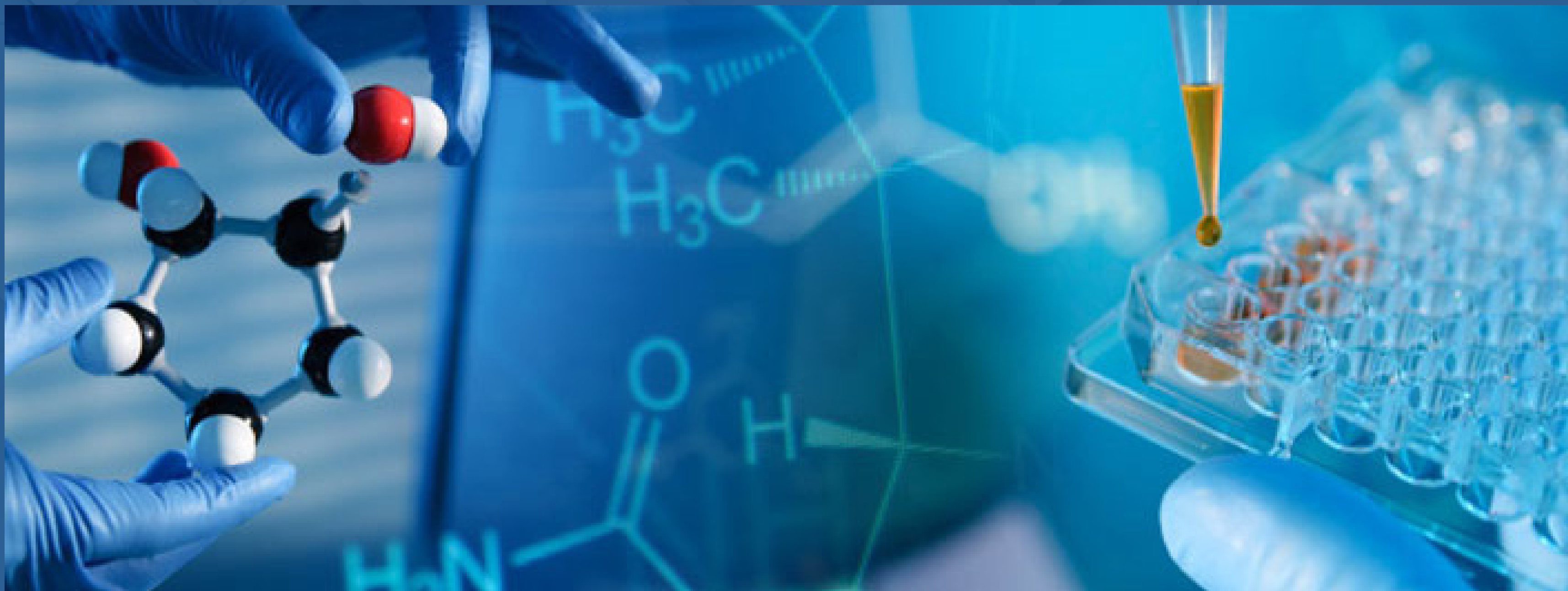

Pharmaceutical Actives and PFOS/PFOA - What Treatment Technologies are Working

Geosyntec consultants

Joseph G. Cleary, P.E., BCEE

AAEES Workshop at NJWEA Annual Meeting | May 6,2019

Presentation Outline

I. Introduction
II. Active Pharmaceutical Ingredients (APIs)
III. API Treatment Technologies and Case Studies
IV. PFOS/PFOAs
V. Technologies and Case Studies
VI. Summary

What is an API?

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- Active pharmaceutical Ingredients (API) are the bioactive chemical agents in our medicines
  - Drug products include pills, tablets, capsules, gels, ointments, oral suspensions & injectable solutions
- Anti-infectives and hormones are the most consequential for the environment
- Modern medicines are built on high potency API
  - Increasingly are high MW biological products
  - Used to be primarily "small molecules" from multi-step chemical synthesis

APIs in the Environment

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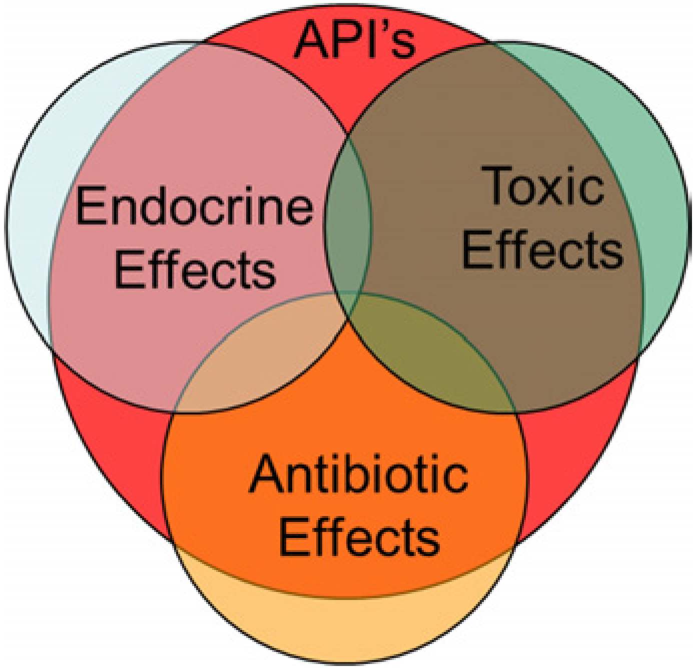
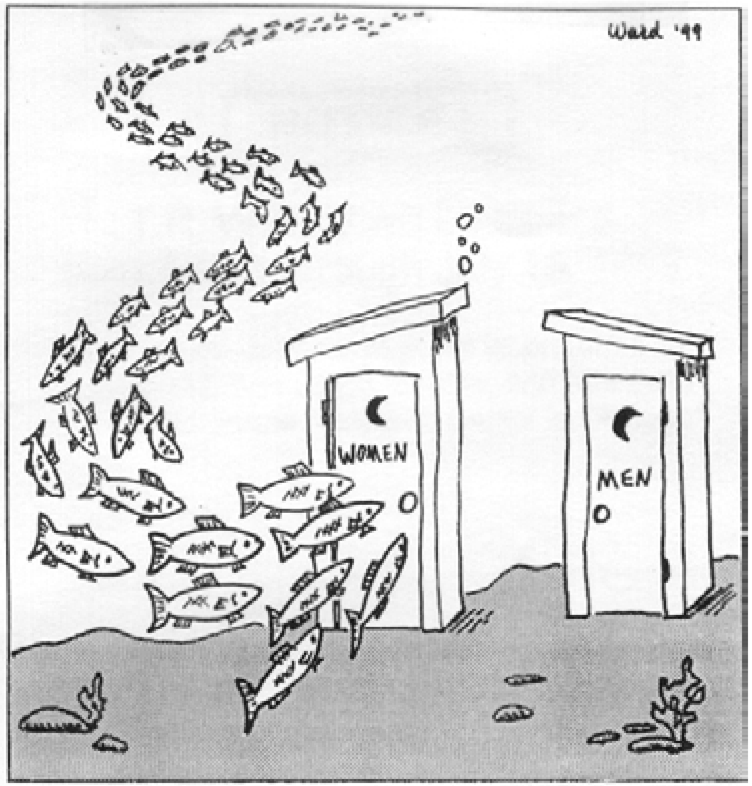
- APIs can be classified into three potentially harmful categories:
  - Toxic Compounds
  - Endocrine Disrupting Compounds (EDCs)
  - Anti-Infectives: Antibiotic & Antimicrobial Agents



Environmental Endocrine Disruptors



The first clue that your new chemical might be an endocrine disruptor.

- Feminization of male fish (e.g. testis-ova induction)
- Modulation of endogenous hormones, receptors, and proteins
- Potential impacts on both human and environmental health

Antimicrobial resistance (AMR)

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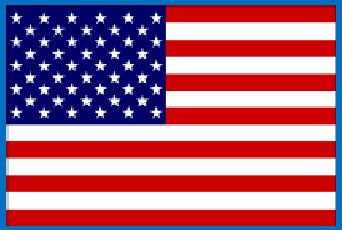
- AMR is the resistance of a microorganism to an AI which was originally effective for treatment
- 3 major causes:
  - Over-prescription in humans, inappropriate use (e.g. non-bacterial infections), & failure to complete treatment courses
  - Routine, non-therapeutic use in livestock
  - Releases of AI into wastewater from human/animal metabolism, pharma production discharges, improper disposal

United States
population 300m

>23,000 deaths

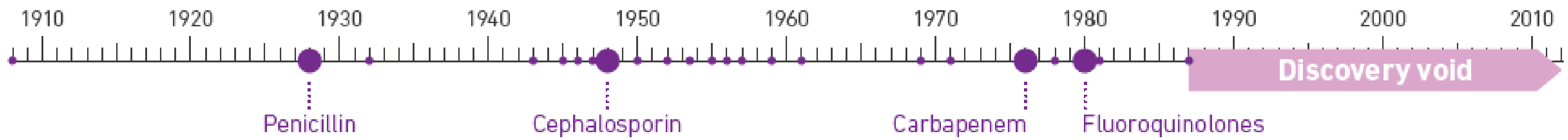
>2.0m illnesses

Overall societal costs
Up to $20 billion direct
Up to $35 billion indirect

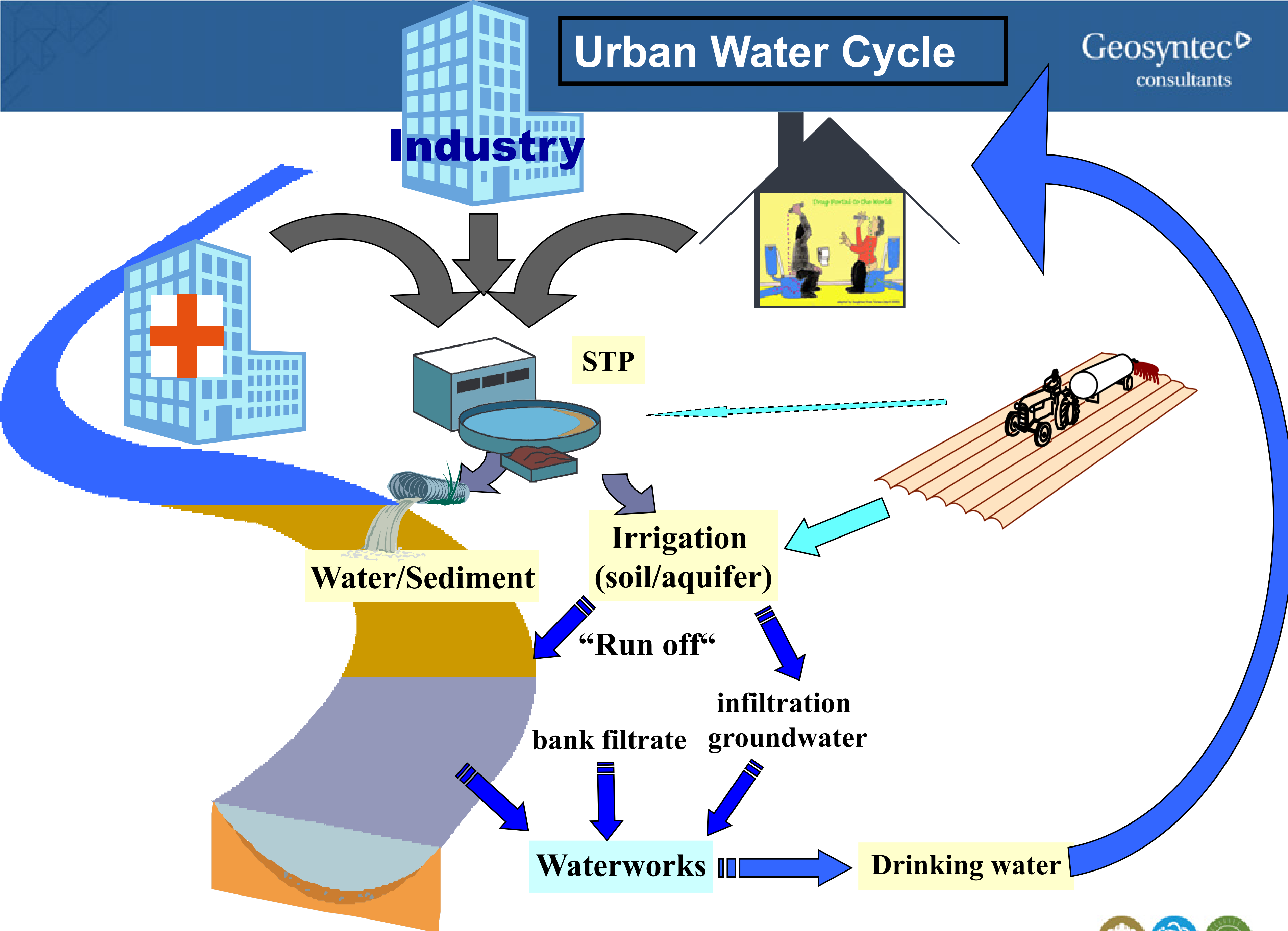


Source: US CDC 2013

Over the last 30 years, no major new types of antibiotics have been developed



Urban Water Cycle



Importance of Physicochemical Properties

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- WWTPs designed to reduce loads of C, N, and P in the influent at concentrations of mg/L
  - API typically are present at concentrations in the ng/L to μg/L
  - Dilution is a factor in influencing degree of treatment
- Some API can be degraded >90% by activated sludge but many are only partially treated
- Physicochemical properties strongly influence both environmental fate and treatment technology selection
  - Polar groups (e.g. –OH, –COOH, – NH_2 etc.) enhance solubility, lessen sorption potential, impart reactivity (acid-base)
  - Degree of saturation of carbon framework
  - Presence of zwitterionic (both "+" and "–") groups

Doxycycline

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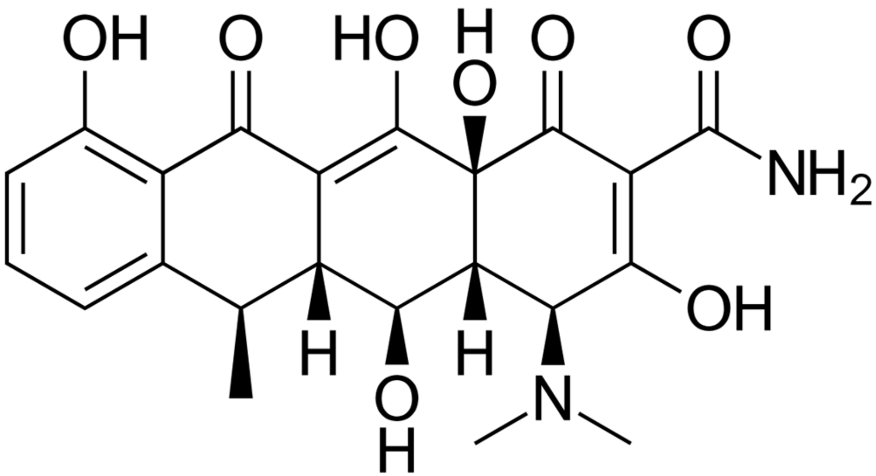

$C_{22}H_{24}N_2O_8$

- Aq. Sol. = 630 mg/L @ T=25°C
- Log K_{ow} = -0.16 @ pH 5 to -1.65 @ pH 9
- K_{oc} soil = 42,246-237,225

- Significant solubility in water
- Progressively more hydrophilicity as pH increases
- No significant acid-base behavior
- Moderate sorption potential
- C:H ratio suggests a highly unsaturated C framework, multiple aromatic and olefinic C=C bonds
- Reasonably well biodegraded by AS
- Frequently found in WWTP effluent and in sludges (~1,000 µg/kg)
- Amine functions, multiple C=C bonds make ozone an excellent treatment option

Fluconazole

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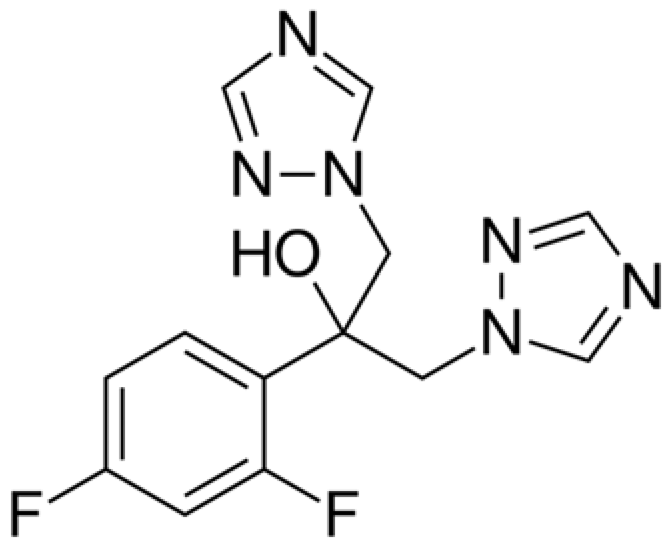

$C_{13}H_{12}F_2N_6O$

- Aq. Sol. = 4,363 mg/L @ T=25°C
- Log K_{ow} = 0.25-0.40

- Substantial aqueous solubility
- Relatively low sorption potential
- C:H ratio suggests a relatively saturated C framework, 1 aromatic ring & 2 azole groups
- A Chinese study of azole antifungals indicated pass through at the WWTP with little biodegradation or sorption to sludge
- Aromatic ring and fluorines will promote sorption & deactivate reactivity of ring
- Aromatic C=C bonds and amino functionality of azoles are good targets for ozone

Known/Unknown Losses to Water Vary

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Processes

1. API* - Organic Synthesis
2. API - Fermentation
3. DP** - Oral Solid Dosage
4. DP - Liquid Formulation
5. Type of Equipment Cleaning

Clean in Place (CIP) System

* API synthesis – 50 to 100%

** Drug Product (DP) – 10-50% for solids, dry wiping/vacuum cleaning
closer to 100% for liquids, liquid cleaning

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Collect Wastewater at Point of Generation (POG)

- Collect 1st & 2nd equipment cleaning rinses before CIP
- Treatment (e.g., alkaline treatment, advanced oxidation)
- Zero liquid discharge – Evaporation Technology
- Off-site disposal (e.g., incineration)

Emphasize Dry Cleaning Practices

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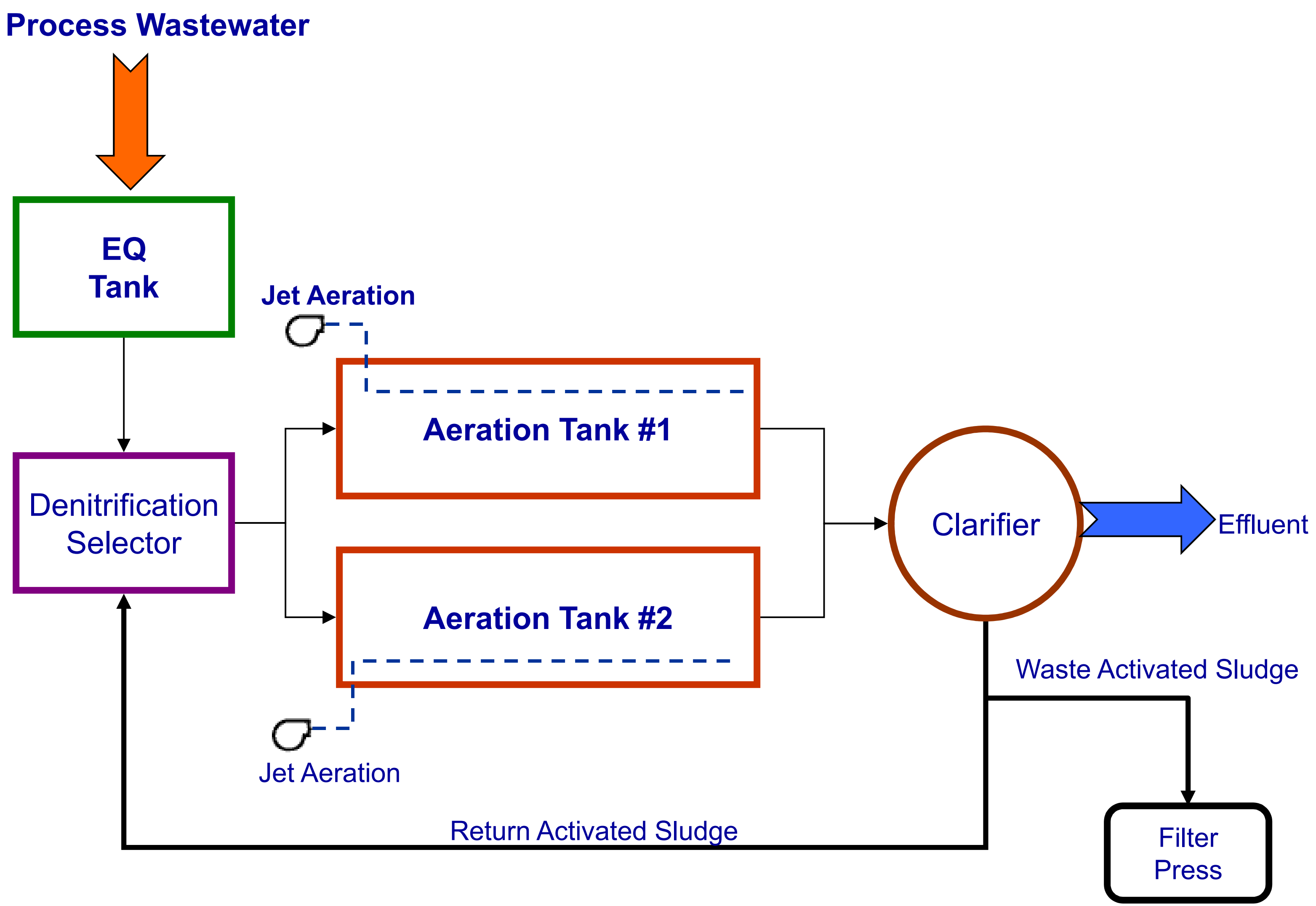
- Minimize the use of liquid equipment cleaning
- Maximize the use of dry cleaning/vacuuming

API and excipient powder everywhere!

Removing residual API from filling reservoir of tablet press

Activated Sludge



Membrane Bioreactor Process

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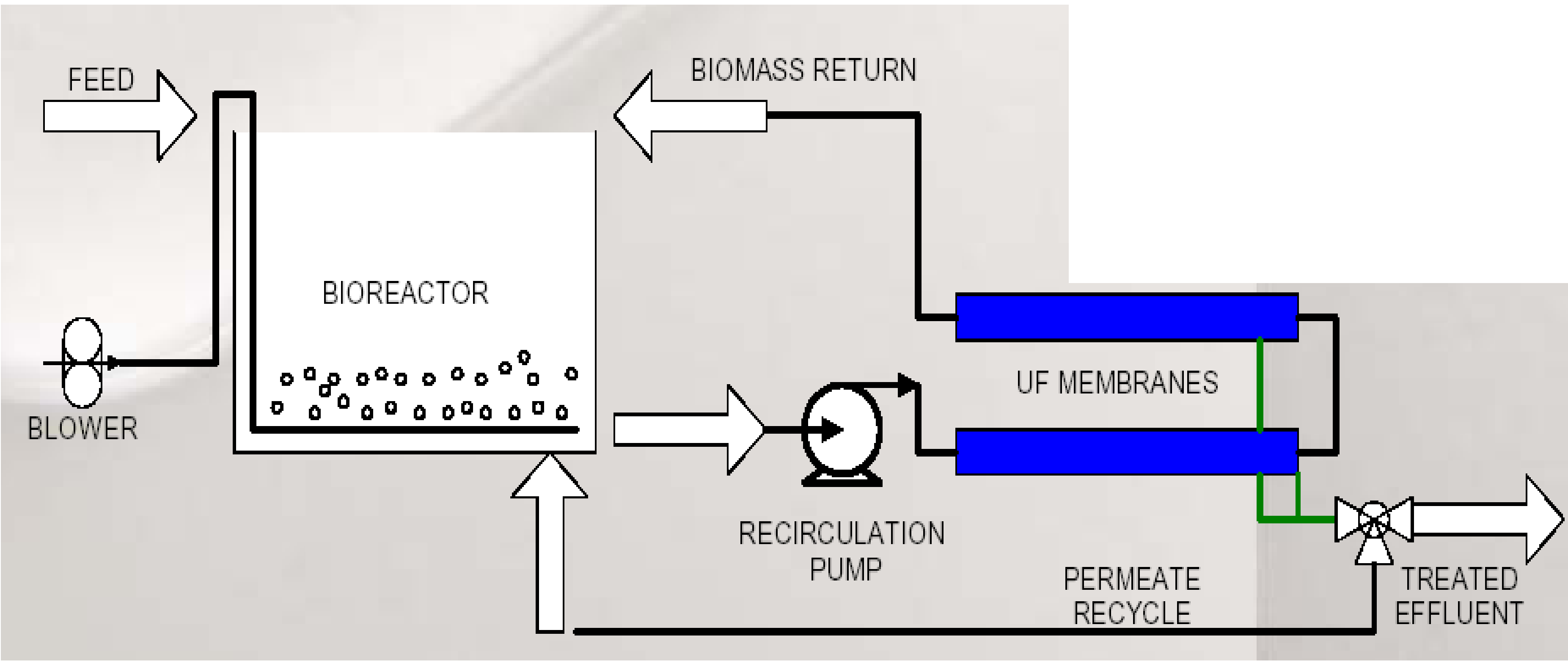

Case Study: Biological Treatment Mass Balance

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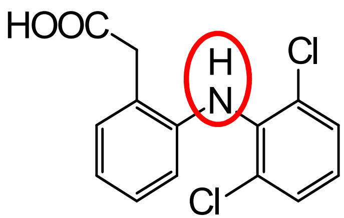
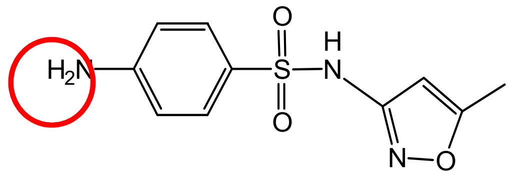
	Plant 1	Plant 2
Influent API (ug/l)	32.6	13
Effluent API (ug/l)	11	0.1
Sludge API (ug/l)	2	0.8
% Effluent	34	< 1
% Adsorbed to Sludge	< 1	< 1
% Volatilized (assumption)	0	0
% Biodegraded	66	99
Sludge Age (days)	15	29
Aeration Basin Temperature (˚C)	26	30

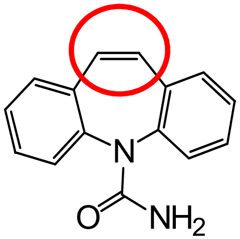
Ozone Treatment



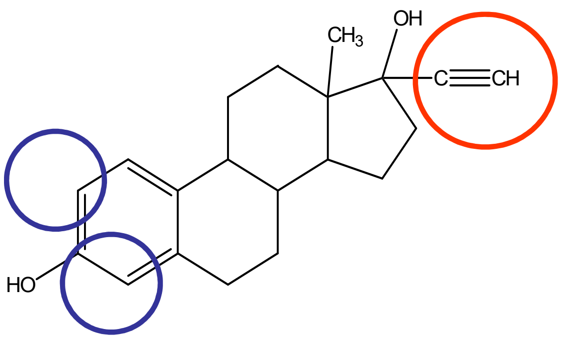
Diclofenac



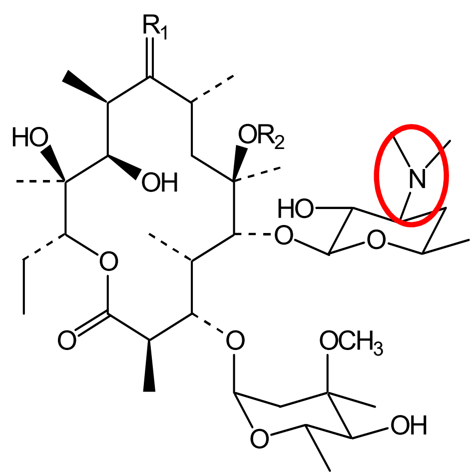
Sulfamethoxazole



Carbamazepine



17 α-Ethinylestradiol



Roxithromycin

Huber et al., 2003, Env.Sci.Technol.

Case Study: Chemical Oxidation Technology Evaluation

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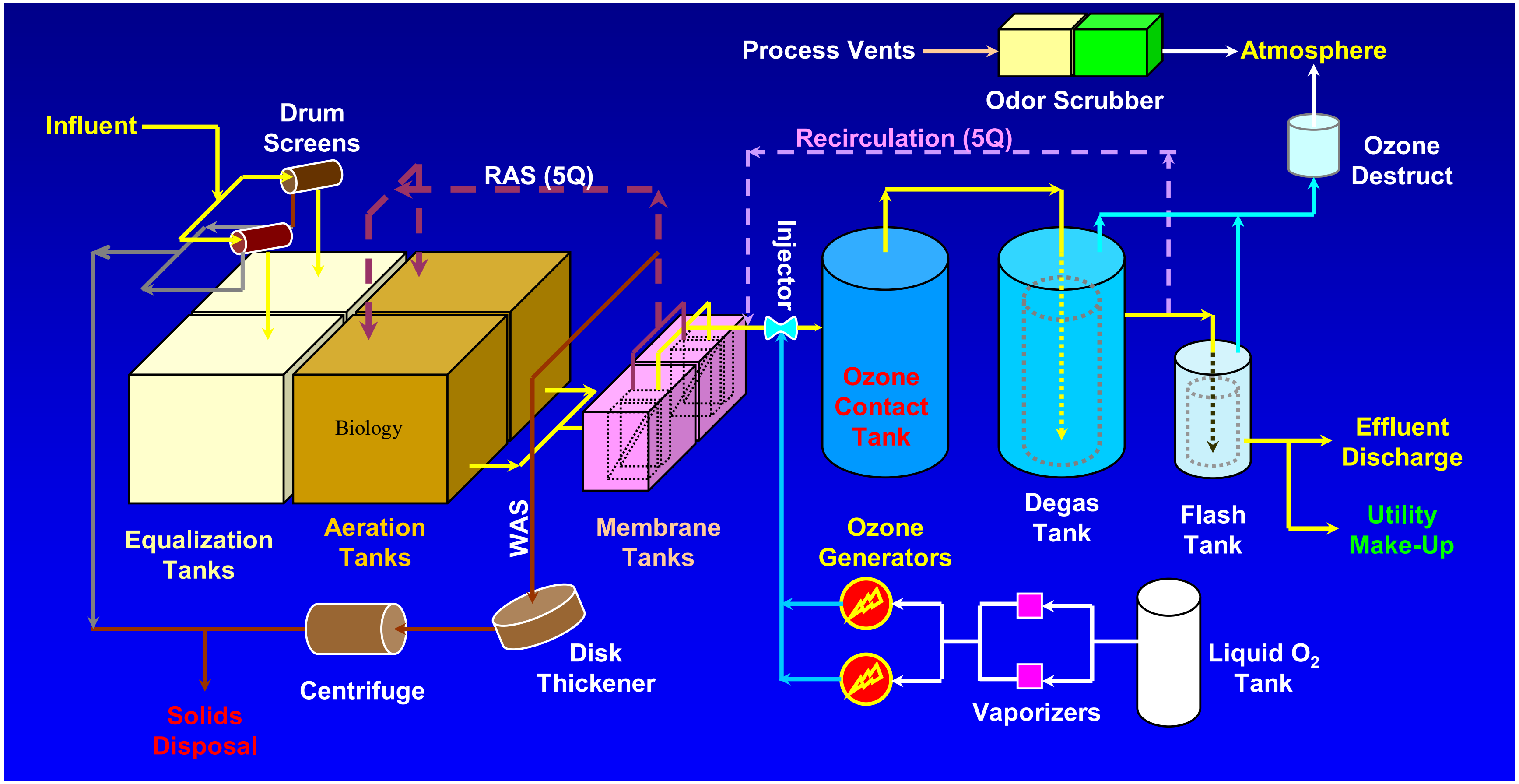
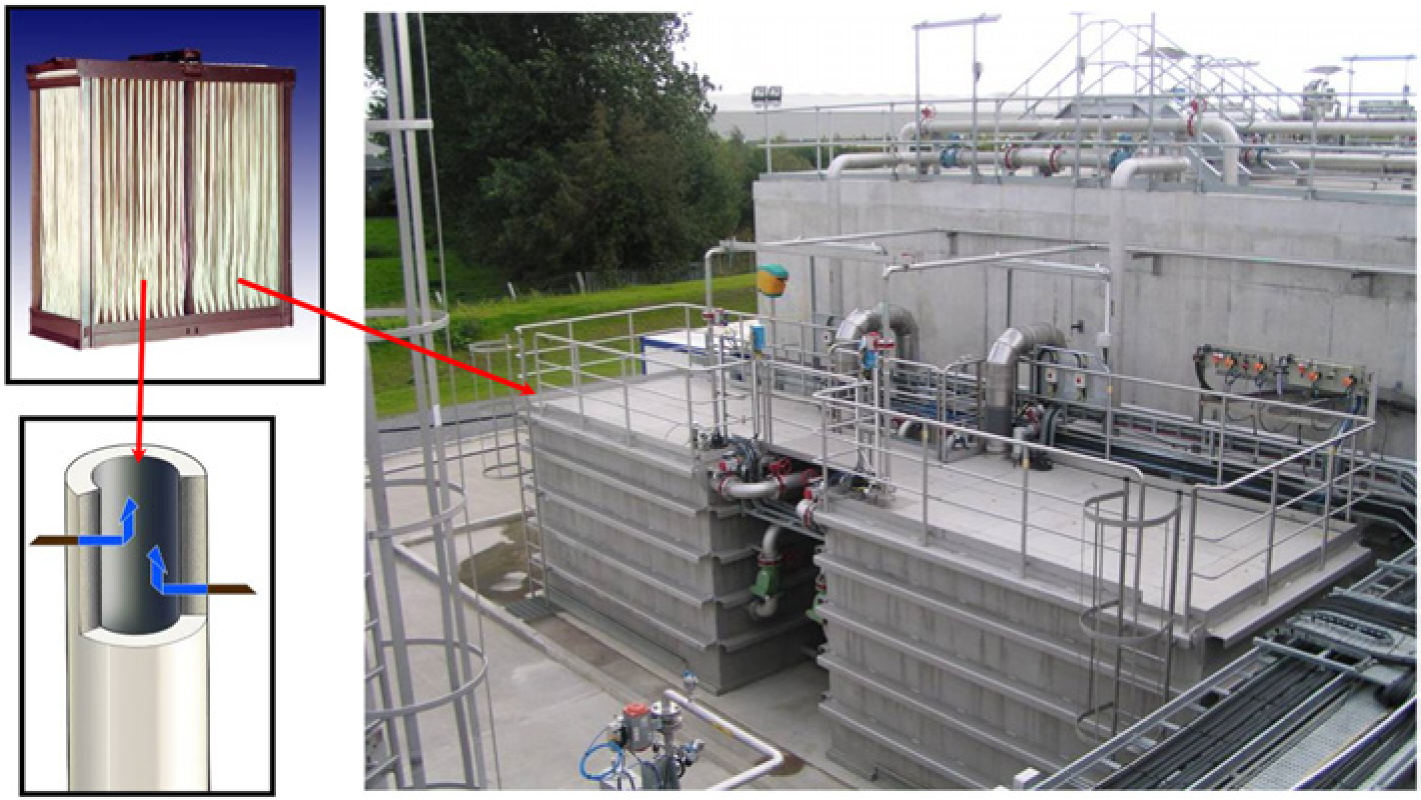
Run Number	Treatment Process	Compound Reduction	Toxicity Reduction
1	UV, hydrogen peroxide	99.5%	58%
2	Catalyzed UV, hydrogen peroxide	99.8%	88.2%
3	UV, ozone	99.4%	99.1%
4	UV, ozone, hydrogen peroxide	99.5%	95%

- Hormone Replacement Therapy (HRT):
  - Medroxy Progesterone Acetate (MPA),Trimegestone,17-α-estradiol,17-β-estradiol,17-α-dihydroequilin and Estrone
- Oral Contraceptives (OC):
  - 17-α-ethinyl estradiol, Norgestrel, Gestodene, Estriol, Medrogestone and Estradiol Valerate
- Tranquilizers:
  - Oxazepam, Lorazepam and Lormatazepam

Case Study: Process Flow Diagram



Bioreactor and Membrane Tanks



2 GE/Zenon Z-500 C cassettes (0.04/0.1 micron pore size) with filtration area of 2,241 m^2 per cassette and header for 1 additional cassette per tank. There are 88 modules per cassette. RAS is 6Q.

Case Study: Yeast Estrogen Screen (YES) Results

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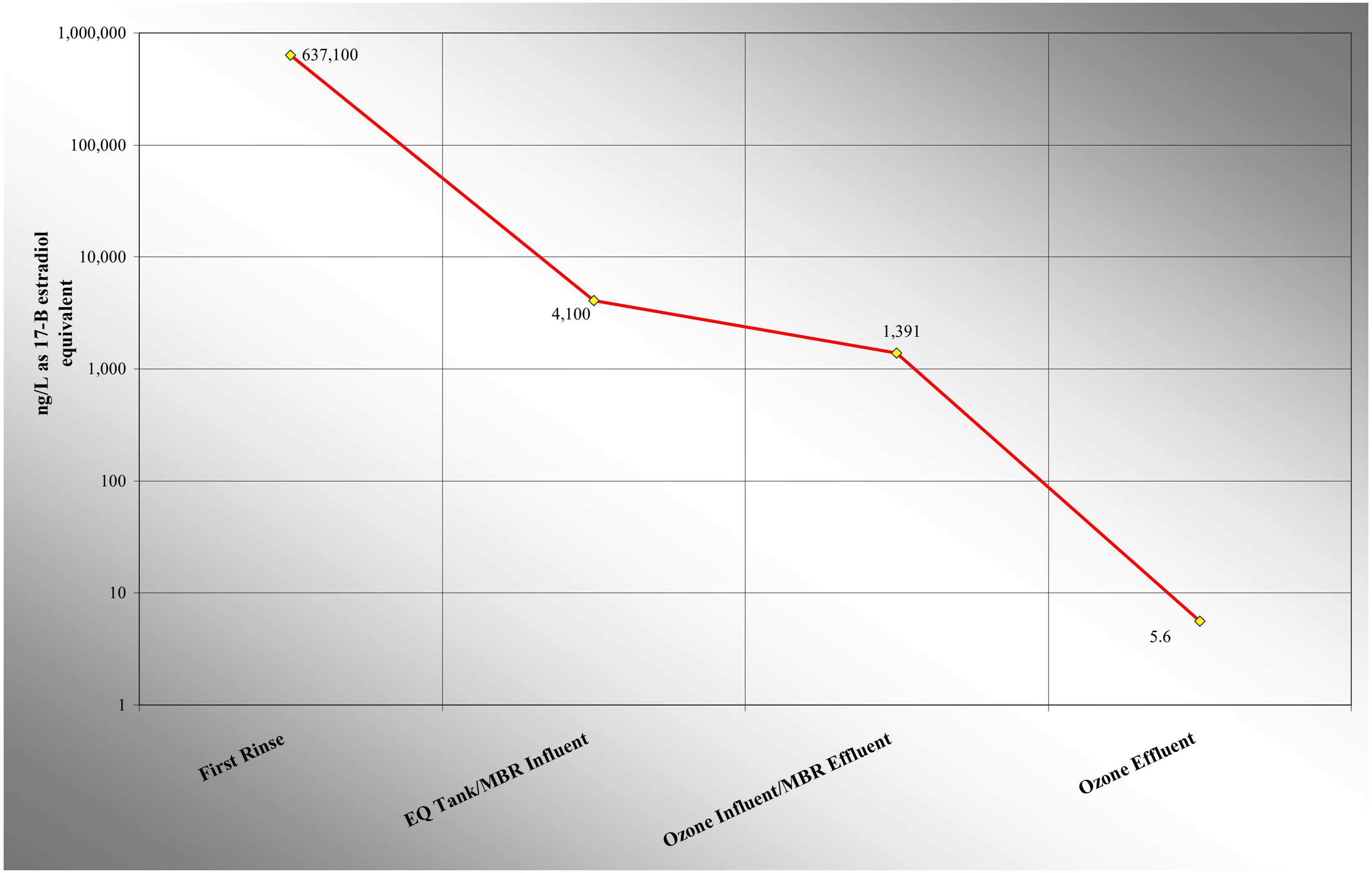
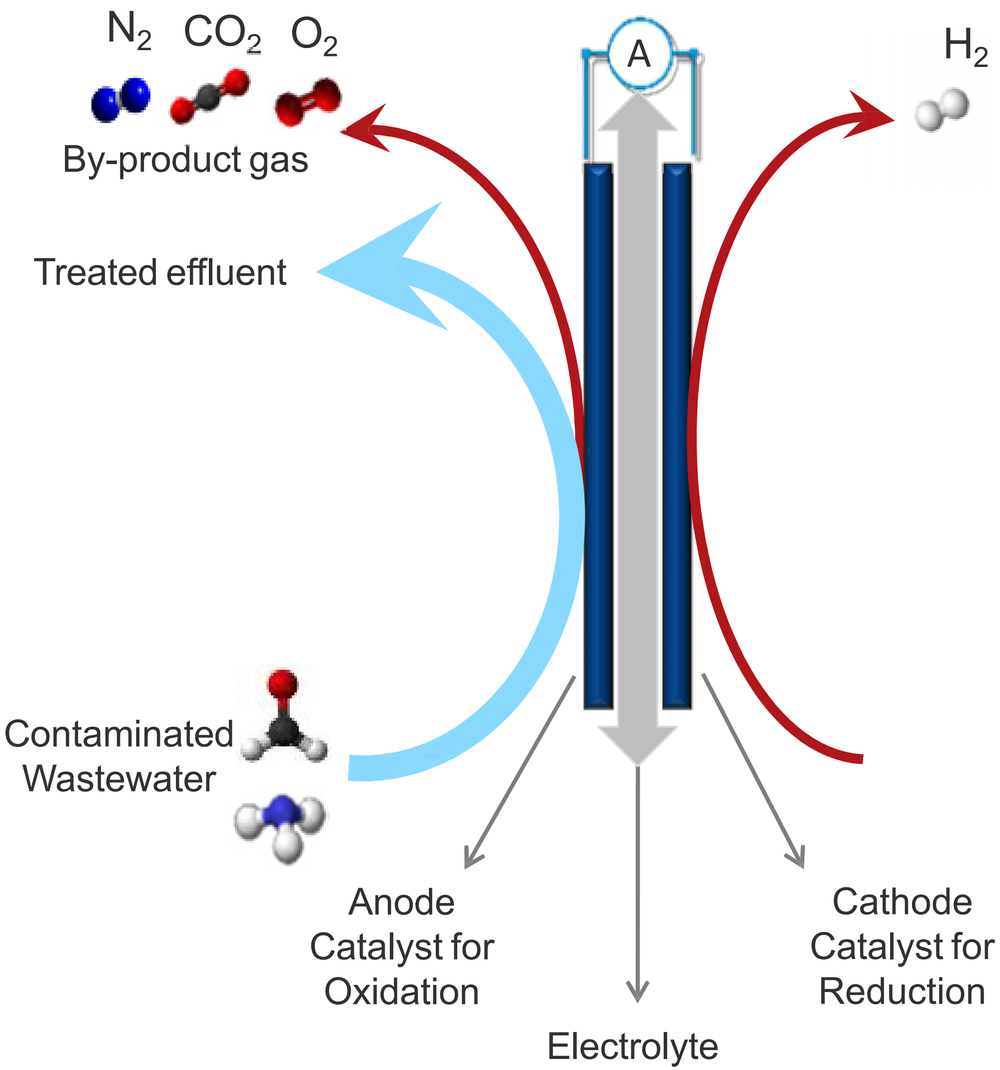
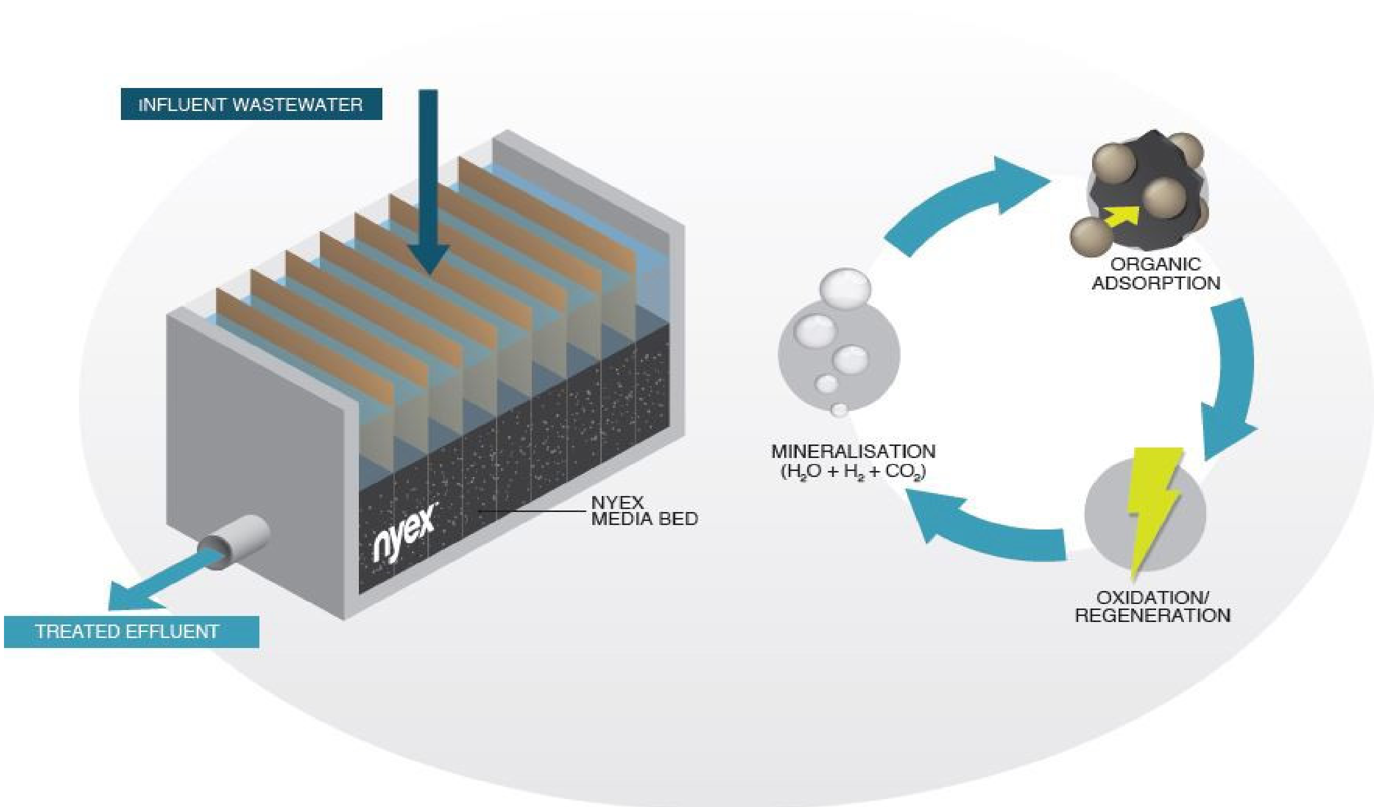


Electrochemical AOP



- Core technology is based on electrochemical process
- Electricity is applied to advanced catalysts
- Catalysts generate oxidants to breakdown organics
- Organics oxidized to gases e.g. N_2, H_2, O_2 , CO_2
- No other waste or by-products are generated
- Technology protected by an extensive patent portfolio

Introduction to the Nyex™ System



Case Study: Antibiotic Removal

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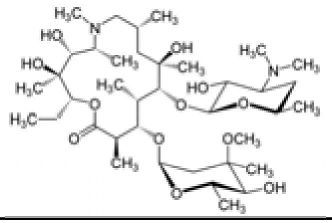
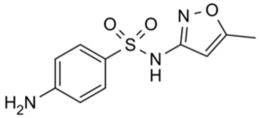
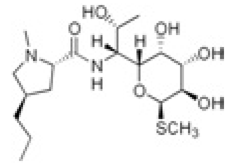
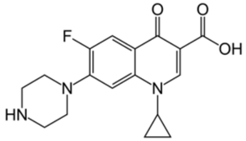
Name	Removal (%)	Structure
Clarithromycin	96.3	
Sulfamethoxazole	99.0	
Lincomycin	Below limit of detec=on	
Ciprofloxacin	78.0	

At Source Treatment Screening Table

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Table 6-1 Comparison of Non-Cost Criteria – At Source Treatment								
At-source treatment		**Screening Criteria**						**Comments**
		Proven Technology	**Ability to Achieve Low Effluent Limits**	**Safety**	**East of operation**	**Total**	**Alternatives Selected or Rejected (preliminary)**	
Alternative 1	Alkaline Chlorination	3	2	3	2	10	Retain	Most proven and has been used by Pfizer on anti-fungals in Europe
Alternative 2	Ozone	3	3	2	2	10	Retain	Proven in Puerto Rico and China and is another very good option. One chemical versus two for alkaline chlorination
Alternative 3	Carbon	1	1	3	3	8	Retain	Effective for some APIs, but transfers to carbon.
Alternative 4	Biological	1	1	3	3	8	Reject	Not used at all for at source only for total wastewater
Alternative 5	Physical Chemical	1	1	2	2	6	Reject	It not a destructive technology, transfers APIs to sludge
Alternative 6	Fenton's Chemistry	2	1	2	2	7	Retain	Proven chemical oxidation technology that can be used to create hydroxyl radicals that destroy APIs
Alternative 7	UV Peroxide	2	2	2	2	8	Reject	Has been used instead of ozone but is not as commonly selected. Requires cleaning and maintenance of UV lamps
Alternative 8	UV Ozone	3	3	2	2	10	Reject	More complicated than ozone by itself
Alternative 9	Electrochemical AOP	1	1	1	1	4	Reject	No testing done on pharmaceutical wastewater

Types of PFAS: Where do PFOA & PFOS fit?

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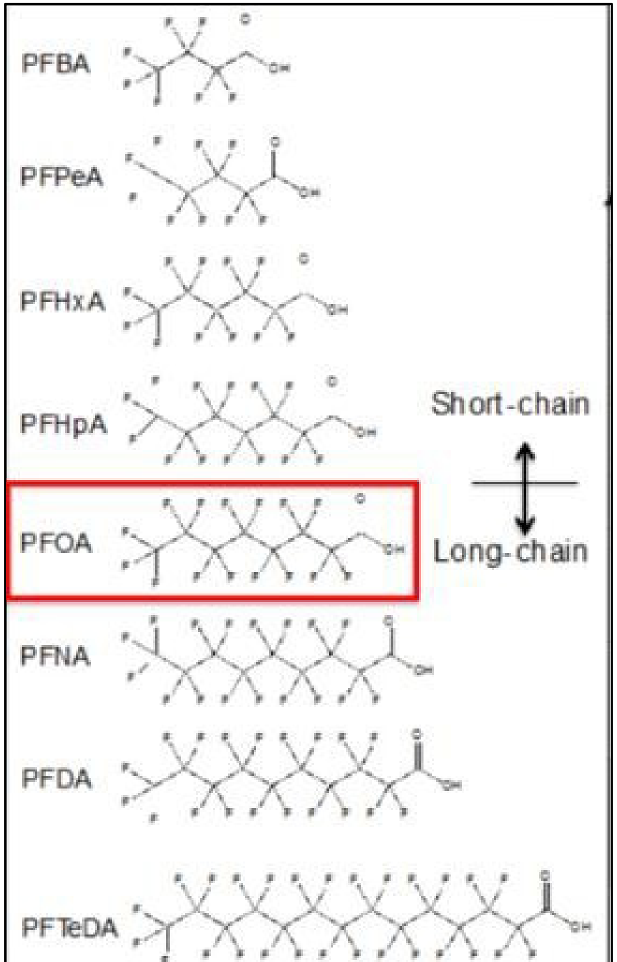
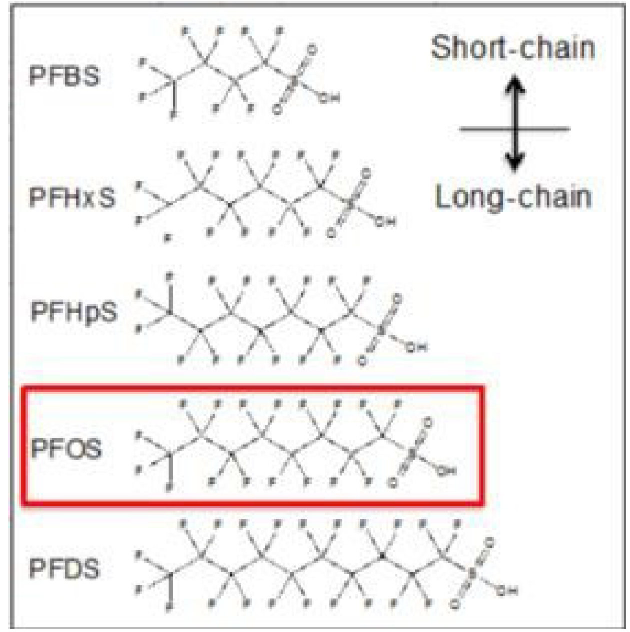
Carboxylic Acids



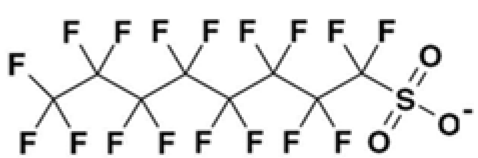
Sulfonic Acids

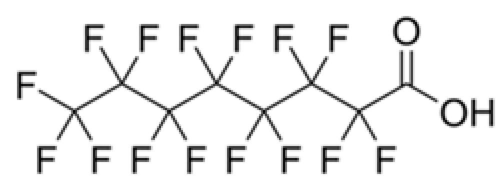


And many more

Treatment Challenges

- PFAS have unique properties
  - Hydrophobic and oleophobic
  - Persistent, bioaccumulative and toxic
  - Moderate solubility – can be transported long distances
- Chemically and biologically stable
  - Resistant to typical environmental degradation processes
  - C-F bond is shortest and strongest in nature
- Treatment approaches challenging and costly





PFAS Removal Solutions

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Granular Activated Carbon

- Named Best Available Technology by EPA for organic contaminant removal
- Removes other organic contaminants
- Reactivation removes liability
- Minimal maintenance

Effective Products:

AquaCarb® CX Carbon

UltraCarb® 1240AW Carbon

UltraCarb® 1240LD Carbon

Single Pass Ion Exchange

- Lower EBCT / Higher flowrate
- Small footprint
- No chemicals or liquid waste
- Spent resin can be incinerated, destroying the contaminants (PFAS)
- Minimal maintenance

Effective Products:

PSR2 Plus
APR-2

Membranes

- Highly effective
- Removes dissolved solids

Effective Products:

Vantage® Product Line

evoqua WATER TECHNOLOGIES

Ion Exchange (IX)

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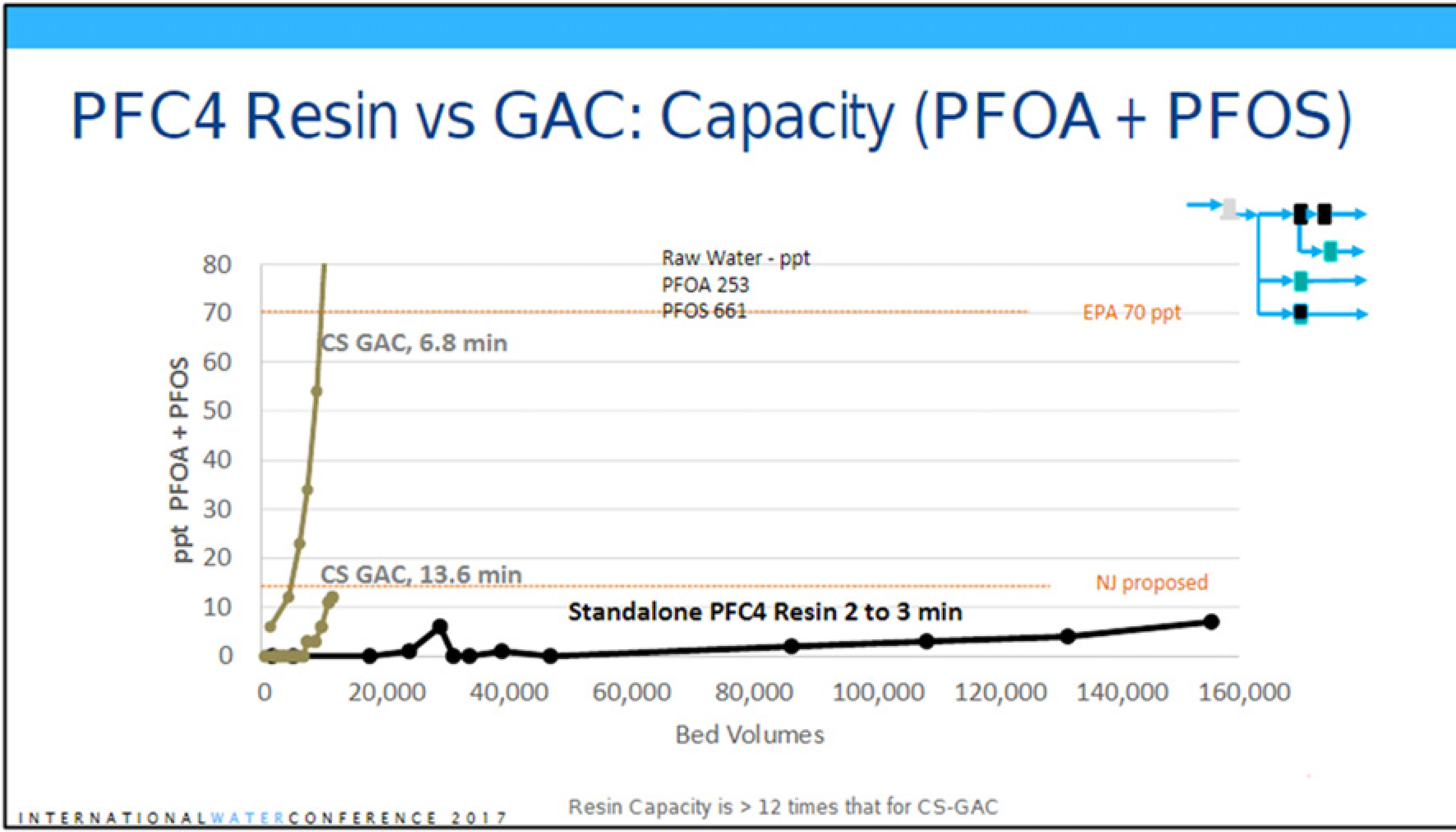

Boodoo, Francis & Kennedy, Sean & Campos, Jonathan. (2017). REMOVAL OF PFOA, PFOS AND OTHER PFAS SUBSTANCES USING ION EXCHANGE.

Summary

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- Biological Treatment & Advanced Oxidation Process (AOP) are proven technologies for APIs
- At-Source Treatment is the best
- Estrogenicty & API removal of greater than 99.9% have been achieved in full scale treatment
- Carbon and Ion Exchange are best for PFOS/PFOA
- Treatability studies & process modeling tools are very helpful to develop design criteria & fate assessments

Thank You!

Jcleary@Geosyntec.com