# Attachment D.1

# Operational Information Requirements

## Attachment No. D1. Operational Information

### D1.A. Review of Site Activities

Forest Laboratories Limited is comprised of 3 no. Buildings within the Clonshaugh Industrial Estate; Building 1 and Building 2, both of which are FDA approved. In addition Forest Laboratories has ownership of a third Building, Building 3 within the industrial estate. Building 3 is a vacant site which has no buildings. The overall location plan (DG0001), which includes the site boundaries for each building, is included in **Attachment C**.

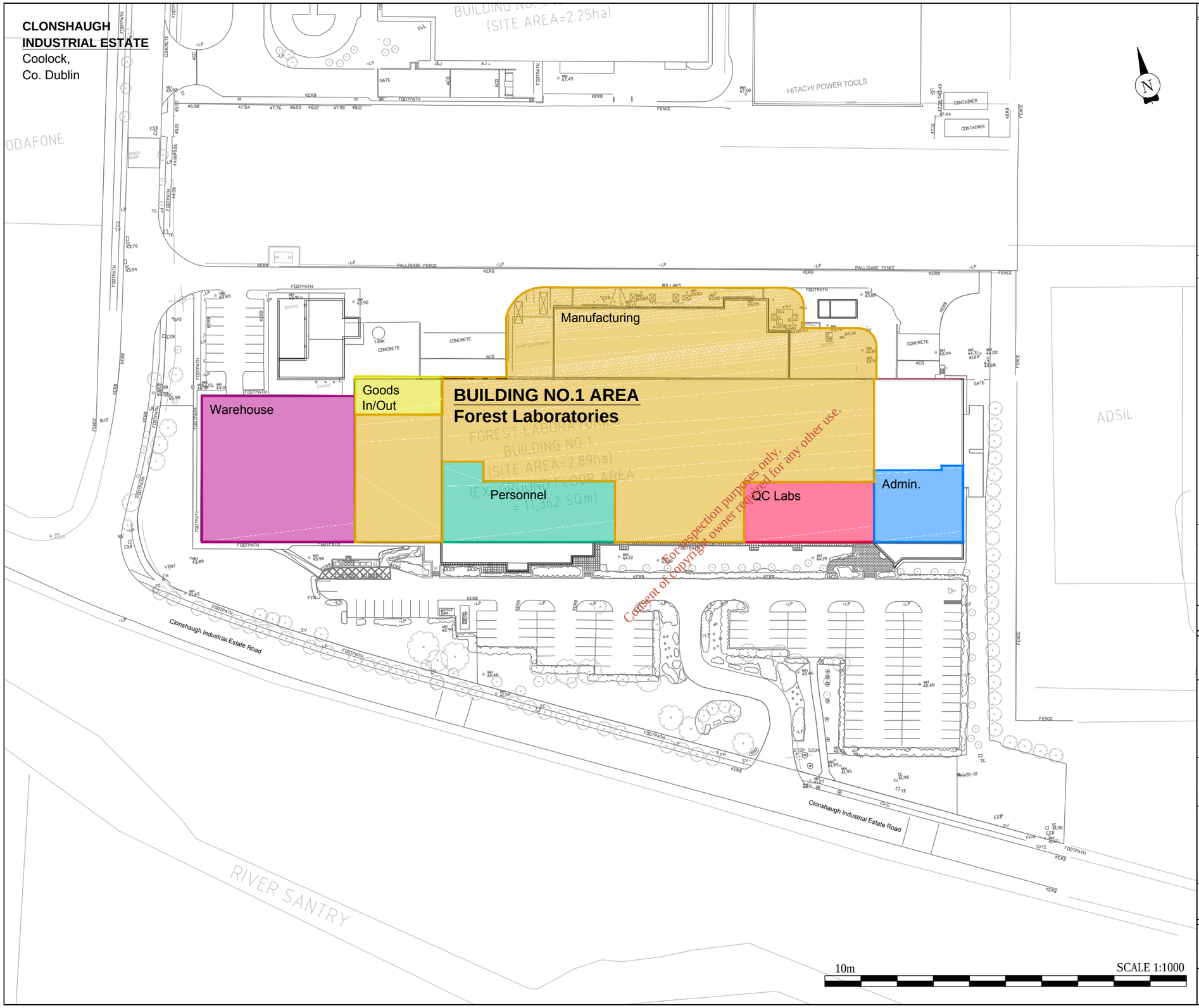
The original plant; Building No. 1, which had its planning permission granted in 1978 at the Clonshaugh Industrial Estate, was occupied by Forest Laboratories in 1994 for the production of pharmaceutical products in the form of tablets and capsules. Planning permission for a change in use from an existing factory to pharmaceutical manufacturing along with internal refurbishment and storage extension was submitted in 1993 along with an Environmental Impact Statement (EIS), which was requested by Dublin Corporation. A number of expansions have occurred since then.

The second plant, Building No. 2 is located to the northwest of Building 1 in the Industrial Estate. Dublin City Council granted planning permission to Forest Laboratories for the change of use of an existing industrial facility to a pharmaceutical processing Building in 2005 (Ref: 1457/05).

Details of planning permissions are presented in **Attachment B.5**.

The activities at both sites comprise of weighing, mixing, granulation, coating and tabletting. The operations at both sites are physical/mechanical and involve no chemical synthesis. The operational areas which illustrate the demarcation of areas for Building 1 and Building 2 are outlined in Drawing DG1000 and DG2000 respectively, which is included in this attachment.

**CLONSHAUGH INDUSTRIAL ESTATE**
Coolock,
Co. Dublin






## NOTES

1. Verifying Dimensions.
   The contractor shall verify dimensions against such other drawings or site conditions as pertain to this part of the work.
2. Existing Services.
   Any information concerning the location of existing services indicated on this drawing is intended for general guidance only. It shall be the responsibility of the contractor to determine and verify the exact horizontal and vertical alignment of all cables, pipes, etc. (both underground and overhead) before work commences.
3. Issue of Drawings.
   Hard copies, dwf and pdf will form a controlled issue of the drawing. All other formats (dwg, dxf etc.) are deemed to be an uncontrolled issue and any work carried out based on these files is at the recipients own risk. RPS will not accept any responsibility for any errors arising from the use of these files, either by human error by the recipient, listing of un-dimensioned measurements, compatibility issues with the recipient's software, and any errors arising when these files are used to aid the recipients drawing production, or setting out on site.
4. Datum: Ordnance Survey Datum, Malin Head

## KEY - Service Area Demarcation (B1)

- Goods In/Out
- Administration
- Manufacturing
- Personnel
- QC Labs
- Warehouse



| No. | Date | Dm. | Chk. | Amendment / Issue | App |
|---|---|---|---|---|---|
| F01 | Nov.'13 | DB | CR | Final Issue | PC |

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Forest Laboratories Ireland Limited

Project
IPCC Licence Implementation

Title
BUILDING No.1 -
Layout & Service Areas Demarcation

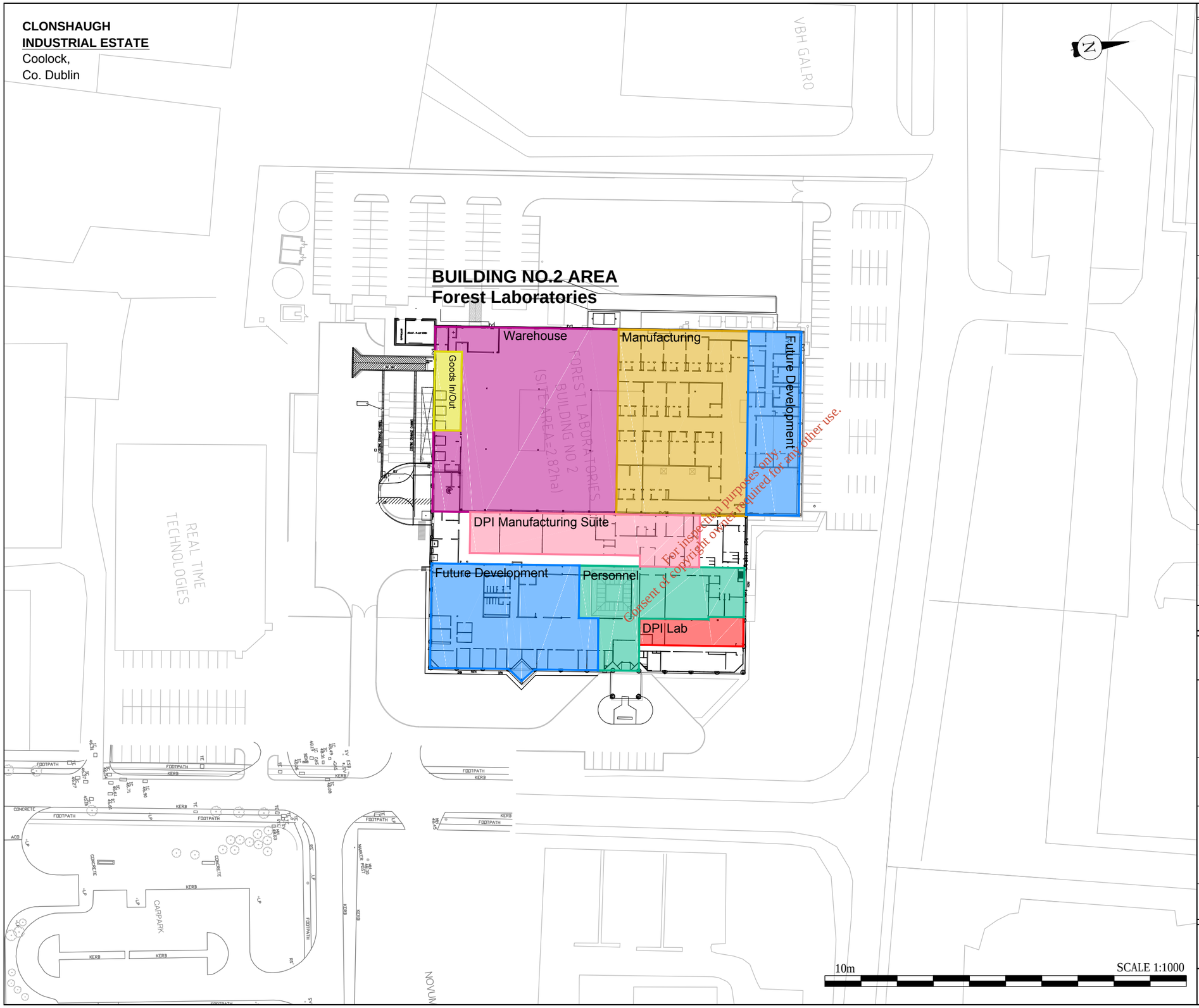
| Drawing Status | Sheet Size | Drawing Scale |
|---|---|---|
| Final Issue | A3 | 1:1,000 @ A3 |

| Drawing Number | Rev |
|---|---|
| MDE0977/DG1000 | F01 |

| Drawn By | Checked By | Approved By | Date |
|---|---|---|---|
| D. Byrne | C. Reilly | P. Chadwick | Nov. '13 |

MDE0977DG1000F01.dwg

**CLONSHAUGH**
**INDUSTRIAL ESTATE**
Coolock,
Co. Dublin






## NOTES

1. Verifying Dimensions.
The contractor shall verify dimensions against such other drawings or site conditions as pertain to this part of the work.

2. Existing Services.
Any information concerning the location of existing services indicated on this drawing is intended for general guidance only. It shall be the responsibility of the contractor to determine and verify the exact horizontal and vertical alignment of all cables, pipes, etc. (both underground and overhead) before work commences.

3. Issue of Drawings.
Hard copies, dwf and pdf will form a controlled issue of the drawing. All other formats (dwg, dxf etc.) are deemed to be an uncontrolled issue and any work carried out based on these files is at the recipients own risk. RPS will not accept any responsibility for any errors arising from the use of these files, either by human error by the recipient, listing of un-dimensioned measurements, compatibility issues with the recipient's software, and any errors arising when these files are used to aid the recipients drawing production, or setting out on site.

4. Datum: Ordnance Survey Datum, Malin Head

**KEY - Service Area Demarcation (B1)**

- Goods In/Out
- DPI Manufacturing Suite
- Manufacturing
- Personnel
- DPI Laboratory
- Warehouse
- Future Development



| No. | Date | | Amendment / Issue | App |
|---|---|---|---|---|
| F01 | Nov.'13 | DB CR | Final Issue | PC |

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Client
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Project
IPCC Licence Implementation

Title
BUILDING No.2 -
Layout & Service Areas Demarcation

| Drawing Status | Sheet Size | Drawing Scale |
|---|---|---|
| Final Issue | A3 | 1:1,000 @ A3 |

| Drawing Number | Rev |
|---|---|
| MDE0977/DG2000 | F01 |

| Drawn By | Checked By | Approved By | Date |
|---|---|---|---|
| D. Byrne | C. Reilly | P. Chadwick | Nov. '13 |

MDE0977DG2000F01.dwg

**D1.B. Process Unit Operations**

The following table presents a description of the various process unit operations, aspects of these operations that cause emissions and process control.

All process operations are conducted in strict compliance with Good Manufacturing Practice (GMP). Good Manufacturing Practice is that part of Quality Assurance which ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the product specification or the relevant regulatory bodies e.g. FDA or IMB.

Standard Operating Procedures are followed for each stage of every batch of product and records are kept for all critical parameters e.g. Batch Manufacturing Records (BMR's).

| Process Description | Emissions | Control |
|---|---|---|
| **1. Weighing of Raw Materials**<br>Raw materials are dispensed and weighed within designated rooms using calibrated scales. All materials usage is recorded using ERP software (SAP). | ▪ All process rooms are supplied with conditioned and filtered air, which exhausts to atmosphere via extraction systems with integrated high-efficiency filters.<br>▪ Spillages of powder do occur occassionally.<br>▪ Floors and walls are regularly washed | ▪ When in use, a relative negative pressure is maintained within all process rooms to ensure that any airborne contamination is contained within the room. All room air passes through hepa filters. In the event of a power loss or failure of equipment, all operations stop.<br>▪ Powder spillages are cleaned with a vacuum cleaner. Dry waste is stored and later sent out for incineration.<br>▪ Floor washings are released into the process drains which feed into the effluent mixing tank. (The pH of water effluent is monitored and controlled. Samples of effluent are analysed every month) |
| **2. Blending of Raw Materials**<br>Blending is done in designated process rooms using one of two types of equipment:<br>▪ Y-cone blenders (10 cu.ft or 20 cu.ft)<br>▪ Matcon IBC blender using 2,000-litre IBCs | ▪ All process rooms are supplied with conditioned and filtered air, which exhausts to atmosphere via extraction systems with integrated high-efficiency filters.<br>▪ Spillages of powder do occur occassionally.<br>▪ Floors and walls are regularly washed. | ▪ Powder spillages are cleaned with a vacuum cleaner. Dry waste is stored and later sent out for incineration.<br>▪ Floor washings are released into the process drains which feed into the effluent mixing tank. |
| **3. Milling & Sieving**<br>Milling may be carried out at various stages of processes using either:<br>▪ Russell Finex sieve<br>▪ Frewitt oscillating mill<br>▪ Cone mill<br>The purpose of this step is to remove any foreign | ▪ All process rooms are supplied with conditioned and filtered air, which exhausts to atmosphere via extraction systems with integrated high-efficiency filters.<br>▪ Spillages of powder do occur occassionally.<br>▪ Floors and walls are regularly washed. | ▪ Powder spillages are cleaned with a vacuum cleaner. Dry waste is stored and later sent out for incineration.<br>▪ Floor washings are released into the process drains which feed into the effluent mixing tank. |

| Process Description | Emissions | Control |
|---|---|---|
| material or lumps and to ensure the product is of a consistent particle size.<br><br>Different mesh/sieve sizes are used depending on the product.<br><br>Mills and sieves are usually mobile equipment but are always used within a designated process room. | | |
| **4. Granulation**<br><br>Some processes require that the ingredients are granulated to allow compression into tablets.<br><br>This may be done in one of two ways, depending on the product:<br>▪ A High Shear Mixer Granulator (HSMG) in which powders are dry-mixed before a granulation solution is added to create a moist sludge.<br>▪ Inside a Fluid Bed Drier in which the granulation solution is sprayed on the fluidized powders. (see below)<br><br>A HSMG is a chamber with a top-opening lid in which there is bottom-entry agitator and a high speed side-entry agitator. The solution used is always aqueous-based. No solvent-based solutions are used. While the operation is largely enclosed there may be some dust emissions during loading or discharge. These are captured using local exhaust. This equipment is used in conjunction with a fluid bed drier and is used in the same process room. | ▪ All granulation is carried out in equipment installed in process rooms.<br>▪ All process rooms are supplied with conditioned and filtered air, which exhausts to atmosphere via extraction systems with integrated high-efficiency filters.<br>▪ Spillages of powder do occur occassionally. | ▪ Powder spillages are cleaned with a vacuum cleaner. Dry waste is stored and later sent out for incineration.<br>▪ Floor washings are released into the process drains which feed into the effluent mixing tank.<br>▪ Any non-aqueous emissions are exhausted through the local exhaust and are not treated. |

| Process Description | Emissions | Control |
|---|---|---|
| There are three HSMGs installed at Forest Laboratories. | | |

| Process Description | Emissions | Control |
|---|---|---|
| **5. Fluid Bed Drying**<br><br>Fluid bed driers (FBD) are used in one of three ways:<br>▪ To dry a wet granulation mix from a HSMG<br>▪ To granulate a powder mix, as in #4 above, and dry the granulation at the same time<br>▪ To produce beads coated with active ingredients and other materials ('Wurster' process). These are usually controlled-release products that are later filled into capsules.<br><br>The equipment consists of a central chamber into which the materials are placed. Conditioned air is forced through the bed of materials causing it to fluidise and dry. The exhaust air passes through a filter above the chamber and later through additional finer filters to remove any dust before exhausting to atmosphere.<br><br>If the solvent used is not water, further treatment may be required using a Regenerative Thermal Oxidiser (RTO – Emission Point A2-20).<br><br>There are five Fluid Bed Driers at Forest:<br>▪ Fluid Air 0300 (Emission Point A3-22)<br>▪ Fluid Air 0500 (Emission Point A3-23)<br>▪ Glatt 120 (Emission Point A3-21)<br>▪ Glatt 120 (Emission Point A3-24)<br>▪ Glatt 120 (Emission Point A3-19) | ▪ All drying/granulation is carried out in equipment installed in process rooms.<br>▪ All process rooms are supplied with conditioned and filtered air, which exhausts to atmosphere via extraction systems with integrated high-efficiency filters.<br>▪ Spillages of powder may occur occassionally.<br>▪ Floors and walls are regularly washed.<br>▪ Air is exhausted from the air handling equipment associated with the FBDs.<br>▪ A non-aqueous solvent (ethanol) may be used to dissolve the ingredients used in the process (this is limited to one of the Glatt 120 machines (Emission Point A2-21). | ▪ Powder spillages are cleaned with a vacuum cleaner. Dry waste is stored and later sent out for incineration.<br>▪ Floor washings are released into the process drains which feed into the effluent mixing tank.<br>▪ The exhaust air from the process passes through high efficiency filters to remove any dust before exhausting to the atmosphere.<br>▪ As Ethanol emissions are in excess of 10 tonnes per annum a Regenerative Thermal Oxidiser (RTO) has been installed to treat this emission. |

| Process Description | Emissions | Control |
|---|---|---|
| **6. Compression**<br>Tablets are produced by compressing blended materials on one of a variety of compression machines:<br>▪ Manesty Rotapress (3 no.)<br>▪ Manesty Xpress (3 no.)<br>▪ Korsch XL400 (2 no.)<br>Each type of tablet differs in dimensions, weight and logo imprinted on the surface. | ▪ All compression is carried out in equipment installed in process rooms.<br>▪ All process rooms are supplied with conditioned and filtered air, which exhausts to atmosphere via extraction systems with integrated high-efficiency filters.<br>▪ Some dust is generated on the machine during the compression process.<br>▪ Spillages of powder may occur occassionally.<br>▪ Floors and walls are regularly washed. | ▪ Dust from the machines is drawn off by central dust extractors and captured by the filtration system. This is later removed from the dust extractors as solid waste and sent out for incineration.<br>▪ Powder spillages are cleaned with a vacuum cleaner.<br>Dry waste is stored and later sent out for incineration.<br>▪ Floor washings are released into the process drains which feed into the effluent mixing tank. |
| **7. Encapsulation**<br>Some products (powders and beads) are filled into gelatin capsules using specific filling machines:<br>▪ Bosch GKF 701 encapsulator<br>▪ Bosch GKF1400 encapsulator<br>▪ Bosch GKF 2500 (3 no.) | ▪ All encapsulation is carried out in equipment installed in process rooms.<br>▪ All process rooms are supplied with conditioned and filtered air, which exhausts to atmosphere via extraction systems with integrated high-efficiency filters.<br>▪ Spillages of powder may occur.<br>▪ Floors and walls are regularly washed. | ▪ Powder spillages are cleaned with a vacuum cleaner. Dry waste is stored and later sent out for incineration.<br>▪ Floor washings are released into the process drains which feed into the effluent mixing tank. |
| **8. Film Coating**<br>In some cases tablets are coated with a thin film to protect the tablet and give it a colour. This is done by spraying an aqueous dispersion on to the tablet cores while they rotate inside an enclosed drum.<br>The drum is perforated to allow conditioned air to pass through and dry the tablets as they are | ▪ All coating is carried out in equipment installed in process rooms.<br>▪ All process rooms are supplied with conditioned and filtered air, which exhausts to atmosphere via extraction systems with integrated high-efficiency filters. | ▪ Powder spillages are cleaned with a vacuum cleaner. Dry waste is stored and later sent out for incineration.<br>▪ Floor washings are released into the process drains which feed into the effluent mixing tank.<br>▪ The exhaust air from the process passes |

| Process Description | Emissions | Control |
|---|---|---|
| sprayed.<br>This process is carried out using:<br>▪ Manesty XL cota 300 (6 no.)<br>▪ Manesty Accelacota 150 (1 no.) | ▪ Spillages of powder or film-coat dispersion may occur occassionally.<br>▪ Air is exhausted from the air handling equipment associated with the film coaters. | through filters to remove any dust before exhausting to the atmosphere.<br>▪ (Non-aqueous solvents are not used.) |
| **9. Powder Conditioning**<br>A dedicated conditioning chamber is used to alter the moisture content of Hydroxy Propyl Methyl Cellulose (HPMC). The HPMC powder is layered on to trays and placed inside the chamber where it is exposed to warm and moist air for an extended time. It is later dried to remove excess moisture. The powder is blended and weighed into drums for export. | ▪ All coating is carried out in equipment installed in process rooms.<br>▪ All process rooms are supplied with conditioned and filtered air, which exhausts to atmosphere via extraction systems with integrated high-efficiency filters.<br>▪ Spillages of powder may occur occassionally.<br>▪ Floors and walls are regularly washed.<br>▪ Air is exhausted from the conditioning chamber. | ▪ Powder spillages are cleaned with a vacuum cleaner. Dry waste is stored and later sent out for incineration.<br>▪ Floor washings are released into the process drains which feed into the effluent mixing tank.<br>▪ Air from the conditioning chamber does not contain any dust. |
| **10. Dry Powder Inhaler Production**<br>Dedicated production equipment within a dedicated suite of rooms is used to manufacture dry powder inhaler (DPI) devices. The suite of rooms is maintained as a Class D cleanroom with restricted access.<br>Powders are weighed within a self-contained weigh booth (no emissions) and blended and sieved in dedicated equipment. The blend is filled into cartridges, which are then placed in devices on a custom-built filling and packaging line. | ▪ All DPI production is carried out in equipment installed in process rooms.<br>▪ All process rooms are supplied with conditioned and filtered air, which exhausts to atmosphere via extraction systems with integrated high-efficiency filters.<br>▪ Spillages of powder may occur occassionally.<br>▪ Floors and walls are regularly washed.<br>▪ Some air is exhausted from the air handling equipment. | ▪ While all other process rooms have a relative negative pressure, this suite of rooms requires a cascade of relatively higher pressures keep contamination out and achieve Cleanroom status.<br>▪ Powder spillages are cleaned with a vacuum cleaner. Dry waste is stored and later sent out for incineration.<br>▪ Floor washings are released into the process drains which feed into the effluent mixing tank.<br>▪ Room air passes through HEPA filters. |

The following commercial products are produced at the facilities:

- Lexapro (Antidepressant);
- Namenda (Alzheimer's);
- Bystolic (Hypertension);
- Savella -Milnacipran (Fibromyalgia)
- Celexa (Antidepressant)
- Fetzima (Antidepressant)
- Linzess (Irritable Bowel Syndrome), and
- Tudorza (COPD).

**Plant utilities**

Site utilities are as follows:

- Mains water (Dublin City Council)
- Natural Gas (Bord Gais)
- Electricity (Electricity Supply Board)

**D1.B.1 Lexapro**

Lexapro is a central nervous system product; an antidepressant used to treat major depressive disorder and generalized anxiety disorder. The active ingredient is Escitalopram Oxalate. Lexapro is produced in three tablet strengths – 5mg, 10mg and 20mg.

Raw materials are weighed and are then passed through a sieve using a vacuum transfer system and mixed together in a blender. The blend is compressed into tablet cores on a Manesty Rotapress or Xpress (10mg and 20mg) compression machine.

The tablet cores are film coated in an Accelacota 150 (5mg) or an Accelacota 300 (10mg and 20mg). The film coating process uses an aqueous solution.

**Emissions to Environment**

| Emission Type | Description |
|---|---|
| Solid Waste | Paper, cardboard from packaging sent-off for recycling. |
| | General waste sent to landfill. |
| | Contaminated PPE, waste batches etc. collected by licensed waste contractor. |
| Emissions to Air | The air handling units are either<br>▪ supply only, with separate filtered exhausts through dedicated fans, or filtered Dust Extract Units,<br>▪ supply/return air units with mixing/spill air sections as appropriate to the area being served, and exhausting through filtered fan units. |
| Emissions to Process Drain | Wash waters arising from process are sent to the process drain |

**D1.B.2 Namenda**

Namenda is also a central nervous system product; for the treatment of Alzheimer's disease. The active ingredient is Memantine Hydrochloride. Namenda is produced for oral administration in two tablet strengths - 5mg and 10mg. The tablets are capsule shaped and are film-coated.

The tablets also contain the following inactive ingredients: microcrystalline cellulose/colloidal silicon dioxide, talc, croscarmellose sodium, and magnesium stearate.

The raw materials are weighed, and after weighing are passed through a sieve using a vacuum transfer system and mixed together in a blender.

The blend is compressed into tablet cores on a Manesty Rotapress or Xpress (10mg) compression machine.

The tablet cores are film coated in a Manesty Accelacota 300. The film coating process uses an aqueous solution.

**Emissions to Environment**

| Emission Type | Description |
|---|---|
| Solid Waste | Paper, cardboard from packaging sent-off for recycling. |
| | General waste sent to landfill. |
| | Contaminated PPE, waste batches etc. collected by licensed waste contractor. |
| Emissions to Air | The air handling units are either<br>▪ supply only, with separate filtered exhausts through dedicated fans, or filtered Dust Extract Units,<br>▪ supply/return air units with mixing/spill air sections as appropriate to the area being served, and exhausting through filtered fan units. |
| Emissions to Process Drain | Wash waters arising from process are sent to the process drain |

### D1.B.3 Bystolic

Bystolic is a cardiovascular product used for the treatment of hypertension. The active ingredient is Nebivolol Hydrochloride. Bystolic is available as tablets for oral administration, with four tablet strengths - 2.5mg, 5mg, 10mg and 20mg.

The tablets are triangular shaped, biconvex, and are differentiated by colour and imprinted on one side and the number of mg (tablet strength) on the other side.

The tablets contain the following inactive ingredients: colloidal silicon dioxide, croscarmellose sodium, D&C Red #27 lake, FD&C Blue #2 lake, FD&C Yellow #6 lake, hypromellose, lactose monohydrate, magnesium stearate, microcrystalline cellulose, pregelatinized starch, polysorbate 80 and sodium lauryl sulphate.

Raw materials are weighted and then are milled with a Quadro Comil U20 cone mill and pre-blended prior to granulation.

An aqueous granulation solution is made up in a stainless steel vessel.

The product is granulated and dried using a top-spray process in a Fluid Air 0500 fluid bed drier (5mg) or a Fluid Air 0300 fluid bed drier (other strengths). The dried granulate is passed through a Quadro Comil cone mill model U20 or U30. The granulate and additional raw materials are passed through a Russell Finex screen using a vacuum transfer system and then blended. The final blend is compressed into tablet cores on a Manesty Rotapress compression machine.



**Emissions to Environment**

| Emission Type | Description |
|---|---|
| Solid Waste | Paper, cardboard from packaging sent-off for recycling. |
| | General waste sent to landfill. |
| | Contaminated PPE, waste batches etc. collected by licensed waste contractor. |
| Emissions to Air | The air handling units are either<br>▪ supply only, with separate filtered exhausts through dedicated fans, or filtered Dust Extract Units,<br>▪ supply/return air units with mixing/spill air sections as appropriate to the area being served, and exhausting through filtered fan units. |
| Emissions to Process Drain | Wash waters arising from process are sent to the process drain |

**D1.B.4 Savella**

Savella is central nervous system product for the treatment of Fibromyalgia. The active ingredient in Savella is Milnacipran Hydrochloride. Savella is available for oral administration as film-coated tablets containing 12.5mg, 25mg, 50mg and 100mg milnacipran hydrochloride.

Each tablet also contains dibasic calcium phosphate, povidone, carboxymethylcellulose calcium, colloidal silicon dioxide, magnesium stearate and talc as inactive ingredients.

Raw materials are weighed and then are added to a GEA Aeromatic-Fielder PMA 800 high shear granulator and granulated with an aqueous solution. The wet granulation is passed through a Frewitt mill and dried in a Fluid Air 0500 fluid bed drier.

The dried granulation is milled through a Quadro Comil model U20 or U30 cone mill. The milled granulate and additional raw materials are mixed in a blender.

The blend is compressed into tablet cores on a Manesty Rotapress (50mg and 100mg) compression machine.

The tablet cores are film coated in a Manesty Accelacota 150 (12.5mg and 25mg) or an Accelacota 300 (50mg and 100mg). The film coating process uses an aqueous solution.

**Emissions to Environment**

| **Emission Type** | **Description** |
|---|---|
| Solid Waste | Paper, cardboard from packaging sent-off for recycling. |
| | General waste sent to landfill. |
| | Contaminated PPE, waste batches etc. collected by licensed waste contractor. |
| Emissions to Air | The air handling units are either<br>▪ supply only, with separate filtered exhausts through dedicated fans, or filtered Dust Extract Units,<br>▪ supply/return air units with mixing/spill air sections as appropriate to the area being served, and exhausting through filtered fan units. |
| Emissions to Process Drain | Wash waters arising from process are sent to the process drain |

**D1.B.5 Celexa**

Celexa is a central nervous system product used for the treatment of depression. The active ingredient of this antidepressant is Citalopram Hydrobromide (HBr). Celexa is produced in three tablet strengths – 10mg, 20mg, and 40mg.

The tablets also contain the following inactive ingredients: copolyvidone, corn starch, crosscarmellose sodium, glycerin, lactose monohydrate, magnesium stearate, hypromellose, microcrystalline cellulose, polyethylene glycol, and titanium dioxide. Iron oxides are used as coloring agents in the beige (10 mg) and pink (20 mg) tablets.

Raw materials are first weighted. The materials are added to a GEA Aeromatic-Fielder high shear granulator and granulated with an aqueous solution.

The wet granulation is passed through a Frewitt mill and dried in a Fluid Air model 0300 (10mg and 40mg) or model 0500 (20mg) fluid bed drier.

The dried granulation is milled through a Frewitt mill blender.

After blending with additional materials, the blend is compressed into tablet cores on a Manesty Rotapress (20mg) compression machine.

The tablet cores are film coated in a Manesty Accelacota 150 (10mg) or an Accelacota 300 (20mg and 40mg). The film coating process uses an aqueous solution.



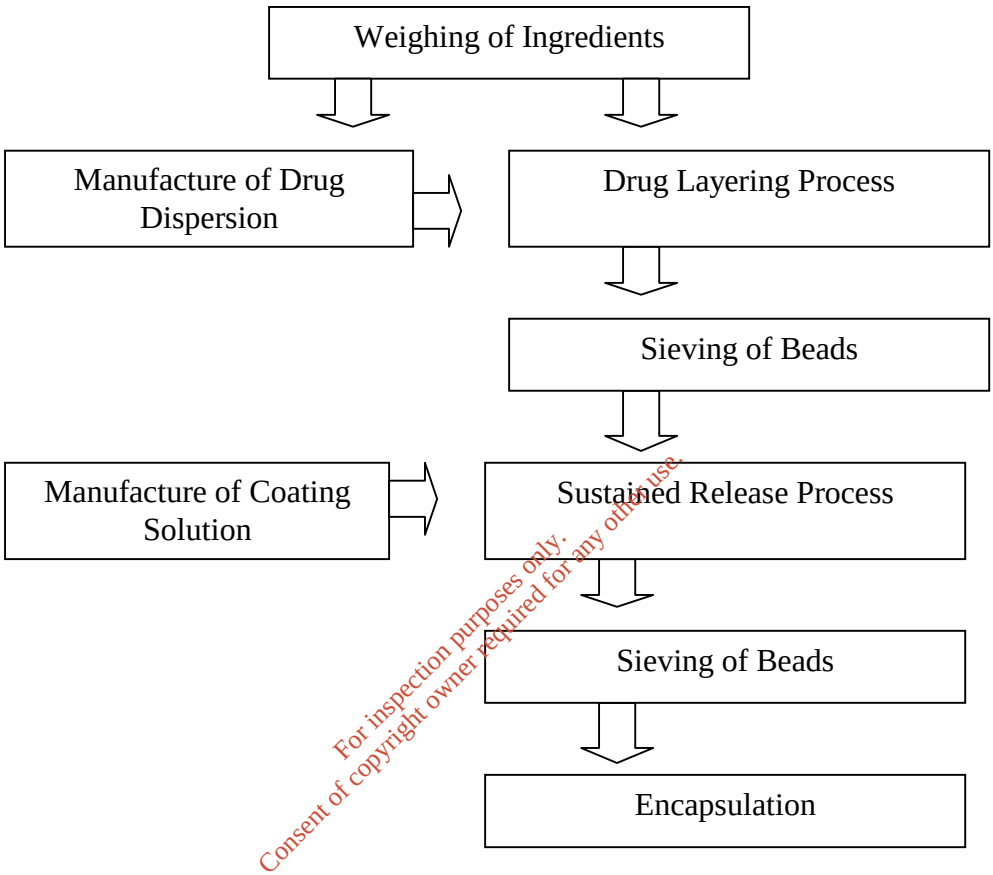
**Emissions to Environment**

| **Emission Type** | **Description** |
|---|---|
| Solid Waste | Paper, cardboard from packaging sent-off for recycling. |
| | General waste sent to landfill. |
| | Contaminated PPE, waste batches etc. collected by licensed waste contractor. |
| Emissions to Air | The air handling units are either<br>▪ supply only, with separate filtered exhausts through dedicated fans, or filtered Dust Extract Units,<br>▪ supply/return air units with mixing/spill air sections as appropriate to the area being served, and exhausting through filtered fan units. |
| Emissions to Process Drain | Wash waters arising from process are sent to the process drain |

**D1.B.6 Fetzima**

Levomilnacipran is an antidepressant and the active ingredient is Milnacipran Hydrochloride. It is produced in one common bead strength and filled into four capsule strengths.

Figure 1 below outlines the Levomilnacipran Capsule Process Flow.






The manufacturing process consists of the mixing of pharmaceutical ingredients with ethanol in a sealed vessel, and the mixed solution is then sprayed onto sugar spheres. On completion of the spraying, the waste ethanol will be emitted through the Regenerative Thermal Oxidiser (A2-20).

Sugar spheres are coated and dried in a Glatt 120 fluid bed drier using a Wurster process. All of the ethanol is dried off the beads. The dry beads are then sieved through a Russell Finex sieve.

A coating solution is manufactured using 372kg of Ethanol USP.

The sieved beads are re-loaded into the Glatt 120 fluid bed drier and the coating solution is applied using a Wurster process. All of the ethanol is dried off the beads and the exhaust passed through the RTO before being emitted to the atmosphere.

The dry beads are then sieved once more through a Russell Finex sieve.

The beads are filled into capsules using a Bosch GKF2500 encapsulations machine to produce 20mg, 40mg, 60mg or 80mg capsule strengths.

**Emissions to Environment**

| Emission Type | Description |
|---|---|
| Solid Waste | Paper, cardboard from packaging sent-off for recycling. |
| | General waste sent to landfill. |
| | Contaminated PPE, waste batches etc. collected by licensed waste contractor. |
| Emissions to Air | Potential emissions of ethanol (as TOC) to atmosphere from the RTO.<br>The air handling units are either<br>▪ supply only, with separate filtered exhausts through dedicated fans, or filtered Dust Extract Units,<br>▪ supply/return air units with mixing/spill air sections as appropriate to the area being served, and exhausting through filtered fan units. |
| Emissions to Process Drain | Wash waters arising from process are sent to the process drain |

### D1.B.7 Linzess

Linzess is a product used to treat Irritable Bowel Syndrome and the active ingredient is Linaclotide. It is produced in one common bead strength and filled into 2 capsule strengths.

The manufacturing process consists of the mixing of pharmaceutical ingredients with water in a solution vessel, and the mixed solution is then sprayed onto spheres. The spheres are coated and dried in a Glatt 120 fluid bed drier using a Wurster process. All of the water-based solution is dried off the beads. The dry beads are then sieved through a Russell Finex sieve.

The beads are filled into capsules using a Bosch encapsulation machine to produce 290mcg and 145mcg capsule strengths.

**Emissions to Environment**

| Emission Type | Description |
|---|---|
| Solid Waste | Paper, cardboard from packaging sent-off for recycling. |
| | General waste sent to landfill. |
| | Contaminated PPE, waste batches etc. collected by licensed waste contractor. |
| Emissions to Air | The air handling units are either<br>▪ supply only, with separate filtered exhausts through dedicated fans, or filtered Dust Extract Units,<br>▪ supply/return air units with mixing/spill air sections as appropriate to the area being served, and exhausting through filtered fan units. |
| Emissions to Process Drain | Wash waters arising from process are sent to the process drain |

### D1.B.8 Tudorza

Tudorza is a Dry Powder Inhaler product used to treat Chronic Obstructive Pulmonary Disease and the active ingredient is Aclidinium. It is a powder produced in one common blend strength and filled into a cartridge inside an application inhaler.

The manufacturing process consists of the dispensing and blending of pharmaceutical ingredients in a batch quantity of 80kg, which is then filled into the individual 1 g cartridges on an automatic filling machine. The cartridges are then assembled into the inhaler device, which is then individually packaged into a pouch and carton.

**Emissions to Environment**

| Emission Type | Description |
|---|---|
| Solid Waste | Paper, cardboard from packaging sent-off for recycling. |
| | General waste sent to landfill. |
| | Contaminated PPE, waste batches etc. collected by licensed waste contractor. |
| Emissions to Air | The air handling units are either<br>▪ supply only, with separate filtered exhausts through dedicated fans, or filtered Dust Extract Units,<br>▪ supply/return air units with mixing/spill air sections as appropriate to the area being served, and exhausting through filtered fan units. |
| Emissions to Process Drain | Wash waters arising from process are sent to the process drain |

### D.1.C.1 Ancillary Processes

### D.1.C.1.A Laboratory Activities

The laboratory activities carried out at Forest Laboratories fall under the function of the Quality control (QC) Department. The QC department is responsible for the analytical testing and general laboratory activities.

The role of the laboratory is to carry out chemical testing associated with tablet, capsule and granule manufacture, and testing is carried out at all stages of production:

Raw Material Testing:

Raw materials, consisting of active drugs and excipients, are tested prior to being used in manufacture. Methods may include U.V. Spectrophotometry, IR spectrophotometry, "Wet" chemistry, polarimetry, TLC, HPLC, GLC and particle size analysis.

Finished Product and Stability Testing:

Finished products must be checked for physical and chemical parameters such as dissolution rate and purity and composition before being released for sale. Methods are predominately HPLC and GC.

In-Process Testing:

In-process testing of preset parameters typically physical parameters and potency.

Other laboratory activities include instrument calibration, validation and technical support.



**Emissions to Environment**

| Emission Type | Description |
|---|---|
| Solid Waste | Paper, plastic, cardboard sent off-site for recycling. |
| | General waste sent to landfill |
| | Laboratory glass and vials sent off-site for incineration by approved waste contractor |
| | Expired Chemicals sent off-site for incineration by approved waste contractor. |
| | Any other hazardous waste materials sent off-site for incineration by approved waste contractor, |
| Emissions to Air | Minimal fugitive emissions from chemical use in the laboratory fumehoods. |
| Emissions to Process Drain | Wash waters arising from the laboratory are sent to the process drain. |

### D.1.C.1.B Canteen

The activities of the facility restaurant service comprise of preparing, cooking and serving food, and post service operations such as washing, cleaning.

The canteen facility consists of

- storage room for food storage,
- washroom for cleaning/washing operations,
- preparatory area for food preparation and cooking,
- serving area where food is served
- dining area for food consumption.

**Emissions to Environment**

| Emission Type | Description |
|---|---|
| Solid Waste | Plastic bottles, drink cans, glass, Paper, Cardboard, sent off-site for recycling |
| | General waste such as food waste, contaminated food packaging are sent to landfill |
| | Waste cooking oil is collected in dedicated containers and collected by an approved waste contractor where it is recycled. |
| Emissions to Air | Steam and vapour from ovens, cooking operations. |
| Emissions to Process Drain | Cleaning agents such as diluted detergents and sanitizing agents are sent to drain. |
| | Liquid food wastes are sent to process drain. |

### D.1.D.1 Abatement, Treatment and Control Systems

**Air Abatement**

Air Handling Units within Buildings 1 and 2 provide space heating, cooling and humidity requirements for production and general areas as required. The Air Handling Units are, typically, constant volume units and comprise of steam/LTHW heating batteries, chilled water cooling coils, panel filters, bag filters, supply fan, return air fan, steam humidifier and access sections. The air-handling units are either supply only, with separate exhausts through dedicated fans or through Dust Extract Units, recirculation units or supply/return air units with mixing/spill air sections as appropriate to the area being served.

Powder containment is controlled via the maintenance of room differential pressures with Dust Extract Units (DEU's) capturing any fugitive dust emissions to atmosphere. Dust Extract Units are fitted with EU9 cartridge filters. Filter differential pressures are routinely monitored and changed out as per supplier and equipment manufacturer requirements.

Abatement of process air directly from the production units is through H13 HEPA Filters (Efficiency 99.95%). This includes abatement from the Accelecota, the Glatts and the Fluid Bed Dryers.

**Regenerative Thermal Oxidiser (RTO):**

Since grant of the IPPC licence, Forest Laboratories has developed a process at the facility, involving greater use of the solvent, ethanol, at the plant. In order to minimise the impact of releases of solvent to atmosphere, Forest have abated the emissions through the installation of a Regenerative Thermal Oxidiser (RTO).

The relevant manufacturing process consists of the mixing of pharmaceutical ingredients with ethanol in a sealed vessel. On completion of the mixing, the waste ethanol will be emitted through a thermal oxidiser.

The RTO is installed on the existing Forest Laboratories Building No. 2 site. The RTO discharges through a licensed emission point (A2-20). During the commissioning process in July-August 2013, emissions monitoring for TOC was carried out at the discharge point to verify compliance. This RTO has achieved compliance and a report on the test programme for the RTO has been completed.

A copy of the technical specification for the RTO is included in this attachment. This specification includes a description of the design and a functional description of the RTO system.

## Description of Ecopure®-RTO 3020

### 3.1.4 Design of the Ecopure-RTO system

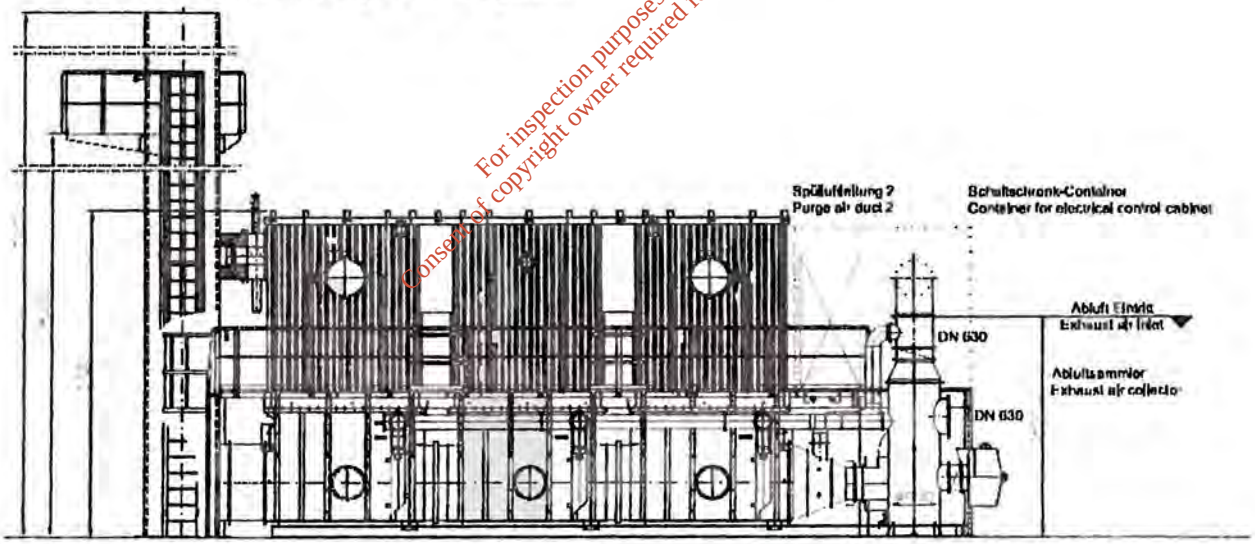
The Ecopure-RTO System which is also referred to as a thermal reactor consists of one compact regenerator column which is divided into three sections in line beside each other. These sections are clad with a multi-layer fire-proof insulation layer corresponding to the high reaction temperatures.
The sections of the column are packed with ceramic packing material which serves as temperature-resistant heat storage elements.

The regenerator sections are interconnected in the upper area by way of a column cover. This cowling serves as combustion chamber; two gas burners are installed on the side. The burners are arranged on the side, while accessible from the grid platform and feature a separate combustion air connection.

The air control system including the crude gas inlet, cleaned gas outlet and purge connection are arranged in the lower area of the column. Each of the column sections is connected by means of a valve box to the crude gas, cleaned gas and purge duct.
One valve box consists of two valve charges with pneumatically operated poppet valves via which the crude gas inlet and the cleaned gas outlet are controlled.



Figure: Design of an Ecopure-RTO system:



### 3.1.5 Functional Description

The exhaust air to be purified comes from the production lines.

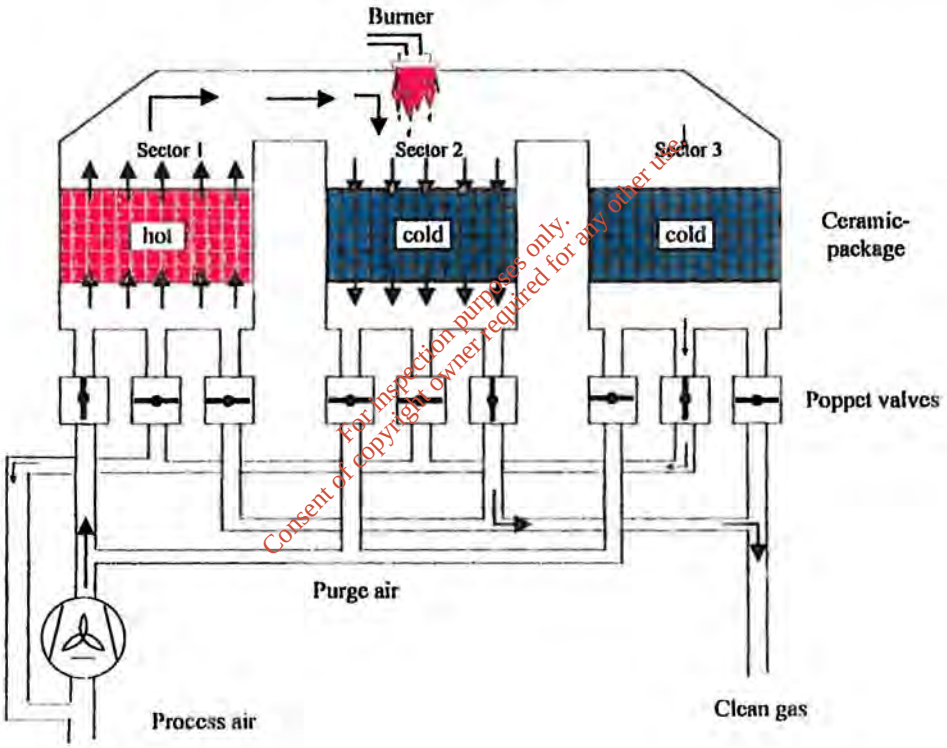
Initially, the burner heat up the cold system in fresh air operation mode until the operating temperature is attained.
The solvent-laden air is drawn in by means of exhaust air fans and routed through the system. During this process, the solvent-laden air is initially drawn through a column sector with hot ceramic material. In this way, the crude gas is heated to a temperature of approx. 780 °C such that the solvent particles begin the oxidation process.
The air is then routed through the column cover, the combustion chamber. Here, the gas burners increase the temperature of the crude gas to approx. 820 °C, thus enabling residual oxidation. As it flows through a second column sector, the hot cleaned air heats up a cold arrangement of ceramic material such that the air is cooled to a temperature of approx. 95 - 120 °C as a result of this heat exchange process.

Fluctuations in the heat produced by the combustion of the pollutants are compensated by the combustion chamber temperature control system. The fuel flow is adapted to current heat requirements in the combustion chamber by means of a control valve.
The temperature in the combustion chamber is recorded by a multi-channel-recorder in the control cabinet.

The exhaust air is heated on the hot ceramic material and the pure gases are cooled on the cold ceramic material in accordance with a defined time cycle since the heat storage elements are cooled down by the solvent-laden air and, in turn, the cold honeycomb blocks absorb the energy from the hot clean air.
When the ceramic material has reached its optimum storage point or a certain temperature, the system switches over between the column sections, i.e. after the cycle time has elapsed, the solvent-laden air flow is switched over by the poppet valve assembly and is allowed to flow through the second regenerator section containing the previously heated storage layers, and the clean air is allowed to flow through the previously cooled ceramic packing of the first column section.

This exhaust air purification system consists of 3 column sectors
As it passes through the hot regenerative heat exchanger, the crude gas reaches a preheating temperature in excess of 780 °C. Depending on the type and concentration of the pollutants, partial thermal oxidation of the hydrocarbons takes place in the centre area of the thermal reactor at the hot contact surfaces of the ceramic elements. The solvent-laden air is then routed into the combustion chamber.
If the energy released during oxidation of the pollutants is not sufficient to ensure complete combustion, the air is heated by the gas burners to above the oxidation temperature of the relevant pollutants. The term autothermic process is used when the energy of the pollutants is sufficient, thus rendering the use of the burners unnecessary.

The pure gas flowing out of the thermal reactor is released into the atmosphere via the stack.



**Emissions to Sewer Abatement**

Process waste from Building No. 1 arises from the cleaning of plant equipment and vessels in the manufacturing area, in addition to laboratory effluent, and blowdown waste from boilers. This Process waste is combined through the piping distribution system and is discharged to a holding tank before discharge to sewer.

In Building No. 1, the holding tank has a capacity of 20,000 $m^3$ with a facility for agitation and pH correction installed to continuously receive process effluent discharged by gravity. The holding tank mixes the treatment tank contents, which is necessary for pH control. The effluent is continuously agitated in the balancing tank by a submersible electric mixer. Agitation helps to reduce the BOD and COD values. A pH probe fitted in the tank controls and monitors the acidity/alkalinity of the effluent by sending a signal to the caustic and acid pumps to dose accordingly to ensure the required specification is maintained.

The Process effluent discharges to a flume fitted with a pH monitor and a sampling pump (Emission point SE1). The treated effluent is sampled using an ISCO 4700 fixed site wastewater sampler, incorporating 4 sample bottles each capable of holding 10 litres. The automatic sampler is operated by a pulse or pulses from the flowmeter depending on flow from the process effluent tank to sewer.

The treated effluent arising at the building is discharged into the local authority sewer, located in the Estate Roadway in Clonshaugh Industrial Estate. Effluent is discharged to the foul drain, which flows easterly to the sanitary authority sewer.

Foul Waste effluent arising from employees will discharge to the main sewer separately process effluent discharge.

Foul and Process effluent discharge both connect to the main sewer line leaving Building 1. The process effluent line joins with the foul drain behind the building near the chemical storage area.



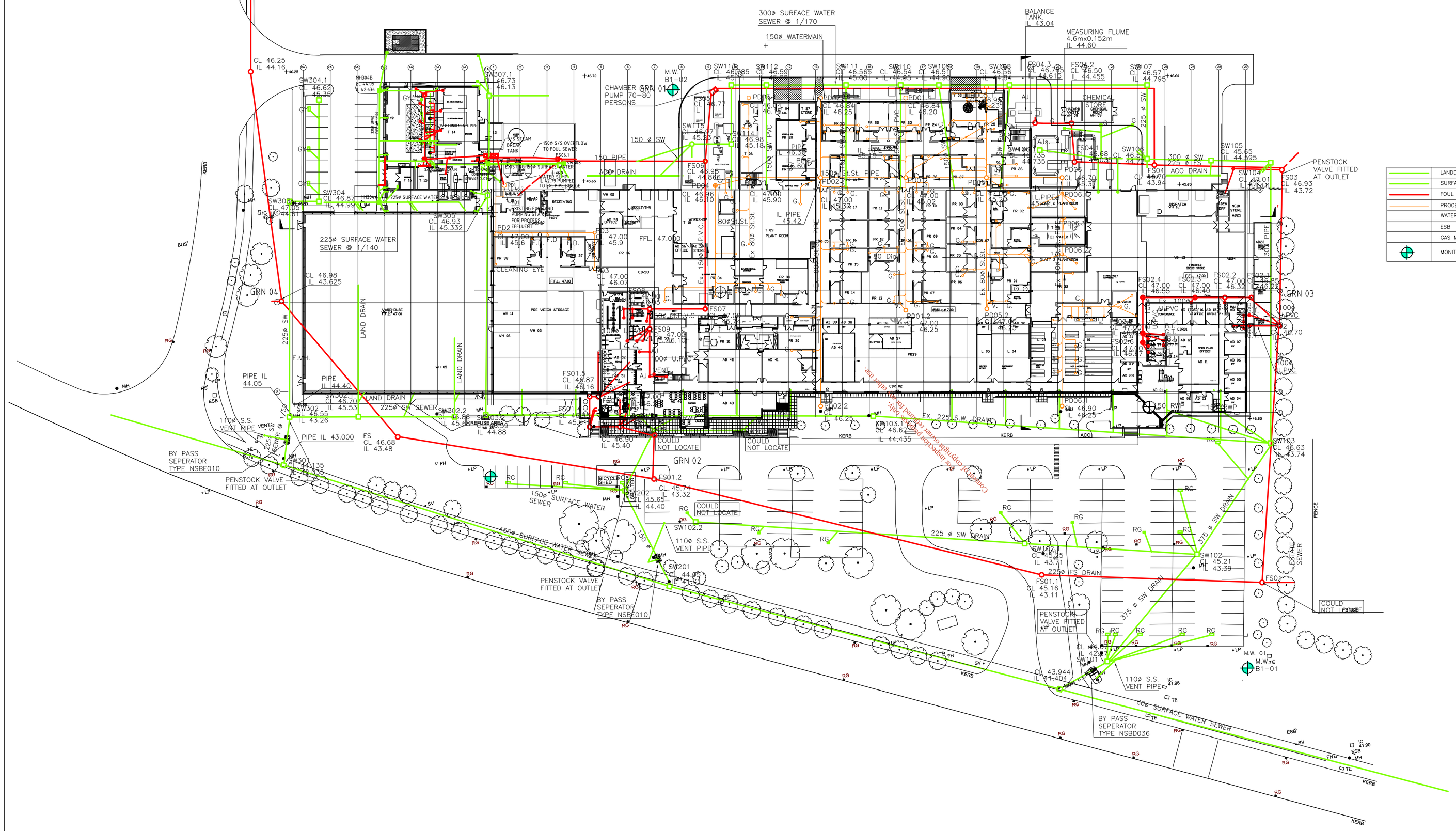
Similarly, in Building No. 2, the process effluent arising from pharmaceutical processes is discharged to a holding tank. This holding tank is located at the rear of the Building No. 2. All process drainage is contained in stainless steel piping and discharged on-site to the holding/balance tank. This holding tank has a capacity of 20,000 $m^3$. A pH probe in the balance tank controls and monitors the acidity/alkalinity of the incoming effluent by sending a signal to the caustic and acid pumps to dose accordingly to ensure the required specification is maintained.

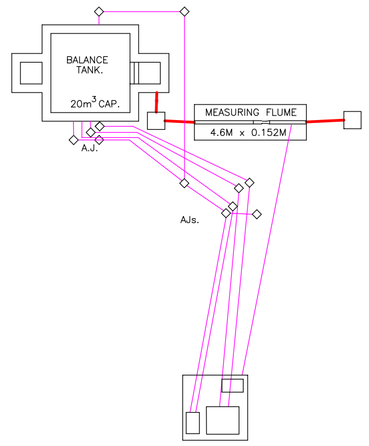
The Process effluent discharges to a flume fitted with a pH monitor and a sampling pump (Emission point SE2). The treated effluent is sampled using an ISCO 4700 fixed site wastewater sampler, incorporating 4 sample bottles each capable of holding 10 litres. The automatic sampler is operated by a pulse or pulses from the flow meter depending on flow from the process effluent tank to sewer.

The drainage layout for Building 1 and Building 2 are included in the attachment in Drawings FLIB1/AR08 and FLIB2/AR08. The drawing illustrates the location of the process drainage, foul sewer and surface water layouts.

NOTES:

1. ALL UTILITY SERVICES SUCH AS GAS, ESB, I.T. ETC. TO BE VERIFIED BY PROVIDERS AND CAREFULLY CHECKED ON SITE




LAYOUT OF PIPES AROUND BALANCE TANK.
(SCALE 1:200)

| Rev: | Description:: | By: | App: | Date: |
|---|---|---|---|---|
| E | GENERAL UPDATE | LLA | LL | 24/09/13 |
| D | GENERAL UPDATE | LLA | LL | 28/02/13 |
| C | INTERCEPTORS ADDED | LLA | LL | 19/12/12 |
| B | GENERAL UPDATE | LLA | LL | 02/11/12 |
| A | ISSUED FOR INFORMATION | LLA | LL | 08/02/12 |

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Project:

Forest Laboratories
Building 1

Title:

Drainage Services Layout

| Drawing Status: | Discipline: | Drg Scale: |
|---|---|---|
| As Built | ARCHITECTURAL | 1:500 @ A1 |

| Drawing Number: | Rev: |
|---|---|
| FLIB1/AR08 | E |

| Date: | Drawn By: | Design By: | Checked By: | Approved By: |
|---|---|---|---|---|
| 16/09/11 | S.C. | S.C. | M.F.D. | L.L. |

NOTES:

| Rev: | Description:: | By: | App: | Date: |
|---|---|---|---|---|
| C | GENERAL UPDATE | LLA | LL | 05/06/13 |
| B | GENERAL UPDATE | LLA | LL | 02/11/12 |
| A | ISSUED FOR INFORMATION | LLA | LL | 08/02/12 |

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Project:
Forest Laboratories
Building 2

Title:
Drainage Layout

| Drawing Status: | Discipline: | Drg Scale: |
|---|---|---|
| As Built | ARCHITECTURAL | 1:250 @ A1 |

Drawing Number: FLIB2 /AR08 Rev: C

| Date: | Drawn By: | Design By: | Checked By: | Approved By: |
|---|---|---|---|---|
| 16/09/11 | S.C. | S.C. | M.F.D. | L.L. |

| | |
|---|---|
| | LANDDRAIN |
| | SURFACE WATER |
| | FOUL SEWER |
| | PROCESS DRAINAGE |
| | WATERMAIN |
| | ESB |
| | GAS MAIN |
| | MONITORING WELL |

ALL UTILITY SERVICES SUCH AS GAS, ESB, IT ETC. TO BE VERIFIED BY PROVIDERS AND CAREFULLY CHECKED ON SITE