Agenda

- Project Background
- Treatability Testing
- Biological Bench Testing
- Permitting Pharmaceutical Discharge
Background

Pharmaceutical manufacturer (The Client) was preparing to manufacture a new medication.

Minimal mass of the residual prodrug to be discharged into process wastewater from equipment rinsing.
Existing Pretreatment System

Process wastewater with residual Active Pharmaceutical Ingredients

Base Addition

- Tank 1
  - 10,000 gals
  - Target pH: 10

Acid Addition

- Tank 2
  - 10,000 gals
  - Target pH: 8

Comingled with sanitary and utility wastewater discharged to POTW
Prodrug Hydrolytic Pathway

Prodrug → Byproduct A → Byproduct C

- Byproduct A
- Byproduct B
- Byproduct C
Overall Project Objectives

• Can the Client's existing pretreatment system be used for pretreatment of the prodrug prior to discharging wastewater to the POTW?

• Will the prodrug or degradation byproducts inhibit nitrification or impact the POTW's whole effluent toxicity?
Project Process

1. Develop Analytical Method
2. Develop Testing Protocol
3. Approval from POTW
4. Perform Test
5. Present Results
Treatability Testing Objectives

• Will the Client's existing pretreatment system be capable of treating the new prodrug via hydrolysis?
• What will the concentrations of the prodrug and byproducts leaving the pretreatment system be?
Treatability Testing Protocol

Prodrug Concentration 4.5 mg/L

- pH 7
- pH 8
- pH 9
- pH 10

Sample at 10 time intervals: 15 minutes - 72 hours

Analyze samples for Prodrug and Byproducts
Treatability Testing Results
Treatability Testing Results

- Prodrug degradation proceeds quickly at pH 10,
- Safety factor of 2 over projected Prodrug discharge rates.
- Prodrug and byproducts will continue to degrade in Tank 2 when the pH is reduced to approximately pH 8

<table>
<thead>
<tr>
<th>Flow Condition</th>
<th>Prodrug (mg/L)</th>
<th>Byproduct A (mg/L)</th>
<th>Byproduct B (mg/L)</th>
<th>Byproduct C (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak Instantaneous Flow Rate</td>
<td>0.1</td>
<td>1.2</td>
<td>1.4</td>
<td>0.35</td>
</tr>
<tr>
<td>Average Flow Rate</td>
<td>&lt;0.0761</td>
<td>1.0</td>
<td>1.3</td>
<td>0.75</td>
</tr>
</tbody>
</table>
Biological Bench Testing Objectives

• Will discharge of residual concentrations of the prodrug and its' byproducts inhibit nitrification at the POTW?

• Will discharge of residual concentrations of the prodrug and its' byproducts impact the POTW 's whole effluent toxicity?

• Does removal of the prodrug and its byproducts occur in the POTW?
Biological Testing Conditions

Control Reactors  Condition 1 Reactors  Condition 2 Reactors  Condition 3 Reactors
### Biological Testing Conditions

**Prodrug and Byproduct B Concentrations simulated in POTW WWTP Influent**

<table>
<thead>
<tr>
<th>Test Condition</th>
<th>Prodrug (ug/L)</th>
<th>Byproduct B (ug/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-Peak flow through manufacturer's pretreatment system</td>
<td>1.0</td>
<td>14.4</td>
</tr>
<tr>
<td>2- No pretreatment, Discharge of wastewater directly to sewer</td>
<td>42.6</td>
<td>0.0</td>
</tr>
<tr>
<td>3-Concentrations 2.5x's the laboratory MDL</td>
<td>200</td>
<td>1,000</td>
</tr>
</tbody>
</table>
Impact on nitrification is evaluated by comparing the rate at which Ammonia-Nitrogen was converted to nitrate & nitrite in the control and test condition reactors. (Oxidized Nitrogen Generation Rate)
Biological Bench Testing Results

- Results indicate the Prodrug and Byproduct B at the concentrations tested do not inhibit nitrification.

<table>
<thead>
<tr>
<th>Approximate Hour Range</th>
<th>Mean Oxidized Nitrogen Generation Rate (µg/h/mg biomass)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
</tr>
<tr>
<td>0 to 7.1 hours</td>
<td>0.96</td>
</tr>
<tr>
<td>18.6 to 29.5 hours</td>
<td>0.87</td>
</tr>
</tbody>
</table>

- Calculations were normalized to mass of biomass.
- **Condition 1** and **Condition 2** were not statistically different than the control reactors.
Whole Effluent Toxicity

• **Condition 1** and **Condition 2** passed for both *Ceriodaphnia dubia* (water flea) and the *Pimephales promelas* (fathead minnow)
• The water flea WET test for **Condition 3** failed based on reproduction
Percent Removal of Prodrug and Byproduct B

- Percent removal could not be determined
- Prodrug adsorbed to solids
- Matrix interferences
Conclusions and Permitting

The Client’s existing pretreatment system successfully degrades the prodrug.

The Prodrug and Byproduct B do not inhibit nitrification at the POTW at the concentrations tested.

Treated effluent at the concentrations tested does not impact WET for conditions that represent actual potential discharge conditions.

A permit limit of 435 grams per day was issued based on 60% of the Maximum Allowable Headworks Loading.
Lessons Learned

Manufacturer desired to discharge water that could be safely managed by the POTW and protect the environment.

New discharge was a concern for the POTW. POTW did not want to negatively impact the WWTP performance or the environment.

With a team of consultant, industry and POTW working collaboratively, testing was performed, and a permit was issued in approximately 13 months.