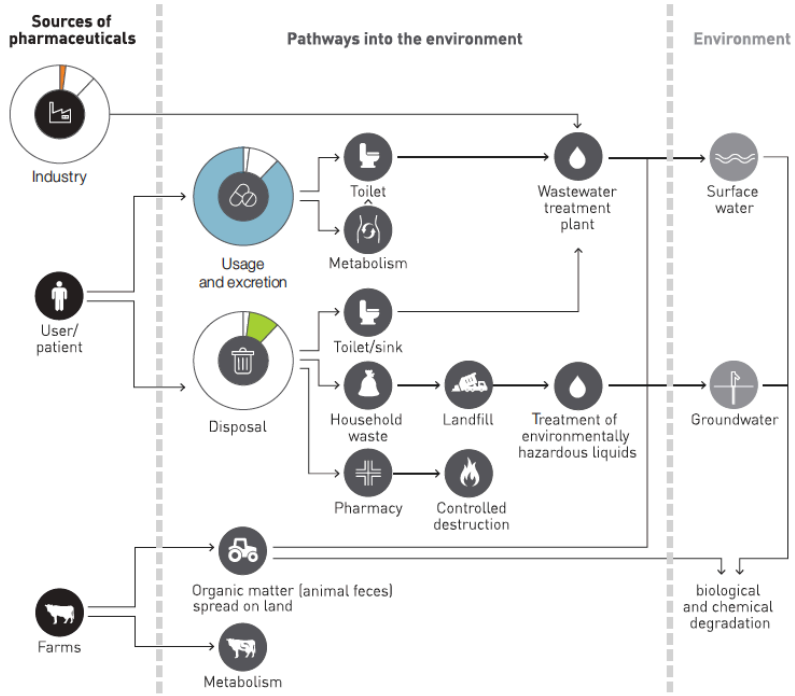
# API Removal – PIE project

## The Customer:

The customer is a leading pharmaceutical company, one of world's largest and most comprehensive manufacturers of healthcare products serving the consumer, medical devices & diagnostics and pharmaceutical markets.

## Project:

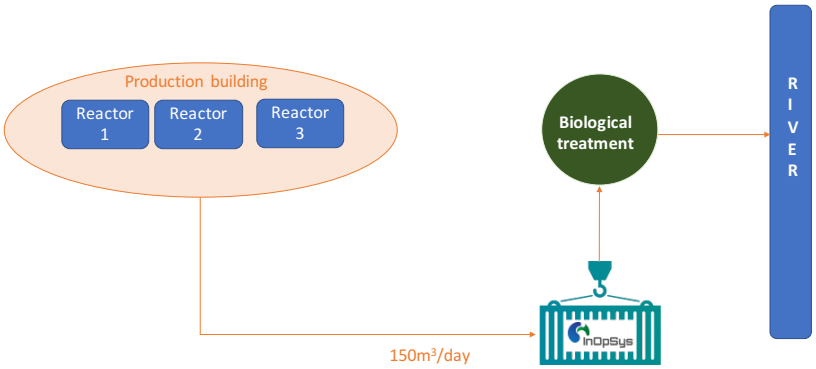
InOpSys developed the solution for a formulation plant for API containing products. Gels, crèmes, shampoos are some of the products which are produced on site. When cleaning their formulation reactors, the cleaning water gets contaminated with API's. A solution for the treatment of the different API's was requested.
PIE (**P**harmaceuticals **I**n the **E**nvironment) is an emerging problem. Pharmaceuticals discarded in the environment have been shown to pose a risk to fish or other wildlife, for example by affecting their ability to reproduce, by altering their behaviour in ways jeopardising their survival, or through direct toxic effects. In addition, incorrectly disposed medicines may contribute to the serious problem of antimicrobial resistance. Increased awareness has prompted further investigation, as well as calls and proposals for action to reduce emissions to the environment, in particular to water but also to soil.



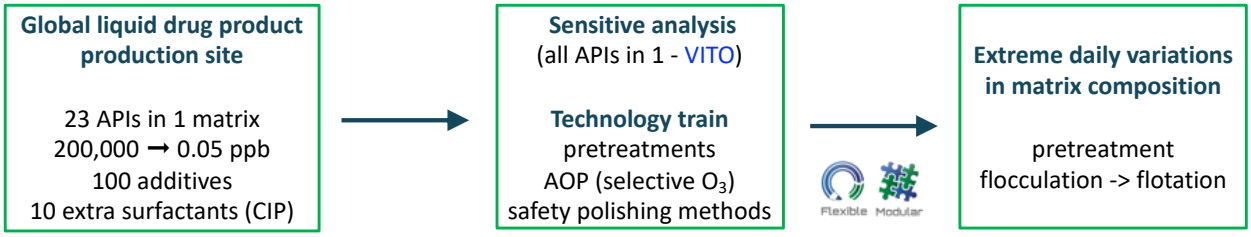

(Source EFPIA)

The customer has a biological treatment unit installed. But persistent, non-biodegradable or difficult to degrade API's will enter the surface water via the biological treatment effluent. This is also the case for municipal biological treatment units. So, the customer decided to implement an innovative solution, developed by InOpSys, for the removal of the API's and to discharge fully PIE (**P**harmaceuticals **I**n the **E**nvironment) free.

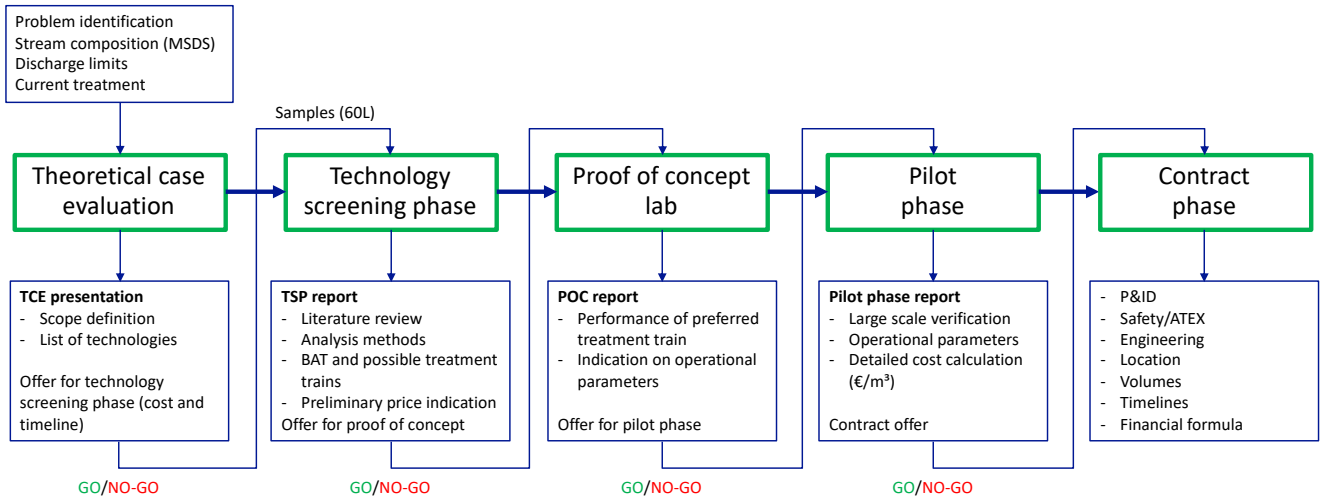
The InOpSys solution is installed in between of the production and the biological treatment unit.




The scope of the project is to remove more then 23 different API's, with 100 additives and different 10 surfactants (CIP). A minimum volume of 150 m3/day will be treated.




In less than 6 months the R&D team of InOpSys developed the analytical method and the hybrid technology concept to remove all the API's out of the wastewater (<0,1 ppb). Together with the customer a stage gate process was executed from theoretical evaluation up to pilot phase testing on-site.



The hybrid technology concept InOpSys developed includes AOP (Advanced Oxidation Process). InOpSys has more than 10 years of experience in all types of AOP technologies (ozone, UV, Fenton, BDD, …). The challenge is to develop a solution that is efficient and economical. The implemented solution also has to be able to treat fluctuating wastewater compositions and future API's.

InOpSys has also developed multiple on-site solutions for the removal of API's, surfactants, … out of aqueous and pure solvent streams from small molecule production.

Overview of some API's for which InOpSys has a developed on-site removal solution (info source https://www.drugbank.ca):

- **Acetaminophen** (paracetamol), also commonly known as *Tylenol*, is the most commonly taken analgesic worldwide and is recommended as first-line therapy in pain conditions by the World Health Organization (WHO).
- **Cetirizine**, also commonly known as *Zyrtec*, is an orally active second-generation histamine H1 antagonist proven effective in the treatment of various allergic symptoms, such as sneezing, coughing, nasal congestion, hives, and other symptoms;
- **Ibuprofen** is a non-steroidal anti-inflammatory drug (NSAID) derived from propionic acid and it is considered the first of the propionics
- **Miconazole** is an anti-fungal medication related to fluconazole (Diflucan), ketoconazole (Nizoral), itraconazole (Sporanox), and clotrimazole (Lotrimin, Mycelex). It is used either on the skin or in the vagina for fungal infections. Miconazole was approved by the FDA in 1974.
- **Hydrocortisone**, or cortisol, is a glucocorticoid secreted by the adrenal cortex.7 Hydrocortisone is used to treat immune, inflammatory, and neoplastic conditions.10,11,12,13,14,15 It was discovered in the 1930s by Edward Kendall and named Compound F, or 17-hydroxycorticosterone.
- **Flubendazole** is an anthelmintic that is used to treat worm infection in humans. It is available OTC in Europe.
- **Econazole** is a broad spectrum antimycotic with some action against Gram positive bacteria. It is used topically in dermatomycoses also orally and parenterally.
- **Haloperidol** is a high potency first-generation (typical) antipsychotic and one of the most frequently used antipsychotic medications used worldwide.
- **Ketoconazole** is an imidazole antifungal agent used in the prevention and treatment of a variety of fungal infections. It functions by preventing the synthesis of ergosterol, the fungal equivalent of cholesterol, thereby increasing membrane fluidity and preventing growth of the fungus.
- **Triamcinolone** is a corticosteroid used to treat various inflammatory conditions in the body from allergic rhinitis to acute exacerbations of multiple sclerosis.
- **Galantamine** is a tertiary alkaloid and reversible, competitive inhibitor of the acetylcholinesterase (AChE) enzyme, which is a common therapeutic target used in the treatment of Alzheimer's disease.
- **Risperidone** is a second-generation antipsychotic (SGA) medication used in the treatment of a number of mood and mental health conditions including schizophrenia and bipolar disorder.
- **Itraconazole** One of the triazole antifungal agents that inhibits cytochrome P-450-dependent enzymes resulting in impairment of ergosterol synthesis. It has been used against histoplasmosis, blastomycosis, cryptococcal meningitis & aspergillosis.
- **Mebendazole** is a benzimidazole that acts by interfering with carbohydrate metabolism and inhibiting polymerization of microtubules.
- **Pheniramine** is a first generation antihistamine in the alkylamine class, similar to brompheniramine and chlorpheniramine. It is used in some over-the-counter allergy as well as cold & flu products in combination with other drugs. Pheniramine's use as an anti-allergy medication has largely been supplanted by second generation antihistamines such as [cetirazine] and [loratidine].
- **Naphazoline** is a rapid acting imidazoline sympathomimetic vasoconstrictor of ocular or nasal artierioles6,7. It acts to decrease congestion and is found in many over the counter (OTC) eye drops and nasal preparations.
- **Domperidone** is a specific blocker of dopamine receptors. It speeds gastrointestinal peristalsis, causes prolactin release, and is used as antiemetic and tool in the study of dopaminergic mechanisms.

- **Tetryzoline** (also known as Tetrahydrozoline), a derivative of imidazoline, is found in over-the-counter eye drops and nasal sprays. Other derivatives include naphazoline, oxymetazoline, and xylometazoline.
- **Abiraterone** is a derivative of steroidal progesterone and is an innovative drug that offers clinical benefit to patients with hormone refractory prostate cancer. Abiraterone is administered as an acetate salt prodrug because it has a higher bioavailability and less susceptible to hydrolysis than abiraterone itself. FDA approved on April 28, 2011.
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