Licensee Name: AbbVie Ireland NL B.V. **Reg No: P0643-03**

Description of Change

AbbVie Sligo plan to install a waste water treatment system in Q3/Q4 2019 to treat waste water from its Synthroid and Drug Product manufacturing facilities. The treatment technology is UV-Oxidation in combination with hydrogen peroxide provided by a German company Enviolet. The system will be designed to treat waste water from the Synthroid and Drug Product facilities that are currently being shipped off site via road tanker for incineration. This technology provided by Enviolet is already EPA approved and in operation in three other facilities in Ireland, ENVA (Shannon, 2 units), Vistakon (Limerick) and Pfizer (Cork).

The proposed installation at AbbVie Sligo; is already in operation in approximately 120 similar facilities throughout the EU, US and Asia.

Overview of Waste streams

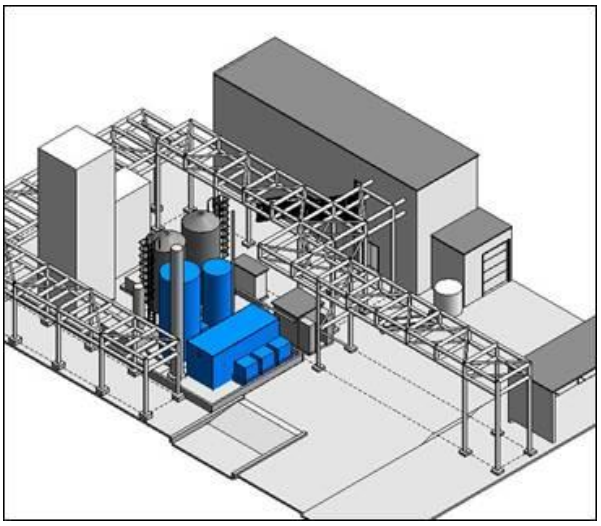
Synthroid active pharmaceutical ingredient is a hormone, Levothyroxine Sodium used to treat hypothyroidism. The stream consists of mostly water, sugar, stearates, povidone, and levothyroxine sodium hormone. Manufacturing of Synthroid is projected to generate approximately 60,000l of waste water per week.

Elagolix is a Gonadotropin Releasing Hormone (GnRH) antagonist for the treatment of endometriosis (management of pain). The waste stream consists of mostly water, sugar, starch, povidone, sodium carbonate monohydrate, stearates and the Elagolix API. Manufacturing of Elagolix depends on supply chain demand and therefore the waste water generation will very. However, in 2020 it is projected that Elagolix production will produce approximately 60,000lt of waste water per week.

In 2018, AbbVie Sligo tankered approximately 4,304,820 litres of waste water offsite for incineration. This accounted for 75% of the total waste produced on site in 2018. The introduction of this waste water treatment system has been identified as a key sustainability project for AbbVie in 2019. The project will ensure AbbVie meet its corporate 2020 & 2025 targets for reduction of waste. It will also significantly reduce its CO2 footprint produced from road tankers usage by a reduction of more than 90%.

Overview of System

The waste water treatment system will be located in the Tank Farm area of the site nearby existing manufacturing waste water tanks. It will consist of a pretreatment storage tank, treatment tank, treatment skid and chemical IBCs required as part of the process.



Feasibility Study of Wastewater treatment technology

A feasibility study was completed by Enviolet and AbbVie in 2018 on representative waste water samples of Synthroid and Elagolix. Samples were taken on site and shipped to Enviolet in Germany where they were treated in the Enviolet lab scale plant. The lab scale plant is the same design as a full scale plant and therefore the system guarantees treatment conditions equal to that of a full scale plant. During the laboratory evaluation process samples were extracted at selected time intervals for analytical purposes of several parameters such as TOC and COD. Additionally BOD tests were carried out for determination of biodegradability. The treatment of all waste water samples resulted in reduced COD and BOD levels and an increase in biodegradability.

Post treatment samples were taken in Germany, frozen and shipped to AbbVie's main laboratory in Chicago where they were also analyzed for any potential residual API content. The resulting analysis confirmed a reduction in COD and API destruction. Results from the treatment study completed by Enviolet are outlined below in the following diagrams and tables.

These results correlate to a previously successful study completed on Synthroid waste water by AbbVie in 2014 with the same technology. Due to changes to the global manufacturing demand for Synthroid in late 2014 the project was postponed.

Diagram 1: Synthroid waste water concentrations of COD, BOD and the resulting biodegradability versus dimensionless time.

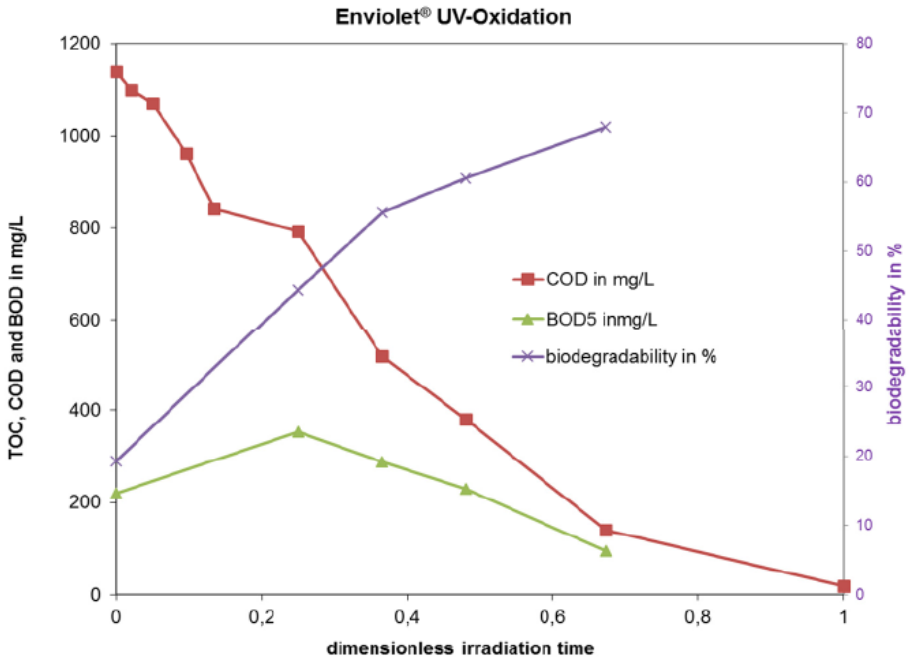


Diagram 2: Synthroid concentrations of TOC and logarithmic concentrations of API versus dimensionless treatment time. Individual API LODs (Level of Detection) are shown in Table 1 in the final column.

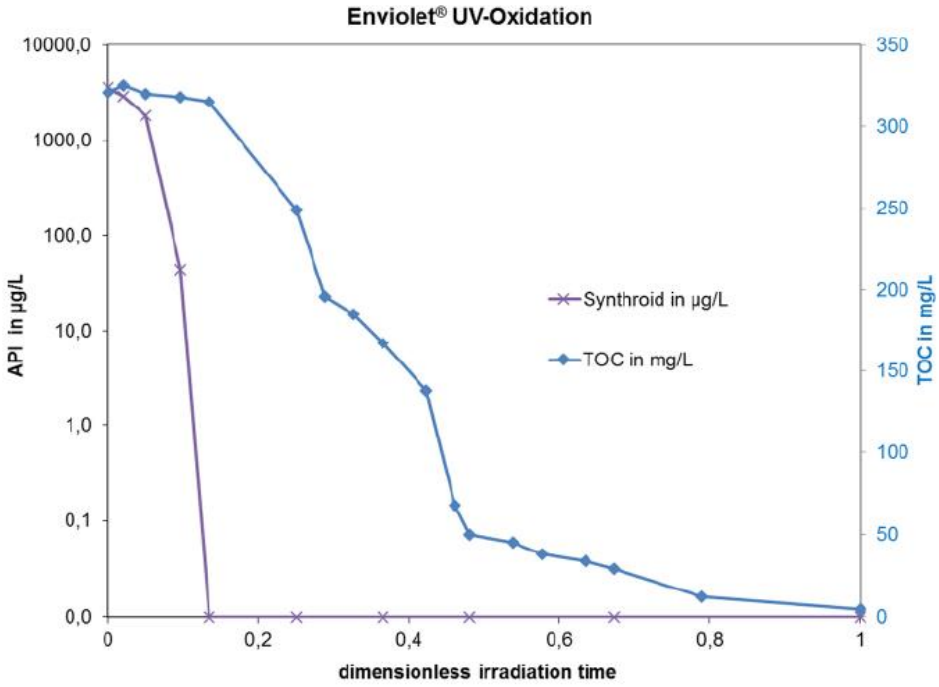


Table 1: **Synthroid** concentrations (Levothyroxine Sodium)

Samples were taken throughout the treatment process to confirm the corresponding reduction in parameters of TOC, COD, BOD and LOD, as well as the increase in Biodegradability.

Irradiation time, normalized	Sample	TOC in mg/L	COD in mg/L	BOD in mg/L	Bio-degrada-bility in %	Synthroid in µg/L
0,00	S0	321	1140	220	19	3500
0,02	S1	325	1100	n.a.	n.a.	2850
0,05	S2	320	1070	n.a.	n.a.	1800
0,10	S3	318	962	n.a.	n.a.	44
0,14	S4	315	842	n.a.	n.a.	<10
0,25	S5	249	793	352	44	<0,5
0,37	S6	167	516	287	56	<50
0,48	S7	50	380	230	61	<50
0,67	S8	29	140	95	68	<50
1,00	S9	5	18	n.a.	n.a.	<25

Diagram 3: Elagolix concentrations of COD and BOD and the resulting biodegradability versus dimensionless time

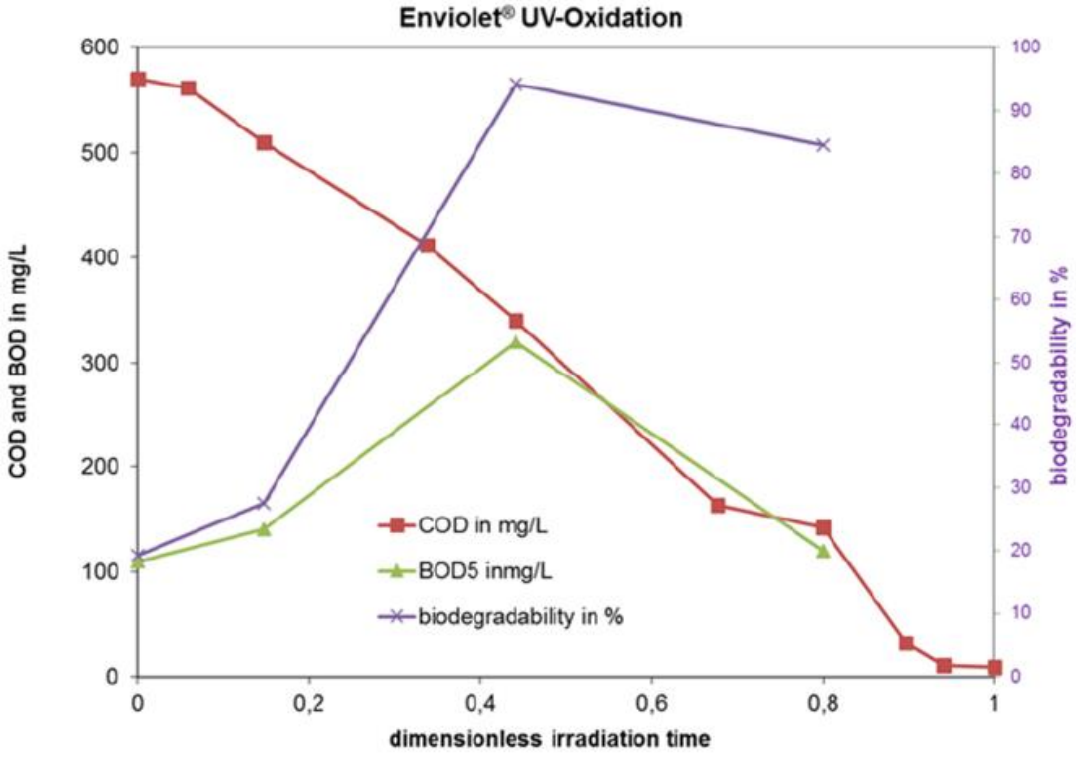


Diagram 4: Elagolix Concentrations of TOC and API (logarithmic) degradation versus dimensionless treatment time.

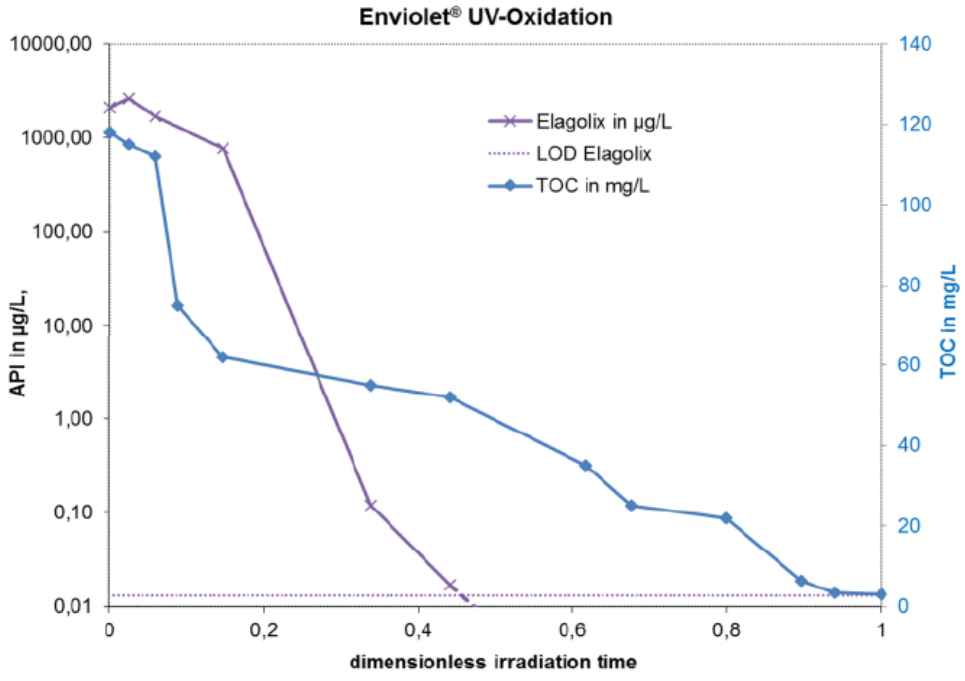


Table 2: **Elagolix** Concentrations

Samples were taken throughout the treatment process to confirm the corresponding reduction in parameters of TOC, COD, BOD and LOD, as well as the increase in Biodegradability.

Irradiation time, normailised	Sample	TOC in mg/L	COD in mg/L	BOD in mg/L	Biodegradibility %	Elagolix in ug/L
0,00	E2-0	118	570	110	19	2100
0,03	E2-1	115	n.a	n.a	n.a	2600
0,06	E2-2	112	562	n.a	n.a	1700
0,15	E2-3	62	510	140	27	780
0,34	E2-4	55	412	n.a	n.a	0.,12
0,44	E2-5	52	340	320	94	0,017
0,62	E2-6	35	n.a	n.a	n.a	<0,013
0,80	E2-7	22	142	120	85	<0,013
0,90	E2-8	6,3	32	n.a	n.a	<0,013
0,94	E2-9	3,3	10,8	n.a	n.a	<0,013
1,00	E2-10	3,1	9,3	n.a	n.a	<0,013

Pre Validation

It is planned to complete pre-validation of Elagolix and Synthroid waste water treatment at an EPA licensed third party site, with the same technology, prior to the systems installation at AbbVie Sligo. These waste streams will be diverted via road tanker to this facility where they will be treated. During treatment a complete analytical program will establish a correlation with COD as the guiding parameter. This treatment technology will operate as a batch system when installed at AbbVie. During pre-validation 6 tankers of wastewater, each of which will represent a batch, will be treated at the third party facility and analysed for COD levels before release to sewer. A sample of the treated waste water will also be shipped to AbbVie's main laboratory in Chicago for confirmation of complete API destruction.

This pre-validation is planned to take place during Q2/Q3 2019, with individual monitoring of several concentrations to establish an AbbVie-Sligo SOP within a chemical correlation study, according to the following EU-rules:

EU (Hormones): Community Strategy for Endocrine Disruptors. A Range of Substances Suspected of Interfering with the Hormone Systems of Humans and Wildlife, Brussels, 17.12.1999 COM (1999) 706 final.

EU (General): European Commission: Integrated Pollution Prevention and Control Reference Document on Best Available Techniques in Common Wastewater and Waste Gas Treatment/Management Systems in the Chemical Sector, February 2003.

EU: Directive 2010/75/EU of the European Parliament and of the Council of 24 November 2010 on Industrial Emissions (Integrated Pollution Prevention and Control) (Recast).

EU: Directive 2000/6o/EC of the European Parliament and of the Council of 23 October 2000, Establishing a Framework for Community Action in the Field of Water Policy Official Journal L.327, 22/12/2000, P. 0001–0073.

On Site Commissioning

During the pre-validation works outlined above the operating parameters for the waste water treatment system will have been determined along with a COD threshold level. It is proposed to the Agency that AbbVie Sligo will verify the systems operation on site by completion of COD analysis on site for each batch over an agreed period. Samples for each batch will be tested for COD prior to discharge to ensure the system is operating within specified limits.

After this agreed period sampling for COD for each batch will no longer be required. Abbvie, as part of its internal environmental management system, will on a quarterly basis, collect an ad-hoc grab sample for COD by an external laboratory to verify the continued correct operation of the unit. The results of this sample will be forwarded to Irish Water as part of its quarterly Emission to Sewer report as per the conditions of the sites industrial emissions licence.

Project Timeline

AbbVie plan to implement commissioning of this waste water treatment system on site between August and September 2019

Request for Approval

AbbVie have reviewed, "EPA Guidance for Licensees on Requests for Alterations to the installation/facility" and believe this change should be captured under category (i) a request for approval (Condition 1 approval) to the Office of Environmental Enforcement via a 'licensee return' on EDEN.