

Summary of Proposed “Imidazole” Project

Introduction

A new product is proposed to be introduced to the Arklow site in 2023, details are provided below.

PROCESS DESCRIPTION

Proposed Process:

Imidazole is a critical buffer substance for bioprocesses to enhance the purity of the target protein. Imidazole has been manufactured and supplied by Merck, Schaffhausen in Switzerland, SCH, for several years. For business reasons it is now planned to relocate the chemical synthesis steps to Arklow. Merck Darmstadt, MDa, will also perform product packaging and distribution while product analysis will remain in SCH to simplify the initial transfer.

The Arklow output will be **Imidazole min. 99%**, which will be supplied to MDa for final packaging and distribution. Individual batch sizes will be in the range of 500-800KG while the total annual output will be in the 1500-3000KG range.

Specifically, for this first production campaign, which is planned for Q1 of 2023, validation of the methods in Arklow is not relevant at present as analysis of the product will continue to be performed in SCH. If, at some point in the future, a decision is made to perform the testing in Arklow, then this will be managed as a new project.

Instrumentation and Control:

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

Capacities and Throughput

As in the existing plant, throughput will vary depending on the products and batch sizes required by the customer. Typical vessel capacities are given below.

Item	Equipment	Material	Capacity
A10	Glass lined reactor	GL	8000L
A11	Glass lined reactor	GL	4000L
E4	Glass lined dryer	GL	4000L
C5	Hastelloy Centrifuge	Hastelloy	100KG

Note: GL= Glass Lined.

GMP All items meet GMP standard.

Explosion protection: All motors are of E Ex dII A + IIB standard.

Raw Materials and Product.

Details are attached on the following page

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

Ref. N° or Code	Material/ Substance ⁽¹⁾	CAS Number	Danger ⁽²⁾ Category	Amount Stored (tonnes)	Annual Usage (tonnes)	Nature of Use	H Statement	P Statement
RM	Imidazole	288-32-4	Danger	2000 kg	Initially 2000kg Potential increase to approx. 4000 kg in future years	Raw material for production of product for supply	H302 Harmful if swallowed H314 Causes severe skin burns and eye damage H360D May damage the unborn child	P260 DO not breathe dusts or mists 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 P304 + P340 + P310 IF INHALED: Remove person to fresh air and keep comfortable for breathing. Immediately call a POISON CENTER/ doctor. P305 + P351 + P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
FP	Imidazole	288-32-4	Danger	1600KG	1600KG	Product for Sale	H302 Harmful if swallowed H314 Causes severe skin burns and eye damage H360D May damage the unborn child	P260 DO not breathe dusts or mists 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 P304 + P340 + P310 IF INHALED: Remove person to fresh air and keep comfortable for breathing. Immediately call a POISON CENTER/ doctor. P305 + P351 + P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.

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 N° 77/94
3. c.f. Schedules 9 and 10 of SI No 62/2004

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			
Organic solvent-based Mother Liquors from the process	07 05 04	Filtration steps within the process	9 tonnes in 2023 Increasing to 18 tonnes in future years	Production scheduling dependent – some months will be zero, while one month might be the full annual quantity	Waste solvent tank	Offsite by approved contractor	Managed as per all similar existing waste streams

1 All organic solvent waste will be disposed of off site for recovery or incineration

Emissions to Atmosphere

Process Emissions

Process emissions will be combined into the main header system and directed to a dual scrubber system and then directed to the Waste Air Treatment Plant (Thermal Oxidiser).

Vent Listing

Vent No.	Building	Description	Major	Minor	Potential	Connected to Header
A1-7	Thermal Oxidiser vent	Thermal Oxidiser	✓	-	-	Combination of all vents in header system

Abatement and Treatment and Recovery Systems

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

Emissions Monitoring

As all process vents are connected to the dual scrubber system emission monitoring from the proposed new product shall take place at A1-7 (Thermal Oxidiser stack). Any samples shall be taken and analysed as per routine method.

Emissions to Surface Water

There are no 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 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 product is being produced, the type of wastes generated will not vary from the waste currently being produced now. 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 and replaces existing production while it is running, there will not be an increase in the amount of overall waste being produced.

Training

Operator training for the new product manufacture will be carried out on-site and will be fully documented

Cessation of Activity

The site's Residual 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:

- Sigma Aldrich Ireland Ltd. Environmental, Health and Safety Policy.
- Organisational charts.
- ISO14001 Overview Manual