from the aquifer and supplied by the municipality of Ascoli Piceno.

Water is essential for the survival of life on Earth, but under the pressure of population growth and climate change, freshwater resources are becoming scarce.
For this reason, wastewater reuse, also known as water recovery or recycling, is increasingly recognized as a sustainable solution to the growing global water crisis. Rather than considering wastewater as a product to be disposed of, it can be treated and purified to limit freshwater consumption. The treated water can be used for agricultural and/or industrial purposes or for the reconstitution of aquifers. Some countries have already taken large-scale actions.
In Italy and Spain, for example, 8% and 14% of wastewater is reused respectively.

Freshwater conservation depends on the guiding principles of the circular economy: reduce, reuse and recycle. However, the reuse or recycling of wastewater, which represents an effective solution to address resource scarcity, will not solve all the water-related problems that will be faced in the coming decades. Optimized usage methods are needed to reduce water consumption. Agriculture, which accounts for more than 70% of global consumption, remains a priority. Reducing water pollution is also a related goal.
Water contamination interrupts the water cycle and has a negative impact on available resources.

One of Pfizer's objectives is to contribute to reducing the use of fresh water, to implement the measures necessary to combat the water crisis and the pollution of surface water bodies which are the basis of a sustainable ecosystem.

Chapter 1. Pfizer

Pfizer is an American company, headquartered in New York, and the largest company in the world operating in the research, production and marketing of drugs. The business areas in which it is engaged are:

- Human pharmaceuticals with 91.8% of total turnover, for which the strategic sectors are: Cardiology, CNS, Infectious, respiratory, urological and ophthalmic diseases, which generate 96.7% of human pharmaceutical revenues, while the remaining 3.3% is generated by the oncology sector;
- Veterinary with 5.4% of total turnover;
- Other with 2.8% of total turnover.
- The geographical areas are:
- USA 43.5%;
- Europe 29.1%;
- Asia 16%;
- Other continents 11.4%.

Pfizer was born in New York in 1849, thanks to two cousins of German origin, Charles Pfizer and Charles Erhardt, who began their chemical products business at *Charles Pfizer and Company*, in a building on the corner of Harrison Avenue and Barlett Street in Williamsburg (Brooklyn). The first product created was an intestinal pesticide, called *santonin*, which was combined with almonds and coffee to improve its flavor. It was an immediate success, but what really began Pfizer's development in the 1880s and 1890s was the production of *citric acid*. Citric acid, which can be found in a wide variety of fruits and vegetables, particularly citrus fruits, was first isolated from lemon juice by crystallization (1784) by Carl Wilhelm Scheele, while its industrial-scale production began in Italy in 1890, where it was obtained from lemon juice through a complex process. In 1893, Carl Whemer discovered that the *Penicillium* mold could produce citric acid from sugar, but microbial production of citric acid did not become industrially important until World War I stopped citrus exports from Italy. In particular, the American chemist James Currie discovered that some strains of Aspergillus niger could efficiently produce citric acid, and from there the pharmaceutical company Pfizer began industrial production using this technique.
The success recorded led the company to purchase various properties to expand its laboratory and factory in the neighborhood between Barlett Street, Harrison Avenue, Gerry Street and Flushing Avenue.

1899 marked the fiftieth anniversary of Pfizer, which with its two offices in New York and Chicago presented itself as the leading company in the chemical-pharmaceutical sector, entering the twentieth century determined to face the challenges of an increasingly competitive market.
By 1910, sales were nearly $3 million, and Pfizer was an expert in fermentation technology, a skill later applied to the mass production of *penicillin* in response to a call from the U.S. government during World War II. The antibiotic soon became known as the "miracle drug", necessary for the treatment of Allied soldiers, and it was Pfizer itself that produced the largest quantity of the penicillin used by the troops. Penicillin was only the beginning of an era of unprecedented chemical-pharmaceutical discoveries: in fact, Pfizer began an intense research activity to find new organisms capable of fighting bacterial diseases and its centenary coincided with another epochal success: the discovery of a new broad-spectrum antibiotic, the *Terramycin*. This was the first pharmaceutical product sold in the United States under the Pfizer label, which until then had sold its products wholesale to other companies who then marketed them under their own name.

After the Second World War the following main events can be remembered:

- in 1951, branches were created all over the world (Belgium, Brazil, Puerto Rico, Canada, Cuba and England);
- in 1952 Pfizer began setting up an agricultural sector;
- in 1953 it acquired a company specializing in food supplements, J.B. Roerig & Co;
- in 1971 it acquired the German drug manufacturer, Heinrich Mack Illertissen;
- in 1992 the formidable "hat-trick" was recorded, given that Pfizer marketed three of the most important drugs of the last twenty years: *Zoloft* (sertraline hydrochloride), for the treatment of depression, *Norvasc* (amlodipine besylate), for the control of angina and hypertension, and *Zithromax* (azithromycin dihydrate), against skin and respiratory infections;
- in 1999 Pfizer celebrated its 150th birthday;
- in 2000 it acquired the German Warner-Lambert, for which founder William R. Warner invented a tablet coating process;
- in 2003 it acquired Pharmacia and launched a new drug for the treatment of migraines (*Relpax*, eletriptan HBr);
- in 2005 *Lyrica* was launched, the first treatment approved by the FDA (Food and Drugs Administration) for the treatment of two different forms of neuropathic pain;
- in 2006, *Sutent* was launched, a new oral treatment to combat stromal tumor of the gastrointestinal tract and metastatic renal cell carcinoma;

- in 2009 Wyeth was acquired and, in that same year, there was an agreement between Pfizer and GlaxoSmithKline plc for joint research on HIV through the creation of a new company called ViiV Healthcare;
- in 2009, in Fortune magazine, Pfizer is in 46th place in the ranking of world companies, and furthermore, according to IMS Health Midas, Pfizer is the first pharmaceutical company with a turnover of $57,024 billion.

Other important events are:

- in October 2010 the acquisition of King Pharmaceuticals for 3.6 billion dollars; furthermore, in that same month, Pfizer signed a strategic agreement with Biocon for the marketing of various insulin formulations produced by the same. Pfizer's strategic objective was to be present in the field of biosimilar drugs and to gain market share in the insulin sector. Shortly afterwards, Pfizer purchased 40% of the Brazilian group Teuto Brasileiro SA in order to strengthen its position on the Brazilian market, with a portfolio of over 250 molecules;
- in 2011 Pfizer purchased Ferrosan, a company specialized in the production of dietary supplements, very present in the regions of Northern Europe;
- in 2020 Pfizer committed to financing and supervising clinical trials and logistical activities related to the development of a vaccine against the COVID-19 disease, caused by the SARS-CoV-2 coronavirus, which started a serious pandemic in 2019. The development was carried out together with BioNTech, the German biotechnology and biopharmaceutical company that created the actual vaccine technology. On November 9, 2020, the drug was declared effective in 94% of cases tested and in the following two months it began to be distributed for administration to populations. It is an mRNA vaccine, provisionally called Tozinameran, which must be stored at temperatures not exceeding -70°C and which is administered via two intramuscular injections three weeks apart.

1.1 Pfizer Italy

Pfizer has been present in Italy since 1955 and is an important industrial reality in the country, with a turnover in 2020 of approximately 800 million euros and 2000 employees. The main office is in Rome, where it houses the administrative headquarters. The offices of the Pharmacovigilance Unit of the Clinical Oncology Research and Regulatory Strategy group, which work at a global level, and of Consumer Healthcare are located in Milan. These structures are flanked by two production plants:

• in Ascoli Piceno, an excellent production plant and key site for the global production of some of Pfizer's main products, such as oncology drugs;

• in Catania, global supplier of injectable penicillin and non-penicillin antibiotics.

with important export volumes worldwide.

FIgure 1: Pzifer in Italy

Pfizer research in Italy is mainly oriented towards research in the oncology field and in infectious diseases, in the central nervous system, in endocrinology and in cardiovascular diseases. Furthermore, in Italy there are active research centers in Milan, in the therapeutic area of oncology, and in Catania, dedicated to preclinical toxicology studies.

1.2 Pfizer factory in Ascoli Piceno

FIgure 2: Pfizer productive plant in Ascoli Piceno

The Pfizer plant in Ascoli Piceno was born in 1972 as the production hub of Carlo Erba Conte Visconti di Modrone, with a staff of 60 employees and production limited to the Italian market. In 1979 the company was merged with Farmitalia of the Montedison Group and both, in 1993, were acquired by the Swedish Pharmacia group. In 1995 there was the acquisition of Farmitalia-Carlo Erba by Kabi-Pharmacia and the birth of the Pharmacia group. Following the merger with the Upjohn Company, Pharmacia & Upjohn (P&U) was born. In 2000, P&U merged with Monsanto/Searle taking the name Pharmacia Co. Finally, in 2003, Pfizer acquired Pharmacia and starting from December 2005, the company name was changed to Pfizer Italia S.r.l.

The Pfizer site in Ascoli Piceno is one of the production centers of excellence in the global pharmaceutical scene, highly specialized in the production of solid oral tablets and capsules (CNS, anti-inflammatories, oncology), and related primary and secondary packaging. The strong innovation of the technologies implemented, the great skills in the production of drugs "with a strong impact and high pharmacological profile", especially in oncology and disorders of the central nervous system, as well as the professional level of its employees, guarantee the competitiveness of the site and the position themselves as one of the main key suppliers for Pfizer.

The production volume stands at 115 million packs, with 3.5 billion tablets/capsules.

This allows the site to confirm itself as one of Pfizer's key suppliers with some of the most important key products of the company's core business in the world.

This site produces an anticancer drug for gastrointestinal stromal cancer and kidney cancer of international importance.
The markets served are more than 100: the largest market share is the European one (29%), which does not include the Italian one (with a further 17%), then there are the Central and Eastern Europe Region markets (14%), Asian (20%), American (4%), Africa and the Middle East 6%, USA (9%).
The Pfizer plant in Ascoli Piceno occupies a total area of 164,000 square meters, of which 24,000 square meters are covered by plants, warehouses and other structures, and 140,000 square meters of land. The volume occupied by the buildings is 125,362 m^2, of which 29,680 m^2 intended for the production cycle, 67,904 m^2 intended for warehouses and 11,637 m^2 for offices. The large spaces, intended for the production departments and services, allow for the most rigorous compliance with good manufacturing practices and the handling of raw materials and finished products according to criteria of maximum rationality.
The site is equipped with 2 warehouses: one for the management and storage of incoming raw materials, entirely automatic, with 10,000 automated pallet spaces, and the other, with approximately 3,000 pallet spaces, for the management and storage of finished products ready to ship. Furthermore, the site has technologies that allow the highest levels of automation and maximum control in the movement of the active ingredients which never come into contact with the production operators.
Particular attention is also paid to the environment: the photovoltaic system and cogenerator installed on the site, which support around 70% of electricity consumption, have made it possible to reduce the plant's $CO2$ emissions by 50%.

1.3 The Pfizer productive plant of Ascoli Piceno

The layout of the production plant of the Pfizer plant in Ascoli Piceno has been defined in such a way as to maximize the efficiency of the processes, therefore the level of productivity. In particular, the production plant was designed "in cascade", precisely to facilitate the flow of raw materials, which therefore fall by gravity.

FIgure 3: Pfizer factory layout in Ascoli Piceno

There are a total of four floors, which are named according to the height from the ground:

• Level +11.90 m: here there is the Batch 2 Formulation Center (CFL2), where the various raw material powders are weighed, to then be sieved and mixed in the proportions foreseen for each drug, and then inserted into the hoppers, containers in the shape of a truncated pyramid, which allow the passage of dust to the floor below, i.e. at a height of +8.50 m;

• Height +8.50 m (2nd floor): here there is still the Batch 2 Formulation Center (CFL2), where the collection of powders takes place which are sent to the two tablet departments (Tablets 1 and Tablets 2); in particular, in Tablets 1, and only for some drugs, a second mixing takes place;

• Level +4.25 m (1st floor): here there is the MFC Multipurpose department, which includes several rooms with the tablet presses that allow the tablet to be shaped, the Packaging Area where the primary and secondary packaging of the different types of tablets takes place, a separate area dedicated to other products (the Provera-Farlutal), the Automatic Warehouse and the Sampling Area where product sampling takes place;

• Level -1.05 m (ground floor): here there are the chemical and microbiological laboratories, the CE2 Electrical Cabin, and dedicated departments, called "High Active", which due to contamination problems carry out the entire process in a single room on the same floor.

Furthermore, the entire production area is organized into three main teams, depending on the product processing phase or the type of product to be made:

- Team Manufacturing: includes all departments ranging from preparation of the powder to production of the product (oral solid tablets), with the exception of those intended for the production of High-Active products;
- Team Packaging: includes the product packaging lines, with the exception of those intended for the packaging of High-Active products;
- Team Hi-Act: includes all the processing and packaging departments of highly contaminated products.

1.4 Pfizer utilities department of Ascoli Piceno

The Utilities department of the Pfizer plant in Ascoli Piceno is the area dedicated to the management and monitoring of the energy consumption of the various services offered by the different plant systems. The main intent of this department is aimed at minimizing consumption, in order to reduce costs and environmental impact.

In particular, the main services present in the pharmaceutical plant are:

- Electric energy
- Compressed air
- Clean steam and technical steam
- Hot, chilled and superheated water
- HVAC (Heating Ventilation & Air Conditioning)

For these services, reference is made to the three fundamental areas of the Utilities department:

- Thermal power plant
- Central refrigeration unit
- Compressor control unit
- Specifically, the main energy carriers present in the plant are:
- Methane gas
- Electric energy
- Waterfall

Each of which is characterized by points of production or purchase (sources) and points of use (destinations).

Specifically, methane gas is purchased from the supplier, reaches the factory in the methane cabin and is then distributed to power the cogenerator, the canteen and the thermal power plant.

Electricity is purchased from the network and produced by a generator and photovoltaic system, and then distributed to all users.

Finally, as regards water, there is municipal water taken from the public network, which once it enters the plant is treated according to use, and then there is a part of the drinking water which is taken from three wells and is intended for filling a collection tank. In particular, the water present in this tank is used partly to replenish the chilled water collection tank and partly for the fire prevention system, sanitary waste and irrigation.

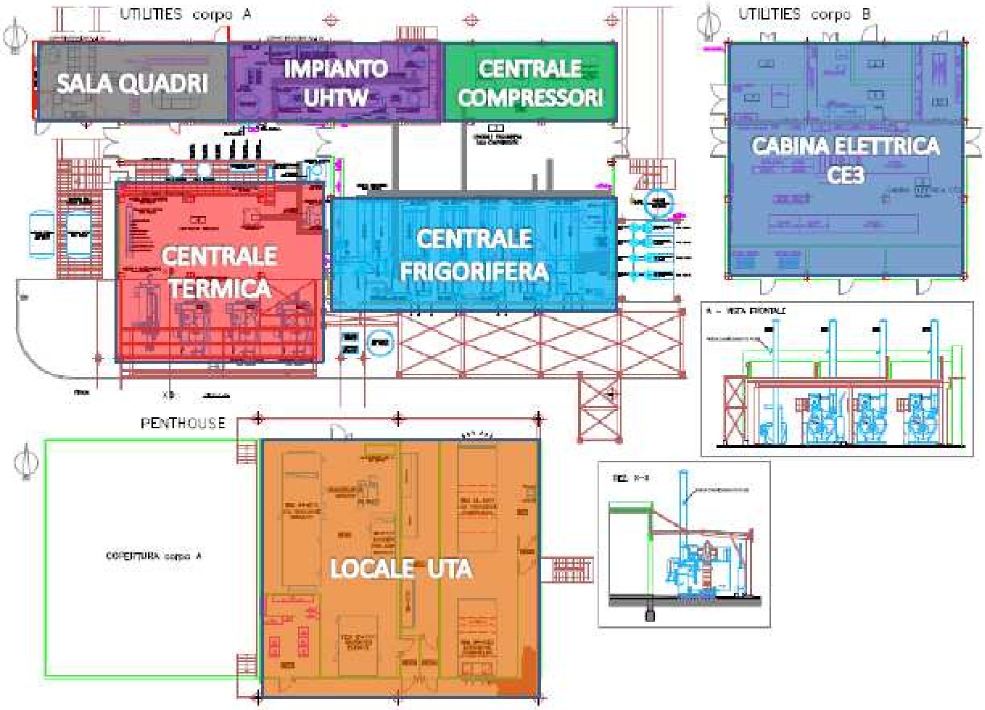

FIgure 4: Pfizer utilities department layout in Ascoli Piceno

Chapter 2. Water resource management – Pfizer case

Water is not only a commercial product, but also a common good and a limited resource that must be protected and used sustainably, in terms of both quality and quantity. However, its use in a wide range of sectors, such as agriculture, industry, tourism, transport and energy, generates pressure on this resource.

The **EU Water Framework Directive 2000/60/EC** establishes a legal framework to protect clean water and restore its quality within the Union, as well as to ensure its sustainable use in the long term.

In 2012, the Commission presented the Europe's Water Resources Safeguarding plan, a long-term strategy aimed at ensuring adequate qualitative and quantitative water supplies for all legitimate uses, improving the implementation of existing EU policy in water sector, integrating its objectives into other sectoral policies and filling the gaps in the existing framework. This plan involves the development by Member States of water resource accounting and water efficiency objectives, as well as the definition of EU standards for water reuse.

EU policy has established two main legal frameworks for the protection and management of freshwater and marine water resources through a holistic ecosystem-based approach, namely the Water Framework Directive and the Marine Strategy Framework Directive.

The EU Water Framework Directive sets out a framework for the protection of inland surface waters, transitional waters, coastal waters and groundwater. It aims to prevent and reduce pollution, promote sustainable use, protect and improve the aquatic environment and mitigate the effects of floods and droughts. The main objective is to ensure that all waters achieve good ecological status. Member States are therefore required to develop so-called river basin management plans based on natural river basins, as well as specific programs containing measures to achieve these objectives.

An evaluation of the Water Framework Directive was conducted in 2019, which determined that the Directive is broadly fit for purpose, but that its implementation needs to be accelerated. As a result, in June 2020 the Commission announced that the Water Framework Directive would not be amended and that instead the focus would be on the implementation and enforcement of the existing Directive.

The Water Framework Directive is complemented by more targeted directives, such as the Groundwater Directive, the Drinking Water Directive, the Bathing Water Directive, the Nitrates

Directive, the Urban Wastewater Treatment Directive, the environmental quality standards and the Floods Directive.

The Directive on the protection of groundwater against pollution and deterioration establishes specific criteria to assess the good chemical status of groundwater, to identify significant and sustained increasing trends and to determine the starting points to be used for trend reversal. All threshold values for pollutants (with the exception of nitrates and pesticides, for which limits are set by specific EU legislation) are set by Member States.

In October 2022, the Commission presented a proposal to amend the framework for Community action on water, the Directive on the protection of groundwater against pollution and deterioration and the Directive on environmental quality standards in the field of water policy.
The Environmental Quality Standards Directive sets concentration limits for 33 priority substances that pose a risk to, or transmitted through, the aquatic environment at EU level and for 8 other pollutants in surface waters. During the 2013 review, 12 new substances were added to the existing list and an obligation was introduced for the Commission to establish an additional list of substances for which monitoring is necessary in all Member States in order to facilitate future revisions of the list of priority substances. The Commission's October 2022 proposal foresees the addition of 23 individual substances to the list of priority substances for surface waters, including pesticides such as glyphosate, some pharmaceuticals (painkillers, anti-inflammatory drugs and antibiotics), bisphenol A and a group of 24 polyfluoroalkyl substances (PFAS).

The Urban Wastewater Treatment Directive aims to protect the environment from the negative impacts of the discharge of urban wastewater and wastewater originating from industry. The directive establishes minimum requirements and timetables for the collection, treatment and discharge of urban wastewater, introduces controls on the disposal of sewage sludge and requires the gradual elimination of sludge discharge into the sea. In October 2022, the Commission adopted its proposal to revise the Directive.

The Nitrates Directive aims to protect waters from pollution caused by nitrates from agricultural sources. A complementary regulation requires Member States to send to the Commission, every four years, a report containing information on codes of good agricultural practice, designated nitrate vulnerable zones and water monitoring, accompanied by a summary of the action programs. The objective of both the directive and the regulation is to safeguard drinking water and prevent damage caused by eutrophication. In October 2021, the Commission published its latest implementation report, warning that nitrates still cause harmful pollution in EU waters and that over-fertilization remains a problem in many parts of the Union.

The sustainable future of water resources is critical to people, ecosystems and global economies, yet pollution and climate change are putting pressure on water systems.
It is estimated that water consumption will grow by 1% per year over the next 30 years1, driven by increased use by the industrial and energy sectors, global population growth, economic development and changing consumption habits. Currently, 88% of water consumption comes from companies, which are gradually becoming aware of the scarcity of this vital commodity, thus encouraging the demand for innovative technologies to conserve water and manage complex water needs.

2.1 Italian water directive

In Italy, the protection of water is regulated by **Legislative Decree 152/2006** deriving from the previous decree 152/1999 which focused on the treatment of wastewater and the protection of water from pollution and represents the implementation of the European directive on the protection of water resources 2000/60/EC.
This decree manages soil protection, waste, air pollution and, as we have said, water protection; in particular it is divided into six parts:

1. Common provisions;
2. VIA, VAS, IPPC;
3. Soil defense, water protection from pollution and water resource management;
4. Waste management, remediation of contaminated sites;
5. Air pollution;
6. Environmental damage.

The main aspect of this decree is the regulation of discharges which must be controlled to reach the acceptability limits of polluting substances.
Discharges are regulated according to compliance with the quality objectives of water bodies and must be authorized.
The discharge limits established by the decree are tabulated in Annex 5; in particular:

- Discharges from wastewater treatment plants with a capacity between 2000 and 10000 and greater than 10000 person equivalent must comply with the limits of table 1;
- Discharges of urban wastewater into surface water bodies, falling in sensitive areas or in an area at risk of eutrophication, are added to the limits shown in table 2;
- Table 3 is provided for discharges from plants that treat industrial wastewater, which distinguishes between discharge into public sewers and discharge into surface water.

Tabella 1. Limiti di emissione per gli impianti di acque reflue urbane

PARAMETRI (MEDIA GIORNALIERA) (1)	POTENZIALITÀ IMPIANTO IN A.E. (ABITANTI EQUIVALENTI)			
	2.000 – 10.000		>10.000	
	Concentrazione (mg/l)	% di riduzione	Concentrazione (mg/l)	% di riduzione
BOD_5 (senza nitrificazione) (2)	25	70-95 (5)	25	80
COD (3)	125	75	125	75
Solidi sospesi (4)	35 (5)	90 (5)	35	90

FIgure 5: tabella 1, Allegato V, D.lgs. 152/06

Tabella 2. Limiti di emissione per gli impianti di acque reflue urbane recapitanti in aree sensibili

PARAMETRI (MEDIA ANNUA)	POTENZIALITÀ IMPIANTO IN A.E.			
	10.000 – 100.000		>100.000	
	Concentrazione (mg/l)	% di riduzione	Concentrazione (mg/l)	% di riduzione
Fosforo totale (P) (1)	2	80	1	80
Azoto totale (N) (2)(3)	15	70-80	10	70-80

FIgure 6: tabella 2, Allegato V, D.lgs. 152/06

Acque di scarico – valori limite di emissione
ALL. 5, P. Terza, D.Lgs n. 152 del 03.04.06

N°	PARAMETRI	Tab. 3 – SCARICO IN ACQUE SUPERFICIALI		Tab. 3 – SCARICO IN RETE FOGNARIA		Tab. 4 – SCARICO SU SUOLO	
1	pH	5,5 – 9,5		5,5 – 9,5		6 - 8	
2	Temperatura (°C)	Variabile in funzione della tipologia del recapito				/	
3	colore	n.p. 1:20		n.p. 1:40		/	
4	odore	no molestie		no molestie		/	
5	materiali grossolani	assenti		assenti		Assenti	
6	Solidi sospesi totali	80	mg/l	200	mg/l	25	mg/l
7	BOD_5 (come O_2)	40	"	250	"	20	"
8	COD (come O_2)	160	"	500	"	100	"
9	Alluminio	1	"	2,0	"	1	"
10	Arsenico	0,5	"	0,5	"	0,05	"
11	Bario	20	"	/		10	"
12	Boro	2	"	4	"	0,5	"
13	Cadmio	0,02	"	0,02	"	(*)	
14	Cromo totale	2	"	4	"	1	"
15	Cromo VI	0,2	"	0,20	"	(*)	
16	Ferro	2	"	4	"	2	"
17	Manganese	2	"	4	"	0,2	"
18	Mercurio	0,005	"	0,005	"	(*)	
19	Nichel	2	"	4	"	0,2	"
20	Piombo	0,2	"	0,3	"	0,1	"
21	Rame	0,1	"	0,4	"	0,1	"
22	Selenio	0,03	"	0,03	"	0,002	"
23	Stagno	10	"	/		3	"
24	Zinco	0,5	"	1,0	"	0,5	"
25	Cianuri totali (come CN)	0,5	"	1,0	"	(*)	
26	Cloro attivo libero	0,2	"	0,3	"	0,2	"
27	Solfuri (come H_2S)	1	"	2	"	0,5	"
28	Solfiti (come SO_3)	1	"	2	"	0,5	"
29	Solfati (come SO_4)	1000	"	1000	"	500	"
30	Cloruri	1200	"	1200	"	200	"
31	Fluoruri	6	"	12	"	1	"
32	Fosforo totale (come P)	10	"	10	"	2	"
33	Azoto ammoniacale (come NH_4)	15	"	30	"	(**)	
34	Azoto nitroso (come N)	0,6	"	0,6	"	(**)	
35	Azoto nitrico (come N)	20	"	30	"	(**)	
36	Grassi e olii animali / vegetali	20	"	40	"	/	
37	Idrocarburi totali	5	"	10	"	(*)	
38	Fenoli	0,5	"	1	"	0,1	"
39	Aldeidi	1	"	2	"	0,5	"
40	Solventi organici aromatici	0,2	"	0,4	"	0,01	"
41	Solventi organici azotati	0,1	"	0,2	"	0,01	"
42	Tensioattivi totali	2	"	4	"	0,5	"
43	Pesticidi fosforati	0,10	"	0,10	"	(*)	
44	Pesticidi tot. (esc. fosf.) tra cui:	0,05	"	0,05	"	(*)	
45-46	- aldrin; dieldrin (ciascuno)	0,01	"	0,01	"	(*)	
47-48	- endrin; isodrin (ciascuno)	0,002	"	0,002	"	(*)	
49	Solventi clorurati	1	"	2	"	(*)	
50	Escherichia coli (UFC/100ml)	Consigliabile inf. 5000 UFC/100 ml		/		Consigliabile inf. 5000 UFC/100 ml	
51	Saggio di tossicità acuta	o.i. ≤ 50%		o.i. ≤ 80%		o.i. ≤ 50%	
						SAR	10
						(**) Azoto tot.	15 mg/l
						Berillio	0,1 mg/l

(*) Sostanza pericolosa di cui è vietato lo scarico in suolo/sottosuolo
(**) in scarico su suolo è regolamentato l'azoto totale
o.i. = organismi immobili dopo 24 ore

Figure 7: tabella 3 e 4, Allegato V, D.lgs. 152/06

2.2 Water in the pharmaceutical sector and its treatments

As in many other industries, water represents the most used resource also in the pharmaceutical sector and, in many cases, also the first ingredient of the products that will ultimately be put on the market, indeed the 22% of the freshwater present in the Earth is the global request for the pharmaceutical industry.

Water is used both as a basic ingredient in many formulations and as a heating or cooling fluid for systems. It is also used for particular washing and purification processes as well as for more common uses such as refreshments, toilets and fire protection. It is therefore easy to understand that, by their nature, all plants that produce water for pharmaceutical use will have to be built in full compliance with standards that are decidedly more restrictive than other industrial water plants.

At a qualitative level, all this water must be free of organic and inorganic contaminants, such as bacteria, mold, yeasts, pesticides, viruses, particles and dissolved gases.

As regards the origin of the water used, it may be meteoric (i.e. coming from normal atmospheric precipitation such as rain, snow and hail), underground, spring, superficial (i.e. coming from lakes, rivers and surface water) or mixed, i.e. partly coming from wells or aqueducts.

Typically, in the pharmaceutical sector, water is always subjected to two types of treatments: one at the beginning of the production cycle and one at the end of it.

As regards the process water used in pharmaceutical companies, it is generally classified according to its different uses as purified or sterile (for injectable or inhalable preparations), as dilution water (to be used in combination with concentrated solutions), for hemodialysis, bacteriostatic and for biotechnological uses.

For pharmaceutical production, the quality of the feed water that passes through an internal treatment to generate water for pharmaceutical use is important.

All water treatment phases must guarantee the achievement of two objectives: purity and sustainability.

Contamination represents real threats to health and therefore their prevention is vital to guarantee the safety of products.

Treatments must meet the standards of the main pharmacopoeias regarding the use of water for the different pharmacological classes. These are different types of treatment for purified water (PW), highly purified water (HPW) and maximum purity of water for inoculation (WFI). Pharmaceutical companies are focusing heavily on sustainability to reduce the effects of water scarcity and environmental impact. The main areas of intervention are water efficiency through internal recycling and advanced treatment of final effluents.

While the treatments vary depending on the main pharmacopoeias, on the other hand it must be remembered that most treatments tend to generate purified water or WIFI using membranes (UF and/or RO), deionization, distillation and/or or disinfection. However, thermal disinfection and distillation treatments consume large amounts of energy. This is why by improving water efficiency the quantities to be treated are reduced and energy efficiency is improved. The internal reuse of washing water allows to reduce the volumes discharged and the costs for wastewater treatment.

Since disinfection is particularly important, a variety of methods are used including heat treatment, UV treatment and ozonation during the various stages of the process. These disinfection processes do not generate chemical byproducts, even if the use of ozone involves the use of ozone-depleting devices. UV is becoming very popular but is used to disinfect the point of application and does not destroy the biofilms of microbes that can accumulate in the pipe. To eliminate these biofilms, it is necessary to slide a disinfectant, normally ozone, along the pipes.

Ozone, together with peroxide and/or UV are extremely effective for the oxidation of biofilms of microbes and bacteria.

2.3 Water resource management in Pfizer

At Pfizer, two types of water resources can be distinguished: municipal water and well water.

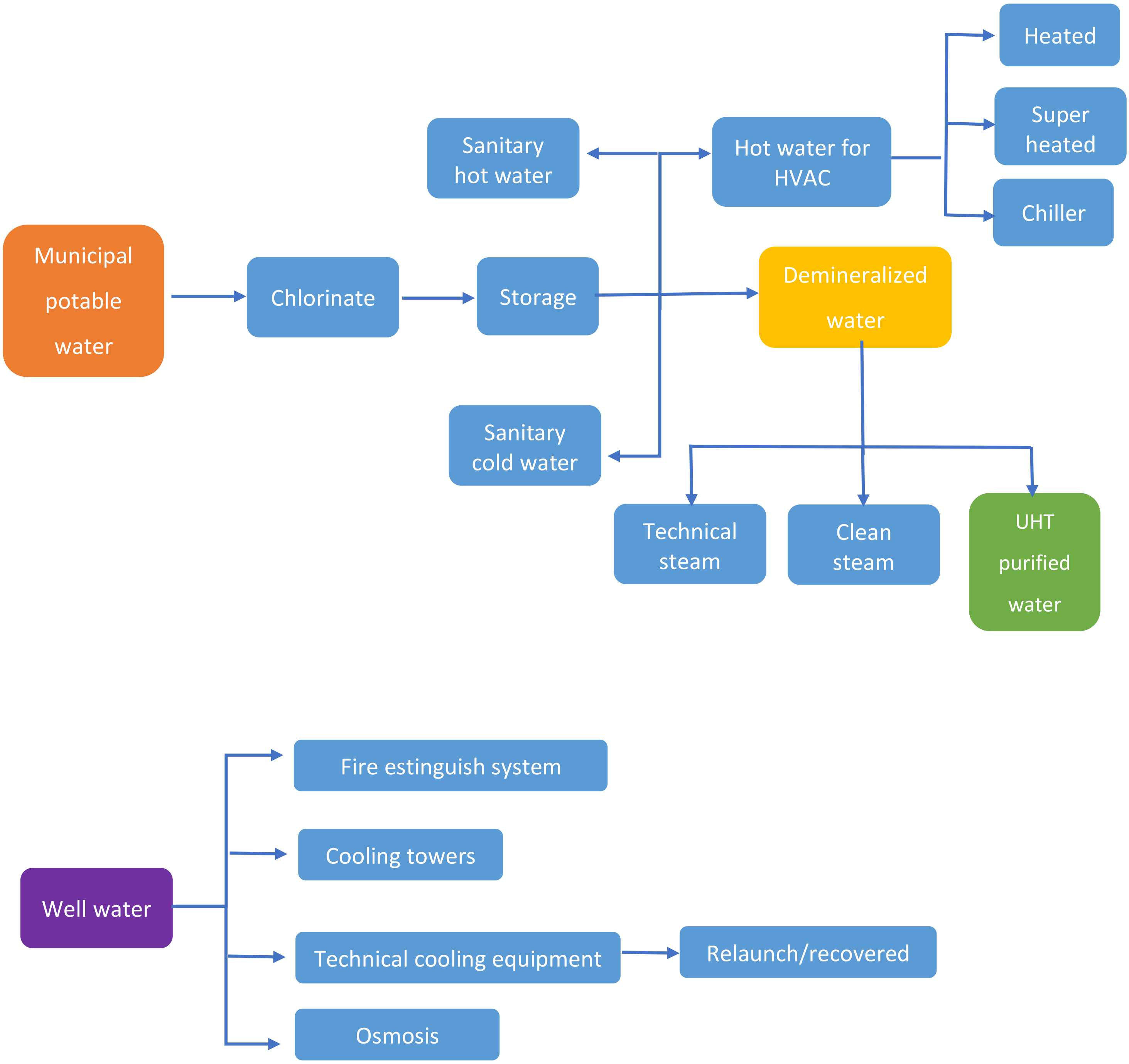

Figure 8: Pfizer water use

2.3.1 Municipal water

Municipal water (drinking water) is supplied by the network of the Municipality of Ascoli Piceno with an inlet at 6 bar; it is subsequently sent to a collector which distributes it to the various uses:

- Chlorinated water
- Demineralized water
- UHT water
- Sanitary water
- HVAC water
- Overheated water
- Technical steam and clean steam

Chlorinated water: after entering the plant, municipal water is treated by adding chlorine dioxide in the two main communicating tanks, where the water continuously recirculates thanks to a pump to avoid bacterial growth (monitored CO_2 content: 0.2 - 0.4 ppm). It is distributed to health services and for the initial rinsing of equipment. It is also used to prepare demineralized water.

Demineralized water: The chlorinated water is filtered through a 20 µm filter and then passed through an activated carbon column. The chlorine content is constantly monitored (n.m.t. 0.2 ppm). The water then passes through a bed of cationic resin, a bed of anionic resin and a mixed bed column (cationic + anionic), all of which serves to intercept the calcium and magnesium salts. After the last column, the conductivity is continuously monitored and an automatic alarm stops the water supply if the conductivity exceeds the limit (n.m.t. 0.8 µsiemens/cm) or if it exceeds 400 m3 of production. The water is then filtered through a 1 µm pre-filter and through a 0.2 µm filter which is tested (integrity) and sterilized monthly. The test is monitored by a special instrument that certifies the process.
The two demineralization systems work in parallel: one is active and the other acts as a reserve. It takes 4 hours to regenerate the resins in the system and each system can produce approximately 350 m3 before requiring resin regeneration. Demineralized water is used for: preparation of UHTW (Ultra High Temperature Water), clean and technical steam, Labs.

The difference between **technical steam** and **clean steam** lies in the production systems and in the metal of the circuits in which the steam flows.
The technical steam is produced thanks to three boilers with forced flow methane gas burner (if necessary it can also burn btz diesel oil) and smoke tubes which work at an operating pressure of

around 6.5 bar. Further steam production comes from the cogenerator boiler which uses the engine combustion fumes to create steam. The steam flows into a manifold from where it branches out to all areas of the plant that use this fluid thanks to soft iron piping.
The clean steam is produced by the technical steam which enters an exchanger, heats the demi water and when it transforms into steam it flows into a tank.
The clean steam is used solely for production processes or for sterilization phases (UHTW detachments, UHTW lines...) and flows through Asi 136 stainless steel piping.

UHT (Ultra High Temperature) water: The water from the system, called E89, is used as a process fluid and for the final rinse in washing operations. To produce this water, the demineralized water is first analyzed by TOC (Total Organic Compound) which measures the carbon particles present in the water, from here it is passed through heat exchangers where it is heated to a temperature of 135°C for 5 minutes to make it purified . It is subsequently stored in a tank kept under pressure with nitrogen (0.2-0.4 bar) to avoid the creation of bacterial load and kept at a temperature between 75 and 85°C. From storage, the UHTW is sent by a pump, and kept constantly in circulation at a temperature of 85°C, in a ring that has various use gaps. Each outlet has a regulator that determines the withdrawal temperature according to need. On a weekly basis the detachments are sterilized.
There are other UHTW systems that supply various departments of the plant:

- The E89/25 plant which is composed exclusively of the storage section and the distribution section (including points of use) as the production is common to both units (E89).
- The section dedicated to the distribution of UHTW in the Sutent department which has its own tank and dedicated loops and sub-loops, the tank is powered by the main E89-25 loop.
- The section dedicated to the distribution of UHTW in the New Coating department has its own tank and dedicated loops and sub-loops, the tank is powered by the main E89 loop.

Sanitary water: This is drinking water heated to 35C°, treated with chlorine dioxide and kept constantly in circulation at a pressure of 2.5/3 bar. It does not have a storage tank, but a series of exchangers fed with HVAC water. It is used for some production processes and for sanitary services (showers, sinks...)

HVAC and Superheated Water

The HCAC water is heated to a temperature of 65/70 °C, circulates in a stainless-steel ring via a pump and subsequently stored in a pressure tank at 3 bar.

This water is produced by an exchanger powered by the cooling water from the cogenerator jacket, by a condensing boiler or, if necessary, by technical steam.
Initially the superheated water was designed to have an operating temperature of 120°C at a pressure of 3 bar (thanks to this pressure the water does not transform into steam) in a ring thanks to a pump and stored in a tank.
Currently the superheated water is run at 80°C because it has been seen that, as we do not have harsh winters, a much lower temperature can be used with considerable economic savings; it is produced by an exchanger powered solely by technical steam.
These two types of water are used almost exclusively to treat air in air conditioners.
To better understand their use, a brief description of the operation of an industrial air conditioner is needed.
External air enters the machine (usually called HVAC or CDZ and specifically with an acronym that identifies the area it is going to treat), which is initially treated (cold period) with a heating battery (superheated water), which is then placed a cold battery (chilled water) which has two functions: the first is, in fact, to cool the air (hot period), the second is, if necessary, to reduce humidity. Subsequently, after the air has undergone the first two treatments, according to the temperature set in the room it is going to treat, the post-heating coil (HVAC water) is activated.

2.3.2 Well water

Well water means, in fact, water drawn from the aquifer and Pfizer has three wells where this happens, called wells 4, 5 and 7.
From these wells the water is introduced, using pumps, into two tanks with a capacity of 400 cubic meters each. The action of the wells is regulated by the levels of the reservoirs which work at around 80% and which are communicating.
A part of the well water, after being used inside the plant, flows into an underground tank, called RELAUNCH, from which it is sent back to the two tanks.

In the WATER STATION room there are three inverter pumps with a capacity of 50 cubic meters each, which, drawing from the tanks as needed, come into operation to maintain the well water circuit at a pressure of 5 bar.
The use of well water in the factory is for the following sectors:

- Cooling of exchangers and jackets;
- Tower water;
- Fire system.

Cooling of exchangers and jackets

Most of the exchangers present in the company, which require the cooling of a fluid, such as the exchangers of the UHTW branches, use well water. This, after being used, ends up in the before mentioned RELAUNCH tank.

The same goes for well water used to cool the jackets of bonze or tanks.

Tower water

By tower water we mean a system composed of a concrete tank with a decreasing bottom, with an operating level of 1.75 metres, with a capacity of 500 cubic metres. Above this large tank there are 9 evaporative towers with 21 fans.

This system serves to supply cooling water to the refrigeration units and air compressors, as well as being a water reserve for the fire prevention circuit.

Fire prevention

The fire prevention circuit is powered by well water.

As a water supply for this circuit there is a 400 cubic meter tank connected to the pump serving the sprinkler system while the tower water tank serves the pump serving the hydrant and hose circuit.

Referring to Pfizer data, in 2019 approximately 140,000 m3 of water were withdrawn, considering both that from the well and that taken from the water network. While in 2020 a total quantity of approximately 136,000 m3 was withdrawn.

It is estimated that of the drinking water taken from the network, approximately 45% is used for the production process, while the remaining part is used for the various services (bathrooms, canteen, etc.). While the largest quantity of well water (around 90%) is estimated to be used for the evaporative towers and heat exchangers, and the remaining part for the toilets.

Drinking water withdrawal from 2015 to 2019 remained around 35,000 - 40,000 m3.

As regards the water leaving the evaporative towers, this has suffered a decline over the years: in 2015 it was equal to 52,700 m3 while in 2019 it reached 41,500 m3. While the evaporated water increased from 31,800 m3 in 2015 to 38,900 m3 in 2019. In 2020 the water leaving the evaporative towers was 43,900 m3 and the evaporated water was 40,100 m3.

The peak flow rate reached by the system is equal to 350 m3/d, while considering 230 working days in the year the average flow rate to be considered is 220 m3/d.

Flow meters are installed inside the Pfizer plant to keep the incoming and outgoing water under control. Furthermore, to monitor and reduce water consumption, volume meters are installed at the collection and discharge points. In this way it is possible to check the average daily flow, the maximum withdrawal and discharge value and report anomalies and losses in the water circuit.

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2.4 Wastewater management in the pharmaceutical industry

In Europe the chemical industry produces 11,5 million of tons of wastewater per year and it's discharge in water bodies can cause environmental impact for local flora and fauna.
In Europe, Italian companies are among influent producers.

All the water used by the pharmaceutical industry must necessarily be subjected to specific and diversified treatments in order to always ensure the highest quality standards; in fact, at the end of each production cycle, the water that comes from the production lines washing may have been contaminated by bio-resistant substances and its waste treatment will therefore have to be managed with customized solutions for each individual industrial reality.
Starting from the design of the water systems, specific measures will therefore be envisaged aimed at limiting bacterial proliferation such as recirculation systems, filtration of the water entering the production lines, reverse osmosis, distillation.

The wastewater resulting from the manufacturing process presents a series of pollutants, moreover the pharmaceutical sector is diversified; for these reasons it is necessary to examine the process

and analyze the wastewater produced; the water treatment plant could be a chemical-physical purification plant, with chelating resins, or a biological activated sludge plant.
In the pharmaceutical industry we can distinguish two complementary sectors: the first is the one in which chemical synthesis is carried out, the method through which the Active Pharmaceutical Ingredients (APIs) and their intermediates are produced; the second is the one in which the final packaging preparation phase of the drug is concluded.
Drug producers must indicate APIs in their wastewater streams. Municipal wastewater treatment plants and agencies responsible for overseeing the sector have begun to regulate certain pollutants more and more strictly. The regulated pollutants are: antibiotics, steroids, hormones, concentrations of endocrine disruptors (EDC) and all other pollutants that have a negative impact on the environment, on aquatic fauna and consequently on human health if discharged into surface waters. Wastewater treatment must break down not only these pollutants but also all other components of BOD, TSS, ammonia, toxicity and pH.

Public opinion trusts the pharmaceutical industry which is able to provide safe products to improve people's health, but also to manage production sites that safeguard the environment and people's health.

Due to the fact that drugs are designed to have special functions such as long shelf life, resistance to acid hydrolysis for oral receptions, resistance against enzymes and toxic substances against special bacteria, problems are not out of the question.

Several investigations have been able to establish the typical composition of wastewater from the pharmaceutical sector (Debska et al. 2004; Heberer 2002). This characterization can be viewed in the following tables:

Parameters	Reference						
	Gome and Upadhyay (2013)	(Choudhary and Parmar 2013)	Wei et al. (2012)	Lokhande et al. (2011)	Saleem (2007)	Idris et al. (2013)	(Imran 2005)
pH	6.9	5.8–7.8	7.2–8.5	3.69–6.77	6.2–7.0	5.65 ± 0.65–6.89 ± 0.12	5.8–6.9
TSS (mg/l)	370	230–830	48–145	280–1,113	690–930	29.67 ± 4.22–123.03 ± 4.56	761–1,202
TDS (mg/l)	1,550	650–1,250	–	1,770–4,009	600–1,300	136.33 ± 5.83–193.05 ± 5.35	1,443–3,788
Total solids	1,920	880–2,040	–	2,135–4,934	–	–	–
BOD (mg/l)	120	20–620	480–1,000	995–1,097	1,300–1,800	–	263-330
COD (mg/l)	490	128–960	2,000–3,500	2,268–3,185	2,500–3,200	–	2,565-28,640
Biodegradability (BOD/COD)	0.259	–	0.20–0.39	–	–	–	–
Alkalinity (mg/l)	–	130–564	–	–	90–180	–	–
Total nitrogen (mg/l)	–	–	80–164	–	–	–	–
Ammonium nitrogen (mg/l)	–	–	74–116	–	–	–	–
Total phosphate (mg/l)	–	–	18–47	–	–	–	–
Turbidity (NTU)	–	–	76–138	–	2.2–3.0	17.22 ± 0.78–28.78 ± 1.18	–
Chloride (mg/l)	–	–	–	205–261	–	–	–
Oil and grease (mg/l)	–	–	–	0.5–2.9	–	–	1,925–3,964
Phenol (mg/l)	–	–	–	–	95–125	–	–
Conductivity (µS/cm)	–	–	–	–	–	157 ± 115.84–1,673 ± 119.36	–
Temperature (°C)	–	–	–	–	–	32 ± 2.23–46 ± 3.41	31–34

Parameters	Reference					
	(Ramola and Singh 2013)	(Rohit and Ponmurugan 2013)	Rao et al. (2004)	Mayabhate et al. (1988)	Vanerkar et al. (2013)	Sirtori et al. (2009)
Iron (mg/l)	8.5–10.8	–	–	–	–	–
Chromium (mg/l)	0.12–0.31	0.01	–	–	0.057–1.11	–
Lead (mg/l)	0.158–0.262	0.03	–	–	0.559–6.53	–
Cadmium (mg/l)	0.16–0.56		–	–	0.036–0.484	–
Nickel (mg/l)	0.05–0.12	0.02	–	–	0.892–2.35	–
Zinc (mg/l)	1–1.3	0.20	–	–	0.583–0.608	–
Dissolved organic carbon (mg/l)						775
Copper (mg/l)	–	0.02	–	–	0.649–1.67	–
Selenium (mg/l)		–	–	–	0.428–0.666	–
Arsenic (mg/l)	–	–	–	–	0.0049–0.0076	–
Manganese (mg/l)	–	–	–	–	6.41–8.47	–
Sodium (mg/l)	–	–	–	–	155–266	2,000
Potassium (mg/l)	–	–	–	–	128–140	–
Oil and grease (mg/l)	–	10.27	–	–	140–182	–
Calcium (mg/l)						20
BOD (mg/l)	–	410	7,200	1,200–1,700	11,200–15,660	–
COD (mg/l)	–	548	25,000	2,000–3,000	21,960–26,000	3,420
Dissolve phosphate (mg/l)	–	6.80	–	–	–	10
Nitrogen (mg/l)	–	185	–	–	389–498	–
TDS (mg/l)	–	622	20,000	–	2,564–3,660	–
TSS (mg/l)	–	110	7,500	300–400	5,460–7,370	407
Total solids (mg/l)	–	–	–	–	8,024–11,030	–
Electrical conductivity (µS/cm)	–	945	–	–	–	–
pH	–	6.01	7.5	6.5–7.0	3.9–4.0	–
Phosphate (mg/l)	–	–	100	–	260–280	10
Sulphide (mg/l)	–	–	100	–	42–54	–
Sulphate (mg/l)	–	–	360	–	82–88	160
Nalidixic acid (mg/l)	–	–	–	–	–	45
Colour	–	White	Orange	–	Dark yellow	–
Chloride (mg/l)	–	–	200	–	–	2,800
Alkalinity (mg/l)	–	–	2,500	50–100	–	–
VFA (mg/l)	–	–	6,000		–	–
Phenols (mg/l)	–	–	–	65–72	–	–
Volatile acids (mg/l)	–	–	–	50–80	–	–
Total acidity (mg/l)	–	–	–	–	3,000	–

Table 1: typical composition of wastewater from the pharmaceutical sector

In Italy, as regards the discharge of industrial wastewater, reference must be made to Table 3 of Annex 5 of Part III of Legislative Decree 152/06, which establishes the limits in terms of concentration of pollutants in water coming from production processes.

Chapter 3. Pfizer case

3.1 Why it was decided to build the plant?

The choice to design a wastewater treatment plant is mainly due to compliance with the limits given by the national legislation on the quality of the wastewater exiting the drains (in reference to Legislative Decree 152/2006 and subsequent amendments) and the possibility of internal reuse of the water treated.

Another fundamental aspect that contributed to the creation of this plant is linked to the discharge of active pharmaceutical ingredients API which nowadays concern an issue of considerable importance for the environment, the ecosystem and the health of all forms of life, animals and humans.
In fact, more than 100,000 tons of pharmaceutical products are consumed worldwide every year, with Europe contributing to a quarter of the consumption of this value.

These substances are used by man to treat and prevent diseases, also affecting the animal species; therefore, they are inevitably emitted into the natural environment both through the companies that produce them and through their metabolization, therefore feces and urine.
This involves their presence in wastewater which is subsequently purified by plants which are not always capable of treating these compounds; for this reason, many of these substances inevitably end up in rivers.
The dispersion of these substances also represents the cause of the appearance of microbes resistant to the action of antibiotics, the so-called antibiotic resistance. This means that some pathogens, once eliminated with certain antibiotics, today cannot be treated because they have developed resistance.

Despite their vital importance, active pharmaceutical ingredients constitute a problem that must be addressed starting from the production process using effective wastewater treatment technologies. In fact, in the European Union one of the main causes of their presence in the environment is given by the residue deriving from their production cycle, therefore, it is essential for companies to intervene at a global level in approaching a sustainable environmental policy and solutions that allow to minimize their production and improve their disposal.

In this sense, Pfizer is committed to contribute to this purpose precisely with the creation of waste water treatment plants within the industry with efficient technologies in order to make a significant contribution aimed at reducing the global problem of pharmaceutical pollution, also satisfying one of the 17 United Nations Sustainable Development Goals: “Clean water and sanitation”.
In 2001, the World Health Organization (WHO) described AMR as a global problem requiring a global response (WHO, 2001).

The “**One Health**” approach, defined by the American Veterinary Medical Association in 2008 as '[...] *the collaborative effort of multiple disciplines - working at local, national and global levels - to achieve optimal health for people, animals and the environment* [...]', believes that the health of humans, animals and the environment are connected like that of a single organism. In addition to being a 'One Health' problem, AMR is a 'One World' problem due to the globalization of the food supply system, with increasing movement of livestock and agricultural products, combined with increased international travel and intercontinental, which facilitates the rapid spread and combination/association of emerging AMR genes (Robinson TP et al., 2016).

A study carried out by the Department of Environmental Geography at the University of York (UK) found that 43.5% of the 1,052 locations examined in 104 countries had concentrations of active pharmaceutical ingredients above the safety threshold. Approximately 34.1% of the 137 sampling campaigns had at least one place where the concentrations were dangerous for the organisms present in the rivers and for entire ecosystems.
This means impacting the life and reproduction of fish and other organisms since APIs were synthesized to treat human diseases but can also act with the same mechanisms in other species.

The antibiotic resistance represents another major global problem which, according to the World Health Organization, will be responsible for at least 2.4 million deaths in the following 20 years. This problem also has an impact on the economy, in terms of loss of productivity and the healthcare system, which according to the World Bank could be worse than that of the 2008-2009 financial crisis with a consequent reduction in GDP of more than 5 percentage points.

Italy, together with Greece and Romania, is one of the countries in Europe with the highest rates of resistance to Gram-positive and Gram-negative bacteria, i.e. bacteria that are distinguished from each other by the characteristics of their cell walls. For example, in Italian hospitals, strains of

Klebsiella pneumoniae are around 50% resistant to carbapenems, a class of broad-spectrum antibiotics with a structure similar to that of penicillin and cephalosporins. For Acinetobacter there is even talk of a resistance rate of 80-90%.

Nowadays, given the new conflicts that have arisen in recent months and years, we must consider that antibiotic resistance is also linked to armed conflicts since at the base there are poor conditions of hospital infrastructures, inappropriate therapies, resources limited, high heavy metal contamination in humans and the environment, lack of water and sanitation.
The alarm was raised by an analysis published by the British Medical Journal Global Health which particularly concerned Iraq, subjected to decades of war, which brought antibiotic resistance to levels never reached before.

Following these problems detected worldwide, Pfizer inc. since 2010 has issued a standard to minimize the release of active ingredients into the environment.
In fact, at a national level, legislation does not provide for limits on the discharge of active pharmaceutical ingredients, but Pfizer has established its own values to combat this environmental problem.

3.2 Current state – before the plant

The industrial water collection network present in the Pfizer plant is characterized by 3 discharge lines: line L1, line L2 and line L3.
The L1 line is a line where the industrial component is predominant, consisting of water coming from manufacturing, from washing the BINs and granulators and from utilities.
The L2 line, with a domestic predominance, is related to warehouse and packaging services, as well as the microbiological laboratory, packaging washing and the discharge of the ozonation system.
The L3 line is dedicated to water coming from the canteen, which operates on three shifts at lunch and one shift at dinner.
The L2 line merges into the L1 at the height of a well called number 15, while the L3 subsequently merges at the height of the well 14.
The three joined lines subsequently reach another well (MW9901 called also S6 – SCINDO2075), where the fiscal and analytical sampling point is present.

These waters, at present, before the construction of the WWTP, discharge into the consortium sewerage managed by Piceno Consind.
The cost related to this discharge corresponds to €65,000 for the year 2023-2024; therefore, with the construction of the new wastewater treatment plant there will be an advantage in terms of costs relating to the saving of this cost which will be eliminated.
In addition to these three lines, there is a separate network for rainwater wastewater, which discharges into the canal that runs along “Via della Mezzadria”.
Finally, within the Pfizer site there is also a disused equalization tank.

As regards the wastewater treatment line, there are no particular depuration stages within the Pfizer site.
The only system present is an ozonation system for production wastewater serving the Sutent department. The ozonation system has the objective of effectively reducing substances that are not readily biodegradable or totally non-biodegradable such as phenols, oils and fats, polycyclic aromatic hydrocarbons, halogenated organic compounds, dyes, pesticides, cyanides, sulphides and many others.
In this case, this type of treatment was included because the water leaving the Sutent department presents color problems.
The water leaving this plant is discharged into the L2 line.

The chemical-physical characteristics of the wastewater analyzed are: COD, BOD5, surfactants, Total Suspended Solids, phosphorus, ammoniacal nitrogen and oils.

The carried-out study revealed a linear growth of the parameters, in particular for BOD5 and COD, a growth of up to 90% of the authorization limits for discharge into surface waters and sewers was noted.
As regards the analysis on COD and BOD5, there is also a growth due to the increase in production within the plant from 2015 to 2019; in fact, during this period of time there was also a growth in staff which increased by 205 people.
Furthermore, active ingredients (APIs) are also present in wastewater that are used inside the Pfizer factory in Ascoli.
In processing there are also various excipients that can affect the chemical quality of the wastewater, including lactose, microcrystalline cellulose, corn starch.

The temperature of the wastewater depends on the individual processes and varies over time and per production cycle; the discharges also contain domestic water at 50°C and UHT water at 80°C. The discharges are underground therefore there are no particular smells.

3.2 Proposed treatment process train

A process chain was initially proposed starting from the data collected by Pfizer.
The proposed chain was structured on the basis of the discharge limits into surface water, of all the parameters required by current legislation, the main ones of which are BOD5, COD, Total Suspended Solids, surfactants, as well as the treatment of APIs.
Initially, a modular system chain was proposed with the possibility of adding any purification states or modifying those already present based on production variations.

From the study of the analysis of the incoming water, including the excipients used in the production process, it was assessed that the AOP (Advanced Oxidation Process) was the most suitable choice for the treatment chain.

Advanced oxidation processes are wastewater treatment techniques, used especially in the industrial field, for the removal of the most recalcitrant organic compounds.
An AOP process is based on the production of hydroxyl radicals (HO•), which can be generated by hydrogen peroxide (H_2O_2), ozone, photo-catalysis processes or oxidants in combination with ultraviolet (UV) radiation. In some cases, two or more radical generators can be used in combination.
The HO• radical is a strong, non-selective chemical oxidant that allows the reduction of the polluting concentration by breaking organic bonds by binding to organic complexes.
The advantages of AOP treatments are due to the high reaction speeds and non-selective oxidation which allows the simultaneous treatment of many contaminants.

Taking this into account, the process chain initially proposed included initial fine screening, excluding the presence of fine sands and oils in concentrations higher than those foreseen in the literature, an equalization tank aimed at relaunching towards the degradation section with AOP. Subsequently the wastewater would be conveyed into a closed tank into which ozone (O3),

produced by pure oxygen or by separation from the air, is blown, with the aim of oxidizing the APIs present in the wastewater, reducing the COD value and disinfecting the wastewater.
Furthermore, in the first treatment chain proposal, the subsequent use of MBR (Membrane BioReactor) technology was expected, linked to the possibility of reducing overall dimensions and optimizing the performance of the system in terms of pollutant abatement.
Having no information initially regarding Kjeldahl nitrogen, it was not possible to define a priori whether a denitrification section was necessary.
After the MBR reactor, the UV disinfection unit was planned.
As regards the sludge treatment section, this was considered without digestion systems given the limited quantity of sludge expected and its almost complete stabilization without such use.

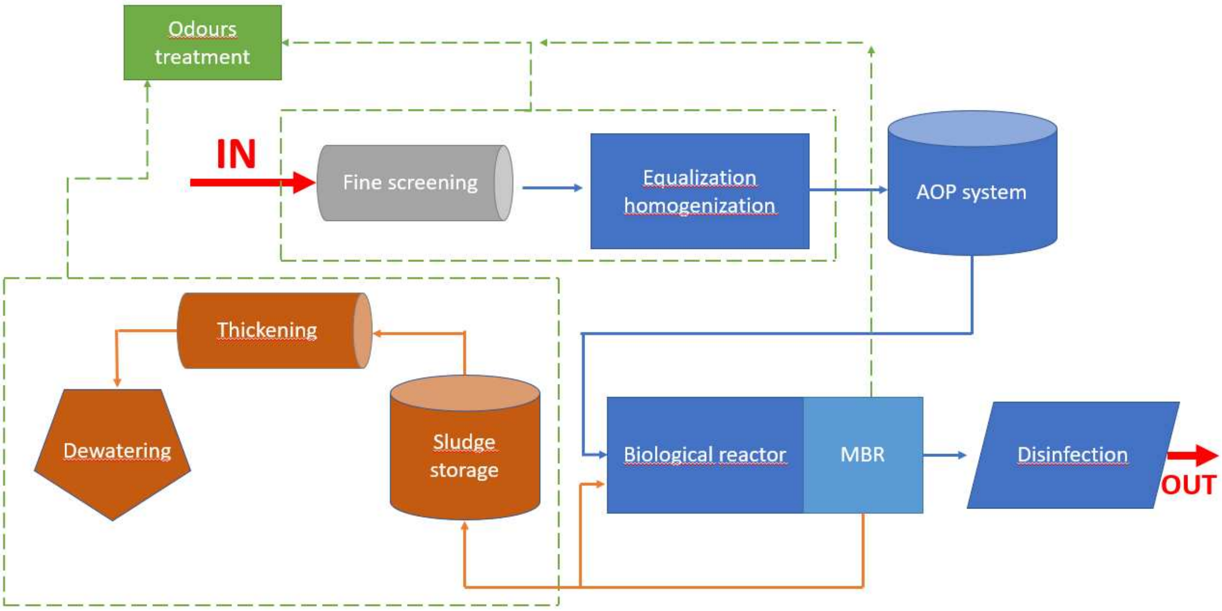


Figure 9: first configuration blockflow diagram

As regards the estimate of management costs, the following parameters must be taken into account:

- MBR membrane replacement: +/- 5 years;
- the management of the system which must include the daily presence of a dedicated person to control the running parameters.

As regards the estimate of management costs, the following parameters must be taken into account:

	ANNUAL COST (%)
Electric energy (average usage)	50-60
Membrane & UV replacement	2-6
Chemical products	8-16
Dried sludge disposal	15-21
Manpower and maintenance	6-8
Technical management of the process and analysis	4-6

Table 2: Management cost items

In particular, the main opex costs in a plant are the personnel, energy consumption and the sludge management.

In ordinary conditions more or less all these contribute in one third.
Now the cost of energy is much higher (0,5 euro/m3) so it contributes to 50% nowadays and the cost of sludge management is increased (100-250 euro/ton).
In terms of personnel more and more high skills personnel are required.

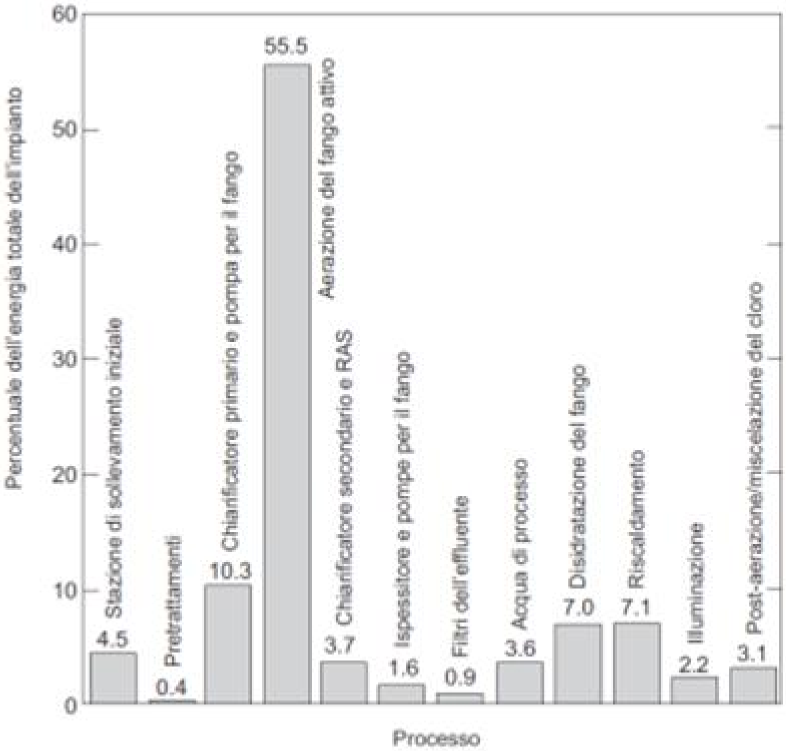


Figure 10: % of total plant energy according to the process type

We have to consider that the energy consumption is not constant but depends on the scale of the treatment, the smaller the treatment the higher the specific energy consumption.

We can see a comparison between nitrification activated sludge process with filtration, conventional activated sludge process and the traditional treatment filters (Figure 10). In particular, we can see that the nitrification activated sludge process with filtration consumes always much more energy than the other two processes and that the higher the flowrate the lower the energy consumption.

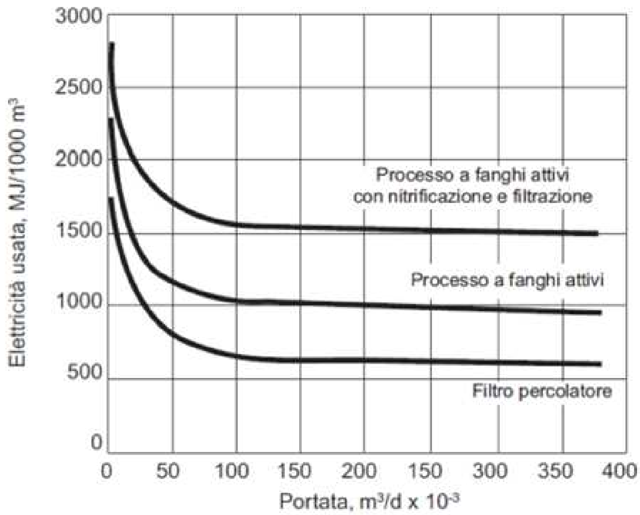


Figure 11: Electricity used based on process type and flow rate

A control of the main parameters such as pH and ammonium, COD, BOD, TOC equivalent and nitrates ion concentration is expected.

To carry out these measurements, it is necessary to provide the installation of probes that allow the registration of the above parameters at a fixed deadline.

Such an acquisition system will make it possible to promptly verify the quality of the wastewater and to have an archive of the monitored parameters and the possibility of verifying any trends or aggregate data.

These measurements must then be compared periodically with the results coming from the samples taken and analyzed by an external laboratory to verify their performance and possibly identify any corrective/maintenance actions.

3.3 Pilot plant

Given the variability found and the data present, the presumed treatment chain was verified through the application of a full-scale pilot plant through the assembly of multiple parts made available by individual producers.

The present variability concerns the possibility of sectioning the production wastewater and possibly carrying out advanced oxidation processes only on the production wastewater, as it is more contaminated, which AOP technology to use and whether to place this technology upstream or downstream.

The experimentation proved to be of fundamental importance because it allowed all the sections to be correctly designed both in terms of the overall dimensions/sizes of the machines and the real management costs resulting from them.
To evaluate the design of the plant and, therefore, of the various treatments suitable for obtaining a certain type of wastewater output, a study was carried out considering the following design characteristics:

- design flow rate of 220 m3/d;
- maximum flow rate of 350 m3/d;
- COD/BOD ratio equal to 2;
- compliance with the limits identified by Pfizer.

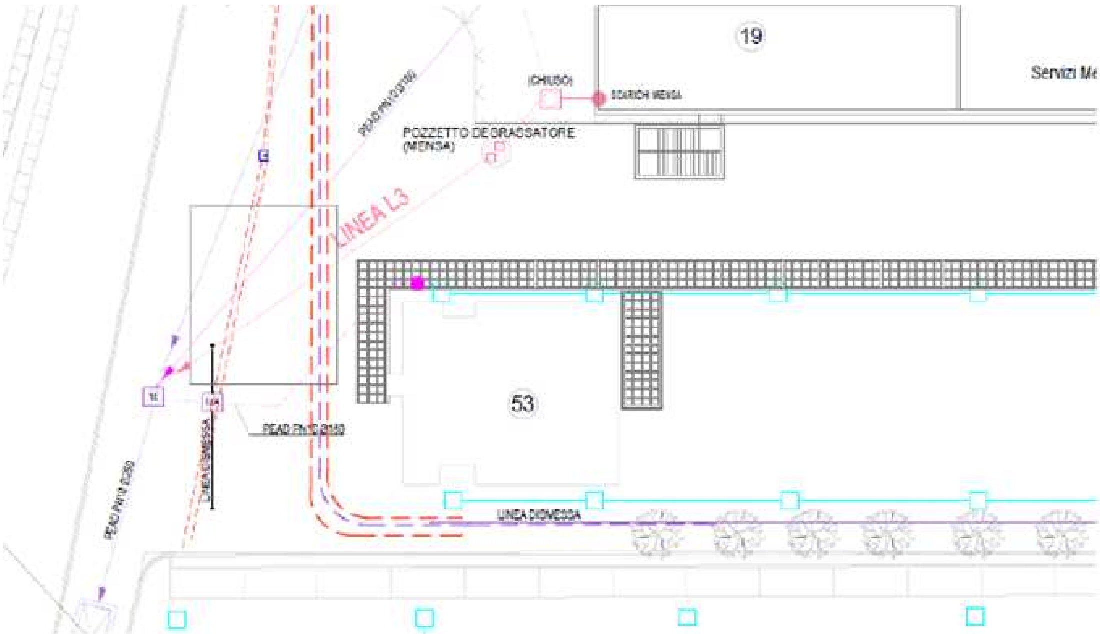


Figure 12: pilot plant installation area

Before installing the pilot plant, the ozone section was subjected to a preliminary laboratory study to verify and evaluate the most suitable size of the ozonizer.
In particular, 4 samples of wastewater treated with increasing doses of ozone were taken and an analysis of pH, COD, BOD5 was carried out.

The first part of the test with the pilot plant concerned the most energy-intensive but at the same time most efficient supply chain with regards to the degradation of API molecules.
During this phase, different process chain combinations were evaluated:

1. ozonation+ MBR + UV
2. Ozonation + UV AOP + MBR + UV
3. AOP with H2O2 + MBR + UV
4. H2O2 + UV AOP + MBR + UV
5. H2O2 + ozonation + MBR + UV
6. Ozonation + MBR + UV
7. MBR + ozonation + UV

The second part of the experiment was conducted to verify a less expensive solution from a management point of view and to evaluate how much API molecules remain in their entirety in the drain. This phase used a scheme consisting of only use of ozone in the AOP reactor without subsequent UV models.

The pilot was composed by:

- an initial pumping section from the supply sump,
- a 2000-liter equalization tank equipped with mixer-agitator,
- AOP reactor consisting, based on the configuration to be tested, of:
  - ozone contact section: through two steel contact columns the ozone, produced from oxygen via a generator, reacts with the wastewater; subsequently the residual ozone is eliminated by a catalytic destroyer
  - UV reactor: composed of a cylindrical body in stainless steel inside which the UV lamps are inserted parallel to the water flow; accompanied by a monitoring and control system.
  - hydrogen peroxide dosing section: composed of a polyethylene tank with suction lance and dosing pump that introduces the peroxide
- MBR reactor: positioned inside a container with a fine grid placed on the top through which the wastewater passes; the retained grating is discharged laterally via a pipe which conveys it into a collection drum. Inside the container there is the biological section, consisting only of the aerobic section having highlighted a low presence of nitrogen, and the filtering section. Upon startup, the reactor was subjected to an inoculation of biological sludge taken from a nearby urban wastewater treatment plant.
- final disinfection section using a UV lamp: made up of a steel body and 250W lamps.

During the use of the pilot plant, 4 weekly samplings were carried out: two aimed at the complete characterization of the wastewater to evaluate all the polluting parameters of Table 3, Annex 5, Part Three of Legislative Decree 152/06 and the main parameters to verify reuse in cooling towers; the other two were carried out for partial sampling to evaluate only the organic substance, the nitrogen component and the surfactants.
Furthermore, a weekly spot sampling was also provided between the two main components, i.e. AOP and MBR or MBR and AOP, to monitor pH, TSS, COD and nitrogen component after the main treatment.
Another weekly punctual sampling was planned to monitor the parameters in the biological tank, i.e. pH, TSS, VSS, COD, alkalinity.

Additional laboratory tests were also carried out because variations in the incoming wastewater, pH changes and plant shutdowns were found during the pilot test.
These tests were based on configurations with AOP pre-oxidation with ozone and AOP post-oxidation with ozone and consist of the characterization of the wastewater and sludge upstream and downstream of the two main sections, biomass respiration tests, respirometric tests for the definition of total biodegradable COD and an analysis of filtration parameters.

3.3.1 Influent wastewater characteristics

The pilot test was conducted also to verify and confirm the characteristics and quality of the wastewater.
Through this test, a variation was found compared to the sampling carried out by Pfizer in previous years of +27% for COD, +38% for BOD5, +3% for TSS, +85% for ammoniacal nitrogen, -25% for surfactants, +30% for phosphorus and +42% for oils.
During the test with the pilot plant the average ratio between COD and BOD is equal to approximately 2 with some peaks to be linked to industrial variability and the trends of COD and BOD5 are similar with a general decrease in values over time, which can also be linked to seasonality.

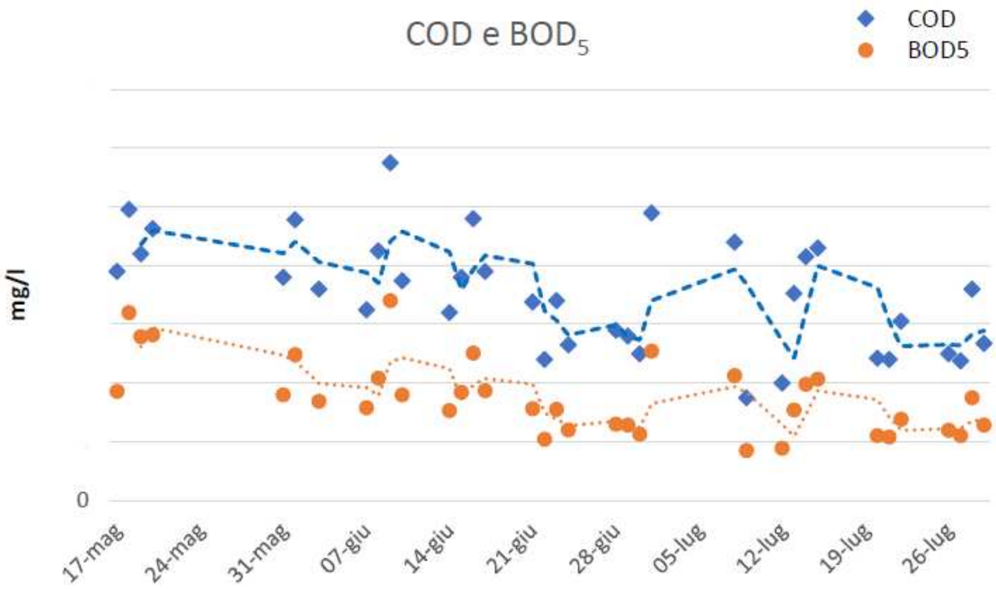


Figure 13: COD trend during the pilot test

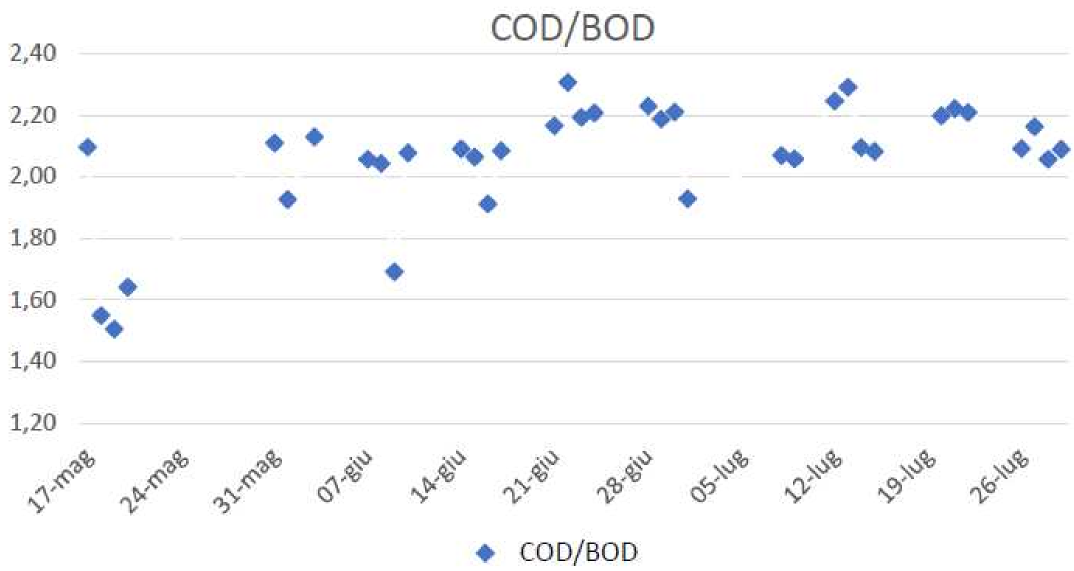


Figure 14: COD/BOD trend during the pilot test

The ratio between COD and nitrogenous forms is high, on average greater than 15, which means that the wastewater is characterized by a carbonaceous fraction of good biodegradability and has an average content compared to the literature values for industrial wastewater.

Ammoniacal nitrogen presents a wide spectrum of values, confirming values equal to or higher than the average value over time.

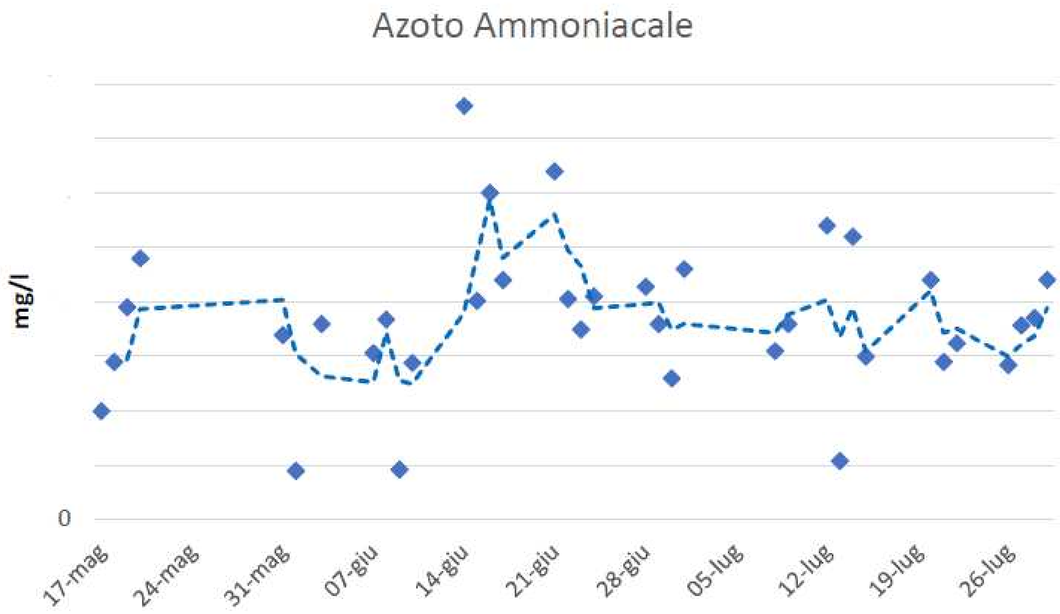


Figure 15: N-NH4 trend during the pilot test

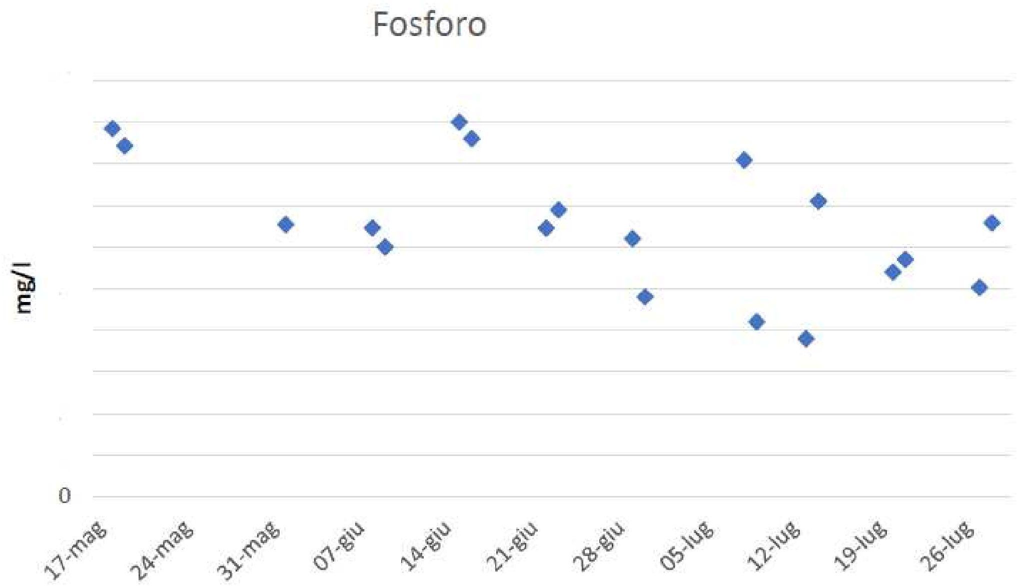


Figure 16: P trend during the pilot test

The TSS have a constant trend over time with peaks and the trend has few similarities with that of the COD.

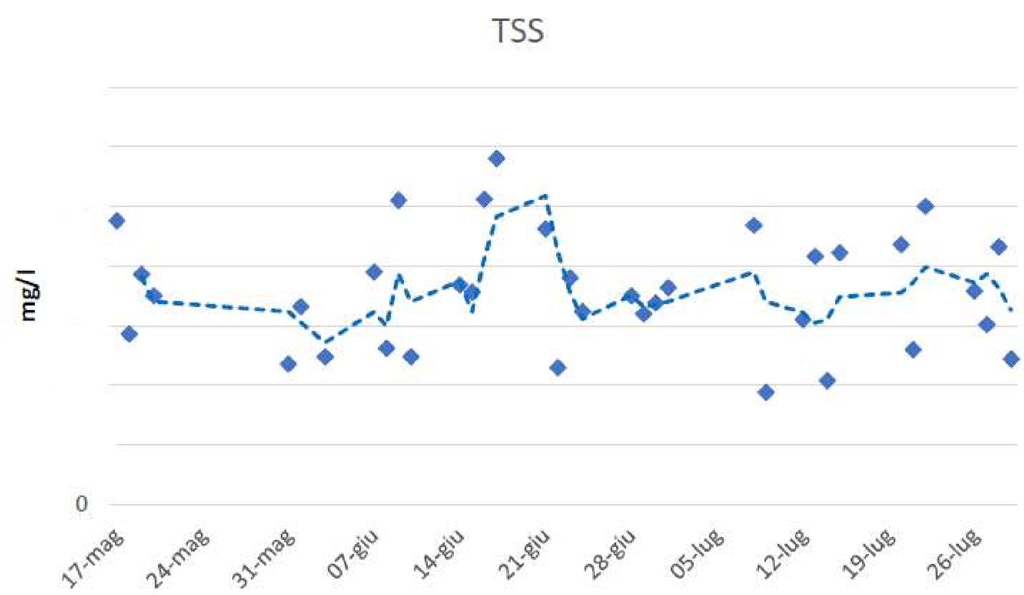


Figure 17: TSS trend during the pilot test

The surfactants show an almost constant trend except for a short period with higher values due to an interference between some compounds present in the wastewater and the analytical method carried out.

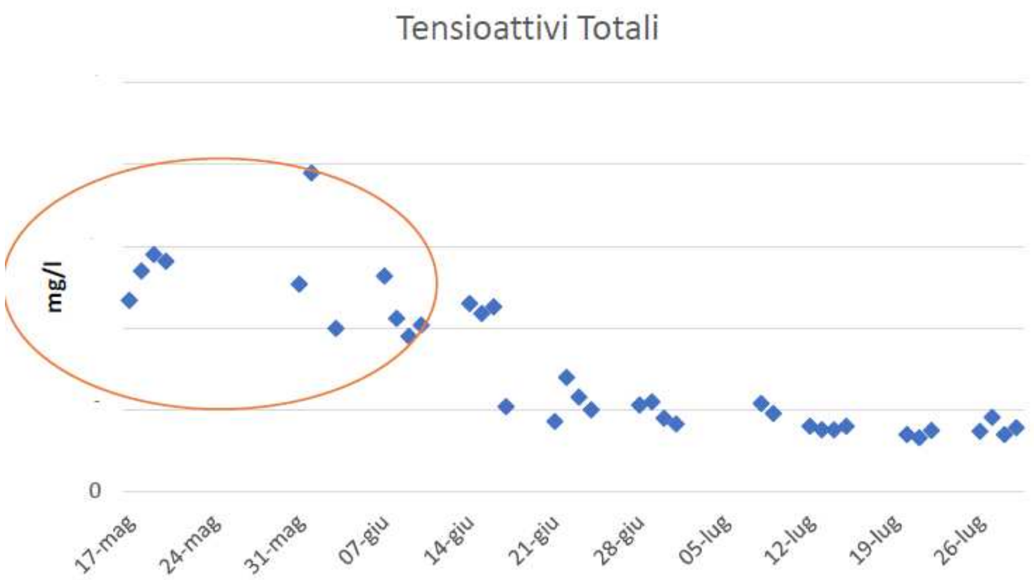


Figure 18: Surfactants trend during the pilot test

The influent pH is very variable, as an average sample, with acidic and basic peaks.

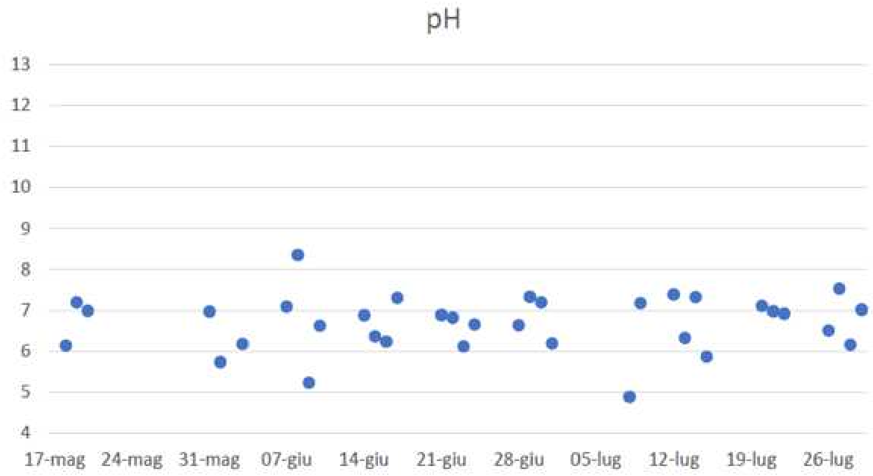


Figure 19: pH trend during the pilot test

The average temperature of the incoming wastewater was found to be 24.4°C.

Based on the characteristics of the sewage, the most suitable process to satisfy the purification requests is an **activated sludge process** with **suspended biomass** at a high sludge load.

3.3.2 Pilot plant results

From the pilot plant, essential information was obtained regarding the type of wastewater to be treated and the most suitable treatment configuration.

In particular, it was found that the average sample over 8 hours of conduction presents different values, especially with regards to pH, COD, BOD5 and TSS, compared to the average sample over 24 hours of the same day; this indicates that it is essential to use an equalization tank upstream of the system to equalize the water flow rate and the polluting load, which is based on the trend of the average hourly flow rates obtained from a flow meter positioned near the drain of the wastewater into the sewer.

During this pilot test, a significant quantity of rags and coarse materials coming from the wastewater was found; this condition made it necessary to use grinding pumps in the supply well and a subsequent screening phase.

Given the variations in pH during the treatment from acid peaks to basic peaks, the pilot test confirmed the need for a pH monitoring and control system and dosing of appropriate reagents to have acceptable values. This need will also allow for better treatment efficiency without

compromising the biological process, which is highly influenced by pH, and guaranteeing its stability.
The reagents used will be sulfuric acid [98%] (H_2SO_4) and sodium hydroxide [20%] (NaOH). An average annual consumption of 107.7 m3 for soda and 14.6 m3 for acid is estimated.

The pilot test also evaluated the different positioning of the AOP treatment with pre-oxidation to allow a pre-treatment of the organic fraction and APIs for the following MBR treatment or with post-oxidation where the MBR treatment plays the main role and the AOP performs a final polishing treatment.

All configurations showed good removal efficiency; in particular, an average removal efficiency of 80% was found for COD, 87% for BOD5, 85% for NH4, 86% for TSS, 89% for surfactants, 98, 9% for APIs and removal of all metals.

Removal (%)						
Week	**COD**	**BOD5**	**NH4**	**TSS**	**API**	**Surfactants**
1	92,9	98,4	92,9	98,6	99,9	96,4
3	90,3	97,3	92,7	96,8	99,1	91,4
4	90,7	97,4	96,4	95,7	96,8	95
5	89,4	96,2	94,9	97,6	96,4	93,3
6	86,3	95,6	95,7	95,3	97,7	90,5
7	88,4	96,4	95,1	94,1	99,5	90,4
8	73,6	85,2	84	78,6	99,7	57,2
9	89,6	96,4	93,1	93,2	99,8	93,9
10	93,3	97,7	96,5	97,1	99,9	94,9
11	87,1	95,5	94,1	99,8	99,9	84,7

Table 3: Removal percentages of different pollutants

From the analysis carried out, the MBR and AOP configuration appears to be the best as the use of the UV lamp upstream of the MBR in synergy with ozone or hydrogen peroxide presents low efficiency with sudden fouling which would require an automatic cleaning treatment increasing maintenance and management costs and the hydrogen peroxide used as pre-oxidation and together

with the AOP UV reactor has a lower effectiveness on the different APIs; on the other hand, ozone appears to be more effective in removing APIs.
In this regard, the positions of the MBR and AOP sections were subsequently evaluated; in particular, pre-oxidation showed a 40% increase in the biodegradability of the sludge, reduction of nbsCOD, protection of the nitrifying biomass since the detected kinetics were greater than those evaluated in the case of post-oxidation.
At the same time, the pre-oxidation configuration involves a higher energy consumption than the post-oxidation configuration corresponding to 30-40%; despite this, pre-oxidation could reduce the volumes of air required in the biological reactor by feeding it with oxygen obtained from the destruction of excess ozone.

Although the pilot test predicted that the ozone-MBR option was preferable, the MBR-ozone configuration was also found to be applicable with lower management costs which requires sizing aimed at avoiding inhibitory effects of the nitrifying biomass.

Furthermore, the pilot test found the need for a denitrification compartment in the biological treatment since the ammoniacal nitrogen has been correctly transformed into nitrates in the aerobic section and needs to be converted into nitrogen gas.

The analysis also suggests dehydration for the treatment of sludge, having good filterability, sending the smallest possible quantity for disposal, as the disposal of sludge is one of the most expensive and environmentally impacting activities in the treatment chain, this is how we go to reduce both costs and environmental impact.

3.4 After plant state

With the construction of the wastewater treatment plant it is expected to make changes to the current configuration of the wastewater discharge network.
In particular, as regards the water coming from the Sutent department, it is intended to flow directly to the L2 line, without being previously treated by the ozonation system, which will be removed. Furthermore, it is intended to modify the final part of the water drainage network, i.e. the part that currently flows into the MW9901 well, to be able to be connected to the recovery well.

The disused equalization tank will be redeveloped and reused with the same purpose of equalizing flow rates and mass loads.

In terms of energy, there will certainly be a higher consumption compared to the previous situation without a purification plant. A maximum energy consumption corresponding to 92 kW/h has been estimated for a total of 2208 kW/day, which will have to be subsequently verified when the system comes into operation.
In this context, energy recovery from the ozonation system used for the water of the Sutent department, which will subsequently be removed, should be considered. This energy saving would correspond to the current average use by the system of 24 kW/h for 6 hours of operation per day, i.e. 144 kW/day.

The wastewater treated by the plant will be discharged into a consortium canal owned by Piceno Consind and then discharged into the river avoiding passage through the sewerage network.
Furthermore, as previously described, after the construction of the plant the wastewater is obviously better than that which was discharged into the sewer and then treated, therefore with much lower pollutants concentrations and mass loads, with an average reduction percentages of 80% for COD, 87% for BOD5, 85% for NH4, 86% for TSS, 89% for surfactants, 98.9% for API and removal of all metals. These reduction percentages would guarantee compliance with the discharge limits; these limits considered are shown in the following table:

Pollutant	**Limit (mg/l)**
BOD5	40
COD	160
TSS	80
NH4	15
NO3	20
Surfactants	2
Alluminium	1
Arsenic e zinc	0,5
Barium	20
Boron, total chrome, Iron, Manganese, Nichel	2
Cadmium	0,02
Chrome IV, Lead	0,2
Copper	0,1
Selenium	0,03
Tin	10
Mercury	0,005

Table 4: discharge limits

Chapter 4. Wastewater treatment plant

The wastewater treatment plant was designed based on compliance with the specific requirements of the area, the Pfizer plant and the activities carried out within it.
Furthermore, the expected objectives are tried to be reached by guaranteeing an aesthetic appearance suited to the needs of use, ease of monitoring, flexibility, safety and modularity.
The plant will be composed of a pre-treatment, i.e. screening for the removal of coarse material, a biological compartment for the degradation of organic compounds and reduction of nutrients, an advanced oxidation system, i.e. ozonation and the sludge treatment line, consisting of a thickener and dehydration by centrifuge.
Furthermore, a GAC activated carbon filter unit will be added if it is deemed appropriate to further reduce the concentration of APIs.

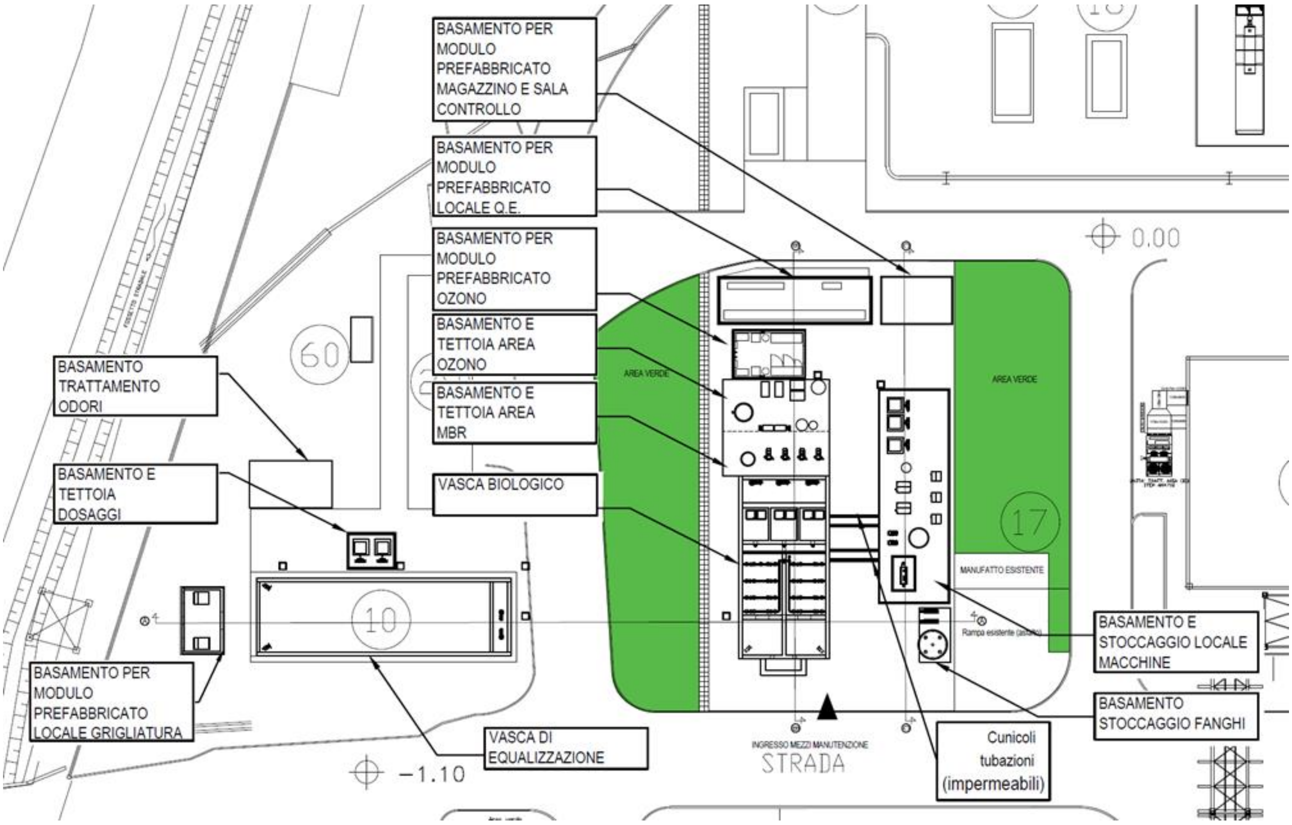


Figure 20: wastewater treatment plant layout

Based on the design data obtained from the pilot plant, and on laboratory analyzes only regarding the oil concentration, it was possible to carry out the sizing of the activated sludge biological reactor with sludge separation using MBR technology. This project was based on the action of microorganisms, such as bacteria and fungi, which metabolize and remove organic pollutants dissolved in wastewater.

In particular, the following data were considered for the design:

Daily average flow rate	350 m3/day
Hourly average flow rate	14,6 m3/h
Daily maximum flow rate	480 m3/day
Peak flow rate	20 m3/h
Annual flow rate	120.000 m3/year
Minimum hourly flowrate	10 m3/h
Pressure	3 barg
Temperature	15 °C

Table 5: project-based data

4.1 Pumping station

The pumping station is designed to manage the wastewater coming from three waste lines (L1, L2 and L3) through a single pipe and has the function of relaunching this water to the screening through an above-ground pipe.

It consists of a polyethylene tank, inside which there are two booster pumps: an operational pump and a backup pump. To avoid their damage, these pumps are grinding since the analysis carried out with the pilot plant revealed a considerable quantity of rags and coarse materials in the influent wastewater.

The operating point of the pumps is: 60 m3/h @13.3 m. The presence of level transmitters allows to monitor and control boosters, ensuring efficient management even in emergency situations.

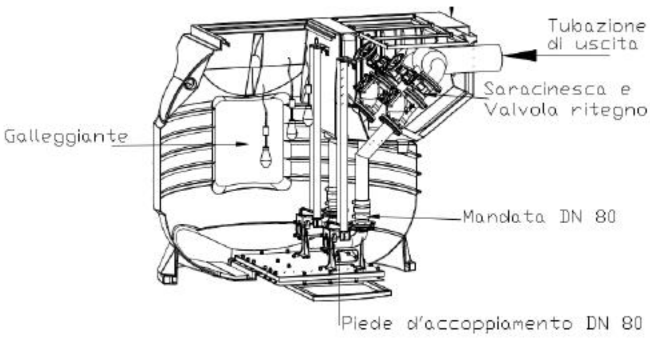


Figure 21: Pumping station

To avoid direct water leaks if the tank breaks, the latter has been positioned inside a concrete sump together with the addition of a pump which would serve to send the leaked water to the tank, avoiding the pollution.

4.2 Screening

The function of screening is to remove coarse solids from the water. To this end, a rotating drum screen is used consisting of a series of bars or blades representing the filtering surface which, by rotating, allow the solid material to be captured on the screen; while the water passes through the latter. The retained material is then collected in bins and disposed of as waste.

The screening is positioned upstream of all treatments, even upstream of equalization, to protect the other components of the system and the subsequent pumps.

The filtered water is then sent to the equalization tank by gravity.

4.3 Equalization tank

As already described previously, equalization tanks are used to compensate for flow peaks related to rainfall events or an increase in water consumption in production and at the same time also mass loads.

For this purpose, the existing totally underground tank measuring 21.6 m x 6.6 m x 3.3 m (LxWxH) is used.

To facilitate mixing and homogenization and avoid sedimentation of the solids, two submerged mixers are used; while, for the relaunch of the water to the subsequent biological compartment, two adjustable submersible cast iron pumps are used.

The operating point of the pumps is: 30 m3/h @15 m.

For the operation of the pumps, alternating use is envisaged, therefore they do not work at the same time.

As indicated by the results obtained from the pilot test, in this step of the system the dosage of H_2SO_4 and NaOH must be considered to correct the pH and guarantee an almost neutral value.

To monitor this value, a pH analyzer is provided which measures the temperature at the same time, as the pH is sensitive to temperature variations.

A level transmitter is used to monitor flow peaks.

In this case the water is sent back to a distribution tank via underground pipes and then sent to the oxidation compartment.

Chemical consumption				
Reagent	**Concentration [ppm]**	**Flow [l/h]**	**Average consumption [mc/year]**	**Note**
Sulphuric acid H2SO4 [98%]	200	1,7	14,6	In equalization
Caustic soda NaOH [20%]	200	12,5	107,7	In equalization

Table 6: Chemical consumption for equalization

4.4 Biological compartment

The technology expected for this plant is MBR, an acronym for Membrane Bioreactor: it is an advanced technology for wastewater treatment. It combines a biological process with membrane separation. In an MBR system, the bacteria responsible for biodegradation are retained inside a reaction chamber and the treated water is separated by porous membranes. These membranes work as a filter that traps suspended solids and bacteria, allowing only clean water to pass through them. This leads to improved removal of pollutants and solids, producing high-quality water that can be reused or safely discharged into the environment. The biological compartment is therefore made up of 3 phases: denitrification, oxidation and filtration.

4.4.1 Denitrification

The wastewater arrives from the previous distribution tank by gravity and is divided into the two treatment lines provided with the aid of manual valves to guarantee correct maintenance.
Denitrification is carried out by heterotrophic microorganisms that live in anoxic conditions, therefore dissolved oxygen concentrations lower than 0.5 mg/l and use nitrates (NO3) as electron acceptors, transforming them into nitrogen gas (NO2). Being an anoxic compartment, a mixer will be used to facilitate mixing and the process.
The denitrification section has dimensions: 3 x 3.4 x 5.5 m (LxWxH) for each treatment line for a total volume of 102 m3.

4.4.2 Oxidation

The oxidation process has the function of removing organic substance and ammoniacal nitrogen and is carried out by microorganisms that live and develop in an aerobic environment, therefore with a concentration of dissolved oxygen equal to 2 mg/l which is supplied by three lobe blowers, each of which can provide 50% of the design air flow, via diffusers positioned on the bottom of the tank.

These microorganisms oxidize organic substance and ammoniacal nitrogen using oxygen as an electron acceptor. The ammoniacal nitrogen is transformed into nitrites and nitrates during the oxidation process, which will then be removed during denitrification.

A level transmitter is installed in the tank for the management of wastewater flows, a dissolved oxygen and temperature analyzer for the management of the process and the blowers, and a suspended solids and pH analyzer for the management of the sludge recirculation pump.
The oxidation section has dimensions: 6 x 3.4 x 5.5 m (LxWxH) for each treatment line for a total volume of 204 m3.

The oxidation system also includes the use of an anti-foam.

The wastewater then reaches an overflow distribution tank to be subsequently sent to the filtration system divided into three lines.

4.4.3 Ultrafiltration

The filtration tank is made up of three lines each capable of managing 50% of the flow rate in such a way as to guarantee the redundancy necessary to allow ordinary and extraordinary maintenance. Filtration takes place via hollow fiber membranes in polymeric material: the degree of filtration of this membrane is in the ultrafiltration range (nominal 0.035 µm), allowing not only the retention of solids and all bacteria that may be present in wastewater but also the removal of a good part of the colloidals and viruses.

The sludge in contact with these membranes must have very specific characteristics so as not to compromise their use; these parameters can be summarized in the following table:

Parameter	Value
MLSS concentration	≤11 g/l
MLSS temperature	5-30 °C
Soluble N-NH4 concentration	<1 ppm
Soluble BOD5 concentration	<5 ppm
Dissolved oxygen concentration	<50 ppm
Mixed liquor pH in the membrane tank	>1,5 ppm
CaCO3 fouling	6-8
Alkalinity (CaCO3)	ABSENT
Time to filter (TTF100ml)	50-300 ppm
Materials with size higher than 2mm	<300 sec
Colloidal TOC concentration	<2 ppm

Table 7: Characteristics of activated sludge in contact with membranes

The main elements of the ZeeWeed ultrafiltration system are the membrane fiber, the membrane module and the cassette.

The membrane fiber is a hollow tube made of polyvinylidene fluoride (PVDF).

The membrane fibers are arranged vertically between the two heads of the membrane module.

The cassettes provide support for the modules and consist primarily of a reinforced frame, permeate collection piping, and an integral aeration assembly.

To guarantee correct management of the filtration process and ordinary maintenance operations, the cassettes are installed in dedicated tanks.

The filtration process consists of the following phases:

1. Permeate extraction: occurs through a driving force that is generated by a positive pressure applied upstream of the membranes, for example a column of water or by a negative pressure generated downstream of the membranes, for example, by a suction pump.
2. Relaxation: it is carried out by stopping, for a time predefined by the operator, and without interrupting the air supply, the flow of water that passes through the membranes. The duration of this phase is usually between 45 and 60 seconds.
3. Backwash cycle: It is carried out by reversing the direction of the filtration flow in the opposite direction to that of the previous phase, causing the removal of any material that may have deposited on the surface of the membrane.

4. Aeration (scouring): necessary for shaking the membranes to mitigate the formation of the biomass polarization layer and usually lasts 10-12 minutes.

5. Cleaning cycles: necessary to deal with problems related to the natural fouling of the membranes. They are divided into Maintenance Cleaning (MC) which is the chemically enhanced backwashing procedure (CEB) and is carried out by keeping the cassettes immersed in the activated sludge and Recovery Cleaning (RC) which is carried out by removing the active sludge from the membrane containment tanks and filling it with aqueous solutions of appropriate reagents in which the cassettes will remain immersed for pre-established times.

They are carried out with chemical agents less frequently than backwash cycles, generally every 2 times a week for ordinary wash cycles and 2-3 times a year for extraordinary maintenance. The chemical agents used are sodium hypochlorite [125%] (NaOCl) for which a consumption of 1.7 m3/year is estimated for ordinary maintenance and 0.6 m3/year for extraordinary maintenance; hydrochloric acid (HCl) for extraordinary maintenance, the use of which cannot be estimated a priori; citric acid [50%] for which a consumption of 1.8 m3/year is expected for ordinary maintenance and 0.3 m3/year for extraordinary maintenance and an anti-foam agent.

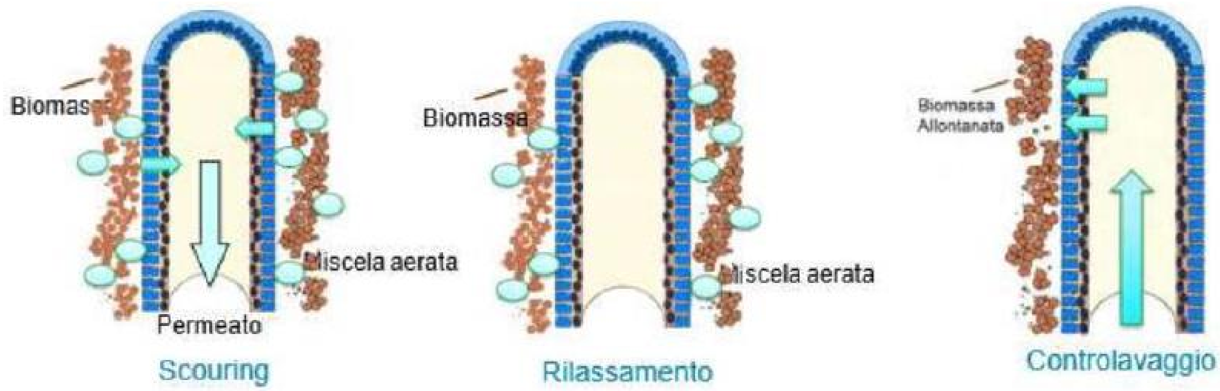


Figure 22: MBR cleaning cycles

Chemical consumption					
Reagent	**Concentration [ppm]**	**Flow [l/h]**	**Average consumption [mc/year]**	**Frequency**	**Note**
NaOCl (for MC) [12,5%]	200	90	1,1	2 times/week	In MBR
Citric acid (for MC) [50%]	2000	5’	1,8	2 times/week	In MBR
NaOCl (for RC) [12,5%]	1100	90	0,6	2-3 times/week	In MBR
Citric acid (for RC) [50%]	2200	50	0,3	2-3 times/week	In MBR
Cloridric acid (for RC)			To be defined		In MBR
Antifoaming			To be defined		In MBR, oxidation-denitrification tank and in ozonation

Table 8: Chemicals consumption for MBR

In particular, the permeate extraction phase occurs through a reversible pump which produces a slight depression of 0.15-0.55 bar and is sent to the accumulation tank before being subsequently sent to the ozonation system; instead the suspension of activated sludge reaches an accumulation tank by overflow and is subsequently relaunched, by 2 submersible pumps plus a reserve one, to be sent partly to the top of the biological compartment to guarantee the concentration of biomass necessary to carry out the action purification and partly to the decanter and then to the sludge line.

The ultrafiltration compartment can be compromised by the accumulation of solids on the surface of the membranes, reducing the efficiency and permeability of the system; for this reason it is necessary to provide a backwashing cycle which is carried out by the same pump that carries out the filtration and consists in the use of the permeate, which has been filtered previously, to be sent back to the membranes and cause the removal of the clogging, so-called fouling.

In order to evaluate the efficiency of the membranes and any damage suffered by the latter, redox and pH analyzers are inserted on the line of the permeate filtered by the pumps and temperature and turbidity transmitters in the line of the permeate which is sent to the storage tank.

The estimated filtration surface is 1,920 m2 and the internal dimensions of each containment tank have been designed with the aim of guaranteeing the possibility of adding an extra filtration box for each train in the future. These dimensions correspond to 2.5 m in length, 2.15 m in width and 2.74 m in minimum hydraulic level.

4.5 Ozonation

Ozonation is an advanced oxidation process in which ozone (O3) is used for the disinfection and oxidation of pollutants present in water. Ozone is produced by generators and introduced into wastewater. This substance reacts with organic contaminants, including bacteria, viruses, organic compounds and chemicals, degrading them effectively.
The system consists of a compressor, which supplies filtered and dried air to the Pressure Swing Adsorption (PSA) to produce oxygen. Subsequently, the O2 is sent to the ozone generator, which, through dielectric systems and electrical discharges, allows the production of O3. The contact between the gas and the wastewater occurs in two stainless steel contact tanks measuring $7m^3$ (called contact tank) and $3,5m^3$ (called quench tank) via a nozzle system. The plant is completed with a residual ozone destruction system based on the principle of thermo-catalytic decomposition. Furthermore, the ozonation system envisages the use, when necessary, of an anti-foam agent.

4.6 Sludge line

Sewage sludge is an essential by-product of biological treatment processes and used in wastewater treatment plants. During the biological purification process, microorganisms decompose and metabolize pollutants present in wastewater, generating sludge as a result. This sludge consists of a mixture of microbial biomass, organic and inorganic substances and residual water. Correct management of sewage sludge is vital to ensure the efficient and sustainable operation of sewage treatment plants. The sludge can be subjected to stabilization, dehydration, anaerobic digestion or chemical treatments to reduce its volume, improve its manageability and recover any resources or energy.

The sludge produced by the plant has a concentration of 1% and a quantity equal to 5 m3/day which will be sent to a thickener together with a plasticizing material, which facilitates the thickening of the sludge, in order to increase the concentration of solids in the sludge up to 2-3% and separate the latter from the liquid component; this process occurs by gravity, i.e. the solids settle on the bottom of the decanter and the liquid part remains suspended and sent to a storage tank to then be sent back to the equalization tank; instead the sludge is sent to the centrifugal dehydration system.

This system exploits the fast rotation of its internal drum and the difference in density between the solids and the liquid; the heavier solids are deposited on the walls of the drum, forming a solid cake of sludge which is stored in a tank to then be disposed of, while the clarified liquid is expelled from the upper part of the decanter and sent to the storage tank and subsequently to the tank of equalization.

4.7 Odors treatment

Wastewater treatment plants can release unpleasant odors resulting from the production of gases such as hydrogen sulfide (H2S) and volatile amines; for this reason, to guarantee an adequate working environment and quality of life, a system of covering the tanks using GRP panels and a system for conveying odors towards abatement filters is provided in order to reduce direct emission in the atmosphere positioned near the equalization tank.

The GRP panels are equipped with EPDM gaskets to prevent the leakage of smelly substances, are resistant to UV rays and have a multi-radius or simple curved arch geometry.

As regards the odor abatement system with carbon filters, it has dimensions of 2.8 m x 2 m (DxH) with a mass of carbon equal to 3,800 kg to be able to treat a flow rate of 5,380 m3/h. The emission point is located at the top, at a height of approximately 2 meters.

4.8 Management and control panel

Electrical and instrumental control systems in wastewater treatment plants are essential to ensure the efficient and safe operation of the process. Two fundamental components of these systems are PLCs (Programmable Logic Controllers) and MCCs (Motor Control Centers).

PLCs are programmable electronic devices that control and monitor the different phases of the wastewater purification process. They manage the sequence of operations, the control of valves, pumps and other electrical devices within the system. The PLCs are programmable to adapt to the specific needs of the plant, allowing automated and precise management of the process.

MCCs, on the other hand, are motor control systems that control the pumps, compressors and other mechanical devices in the plant. These systems ensure the correct start, stop and control of motorized equipment, ensuring safe and reliable operation.

PLCs and MCCs work synergistically to control and monitor the entire wastewater treatment plant, enabling the regulation of various operational variables, performance monitoring, emergency management and data collection for process analysis and optimization.

The electrical lighting panel for the entire plant area is also installed. They include:

• Plant grounding;

• Atmospheric discharge protection report;

PLC, MCC and electrical lighting panel are installed in the Electrical Panel Room.

Chapter 5. Permitting

The process is mainly based on the **Autorizzazione Unica Ambientale (AUA)**, a provision authorization established with the **D.P.R. n. 59 of 13.3.2013**, which replaces and includes titles environmental qualifications.

The current AUA number 3413 referring to the date 28/09/2023 authorizes:

- Authorization for the discharge of industrial wastewater S2, S3 into surface water (**art. 124 of Legislative Decree 152/06**);
- Authorization for the discharge of industrial waste water S6 into public sewers (art. 124 of Legislative Decree 152/06) relating to the "Campolungo Piceno CONSIND" plant;
- Authorization for emissions into the atmosphere (**art. 269 Legislative Decree 152/06**);
- Communication or Authorization **Law 447/1995** regarding the acoustic impact.

The following discharges can be distinguished:

- **S1**: rainwater runoff from yards and roofs;
- **S2**: industrial wastewater from the osmosis system together with rainwater runoff from yards and roofs. This discharge is characterized by the following parameters: TSS, COD, aluminium, iron, manganese, sulphates, chlorides, total phosphorus, ammoniacal nitrogen, nitrous and nitric nitrogen;
- **S3**: industrial wastewater coming from the purging of the cooling towers together with the rainwater run-off from the yards and roofs. This discharge is characterized by the following parameters: TSS, COD, iron, sulphates, chlorides, ammoniacal nitrogen, nitrous and nitric nitrogen, free active chlorine, copper and zinc. The parameters "copper" and "zinc" are dangerous substances pursuant to art. 108 of Legislative Decree 152/2006 and subsequent amendments. listed in Table 5 of Annex 5 to Part Three of Legislative Decree 152/2006 and subsequent amendments, art.3, paragraph 5, of Presidential Decree 59/2013 applies;
- **S4**: rainwater runoff from yards and roofs;
- **S5**: rainwater runoff from yards and roofs;
- **S6**: water from the L1 waste lines, i.e. water coming from manufacturing, from washing the BINs and granulators and from utilities, L2 relating to warehouse and packaging services, in addition to the microbiological laboratory, packaging washing and waste disposal ozonation system and L3 dedicated to water coming from the canteen.

Pursuant to art.101 of Legislative Decree 152/2006 and subsequent amendments and art.29 of the NTA of the PTA of the Region Marche (DAALR 145/2010) both aforementioned industrial wastewater discharges, S2 and S3, as well as the sampling wells: S2A, S3A and S3B, in surface waters (Tronto river) must comply with the emission limits in surface waters indicated in table 3 of annex 5 (Part Three).
The S1, S2, S3, S4 and S5 drains lead to the Tronto river via a consortium canal, for which the Piceno Consind has granted authorization pursuant to art. 29 of the NTA of the PTA of the Marche Region.
The ARPAM department of Ascoli Piceno is responsible for carrying out periodic checks at the system in question pursuant to art.5, paragraph 1, letter. i of LR 60/97.
Periodic self-checks for some parameters on the discharge are required.
The expiration of this single environmental authorization is scheduled for 02/27/2034.
In particular, with regard to the existing ozonation system, to support the water coming from the Sutent department, article 272, paragraph 1 of Legislative Decree 152/06 underlines that plants and activities with emissions that are of little relevance to the effects of air pollution they are not subjected to ordinary authorization, but exclusively to communication to the competent authority.

An amendment to the AUA is planned for the new wastewater treatment plant.
This change concerns the additional emissions of the carbon and ozonation filter and the discharge of water which will take place directly on the canal owned by Consind; therefore, the S6 drain will be removed, and the water will flow to the S3 drain.
Only in the unlikely event that there is a problem with both pumps for relaunching the wastewater towards the treatment plant or if an exceptional and unforeseeable event occurs, will it be possible to activate an emergency discharge into a body of surface water at the discharge point named S2.
Furthermore, there will also be a change to the acoustic impact.

The duration of the process varies and depends on the territorial structures; in principle the authorization requires a minimum of 90 days from the time the application is submitted.
Once the AUA has been obtained, the procedural activity moves on to the presentation of the SCIA and filing of the reinforced concrete with the Civil Engineers, pursuant to Presidential Decree 380/2001.

As regards the start-up period of the plant, reference must be made to article 48 of the Water Protection Plan of the Marche region, which states that:

"in the start-up phase, or for the return to normal conditions following the cases referred to in paragraph 1, letter b), the following time frame is defined:
a) first 30 days: without exhaust emission limit values;
b) from the 31st to the 90th day: possibility of exceeding the emission limit values by up to 100%;
c) from the 91st day until the end of the start-up period established pursuant to the art. 46 of the regional law 10/1999 and subsequent amendments: possibility of exceeding the emission limit values up to 50%.
In the application for discharge authorization for a new biological purification plant, authorization must also be requested for the start-up period, justifying the need for duration. During the start-up period referred to in paragraph 2, fortnightly self-checks of the parameters established by the authorization must be carried out on the final discharge. The results of the self-checks must be made available to the supervisory authorities."

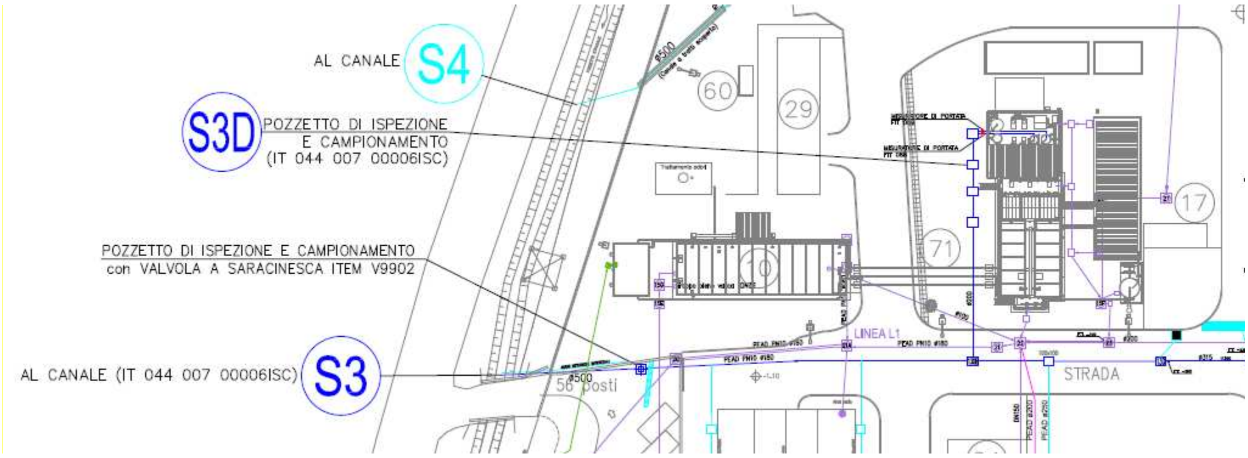


Figure 23: wastewater and emissions plan

Chapter 6. Reuse of water treated by the purification plant

6.1 Introduction: drought problem and water crisis

A further critical issue to which importance must be given in pharmaceutical production is the requirement for significant quantities of water.

The management of all aspects of the water cycle represents an important source of competitiveness between companies, enabling large-scale synergies with the goal of creating a circular economy.

In recent years, our planet is feeling the effects of climate change due to global warming, which contributes to an ever-increasing decrease in precipitation, with more frequent extreme weather events and droughts.

According to the latest report from the Intergovernmental Panel on Climate Change (IPCC) of the United Nations (*Climate Change, 2022*), in the last twenty years climate change is causing greater impacts than expected and temperatures higher than those estimated, upsetting natural systems and affecting the lives of at least 2.3 billion people, who face situations of water stress.

Numbers - according to UNICEF - destined to grow: by 2040 one in four children will live in areas with serious water shortages, while by 2050 three-quarters of the world's population will experience severe drought conditions.

In 2021, there were 187 calamitous events in the world, of which over 70% were linked to excess water or its absence.

Last year, our peninsula recorded nine drought events of such intensity and duration as to impose a state of emergency.

We will certainly remember 2022, because in the only first four months of the year, extreme climatic events in Italy increased by 29% compared to the same period of the previous year, violently hitting the North of the country, where it caused an unprecedented water crisis by intensity, extension and severity (Figure 24).

Figure 24: Drought in Italy in 2022

The drought of 2022 has new and absolutely serious characteristics, because the absence of rain and snow is also affecting water reserves, primarily intended for drinking use, "*causing a deficit that will continue over time*" (*ANBI source*). The most evident climatic anomaly during this year occurred in the month of June, which recorded an average temperature that was +2.88 ºC higher than the average (*Coldiretti data*).

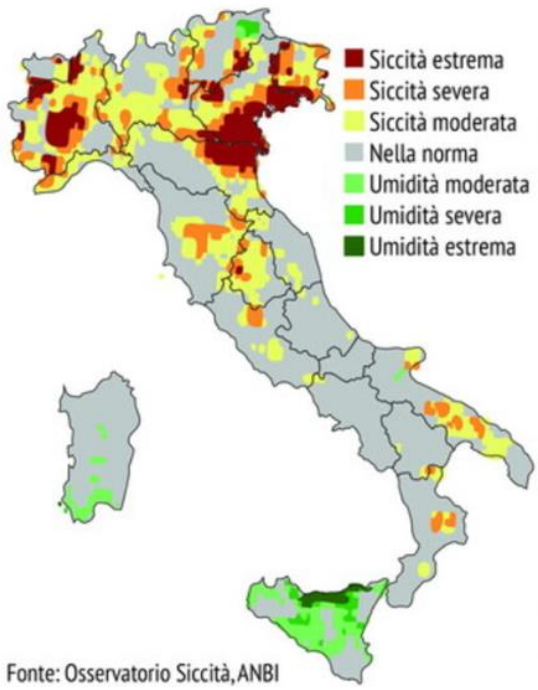


Figure 25: Drought in Italy in June 2022

With precipitation, water reaches the ground; to this can be added the melting of glaciers and snow in the highest mountains. Part of it flows onto the surface, feeding the hydrographic network (surface runoff); a part soaks the soil and returns to the atmosphere by evaporation from the soil and by transpiration of the plants; another penetrates the subsoil depending on the permeability of the materials, constituting the domain of groundwater. Throughout the entire globe, these are over 5,000,000 km3, approximately 0.4% of the total terrestrial water, 13 times that of surface continental waters (lakes and rivers) and less than 1/6 of the solid water in alpine and polar glaciers. Considering that the waters "imprisoned" in the glaciers cannot be used by humans unless they melt, the underground waters constitute an important "reservoir"; a reserve of fresh water with a volume 10 times that of surface water, often polluted.
Overexploitation and pollution represent, according to *Legambiente*, two great dangers for this water reserve.
According to the latest estimates reported in the United Nations' global report on the development of water resources 2022, 99% of the volume of fresh water in the planet's liquid state is concentrated underground.

The data on withdrawals amount to 959 cubic kilometers per year extracted in 2017, the equivalent of approximately twenty-four times that of Lake Maggiore. In Europe, aquifers provide 65% of drinking water and 25% of irrigation water and according to the *European Environment Agency (EEA)* they represent a key resource to be protected according to the targets of Objective 6 of the 2030 Agenda.

As reported by the *IPCC (Intergovernmental Panel on Climate Change)*, i.e., the scientific forum formed in 1988 by two United Nations bodies, the World Meteorological Organization (WMO) and the United Nations Environment Program (UNEP) for the purpose to study global warming, during the 20th century, total precipitation increased in areas of high northern latitudes and decreased in some sub-tropical regions and in those of low-mid latitudes. Average global air and ocean temperatures have also increased, and warm days, warm nights and heat waves have become more frequent over the past fifty years. Climate model simulations indicate that these trends will continue into the 21st century. Not only will precipitation as a whole change, but also the intensity and variability of precipitation.
Since 1970, the frequency of heavy rainfall has increased, while the surface area of land classified as very dry has more than doubled. These extreme weather conditions are causing an increase in the frequency of severe droughts and floods.

A change in precipitation along with increased evapotranspiration linked to rising temperatures will affect natural groundwater recharge rates and aquifer depths.

The Italian water consumption situation is among the most delicate in Europe; water stress in the country has always been considered medium-high, Legambiente states in the dossier.
According to the latest ISTAT survey of 2018, Italy holds the European record for the quantity of drinking water withdrawn per capita, with a total of 9.2 billion cubic metres, of which 85% comes from underground sources (wells and springs).
However, this water reserve does not receive the necessary protections. In particular, considering two aspects, the quality of the water and the flow rate of the aquifer, the situation presents several critical cases.
According to the *EEA's European Waters* 2018 report, only 58% of Italy's groundwater reserves met the European parameters of good chemical condition, a percentage well below the European average of 75%.
The most common substances detected in groundwater analyzed in the twenty-seven Member States are nitrates and pesticides used in agriculture. In our country, Legambiente reports four critical cases, in particular, two serious cases of pollution by perfluoroalkyl substances, called PFAS, used as waterproofing in numerous industrial processes and suspected of being carcinogenic.

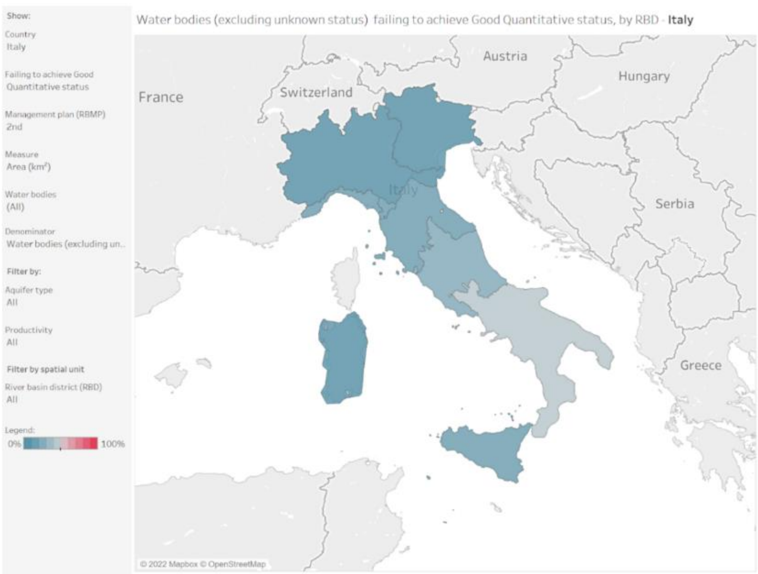


Figure 26: qualitative state of groundwater in our country according to data collected by the EEA

The situation is not the best regarding the quantitative conditions of underground water reserves. Again, according to the EEA report, in Italy almost 10% of the underground water bodies analyzed are in a situation of scarcity.
Most cases of shortages in Europe are due to too rapid overexploitation, which leads to a lowering of the water table with loss of head, and/or saline intrusions. Climate change will accentuate the problem with the increase in water required for irrigation, particularly in Southern Europe.

The factor that most influences the height of the water table surface is the hydrometeorological situation (Figure 27). During droughts the water table drops due to lack of precipitation and the conspicuous processes of evaporation from the soil, favored by the high air temperatures and transpiration of the vegetation. As the drought continues, the groundwater level can drop to such an extent that capillarity processes are insufficient to bring water to the surface; therefore, it no longer evaporates from the soil and is no longer available to the deep portions of the plants' root system. Occasional storms or the first rainfall of a day or two are generally not enough to bring water to the aquifer; the water wets a few centimeters (at most a few decimeters) of soil with the benefit of the plants limited to a short period; within a short time (a few days), the soil is dry again.

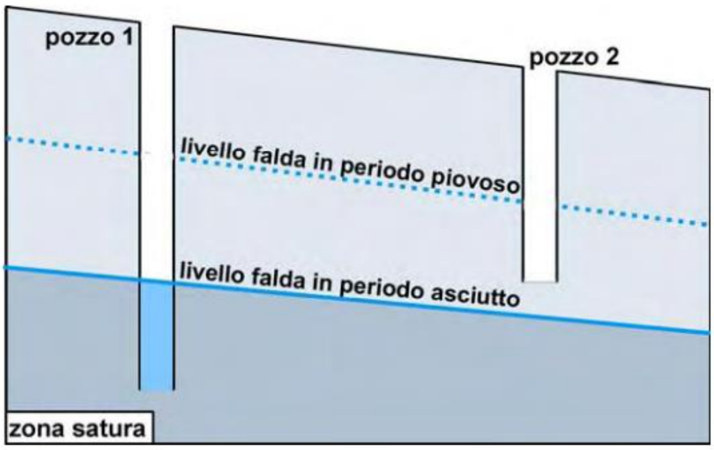


Figure 27: groundwater level trend as a function of rainfall

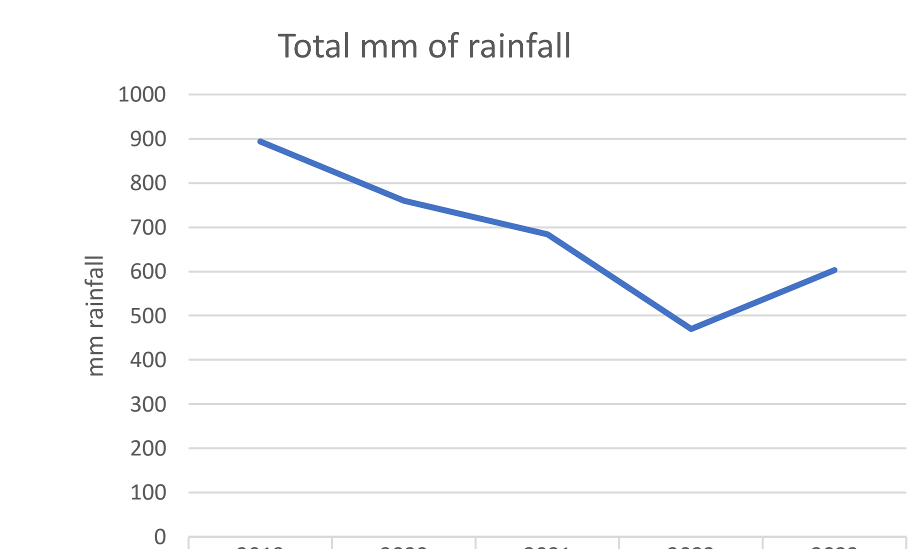
In the current year, the rains that occurred during the spring were unable to rebalance a water deficit that has now continued approximately since December 2021. Overall, groundwater levels in the months of May and June 2023 were temporarily returning to multi-year average values. However, the lack of rainfall in July and August but above all their type (extreme events of high intensity but short duration) did not allow adequate recharge of the aquifers.
Failure to recharge the aquifers entails serious inconvenience for those municipalities that are almost exclusively dependent on springs for their water supply: if a source significantly reduces

the flow rate or even temporarily disappears, the quantity of water that can be captured will be much lower. Subsequently, prolonged water stress in alluvial aquifers also leads to limit water consumption to only fundamental needs, therefore drinking, agricultural and industrial.
Non-essential uses are prohibited by drinking water companies to rationalize the resource, which is primarily intended for drinking use.

Another factor that influences the morphology of the phreatic surface is represented by the water levels in rivers. In case of drought the river level drops and is partially fed by water from the underground reserve. In the event of a flood, the water level in the riverbed suddenly rises, partially feeding the aquifer. The river can also receive water from the aquifer on one side and send water into the aquifer on the other.

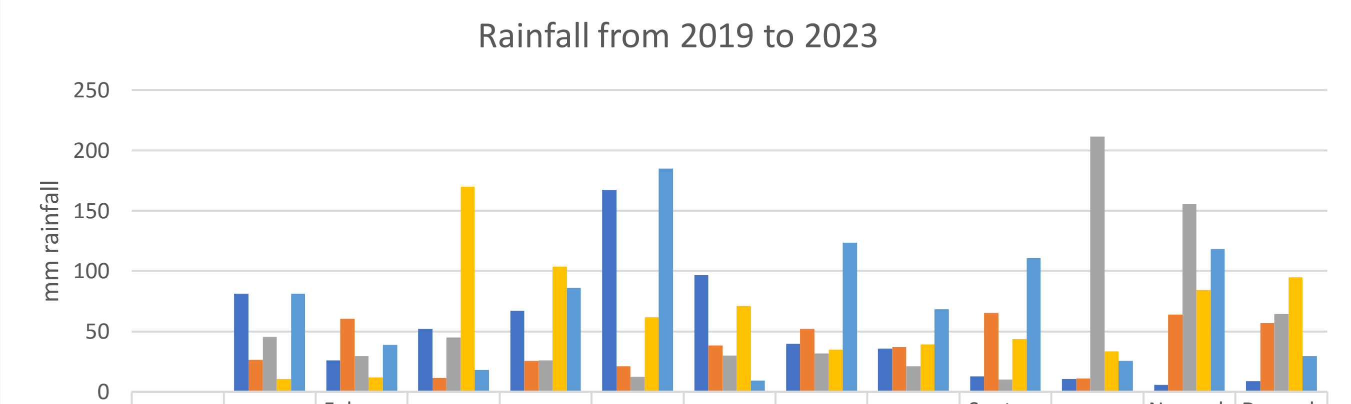
Thanks to the data provided by the *Multi-Risk Functional Center of the Marche Region*, relating to the Brecciarolo (AP) RT-3017 rain gauge, it is possible to observe how, over the last 5 years, the millimeters of annual precipitation in the city of Ascoli Piceno have decreased with the exception of the year 2023 which has a greater annual precipitation total than the previous year (Figure 28); this is due to the occurrence of short and intense phenomena in the months of April, May and June 2023; in particular, in this period a quantity of precipitation exceeding 50% of the precipitation recorded during the same year was recorded (Figure 30).
These short and intense events, as stated previously, only cause damage to the territory without contributing to the rise in the level of aquifers, which represent one of the most precious sources of water intake.

As can be seen in the graph shown in figure 31, the rainfall trend for the year 2019 represents the classic trend of a season in which periods of rainfall and periods of drought alternate; instead, in the blue line, which represents the summer and autumn season of 2023, we have a constant and continuous decrease in precipitation.



	2019	2020	2021	2022	2023
mm rainfall	893,8	759,8	683,8	469,8	603,4

Figure 28: Total rainfall mm for 2019-2022



	month	January	February	March	April	May	June	July	August	September	October	November	December
2023		81	26	52,2	67,2	167,4	96,6	39,6	35,8	12,8	10,4	5,6	8,8
2022		26,4	60,6	11,4	25,4	21,4	38,2	52,2	37	65,4	11,2	63,8	56,8
2021		45,4	29,6	45,2	26,2	12,4	30,2	31,8	21	10,2	211,4	155,8	64,6
2020		10,8	11,8	169,8	103,6	62	71,2	35	39,4	43,6	33,4	84,2	95
2019		81,2	38,8	18	86	184,8	9,2	123,6	68,2	110,8	25,4	118,2	29,6

Figure 29: Rainfall from 2019 to 2023

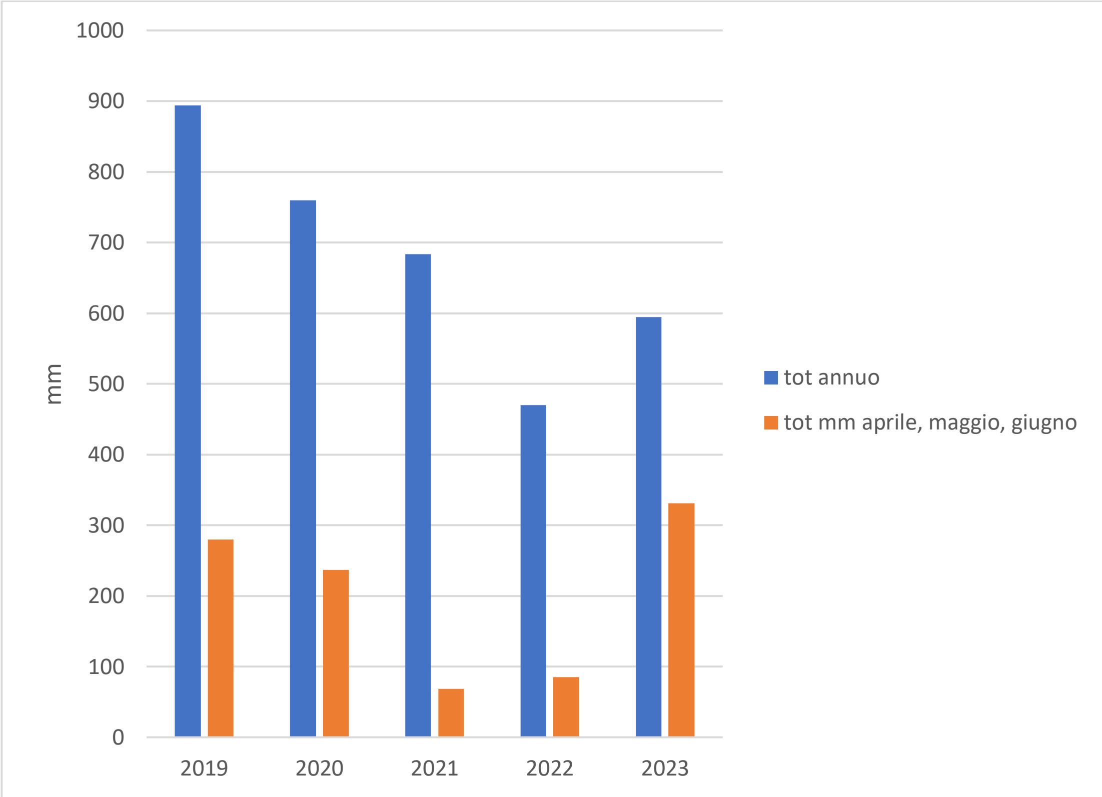
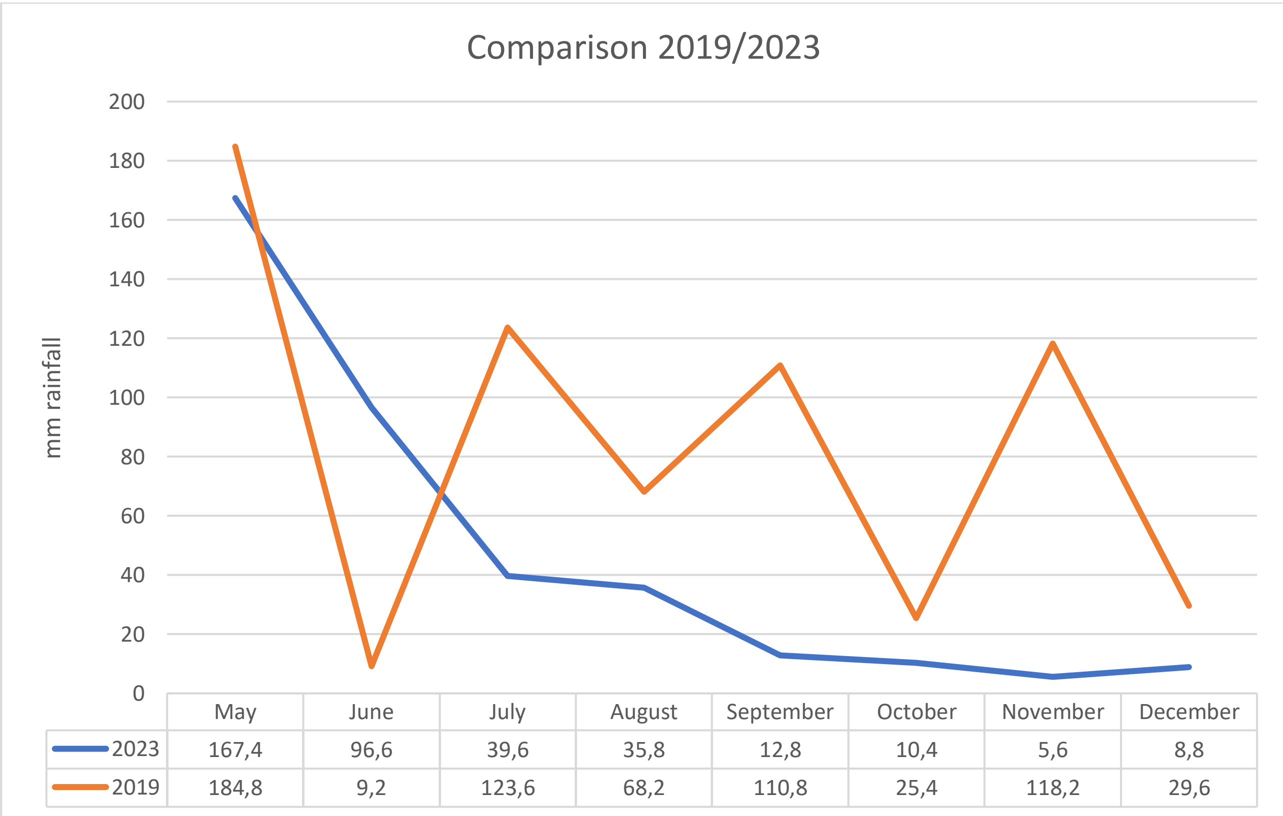


Figure 30: comparison of rainfall in the months of April, May, June



	May	June	July	August	September	October	November	December
2023	167,4	96,6	39,6	35,8	12,8	10,4	5,6	8,8
2019	184,8	9,2	123,6	68,2	110,8	25,4	118,2	29,6

Figure 31: Comparison 2019-2023

In consideration of the serious repercussions that the persistent situation of water scarcity could have on the economic and social fabric, a measure of considerable importance is the **Drought Decree DL 39/2023**, which introduces specific measures aimed at increasing the resilience of water systems to climate change and to reduce the waste of water resources.
In particular, the text identifies specific measures aimed at preventing drought, with attention to the resilience of water systems, water losses, increase in reservoirs, reuse of water.
Among the objectives of the decree: speeding up authorization procedures, speeding up the construction of water infrastructures, and making the action of the Government and the Regions highly effective and more coordinated.
For the implementation of these measures, the establishment of the control room and the appointment of a national extraordinary commissioner for water scarcity is envisaged to ensure the coordination of all initiatives and the strengthening and adaptation of water infrastructures.

Climate change and environmental degradation represent an existential threat to Europe and the world. To overcome these challenges, the **European Green Deal** will transform the EU into a modern, resource-efficient and competitive economy by ensuring:

• no net greenhouse gas emissions by 2050;
• economic growth separated from the use of resources;
• No person and no place left behind.

The European Commission has adopted a set of proposals to make EU climate, energy, transport, and taxation policies capable of reducing net greenhouse gas emissions by at least 55% by 2030, compared to 1990 levels.

Groundwater is an important resource, particularly vulnerable to the direct or indirect effects of climate change and therefore needs careful management. The technological advances achieved in the 19th and 20th centuries are not sufficient on their own to manage the "common good" that is underground water.
In conclusion, political institutions and governance structures are also important: methods and policies directed at sustainable use of global resources such as groundwater, in response to climate-driven hydrological changes and in combination with additional stresses of population growth and consumption, associated with changes in land use, will be the main challenge for water management in the 21st century.

1.2 Possible scenarios for the reuse of purified water

At Pfizer, groundwater is used extensively for several purposes, as described in Chapter 2, Section 2.3.

This use can be observed in the following graphs.

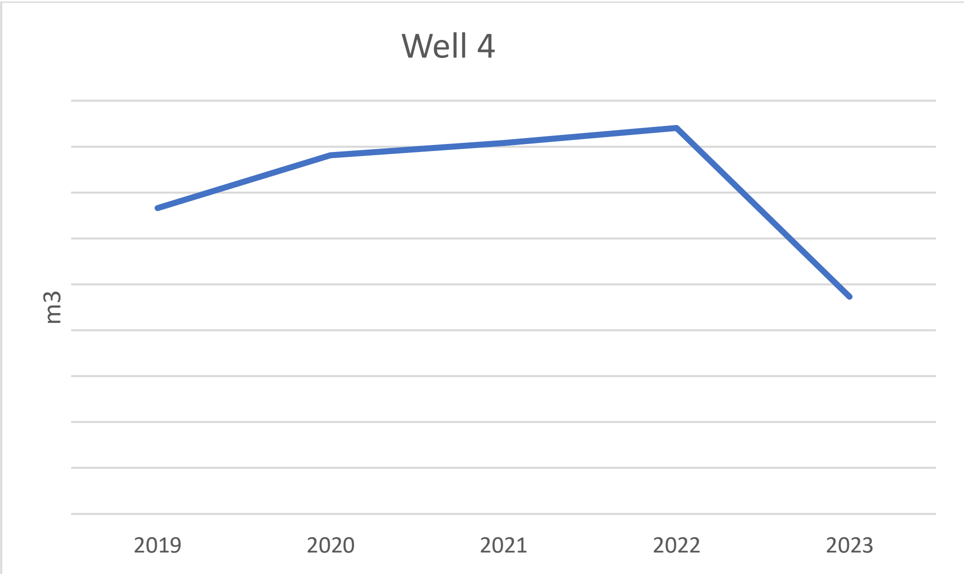


Figure 32: trend of water withdrawal from well 4 over the last 5 years

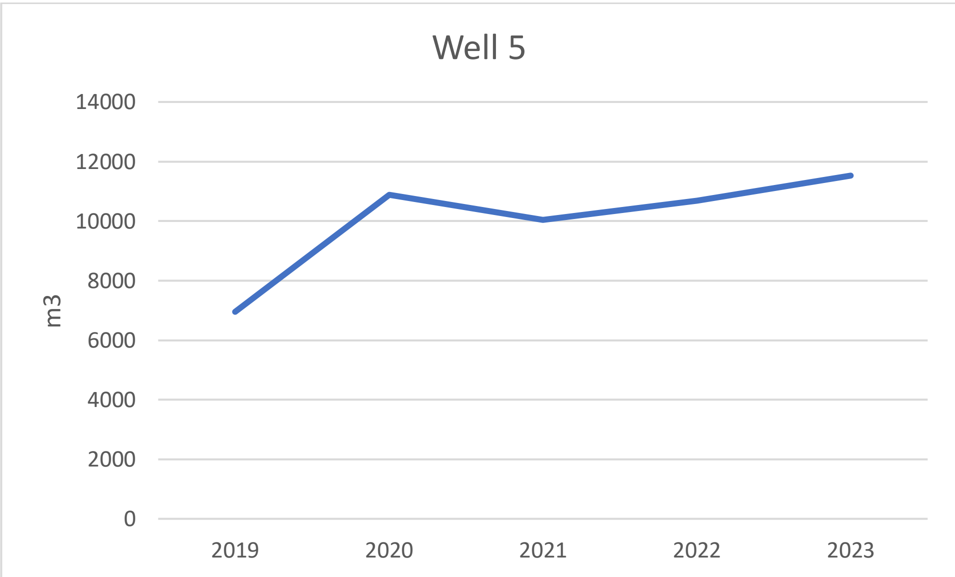


Figure 33: trend of water withdrawal from well 5 over the last 5 years

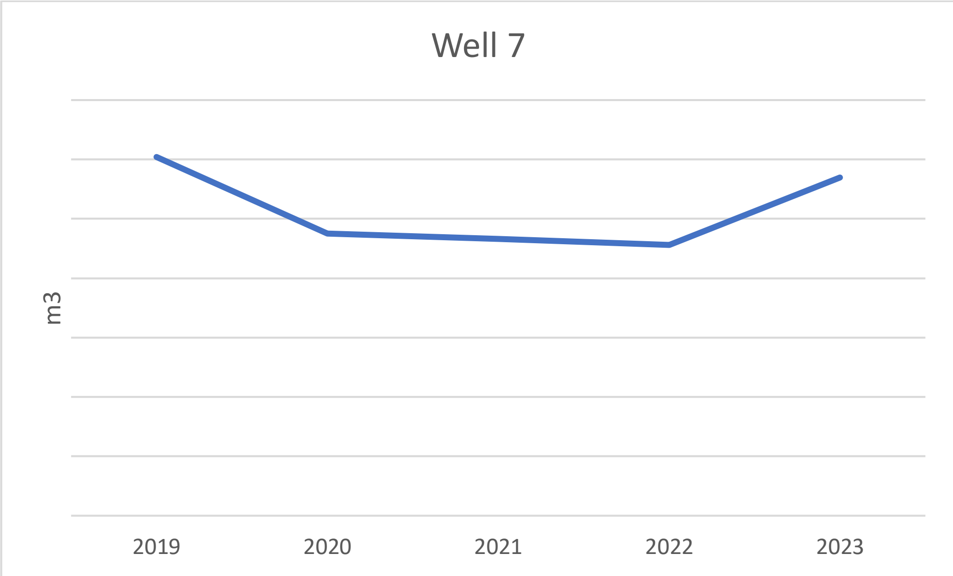


Figure 34: trend of water withdrawal from well 7 over the last 5 years

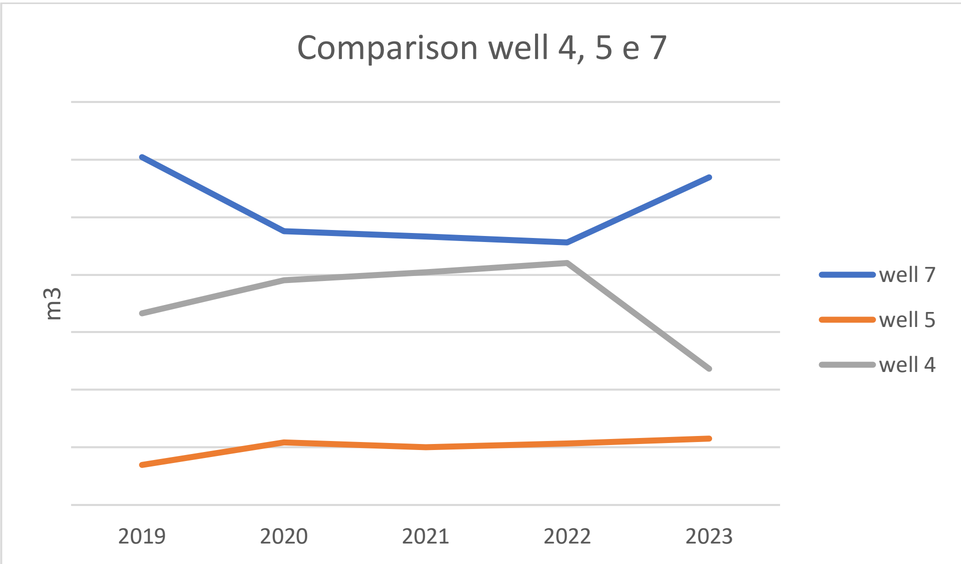


Figure 35: comparison of water withdrawal from the three wells in the last 5 years

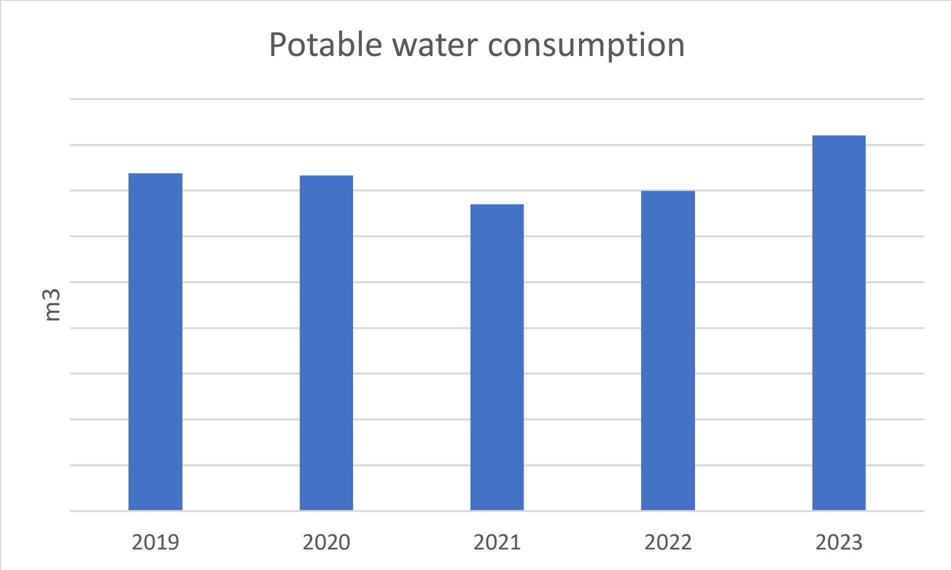


Figure 36: drinking water consumption in the years 2019-2023

In 2020, a quantity of well water equal to 92% of that withdrawn in 2019 was withdrawn.
It is estimated that of the drinking water taken from the network, approximately 45% is used for the production process, while the remaining part is used for the various services (bathrooms, canteen, etc.).
While the largest quantity of well water (around 90%) is estimated to be used for the evaporative towers and heat exchangers, and the remaining part for the toilets.
The well water withdrawal from 2019 to 2023 remained on the order of 33% – 25% for well 4, 7% – 13% for well 5 and 60% – 62% for well 7 compared to the total drawn in the respective years.

From the graphs shown in figures 34, 35, 36, it is possible to observe how the consumption of well water varies over the years based on needs, but also on the capacity of the different wells to supply water.
In particular, it is possible to observe (Figure 37) how wells 4 and 7 are able to supply more water than well 5.

Flow meters are installed inside the Pfizer plant to keep the incoming and outgoing water under control. Furthermore, to monitor and reduce water consumption, volume meters are installed at the collection and discharge points. In this way it is possible to check the average daily flow, the maximum withdrawal and discharge value and report anomalies and losses in the water circuit.

Based on this data and what was previously said regarding the water crisis and all the related critical issues, wastewater treatment can offer opportunities to reduce water consumption and limit discharge into the sewer.
In particular, the water reclaimed in the purifiers can be reused as evaporative cooling water or, depending on the case, in the supply of boilers, as maintenance and irrigation water for industrial green areas.

There are 3 options that could be taken into consideration for water reuse:

- send the treated water directly to the cooling tower tank;
- send the water directly to the collector upstream of the osmosis system;
- send the treated water to the relaunch well and then to the well water tanks.

Below we will discuss the different options in detail.

1.2.1 Option 1

Among the various applications of reuse for industrial purposes, the replenishment of water in the cooling tower tank constitutes an important use in the industrial world.
Cooling towers represent the section where the greatest quantity of water is lost; for this reason they require constant replenishment and this replenishment could be provided by the water purified by the new system which would replace the so-called well water, in such a way as to guarantee the aforementioned replenishment even in periods of extreme drought and notable lowering of the level of water in the aquifer which can compromise the supply of the necessary quantity of water to the plant.

The **cooling tower** - sometimes also called evaporative tower - is a heat disposal system which, exploiting the natural operating principle of evaporative cooling, allows a mass of water to be cooled through exchange with ambient air.
As anticipated, open circuit evaporative towers are cooling systems which, by placing water and air in direct contact, exploit the operating principle of evaporative cooling, ensuring low energy consumption.
Water cooling towers work like a heat exchanger:

1. The open circuit evaporative tower receives from the user a large mass of process water at high temperatures which needs to be cooled.

2. The water used to cool the refrigeration units and air compressors is distributed uniformly from above onto the exchange packs using spray nozzles.
3. The exchange pack, which represents the section inside the evaporative tower where the heat exchange with the air takes place in countercurrent, has the function of expanding the useful surface of the heat exchange and promoting the evaporation of a small amount of water.
4. The direct encounter of the air with the process water causes the evaporation of a small quantity of water and the cooling of the remaining part, bringing it to a lower temperature (e.g. 30°C), which can therefore be recirculated in the industrial process.
5. Once cooled, the process water is conveyed into the evaporative tower basin from which pipes connected to booster pumps which allow the cycle to be restarted within the user.

As regards the water balance of the evaporative towers, the share of water lost from the towers is given by its purging and evaporation.
The purging is carried out because the water evaporating from the tank creates an increase in the concentration of salts.
In particular, via a piezometric sensor, the tank level is monitored and when the latter drops below 170 cm, replenishment is activated.
Furthermore, since the tank is open-air, there will be an evaporation of the water contained in the tank and this contribution also considers the amount of water lost due to the dragging upwards of micro-droplets of water from the heat exchanger.

The amount of water lost through evaporation depends above all on the season, on external temperatures and is measured as the difference between replenishment and purge.
From the graphs below it is possible to observe how in summer there is a significantly higher evaporated value compared to the same during the winter.

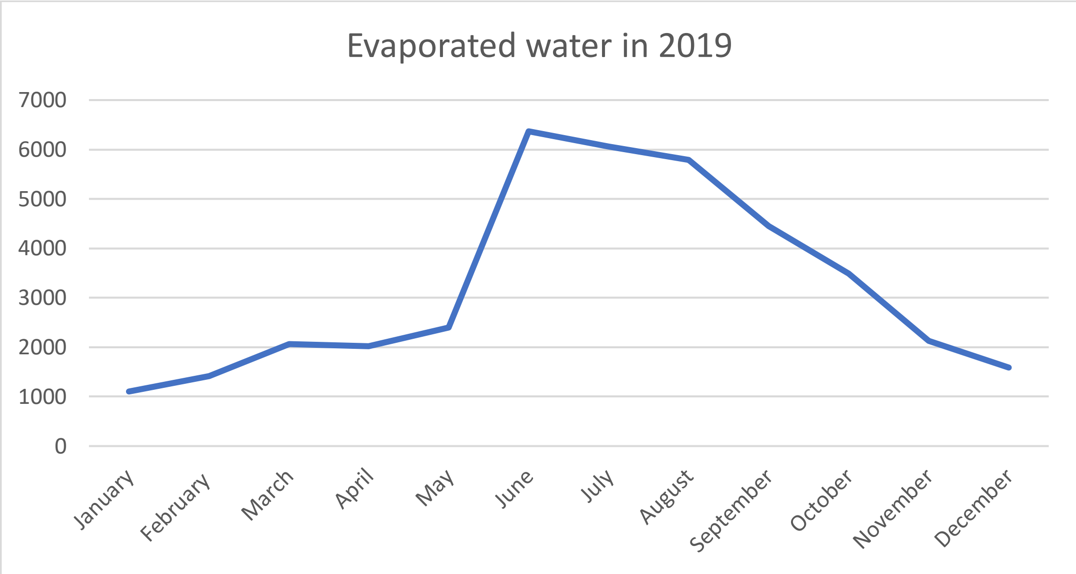


Figure 37: Evaporated trend in 2019

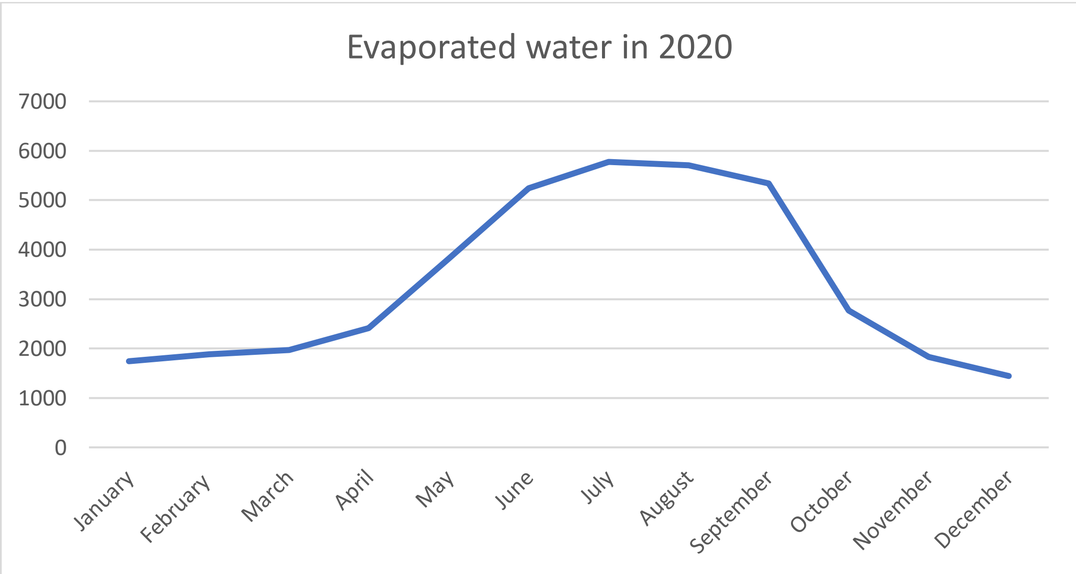


Figure 38: Evaporated trend in 2020

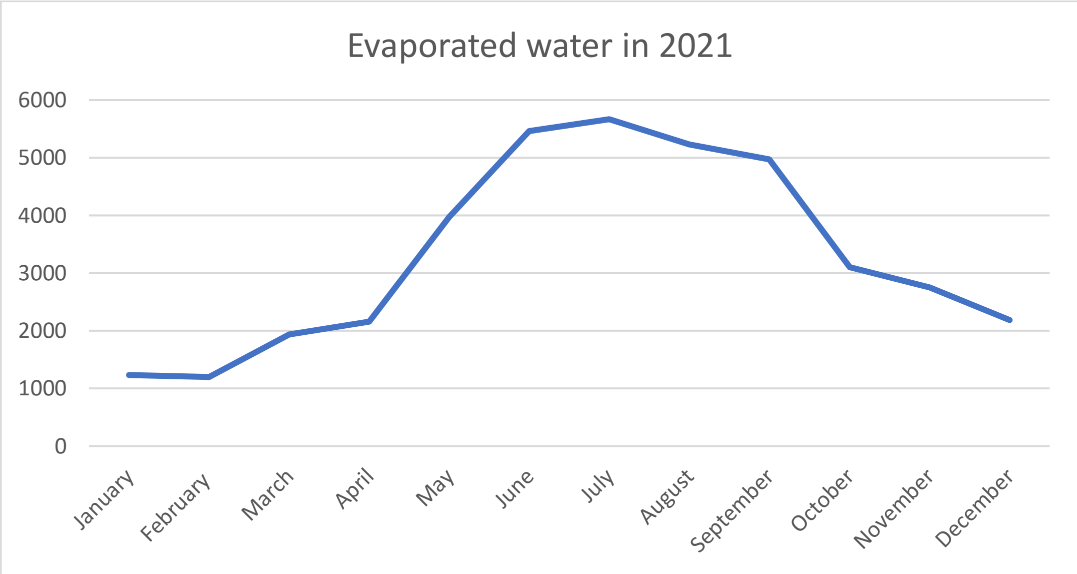


Figure 39: Evaporated trend in 2021

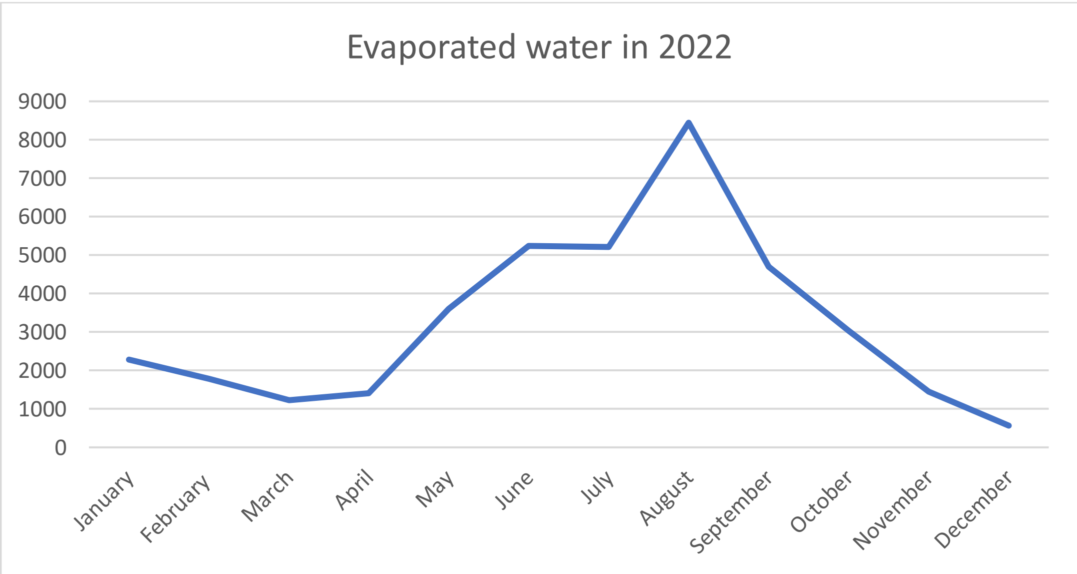


Figure 40: Evaporated trend in 2022

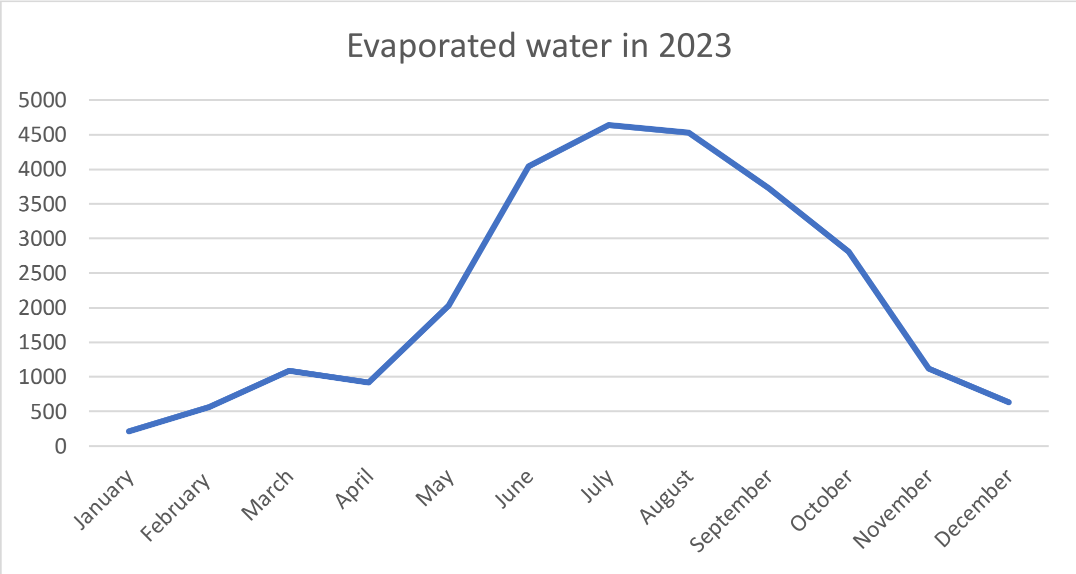


Figure 41: Evaporated trend in 2023

As regards the water leaving the evaporative towers, this has increased in the last 5 years: in 2023, 23% more purging was achieved compared to 2019.

While the evaporated water remained almost constant from 2019 to 2022, with a decrease of 32% in 2023.

The following cooling towers are present at the Pfizer plant in Ascoli:

- DECSA model TVA-24-268-SS+SG;
- ILMED model ITEM A 3/aTG/P3/11/DS/S.
-

Figure 42: ILMED cooling tower system

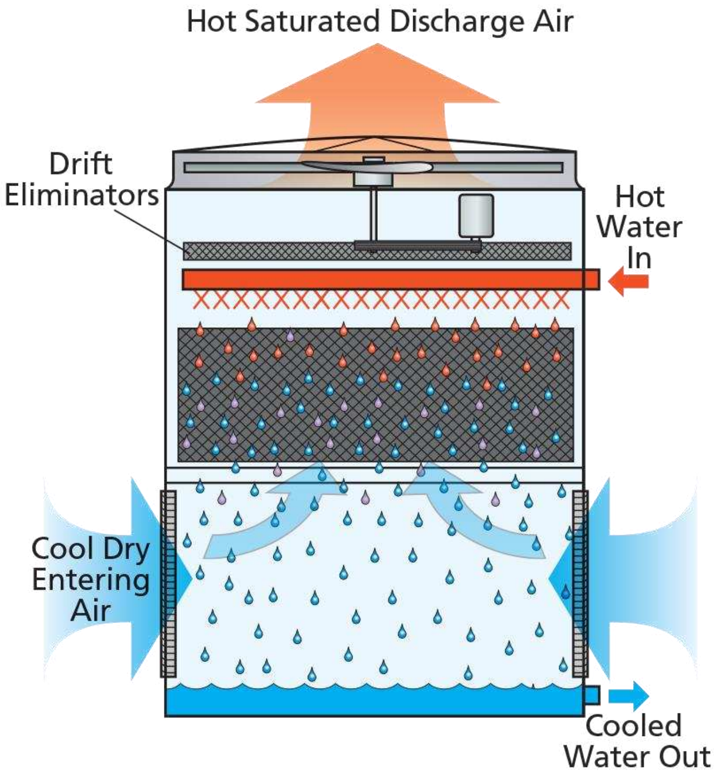


Figure 43: cooling towers functioning

Figure 44: focus water cooling through the spray nozzles

Suppliers recommend the following values of water entering the towers:

		ILMED	ILMED	DECSA	DECSA
Substances	**Unit of measure**	**min**	**max**	**min**	**max**
Total hardness	°F	20	100	5	80
Alcalinity	Mg/l CaCO3	50	300		650
pH	-	7	8,5	6,5	9,5
Coductivity (at 20°C)	µS/cm	500	2500		3300
Total suspended solids	mg/l		25		25
Iron	mg/l		2		
Manganese	mg/l		0,1		
Free active chlorine	mg/l				1,2
Sulphates (as SO4)	mg/l		250		350
Clorides	mg/l		250		300
Fats and vegetable and animal oils	mg/l		10		
Organic substances (COD)	mg/l		30		N.D.

Table 9: water parameters for cooling towers

Therefore, the following ranges will be considered:

SUBSTANCES	UNIT OF MEASURE	MIN	MAX
Total hardness	°F	20	80
Alcalinity	Mg/l CaCO3	50	300
pH	-	7	8,5
Conductivity (at 20°C)	µS/cm	500	2500
Total suspended solids	mg/l	0	25
Iron	mg/l	0	2
Manganese	mg/l	0	0,1
Free active chlorine	mg/l	0	1,2
Sulphates (come SO4)	mg/l	0	250
Clorides	mg/l	0	250
Fats and vegetable and animal oils	mg/l	0	10
Organic substances (COD)	mg/l	0	30

Table 10: water parameters for cooling towers taken into consideration

One of the most limiting parameters for water reuse is COD since the value of the treated water is much higher than the limit of 30 mg/l obtained from the tower suppliers; in this case it is necessary to provide a further refinement treatment or increase the purification efficiency of the chosen solution.

Let's assume we have a concentration in the treated water equal to that of the discharge limit value, evaluating the possible treatment in the worst and most precautionary case.

One of the possible treatments to reduce COD is an adsorption on granular activated carbon, the so-called GAC.

Adsorption is a mass transfer phenomenon in which one or more constituents, present in the liquid or gaseous phase, are fixed on a solid porous surface. The process is classified among the advanced treatments, aimed at removing pollutants in suspended, dissolved and colloidal forms, still present in the wastewater downstream of the secondary treatments. The use of this type of treatment is essential where there is a need to reduce nutrient concentrations, to avoid eutrophication phenomena, or to reuse wastewater, with reference to industrial applications or dispersion interventions of treated water on the soil or underground.

This process is influenced by several factors:

- Surface area: the more porous and particle-sized the adsorbent is the greater the adsorption capacity (Weber, 1972).
- The adsorbate: As regards inorganic compounds, the fundamental factor seems to be the presence of the solute in neutral or ionic form (Cooney, 1999). However, with reference to organic compounds, the key factor is the solubility of the compound. The lower the compound solubility in the solvent the more the compound is adsorbable.
- pH: the adsorption of organic substances presents in an aqueous solution decrease as the pH increases, in particular pHs far from neutrality negatively influence the results as they could induce ionization phenomena.
- Temperature: the process improves as the temperature decreases.

The activated carbons normally used for the treatment of drinking water, wastewater and gas are prepared from different types of material, such as mineral coal, peat, wood, or lignite.

Activated carbon acts on organic molecules which include phenols, chlorinated and non-chlorinated hydrocarbons, pesticides, pesticides, surfactants as well as eliminating excess oxidants such as chlorine.

The preparation of a coal consists of the pyrolysis of the base material, followed by an oxidation phase. The first phase consists of subjecting the material to temperatures varying between 600 and 900 °C in the absence of air. The addition of metal chlorides promotes the development of pores. The subsequent oxidation phase, the function of which is to “activate” the carbon, is usually carried out using steam, although air (less frequently CO2) is sometimes chosen, at temperatures varying between 600 and 900 °C. During this phase, oxidizing gases erode the surface of the coal, developing a vast internal network of pores.
The reactions that occur during the activation phase are the following:

$C + H_2O \rightarrow H_2 + CO$

$C + CO_2 \rightarrow 2CO$

$C + {}^{1}/_{2}\, O2 \rightarrow CO$

The treatment with granular activated carbon involves the passage of the water to be treated through a filter bed, in which the carbon is arranged within containers, usually metallic, and is a product in granules, of an amorphous type, which presents a porous appearance under the microscope.
In fact, they are distinguished into:

- Micropores: pores with a diameter greater than 1000 A
- Macropores: pores with a diameter between 10 A and 1000 A

and it is precisely the large internal surface (of the order of 500 to 1500 m2/gr) and the structure of the pores that determine the adsorbent properties of activated carbon.
Different phases can be distinguished inside the bed:

- a first zone consisting of completely exhausted carbon in phase equilibrium with the contaminants present in solution.
- a second band called mass transfer zone (MTZ – Mass Transfer Zone) in which the concentration of solutes decreases from the value that characterizes the incoming liquid to the outgoing liquid with a characteristic S-curve.
- a third zone in which the activated carbon is assumed to be "virgin" as the liquid that has passed through the previous layer has minimal concentrations of pollutant.

Let's say we have a downflow column filled with GAC. The carbon adsorbs the pollutants and progressively becomes saturated as the liquid travels. Figure 45 shows the operating scheme of a down flow filter column, which is usually represented by the variation in concentration over time or by volume of treated bed. This curve is called the breakthrough curve.
The area of the column in which the adsorption process takes place is known as the mass transfer zone (MTZ). Leaving the MTZ the polluting compounds will have concentration values close to the minimum achievable ones. Beyond the MTZ there is a still unused coal area which therefore keeps its adsorbent capacities unchanged.
As the process continues, the mass transfer zone gradually moves downwards, resulting in a reduction of the virgin coal zone until it disappears. At this point the concentration of solute in the effluent tends to increase, until it reaches a maximum acceptable value at which perforation of the bed occurs. This condition, also known as the breakdown condition, occurs when the concentration of the solute at the exit is equal to 5% of the concentration at the entrance. At this point it is necessary to regenerate the carbon even if the carbon in the MTZ has not yet completely exhausted its adsorption capacity. The filter exhaustion condition, however, is considered to have been reached when the exit concentration of the adsorbate is equal to 95% of the input concentration.

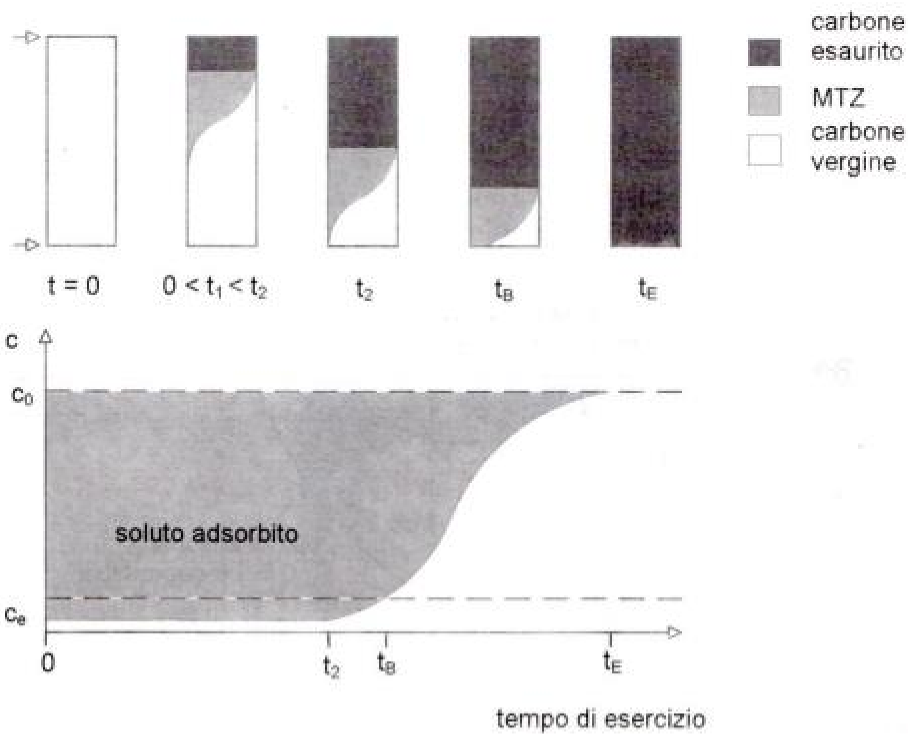


Figure 45: break-through curve for a down-flow adsorption column

The sizing of an adsorption column must be carried out considering the contact time, defined as the ratio between the volume of the empty reactor and the flow rate fed, also known as EBCT (Empty Bed Contact Time), and the filtration speed or surface hydraulic load. Once these two parameters have been set, we proceed to evaluate the geometric dimensions of the various units. EBCT values are usually between 5 and 30 min; while values of the surface hydraulic load are set varying between 5 and 15 m/h (Metcalf & Eddy, 2006).
Another parameter to consider is the height of the filter medium. It is obvious that the higher the heights of the reactors, the longer the contact times between the substances to be adsorbed and the adsorbent material. It is good to remember, however, that as the height increases the pressure losses also increase. For this reason, values of 3 m are generally not exceeded (Bonomo, 2008).

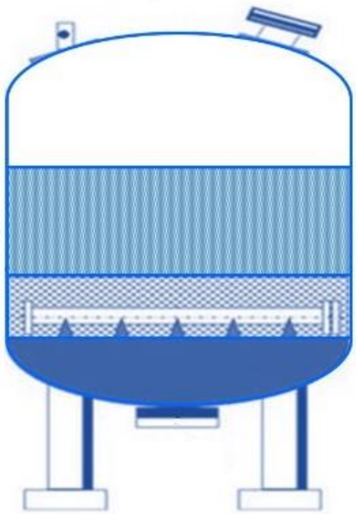


Figure 46: example of activated carbon filtration (osmo systems water treatment technologies)

In the Pfizer case, it is necessary to reduce the COD in particular from 160 mg/l to 30 mg/l; to obtain this result it is necessary to consider the average hourly flow rate that will have to be treated equal to 14.6 m3/h which would significantly compensate for the water necessary to maintain the adequate level for the cooling tower basin which corresponds to 170 cm.
It will be necessary to connect the two final tanks where the ozonation will take place to the activated carbon filter with a 23 m underground polyethylene pipe.

It will also be necessary to provide two booster pumps to ensure the necessary redundancy in the event of failure of one of the two or maintenance. Only one pump will work at a time which will send the flow of treated water from the ozonation tanks to the carbon filters. These pumps will be multi-impeller vertical centrifugal pumps with inverter, capable of lifting a maximum flow rate of 15 m3/h and a hydraulic head not exceeding 3 bar.

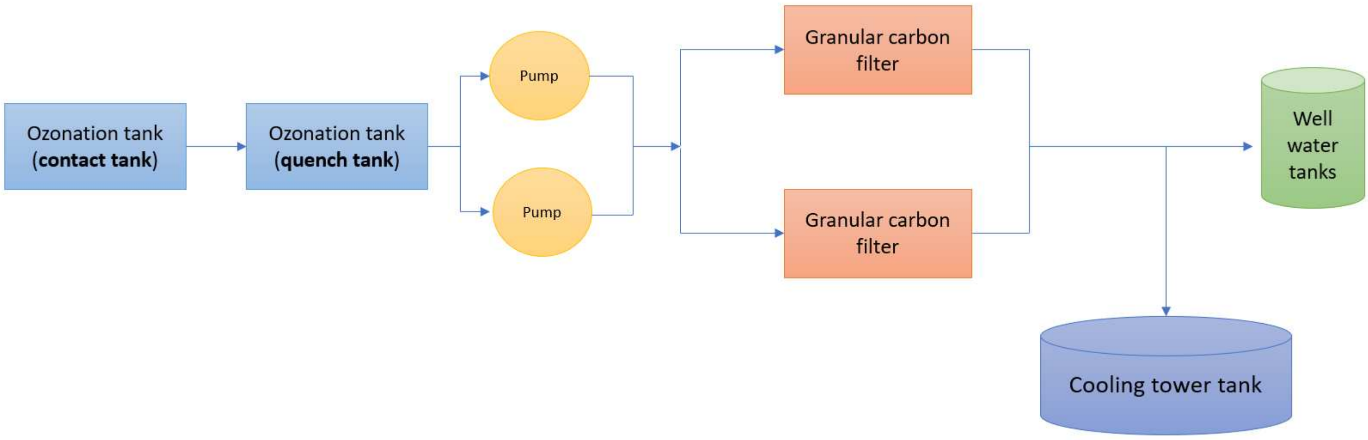


Figure 47: Blockflow diagram for option 1

Assuming a filtration speed of 10 m/h for carbon filters, we will have a filter surface of 1.46 m2, consequently the diameter will be 1.4 m.

With a contact time of 20 min. we will need 4.8 m3 of carbon, which, inserted in a column with a diameter of 1.4, leads to a height of carbon of 3.13 m.

The height of the carbon is excessive, both for the pressure drop that would be needed for crossing the carbon and for the construction of a filter with large height dimensions.

It is good practice to keep the height of the carbon inside the filter from a minimum of 1 m to a maximum of 1.5 m.

For this reason and since the depletion of carbon does not occur in a linear way as previously described, it is better to divide the quantity of carbon into 2 columns, having a diameter of 1500 mm (surface area 1.7 m2) loaded with 2.4 m3 of carbon each, which leads to a layer height of 1.4 m.

In fact, the use of a single stage does not allow the full potential of the system to be exploited, since the unit needs to be deactivated before the column is completely exhausted.

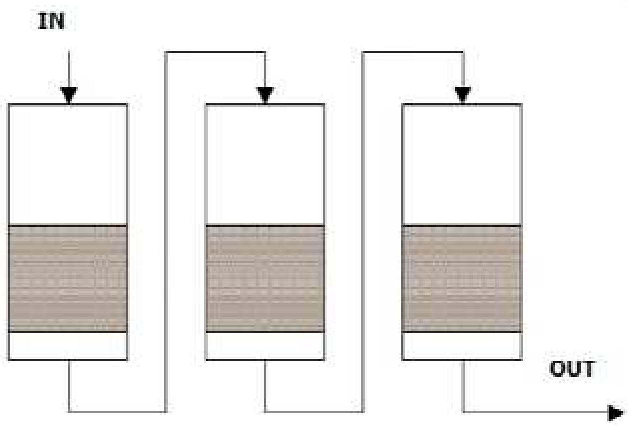


Figure 48: In series down-flow adsorption column example

However, it is advisable to periodically carry out backwashes to eliminate any accumulated solids. In fact, the filters must have a height of at least 600 – 700 mm of empty space to allow the carbon to expand during the backwashing phase which must be carried out at a speed of 15 m/h, since higher speeds could lead to a leak of carbon.
Since it is clean water, coming out of UF membranes, the backwash can even exceed one month of operation.
To perform backwashing, we will need a pump following the carbon filters and a bypass channel in case of pump malfunction or maintenance.
To start the backwash, we could use a differential pressure gauge on each filter with a difference of 0.8 - 1 bar which indicates the clogging of the filter, but since it is a backwash per month, it would be more appropriate to carry it out manually by reading the difference between the pressure gauges placed in test the filters.

The two-column system, through a panel of valves, allows them to rotate, leaving the column with fresh activated carbon to be discharged.
To better understand the transition, let's explain the various phases. Initially the passage will be:

- Column 1 + column 2; in this way the column that runs out completely will be number 1 but column 2 can adsorb any leakage of organic substance and the carbon in column 1 can be replaced.

After replacing the carbon in column 1 the step will be:

- Column 2 + column 1; in this way the column that runs out completely will be number 2 (which has already partially worked), but column 1 can adsorb any leakage of organic substance and the carbon in column 2 can be replaced, restoring the initial system.

Figure 49: example of two column filtration system (Boer group)

Based on the pollutants present in the water to be treated, the type of carbon used will have an iodine number of around 900 and preferably of vegetal origin, which also allows the adsorption of most solvents.

With a two-column system as described, a 90% reduction in COD is expected, naturally dependent on the type of pollutants present, the quantities of which will need to be verified once the plant is started.

The adsorption capacity of organic substance by carbon is approximately 20% of its weight and the organic substance is 1/3 of the COD; from this it can be deduced how often the carbon in a column will have to be replaced.
To make the most of the carbon's potential, it will be replaced when the COD entering and leaving the filter is the same.

The application of an adsorption process on activated carbons in a cost-effective manner is related to the possibility of being able to regenerate the carbons once exhausted at a specialized company. Regeneration allows us to restore the adsorbent capacity of the carbon and can be carried out by:

- chemical method, which involves the use of chemical reagents for the oxidation of adsorbed organic substances or their extraction with solvents;
- flow of steam or inert gas at relatively high temperatures to remove adsorbed volatile substances;
- biological regeneration processes;
- thermal processes, implemented by heating the material in controlled atmosphere rotary ovens up to temperatures of 800-900 °C.

The life of an activated carbon filter is linked to the quantity of pollutants that the carbon is able to adsorb before reaching saturation. The time is of the order of 1 – 2 years.

However, it is important to underline that during the regeneration cycles there is a loss of 5-10% by weight of the material and the adsorbent capacity is not completely recovered; and, therefore, after a certain number of cycles, the complete replacement of coal becomes necessary (Bonomo, 2008).

This treatment will require a 10m x 5m bed with a double electro-welded mesh.

Considering that the flow coming from the depuration plant could, in some periods of the year, be greater than the necessary replenishment, it will be necessary to provide a three-way valve on the pipe that will be built, controlled by the level sensor: in the event that the level of water in the tank is lower than the minimum (170 cm), the flow rate of treated water is directed to the tower tank; upon reaching the appropriate level, the valve begins to switch towards the pipe directed to the two well water tanks.

This valve must be equipped with a proportional band, to offer a regulation as close as possible to the operating needs of the tub, i.e. 170 cm, rather than working with an on/off valve which would work between a minimum and maximum value.

Furthermore, a polyethylene pipe with a nominal diameter of 80 and a length of approximately 335 meters in total will be required, of which 55 are needed to get from the GAC to the evaporative towers and a further 280 meters to get to the storage tanks.

It is possible to estimate a flat rate cost of such operations:

	Quantity	**Cost**
GAC		115.000 €
Pump	3	8.000 €
Valve	7	14.000 €
Conduit	360 m	200 €/m linear = 72.000 €
Excavation	255m 25m	100 €/m linear on an asphalt road 60 €/m lineare for ground = 30.000 €
Pipe laying		40 €/ m linear= 14.400 €
Energy consumption	84.000kW/year	12.600 €
Additional costs		35.000 €
Total flat rate		300.000 €

Table 11: Option 1 costs

For this option it will be necessary to provide for an update of the Autorizzazione Unica Ambientale regarding the additional emissions, the modification of the water discharge which will no longer occur at the S4 discharge, but there will be a recirculation of the water within the company and only in the event of malfunctioning of the system or in the event of an exceptional and unforeseeable event, a discharge into a body of surface water is expected. Furthermore, a modification will also need to be made for the acoustic impact.

In conclusion, by adopting this option there would be a total recovery of well water since an average annual withdrawal from the wells of 97078 m3 is estimated, on the other hand from the purification plant an average annual recovery available of 122000 m3 is estimated. Obviously, these data were considered and processed on a predictive basis as the plant is still under construction. Once the start-up has been carried out and working stability has been achieved, it will be necessary to verify what has been said based on certain and measured values.
The project certainly involves a significant cost which however will be amortized over the years thanks to the energy savings due to the withdrawal and operation of groundwater.
Furthermore, a fundamental aspect to consider is the environmental impact, since this project safeguards the aquifer and water resources, since the same water would always be reused, creating a continuous cycle.

In this regard, this reuse is necessary by analysing the level of the tanks that collect the well water; since, it is possible to observe how in the summer period this level reaches its minimum due to the lowering of the water table, which causes the wells to dry up and consequently a sufficient quota for the operation of the pumps is not guaranteed.
The graph below refers to the year 2023 which shows the same trend as previous years.

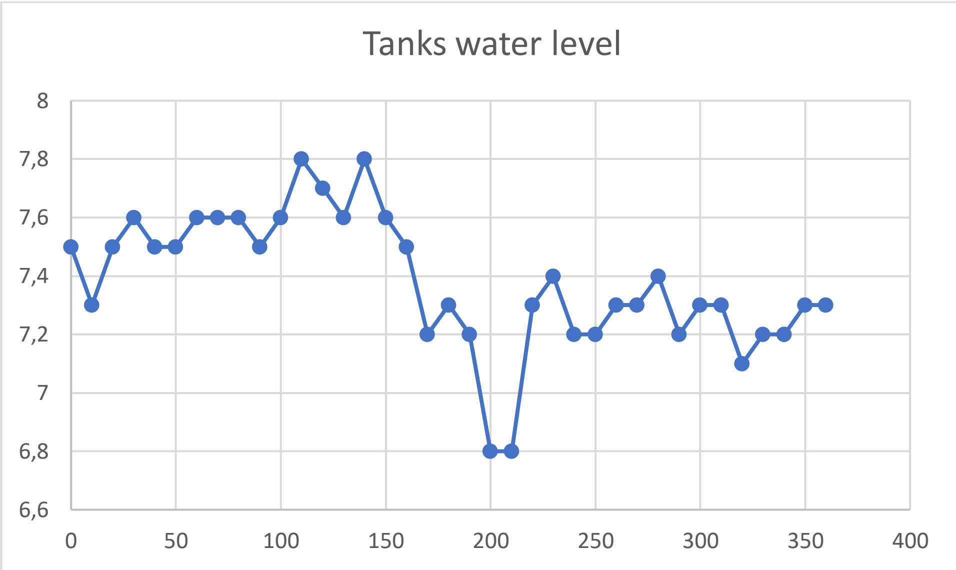


Figure 50: Tanks water level trend during 2023

What was previously mentioned underlines the main element of this study: given the constant demand for well water from the plant, given the climate crisis with consequent shortage of rainfall, it may lead to a plant shutdown due to lack of water in the tanks.
For this reason, the reuse of water would guarantee continuity of operation even in the summer period.

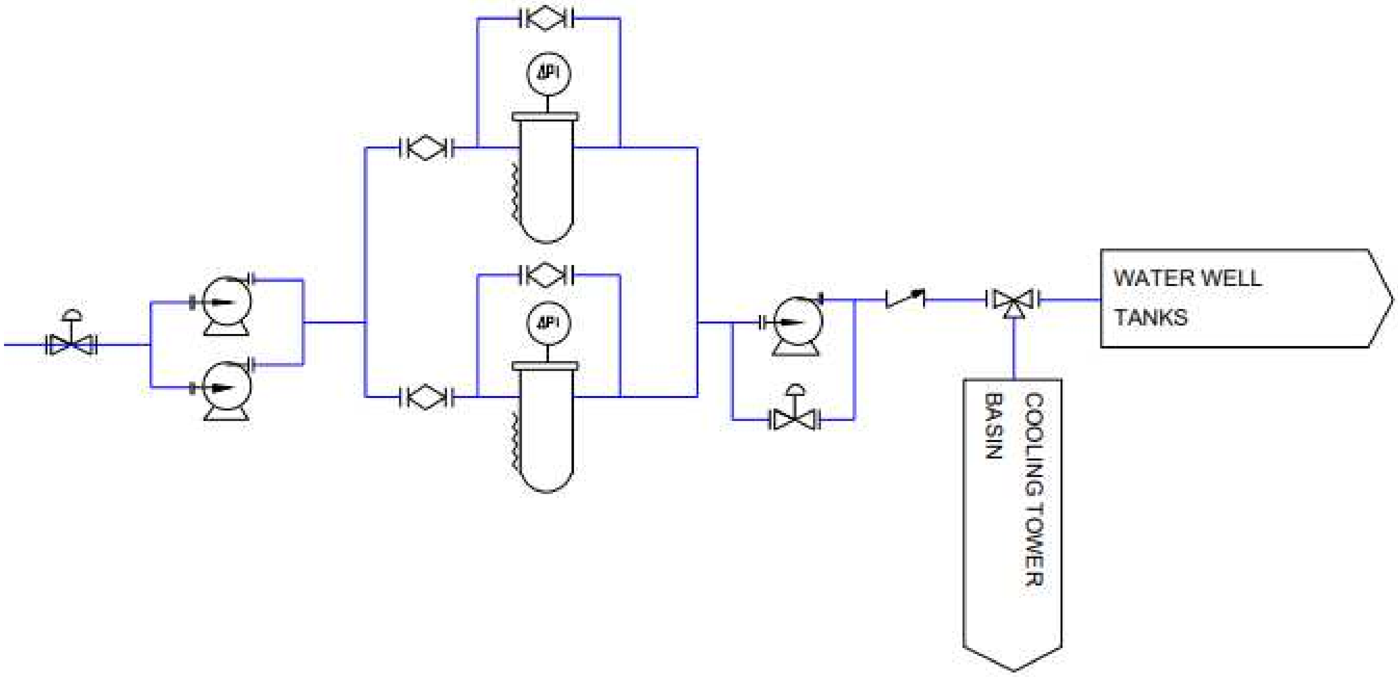


Figure 51: Possible P&I for option 1 additional part

1.2.2 Option 2

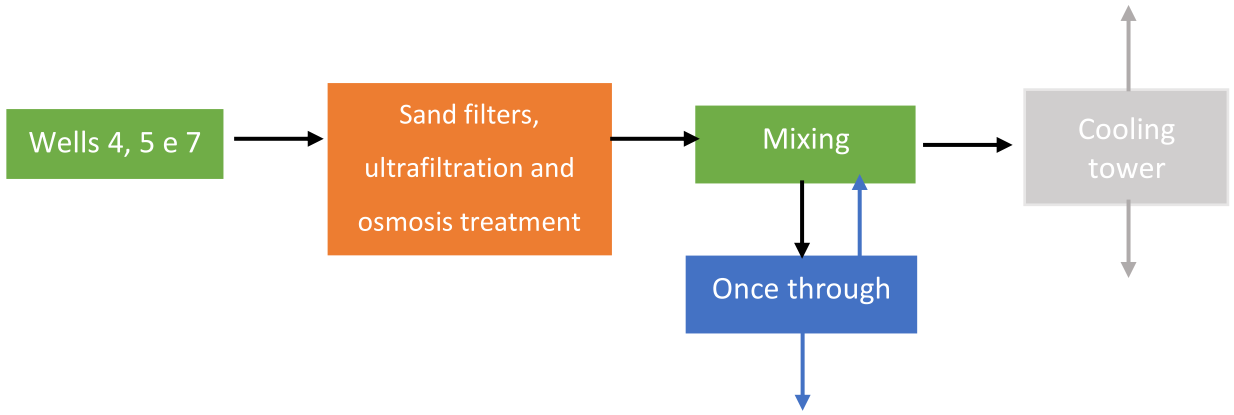
This procedure would consist of sending the treated water to the tank that feeds the osmosis treatment characterized by a volume of 25 m3.

This plant was built to treat well water and allow to feed cooling systems with water of better quality in terms of salinity and suspended solids. The water supplied to the circuits will be the result of a mixture of well water and osmotic water. The expected cut varies approximately between 40% and 60% of osmotic water. The cutting ratio is manually adjusted according to the size of the characteristics of the water and specific management needs to be assessed contingently. This mixture allows the systems to be operated while minimizing the corrosion and inorganic fouling phenomena currently found in systems.

The osmosis system operates in the following way: the pressure booster pump sucks the well water, coming from wells 4, 5 and 7, from a 25 m3 tank and pushes the water through the multimedia filters and the ultrafiltration to fill another 20 m3 tank; when the latter is full, the pump stops. Sodium hypochlorite is dosed into the 25 m3 tank from a dosing pump.

The dosage is in proportion to the flow rate of water entering the same tank after multimedia filtration.

A part of the ultrafiltered water is accumulated in another tank for washing the UF itself.
The media filters are washed with the same incoming chlorinated well water.
The ultrafiltered water contained inside the 20 m3 tank is then relaunched by a pump towards reverse osmosis. An optional softener is also installed on the same osmosis feed line.
The water coming out of the reverse osmosis is mixed with a part of chlorinated well water which is relaunched into the same pipe coming out of the reverse osmosis.
This mixture is sent to the accumulation tanks, which are currently the well water storage tanks, of 400 m3 of treated water.
This mixed water will be sent to the plant's once-through cooling systems and part of this water will be lost and part will constitute the so-called relaunch. The other destination of the mixed water will be the evaporative towers.
The unit can treat water up to 35ºC, with a pressure between 0.1 and 2 bar.



The system requires the supporting tank to constantly have a water level equal to 60% of its volume, such as to function continuously without interruptions, since when the tank reaches 30% full the osmosis system will stop its operation until 60% full is reached again.

Sending the flow of treated water directly to the osmosis system would mean having continuity of operation of this system, as previously mentioned; furthermore, making osmosis work continuously has benefits in terms of less clogging of the membranes, less quantity of chemical agents to use because we would have better incoming water as it is treated water diluted with water coming from the 3 wells serving Pfizer.
Furthermore, by sending this contribution of water to the osmosis system it is possible to exploit it for different uses and not only for the evaporative towers, guaranteeing a constant supply to the various users.

On the other hand, this alternative is not effective for several reasons:

- The osmosis system was designed to treat well water and the related concentrations of hardness, conductivity, alkalinity, etc.; therefore, sending water with different characteristics to the tank that feeds the osmosis system would not be so effective and the osmosis working parameters would have to be modified.
- The treated and recovered water would already be good to be sent to the towers so it would not make sense to have to reprocess it and be diluted again with untreated water.
- If the water coming from the wells were not sufficient to fill the osmosis feed tank, the latter would not be used and sulfuric acid would be dosed, thanks to which parameters would be reached such as to consider the water osmotic well.
- the treated water sent to the osmosis could be more than necessary for the osmosis feed tank so there would be a waste of already purified water which would have to be discharged.

1.2.3 Option 3

This option involves sending the purified water to the recovery tank which receives the water used internally at the plant and then sends it to the two tanks which currently collect the well water.

To carry out this procedure it is necessary to verify that the purified water has parameters consistent with the osmotized water since these two types of water would be mixed and combined in the two tanks.

Furthermore, the recovery tank doesn't have a capacity sufficient to also accommodate the water leaving the purification plant.

Furthermore, it would not be very effective as a practice since we would be sending water to the two tanks which will then be sent partly to the towers; therefore, we would recirculate the water unnecessarily with a subsequent economic expense that could be avoided if the treated water was sent directly to the towers, therefore to the direct and main use.

Chapter 7. Plant maintenance

In the industrial context, the concept of use of a system is immediately associated with that of its maintenance.
Maintenance thus constitutes a fundamental strategic activity for the conservation and safety of the things in our daily lives, both working and otherwise, and has a strong impact on the functional efficiency and safety of environments, systems, equipment and devices, indispensable elements to guarantee the main objective, the safety of workers and people in general.
A system that is not regularly maintained can break or malfunction, causing delays or stops in the production cycle, with consequent economic damage.

The UNI Maintenance Commission, in the UNI EN 10336 standard, defines maintenance as: *"the combination of all technical, administrative and management actions, including supervisory actions, foreseen during the life cycle of an entity and intended to maintain or restore it to a state in which it can perform the required function"*.
These standards were replaced by UNI EN 13306, which sees maintenance as:
"Combination of all technical, administrative and managerial actions, foreseen during the life cycle of an entity, intended to maintain or restore it to a state in which it can perform the required function".

In the workplace, this perspective of bilaterality in the relationship between safety and maintenance is consolidated by the reference standards for the protection of the health and safety of workers and the standards, as we know, constitute a fundamental aspect for establishing and directing towards shared behaviour.
In the Legislative Decree 81/08, for example, the term maintenance appears significantly hundreds of times and is expressly included among the general protection measures.

In the Pfizer plant in Ascoli Piceno, the functionality, efficiency and functioning of all systems are essential requirements to ensure:

- the safeguarding and protection of people;
- the safeguarding and protection of assets;
- safeguarding and protecting the environment.

It follows that the systems, devices, equipment, and various systems require correct management, which is implemented through surveillance, control and maintenance, all in compliance with the provisions of the laws and regulations in force. These activities allow us to detect and remove any cause, deficiency, damage or impediment that could jeopardize the correct functioning and use of the same.

The surveillance activity is carried out through visual inspection by the staff of the Utilities department of the pharmaceutical plant, who have the duty to know the instructions contained in the installation, use and maintenance manual of the machines covered by the company SOP (Standard Operating Procedure), and refer to the latter for every planned and requested activity.

Instead, control, maintenance and overhaul activities require specific skills and resources; therefore, they are entrusted to external companies in possession of the technical-professional requirements required by Ministerial Decree 37/2008.

A critical issue that needs to be focused on is the qualification of those who carry out the maintenance operations, which has a major impact on the effectiveness of the intervention itself.

For this reason, at Pfizer there are three main figures for the management of the systems of the pharmaceutical plant in Ascoli Piceno:

1. The Maintainer
2. The Plant Maintenance Manager
3. The relevant Department Manager.

Who have specific tasks and responsibilities. In particular:

- the Maintainer, in accordance with his training and the instructions and means provided by the employer: takes care of his own safety and health and that of all other people on whom his actions or omissions impact; pursues collective and individual protection; uses the individual and collective protective devices provided appropriately; immediately reports all possible dangerous situations to the manager of the area and/or department; does not remove or modify safety, signalling or control devices without authorization; handles weights exceeding 25 kg with the aid of the equipment supplied; complies with the indications of the company procedure; records all verification and maintenance activities carried out, in accordance with the maintenance management procedure.
- the Plant Maintenance Manager carries out the following activities: ensures that maintenance is carried out in accordance with the company procedure, as established by preventive maintenance; ensures that all staff, both internal and external, have received adequate training and that this is documented; annually evaluates any changes to be implemented on the planned

operations; ensures that activities are carried out in safe conditions; in the event of an anomaly and/or deviation from the company procedure, consider whether to notify Product Assurance.

- the relevant Department Manager carries out the following tasks releases the system in conditions suitable for scheduled maintenance interventions; guarantees that only authorized people can access the various zones of the areas; takes charge of the system after maintenance operations.

Pfizer uses a maintenance management system called EAMS within which maintenance sheets are created describing the type of intervention, frequency, who carries out the activity, whether it is an internal or external employee, reference equipment or whether it is a device or a plant. Once the card has been created, this software ensures that based on the established frequency, it generates a work order, which is in the "ready to be scheduled" state. Subsequently, based on the deadlines, the software inserts this work order into the "in progress" status, that is, it defines who must carry out the work and how much time this work requires, it is subsequently printed and delivered to the person carrying out the activity, it is compiled by the latter and is returned to the Expert who completes, reviews, and archives it.

The Maintenance Execution process receives operational orders from the Maintenance Management process and reports their progress to it, as well as all the information on preventive or fault interventions.

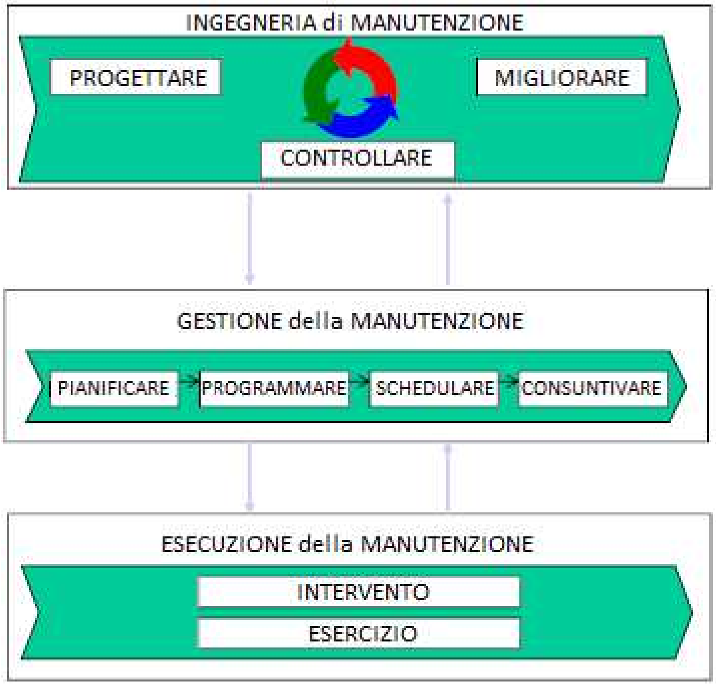


Figure 52: Maintenance process

The Maintenance Management process generates a report of the activities that concern the organization of the interventions, from the planning phase to their final assessment, and sends it to the Maintenance Engineering function.

Finally, the Maintenance Engineering process, using a set of support techniques and tools, has the task of deducing from the analysis of the data received, adequate proposals for improving maintenance activities, from a technical and managerial point of view. The deductions and plans made by Maintenance Engineering are then transferred as input to Maintenance Management, which has the task of preparing their implementation.

Conclusion

This work focused on sustainability applied to wastewater treatment technologies in the pharmaceutical field.
It was possible to take part in the final design of the wastewater treatment plant, examining the details of its construction with a comparison of the possible risks and scenarios of the various treatment phases, highlighting the importance of cooperation during the work activity.

This document was drawn up with the aim of paying attention to all environmental aspects concerning water, considering the influence of active pharmaceutical ingredients which play a fundamental role on the health of humans and the ecosystem nowadays.

Having had the opportunity to analyse the data made available by Pfizer on water consumption within the Ascoli Piceno site, considering the current climate crisis and the increasingly evident scarcity of water resources caused by climate change and estimating the significant daily quantity of treated water equal to 350 m3 which would end up in a body of surface water, it was decided to develop a project for the recovery of this water.

In this project, three options were evaluated, among which one appears to be more valid than the others in terms of implementation and benefits.
Starting from the assumption that in all 3 options the addition of a final activated carbon filtration treatment is expected to improve the quality of the water, the chosen option is to send, as needed, the water directly to the tank of the cooling towers and any surplus to the well water storage tanks.
This conclusion was reached because:

- the evaporative towers are the part of the system that requires a greater supply of water on a constant basis due to the continuous losses that occur due to purging and evaporation.
- the evaporative towers guarantee the operation (through cooling) of the refrigerator and air compressors; especially the latter represent, after electricity, one of the most important sources of the plant.
- at a plant engineering level it appears to be the simplest solution to implement;
- this option guarantees continuity of service especially in the summer period when there is a shortage of well water.
- this option would completely replace the current withdrawal of groundwater through wells.

In conclusion, the experience carried out during the internship at Pfizer in the Utilities department was constructive from several points of view:

- The growth of knowledge acquired throughout the course of studies,
- On a personal level, knowing and learning to relate to other people in the working world.
- On a professional level, working following procedures to which Pfizer pays great attention regarding production and worker safety.
- The possibility of having a first approach to the world of work in a large company reality.
- All this was facilitated by the friendly and serene climate within the company.

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