

Lilly Mondrian Concept Phase

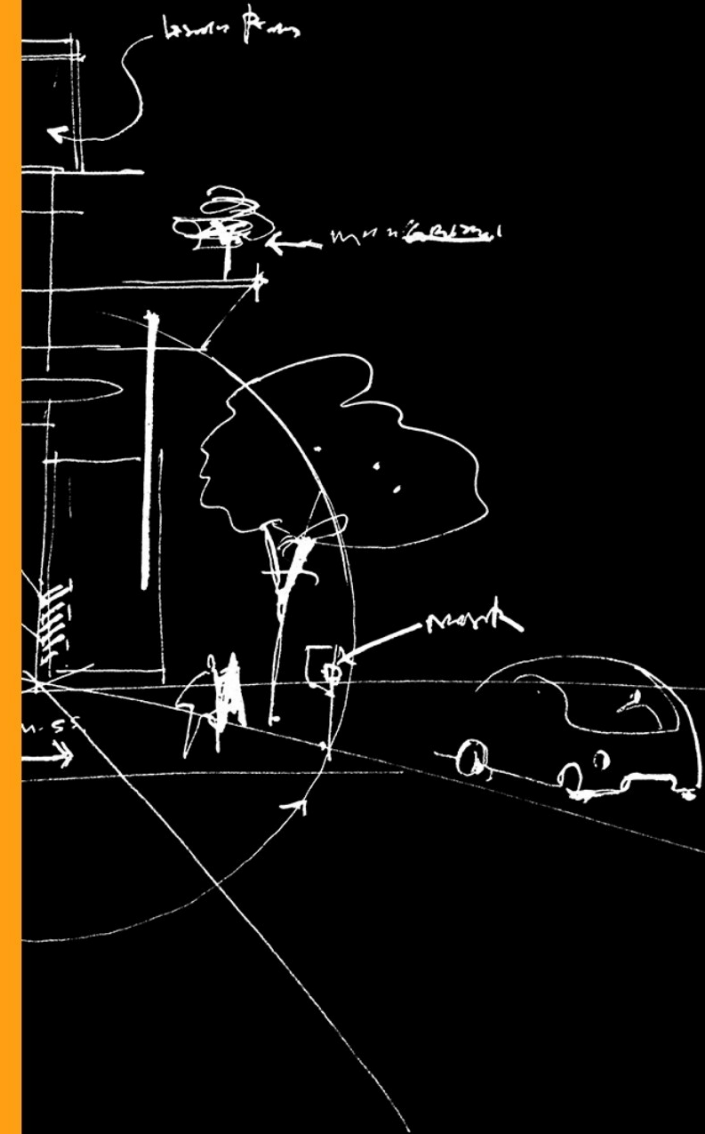
SEVESO Analysis

21st Jan 2026

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Introduction

- **Purpose of Evaluation**

- Assess compliance with Seveso III Directive (2012/18/EU)
- Identify major accident hazards and mitigation measures

- **Scope**

- Covers hazardous substances & Determine if Seveso is applicable to the site.

- **Regulatory Context**

- Non-Tier vs Lower-tier vs Upper-tier classification
- Key obligations: Safety Report, Emergency Plan, Public Information

Executive Summary

This Seveso III regulatory evaluation was undertaken to determine whether the Eli Lilly “Project Mondrian” Oral Solid Dosage (OSD) facility falls within the scope of the Seveso III Directive (2012/18/EU).

The assessment is based on data and information supplied by Lilly, reflecting the best available data at the time of evaluation, and was used to develop an accurate representation of the site’s projected hazardous substance inventory and operational conditions.

A comprehensive review of all hazardous materials used or stored on site was completed, including process solvents, laboratory chemicals, utilities, and cleaning/passivation materials. Attention was given to denatured ethanol containing 5% methanol, due to methanol’s classification as a named Seveso substance. Following mixture evaluation aligned with CLP (Classification, Labelling and Packing) rules, the material was categorised under hazard class P5c with a corresponding 5,000 tonne threshold.

All Seveso-relevant substances were incorporated into the aggregation methodology defined in Note 4 of the Directive. Using the operational assumptions provided by Lilly—such as batch frequencies, solvent recovery, maximum inventories, and multiproduct capacity—the cumulative lower-tier result was calculated as 0.8346, below the threshold value of 1.0.

Accordingly, **the Project Mondrian facility is not deemed to fall within the Seveso classification**, with no lower-tier or upper-tier obligations triggered. As the evaluation relies on currently supplied data, any future changes to materials, storage volumes, process conditions, or facility configuration should be reassessed to ensure ongoing compliance with Seveso III requirements.

Evaluation Approach

■ Inventory Assessment

- Identify all hazardous substances and quantities.

■ Classification

- Apply CLP hazard categories.

■ Threshold Comparison

- Compare site inventory against Annex I thresholds.
- If Material is a named substance – Compare inventory against Annex II thresholds

■ Calculate the Cumulative

- When no single substance exceeds its qualifying quantity, the Seveso Directive requires an aggregation calculation to determine if the site falls under Lower-tier or Upper-tier obligations.

Site Layout



PROJECT MONDRIAN
Site Master Plan 1:1200 @A1
OPTION A - 16.01.2026



Facility Description

- The Eli Lilly Katwijk plant (Project Mondrian) is designed as a high-tech oral solid dosage (OSD) manufacturing facility with two primary unit operations.
 - The first is Spray Drying, where the active pharmaceutical ingredient (API) is dissolved in a solvent solution and spray-dried with excipients to achieve the required solubility profile.
 - The second is the OSD area, which includes multiple suites for direct compression tablet manufacturing, followed by aqueous-based tablet coating. Additionally, the facility features a multiproduct wing capable of wet and dry granulation with advanced containment systems achieving exposure levels of $<0.1 \text{ } \mu\text{g}/\text{m}^3$, enabling safe handling of highly potent compounds and supporting a broad future product portfolio.

Denatured Ethanol Evaluation

- The primary solvents used on site for the Spray Drying Process are:
 - Ethanol denatured with 5% Methanol (w/w)
 - Methanol is a named substance under Seveso; Ethanol is not
 - A separate evaluation was conducted by TAUW (local Dutch partner)
 - Assessment determined:
 - Mixture classification under CLP and Seveso III
 - Applicable hazard category and thresholds
 - Full TAUW report is attached
- **CLP Classification**
 - Mixture properties estimated per Regulation (EC) No. 1272/2008
 - Summation rules applied for toxicity categories:
 - LD50 oral: 2000 mg/kg
 - LC50 inhalation: 64,000 ppm
 - Mixtures with 5% Methanol:
 - Not categorized as toxic category 3 or higher
 - Methanol <10% → Specific organ toxicity (single exposure) category 2
 - Classification aligns with CLP estimation rules for ethanol-5% methanol mixture
- **Conclusion**
 - Mixture of ethanol with 5% methanol falls under:
 - Seveso Hazard Category P5c (Flammable liquid category 2)
 - Applies only if not stored or used under elevated temperature or pressure
 - Threshold for Category P5c: 5,000 metric tonnes



Kenmerk

N001-1300671RFU-V01-mvg-NL

CLP classification

In case hazard properties of mixtures are not available, rules for estimating properties of mixtures are established in Regulation (EC) No. 1272/2008². In this regulation, summation rules are provided for estimating the toxicity categories of mixtures. Using LD50 of 2000 mg/kg (oral)³ and LC50 of 64,000 ppm (inhalation)³, mixtures containing 5% methanol are not categorized as toxic category 3 or higher according to the summation rule. Methanol mixtures of <10% by weight are categorized as specific organ toxicity – single exposure category 2 in Regulation (EC) No. 1272/2008. The results from the estimation rules in this regulation thus align with the aforementioned information available for the ethanol-5%methanol mixture.

Conclusion

Both on the basis of available information about the mixture and toxicity estimation based on Regulation (EC) No. 1272/2008, a mixture of ethanol with 5% methanol is considered only in Seveso Hazard category P5c (flammable liquid category 2), as long it is not stored or used under elevated temperature or pressure conditions. The threshold for this category is 5.000 metric tonnes.

Hazardous Materials

Process Materials

Material Name	Chematic 82 Euro	Chematic 501	IMS	Isopropanol	Acetone	Opadry II	Copovidone	LY3502970 Hemicalcium	LY3502970 SDD	Magnesium Stearate	Sodium Carbonate	Crospovidone XL- 10	Microcrystalline Cellulose
Seveso Applicable	Non-Seveso	Non-Seveso	Seveso !	Seveso !	Seveso !	Non-Seveso	Non-Seveso	Seveso !	Seveso !	Non-Seveso	Non-Seveso	Non-Seveso	Non-Seveso
Reason	N/A	N/A	P5c	P5c	P5c	N/A	N/A	E2	E2	N/A	N/A	N/A	N/A

Non-Process Materials

Material Name	Sodium Hydroxide	Sodium Bisulphite solution	Sodium Metabisulfite (Solid)	Ethylene Glycol	Sodium Hypochlorite	Sulphuric Acid	Citric Acid	Phosphoric Acid	Nitric Acid	Oxygen	Hydrogen	Helium	Ethylene	Carbon Dioxide	Acetylene
Seveso Applicable	Non-Seveso	Non-Seveso	Non-Seveso	Non-Seveso	Seveso !	Non-Seveso	Non-Seveso	Non-Seveso	Seveso !	Seveso !	Seveso !	Non-Seveso	Seveso !	Non-Seveso	Seveso !
Reason	N/A	N/A	N/A	N/A	E1	N/A	N/A	N/A	P8	P4	P2	N/A	P2	N/A	P2

Assumptions & Basis

- No of SDD Batches per annum = 216
- No of OSD Batches per annum = 1794
- Fresh & Waste Solvent Inventory = 4 Weeks Production
- Solids Material Inventory = 12 Weeks
- Cleaning Frequency = 4 Weeks
- Assumes 100% Solvent Recovery.

■ Multiproduct

- Assumes a max H1 & E1 Material of 300kg onsite at any given time
- Existing infrastructure will support and no additional solvent foreseen in MP Suites

■ Labs

- Assumed list of Lab Gases included as per previous page
- Small volumes of solvents will be used and inventory will be managed to ensure Seveso thresholds are not exceeded

■ Sitewide

- As the project is phased additional chemicals for Passivation (Citric, Nitric and Phosphoric acid have been included – 2 IBCs of each onsite at a given time

Results & Conclusions

■ Calculation basis

- The evaluation was performed using the aggregation formulas defined in Seveso III, specifically Note 4, which requires summing the ratios of each substance quantity to its respective lower-tier qualifying quantity.

■ Threshold Requirements

- To remain classified as a Non-Seveso site, the aggregated lower-tier value must stay below 1. This ensures that the combined presence of hazardous substances does not trigger Seveso obligations.

■ Current Result

- Based on the current inventory, assumptions, and supplementary notes, the calculated sum is 0.80, confirming that the site does not meet the criteria for Seveso classification and therefore remains outside the Directive's scope.

■ Future Considerations

- Any changes to material types, quantities, or process conditions must prompt a re-evaluation to verify compliance. All modifications should be documented to maintain transparency and ensure the site continues to operate below the lower-tier threshold.

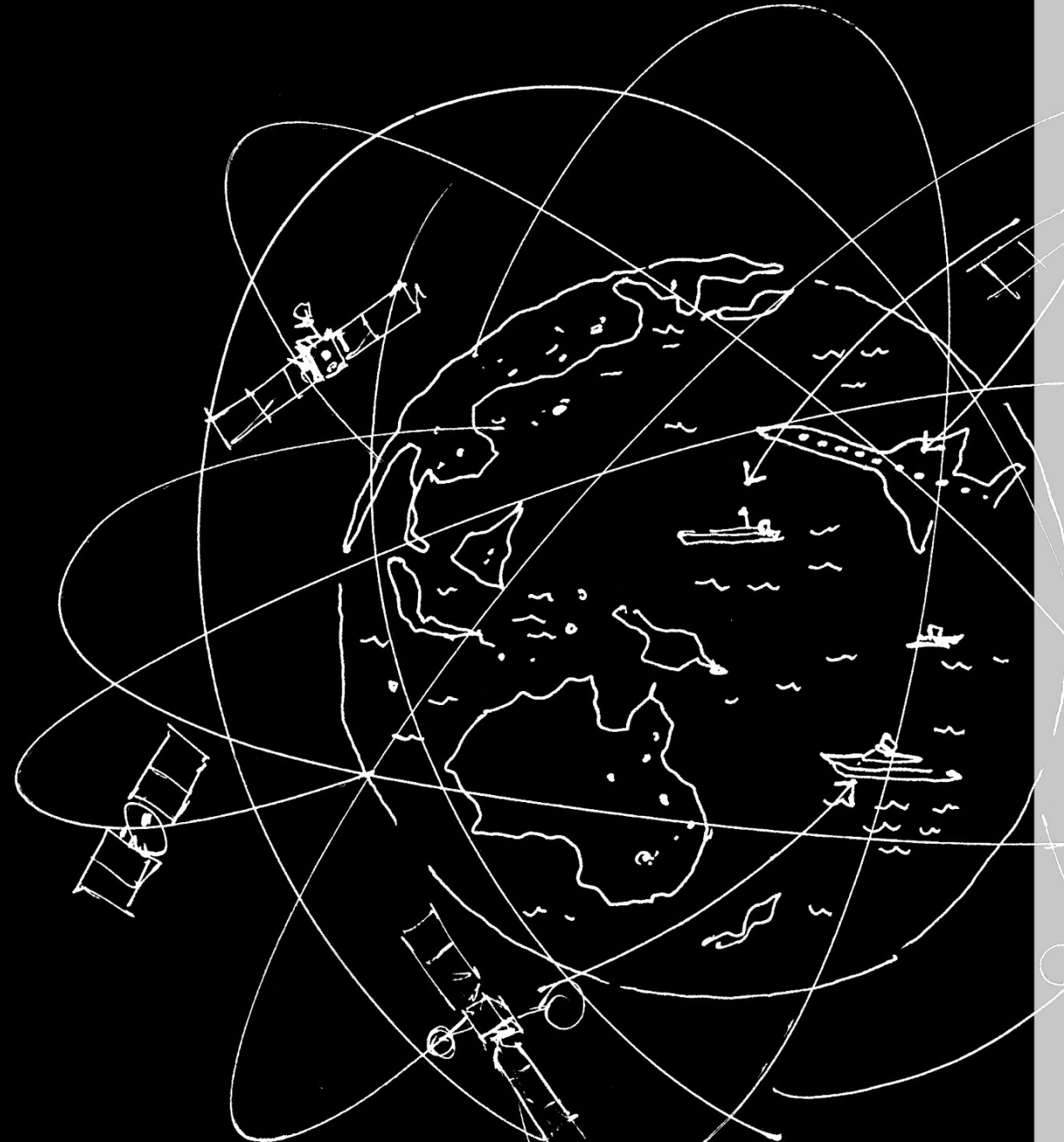
Hazard Category	Classification	Lower-tier qualifying quantity	Upper-tier qualifying quantity	Dangerous Substance	< 1 = Lower-tier Seveso	Health, Physical and environment hazards > 1 = Lower-tier Seveso (Note 8)	≥ 1 = Upper-tier Seveso	Health, Physical and environment hazards ≥ 1 = Upper-tier Seveso (Note 8)
H1	H1 Acute Toxic Cat 1	5	20	Sodium hypochlorite, OEB5 Materials	0.2200		0.055	0.055
H2	H2 Acute Toxic Cat 2, 3	50	200		0.0000	0.220	0.000	
H3	H3 - STOT SE Category 1	50	200		0.0000		0.000	
P5c	Flammable P5c	5000	50000	Denatured Ethanol (Methanol), Acetone	0.1183	0.118	0.012	0.012
E1	E1 Environmental Hazard Cat Acute 1 or Chronic 1	100	200	OEB5 Materials LY3502970 Hemicalcium, LY3502970 SDD	0.0110		0.006	0.170
E2	E2 Environmental Hazard Cat Chronic 2	200	500		0.4122	0.423	0.165	
P8	Oxidising liquids/solids Cat 1-3	50	200		0.0603	0.060	0.015	0.015
Named Substance 1	<5% Sodium Hypochlorite	200	500	N/A	0.0116		0.005	
Named Substance 2	Oxygen	200	2000	N/A	0.0000		0.000	
Named Substance 3	Hydrogen	5	50	N/A	0.0000		0.000	
Named Substance 4	Acetylene	5	50	N/A	0.0006		0.000	
Named Substance 5	Ethylene	5	50	N/A	0.0005		0.000	
					0.8346		0.2570	

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