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

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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?

• Active pharmaceutical Ingredients (API) are the bioactive chemical agents in our medicines
  o 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
  o Increasingly are high MW biological products
  o Used to be primarily “small molecules” from multi-step chemical synthesis
APIs in the Environment

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

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

The first clue that your new chemical might be an endocrine disruptor.
Antimicrobial resistance (AMR)

• AMR is the resistance of a microorganism to an AI which was originally effective for treatment

• 3 major causes:
  o Over-prescription in humans, inappropriate use (e.g. non-bacterial infections), & failure to complete treatment courses
  o Routine, non-therapeutic use in livestock
  o Releases of AI into wastewater from human/animal metabolism, pharma production discharges, improper disposal

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

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
Water/Sediment

Industry

STP

Urban Water Cycle

Irrigation
(soil/aquifer)

“Run off”

infiltration

bank filtrate

groundwater

Waterworks

Drinking water
Importance of Physicochemical Properties

• WWTPs designed to reduce loads of C, N, and P in the influent at concentrations of mg/L
  o API typically are present at concentrations in the ng/L to µg/L
  o 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
  o Polar groups (e.g. –OH, –COOH, –NH₂ etc.) enhance solubility, lessen sorption potential, impart reactivity (acid-base)
  o Degree of saturation of carbon framework
  o Presence of zwitterionic (both “+” and “−”) groups
Doxycycline

- 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

\[
\text{C}_{22}\text{H}_{24}\text{N}_2\text{O}_8
\]

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

- 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

\[ \text{C}_{13}\text{H}_{12}\text{F}_2\text{N}_6\text{O} \]

- Aq. Sol. = 4,363 mg/L @ T=25°C
- Log \( K_{ow} \) = 0.25-0.40
Known/Unknown Losses to Water Vary

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

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

Clean in Place (CIP) System
Collect Wastewater and Treat/Dispose

Collect Wastewater at Point of Generation (POG)

- Collect 1\textsuperscript{st} & 2\textsuperscript{nd} 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

- 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

Process Wastewater

- EQ Tank
  - Denitrification Selector
  - Aeration Tank #1
  - Aeration Tank #2
  - Clarifier

- Jet Aeration
- Return Activated Sludge
- Waste Activated Sludge

- Filter Press
- Effluent
<table>
<thead>
<tr>
<th></th>
<th>Plant 1</th>
<th>Plant 2</th>
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<tbody>
<tr>
<td>Influent API (ug/l)</td>
<td>32.6</td>
<td>13</td>
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<tr>
<td>Effluent API (ug/l)</td>
<td>11</td>
<td>0.1</td>
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<tr>
<td>Sludge API (ug/l)</td>
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<tr>
<td>% Effluent</td>
<td>34</td>
<td>&lt; 1</td>
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<tr>
<td>% Adsorbed to Sludge</td>
<td>&lt; 1</td>
<td>&lt; 1</td>
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<tr>
<td>% Volatilized (assumption)</td>
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<td>0</td>
</tr>
<tr>
<td>% Biodegraded</td>
<td>66</td>
<td>99</td>
</tr>
<tr>
<td>Sludge Age (days)</td>
<td>15</td>
<td>29</td>
</tr>
<tr>
<td>Aeration Basin Temperature (°C)</td>
<td>26</td>
<td>30</td>
</tr>
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</table>
Ozone Treatment

Diclofenac

Sulfamethoxazole

Carbamazepine

17 α-Ethinylestradiol

Roxithromycin

Huber et al., 2003, Env.Sci.Technol.
### Case Study: Chemical Oxidation Technology Evaluation

<table>
<thead>
<tr>
<th>Run Number</th>
<th>Treatment Process</th>
<th>Compound Reduction</th>
<th>Toxicity Reduction</th>
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<tbody>
<tr>
<td>1</td>
<td>UV, hydrogen peroxide</td>
<td>99.5%</td>
<td>58%</td>
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<tr>
<td>2</td>
<td>Catalyzed UV, hydrogen peroxide</td>
<td>99.8%</td>
<td>88.2%</td>
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<tr>
<td>3</td>
<td>UV, ozone</td>
<td>99.4%</td>
<td>99.1%</td>
</tr>
<tr>
<td>4</td>
<td>UV, ozone, hydrogen peroxide</td>
<td>99.5%</td>
<td>95%</td>
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</tbody>
</table>
Case Study
Pharmaceutical Project in Ireland

• **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
2 GE/Zenon Z-500 C cassettes (0.04/0.1 micron pore size) with filtration area of 2,241 m² 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

- **First Rinse**: 637,100 ng/L as 17-B estradiol equivalent
- **EQ Tank/MBR Influent**: 4,100 ng/L as 17-B estradiol equivalent
- **Ozone Influent/MBR Effluent**: 1,391 ng/L as 17-B estradiol equivalent
- **Ozone Effluent**: 5.6 ng/L as 17-B estradiol equivalent
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. N₂, H₂, O₂, CO₂
- No other waste or by-products are generated
- Technology protected by an extensive patent portfolio
Introduction to the Nyex™ System
## Case Study: Antibiotic Removal

<table>
<thead>
<tr>
<th>Name</th>
<th>Removal (%)</th>
<th>Structure</th>
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<tbody>
<tr>
<td>Clarithromycin</td>
<td>96.3</td>
<td><img src="image1" alt="Structure" /></td>
</tr>
<tr>
<td>Sulfamethoxazole</td>
<td>99.0</td>
<td><img src="image2" alt="Structure" /></td>
</tr>
<tr>
<td>Lincomycin</td>
<td>Below limit of detection</td>
<td><img src="image3" alt="Structure" /></td>
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<tr>
<td>Ciprofloxacin</td>
<td>78.0</td>
<td><img src="image4" alt="Structure" /></td>
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<tr>
<td>At-source treatment</td>
<td>Screening Criteria</td>
<td>Alternatives Selected or Rejected (preliminary)</td>
</tr>
<tr>
<td>---------------------</td>
<td>--------------------</td>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>Alternative 1</td>
<td>Alkaline Chlorination</td>
<td>3 2 3 2 10 Retain</td>
</tr>
<tr>
<td>Alternative 2</td>
<td>Ozone</td>
<td>3 3 2 2 10 Retain</td>
</tr>
<tr>
<td>Alternative 3</td>
<td>Carbon</td>
<td>1 1 3 3 8 Retain</td>
</tr>
<tr>
<td>Alternative 4</td>
<td>Biological</td>
<td>1 1 3 3 8 Reject</td>
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<tr>
<td>Alternative 5</td>
<td>Physical Chemical</td>
<td>1 1 2 2 6 Reject</td>
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<tr>
<td>Alternative 6</td>
<td>Fenton’s Chemistry</td>
<td>2 1 2 2 7 Retain</td>
</tr>
<tr>
<td>Alternative 7</td>
<td>UV Peroxide</td>
<td>2 2 2 2 8 Reject</td>
</tr>
<tr>
<td>Alternative 8</td>
<td>UV Ozone</td>
<td>3 3 2 2 10 Reject</td>
</tr>
<tr>
<td>Alternative 9</td>
<td>Electrochemical AOP</td>
<td>1 1 1 1 4 Reject</td>
</tr>
</tbody>
</table>
Types of PFAS: Where do PFOA & PFOS fit?

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

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
Summary

• Biological Treatment & Advanced Oxidation Process (AOP) are proven technologies for APIs
• At-Source Treatment is the best
• Estrogenicity & 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!

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