PSCI PHARMACEUTICAL SUPPLY CHAIN INITIATIVE

Building responsible supply chains

Introduction to sampling and analysis of APIs in wastewater

JONATHAN STANWAY

BIOTECHNOLOGY & ENVIRONMENTAL DOWNSTREAM MANAGER

GLAXOSMITHKLINE

Speaker Bio

Jon Stanway

BEng (Chemical Engineering) MSc (Biochemical Engineering)

CEng Chartered Engineer of the Institute of Chemical Engineering (IChemE)

14 years at GSK across API development and manufacture.

BIOTECHNOLOGY & ENVIRONMENTAL DOWNSTREAM MANAGER, GSK

- Pharmaceuticals in the Environment expert
  - Manufacturing controls and wastewater treatment
  - AMR Industry Alliance Manufacturing Roadmap risk assessment & compliance
  - Mass Balance calculation and analytical characterisation.
- Small molecule biotechnology industrialization.

Introduction to sampling and analysis of APIs in wastewater

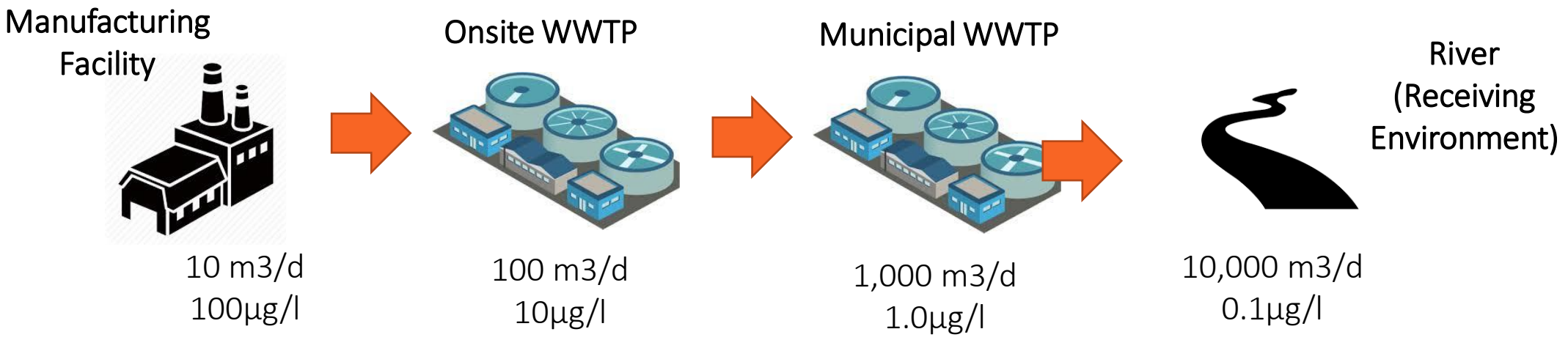
- Why Sample?
- Where to Sample?
- When to Sample?
- How to Sample?
- How to Analyse?

Why Sample Wastewater?

- Assessment of compliance to regulatory or industry discharge limits can be done by mass balance calculation accounting for **worst-case** assumptions for the following;
  - **Losses of API** to wastewater from manufacturing operations e.g. from process waste and cleaning streams.
  - **Removal efficiency** in wastewater pre-treatment and treatment operations.
  - Onsite and offsite **dilution** e.g. accounting for dilution in downstream municipal wastewater treatment and in the location of environmental discharge.
- Refinement with analytical data may be required in some circumstances;
  1. Where the mass balance calculation indicates discharge above or close to the limit.
  2. Where there is limited data to establish worst-case assumptions.
  3. To characterise actual API removal efficiency in wastewater treatment.
  4. For purposes of routine monitoring of performance.

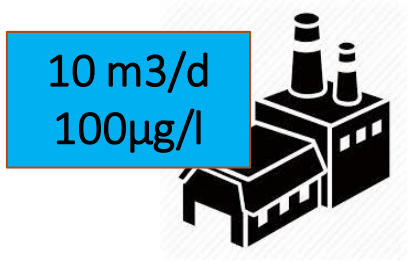
Where to Sample?

- Location of wastewater sampling dependent on several key factors;
  1. Primary rationale for sampling – what's the most important information required?
  2. Constraints of analytical methods.
  3. Access to sampling locations.
  4. Likelihood of noise or interference from other factors.
- Example: **Site wants to determine compliance to a PNEC limit of 0.10µg/l.**

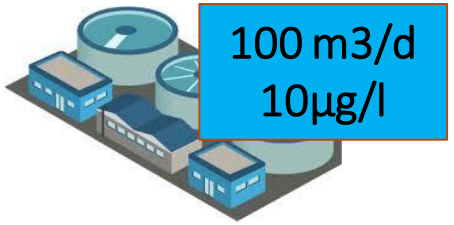


Where to Sample?

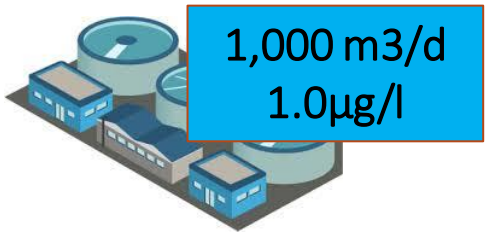
Manufacturing Facility



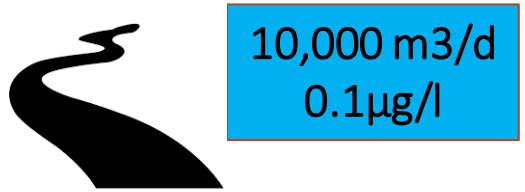
Onsite WWTP



Municipal WWTP



River (Receiving Environment)



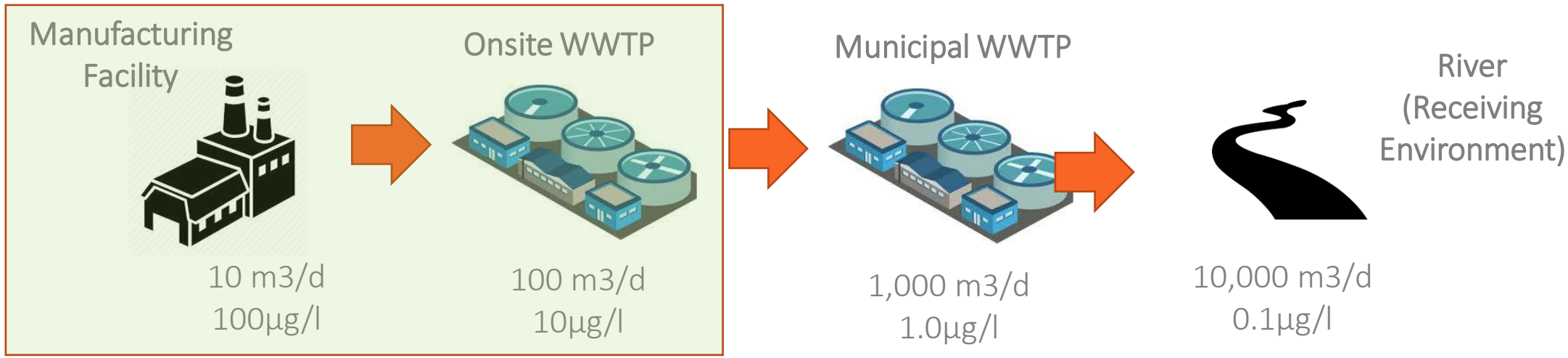
Easy Access for Sampling → Difficult to Access for Sampling

Analysis by HPLC → Analysis by LCMSMS → Difficult to Analyse

No Offsite Noise → Liable to Noise/Interference from Offsite (e.g. other industry, domestic/hospital use)

Doesn't account for removal in WWTP → Removal in WWTP accounted for

Where to Sample?



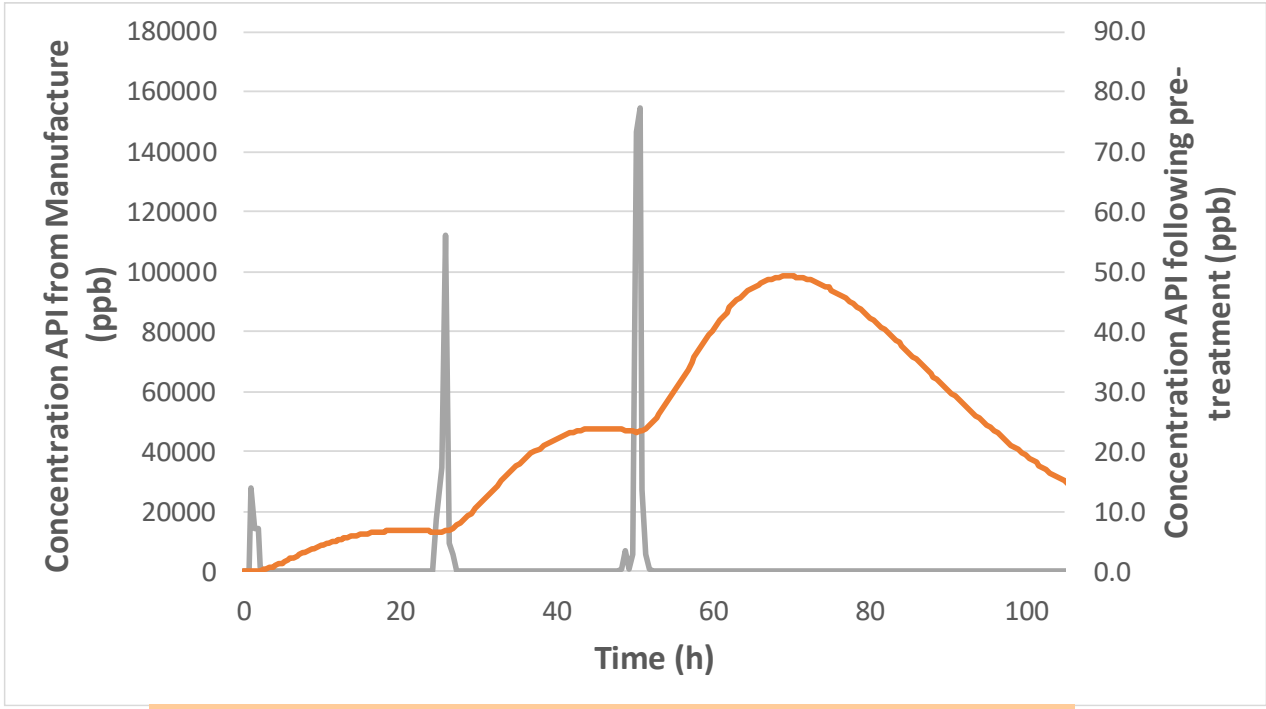
- Optimal sampling programme likely to encompass more than one sample location.
- E.g. sampling of WWTP influent and effluent provides confirmation of concentration discharged from both the manufacturing operation and the site and allows actual API removal efficiency to be determined.
- Other factors such as wastewater pH and presence of biological contaminants (e.g. from WWTP biological treatment) may also impact considerations on location due to sample stability.

What about Zero-Liquid Discharge?

- True ZLD (full recycle) or No offsite discharge?
- Sampling may not be required where treated wastewater is fully recycled e.g. to utilities without any environmental discharge.
  - Sampling of wastewater may still be beneficial to inform antibiotic in the environment risk assessment of e.g. WWTP biosolid.
- For sites discharging treated wastewater for onsite irrigation, understanding API discharge concentration is of particular importance;
  - No dilution/buffering effect from downstream flow.
  - Potential accumulation effects in soil.
- Common approach to apply surface water PNEC limits for soil discharge where soil specific PNEC limits are not available.

When to Sample?

- PNEC concentration limits generally defined for an acute worst-case 24-hour duration.
- Sampling programme design should ensure maximum concentration at the sampling location is measured, accounting for;
    1. **Peak discharge** from manufacturing operations - typically from discrete operations e.g. fermentation harvest, dryer water rinsing.
    2. **Cumulative effects** from overlap in manufacture of an API/DP or multiple formulations containing the same API.
    3. **Residence time** and buffering effects in wastewater collection and treatment.



Delay in peak concentration from manufacturing to WWTP discharge due to residence time in treatment operations.

How to Sample?

- 2 main types of sampling methodology;
  - **Composite sampling:** collected over time through continuous sampling or mixing of discrete samples. Determines average concentration over e.g. a 24 hour period.
  - **Grab sampling:** determines concentration at a specific point of time.
- Use of composite sampling may reduce the number of samples for analysis to assess compliance against a PNEC limit.
- Ensure samples are representative:
  - Taken from centre of the flow channel.
  - Sufficient volume for duplicate analysis.
  - Wearing new gloves for each location.
  - Leakproof containers – and keeping highly contaminated samples segregated from clean samples
  - Using disposable or verified clean equipment for sampling.

Typical composite sample installation

Typical grab sample methodology

How to Analyse?

- Sample transport/storage conditions (time, temperature, exposure to light) should minimise risk of degradation of the API. Ensure couriers can deliver the required conditions.
- Samples with biological contamination e.g. from biological treatment or at high or low pH are liable to degrade APIs resulting in inaccurate results.
- Analysis should be conducted by an accredited laboratory with appropriate technology.
- **Consider risk of signal suppression and limit of detection (LOD).**
- Determine LOD through method development using an equivalent matrix to the wastewater or, ideally, established for each sample through determination of spike recovery.
- Where analysis returns “none detected” or “below the limit of quantification” results, the limit of detection / quantification should be used as a worst-case in mass balance calculations rather than “0”.
- Consider methods utilising sample preparation e.g. US EPA 1694.

LC-MS/MS QTOF for low limit of detection (<ppb) analysis.

CONTACT

pscinitiative.org

info@pscinitiative.org

Annabel Buchan:
+44 (0) 7794 557524

PSCI

@PSCInitiative

For more information about the PSCI please contact:

PSCI Secretariat
Carnstone Partners Ltd
Durham House
Durham House Street
London
WC2N 6HG

info@pscinitiative.org

+44 (0) 7794 557 524

About the Secretariat
Carnstone Partners Ltd is an independent management consultancy, specialising in corporate responsibility and sustainability, with a long track record in running industry groups.

carnstone
partners ltd