Attachment 4.8.1 Operational Report

1.0 OVERVIEW

AbbVie Ireland NL B.V. (hereafter referred to as AbbVie) has decided to develop an integrated biochemical operation at their facility at Ballytivnan Sligo. The facility at Ballytivnan is located approximately 1.7 km north east of Sligo town centre. The site is also located approximately 1 km from another AbbVie facility on the Manorhamilton Road established in 2002. The site location drawing (Drawing 001) shows both facilities.

The purpose of this development is to design a facility to manufacture special medicines for treating illnesses (like cancer) in a highly controlled and contained environment. The main process includes the linking of a bio-pharmaceutical molecule to a cytotoxic molecule providing effective delivery of the medicine within the patient. At this stage it is anticipated that there will be 2 no. drug lines produced in the suite.

The project will consist of internal demolition of part of the existing redundant manufacturing facility, which is located to the west of the new Warehouse, to make way for the proposed filling suite.

The facility in Ballytivnan will provide for conjugation or joining together of bio-pharma molecule and pharmaceutical acute-molecule. The main process steps are Buffer Preparation, Thawing, Formulation, and then Vial Filling and Lyophilisation followed by semi-automatic inspection and Cold Storage before shipping. In order to support these operations additional clean utilities will be required.

The main support functions consist of Water for Injection and Clean Steam, generation, storage and distribution, as well as raw material and Active Pharmaceutical Ingredients (API) storage.

One of the main considerations for this design (typically much like most cancer or oncology medicines) is to address the high containment requirements for the products produced in this suite and to maintain a safe working environment for the operator and maintenance personnel. To achieve the required containment levels, the facility has been designed to prevent exposure of the product or excipients to the operator by means of closed processes or the use of containment equipment. Personnel and material handling procedures also form a significant part of the facility operation to maintain the required level of containment.

The location of the new manufacturing suite is in the north east of the existing site. The area in the building was in use as a production facility until May 2018. It has since been de-commissioned and cleared to allow the construction of the new facility. Internal alterations will be made to accommodate an integrated bio-chemical manufacturing facility sized 3,476 square metres, within the building fabric of the existing AbbVie Ballytivnan building. The alterations consist of the following:

- New roof-mounted plant and Penthouse Louvres 1.8 m high and removal of existing roof mounted equipment;
- The construction of additional plant room internal mezzanines, sized 645 m^2 within the existing building and an external single storey extension sized 20 m^2 and 9.6 m high, located to the north of the existing facility;
- A revised yard layout, located to the north of the existing facility, including a new single storey electrical room extension sized 155 m^2 and 7.1 m high;
- The enclosure of an existing walled yard area with a new roof and cladding, sized 150 m^2, to house chillers;
- The addition of 4 no. new boiler flues, 17.5 m high above ground level and 500 mm diameter;
- 2 no. new bulk bunded waste water holding tanks, housed in a building sized 110 m^2 and 9 m high, and associated tanker un-loading area;
- 2 no. bunded sunken tanks housed in a building sized 75 m^2 and 4 m high;
- 3 no. cooling towers 9 m high. A liquid nitrogen tank sized 8 m high and 2 m diameter, and an emergency generator and its associated diesel tank and its 10 m high stack; and
- Site works include revised road and car parking layouts, additional temporary contractor related car parking for 109 cars, underground and over-ground utilities, landscaping and a landscaped berm.

Approximately 120 personnel currently working at the site will be moved and deployed to a different manufacturing facility in the Sligo area and the circa 179 existing persons manufacturing medical devices will remain onsite. The new development will employ approximately 100 personnel and will operate on a shift basis, similar to existing shift patterns.

Planning permission (Planning Reference PL 18/185) for the development was granted by Sligo County Council (SCC) on 7th August 2018. The application was accompanied by an Environmental Impact Assessment Report (EIAR) together with a Natura Impact Screening Statement which were approved as part of the permission. As these were submitted prior to detailed design, additional and revised detail relating to the project since the time of the EIAR submission to SCC is therefore provided in this IE licence application.

2.0 PLANT DESCRIPTION

The site layout drawing (Drawing 002) shows the general layout of the buildings and car parking areas at the facility. The proposed facility will be located in a shell space in Building 03 on the Sligo Ballytivnan site, along with required support facilities, equipment and utilities.

The following Block Flow Diagram outlines the core processing functionality and the process related support functions.

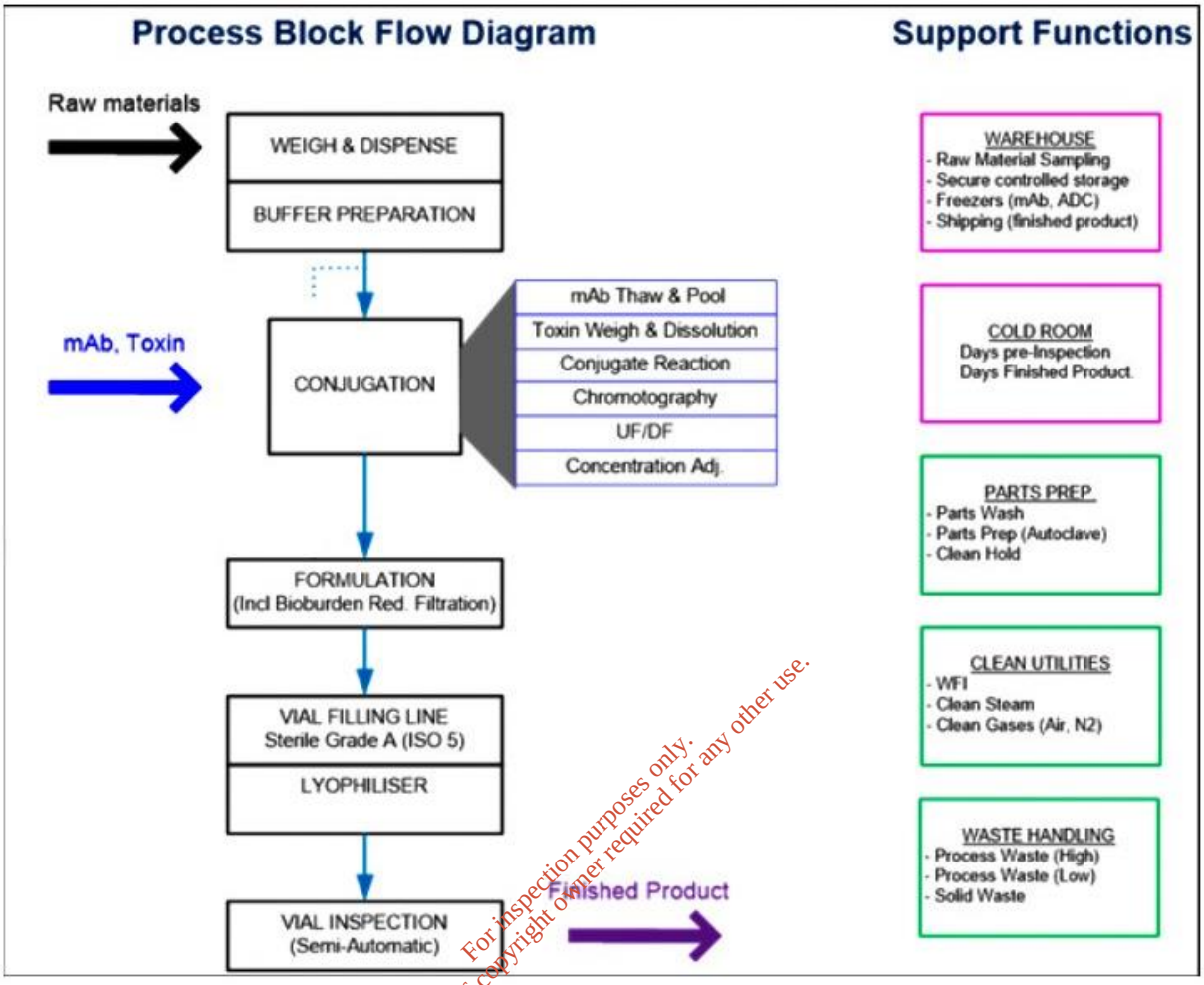

Figure 1 *Process Block Flow Diagram for Bio-Chemical Pharmaceutical Production*

2.1 Unit operations

2.1.1 New Operations

The proposed bio-chemical suite is anticipated to be used for the production of 2 no. drug preparations. Additional drug production lines may be incorporated into the facility processes at a later stage.

The 2 no. drug production lines operate slightly differently; however, the basic process operations can be described as follows:

1. Raw Materials

All raw materials will be brought in through the Warehouse, where there is provision for sampling within a controlled environment, and the materials will be stored until required. The Warehouse will also be used to receive and store process consumables, such as filter cartridges and single use equipment.

2. Weigh & Dispense for Buffer Preparation

Weighing & Dispensing will occur in a small dedicated room adjacent to the Buffer Preparation room. A walk-in downflow booth will be provided for dust minimisation, together with the appropriate bench scales and floor scales. Raw materials (powder and liquid) will be supplied in small quantities (typically bags up to 10 kg) that mitigates the requirement for material handling aids. Small quantities of raw materials (partial bags) will be stored within the raw material storage cabinets provided in the Weigh & Dispense room.

3. Buffer Preparation

Buffer preparation will occur in a controlled room adjacent to the conjugation room. This room will have separate access for personnel and materials from the general circulation corridor. There will be no handling of Active Pharmaceutical Ingredients (API) or potent material in the Buffer Prep room. The equipment will be dedicated to this room and will not move to other High Containment rooms (with the exception of totes).

Excipients will be supplied via the adjacent Weigh & Dispense Room in bags and containers.

Two ambient water for Injection (WFI) points of use will be provided in the room, one adjacent to the area for solution make-up, and the second for direct filling of WFI into single use (SU) bags. WFI will be filtered to 500L or 1000L SU bags (within totes) for pumping via a peristaltic pump through the wall to the Conjugation suite.

Buffers will be made up in large quantities (up to 500L) within Single Use Mixers (SUMs). The SUM can be located within a downflow cabinet for powder dispensing for dust minimisation during the powder addition step.

The complete Buffer will be filtered using a single use 0.2 µm filter into a SU bag (within tote) for storage at ambient temperature in the room, as shown below.

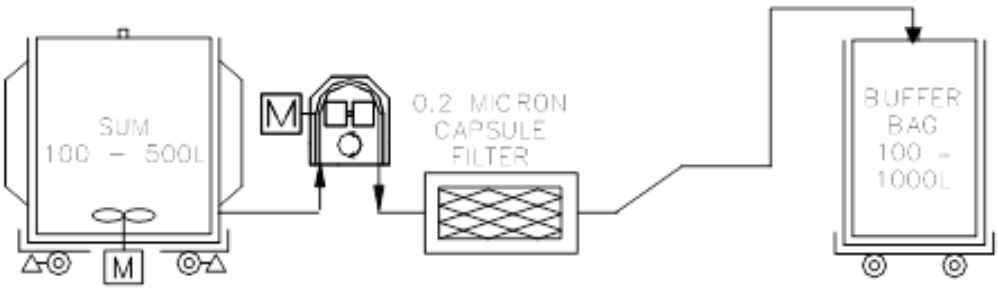

Figure 2 *Buffer Filtration*

When the buffer is required for a process step in the Conjugation Room, the tubing from the SU buffer bags will be bundled and passed through to the Conjugation room using a clean-room wall Hose Transfer Pass-Through device. After use, these hoses will be pulled through to the Conjugation Room for disposal. All hoses will be uniquely identified to prevent mix-up.

For small scale make-ups (<50L) the buffers will be made-up using bottles or carboys within a downflow cabinet (or on a bench) using a magnetic lab mixer and filtered into SU bags or bottles for transfer through the material pass-through (cabinet cleanroom type) into the Conjugation suite. The material pass-through is uni-directional.

Other buffers (<50L) will also be made up in this area and will be transferred (via 0.2-micron filter) to a SU Bag, either small bags (<20L) or alternatively a 100L SU Bag (within tote). These will then be transferred to the Formulation Room in a tote/trolley via the MAL and the corridor.

All process contact components used in Buffer Prep are single use (bags, filters, tubing etc.). There is no requirement for Clean-in-Place (CIP). The externals of equipment (SUMs, totes) will be cleaned by manual wipe down.

4. MAB (Monoclonal Antibody) Thawing & Pooling

MAB product will be delivered to the Conjugation room in a frozen state from the Warehouse, via the material airlock, and the frozen MAB containers will be thawed. After thawing, the MAB product is ready to be pooled into a SUM and diluted with WFI or buffers. The MAB will then be dispensed from a GMP Isolator into a single use mixer

5. Weigh, Dispense and Dissolution of Toxin

Weighing and dispensing of the Toxin (drug linker) will be in a negatively pressurised containment isolator to provide containment controls for the safe handling of potent materials. Solvents for dissolution of the drug linker (DMSO or DMA) will be pumped directly into the dispensing chamber of the isolator as required.

7. Conjugation Reaction

Conjugation of the MAB and the toxin will occur within the conjugate reactors. The reactors will be designed as stainless steel, portable vessels with an agitator, a contained sampling device and an integrated cooling/heating jacket. The cooling/ heating requirements of the process will be controlled by a stand-alone Temperature-Control-Unit (TCU).

Once the toxin and MAB have been transferred to the Reactor, the Buffers, reducing agent, and quenching agent are added to the reactor. Buffers will be transferred in SU Bags via the Material Pass-Through (cabinet type) from Buffer Preparation.

Upon completion of the conjugate process, the in-process material will be transferred to the first purification step (ultra-filtration or chromatography) as required for the specific drug product.

8. Chromatography

Only one of the products requires a Chromatography manufacturing step. The chromatography process consists of a fluid handling skid and pre-packed disposable chromatography column. The use of disposable chromatography columns will be employed to provide a closed system process and eliminate the need for cleaning and column repacking. Buffers will be pumped into the Conjugation Room from the Buffer Prep Room. Upon completion of the chromatography process the in-process material will be transferred to a SUM.

9. Ultra-Filtration / Depth-Filtration

The Ultra-Filtration / Depth-Filtration (UF/DF) process consists of a UF/DF skid and single-use filtration elements. The use of single-use filter elements will be employed to provide a closed and contained system process. Buffers will be pumped into the conjugation room from the buffer prep room.

Upon completion of the UF/DF process the concentrated in-process material will be collected in a SUM.

10. Formulation

The pooled product will then be formulated or diluted with buffer before transfer to the filling suite.

11. Filling

The formulated product will be delivered from the formulation room to the filling suite. A final filtration step will be undertaken in the filling isolator prior to the product being filled into vials.

The Filing Line is a single use product pathway. It is also fully integrated within the Lyophiliser.

Isolators are capable of wipe down and wetting (manual spray lances) for decontamination cleaning. All waste water generated will be directed to the high high strength waste collection system

The vial Filling Line is primarily intended for lyophilised fill with the sequence:

- Fill,
- Stopper,
- Load to Lyophiliser (Lyo),
- Freeze Dry,
- Lyo Unload,
- Cap,
- Tray-off.

Finished vials will be transferred to a Cold Room in preparation for semi-automatic inspection.

12. Lyophiliser (Freeze Dryer)

Filled vials will be transferred to the Lyo via the Lyo automated load/unload system, which is fully contained within an isolator. The Lyo will be used to freeze-dry the final product.

13. Automation

All key process operations will be automated and operated by the process staff from within the process areas. The automation will allow the critical process parameters to be monitored and logged.

The automation will include control of raw materials through monitoring of dispensing operations and dispensed material use in the process.

Critical process utilities will be controlled and / or monitored to ensure product quality is not compromised and system alarms are dealt with in a timely manner.

2.1.2 Existing Operations

The existing site operations involves Moulding, Pad printing and Sub-assembly of plastic components for use in combination devices supporting AbbVie medicinal products.

1. Products

AbbVie Ballytivnan currently produces drug delivery devices, including an auto injector pen that is used by patients around the world who use the company's treatment indicated for a range of immune-related illnesses including rheumatoid arthritis and Crohn's disease. The site also manufactures a combination product that is used to administer a treatment for patients with advanced Parkinson's disease.

Resin, Ink, Springs, Trays and Corrugates are delivered to the site. Once materials are delivered, they are goods receipted on SAP. Samples are collected and tested.

2. Moulding

The site manufactures combination devices. Commercially the site has 14 injection moulding machines, 3 twin shots and 11 single shot moulding machines that manufacture components for an auto-injector pen. Components are moulded using the resin. In process samples are taken for inspection. Moulded parts are left to cure. Once cured, samples are measured in Metrology in-house.

3. Printing

Some components require printing. Numbers are printed on one variant of the pen. This is done in the Pad Printing area on the site. In Process samples are taken and inspected.

4. Assembly

Two halves are then assembled in the automation part of the facility. Post assembly functional testing is carried out in Metrology. AbbVie also manually assemble a nasal duodenum tube for the treatment of Parkinson's. Some of these components are injection moulded onsite and others are purchased and delivered to the site. Once manually assembled they are sent off site for sterilization and then returned for final packaging.

5. Metrology

The site functionally and dimensionally tests all components before they are shipped to distribution centre in the Netherlands.

3.0 ANCILLARY SERVICES AND UTILITIES

3.1 Effluent / Wastewater

Wastewater from the new facility will be segregated into two categories; High High Strength and Low Strength.

High High Strength wastewater is liquid waste from high containment areas or liquid waste which has been identified that may contain some toxin or other harmful substances. This waste is considered hazardous and is not suitable for treatment by conventional WWT (Waste Water Treatment) technology.

High high strength wastewater will be routed via double-contained pipework to the high high strength sump tank. The High high strength sump tank will be a stainless steel, flat bottomed, vertical cylindrical tank with an approximate operating volume of 7000 L. The sump tank will be within the same sunken, chemical resistant coated concrete bund as the low strength wastewater sump tank.

From the sump tank the high high strength wastewater will be pumped to a high high strength wastewater bulk storage tank as required using two (duty and standby) level switch controlled self-priming pumps. The bulk storage tank will be a flat bottomed, vertical cylindrical stainless steel tank with an approximate operating volume of 60,000 L. This tank will be in the same sunken, chemical resistant coated concrete bund as the low strength wastewater bulk storage tank.

Both the sump tanks bunds and the bulk tanks bunds will be roofed over. They will also be equipped with liquid level detection. In the unlikely event that any liquid enters the bund it can be tested and pumped to the appropriate wastewater tank for further treatment or disposal.

The containment of the high high strength wastewater will be subject to Environmental Protection Agency (EPA) licence conditions to minimise potential for leakage/spillage. The bund will be equipped with level detection, and in the unlikely event that any liquid enters the bund it can be tested and pumped to the appropriate wastewater tank for further treatment or disposal. Please see Figure 3 for a cross-section through the sunken sump and bulk tanks area.

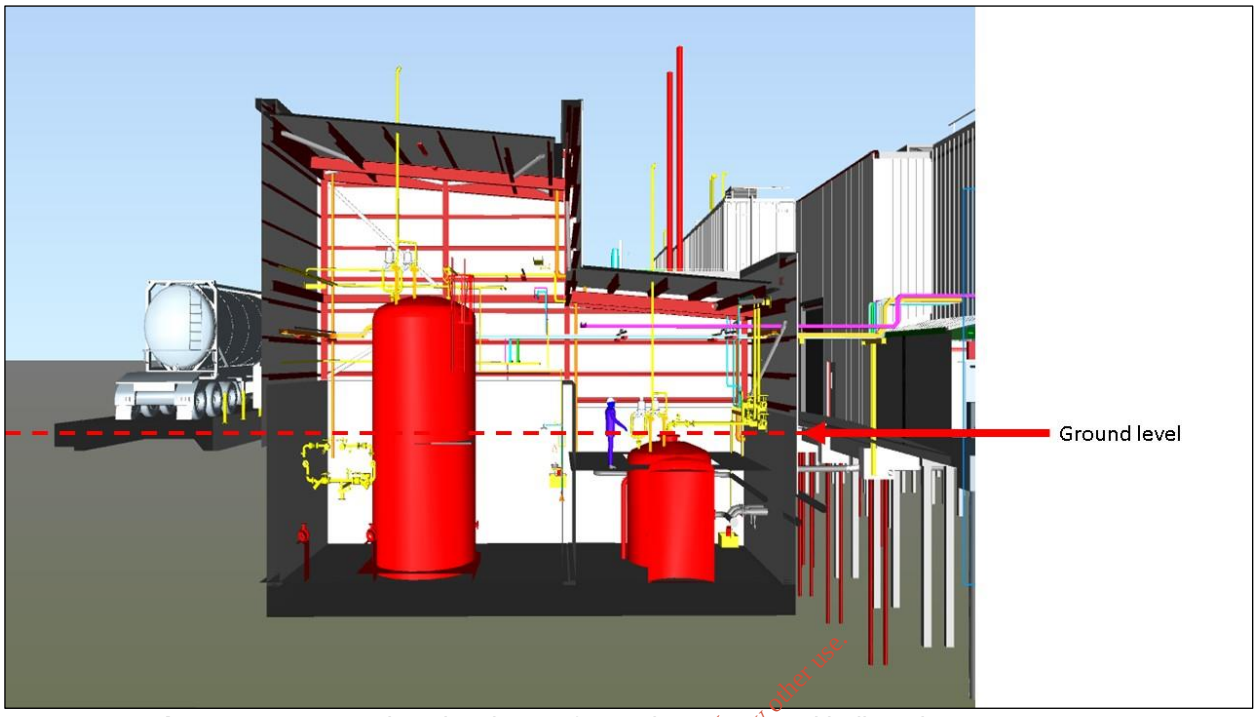

Figure 3 *Cross-section showing 1 of 2 sunken sump and bulk tanks*

Low Strength wastewater is all other process specific wastewater including flashpot condensate drains, and waste from non-toxin / product contacting equipment e.g. autoclave & buffer prep equipment. There is no toxin in this waste.

The low strength wastewater sump tank will be a Glass Reinforced Plastic (GRP) tank with approx. 10,000 L operating volume. It will be bunded in the same sunken bund as the high high strength wastewater sump tank. The waste will be pumped into the low strength wastewater bulk storage tank by two (duty and standby) submersible pumps inside the sump tank.

The low strength wastewater bulk storage tank will be a 30,000 L GRP tank. It will be bunded in the same sunken bund as the high high strength wastewater sump tank.

The high high strength and low strength wastewater drain lines will be stainless steel with the underground drainage transitioning to double contained, gravity drained polypropylene pipe. The locations of the sumps and tanks are shown on Drawing 007.

Figure 3 shows the layout of the low strength and high high strength wastewater tanks and bunds.

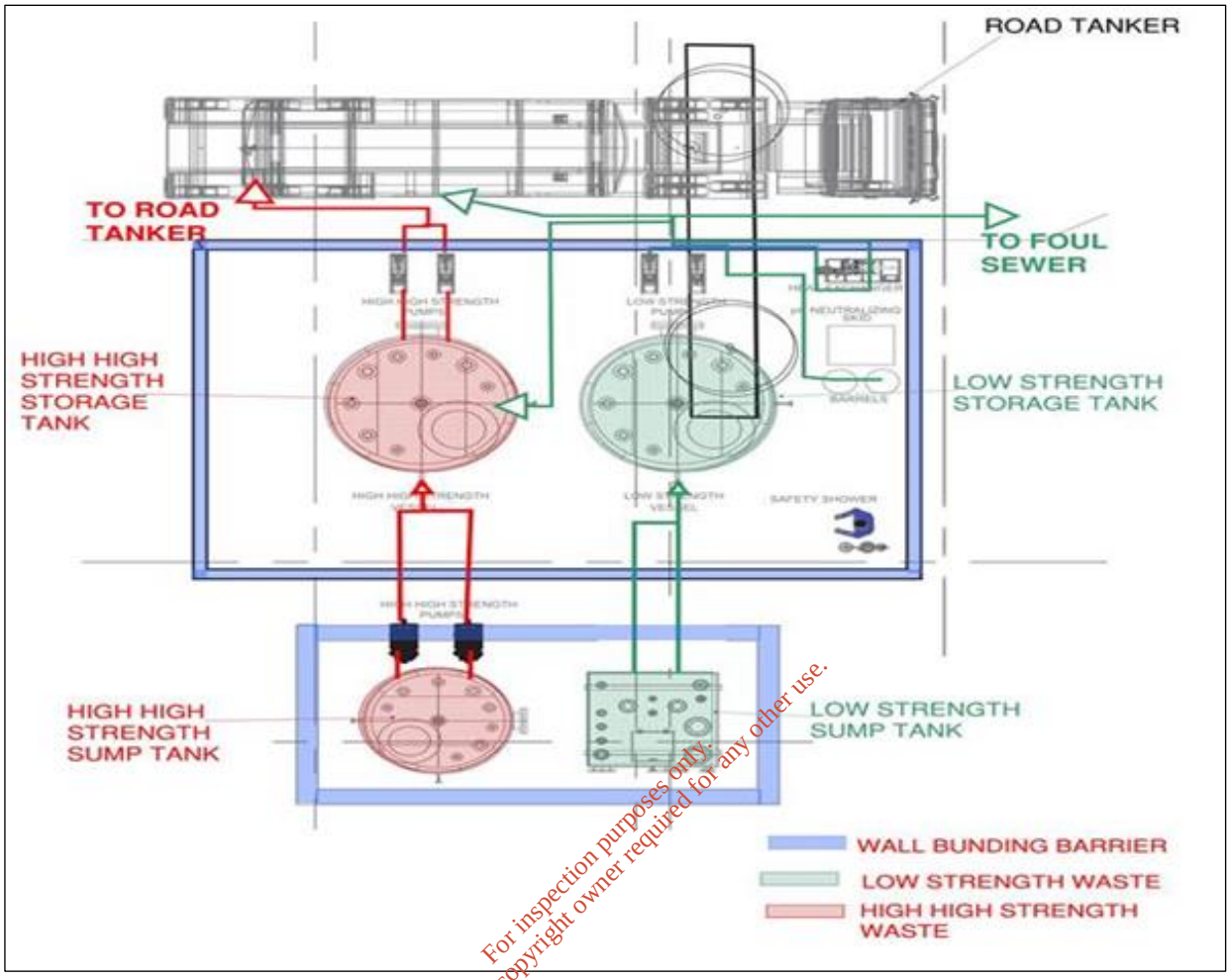

Figure 4 *Wastewater Block Flow Diagram*

The high high strength storage tank will be emptied routinely into a road tanker to be incinerated / disposed of off-site. Approximately two tankers a week are estimated to be required when working at maximum capacity.

The low strength wastewater will be sampled and will generally be sent to the foul sewer (municipal waste water treatment). The facility includes for pH and temperature adjustment should there be a need for this before discharge. The waste can also be pumped into the high high strength wastewater tank or to a road tanker if there is ever a risk of contamination of the waste.

The discharge to sewer will be via SE1 in the south east corner of the site. The main foul line (F15) is constructed of 225mm Polyvinyl Chloride (PVC) pipe. Upstream of this the foul lines are 225mm concrete pipe. The average flow will be 6.7m^3/hour with a max flow of 12.7m^3/hour.

Figure 5 is a process flow diagram of both waste water streams.

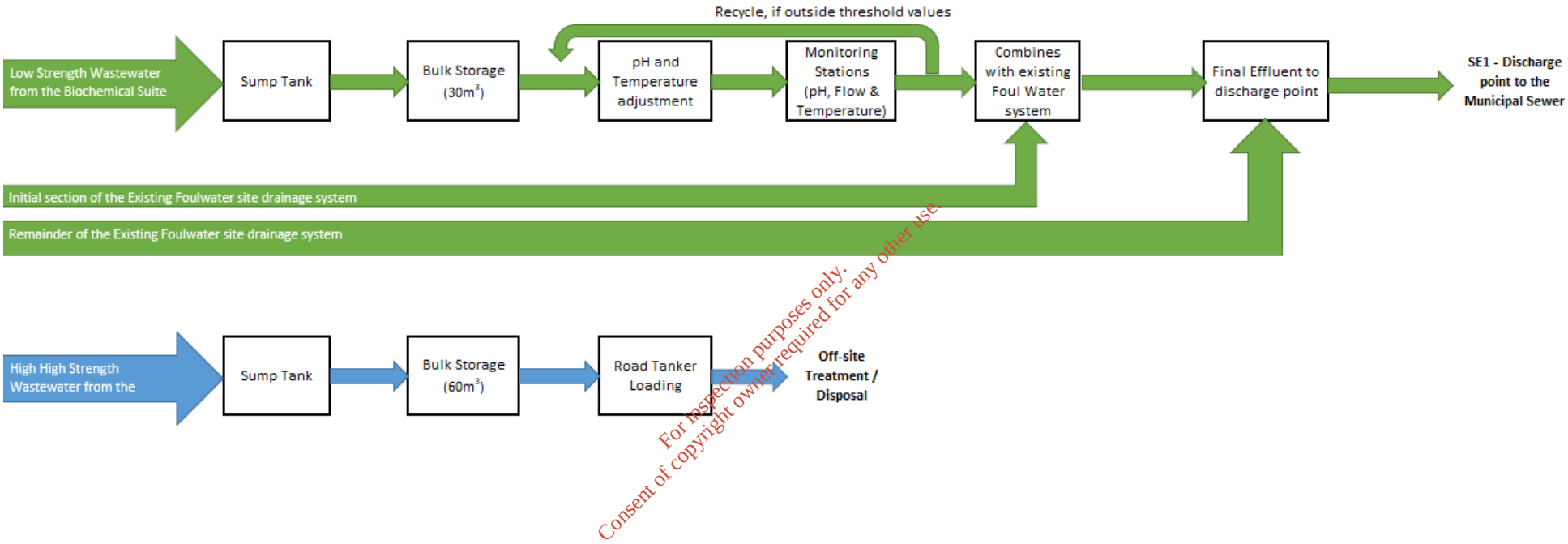

Figure 5. *Process Flow Sequence for Low Strength and High High Strength Wastewaters*

Operation of the wastewater system will be according to BAT (Best Available Technology) principles and in compliance with the licence for the site to ensure that inputs to, and subsequent contamination of, soil and water environments does not occur during normal and/ or emergency conditions (material spillage or fire event situations).

3.2 Stormwater Drainage

Surface water from the buildings and yards is collected via a series of points across the facility. These then discharge to an offsite drainage ditch along the eastern and southern boundaries of the site via 4 no. hydrocarbon interceptors as per existing facility at 3 no. discharge points (SW1 to SW3). The drainage ditch eventually discharges into the Shannon Eighter. The locations of the interceptors and discharge points are shown on Drawing 008.

The onsite stormwater drainage to the north east corner of the site is via a 225mm concrete pipe. The onsite stormwater drainage to the south of the site is via a 300mm concrete pipe. There is no existing flow monitoring or control.

In accordance with BAT, clean stormwater is kept separate from wastewater and there is no inherent risk of cross-contamination. Stormwater run-off is from buildings and car parks only and therefore there is no requirement to undertake regular sampling of the stormwater prior to discharge. Weekly visual inspections will be undertaken for all stormwater discharge points (via manholes) in accordance with the facility's Licence.

3.3 Water Systems

Clean Utilities in this project includes Water for Injection (WFI), Clean Steam and Reverse Osmosis (RO) Water.

3.3.1 Reverse Osmosis (RO) Water

RO Water is required by the WFI Generational Still. RO Water will be generated by a RO Generation Skid, which will consist of multimedia filters, Softeners, organic scavengers, RO membranes and an electro-deionization (EDI) unit. The key features of the system are as follows:

- RO Water System (to United States Pharmacopeia / European Pharmacopeia (USP/ EP) standards for Purified Water);
- Pre-Treatment for Towns Water in Sligo Area (Domestic Water on site);
- Duplex System (for Redundancy purposes only);
- System suitable for periodic Hot Water Sanitisation within the hygienic boundary;
- Break Tank from Domestic Water;
- Capability to feed to a WFI Still and a Coal Seam Gas (CSG) (in an adjacent room), with capability for a Future WFI Still.

3.3.2 Water for Injection (WFI)

WFI will be generated by a new multi-effect still which will be located on the mezzanine level of the Clean Utilities Area. The generated WFI will be sent to a new 23,000 L WFI Storage Tank, which will also be located in the Clean Utilities Area. This storage tank maximizes the available space, adequately supplying the current anticipated requirements, as well as providing extra capacity for future demands.

3.3.3 Clean Steam

Clean Steam is required for the Lyophilizer, Autoclave and steam sanitisation of the WFI POU (and very occasionally for the WFI Storage Vessel). A new Clean Steam Generator will be provided in mezzanine level of Clean Utilities Area and a respective distribution network installed.

3.4 Gas Systems

Gaseous Clean Utilities include Nitrogen and Compressed Air.

3.4.1 Nitrogen

Liquid nitrogen will be supplied from a bulk nitrogen storage vessel and vaporiser external to the building.

3.4.2 Compressed Air

Compressed Air and Instrument Air will be distributed as a single clean service, via new stainless-steel piping.

3.5 HVAC

The Heating, Ventilation and Air Conditioning (HVAC) system will be designed to provide environmentally-controlled air for the facility. This involves maintaining at predetermined pressures, temperatures and humidity levels, as required by area.

Each classified process suite will be equipped with an air handling unit (AHU) and separate material and personnel airlocks which segregate the zone from the adjacent suites. Fresh air will be supplied and extracted from each of the recirculation air handlers by the primary units.

Internal air quality testing will be used to assess compliance of the manufacturing environment with established standards for microbial control and total particulate levels in via the Environmental Monitoring System for the HVAC.

Chilled water will provide the cooling requirements for the HVAC units.

3.6 Cleaning Systems

The bio-chemical production suite has been designed on the basis of single-use technology, minimising the requirement for cleaning. All single use components will be double bagged and sent to a designated waste storage area for specialist disposal (e.g. incineration). Single use components with direct product contact will be double bagged and placed into sealed drums.

The isolators and conjugation reactors are fixed vessels and will be cleaned in place. The isolators will be cleaned with a combination of manual wipe down and washdown (using WFI) with washwater sent to the high high strength wastewater system. The conjugation reactors will be cleaned using a simplified clean-in-place (CIP) system which involves cleaning solutions and WFI being charged into the reactor across multiple cycles. As with the isolators, the washwater generated will be diverted to the high high strength wastewater system. The Lyophiliser is also designed for full CIP.

A parts washer and an autoclave will be installed for equipment and isolators that can be cleaned out of place (COP). The parts washed will be loaded from the equipment wash room and unloaded from the clean preparation room under LAF (laminar air flow) protection. The autoclave will be loaded from the clean preparation room and will be unloaded from the clean hold room under LAF protection. The autoclaves will be validated annually by a specialist contractor.

3.7 Air Locks

The production areas are inter-connected by corridors with airlocks acting as a transition between them. Materials flow into each production area will be via uni-directional air locks.

The transitional personnel air locks proposed for the containment areas will provide uni-directional flow with respect to the gowning and de-gowning operational procedures.

3.8 Building Management System (BMS)

The facility will operate a BMS automation system and an automated Environmental Monitoring System for control, monitoring, data collection and alarm/reporting of the HVAC air handling systems and mechanical utility systems site wide.

Rooms requiring environmental control will be managed by the BMS and identified monitoring signals from pressure transmitters and humidity/temperature instruments will provide readings to the Environmental Monitoring System. A Process Control System (PCS) will provide for the major equipment located in the bio-chemical production suite.

3.9 Utilities

Electrical energy will be used to power the facility and will be supplied from the mains supply as per the existing arrangement for the site. The anticipated energy use for the facility is 15,000 MWh per year.

1 no. 2 MW diesel generator will be available to supply emergency power to critical and essential manufacturing and utility equipment and systems. The emergency generators will be tested 4-6 hours every month and will be used periodically in the event of a power outage. Annual usage of diesel is anticipated to be up to 6000L per year.

Liquid Petroleum Gas (LPG) will be used for Low Pressure Hot Water (LPHW) boilers to provide hot water for AHUs and steam boilers. LPG is currently used in the existing LPHW boilers for the existing AHUs. Annual consumption is anticipated to be 2,000 m^3 per year. Note: LPG use in boilers does not constitute energy generation as boilers are used to produce hot water/steam for direct use.

Water from the mains water supply is required for supply across the building for the WFI tank (including water for the safety showers), domestic water tank, and the chilled water system. On entering the site, the mains water supply will be routed to a central break-tank. Annual consumption is anticipated to be 73,000 m^3.

3.10 Fire Suppression Systems

An L2/L3 type fire detection and alarm system is in place throughout the building including either smoke or heat detectors as appropriate. All air handling units have duct smoke detectors connected to and monitored by the alarm system.

The existing facility is equipped with an automatic sprinkler valve control system to effectively deal with any emergency situation that may occur. The water going to the sprinkler system is fed from the ring main which is filled by the mains supply. Hydrants outside the building are fed direct from Town mains

Portable fire extinguishers are in place around the building and will be used by suitably trained personnel. These comply with the requirements of The Fire Services Act 1981 and the Safety Health and Welfare at Work Act 1989 and IS 291: 2013 The Use, Siting, Inspection and Maintenance of Portable Fire Extinguishers.

3.11 External Storage and Warehousing

Existing separate designated external chemstores are in place at the current facility for the storage of solvents and hydrocarbons. These are lockable with restricted access. There are also 8 no. existing large plastics storage silos located to the south of the existing site.

There is no existing bulk tank storage external to the building. As part of the new facility, bulk diesel storage (for the emergency generator) and bulk liquid nitrogen storage (for the lyophiliser and isolators) will be required.

The majority of the hazardous chemicals that are or will be stored on site are stored in small quantities in drums and Integrated Bulk Containers (IBCs). These will be stored in designated areas within the Warehouse or in the existing self-bunded external chemstores.

3.12 Offices and Support Facilities

The offices are housed in the main building and comprise administration/finance, production planning/purchasing, human resources, manufacturing, quality assurance, engineering/facilities and Environmental Health & Safety (EHS).

The main support facilities on site are the cafeteria, waste management, cleaning, occupational health and the security centre at the entrance to the facility.

4.0 MANAGEMENT OF RAW MATERIALS AND WASTES

Please refer to Attachment 4.6.2 for a comprehensive list of the raw materials which will be required and stored at the site during operations.

There will be no intermediaries stored at the facility.

4.1 Raw Materials Management

Chemical storage is limited to bunded tanks, drums stores and designated process areas. Handling and transfer of fuel and chemicals will be carefully controlled. Any spill of hazardous substances used in the process will be diverted to a designated drainage system and into a designated bund for offsite disposal.

In general, the quantities of new materials are typically low due to the high-value, low-volume nature of the bio-chemical production process.

Raw materials and supplies are delivered to site by contractors/vendors. Access to the site is via the security centre at the west of the site, the goods are then escorted to the delivery unloading platform located at the rear of the Warehouse. Goods will be unloaded by trained operators and stored in the Warehouse until use.

Trolleys and carts will be used for all material movements within the facility. Separate trolleys/ carts will be used for the general circulation areas as opposed to the individual processing rooms. Each individual processing room will have dedicated trolleys/ carts which will stay within the relevant rooms and will only travel to the individual room Materials Air Lock (MAL) to receive materials. Single Use Mixers (SUM) and totes will also be used for movement of materials and single use components around the process areas.

Staff are fully trained in site procedures, including all Standard Operating Procedures (SOPs) and emergency response and safety procedures in relation to the storage and handling of all substances being used at the facility.

4.1.1 Solvents

Isopropyl Alcohol (IPA) at 99.7% and 70% is used within the existing facility for surface decontamination. A 70% solution of Isopropyl Alcohol (IPA), as 70% IPA impregnated wipes, will also be used for cleaning and disinfecting the new production surfaces after use. IPA will be stored in pre-packaged wipes and sealed bottles within the Warehouse.

It is proposed that di-methyl alcohol (DMA) and di-methyl sulfoxide (DMSO) will be used for dilution of the toxin for MAB conjugation in small quantities (6L). 100% DMA will be delivered to site in sealed 5L, 15L or 25L bottles, and will be stored within the designated flammables area of the Warehouse. DMA and DMSO for the MAB conjugation will be pumped directly to the conjugation suite using a peristaltic pump and single use tubing.

Glacial acetic acid required in small quantities as part of the buffer solution formulation will be stored in sealed containers (1L bottles of acetic acid) in the Warehouse prior to use. These will be dispensed directly into the buffer solution within an air-controlled environment.

Within the existing processes, solvents are used as part of the printing process during the final stages of the bio-medical devices production. Solvents used in printing are stored in sealed containers (up to 1L max) in locked cabinets until use.

4.1.2 Sterilising Chemicals other than Solvents

NaOH will be stored in 200L drums in the Warehouse and transferred to the point of use as required. The NaOH will be pumped using a peristaltic pump and single use tubing into the conjugation reactors. The waste NaOH will then be diverted to the wastewater drain to the high high strength wastewater system

Vaporised Hydrogen Peroxide (VHP) will be used for sterilisation of the high containment isolator and will be stored onsite in canisters in the Warehouse. The canisters are located near the isolators loaded into the isolators which is equipped with a vaporised. A catalytic converter is used to make the gas safe for emission to atmosphere (i.e. converts to water and oxygen).

4.1.3 Fuel Storage

A 10m^3 double skinned belly tank will be used to hold diesel for the emergency generator. The bulk diesel tank will also be equipped with leak detection.

A 30m^3 LPG tank is also in place to supply the new and existing boilers. Liquid nitrogen will also be stored in a 10m^3 tank.

4.1.4 Hazardous Chemicals

Linker toxin used in the production of the pharmaceutical product has an Occupational Exposure Limit (OEL) of ≤1 microgram per m^3 and will only be used within high grade isolators. This will be stored within a designated, access

controlled cold room within the Warehouse and will be transferred to the production suite via a bunded trolley.

As outlined in Attachment 4-6-2, up to 500g of toxin will be stored onsite at any one time in 1-50g containers.

4.1.5 Powders

Powders are generally inert and non-combustible and will be stored in the Warehouse in 1kg or 5kg bags. The powders will be transferred directly to the single use mixer room within the sealed bags and opened and dispensed into the mixer within the laminar flow hood. Due to the toxicities of the materials, the equipment is designed for High Containment fully closed processing and the solids will be kept wetted as much as possible.

4.1.6 Single Use Components

Single use components will be stored in bulk within the Warehouse and will be transferred to the facility as required. A designated store room within the production area will also be provided for frequently used items.

Other single use items such as gowning materials and space cleaning consumables will be stored in a separate designated store within the production area.

4.1.7 Refrigerants and Coolants

Refrigerants will be stored across the site within the chiller systems. These are stored in closed loop systems and will be topped up as required. Annual service of refrigeration skid is undertaken by a 3rd party, and the refrigerant will be removed, weighed and returned to system. As such, there is limited or no charging of refrigerant required. Annual use volumes in Attachment 4-6-1 has allowed for removal and replacement of the entire usable volume within the system per year. The following outlines how each is used.

R134A will be used in:

- The chiller in the manufacturing building (used for storing production materials);
- The canteen fridge and freezer (<5kg);
- Printing (<30kg); and
- The MS&T Cold Storage Unit (<10kg).

R404A (c. 50kg) will be used in the cold rooms in the manufacturing building and in the CHW water chillers in the existing plant room (<250kg per chiller for CHW chiller 1 and 2, c. 100kg for CHW chiller 4).

R134A will be used in the fridge doors (<6kg) in the canteen.

R717 is used in the heat pump in the plant room.

R407C is used in the existing site for the chilled water air in the outside switch room (<130kg).

R410A is used in:

- Cassette units (<40kg);
- The IT room;
- Lyo freeze drying unit (<150kg); and,
- The canteen (<30kg).

20% Propylene glycol will be used in the jackets of the temperature control units. Glycol will be arrive on site and be stored 200l drums (up to 1m^3). Waste glycol will be drummed and disposed of off site.

4.1.8 Liquid Nitrogen

Liquid nitrogen will be stored in a 10m^3 bulk tank in the yard. The vaporized nitrogen will provide nitrogen to the lyophiliser and isolators. The nitrogen pad will be free of sumps, open drains or other areas where cold nitrogen gas could accumulate in the event of a release.

4.1.9 Oils and Other Chemicals within Plant

Oils and lubricants will be supplied to the plant equipment (e.g. the Lyo) by an external contractor with responsibility for maintaining the equipment. There will therefore be no storage of these oils/lubricants onsite other than within the plant itself.

Heat transfer oil will similarly be held within the Lyo plant equipment and will not be stored onsite.

4.2 Waste Management

Waste management is covered under Section 8 of this application. The process in the new pharmaceutical manufacturing operation is expected to generate two categories of waste - hazardous and non-hazardous waste. Hazardous wastewater will consist of both liquid and solid waste streams.

All waste documentation will be retained on site in accordance with legislative requirements and will be carried out in accordance with the Environmental Management System for the facility which is designed to meet ISO 14001:2015 standards.

Waste management companies, as authorised by AbbVie, will be responsible for the transfer of all waste off site to authorised recovery/disposal facilities.

All waste types generated on site will be managed according to facility procedures which will comply with Irish and European waste management legislation and the waste management hierarchy.

AbbVie will ensure that all waste contractors and all recovery/disposal outlets used by the facility in its entirety are appropriately permitted and authorised to transport and receive the waste types being removed off site.

The requirements of the Sligo County Development Plan 2016 – 2023 and the targets outlined in the Connacht - Ulster Region Waste Management Plan 2015 – 2021 will also be followed.

4.3 Bunds and Pipelines

Bulk chemical storage at the new facility including the diesel tank and the high and low strength wastewater tanks will be bunded (wastewater tanks) or double lined (diesel belly tank). In the event of a spillage, drainage from bunded areas shall be inspected and diverted for collection and safe disposal if required. Drainage from the unloading facility for the diesel trucks and for the transfer area for the wastewater tanker is also diverted for collection and safe disposal.

Liquid Nitrogen and LPG will also be stored in bulk tanks however these do not require bunding and will vaporise in the event of a leak.

All proposed tanks, bunded storage and pipelines have been designed for their specific purpose and their contents. As required the structures will be rendered impervious to the materials stored therein. Tanks will be stored in bunds meeting the requirements of Agency guidelines on the "Storage and Transfer of Materials for Scheduled Activities".

With respect to integrity testing all bulk tanks, bunds and pipelines are new structures. As such no integrity testing of these structures has been carried out to date. It is anticipated that all bunds will be tested in accordance with standard licence requirements (testing is required typically every 3 years). Integrity testing will be completed in accordance with BS8007 "Code of Practice for design of concrete structures for retaining aqueous liquids" i.e. bunds will be demonstrated to be capable of holding 110% of the capacity of the largest tank or drum within the bunded area or 25% of the total volume of substances stored within the bund (whichever is the larger).

5.0 EMISSIONS

5.1 Air Emissions

Boiler emissions

There are 3 no. existing low pressure hot water boilers which operate on liquid petroleum gas. All three of these boilers connect to a common flue with one emission point and all three boilers are minor emission points i.e. have a rating of under 1MW (540kW).

There will be 7 no. new boilers as part of the proposed development. Five of these will be hot water boilers (4 no. low pressure hot water and 1 no. domestic hot water) and will be minor emissions i.e. have a rating of under 1MW (540kW). The

remaining two will be steam boilers (1 no. duty and 1 no. stand-by) which will be major emissions i.e. have a rating of over 1MW i.e. 1.6MW.

The two major emission steam boilers will have a stack height of 17.4m above ground level. The steam boilers will operate in a standby/duty mode, with only one boiler in operation at any one time. The locations of these boilers are shown on Drawing 004.

Minor emissions

Minor emissions from the facility will include solvent store and pad printing extracts from the existing facility, the new and existing low pressure hot water boilers and domestic hot water boiler, tank and process vents, lyo vents, autoclave vents, and the Vaporized hydrogen peroxide (VHP) vents (from sterilization). All minor emissions will operate up to 80% of the time or up to 7000 hours per year.

AHU units in non-process areas (e.g. canteen, non- airlock corridors, office spaces, Warehouse, laboratory, etc) have not been included as minor emission points in the licence. The locations of minor emission points are shown on Drawing 005.

Potential Emissions

Potential emissions include pressure relief valves and 1 new emergency generator. The emergency generator will be tested on a monthly basis. The locations of potential emission points are shown on Drawing 005.

Fugitive Emissions

Fugitive emissions are defined as low level diffuse emissions, mainly of volatile organic compounds, that occur when either gaseous or liquid process fluids escape from plant equipment. There are no such emissions anticipated from the new facility.

Volatile solvents are used at the existing facility for printing and will be used at the proposed facility for surface cleaning (IPA) and solution prep (DMA, DMSO and Acetic Acid). Solvents will be delivered in sealed bottles or drums and will remain sealed until required for use.

In the case of solution prep solvents, these will be dispensed directly from the container to the point of use in an air-controlled environment. There will be no fugitive emissions from this process.

IPA and solvents used in printing in the existing facility will evaporate from the surface onto which they are applied into the internal room air. However, the volume of solvent lost to internal room air will not be significant.

5.2 Emissions to Sewer (Wastewater Emissions)

Wastewater from the facility will comprise low strength wastewater including reject water from water purification systems, boilers and cooling towers blowdown, and wastewater from non-product contact equipment, as well as domestic effluent from welfare facilities such as toilets, showers and canteen facilities.

Low strength wastewater will be diverted to the 2 no. monitoring stations, SE-1a and SE1-b. Monitoring will be in accordance with the IE licence, and proposed monitoring is presented in Attachment 7.3.1. The low strength wastewater is relatively low in contaminants including phosphorus and nitrogen when compared to the domestic effluents. As the downstream wastewater treatment plant is sensitive to phosphorus, Total Phosphorus will be monitored weekly whist Total Nitrogen will be monitored monthly.

The average low strength wastewater volume for off-site disposal is expected to be in the region of 180m$^{3/}$day. The domestic effluent ties into the wastewater stream downstream from these monitoring stations.

All wastewater will be discharged to sewer via Sewer Emission Point SE -1 to the local foul network and then to Sligo County Council Waste Water Treatment Plant (WWTP). The location of SE-1 is shown on Drawing 006.

5.3 Emissions to Surface Water (Stormwater Emissions)

Stormwater from the site arises from buildings run-off, car-parks, roadways, service yards and other developed areas of the site. There are 3 no. discharge locations which drain to the east of the site i.e. SW1, SW2, and SW3. These discharge points drain via hydrocarbon petrol interceptors before combining in the outfall of the plant to the Shannon Eighter watercourse.

As the area proposed for development is already mostly hard standing there will be no significant change in run-off from the site.

5.4 Emissions to Ground

There are no existing or proposed emissions points to ground from the facility.

There are 3 no. existing groundwater monitoring wells i.e. MW1, MW2 and MW3. There are no current indications of water table pollution arising either upstream of or on the site however it is proposed to undertake bi-annual groundwater monitoring as per other similar AbbVie sites. The locations of MW1, MW2 and MW3 are shown on Drawing 009.

5.5 Noise Emissions

The primary sources of outward noise in the operational context are deemed long term and will involve:

- Building Services and Factory Process Plant; and;
- Additional vehicular traffic on public roads.

The main operational noise sources associated with building services and factory process plant will include cooling towers, boiler stacks, air handling units (AHUs), condenser units and various rooftop mounted fan and exhaust units. It is expected that all the plant items will operate continuously and up to 24/7. The new noise source locations (for the proposed development) are shown on Drawing 011.

Noise monitoring was undertaken at locations across the site as outlined in Attachment 7.1.3.2. Fixed noise monitoring locations are not proposed in this IE licence application and it is advised that monitoring locations be selected to best represent the noise sensitive receptors (NSRs).

6.0 TREATMENT AND ABATEMENT SYSTEMS

6.1 Air Emissions

Existing air quality is generally well within the National and European Union (EU) air quality standards therefore no abatement system is required for the new main air emissions. For the proposed development, no specific abatement is required as the operational phase is predicted to have an imperceptible impact on ambient air quality and climate.

New minor emissions from preparatory and production vessels, emissions from fume hoods, lyo vents, autoclave vents, and low pressure hot water boilers are not considered to be significant and appropriate abatement (i.e. HEPA filters and 2 um filters as appropriate) will be employed to remove trace contaminants. Dual catalytic converters in series will be in place on the Isolator lines to convert H_2O2 to H_2O and O_2.

Existing minor emissions from the pad printer and the solvent store contain small amounts of Volatile Organic Compounds (VOCs); however, the quantities of emissions are not considered significant and abatement systems are not required.

6.2 Wastewater

Wastewater discharged to sewer from the facility will be domestic foul, canteen foul, and low strength process foul waters (including boiler blow down and autoclave wastewater).

A new wastewater collection sump and tank system will provide for pH and temperature adjustment for the low strength wastewater should there be a need for this before discharge at sewer discharge point SE-1.

6.3 Stormwater

The current abatement technique for the stormwater network of the facility comprises all 3 no. stormwater emission points discharging to the drainage ditch along the eastern and southern boundaries via 4 no. existing hydrocarbon interceptors previously installed for the existing facility.

A new Class 1 Full retention hydrocarbon interceptor is proposed for the drainage line draining the area around the new bulk diesel tank as is required.

The potential effects on the local water environment are considered to be low for this proposed development so no abatement is required. However, the facility will continue to adhere to an environmental management plan (EMP) which will be in place to ensure compliance together with stringent EPA licencing requirements. This will include full containment of potential pollutant sources, site-specific

emergency response measures and management of stormwater run-off from the site.

Monitoring will also be undertaken as required by the future IE licence requirement.

6.4 Noise Emissions

The impact assessment has found that predicted noise levels associated with the day to day operations of the new facility (i.e. building services and factory process plant) will be well within the proposed criteria applicable to a site of this nature, so no additional abatement will be required. Notwithstanding this, due consideration as part of the detailed design process will ensure that the new development will operate within the noise limits stipulated in the site IE licence issued by the EPA. Proposed AHUs will be internal and therefore do not require additional abatement.

Noise levels at the existing facility have also been reduced through the removal of operational noise sources from Abbott owned equipment. In particular, the sterilisation equipment which had been previously identified as an undesirable noise source. The Abbott owned equipment was removed between January 2018 and May 2018.

Any change in noise levels associated with vehicles at road junctions in the vicinity of the proposed development is expected to be imperceptible so no abatement will be required.

7.0 MANAGEMENT SYSTEMS

AbbVie has established Environmental Health & Safety (EHS) management requirements that conform to the ISO14001, ISO 50001, ISO 55001 and OHSAS18001 management system standards. The EHS Management System provides a structured process for the achievement of continual improvement based on the Plan-Do-Check-Act cycle.

The management of AbbVie Ballytivnan ensures that the EHS policy is clearly understood, implemented and maintained at all levels of the company and by contractors engaged and working onsite on behalf of the company. The policy is publicly available to interested parties on request.

7.1 Emergency Response Plan

An on-site Emergency Response Plan (ERP) is in place at the facility and will be updated to include the new suite. The ERP details the required response of the AbbVie emergency response personnel in the event of an incident on site. The ERP will include arrangements for contacting the emergency services and those people in the surrounding environment that might be affected. The plan also includes a Post-Emergency Recovery Plan which outlines procedures to follow with regards to Public Affairs, Incident Reporting and Incident Closure and Investigation Protocol.

The primary purpose of the procedure is to protect people on site and in the surrounding community. Secondary objectives of the procedure are to minimise

any impacts to the environment, to protect property and operations, and to establish procedures that enable personnel to report and respond to emergencies.

The procedure will be reviewed and amended as required annually for any of the following:

- Changes to the emergency system;
- Updates to emergency response procedure;
- Changes in applicable regulations (refer to register of legislation);
- Facility changes in design, construction, operation or maintenance that would affect; planned emergency routes, the risk of fire/explosion or the risk of hazardous materials release or spill; and
- Post emergency and drill review.

It should be noted that the proposed facility will operate 24/7, 365 days a year. There is therefore no additional specific procedure required for emergencies outside normal working hours.

7.2 Hazard Identification and Risk Assessment Procedure

The procedure ensures all significant hazards in the workplace are identified and assessed in a systematic way and appropriate control measures are implemented to eliminate or reduce the risk to the lowest level in so far as is reasonably practicable.

The Risk Assessment process is a matrix method, which uses a quantitative process to determine the Risk Index for the hazard identified. The Risk Index number is then translated into the Qualitative method whereby the risk is described in terms of Risk Ranking and Priority. A number is assigned as per the probability and severity of the hazard and control measures are assigned. Control measures from risk assessments are managed as action plans. The risk level must be amended to account for the change in risk when control measures are implemented.

All Risk Assessments are recorded and controlled by the EHS department. Hazards and risks are communicated to all relevant persons and further information and training given as necessary. Risk Assessments are reviewed if there has been an accident relating to the area or type of work and for other possible reasons to suspect the risk assessment is no longer valid.

7.3 Security Procedures

The Security Procedure defines security operations at the AbbVie facility including security management, access, personnel roles and their responsibilities. It applies to all new hires, employees, visitors and contractors at the Ballytivnan site. The procedure gives details of the security steps to be followed with regard to:

- New Hires/Approved Embedded Contractors;
- Visitors –Short-term onsite visiting;
- Employees/Approved Embedded Contractors;
- Amending Existing Badges;

- Departures/Dismissals/Terminations;
- Camera Passes;
- Security Personnel: Unauthorized Access and Intrusion Management Guidelines; and
- Deliveries–Heavy Goods Vehicle (HGV)and Parcel Delivery Contractor.

7.4 Energy Policy

The Energy Policy at the AbbVie facility incorporates a strong energy management program which includes a systematic approach involving:

- Setting long term emissions reduction targets;
- Driving short term and long-term energy efficiency improvements;
- Incorporating energy efficient design into the construction of new buildings and facilities;
- Partnering with key suppliers and vendors on emissions reduction improvements;
- Promoting energy efficiency within the vehicle fleet; and
- Implementing renewable energy projects.

The policy applies to all employees, visitors and contractors that influence or impact the use, procurement or conservation of energy. This policy is fully endorsed by AbbVie management and establishes a global framework to manage greenhouse gas emissions from its operations.

8.0 ALTERNATIVES

In terms of alternative methods for the manufacture of bio-chemical pharmaceutical products, there are two options available. The first uses fixed stainless-steel vessels whilst the second option is an emerging trend using single use bag technology.

Fixed vessels will be used for the conjugation vessels only. The use of stainless steel vessels means the equipment will continue to be used for the production batches. The production equipment therefore requires cleaning after each batch is manufactured. For small batch processes this option tends to be expensive and therefore is only proposed to be used for conjugation due to the larger volume of material used during this stage.

Single use technology reduces the need for cleaning. It is also more flexible and allows the process to be reconfigured to allow for the introduction of new products or technologies. AbbVie plan to use single use technology for buffer and media preparation, production, and chromatography columns.

The process is constrained by Good Management Practice (GMP) regulations and as such there is limited opportunity for alternative processes. However, the facility has been designed to conform with best industrial practice for a high-containment facility.