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New Product Introduction Treatment – EPA Notification

"Project NOAH"

07 October 2022

Priority: Urgent

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1. Introduction

ThermoFisher Scientific is planning the introduction of a new product, Project NOAH, to the Cork site. The product to be manufactured relates to the treatment of cancer. Manufacturing for Project NOAH is proposed to commence on the week commencing 7th November 2022 and will be manufactured in site Building 5.

Priority of this notification: 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.*"

Project NOAH will involve the manufacture of approximately 0.5 kg of product per batch. It is proposed to manufacture two batches in November 2022. 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 Building 5. No changes to site management, infrastructure or control are required.

Within Building 5, 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. 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

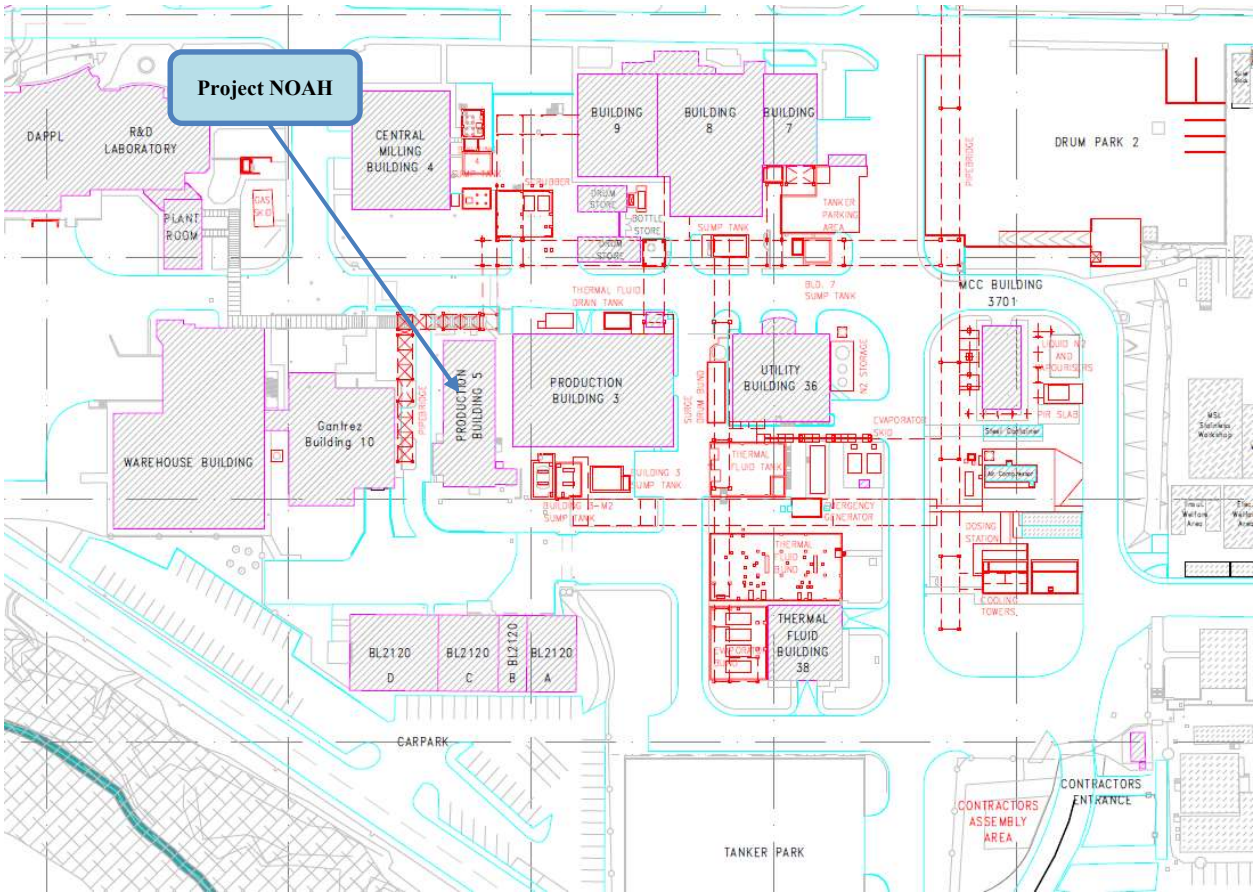

Figure 1.1 Site Layout and Location of Proposed Process for Project NOAH

2. Process Description

As outlined above, there is no change to the range of processes to be carried out in Building 5. The manufacture of the proposed product comprises a number of unit operations.

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 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 for Project NOAH are outlined in Figure 2.1.

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 exceedance.

Figure 2.1 Project NOAH Associated Environmental Emissions

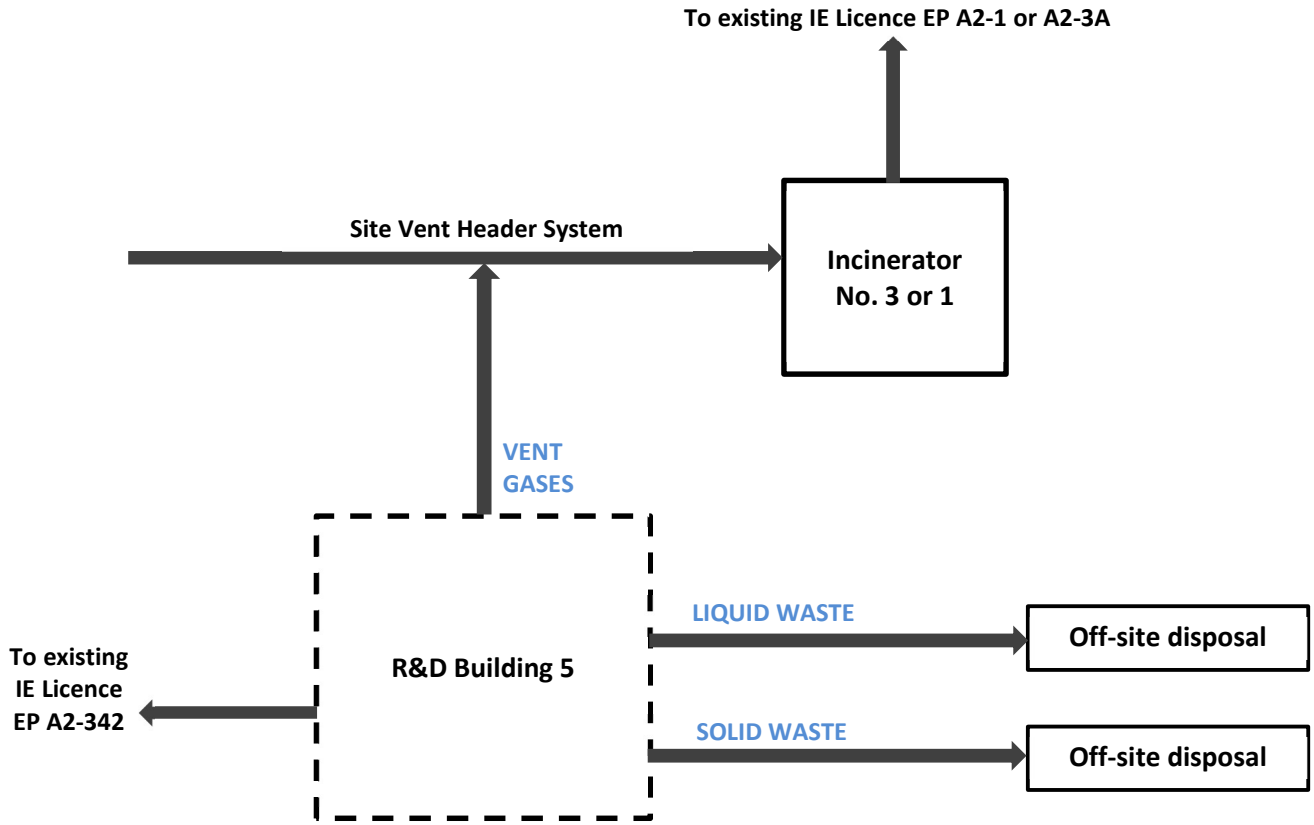

Table 2.1 Raw Materials Associated with Project NOAH

Raw Material	New or Existing to Site	SDS Hazard Phrases (Further details in attachment for new chemicals)
NUV-1511-6	New	H300, H340, H350, H360FD, H372
NUV-1511-7	New	H314
Diisopropylethylamine (DIPEA)	Existing	H302, H318, H331, H335, H225
4-Dimethylaminopyridine (DMAP)	Existing	H301, H310, H331, H315, H318, H370, H411
Dichlormethane (DCM)	Existing	H315, H319, H336, H350, H373
Triflouroacetic acid (TFA)	Existing	H314, H332, H412
t-Butyl methyl ether (tBME)	Existing	H315, H225
NUV-1511-9	New	H302, H314, H318

3. 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 emission point A2-342 (Building 5).

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 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 Average (mg/m^3)
Traces of solvents: DCM, TBME, TFA, DIPEA, isobutylene	CH_2Cl_2 $C_5H_{12}O$ $C_2HF_3O_2$ $C_8H_{19}N$ C_4H_8	CO, CO_2, H_2O, NO_X, HCl, HF	CO: 50 NO_X: 200 HCl: 10 HF: 1

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 vent gases are incinerated at a temperature of 1150^{o}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, NO_X, HCl and HF would be anticipated from N, Cl and F 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/m³	100		50	150
		Column A	Column B		
Total dust	mg/m³	30	10	10	-
Volatile organic compounds expressed as total organic carbon	mg/m³	20	10	10	-
Hydrogen chloride (HCl)	mg/m³	60	10	10	-
Hydrogen fluoride (HF)	mg/m³	4	2	1	-
Hydrogen bromide (HBr)	mg/m³	5	3	2	-
Sulphur dioxide (SO_2)	mg/m³	200	50	50	-
Oxides of Nitrogen (NO and NO_2 expressed as NO_2)	mg/m³	400	200	200	-

Parameter	Sampling Period	Emission Limit Value
Cadmium (as Cd) + thallium (as Tl), and their compounds Note 2	30minute – 8-hour sample	Total 0.05 mg/m³
Mercury (as Hg) and its compounds Note 2	30minute – 8-hour sample	0.05 mg/m³
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/m³
Dioxins/furans (TEQ) Note 3	6 – 8-hour sample	0.1 ng/m³

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 2021, a total of 4,710 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 emission point from the dust handling activities i.e. A2-342. 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.

NUV-1511-6 is categorised as a Thermo Fisher Scientific Occupational Hazard Category 3B material. It is a potent chemical agent which may cause cancer and reproductive affecting indications in humans, therefore, it is necessary to ensure that all personnel and the environment are fully protected. As such, existing emission point A2-342 will be monitored according to standard operating procedure TTP-012 'Environmental Monitoring and Reporting'. Surface (swab) monitoring of the exhaust of the HEPA filtered air vent will be carried out by Thermo Fisher personnel. Results of this testing will be compared with a surface target value of 300ng/100cm^2 for NUV-1511-6.

3.2 Aqueous Emissions

All aqueous waste streams generated during production in Building 5 will be drummed off in line with site health and safety requirements and routed off-site to an approved and permitted hazardous waste facility for incineration as illustrated in Figure 2.1.

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

Table 3.2 Liquid Waste Stream sent offsite for incineration

Waste Stream, L/Batch, Approx Composition	Chemical Formula
Mother Liquors, 31 L. Major constituents: DCM, TBME, TFA-DIPEA, HCl-DIPEA, TFA DAMP, NUV-1511-7, NUV-1511-9, reaction side products	CH_2Cl_2 $C_5H_{12}O$ $C_2HF_3O_2$ $C_8H_{19}N$ $C_7H_{10}N_2$ $C_{10}H_{17}ClN_2O_3$ $C_{28}H_{31}N_5O_6$
Mother Liquors & wash, 10 L. Major constituents: DCM, TBME, TFA-DIPEA, HCl-DIPEA, TFA DAMP, NUV-1511-7, NUV-1511-9, reaction side products	CH_2Cl_2 $C_5H_{12}O$ $C_2HF_3O_2$

Waste Stream, L/Batch, Approx Composition	Chemical Formula
	$C_8H_{19}N$ $C_7H_{10}N_2$ $C_{10}H_{17}ClN_2O_3$ $C_{28}H_{31}N_5O_6$
Interbatch clean, 25 L Water, NUV-1511-9, TFA-DIPEA, TBME	$C_{28}H_{31}N_5O_6$ $C_2HF_3O_2$ $C_8H_{19}N$ $C_5H_{12}O$

3.3 Emissions to Sewer

There are no emissions to sewer from the ThermoFisher 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 for off-site incineration

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 <u>new</u> chemicals, raw materials and products to site

Item	H Phrase
NUV-1511-6	**SECTION 2: Hazard(s) identification** **Classification of the substance or mixture** **Acute toxicity (oral), Category 2** Fatal if swallowed. **Germ cell mutagenicity, Category 1B** May cause genetic defects. **Carcinogenicity, Category 1B** May cause cancer. **Reproductive toxicity, Category 1B** May damage fertility or the unborn child. **Specific target organ toxicity — Repeated exposure, Category 1** Causes damage to organs (digestive, immune, and male reproductive systems, hair follicles) through prolonged or repeated exposure. **Label elements** **GHS Hazard pictograms**  **GHS Signal word** Danger **GHS Hazard statements** H300 - Fatal if swallowed. H340 - May cause genetic defects. H350 - May cause cancer. H360FD - May damage fertility or the unborn child. H372 - Causes damage to organs (digestive, immune, and male reproductive systems, hair follicles) through prolonged or repeated exposure.

Item	H Phrase
NUV-1511-7	**SECTION 2: Hazards identification** **2.1 Classification of the substance or mixture** **Classification according to Regulation (EC) No 1272/2008** Skin corrosion/irritation,Category 1A, B, C,H314
NUV-1511-9	**SECTION 2: Hazard(s) identification** **2.1. Classification of the substance or mixture** **GHS-US classification** Acute toxicity (oral), Category 4 H302 Skin corrosion/irritation, Category 1A H314 Serious eye damage/eye irritation, Category 1 H318 Full text of H statements : see section 16 **SECTION 16: Other information** Other information : The information contained in this Safety Data Sheet (SDS) is believed to be accurate and represents the best information currently available to us. We make no warranty, however, expressed or implied, with respect to such information, and we assume no liability resulting from its use. Users should make their own investigations to determine the suitability of the information for their particular purposes. Full text of H-statements: H302 Harmful if swallowed H314 Causes severe skin burns and eye damage H318 Causes serious eye damage SDS US (GHS HazCom 2012)