Piramal Healthcare UK Limited
Earls Road, Grangemouth

Permit Variation

PPC/A/1008835

Contents

1 Non-Technical Summary of Determination

Provide a non-technical summary of the process and determination

This variation is to include a 'new build' operation within the existing permit. The new build manufacturing suites remain close to its currently permitted site within the multi-operator installation run by CalaChem.

The new manufacturing suites will produce batch sizes of up to 4kg with a capacity of up to 40 batches per year in each Antibody Drug Conjugate (ADC). Although this is classed as a large-scale production, less than 1 tonne of product will be produced annually.

Liquid effluent from the new facility will be treated by CalaChem Effluent Treatment Plant (ETP), other solid and liquid waste will be handled by a responsible waste management company under contract.

The energy use of the site is small. The new build has been designed to incorporate energy efficiency operating systems throughout.

Waste streams to air, aqueous effluent and solid/liquid wastes have been assessed to determine their environmental impact, overall there is minimal environmental impact from the operations activities.

Glossary of Terms

ADC - Antibody Drug Conjugate
BAT - Best Available Techniques
BMS – Building Management System
BREF – Best Available Techniques Reference Document
BAT-C – Best Available Technique Conclusions
CO – Coordinating Officer
ELV – Emission Limit Value
ETP – Effluent Treatment Plant
EWC – European Waste Code
F Gas – Fluorinated Gas
HVAC – Heating, Ventilation, and Air Conditioning
LED – Light Emitting Diode
MHRA – The Medicines and Healthcare products Regulatory Agency
PIR – Passive Infrared Sensor
PMDA – Pharmaceuticals and Medical Devices Agency (Japan)
RHS – Relevant Hazardous Substances
USFDA – The United States Food and Drug Administration
WEEE – Waste Electrical and Electronic Equipment

2 External Consultation and SEPA's response

Is Public Consultation Required? (if no delete rows below)	**Yes**

Advertisement Check:	**Date**	**Compliance with advertising requirements**
Edinburgh Gazette	**25/07/2023**	**Yes**
Falkirk Herald	**03/08/2023**	**Yes**

Officer Checking advert: M MacGregor

No of responses received	No responses to advertisement received.

Summary of responses and how they were taken into account during the determination:

None	
Summary of responses withheld from the public register on request and how they were taken into account during the determination:	
None	
Is PPC Statutory Consultation Required? (if no delete rows below)	**Yes**
Food Standards Agency:	Not consulted
Health Board:	Consulted, no response
Local Authority	Consulted, no response
Scottish Water	Not consulted, no direct release to sewer or environment from process.
Health and Safety Executive	Not Consulted
NatureScot	Consulted, no comments on the application.
Discretionary Consultation required? (if yes provide justification and details below, otherwise delete row)	**Yes**
Consulted local community council on proposal. No response received.	
Enhanced SEPA Consultation required? (if yes provide justification and details below, otherwise delete row)	**No**
"Off site" consultation required (if yes provide justification and details below, otherwise delete row)	**No**
Transboundary Consultation required? (if yes provide justification and details below, otherwise delete row)	**No**
Is Public Participation Consultation Required? (if yes provide justification and details below, otherwise delete rows below)	**Yes**

3 Administrative determinations

Determination of the Schedule 1 Activity

There are no changes to the Schedule 1 activity within the permit.

Determination of the Stationary Technical Unit to be permitted

The Stationary Technical Unit will require changes to incorporate the new manufacturing facility.

Determination of Directly Associated Activities

The Directly Associated activities will be reviewed where required to incorporate the new manufacturing facility.

Determination of Site Boundary

The site boundary will change to include the new manufacturing facility.

4 Introduction and Background

4.1 Historical Background to the activity and variation

Piramal's Grangemouth facility has been operating since 2004 and has held a PPC permit since 2007.

The site provides full process & analytical development services to support proof-of-concept & Toxicology studies with commercial manufacture of Antibody Drug Conjugates (ADCs) since 2012.

Piramal are also regulated and inspected under the USFDA, MHRA & PMDA Japan regulatory frameworks.

4.2 Description of activity

The site manufactures high potency pharmaceuticals on a small scale.

4.3 Outline details of the Variation applied for

A new facility will be purpose built to extend the process which already exists in the current manufacturing facility and is regulated under permit PPC/A/1008835.

Due to increased requirements for this product the new building will manufacture ADC's only. In addition to this there is a goods in/warehouse/storage area on the ground floor.

4.4 Guidance/directions issued to SEPA by the Scottish Ministers under Reg.60 or 61.

None

4.5 Identification of important and sensitive receptors

The site is surrounded by industrial premises.

Sites of Special Scientific Interest and Special Protected area:
The Firth of Forth SSSI/SPA is located approximately 1550m North Northwest of the site.
SSSI Code 8163, European code: 169840
SPA Code 8499, European code: UK9004411
Watercourses:
The River Carron is located 1000m to the north of the site and the Grange Burn 1050m to the west.

Local Amenity:
The Grange Manor hotel is located 500m Northeast of the site.
Falkirk's Helix Park is located approx. 1000m to the West of the site.
Falkirk Stadium is approx. 1000m Southwest of the site.
The nearest housing is located at approx. 500m Southeast of the site at Wood street.

This variation is not anticipated to have consequences for the Air Quality Management Area, the Firth of Forth Special Protection Area or local centres of population.

5 Key Environmental Issues

5.1 Summary of significant environmental impacts

The environmental impacts of the existing facility have been previously assessed and a permit granted with appropriate control measures. Overall emissions associated with the manufacture of antibody and antibiotic drug conjugates are negligible by virtue of the small scale laboratory manufacture and the potent nature of the substances requiring strict control of emissions to prevent worker exposure.

The proposals contained within this application are to add a 'new build' manufacturing facility to the permit to increase the production capacity of their existing products. The new facility remains close to its currently permitted site within the multi-operator installation and the environmental control measures contained within the existing permit will be applied to the new facility.

5.2 Emissions to Air

Point Source emission to air:

N,N-Dimethylacetamide (DMA) and dimethyl sulphoxide (DMSO) are used as co-solvents in the batch manufacturing process; neither are categorised Department of the Environment VOCs. Piramal estimate VOC emissions to air as 0.0087kg per kg of product, the nature and quantity of the emission means that it is not significant.

Air in the laboratory areas is controlled through Heating, Ventilation, and Air Conditioning (HVAC) in accordance with BAT and all air emissions are collected into a filtration system which retains any contamination.
Filter units are changed as per maintenance requirements and disposed of as hazardous waste. In the event of an emergency or abnormal circumstance production would be suspended until normal operation could be resumed.

Fugitive emissions to air:

There are no implications, there is limited solvent storage & use and chiller will be Fluorinated gas (F gas) compliant.
Due to the air handling through the HVAC system the potential for fugitive emissions to air from the process is minimal.

Odour:

The manufacturing process itself does not cause odours and there is no proposed change in substances used. The existing permit contains standard conditions requiring emissions to air be free from offensive odour.

5.3 Emissions to Water

Point Source Emissions to Surface Water and Sewer:

Liquid waste is divided up into two distinct waste streams, hazardous and non-hazardous.
The non-hazardous effluent will be pumped from the laboratory suites via holding tanks to the CalaChem owned and operated Effluent Treatment Plant (ETP) as per a trade effluent agreement.
The waste stream is conveyed through a dedicated route which further precautions in the form of shut off valves, holding tank at site, emergency response team and CalaChem ETP emergency procedures.
The non-hazardous waste stream will produce quantities of approximately 200,000 litres per year the constituents of this waste stream are as follows:
• WFI (Water For Injection taken from purified/distilled water)
• 0.1M NaOH
• 0.5M NaOH

The hazardous liquid waste stream (toxic effluent) is pumped directly from the laboratory suites to a hazardous waste effluent storage tank, as illustrated in appendix 4 of the application. This is a bunded tank on hardstanding. The tank will have shutoff valves and an emergency response team and associated procedures.

The current waste management provider for the site will continue to take the aqueous flammable waste which consists of a liquid waste combined with the toxic product ingredients, The associated waste European Waste Code (EWC) is: 07 05 01, UN code: 1992.
This will be collected by tanker. Regular tanker collections will occur at around 20,000 litres.
This will continue to be disposed via incineration.
Both waste stream containment facilities will have a system of inspection and maintenance to ensure the integrity of tanks, bunds. and tanks will be equipped with overfill prevention and high level alarms. The facilities will be subject to administrative controls including, site rules, procedural controls, supervision of the area during loading, emergency response plans and training

Point Source Emissions to Groundwater:

There are no direct point source emissions to groundwater.

Fugitive Emissions to Water:

Considering storage and containment measures utilised on site it is unlikely that any substances will enter the surface water or groundwater. Any fugitive emissions are contained within the effluent sump.

5.4 Noise

The operation does not produce noise or vibration. The building is part of an industrial park and activities are internal and laboratory based.

5.5 Resource Utilisation

Water use

Water use will increase proportionally with the increase in size of facility and production capacity. Water use is monitored and regulated through resource efficiency data returns

Energy use and generation

Energy consumption for Piramal will increase with the increased size of the estate, once the new building is fully operational.
Electricity will continue to be purchased directly from the grid to manufacture pharmaceutical products. Electricity requirements are minimal and will be used for mainly for HVAC, heating, and lighting (LED). In line with BAT the building has been constructed to incorporate energy efficiency measures and includes a modern Building Management System (BMS) with smart controls around efficiency, heating via heat pumps with heat recovery systems and recovered steam from condensate. PIR systems installed together with LED lighting and motion sensors.
Energy rating will be considered further in the refurbishment/replacement of the existing equipment on site.

Raw Materials Selection and Use

There is no change to the type of raw materials to be used in the process and currently in use on the existing site facilities. The increase in use of raw materials will be proportionate to the increase in production.

5.6 Waste Management and Handling

Waste Minimisation

All wastes generated on site are managed in line with waste management regulations and removed by a licenced waste management contractor. Existing permit conditions require the operator to review all wastes generated by the permitted activities on a regular basis to identify opportunities for minimising the environmental impact from the disposal of waste. These conditions will also apply to the extension to the site proposed in this application.

Waste Handling

Liquid wastes are handled as detailed in section 5.3 above. Other waste generated on site includes solid waste such as food waste, WEEE, and other occasional solid waste streams. All wastes are managed in line with waste management regulations and removed via a licenced waste management contractor. Existing permit conditions require the operator to review all wastes generated by the permitted activities on a regular basis to identify opportunities for minimising the environmental impact from the disposal of waste. These conditions will also apply to the extension to the site proposed in this application.

Waste Recovery or Disposal

As described above all wastes generated on site are managed in line with waste management regulations and removed by a licenced waste management contractor for treated at an appropriate facility.

5.7 Management of the site

Environmental Management System

Piramal operate under an appropriate environmental management system and are also regulated and inspected under the USFDA, MHRA & PMDA Japan regulatory frameworks.

Accidents and their Consequences

The existing permit contains conditions requiring the permit holder to prepare, implement and maintain an ‘Incident Prevention and Mitigation Plan’ along with related conditions for each manufacturing process. The ‘Plan’ will require to be reviewed and updated to take into account the changes authorised by this variation and should be reviewed during future audits of the site.

Closure

The existing permit contains conditions referring to the preparation of a ‘Decommissioning Plan’. This will require updated, as detailed in the permit conditions, to reflect the new area of activities proposed in this variation.

5.8 Site Condition report

A site condition report for the new area was submitted along with the application. SEPAs contaminated land team have reviewed the report and provided the following comments.

'I have now reviewed the following documents:

a) *Ref:001 Variation Application Piramal. Application for Variation with Site Condition Report & Baseline Report. Piramal Earls Road, Grangemouth, FK3 8XG*
b) *Appendix 5 Mason Evans site investigation report*

Based on the information provided for the site condition report and baseline on the documents listed above for this permit variation and taking into account your comments below on email dated 4th Oct 2023; I agree with your requirements for preventing pollution and reporting requirements for this site given the small volumes of Relevant Hazardous Substances(RHS) and level of containment in place.
The only aspect I would like to add is that we should request the applicant to request a waiver for baseline, since the site investigation undertaken did not report soil or groundwater baseline concentrations for any of the RHS listed under table 3.1 of the site condition report.
By requesting a waiver, the applicant is accepting that the baseline concentrations for the RHS used, produced, and stored on their site, is zero ug/l in water and zero mg/kg in soil. Given that it is a new site, the chances of presence in soil and groundwater beneath the site for the RHS associated to Piramal activities I assume it is unlikely otherwise they would have stated to have similar RHS to the encountered historic contamination on site.

If they can put in writing that they are requesting a waiver for baseline and state, they accept that their RHS have a concentration of zero ug/l in water and zero mg/kg in soil, I have no further comments on this.

Based on the above, I see no need to require them to collect soil and groundwater samples for baseline or require soil and groundwater monitoring for this site. It is an unusual site.'

On contacting Piramal they have requested a waiver, text as follows:

'In response to the comments below Piramal would like to request a waiver for baseline and state, accepting that the RHS have a concentration of zero ug/l in water and zero mg/kg in soil.'

With this waiver request in place there is no need to require Piramal to collect soil and groundwater samples for baseline or require soil and groundwater monitoring for this site.
Conditions have been included within the variation to ensure inspection and systematic assessment of the on site drainage is undertaken regularly.

5.9 Monitoring

Air

The existing permit contains conditions relating to the emissions to air from the installation. These conditions will also apply to the extension to the site proposed in this application.

Water

The existing permit contains conditions stating the conditions for discharge to the water environment and these conditions will also apply to the extension to the site proposed in this application.
There are no direct discharges to the water environment from the installation and appropriate measures will be deployed to mitigate against the potential for fugitive emissions

Soil and Groundwater

The existing permit contains conditions relating to the protection of Soil and Groundwater. These conditions will also apply to the extended site authorised under this variation and have been expanded to include further conditions requiring systematic inspection and review of the condition of the internal floors, external yard surfaces, bunding, foul drainage systems and process drains.

Waste

The existing permit contains conditions requiring the operator to maintain a register of waste which is generated by the permitted activities. These conditions will also apply to the extension to the site proposed in this application.

5.10 Consideration of BAT and compliance with BAT-Cs if appropriate

Information submitted suggests that BAT has been applied and manufacture in the new facility will utilise the same techniques as in the existing processes, previously determined to represent BAT.

6 Other Legislation Considered		
Nature Conservation (Scotland) Act 2004 & Conservation (Natural Habitats &c.) Regulations 1994		
Is there any possibility that the proposal will have any impact on site designated under the above legislation? If yes, provide information on the action and justification below:		**No**
The installation has been assessed previously and a permit issued to regulate the risks to the environment from the facility. This variation proposes an expansion of the manufacturing capacity of the site by creation of additional facilities. The control measures already in place will be applied to the new facility to mitigate against any potential for environmental impact.		
Screening distance(s) used	2km	
Is there any other legislation that was considered during determination of the permit (for example installations that may be impacted by the requirements of legislation involving Animal By Products, Food Standards, Waste, WEEE regulations etc). If yes, provide information on the legislation, action and justification below:		**No**

7 Environmental Impact Assessment and COMAH
How has any relevant information obtained or conclusion arrived at pursuant to Articles 5, 6 and 7 of Council Directive 85/337/EEC on the assessment of the effects certain public and private projects on the environment been taken into account?
Articles 5, 6 and 7 of Council Directive 85/337/EEC are not relevant to this application
How has any information contained within a safety report within the meaning of Regulation 7 (safety report) of the Control of Major Accident Hazards Regulations 1999 been taken into account?
The site is not regulated under COMAH

8 Details of the permit		
Do you propose placing any non standard conditions in the Permit?		**No**
Do you propose making changes to existing text, tables or diagrams within the permit?		**Yes**
Outline the changes required and provide justification below:		
Proposed Condition Number:	**Proposed Change:**	**Justification:**
1.1.4.1	The description of the facilities has been altered by the addition of the two new production labs Pharma 1 and Pharma 2.	The change introduces the two new areas of production within the facility proposed within the application.
1.2	The site plan has been changed to clearly indicate the location of the Piramal facilities at the site's location.	The new production facility is located within a newly constructed building and the plan has been altered to include this new building. The new plan also

		clearly identifies the location of the other Piramal properties.
Table 2.1	The table has been updated.	The table has been updated to include the reporting requirements of the conditions included in this variation
2.4	The permit schedule regarding Incidents has been replaced.	The schedule has been replaced in its entirety to reflect the most recent version of these conditions including response, recording, investigation and reporting of incidents. This includes updated contact info for SEPA.
2.5	The permit schedule regarding Resource Utilisation has been replaced.	The schedule has been replaced in its entirety to reflect the most recent version of the conditions relating to raw materials, waste and emissions from the facility. It includes updated reporting requirements.
Table 2.2	The table has been updated.	The table has been updated to include the definitions of Raw material, Energy or Fuel included in the conditions of this variation
2.6	The permit schedule regarding Waste Management has been deleted.	This set of conditions has been deleted as the requirements relating to waste management are now included in condition 2.5 Resource utilisation.
2.7.4 to 2.7.7	The additional conditions in section 2.7 include additional measures to ensure protection of soil and groundwater.	Due to the additional land required and the extension of the drainage network the set of conditions relating to Soil and Groundwater has been expanded to include a requirement to carry out a full inspection and systematic assessment of internal floors, external yard surfaces, bunding, foul drainage systems and process drains. This will minimise the potential for contamination by the on site processes.
5.1.2	The description of where production process can be carried out within the facilities has been altered by the addition of the two new production labs Pharma 1 and Pharma 2.	The change introduces the two new areas of production within the facility proposed within the application.
5.5.1	The description of the spillage protocol for the process facilities has been altered by the addition of the two new production labs Pharma 1 and Pharma 2.	The change introduces the two new areas of production within the facility proposed within the application.
Table 5.1	The table of emissions to air has been updated to include reference to the additional emission points on site and related to the new production facility.	The change is require to clearly identify all vents associated with the production process.

Explanatory Notes	These have been updated to the most recent version of the notes and include updated SEPA contact details	Updated to the most recent version of the notes and include updated SEPA contact details

9 Emission Limit Values or Equivalent Technical Parameters/Measures	
Are you are dealing with either a permit application, or a permit variation which would involve a review of existing ELVs or equivalent technical parameters?	**No**
Outline the changes required and provide justification below:	
No changes are required. The application describes an extension of the site to include new manufacturing facilities to expand the production of their current product lines. Any existing ELVs within the permit will also be applied to the new facilities proposed in the application	

10 Final Determination
Issue of a Permit - Based on the information available at the time
Issue a Permit – Based on the information available at the time of the determination SEPA is satisfied that: • The applicant will be the person who will have control over the operation of the installation/mobile plant, • The applicant will ensure that the installation/mobile plant is operated so as to comply with the conditions of the Permit, • That the operator is able to use all appropriate preventative measures against pollution, in particular through the application of best available techniques. • That no significant pollution will be caused.