Thermo Fisher Scientific Cork Ltd.

New R&D Product - EPA Notification

"Project Callum"

18 May 2021

Priority: Urgent

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1.0 Introduction

Thermo Fisher Scientific Cork Ltd. is planning the introduction of a new product for research and development to the Cork site "Project Callum" in June 2021, this project is similar in scale and nature to other recent R&D notifications approved by the EPA i.e. small scale relative to the main products portfolio manufactured within the main production buildings.

As with all R&D projects the priority of this notification is urgent.

This request for approval in accordance with Condition 1.4 is in keeping with the guidelines from the EPA[1] on seeking alterations which state that:

"*An activity or process at an installation solely for research, development or testing of new products and processes are excluded and may be considered and approved by OEE. New products or processes at an installation adequately controlled by the conditions of the licence may be considered and approved by OEE."*

The proposed product will be manufactured in 6 Stages, 5 of which (Stages 1 & 3 to 6) will be manufactured at the Cork Facility, resulting in the manufacture of approximately 12kg of product. The process is similar to many current and previous process stages manufactured at the Cork facility. Many of the common bulk solvents are being used and standard unit operations are being employed in existing infrastructure within the R&D Building 9 and the Kilo Scale Facility (KSF) in Building 8. No changes to site management, infrastructure or control are required.

Within the existing buildings, the process uses existing modules and associated vent lines, drainage lines and abatement measures.

See Figure 1.1 for Site Layout and location of the proposed process stages. In terms of environmental operation and compliance, this process does not require a new main or minor emission point and can be readily facilitated and controlled within the existing Conditions and limits of the sites IE Licence.

[1] https://www.epa.ie/pubs/advice/licensee/Licence%20Alteration%20Guidance%20rev%20MOC%2021-06-19.pdf

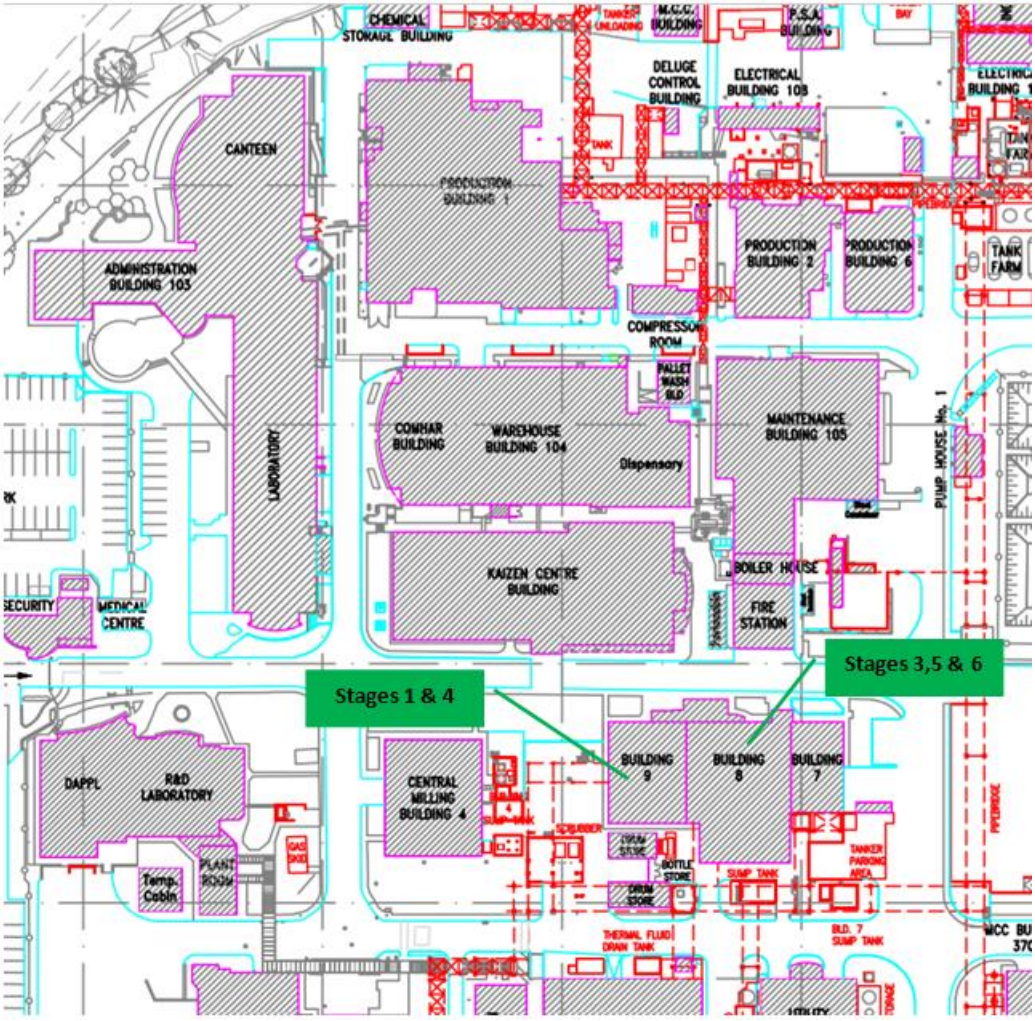


Figure 1.1 Site Layout and Location of Proposed Process Stages for Project Callum

2.0 Process Description

Overview

As outlined above, there is no change to the range of processes to be carried out in Building 8 KSF or Building 9. The proposed product will be generated through a series of 6 stages, with each stage comprising a number of unit operations (note Stage 2 is manufactured at another facility off site).

The following main unit operations will occur in the proposed process stages:

- Charging of solvent and reagents
- Mixing in standard vessels
- Chemical reaction
- Distillation

- Separation
- Drying in filter dryer
- Milling
- Storage of final product in product warehouse

Raw materials as per outlined in Table 2.1 will be subjected to various physical and chemical changes in order to produce the required chemical in the correct form. As a result, solid, liquid and gaseous emissions are generated. These emissions are subjected to physical and chemical treatment to remove any environmentally sensitive substances in accordance with IE Licence Reg. No. P0004-06 prior to discharge from the facility.

No changes to the existing abatement, treatment or recovery systems are required.

The associated environmental emissions are outlined in Figure 2.1.

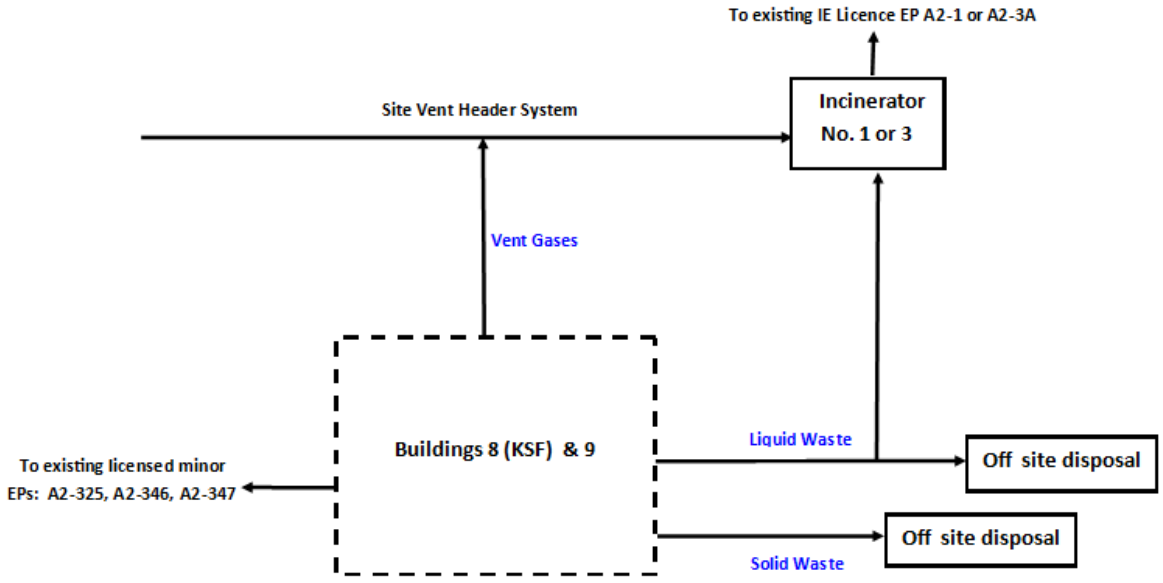


Figure 2.1 Project Callum Associated Environmental Emissions

TFS have reviewed the sites raw materials database and no new H phrases arise from the new raw materials on site. All new wastes to the incinerator are assessed in terms of compatibility with current waste streams as per standard operating procedure ENVP-063 Bulk Waste Characterisation and Storage Compatibility.

In addition, the incinerator burner management system and other critical safety interlocks are monitored and controlled by a Hima-Sella Programmable Logic Controller (PLC-19-004). PLC-19-004 is a dedicated Safety System associated with the incinerators. This will shut down the incinerator in the event of a safety parameter is exceeded.

Table 2.1 Raw Materials Associated with the New Process

Raw Material	New or Existing to site	SDS Hazard Phrases (Further details in attachment for new chemicals)
Stage 1		
CORT-00 (Compound 9 RSM)	New Seed	NA
10% Pd/C	Existing	NA
Methanol (MeOH)	Existing	H225, H301, H311, H331, H370
Toluene	Existing	H304, H225, H315, H373, H361d, H336
CORT-01	New Manufactured Intermediate	H315, H319, H335
Stage 2		
Intermediate from Stage 2 Manufactured off site	New (intermediate from Stage 2)	H315, H319, H335
Stage 3		
Stage 2 brought in from off site: CORT-02 (RSM)	New (intermediate from Stage 2)	H315, H319, H335
Hexyl Lithium (2.5M in hexane)	New	H314, H260, H250
Hexane (Iso-Container)	New	H411, H225, H304, H361f, H336, H315, H373
10% w/w NaCl	Existing	NA
Tetrahydrofuran (THF)	Existing	H225, H302, H319, H335, H336, H351
CORT-03, Stage 3 product	Manufactured Intermediate (liquid)	H315, H319, H335
Stage 4		
CORT-03 Stage 4 Input	Manufactured Intermediate (liquid)	H315, H319, H335
10% w/w NaOH	Existing	H314, H290, H318
Acetonitrile	Existing	H302, H312, H319, H225, H332
10% w/w NaCl	Existing	NA
Methyl tert-butyl ether (MTBE)	Existing	H315, H225
0.1M HCl	Existing	H314, H331, H335, H318, H290

Stage 4: output CORT-05	Manufactured Intermediate (solid) new	H302
Stage 5		
CORT-03 Stage 5 Input	Manufactured Intermediate (liquid)	H315, H319, H335
10% w/w NaOH	Existing	H314, H290, H318
Acetonitrile	Existing	H302, H312, H319, H225, H332
10% w/w NaCl	Existing	NA
Methyl tert-butyl ether (MTBE)	Existing	H315, H225
0.1M HCl	Existing	H314, H331, H335, H318, H290
Stage 5 Output CORT-05	Manufactured Intermediate New	H302
Stage 6		
CORT-05 Stage 5 Product Input to Stage 6	New	H302
Diisopropylethylamine (DIPEA)	Existing	H225, H302, H331, H318, H335
Dichloromethane (DCM)	Existing	H315,H319,H335,H336,H351,H373
N,N-Dimethylethylenediamine (DMEN)	New	H225, H302, H312, H314, H318
Acetone	Existing	H319, H225, H336
2M HCl	Existing	H314, H331, H335, H318, H290
Potassium carbonate 10% w/w	Existing	NA
CORT-06 Stage 6 output (API)	Manufactured API new	Not classified

3.0 Emissions

3.1. Emissions to Atmosphere

There are no new main or minor emission points to atmosphere. As outlined above, the process will use existing modules and associated vent lines and abatement measures. As illustrated in Figure 2.1, all organic vapours from the process will be vented to the onsite abatement system incinerator IN1931 or incinerator IN1951 (Licensed emission points A2-1 and A2-3A) via each buildings vent header system.

Venting from any dust handling activities such as solids charging, solids dig out, filters, dryers and from milling will be double HEPA filtered and routed to existing IE Licenced minor emission points A2-325 (Building 9) and A2-346 & A2-347 (Building 8).

3.1.1 Parameters from the Process

Parameters expected to arise in the emissions to air from the new process before it reaches the onsite abatement system (incinerator IN1931/ incinerator IN1951 (Licensed emission points A2-1/A2-3A)) are outlined in the following Table 3.1 along with the associated IE Licence ELVs.

Table 3.1 Parameters from the proposed new process to incinerator IN1931/ incinerator IN1951

Gaseous Waste pre abatement:	Chemical Formula	Combustion Products	ELV in Licence Daily avg mg/m³
Stage 1			
Traces of solvents: Toluene	C_7H_8	CO_2, H_2O & CO	CO: 50
Stage 3			
Traces of solvents: Methyl tert-butyl ether (MTBE) & Hexane	$C_5H_{12}O$ C_6H_{14}	CO_2, H_2O & CO	CO: 50
Stage 4			
Traces of solvents: Heptane and Hydrochloric acid	C_7H_{16} HCl	H_2O, CO_2, CO & HCl	CO: 50 HCl: 10
Stage 5			
Traces of solvents: Methyl tert-butyl ether (MTBE)	$C_5H_{12}O$	CO_2, H_2O & CO	CO: 50
Stage 6			
Traces of solvents: Acetone, Dichloromethane (DCM)& Disoproplyethylamine (DIPEA)	C_3H_6O CH_2Cl_2 $C_8H_{19}N$	CO_2, H_2O, CO, HCl & NOx	CO: 50 HCl: 10 NOx: 200

It is assumed the maximum concentrations are above the relevant BAT threshold values and appropriate abatement in the form of incineration is being employed. As this is a batch process, gaseous emissions from this process to the vent header system and incineration are not continuous.

In both incinerators on site (A2-1 and A2-3A) waste liquids and vent gases are incinerated at a temperature of 1150°C, in 5% excess oxygen and a two second residence time to ensure complete destruction of all organic components to CO_2 and H_2O. In addition, NOx , SOx and HCl would be anticipated from N, S and Cl containing wastes. No other combustion products are expected from the burning of liquid wastes and vent gases from the proposed process.

The following ELVs and continuous monitoring are in place within the IE Licence for both incinerators to address combustion products from all wastes incinerated.

Parameter	Units	Half Hour Average		Daily Average	10 minute average
Carbon monoxide (CO) Note 1	mg/m^3	100		50	150
		A	B		
Total dust	mg/m^3	30	10	10	-
Volatile organic compounds expressed as total organic carbon	mg/m^3	20	10	10	-
Hydrogen chloride (HCl)	mg/m^3	60	10	10	-
Hydrogen fluoride (HF)	mg/m^3	4	2	1	-
Hydrogen bromide (HBr)	mg/m^3	5	3	2	-
Sulphur dioxide (SO_2)	mg/m^3	200	50	50	-
Oxides of Nitrogen (NO and NO_2 expressed as NO_2)	mg/m^3	400	200	200	-

Parameter	Emission Limit Value	
Cadmium (as Cd) + thallium (as Tl), and their compounds Note 2	30minute – 8 hour sample	Total 0.05 mg/m^3
Mercury (as Hg) and its compounds Note 2	30minute – 8 hour sample	0.05 mg/m^3
Antimony (as Sb), arsenic (as As), lead (as Pb), chromium (as Cr), cobalt (as Co), copper (as Cu), manganese (as Mn), nickel (as Ni), and vanadium (as V) and their compounds Note 2	30minute – 8 hour sample	Total 0.5 mg/m^3
Dioxins/furans (TEQ) Note 3	6 – 8 hour sample	0.1 ng/m^3

No ELV including the flow ELV is likely to be exceeded during the manufacture of the new product. For context, Incinerator No. 3 was designed to burn up to 10,000 MT of hazardous waste per year and Incinerator No. 1 7,000 MT within the limits of our IE Licence. In 2020, a total of 3,084 MT of hazardous waste in total was burned on site. Therefore, there is significant spare capacity in terms of compliant incineration on site.

Notwithstanding the above, incinerator performance and emissions profiles will be monitored carefully during each new campaign on site.

It is not possible to estimate the pre-abatement particulate emissions concentrations for the minor emission points from the dust handling activities i.e. A2-325, A2-346 & A2-347. There is no change in the dust handling activities and the same abatement measures (double HEPA filtration with >99.99% removal efficiencies) will be in place as for the particulate emission points attached to the process on site.

For existing minor emission points A2-325, A2-346 & A2-347 the following monitoring programme will be put in place with 'Element Ireland' (ISO 17025 accredited) and in accordance with the requirements of EPA Air Emission Monitoring Guidance Note AG2.

Monitoring for total particulate matter (TPM), velocity and volumetric flow rate will be carried out in accordance with the following standards:

METHODS & TECHNICAL PROCEDURES USED

Parameter	Standard	Technical Procedure
Total Particulate Matter	EN 13284-1	CAT-TP-01
Velocity & Vol. Flow Rate	EN 16911-1 (MID)	CAT-TP-41

Results will be compared against the following emission limits as specified within Schedule C.1.2 of the IE Licence to demonstrate that the emissions remain minor in nature:

Parameter	Emission Limit Value
Total Particulates	1 mg/m^3
Pharmaceutical dust - as active ingredient	0.15 mg/ m^3 at a mass flow >1 g/hour.

The above emission limit values apply to the following emission points as outlined in Schedule C.1.1 of the sites IE Licence:

Emission Point Reference Nos.: A2-12, A2-13, A2-14, A2-112, A2-116, A2-123, A2-124, A2-128, A2-146, A2-149, A2-150, A2-152, A2-162, A2-163, A2-166, A2-301, A2-303, A2-308, A2-316, A2-317, A2-318, A2-319, A2-320, A2-325, A2-328, A2-338, A2-339, A2-340, A2-341, A2-342, A2-343, A2-344, A2-345, A2-346, A2-347, A2-348, A2-351, A2-352, A2-353, A2-354, A2-355.

Parameter	Monitoring Frequency	Analysis Method/Technique
Total particulates	Annually	Isokinetic/Gravimetric

3.2. Aqueous Emissions

As illustrated in Figure 2.1, aqueous waste will be routed to:

- either of the on-site incinerators IN1931/IN1951 which includes Licensed air emission points A2-1/A2-3A and internal aqueous emission point W1.
- Or offsite to an approved and permitted hazardous waste facility

Table 3.2 provides an overview of the constituents of the aqueous waste.

Table 3.2 Liquid Waste Stream to On Site Incinerator / Offsite to Indaver

Waste Stream, L/Batch, Approx. composition	Chemical Formula	Combustion Products	ELV in Licence Daily avg mg/m³
Stage 1			
Distillate 182L Constituents include Methanol & Toluene	CH_4O C_7H_8	CO_2, H_2O & CO	CO: 50
Stage 3			
Waste aqueous phase 51L Constituents: MTBE, THF, Sodium chloride	$C_5H_{12}O$ C_4H_8O NaCl	CO_2, H_2O, CO, NOx, HCl	CO: 50 NOx: 200 HCl: 10
Stage 4			
Distillate, constituent Heptane	C_7H_{16}	CO_2, H_2O, CO	CO: 50
Organic phase, constituent Methyl tert-butyl ether (MTBE)	$C_5H_{12}O$	CO_2, H_2O, CO	CO: 50
Aqueous phase, constituents include HCl, water	HCl, H_2O	CO_2, H_2O, CO, HCl	CO: 50 HCl: 10
Stage 5			
Mother liquors and waste, constituents water, MTBE, sodium chloride	H_2O $C_5H_{12}O$ NaCl	CO_2, H_2O, CO, HCl & NOx	CO: 50 NOx: 200 HCl: 10
Stage 6			
Aqueous phase, constituents include HCl, diisoproplyethylamine (DIPEA), dimethylethlenediamine (DMEN)	HCl $C_8H_{19}N$ $C_4H_{12}N_2$	CO_2, H_2O, CO, HCl & NOx	CO: 50 NOx: 200 HCl: 10
Distillate, major constituents include Acetone & DCM	C_3H_6O CH_2Cl_2	CO_2, H_2O, CO, HCl	CO: 50 HCl: 10
Mother liquors and wash, major constituents include acetone and water	C_3H_6O H_2O	CO_2, H_2O, CO	CO: 50

3.3. Emissions to Sewer

There are no emissions to sewer from the Thermo Fisher site.

4 Solid Waste Generation and Disposal

All solid waste will be sent off site for incineration, in line with existing site procedures and IE Licence Requirements.

Table 4.1 Solid Waste

Solid Waste Material	Quantity (kg)	Further Treatment	Recovery / Reuse / Recycle	Final Disposal
Bags/liners etc.	2.5 drums approx. per batch	n/a	n/a	Off site incineration

5. SDS Hazardous Data for List of new chemicals, raw materials and products to site

Item	H Phrase
Stage 1: output CORT-01	SECTION 2: Hazards identification **2.1. Classification of the substance or mixture** **Classification according to Regulation (EC) No. 1272/2008 [CLP]** Skin corrosion/irritation, Category 2 H315 Serious eye damage/eye irritation, Category 2 H319 Specific target organ toxicity — Single exposure, Category 3, Respiratory tract irritation H335 Full text of H statements : see section 16 **Adverse physicochemical, human health and environmental effects** No additional information available **2.2. Label elements** **Labelling according to Regulation (EC) No. 1272/2008 [CLP]** Hazard pictograms (CLP) :  GHS07 Signal word (CLP) : Warning Safety Data Sheet according to Regulation (EU) 2020/878 Hazard statements (CLP) : H315 - Causes skin irritation. H319 - Causes serious eye irritation. H335 - May cause respiratory irritation. Precautionary statements (CLP) : P261 - Avoid breathing dust, vapours. P280 - Wear protective gloves, protective clothing, eye protection, face protection. P302+P352 - IF ON SKIN: Wash with plenty of water. P333+P313 - If skin irritation or rash occurs: Get medical advice/attention. P362+P364 - Take off contaminated clothing and wash it before reuse. P403+P233 - Store in a well-ventilated place. Keep container tightly closed. **2.3. Other hazards** PBT: not yet assessed vPvB: not yet assessed

Stage 2: CORT-02 (RSM) [4-bromo-2-(triisopropylsilyl)thiazole]	SECTION 2: Hazards identification **2.1. Classification of the substance or mixture** **Classification according to Regulation (EC) No. 1272/2008 [CLP]** Skin corrosion/irritation, Category 2 H315 Serious eye damage/eye irritation, Category 2 H319 Specific target organ toxicity — Single exposure, Category 3, Respiratory tract irritation H335 Full text of H statements : see section 16 **Adverse physicochemical, human health and environmental effects** No additional information available **2.2. Label elements** **Labelling according to Regulation (EC) No. 1272/2008 [CLP]** Hazard pictograms (CLP) :  GHS07 Signal word (CLP) : Warning 10/02/2021 (Issue date) EN (English) 1/9 Safety Data Sheet according to Regulation (EU) 2020/878 Hazard statements (CLP) : H315 - Causes skin irritation. H319 - Causes serious eye irritation. H335 - May cause respiratory irritation. Precautionary statements (CLP) : P261 - Avoid breathing dust, vapours. P280 - Wear protective gloves, protective clothing, eye protection, face protection. P302+P352 - IF ON SKIN: Wash with plenty of water. P333+P313 - If skin irritation or rash occurs: Get medical advice/attention. P362+P364 - Take off contaminated clothing and wash it before reuse. P403+P233 - Store in a well-ventilated place. Keep container tightly closed. **2.3. Other hazards** PBT: not yet assessed vPvB: not yet assessed

Stage 3: output

SECTION 2: Hazards identification

2.1. Classification of the substance or mixture

Classification according to Regulation (EC) No. 1272/2008 [CLP]

Skin corrosion/irritation, Category 2	H315
Serious eye damage/eye irritation, Category 2	H319
Specific target organ toxicity — Single exposure, Category 3, Respiratory tract irritation	H335

Full text of H statements : see section 16

Adverse physicochemical, human health and environmental effects

No additional information available

2.2. Label elements

Labelling according to Regulation (EC) No. 1272/2008 [CLP]

Hazard pictograms (CLP) :

GHS07

Signal word (CLP) : Warning

Safety Data Sheet

according to Regulation (EU) 2020/878

Hazard statements (CLP) : H315 - Causes skin irritation.
H319 - Causes serious eye irritation.
H335 - May cause respiratory irritation.

Precautionary statements (CLP) : P261 - Avoid breathing dust, vapours.
P280 - Wear protective gloves, protective clothing, eye protection, face protection.
P302+P352 - IF ON SKIN: Wash with plenty of water.
P333+P313 - If skin irritation or rash occurs: Get medical advice/attention.
P362+P364 - Take off contaminated clothing and wash it before reuse.
P403+P233 - Store in a well-ventilated place. Keep container tightly closed.

2.3. Other hazards

PBT: not yet assessed
vPvB: not yet assessed

Stage 3: Hexyl Lithium

SECTION 2: Hazards identification

2.1 Classification of the substance or mixture

Classification according to Regulation (EC) No 1272/2008

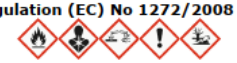
Flammable liquids (Category 2), H225
Pyrophoric liquids (Category 1), H250
Substances and mixtures, which in contact with water, emit flammable gases (Category 1), H260
Skin corrosion (Sub-category 1A), H314
Serious eye damage (Category 1), H318
Reproductive toxicity (Category 2), H361f
Specific target organ toxicity - single exposure (Category 3), Central nervous system, H336
Specific target organ toxicity - repeated exposure, Inhalation (Category 2), Nervous system, H373
Aspiration hazard (Category 1), H304
Long-term (chronic) aquatic hazard (Category 2), H411

For the full text of the H-Statements mentioned in this Section, see Section 16.

2.2 Label elements

Labelling according Regulation (EC) No 1272/2008

Pictogram



Signal word	Danger
Hazard statement(s)	
H225	Highly flammable liquid and vapour.
H250	Catches fire spontaneously if exposed to air.
H260	In contact with water releases flammable gases which may ignite spontaneously.
H304	May be fatal if swallowed and enters airways.
H314	Causes severe skin burns and eye damage.
H336	May cause drowsiness or dizziness.
H361f	Suspected of damaging fertility.
H373	May cause damage to organs (Nervous system) through prolonged or repeated exposure if inhaled.
H411	Toxic to aquatic life with long lasting effects.
Precautionary statement(s)	
P210	Keep away from heat, hot surfaces, sparks, open flames and other ignition sources. No smoking.
P231 + P232	Handle and store contents under inert gas. Protect from moisture.
P280	Wear protective gloves/ protective clothing/ eye protection/ face protection.
P301 + P310 + P331	IF SWALLOWED: Immediately call a POISON CENTER/doctor. Do NOT induce vomiting.
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.
P305 + P351 + P338 + P310	IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a POISON CENTER/doctor.
P370 + P378	In case of fire: Use dry sand, dry chemical or alcohol-resistant foam to extinguish.
Supplemental Hazard information (EU)	
EUH014	Reacts violently with water.

2.3 Other hazards

This substance/mixture contains no components considered to be either persistent, bioaccumulative and toxic (PBT), or very persistent and very bioaccumulative (vPvB) at levels of 0.1% or higher.

Hexane	**2. Hazard(s) identification** **Classification** This chemical is considered hazardous by the 2012 OSHA Hazard Communication Standard (29 CFR 1910.1200) Flammable liquids — Category 2 Skin Corrosion/Irritation — Category 2 Serious Eye Damage/Eye Irritation — Category 2 Reproductive Toxicity — Category 2 Specific target organ toxicity (single exposure) — Category 3 Target Organs - Respiratory system, Central nervous system (CNS). Specific target organ toxicity - (repeated exposure) — Category 1 Target Organs - Respiratory system, Heart. Aspiration Toxicity — Category 1 **Label Elements** **Signal Word** Danger

Hazard Statements
Highly flammable liquid and vapor
May be fatal if swallowed and enters airways
Causes skin irritation
Causes serious eye irritation
May cause respiratory irritation
May cause drowsiness or dizziness
Suspected of damaging fertility
Causes damage to organs through prolonged or repeated exposure

Precautionary Statements
Prevention
Obtain special instructions before use
Do not handle until all safety precautions have been read and understood
Use personal protective equipment as required
Wash face, hands and any exposed skin thoroughly after handling
Wear eye/face protection
Do not breathe dust/fume/gas/mist/vapors/spray
Do not eat, drink or smoke when using this product
Use only outdoors or in a well-ventilated area
Keep away from heat/sparks/open flames/hot surfaces. - No smoking
Keep container tightly closed
Ground/bond container and receiving equipment
Use explosion-proof electrical/ventilating/lighting/equipment
Use only non-sparking tools
Take precautionary measures against static discharge
Keep cool
Response
IF exposed or concerned: Get medical attention/advice
Inhalation
IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing
Skin
If skin irritation occurs: Get medical advice/attention
IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water/shower
Wash contaminated clothing before reuse
Eyes
IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing
If eye irritation persists: Get medical advice/attention
Ingestion
IF SWALLOWED: Immediately call a POISON CENTER or doctor/physician
Do NOT induce vomiting
Fire
In case of fire: Use CO_2, dry chemical, or foam for extinction
Storage
Store locked up
Store in a well-ventilated place. Keep container tightly closed
Disposal
Dispose of contents/container to an approved waste disposal plant
Hazards not otherwise classified (HNOC)
Toxic to aquatic life with long lasting effects
WARNING: Reproductive Harm - https://www.p65warnings.ca.gov/.

Stage 4 and Stage 5: output CORT-05	**2. HAZARDS IDENTIFICATION** **Classification according to Regulation (EC) No. 1272/2008:** Signal Word: **Warning** **Hazard Statements:** H302: Harmful if swallowed **Label according to (EC) No. 1272/2008** **Precautionary Statements:** P101: If medical advice is needed, have product container or label at hand **Carcinogenic:** This product has not been fully tested **Sensitiser:** This product has not been fully tested **Primary route(s) of entry:** Inhalation; Skin-Eyes; Ingestion; Needlestick **Health:** Caution - The toxicological properties of this material have not been fully investigated. Exposure might occur via inhalation; ingestion; skin; eyes. Exercise due care when handling. Handle with appropriate care to minimise exposure. Wash thoroughly after handling. **Environment:** No information is available about the potential of this material to produce adverse environmental effects.

Stage 6: N,N-Dimethylethylenediamine (DMEN)	**SECTION 2: Hazards identification** **2.1 Classification of the substance or mixture** **Classification according to Regulation (EC) No 1272/2008** Flammable liquids (Category 2), H225 Acute toxicity, Oral (Category 4), H302 Acute toxicity, Dermal (Category 4), H312 Skin corrosion (Sub-category 1A), H314 Serious eye damage (Category 1), H318 For the full text of the H-Statements mentioned in this Section, see Section 16. **2.2 Label elements** **Labelling according Regulation (EC) No 1272/2008** Pictogram  Signal word: Danger Hazard statement(s) H225: Highly flammable liquid and vapour. H302 + H312: Harmful if swallowed or in contact with skin. H314: Causes severe skin burns and eye damage. Precautionary statement(s) P210: Keep away from heat, hot surfaces, sparks, open flames and other ignition sources. No smoking. P233: Keep container tightly closed. P280: Wear protective gloves/ protective clothing/ eye protection/ face protection/ hearing protection. P301 + P312: IF SWALLOWED: Call a POISON CENTER/ doctor if you feel unwell. P303 + P361 + P353: IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water. P305 + P351 + P338: IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Supplemental Hazard Statements: none **2.3 Other hazards** This substance/mixture contains no components considered to be either persistent, bioaccumulative and toxic (PBT), or very persistent and very bioaccumulative (vPvB) at levels of 0.1% or higher.

Stage 6: CORT-06 (API)	

SECTION 2 - HAZARDS IDENTIFICATION

Classification of the substance or mixture

SECTION 2 - HAZARDS IDENTIFICATION …continued

Globally Harmonized System [GHS]	Not classified
Other/Supplemental	Substance not yet fully tested
Label elements	
GHS hazard pictogram	None required
GHS signal word	None required
GHS hazard statements	None required
GHS precautionary statements	None required
Other hazards	CORT125329 is an antagonist of the glucocorticoid receptor (GR). No other information identified.
Note	This substance does not meet criteria for classification under GHS as implemented by Regulation EC No 1272/2008 (EU CLP), WHMIS 2015 (Health Canada), and Hazard Communication Standard No. 1910.1200 (US OSHA). Nevertheless, it should be handled with caution as it is pharmacologically active and has not yet been fully tested.

Stage 6: CORT125329 Sulfonyl linker	

SECTION 2: Hazards identification

2.1. Classification of the substance or mixture

Classification according to Regulation (EC) No. 1272/2008 [CLP]

Skin corrosion/irritation, Category 2	H315
Serious eye damage/eye irritation, Category 2	H319
Specific target organ toxicity — Single exposure, Category 3, Respiratory tract irritation	H335

Full text of H statements : see section 16

Adverse physicochemical, human health and environmental effects

No additional information available

2.2. Label elements

Labelling according to Regulation (EC) No. 1272/2008 [CLP]

Hazard pictograms (CLP) :

GHS07

Signal word (CLP) : Warning

Hazard statements (CLP) : H315 - Causes skin irritation.
H319 - Causes serious eye irritation.
H335 - May cause respiratory irritation.

Precautionary statements (CLP) : P261 - Avoid breathing dust, vapours.
P280 - Wear protective gloves, protective clothing, eye protection, face protection.
P302+P352 - IF ON SKIN: Wash with plenty of water.
P333+P313 - If skin irritation or rash occurs: Get medical advice/attention.
P362+P364 - Take off contaminated clothing and wash it before reuse.
P403+P233 - Store in a well-ventilated place. Keep container tightly closed.

2.3. Other hazards

PBT: not yet assessed
vPvB: not yet assessed