Zoetis Belgium S.A. (Irish Branch)
Copse House
Laragh Road
Rathdrum
Co. Wicklow
A67 X704

04th Nov, 2019

Ms Sandra Gleeson
EPA Office of Environmental Enforcement
South East Region,
Environmental Protection Agency Headquarters
PO Box 3000
Johnstown Castle Estate
Wexford.

Ref: P0015-5

Ref: Approval request for new process.

Dear Ms Gleeson

In accordance with Condition 1.4 of the Integrated Pollution Control Licence Register number P0015-5, Zoetis, request prior written agreement of the agency to produce a new Product .

Project Name: Code SLR

Manufacturing to begin in February 2020, expected to produce approximately 3000 kg of product. Further production campaigns, yet to be confirmed, are also envisaged in following years and are likely to increase progressively in the following years.

The company will ensure that the operations shall be carried out in a manner that all emissions shall conform to all emission limit values and conditions of the IPPC license shall be complied with.

We would appreciate the Agency's urgent attention as there is a commitment to manufacture this by Q2 to satisfy customer requirements.

Should you require any additional information, please do not hesitate to contact me.
All relevant details shall be retained on file.

A response from the Agency to this request would be greatly appreciated.

Yours sincerely,

Dora Forde
EHS lead

zoetis

EPA Approval Request for "SLR" project

31st October 2019

Introduction

Zoetis Belgium S.A. Ireland branch, is planning to produce and to supply a material to be used in Veterinary production as follows:

Project Code: SLR

This product will be manufactured on site. This production run is expected to produce approximately 3000kg of product (is this based on annual volumes expected). The API will be packed off in sealed double-lined polythene bags. Further production is anticipated in the future. This product will be made in Production buildings P2 and P3.

Class of the Activity

Class 5.16: The use of a chemical or biological process for the production of basic pharmaceutical products.
Class 11.1: The recovery or disposal of waste in a facility, within the meaning of the Act of 1996, which facility is connected or associated with another activity specified in this Schedule in respect of which a license or revised license under Part IV is in force or in respect of which a license under the said part is or will be required.

Description of the Activity

The product will be produced in a combination of the production building areas and the process is similar to Legacy chemical processes at the Zoetis Belgium S.A. facility (Irish branch under License P0015-5).

Pre- existing Utilities will be utilised. The services required to support production are a combination of existing services. The existing services are Listed below:

- Electricity
- Nitrogen
- Process water
- Purified water
- Air and instrument air
- Cooling water
- Chilled water
- Vacuum
- High Temperature (HT) Marlotherm (180 C)
- Medium Temperature (MT) Marlotherm, with a controlled supply temperature of 20°C.
- Low Temperature (LT) Marlotherm, with a controlled supply temperature of minus 90°C.
- Process vent header to Liquid Vapor Incinerator (LVI)
- Wastewater treatment plant
- Low pressure Steam

P2/P3 chillers are being replaced. HVAC systems are being replaced
There no new services required for the production of this product.

PROCESS FLOW

Step 1
PF-06452787, PF-06458663, cesium carbonate, and TFT are charged to a reactor. This is heated to reflux (100-110°C) and TFT (solvent) is removed by distillation. Cesium carbonate and TFT (solvent) are charged to the reaction and the reaction / distillation continued. The reaction is cooled to 20-25°C, the volume of distilled TFT solvent removed in the final distillation is replaced, and water is added. After stirring for 30 minutes, the aqueous layer is discarded. Alumina is added and the mixture is agitated. The alumina is removed by filtration and the alumina bed which formed is rinsed with solvent. The combined organic layers are concentrated under vacuum distillation. Heptane is charged to the reaction and the . The slurry is cooled to 0-5°C.The product is isolated by filtration and rinsed with cold heptane. The intermediate product (PF-06459514) is dried under vacuum.

Step 2
PF-06459514 and catalyst PF-06560381-Q4 are dissolved in DCM and cooled to -8°C. A cold aqueous solution (0-7°C) of hydroxylamine hydrochloride is added to the reaction solution, then aqueous sodium hydroxide is dosed at a rate such that a steady temperature is maintained. The reaction mixture is stirred and is then warmed to ambient temperature and diluted with water. The aqueous phase is removed. The organic phase is washed sequentially with 1N hydrochloric acid water. DCM is removed distillation. Methanol is added to replace the DCM removed and the sequence is repeated The solution is further diluted with solvent and heated, maintaining a specified temperature range. The solution is cooled and is seeded with PF-06451264. to crystallize the product. The solids are isolated by filtration, washed with a mixture of solvent and water and the intermediate product (PF-06451264) is dried under vacuum

Step 3
PF-06451264is dissolved in solvent and the solution is heated to reflux. A solution of an organic acid in methanol is added at a controlled rate to control the off-gassing. Reflux is continued, then. the reaction solution is cooled and diluted with solvent MTBE. The resulting suspension is cooled. The solids are isolated by filtration, washed first with a mixture of methanol and MTBE and then with MTBE, and the product (PF-06474507-26) dried under vacuum.

Step 4
PF-06474507-26is suspended in isopropyl acetate. Solid reagent PF-06667698 is added, then TEA is dosed at a rate so not to exceed a reaction temperature of 25°C. The TEA feed tank is rinsed with isopropyl acetate and the suspension is stirred until complete conversion is achieved Filter aid is added, and the suspension is agitated for about three hours. The solids (by-products) are removed by filtration and the filter cake is washed with solvent. The organic product solution is washed with aqueous ammonia and water The distillation residue is diluted with a solvent mixture (ethanol and heptane). The solution is heated, followed by dilution with solvent. The solution is seeded with crystalline product (PF-06450567 – sarolaner) and the mixture then cooled. Further heptane solvent is added during the cooling.
The solids are isolated by filtration, washed with pre-cooled n-heptane and dried under vacuum.

Operational information Requirements

Contents

List of unit operations
List of abatement, Treatment and Recovery options
Emissions to the Environment from unit operations
Process control
Capacities and throughputs, i.e. Equipment No, Material of construction, capacity and output
Bund register

List of unit operations

No Change

List of abatement treatment and recovery options

On-site wastewater treatment plant
On-site Liquid Vapor Incinerator
On-site scrubbers
On-site condensers

Emissions to the Environment from unit operations

As Methanol and Dichloromethane considered a Class II solvent under T.A. Luft, the emission is below this limit of 2.0 Kg/hr Ethanol ,IPA , MTBE, triethylamine, Isobutylene, acetic acid and n-Heptane are Class III as a limit of 3.0 kg/hr therefore the mass emissions would be considered minor. All vents from reactors and ancillary equipment are connected into the vent header system and to the LVI.

Reaction synthesis

See Emissions to atmosphere section.

Process Control

Instrumentation and Control:

The equipment and associated tank farm equipment are controlled by an extension of the sites Distributed Control System (DCS). Both DCS systems are validated in accordance with the requirements of FDA regulations.

Capacities and Throughput

As in the existing plant, through put will vary depending on the products and batch sizes required by the customer. Typical vessels and their capacities are given below.

Item	Equipment	Material	Capacity
RG-201	Glass lined reactor	Glass lined Carbon Steel	4,000 L
RG-202	Glass Lined Reactor	Glass Lined Carbon Steel	10,000 L
RG-203	Glass lined reactor	Glass lined Carbon Steel	4,000 L
SE-205	Stainless Steel Separator	316 S.S.	6200 L
SE-206	Stainless Steel Separator	316 S.S.	5000 L
SE-207	Stainless Steel Separator	316 S.S.	5000 L
SE-208	Stainless Steel Separator	316 S.S.	5000 L
CE-203	Horizontal Centrifuge Peeler	Hastelloy C	200 L
D-202	Conical Drier	Hastelloy "C"	2000 L
D-204	Agitated Pan Drier	Hastelloy C22	2560 L
TA-224	Centrifuge wash Tank	316L S.S.	500 L
TA-874	Halogenated Bulk tank	304L S.S.	50m3
TA-882	Bulk tank	304L S.S.	50m3
TA-877	Halogenated waste Bulk tank	304L S.S.	50m3

Note: SS= stainless steel GLCS= Glass lined carbon steel
GMP All items meet GMP standard.
Explosion protection All motors are of E Ex dIIA + IIB standard and Hydrogenator IIC standard.
All reactors can be linked by flexible pipes to inlets and outlets within the plant.

Bund Regwaster
No change

Raw Materials and Product.
Details are attached on the following pages

Table G.1 (i) Details of Process related Raw Materials, Intermediates, Products, etc., used or generated on the site

Note: These materials are previously used on site or present similar hazards to those previously managed in accordance with the License.".

Table G.1 (i) – Table 1 of 1

Ref. Nº or Code	Material/ Substance(1)	CAS Number	Danger(2) Category	Amount Stored (tonnes)	Annual Usage (tonnes)	Nature of Use	H Statement	P Statement
RM	Benzotrifluoride/ trifluorotoluene	98-08-8	Flammable Liquid	5.00	32.00	Manufacture of API	**H225:**Highly flammable liquid and vapour **H332:**Harmful if inhaled **H400:**Very toxic to aquatic life **H410:**Very toxic to aquatic life with long lasting effects	**P210:**Keep away from heat/sparks/open flames/hot surfaces. - No smoking. **P233:**Keep container tightly closed. **P241+P242+P243:**Use explosion-proof electrical/ventilating/lighting equipment. Take precautionary measures against ignition by the static discharge and the spark. **P261:**Avoid breathing. **P271:**Use only outdoors or in a well-ventilated area. **P273:**Avoid release to the environment. **P280:**Wear protective gloves/eye protection/face protection. **[Response] P304+P340+P312:**IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing. Call a POISON CENTER or octor/physician if you feel unwell. **P303+P361+P353:**IF ON SKIN (or hair): Remove/Take off immediately all contaminated clothing. Rinse skin with water/shower.Collect spillage. **[Storage] P403+P235:**Store in a well-ventilated place. Keep cool. **[Disposal] P501:**Dispose of contents/container through a waste management company authorized by the local government.
RM	PF-06452787 RSM 2	NA	Harmful	TBC	TBC	Manufacture of API	May form combustible dust concentrations in air	P210 - Keep away from heat/sparks/open flames/hot surfaces. - No smoking P243 - Take precautionary measures against static discharge P240 - Ground/Bond container and receiving equipment
RM	PF-06458663 RSM 1	NA	Corrosive	1.285	3.088	Manufacture of API	H314 Causes severe skin burns and eye damage. H317 May cause an allergic skin reaction.	Prevention P260 Do not breathe vapour. P264 Ish thoroughly after handling. P272 Contaminated work clothing should not be allowed out of the workplace. P280 Wear protective gloves/protective clothing/eye protection/face protection. Response

								P301 + P330 + P331 IF SWALLOWED: rinse mouth. Do NOT induce vomiting. P303 + P361 + P353 IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with/shower. P304 + P340 IF INHALED: Remove person to fresh air and keep comfortable for breathing. P305 + P351 + P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present easy to do. Continue rinsing. P310 Immediately call a POISON CENTRE/doctor. P333 + P313 If skin irritation or rash occurs: Get medical advice/attention. P362 + P364 Take off contaminated clothing and ish it before reuse. Storage P405 Store locked up. Disposal P501 Dispose of contents/container in accordance with local/regional/national/international regulations.
RM	Heptane	142-82-5	Flammable liquid	4.00	24T	Manufacture of API	H225 Highly flammable liquid and vapour. H315 Causes skin irritation. H336 May cause drowsiness or dizziness. H304 May be fatal if swallowed and enters airways. H410 Very toxic to aquat life with very long lasting effects	P301+P310 IF SWALLOWED: Immediately call a POISON CENTER/ doctor. P321 Specific treatment (see on this label). P331 Do NOT induce vomiting. P303+P361+P353 IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water [or shower]. P362+P364 Take off contaminated clothing and ish it before reuse. P405 Store locked up. P501 Dispose of contents/container in accordance with local/regional/ national/international regulations.
RM	Methanol	67-56-01	Flammable Liquid	25.000	TBC	Manufacture of API	H225 Highly flammable liquid and vapour. H301+H311+H331 Toxic if swallowed, in contact with skin or if inhaled. H370 Causes damage to organs .	P210 Keep away from heat, hot surfaces, sparks, open flames and other ignition sources. No smoking. P260 Do not breathe vapour/ spray. P301+P310 IF SWALLOWED: Immediately call a POISON CENTER/ doctor. P304+P340 IF INHALED: Remove person to fresh air and keep comfortable for breathing. P501 Dispose of contents/ container in accordance with national regulations.

RM	Toluene	108-88-3	Flammable liquid	11.000		Manufacture of API	H225 Highly flammable liquid and vapour. H304 May be fatal if swallowed and enters airways. H315 Causes skin irritation. H336 May cause drowsiness or dizziness. H361 Suspected of damaging fertility or the unborn child. H373 May cause damage to organs through prolonged or repeated exposure. H401 Toxic to aquatic life.	P201 Obtain special instructions before use. P202 Do not handle until all safety precautions have been read and understood. P210 Keep away from heat/sparks/open flames/hot surfaces. No smoking. P233 Keep container tightly closed. P240 Ground/bond container and receiving equipment. P241 Use explosion-proof electrical/ ventilating/ lighting/ equipment. P242 Use only non-sparking tools. P243 Take precautionary measures against static discharge. P260 Do not breathe dust/ fume/ gas/ mist/ vapours/ spray. P264 Ish skin thoroughly after handling. P271 Use only outdoors or in a well-ventilated area. P273 Avoid release to the environment. P280 Wear protective gloves/ protective clothing/ eye protection/ face protection. P301 + P310 IF SWALLOWED: Immediately call a POISON CENTER/doctor. P303 + P361 + P353 IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water/shower. P304 + P340 + P312 IF INHALED: Remove person to fresh air and keep comfortable for breathing. Call a POISON CENTER/doctor if you feel unwell. P308 + P313 IF exposed or concerned: Get medical attention P301 + P310 IF SWALLOWED: Immediately call a POISON CENTER/doctor. P303 + P361 + P353 IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water/shower. P304 + P340 + P312 IF INHALED: Remove person to fresh air and keep comfortable for breathing. Call a POISON CENTER/doctor if you feel unwell. P308 + P313 IF exposed or concerned: Get medical advice/ attention. P331 Do NOT induce vomiting. P332 + P313 If skin irritation occurs: Get medical advice/ attention. P362 Take off contaminated clothing and ish before reuse. P370 + P378 In case of fire: Use dry sand, dry chemical or alcohol-resistant foam to extinguish. P403 + P233 Store in a well-ventilated place. Keep container tightly closed. P403 + P235 Store in a well-ventilated place. Keep cool. P405 Store locked up. P501 Dispose of contents/ container to an approved waste disposal plant.

RM	Acetone	67-64-1	Flammable Liquid	12.1		Manufacture of API	Hazard statement(s) H225 Highly flammable liquid and vapour. H319 Causes serious eye irritation. H336 May cause drowsiness or dizziness	P210 Keep away from heat/sparks/open flames/hot surfaces. - No smoking. P233 Keep container tightly closed. P240 Ground/bond container and receiving equipment. P241 Use explosion-proof electrical/ ventilating/ lighting/ equipment. P242 Use only non-sparking tools. P243 Take precautionary measures against static discharge. P261 Avoid breathing dust/ fume/ gas/ mist/ vapours/ spray. P264 Ish skin thoroughly after handling. P271 Use only outdoors or in a well-ventilated area. P280 Wear protective gloves/ eye protection/ face protection. P303 + P361 + P353 IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water/shower. P304 + P340 + P312 IF INHALED: Remove person to fresh air and keep comfortable for breathing. Call a POISON CENTER or doctor/ physician if you feel unwell. P305 + P351 + P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. P337 + P313 If eye irritation persists: Get medical advice/ attention. P370 + P378 In case of fire: Use dry sand, dry chemical or alcohol-resistant foam to extinguish. P403 + P233 Store in a well-ventilated place. Keep container tightly closed. P403 + P235 Store in a well-ventilated place. Keep cool. P405 Store locked up. P501 Dispose of contents/ container to an approved waste disposal plant.
RM	Acetic acid	64-19-7	Flammable liquid	3.5 T	3.5	Manufacture of API	H226 Flammable liquid and vapour. H314 Causes severe skin burns and eye damage.	P243 Take action to prevent static discharges. P280 Wear protective gloves/ protective clothing/ eye protection/ face protection. P301+P330+P331 IF SWALLOWED: Rinse mouth. Do NOT induce vomiting. P303+P361+P353 IF ON SKIN (or hair): Take off immediately all contaminated clothing .Rinse skin with water or shower. P305+P351+P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. P313 Get medical advice/ attention. 2.3.
RM	Isopropylacetate	108-21-4	Flammable liquid	16.000	35.0	Manufacture of API	H225 Highly flammable liquid and vapour.	P210 Keep away from heat, hot surfaces, sparks, open flames and other ignition sources. No smoking. P261 Avoid breathing vapour/ spray.

							H319 Causes serious eye irritation. H336, may cause dizziness .	P304+P340 IF INHALED: Remove person to fresh air and keep comfortable for breathing. P305+P351+P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. P501 Dispose of contents/ container in accordance with national regulations. **P-statements** Keep away from heat, hot surfaces, sparks, open flames and other igni□on sources. No smokingP210 . Wear protective gloves and eye protec□on/face protec□onP280 . IF INHALED: Remove person to fresh air and keep comfortable for breathingP304 + P340 . IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water/showerP303 + P361 + P353 . IF IN EYES: Rinse cau□ously with water for several minutes. Remove contact lenses, if present and easy to do. Con□nue rinsing. P305 + P351 + P338 Call a POISON CENTER/doctor if you feel unwellP312 .
RM	Process water		Not hazardous	35.0	35	Manufacture of API	Not available	Not available
RM	Di-isopropyl formamide	2700-30-3	Not hazardous	0.221	0.886	Manufacture of API	H317 May cause an allergic skin reaction H319 Causes serious eye irritation	P280 Wear protective gloves/protective clothing/eye protection/face protection. P305+351+338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses if present and easy to do - continue rinsing.
RM	Cesium carbonate	534-17-8		0.350	0.350		H318 - Causes serious eye damage H361f - Suspected of damaging fertility H373 - May cause damage to organs (kidneys, adrenals) through prolonged or repeated exposure	P201 - Obtain special instructions before use P202 - Do not handle until all safety precautions have been read and understood P260 - Do not breathe dust P280 - Wear protective gloves/protective clothing/eye protection/face protection P305 + P351 + P338 - IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing P310 - Immediately call a POISON CENTER P308 + P313 - IF exposed or concerned: Get medical advice/attention P405 - Store locked up P501 - Dispose of contents/container in accordance with local, regional, national and international regulations

RM	36% HCl	7647-01-0	C, Corrosive	1.2T	1.2T	Manufacture of API	H290 May be corrosive to metals. H314 Causes severe skin burns and eye damage. H335 May cause respiratory irritation.	P261 Avoid breathing dust/ fume/ gas/ mist/ vapours/ spray. P280 Wear protective gloves/ protective clothing/ eye protection/ face protection. Response P301 + P330 + P331 IF SWALLOWED: Rinse mouth. Do NOT induce vomiting. P303 + P361 + P353 IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water/shower. P305 + P351 + P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. P304 + P340 + P310 IF INHALED: Remove person to fresh air and keep comfortable for breathing. Immediately call a POISON CENTER/doctor. Disposal: P501 Dispose of contents/ container in accordance with the local/regional/international regulations.
RM	Hydroxylamine hydrochloride	5470-11-1	Xn, Harmful	0.450	0.450	Manufacture of API	H290 May be corrosive to metals. H302 + H312 Harmful if swallowed or in contact with skin. H315 Causes skin irritation. H317 May cause an allergic skin reaction. H319 Causes serious eye irritation. H351 Suspected of causing cancer. H373 May cause damage to organs through prolonged or repeated exposure. H400 Very toxic to aquatic life.	P260 Do not breathe dust/ fume/ gas/ mist/ vapours/ spray. P280 Wear protective gloves/ protective clothing/ eye protection/ face protection. P301 + P312 + P330 IF SWALLOWED: Call a POISON CENTER/doctor if you feel unwell.Rinse mouth. P305 + P351 + P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.

RM	30% sodium hydroxide	1310-73-2	C , Corrosive	1.5		Manufacture of API	H290 Skin Corr. 1A - H314 Eye Dam. 1 - H318	P234 Keep only in original packaging. P260 Do not breathe vapour/ spray. P303+P361+P353 IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water or shower. P305+P351+P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. P501 Dispose of contents/ container in accordance with national regulations.
RM	Formic acid	64-18-06	Flammable	3.0	3.0	Manufacture of API	H226 Flammable liquid and vapour. H331 Toxic if inhaled. H302 Harmful if swallowed. H314 Causes severe skin burns and eye damage	P271 Use only outdoors or in well-ventilated area. P280 Wear protective gloves/protective clothing/eye protection/face protection. P210 Keep away from heat/hot surfaces, sparks, open flames and other ignition sources. No smoking. P260 Do not breathe mist or vapour. P243 Take action to prevent static discharges. P241 Use explosion-proof electrical/ventilating/lighting/equipment. P264 Ish with plenty of water and soap thoroughly after handling. P270 Do not eat, drink or smoke when using this product. P242 Use non-sparking tools. P240 Ground and bond container and receiving equipment. Precautionary Statements (Response): P310 Immediately call a POISON CENTER or doctor/physician. P305 + P351 + P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. P304 + P340 IF INHALED: Remove person to fresh air and keep comfortable for breathing. P303 + P361 + P352 IF ON SKIN (or hair): Remove/Take off immediately all contaminated clothing. Ish with plenty of soap and water. P301 + P330 + P331 IF SWALLOWED: rinse mouth. Do NOT induce vomiting. P370 + P378 In case of fire: Use alcohol-resistant foam, carbon dioxide, dry powder or water spray for extinction. Precautionary Statements (Storage): P403 + P235Store in a well-ventilated place. Keep cool. P233Keep container tightly closed. P405 Store locked up. Precautionary Statements (Disposal):

								P501Dispose of contents/container to hazardous or special waste collection point.
RM	PF-06560381(Chiral catylst)	NA		0.02	0.1	Manufacture of API	H317 - May cause an allergic skin reaction.	Prevent dust accumulation to minimize explosion hazard. Material name: PF-06560381-Q4 SDS EU Version #: 01 Issue date: 13-October-2018 1 / 8 P261 Avoid breathing dust. P272 Contaminated work clothing should not be allowed out of the workplace. P280 Wear protective gloves. P210 Keep away from heat, hot surfaces, sparks, open flames and other ignition sources. No smoking. P240 Ground and bond container and receiving equipment. P302 + P352 IF ON SKIN: Ish with plenty of water. P333 + P313 If skin irritation or rash occurs: Get medical advice/attention. P362 + P364 Take off contaminated clothing and ish it before reuse. P501 P501, Dispose of contents/container in accordance with local/regional/national/international regulations
RM	Benzene sulphonic acid	98-11-3	C Corrosive	1,5 T	1.5 T		H290 May be corrosive to metals. H314 Causes severe skin burns and eye damage.	P280 Wear protective gloves/ protective clothing/ eye protection/ face protection. P305 + P351 + P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. P310 Immediately call a POISON CENTER/doctor.
RM	Aluminium Oxide	1344-28-1	NA				Dust can cause (mechanical) irritation of the cornea and conjunctiva. Inhalation of dust may cause respiratory irritation	Not available
RM	PF-06667689 RSM 3 PNPE		irritant	1.8 T	1.8T		H317 - May cause an allergic skin reaction	P210 - Keep away from heat/sparks/open flames/hot surfaces. - No smoking P240 - Ground/Bond container and receiving equipment P280 - Wear protective gloves/protective clothing/eye protection/face protection P261 - Avoid breathing dust/fume/gas/mist/vapors/spray P272 - Contaminated work clothing should not be allowed out of the workplace P302+ P352 - IF ON SKIN: Ish with plenty of soap and water

								P333 + P313 - If skin irritation or rash occurs: Get medical advice/attention P362 - Take off contaminated clothing and ish before reuse P501 - Dispose of contents/container in accordance with all local and national regulations.
RM	Triethylamine	121-44-8	Flammable	0.8	0.8	Manufacture of API	H225 Highly flammable liquid and vapour. H302 Harmful if swallowed. H311+H331 Toxic in contact with skin or if inhaled. H314 Causes severe skin burns and eye damage. H335 May cause respiratory irritation.	P210 Keep away from heat, hot surfaces, sparks, open flames and other ignition sources. No smoking. P261 Avoid breathing vapour/ spray. P301+P330+P331 IF SWALLOWED: Rinse mouth. Do NOT induce vomiting. P302+P352 IF ON SKIN: Ish with plenty of water. P304+P340 IF INHALED: Remove person to fresh air and keep comfortable for breathing. P501 Dispose of contents/ container in accordance with national regulations
RM	Methylene chloride (DCM)	75-09-2	Toxic	18.0	50	Manufacture of API	H315 Causes skin irritation. H319 Causes serious eye irritation. H336 May cause drowsiness or dizziness. H351 Suspected of causing cancer	P201 Obtain special instructions before use. P261 Avoid breathing vapour/ spray. P302+P352 IF ON SKIN: Ish with plenty of water. P304+P340 IF INHALED: Remove person to fresh air and keep comfortable for breathing. P305+P351+P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. P501 Dispose of contents/ container in accordance with national regulations
RM	MTBE	1634-04-4	Flammable	12.0		Manufacture of API	H225 Highly flammable liquid and vapour. H315 Causes skin irritation.	P210 Keep away from heat, hot surfaces, sparks, open flames and other ignition sources. No smoking. P243 Take precautionary measures against static discharge. P280 Wear protective gloves/ protective clothing/ eye protection/ face protection. P302+P352 IF ON SKIN: Ish with plenty of water.
RM	Ethanol	64-17-5	Flammable				H225 Highly flammable liquid and vapour.	P210 Keep away from heat, hot surfaces, sparks, open flames and other ignition sources. No smoking.

							H319 Causes serious eye irritation	P280 Wear protective gloves/ protective clothing/ eye protection/ face protection. P305+P351+P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. P501 Dispose of contents/ container in accordance with national regulations.
RM	Cellflock filter aid							
RM	PF-06459514 (Chalcone)	NA	NA	0.4	1.0	Manufacture of API	The substance does not meet the criteria for classification.	Observe good industrial hygiene practices
RM	25% Ammonia	1336-21-6	Corrosive	9.8	10	Manufacture of API	H290 May be corrosive to metals. H314 Causes severe skin burns and eye damage. H335 May cause respiratory irritation. H400 Very toxic to aquatic life.	P273 Avoid release to the environment. P280 Wear protective gloves/ protective clothing/ eye protection/ face protection. Response P301 + P330 + P331 IF SWALLOWED: Rinse mouth. Do NOT induce vomiting. P305 + P351 + P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. P308 + P310 IF exposed or concerned: immediately call a POISON CENTER or doctor/ physician
Product	Product SLR		Harmful	3.0	3.0	API	H302 Harmful if swallowed. H410 Very toxic to aquatic life with long lasting effects.	Take precautionary measures against static discharges. Prevent dust accumulation to minimize explosion hazard. Observe good industrial hygiene practices. P264 Wash thoroughly after handling. P270 Do not eat, drink or smoke when using this product. P273 Avoid release to the environment. P210 Keep away from heat/sparks/open flames/hot surfaces. - No smoking. P240 Ground/bond container and receiving equipment. **Response** P301 + P312 IF SWALLOWED: Call a POISON CENTRE/doctor if you feel unwell. P330 Rinse mouth. P391 Collect spillage.

Notes:
1. In cases where a material comprises a number of distinct and available dangerous substances, please give details for each component substance.
2. c.f. Article 2(2) of SI № 77/94
3. c.f. Schedules 9 and 10 of SI No 62/2004

Table G.1 (ii) Details of Process related Raw Materials, Intermediates, Products, etc., used or generated on the site

Table G.1 (ii) – Table 1 of 1

Ref. № or Code	Material/ Substance(1)	TA Luft Class 1, 2 or 3	Odour			EU Lists I and II (Tick and specify Group/Family Number)			
			Odourous Yes/No	Description	Threshold µg/m³	Dangerous Substances Directive 76/464/EEC		Groundwater Directive 80/68/EEC	
						List I	List II +129[2]	List I	List II
RM	Benzotrofluoride/ trifluorotoluene	-	NA	Not available	Not available	√	√		
RM	PF-06452787 RSM 2	-	NA	Not available	Not available	√	√		
RM	PF-06458663 RSM 1	-	NA	Not available	Not available	√	√		
RM	Heptane	Class III	Yes	Characteristic	Not available	√	√		
RM	Methanol	Class II	No	Clear colourless liquid	Not available	√	√		
RM	Acetone	Class III	No	Clear colourless liquid	Not available	√	√		
RM	Acetic acid	Class III	Yes	Clear colourless liquid	Not available	√	√		
RM	Cesium carbonate	-	No	No data available	No data available	-	-		
RM	PUW, process water	-	No	No data available	No data available	-	-		
RM	36% HCl	Class III	Yes	stinging	No data available	-	-		
RM	Hydroxylamine hydrochloride	-	No	No data available	No data available	-	-		

RM	Formic acid	-	No	No data available	No data available	-	-	
RM	PF-06560381(Chiral catylst)	-	-	-	-	-	-	-
RM	Benzene sulphonic acid	-	No	-	-	-	-	-
RM	Aluminium Oxide		No	No data available	No data available	-	-	
RM	PF-06667689 RSM 3	-	No	-	-	-	-	-
RM	Triethylamine	Class III	Yes	Ammonia like	-	-	-	-
RM	Methylene chloride	Class II	Yes	Characteristic ether	200-250ppm			
RM	MTBE	Class III	Yes	Hydrocarbons	NA			
RM	Ethanol	Class III	Yes	Alcoholic	NA	-		
RM	Cellflock filter aid							
RM	PF-06459514	-	NA	NA	NA	-	-	-
RM	25% Ammonia	-	NA	NA	NA	-	-	-
Product	SLR	-	NA	NA	NA	-	-	-

Notes

1. In cases where a material comprises a number of distinct and available dangerous substances, please give details for each component substance
2. The European Commission priority candidate list
3. Groundwater list I, item 7, "Mineral Oils & Hydrocarbons". All organic compounds are "Hydrocarbons" and thus as an organic compound falls under list I.

Table H.1 (i): Waste - Hazardous Waste Recovery/Disposal

Waste material	EWC Code	Main source[1]	Quantity		On-site Recovery/ Disposal (Method & Location)	Off-site Recovery, reuse or recycling (Method, Location & Undertaker)	Off-site Disposal (Method, Location & Undertaker)
			Tonnes	m^3 / month			
Mother Liquors waste (Organic solvents containing Methanol and Water), n-heptane, MTBE, ethanol	07 05 04	Filtration and enclosed ishing washing? of the product	Production volume dependent –	Production scheduling dependent – some months will be zero, while one month might be the full annual quantity	Off-site disposal – onsite is not applicable	Offsite by approved contractor	Offsite by approved contractor

1 A reference should be made to the main activity / process for each waste
2 Note: TBD To be determined
3 All organic solvent waste will be disposed of offsite for recovery or incineration

Treatment of waste Solids.

General non-hazardous waste is disposed of in accordance with current license conditions and applicable regulations. The waste is segregated and recycled /reused for an alternative purpose where practicable. Non-hazardous waste which cannot be reused or recycled is sent to landfill.

Toxic and dangerous waste including packaging which has come in contact with process materials and filters are collected and transported off-site for incineration by licensed specialised companies. All waste is handled in accordance with the appropriate Regulations and also in accordance with conditions with current IPPC /IED License P0015-05.
Wastes arising from the production activity include:
070501 Aqueous washing liquors and other liquors
070504 Non-Halogenated organic solvents
070508 Other still bottoms and reaction residues
Recovered solvent may be stored in a dedicated tank pending re-use on site or customer call-off. Supply Chain and EHS department personnel will generate the appropriate documentation.
These wastes are already generated on site and are transported to an approved Hazardous waste facility in accordance with license requirement

Emissions to Atmosphere

Process emissions

Vent listing

Emission register

Abatement and treatment and recovery systems

Emissions from unit operations

Emissions monitoring

Process Emissions

Process emissions are expected to occur as shown in diagram in Section 9.1.

These emissions are combined into the main header system is then directed to a scrubber system and then directed to the LVI.

Vent Listing and Emission Regisster

Vent No.	Building	Description	Major	Minor	Potential	Connected To Header
LVI	Liquid vapour incinerator	Liquid vapour incinerator via hydrolic flame arrestor	✓	-	-	Combination of all vents in header system from P1,P2,P4,

Abatement and Treatment and Recovery Systems

All relevant process vents are connected to vent header/abatement system.

Emissions from Reaction Synthesis

During normal operation of a reaction, controlled emissions may result from the following operations

- Inerting a vessel with nitrogen
- Chemical reaction-
- Charging liquids to a vessel
- Applying vacuum
- Applying heat
- Transferring contents from one vessel to another
- Filling bulk tanks

The following procedures are applied to control the emissions

- Condensers are cooled using Cooling Water/ dowtherm liquid
- Scrubber systems are used to remove Solvents and Acidic vapours which may by-pass the condenser, prior to venting to the LVI.

Emissions during a Malfunction.

- Bursting disc rupture
- Failure of the cooling medium to condensers

- Failure of cooling medium to reactor.
- Emissions during a conservation vent failure.
- Any potential new malfunctions shall be identified as part of the HAZOP.

Emissions Monitoring

As all process vents are connected to the scrubber system emission monitoring of the proposed expansion shall take place at LVI. Any samples shall be taken and analysed as per routine method.

Emissions to Surface Water

There are no additional emissions to surface water as a result of this process.

Emissions to Sewer

There are no emissions to sewer as a result of this process.

Emissions to Ground

There will be no additional emissions to ground as a result of this process.

Noise

There will be no additional noise sources added as part of this process.

Waste Management

Although a new process is being produced, the type of wastes generated will not vary from the waste historically generated on site. There will therefore be no new requirements for the handling, storage, and disposal of waste. There should not therefore, be any significant adverse environmental impact resulting from the disposal of waste from this project. As the proposed new process will be run in existing equipment, there will not be an increase in the amount of overall waste being produced.

Environmental Considerations

Where appropriate, Zoetis Belgium S.A. (Irish branch), has sought to use the most cost effective methods of reducing its environmental impact.

The following waste minimization technologies as outlined in the relevant Guidance Note for the Chemical Sector will be used.

a) Technologies for load minimization

I Optimisation of Condenser Efficiency.
Checks will be carried out before each distillation on major items of equipment to ensure air leakage is kept to a minimum.

II. Inventory Control
Where possible, only the amount of chemical used in the process will be ordered.
There are regular stock checks done on raw materials inventory
There is a computerised inventory listing
Quantities of raw materials used are specified on batch sheets to avoid overuse of materials.

Catalysts used will be recycled for re use

III. **Separation of Cooling Water, Storm Water and Process Effluent**
Storm water is kept separate to effluent and cooling water is cooled in cooling towers and recirculated for reuse.

b) Technologies for Containment of Emissions

I. Reactor operation is via computerised system to reduce the risk of Operator error.
II. Vent collection from all major items of equipment into the centralised system prior to further treatment.
III. Bunding of all stored materials with separate bunding for incompatibles
IV. Fire protection of bulk tank storage through Foam cannons

c) Technologies for Recovery and Recycle

I. Waste solvent sent off site is recycled where possible and reused as fuel where possible.

II. Re-use in another industry

III. Solvents, steel paper, glass, pallets, are reused/recycled in other industries.

d) Technologies for Treating Air Emissions

I. Selective chemical reaction scrubbers are used; primary treatment is oxidation at the LVI.

e) Technologies for Treating Water Emissions

I.	Primary treatment:	pH correction/ neutralisation
II.	Secondary treatment:	Biological degradation of effluent
III.	Tertiary treatment:	Settleability of final effluent

f) Technologies for Treatment and Disposal of Wastes

I. **Incineration:** Toxic and dangerous waste which is unsuitable for recovery shall be sent offsite for reuse as fuel or will be incinerated.

Accidental Emissions

All tanks are bunded so that in the event of a spill arising all material shall be contained. All bunds shall be constructed in accordance with the agency's guidelines on bund construction as detailed in the Agency's guidance note for the Annual Environmental Report.

All control equipment is maintained and calibrated in accordance with manufacturer's instructions and inspected and tested regularly as part of the sites Preventative Maintenance Programme.

The onsite emergency plan shall be reviewed to take into account any new emergency situations arising on site. The firewater retention Pond shall enable any contaminated effluent to be diverted to the firewater retention pond The effluent can be analysed prior to feeding into the wastewater treatment plant at a pre-controlled rate.

Any contaminated surface water from this area will be detected by an online pH/TOC meter. If elevated levels are detected, the diversion valve will divert this contaminated water to the firewater retention tank. The effluent can be analysed prior to feeding into the wastewater treatment plant at a pre-controlled rate.

The range of measures is dependent on the complexity of the site. Pollution prevention measures may, inter alia, include the following information:
Conclusions on BAT set out in the EU Reference document on BAT on emissions from storage such as a safety management system; corrosion prevention measures on tanks, etc.
Details of storage of all raw materials, products and wastes such as segregation, labelling, designation and impervious surface;
Details of spill or emergency containment measures and structures such as bunds, high level alarms, absorbent materials;
Details of fire detection and fire-water retention facilities in the event of emergencies or other measures to contain fire-water;
Details of transport of material within the site, solid, liquid or sludge transported by pipe, vehicle or conveyor; etc.,

Training

Process training will be carried out on- site and fully documented.

Cessation of Activity

The site's Decommissioning Management Programme (Closure, Restoration and Aftercare Management plan) will not be affected as a result of this new process.

Site Management and Control
A copy of the following is available:

- Zoetis Corporation Environmental Protection, Health and Safety Policy.
- Organisational charts