



"ICM Factory Project"

End to End Continuous
Manufacturing of
Pharmaceuticals

October 27, 2021



Discussion Points

- Background
- Integrated Continuous Manufacturing (ICM) Factory Tour
- End to End Continuous Manufacturing Challenges

Disclaimer: Ernie Penachio and Continuus Pharmaceuticals are not part of FDA.

Background on CONTINUUS Pharmaceuticals

- Spin-out of the Novartis-MIT Center for Continuous Manufacturing
- Backed by a major pharmaceutical equipment manufacturer, i.e. Industria Macchine Automatiche (IMA) and Investors
- Expertise in integrated continuous unit operations (reaction, extraction, crystallization, filtration, drying, drug product, control systems, PATs)
- Projects with generics and pharma to develop ICM processes for their drugs

CONTINUUS to Build US 1st GMP End-to-End Continuous Manufacturing Facility



CONTINUUS Awarded \$69.3M DoD Grant

Will enable construction of the country's first GMP facility for end-to-end, ICM-driven production of small-molecule drugs in Woburn, MA.



Integrated Continuous Manufacturing (ICM) technology

Outsourcing -Pharma.com

Continuus lands \$69.3m US drug manufacturing contract

By Jenni Spinner

21-Jan-2021 - Last updated on 22-Jan-2021 at 15:04 GMT



(aleksejplatonov/ISTock via Getty Images Plus)

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On-shore Production

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January 29, 2021

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Vials and Oral Solid Dosages

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Multi Product Facility
Potent Compounds (OEB 1-5)

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DEA Scheduled Drugs

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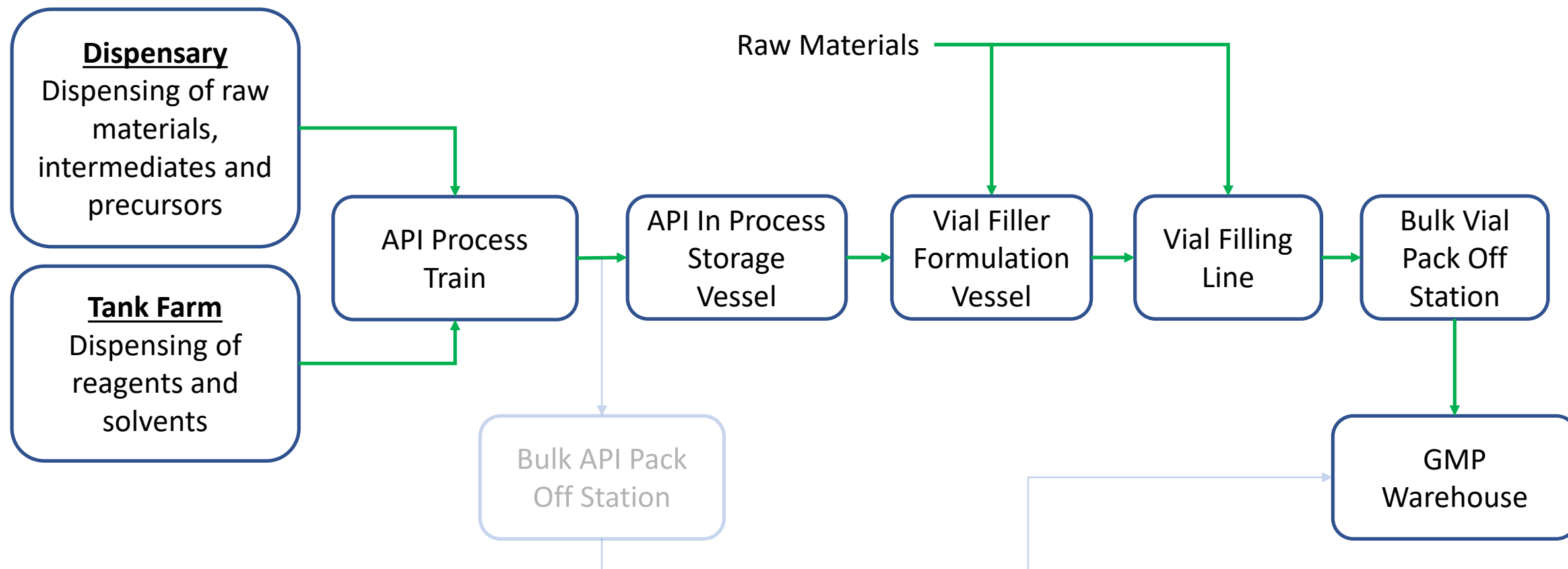
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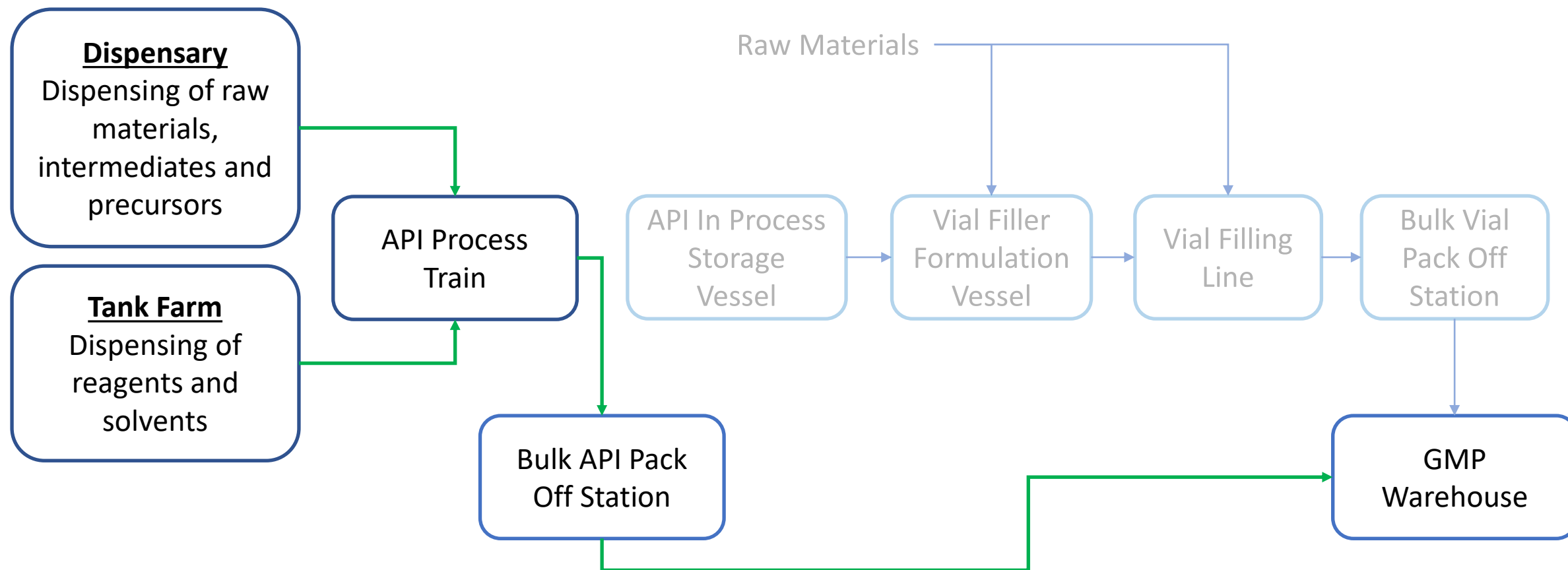
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On-shore Production
Drug Substance & Product
Vials and Oral Solid Dosages
Bulk API
Multi Product Facility
Potent Compounds (OEB 1-5)
DEA Scheduled Drugs
100M Vials Annual Capacity

End to End Continuous Production Pathway of Sterile Vials



Continuous Production Pathway of Bulk API

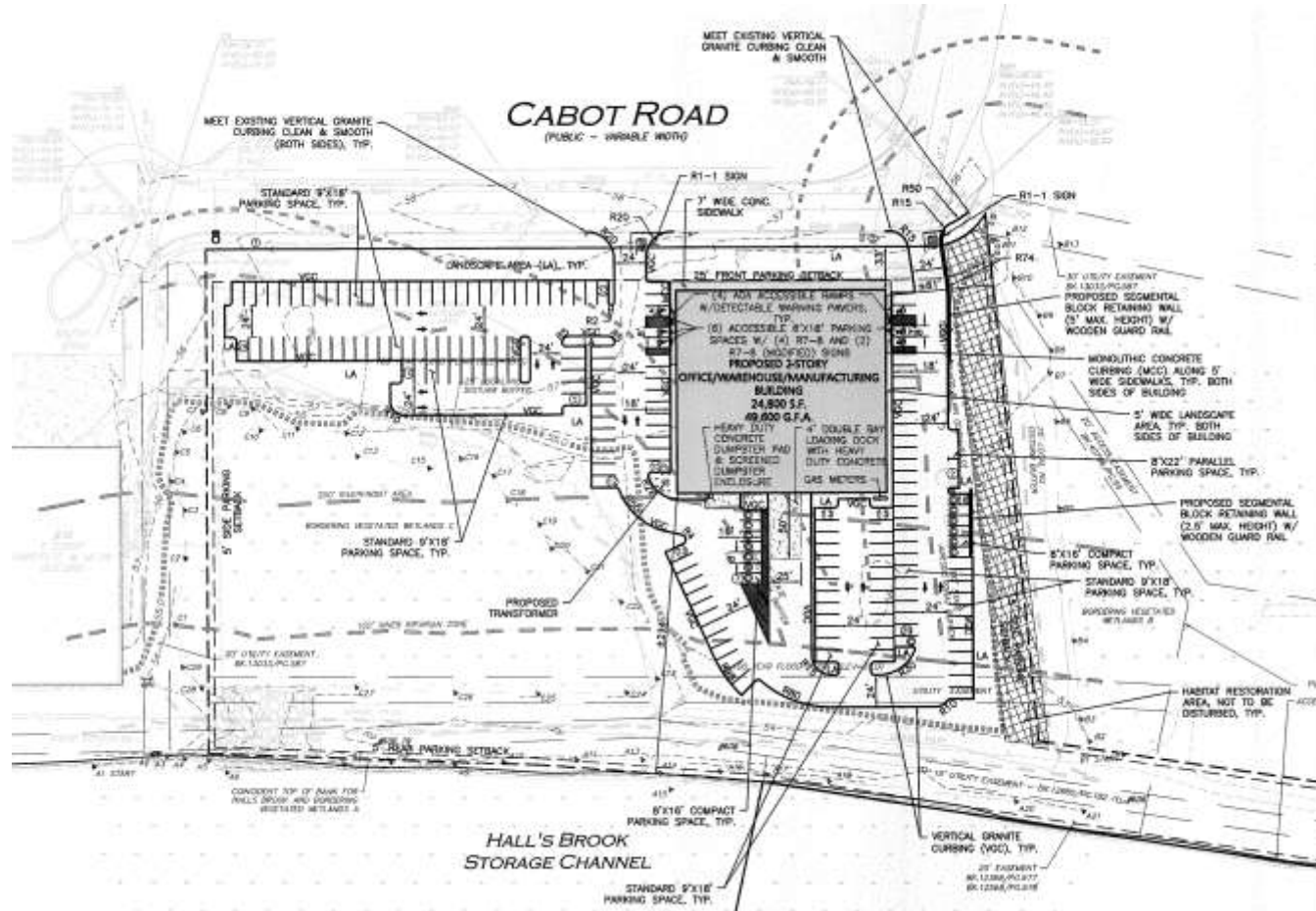


From Pilot Plant to Commercial Production

32 Cabot Road, Woburn MA

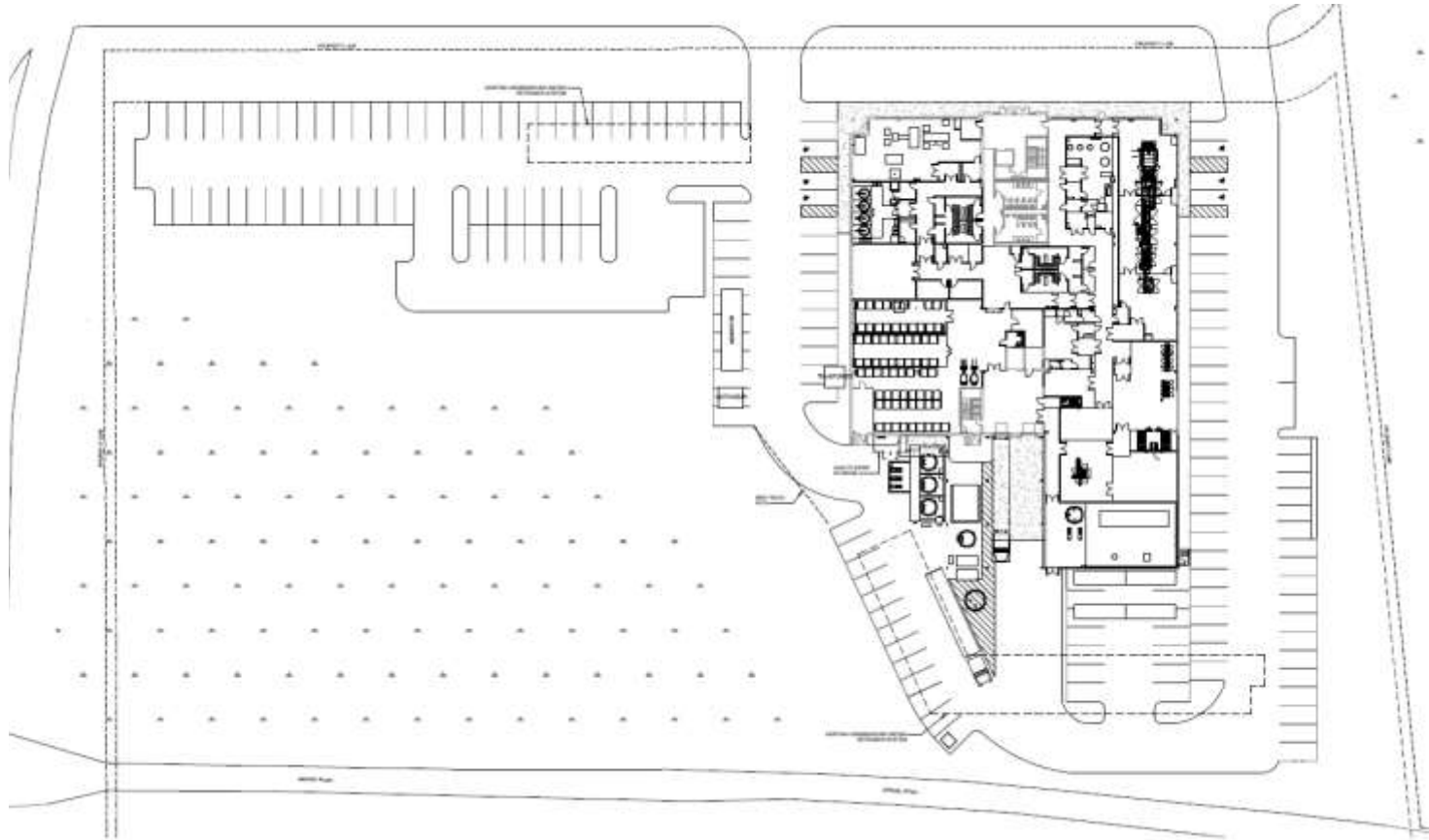


ICM Factory – Existing Conditions Site Plan



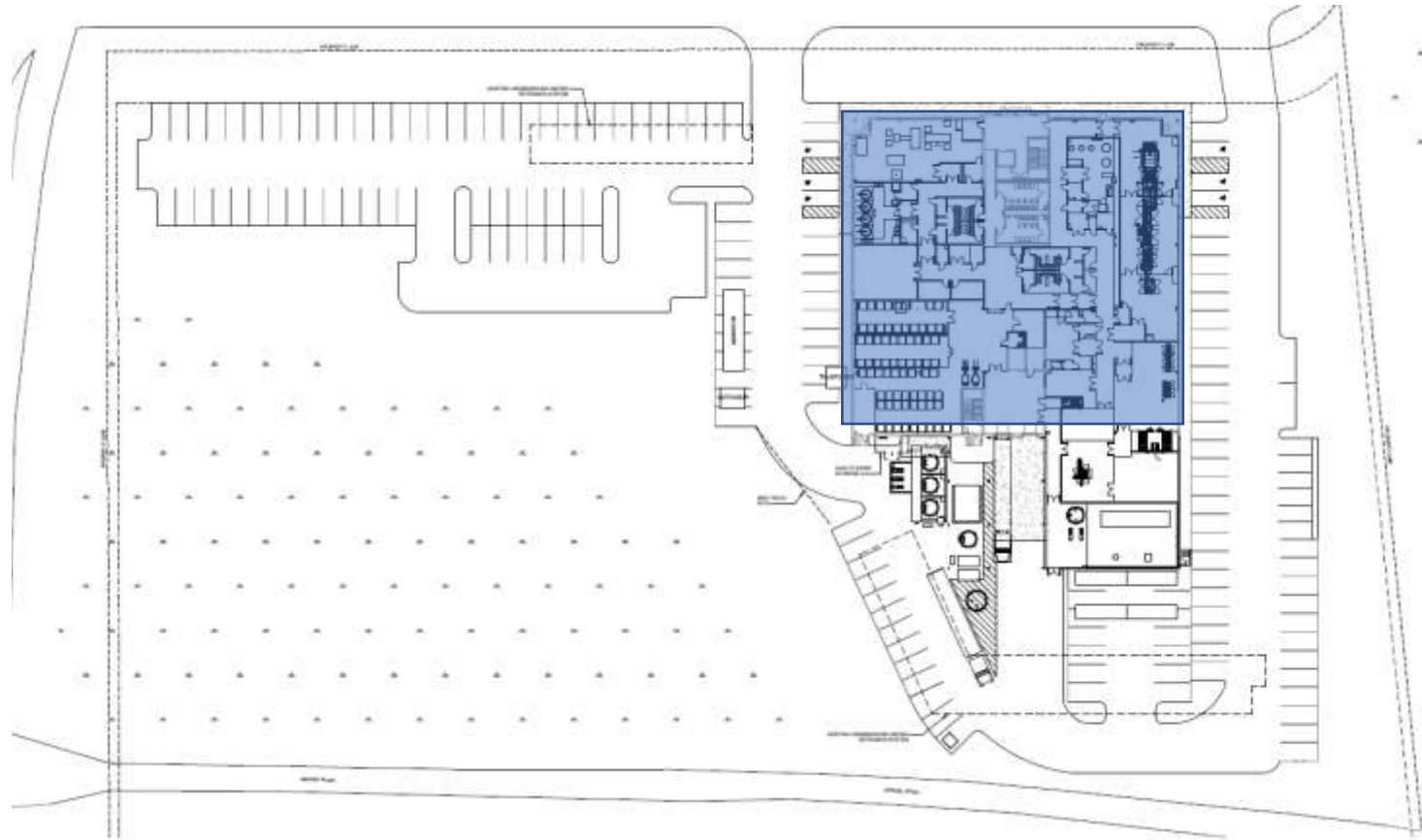
32 Cabot Road, Woburn MA
49,600 ft² Warm Shell

ICM Factory – Site Plan



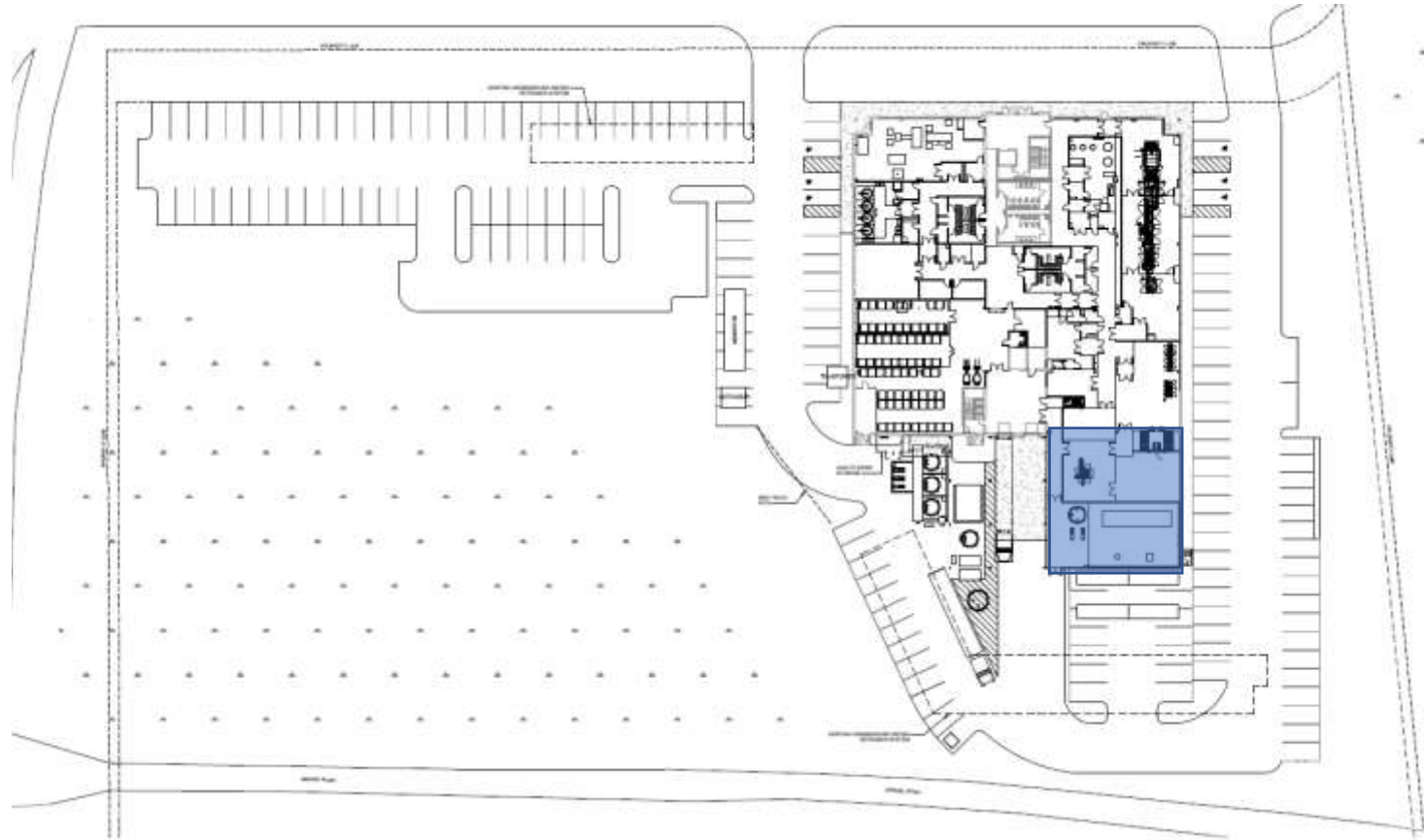
- Master Site Plan
- Detailed Engineering Design

ICM Factory – Site Plan



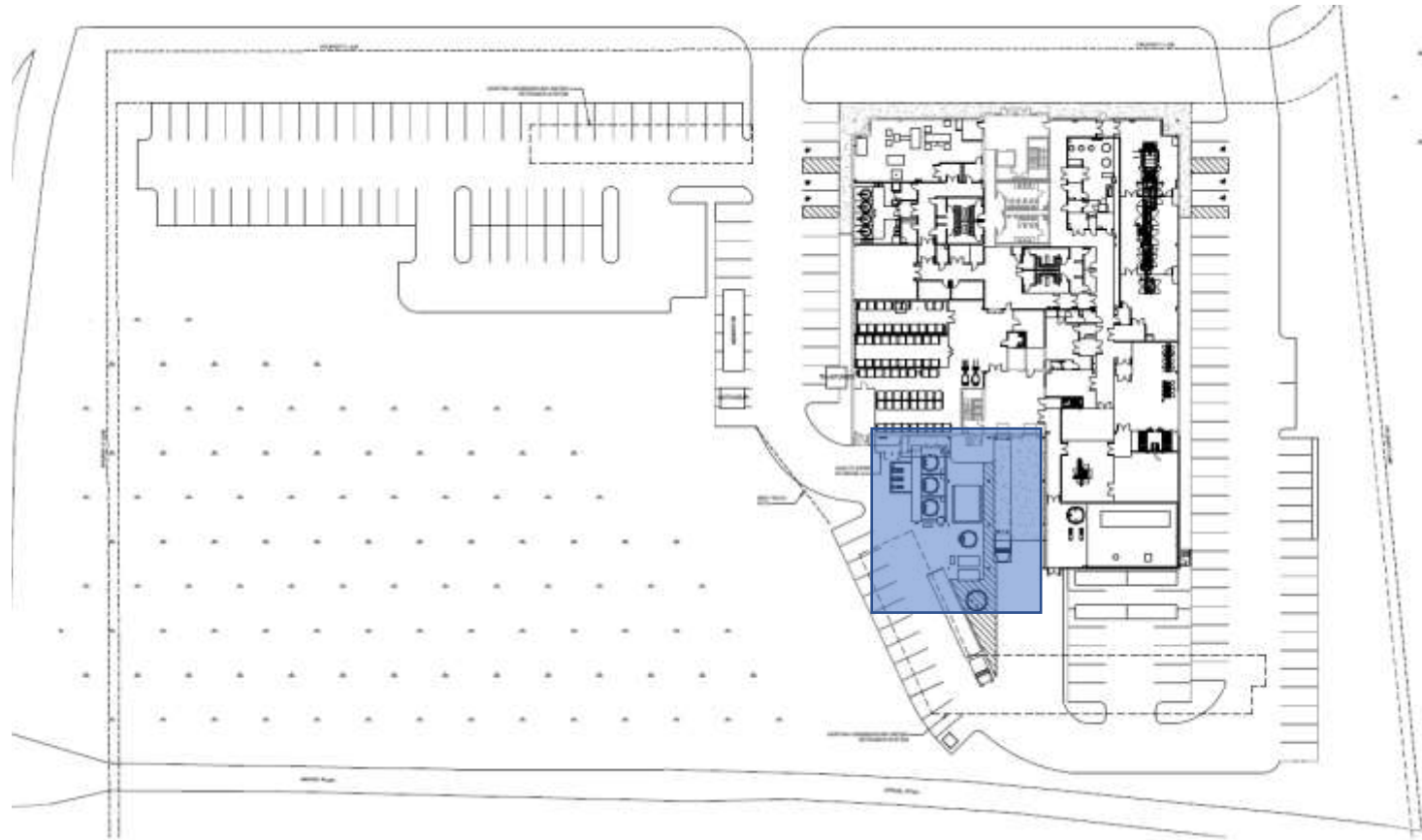
Existing Warm Shell

ICM Factory – Site Plan



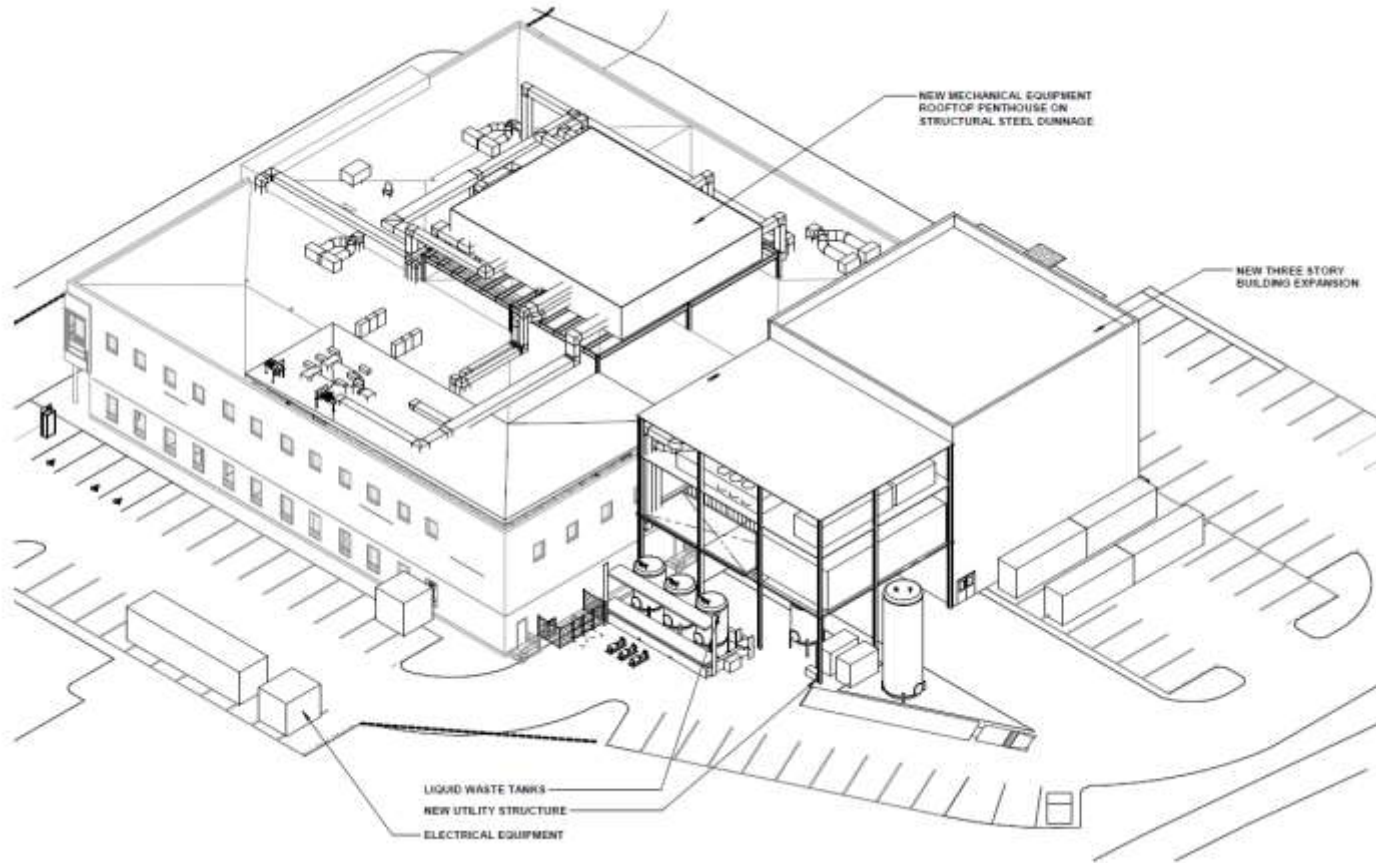
Building Addition

ICM Factory – Site Plan

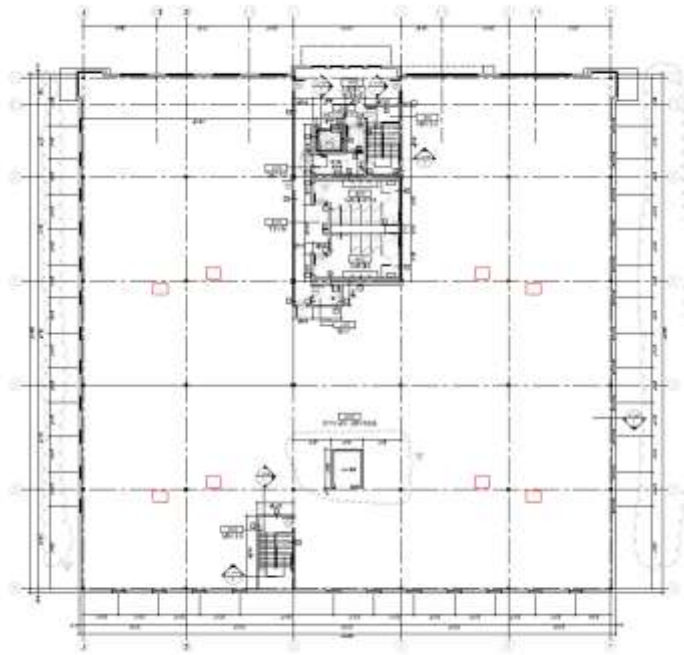
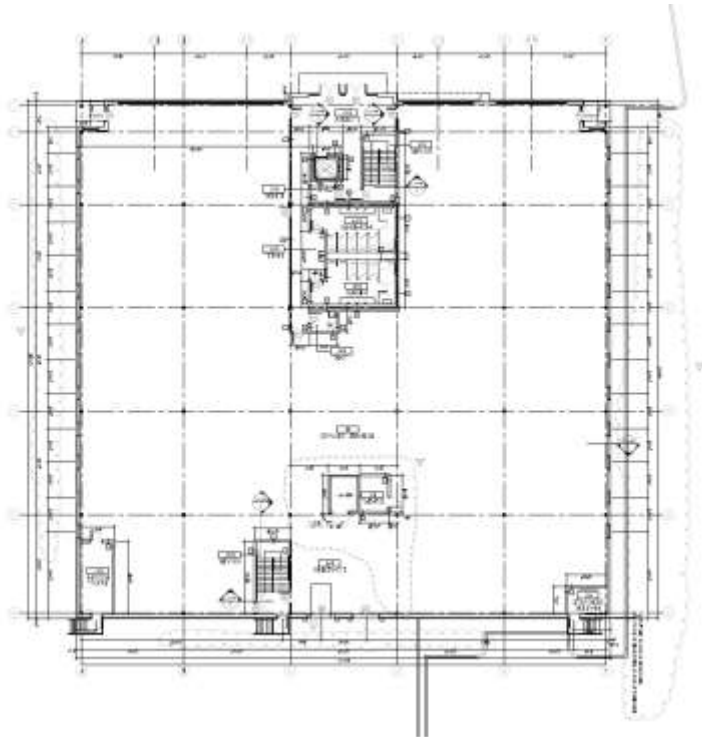


- Utility Structure & Tank
- Farm

ICM Factory – 3D View

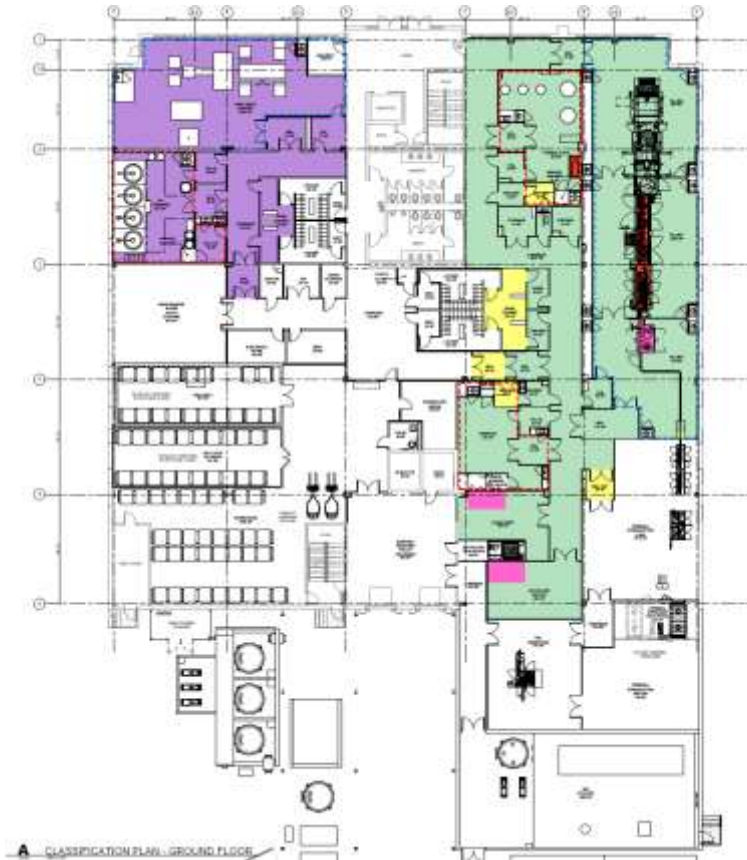


ICM Factory – Existing Conditions Floor Plan



Empty Warm Shell

ICM Factory – Floor Plan



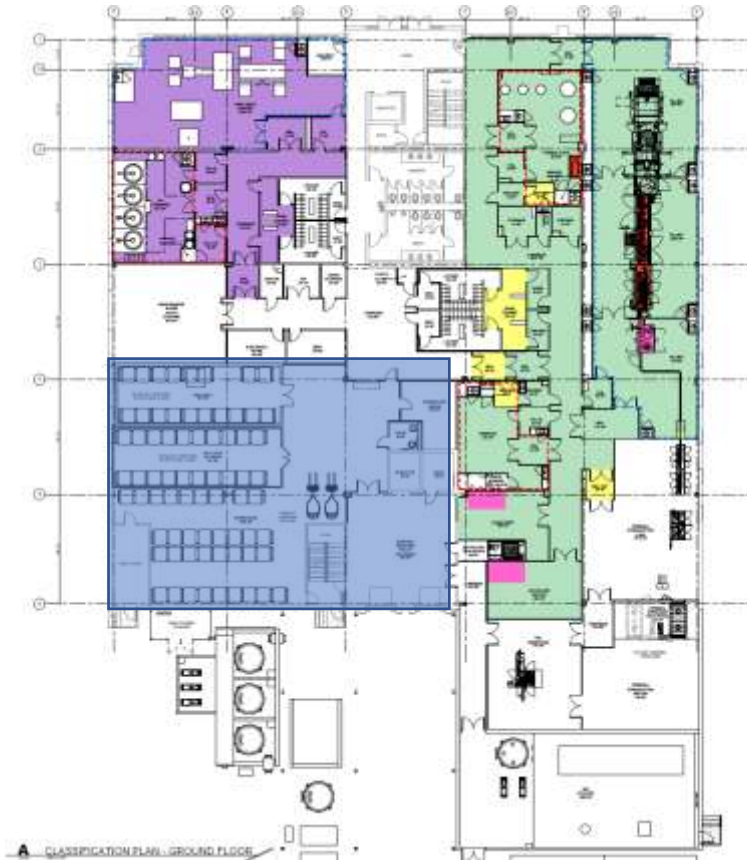
GROUND FLOOR



SECOND FLOOR

Detailed Engineering Design

ICM Factory – Floor Plan



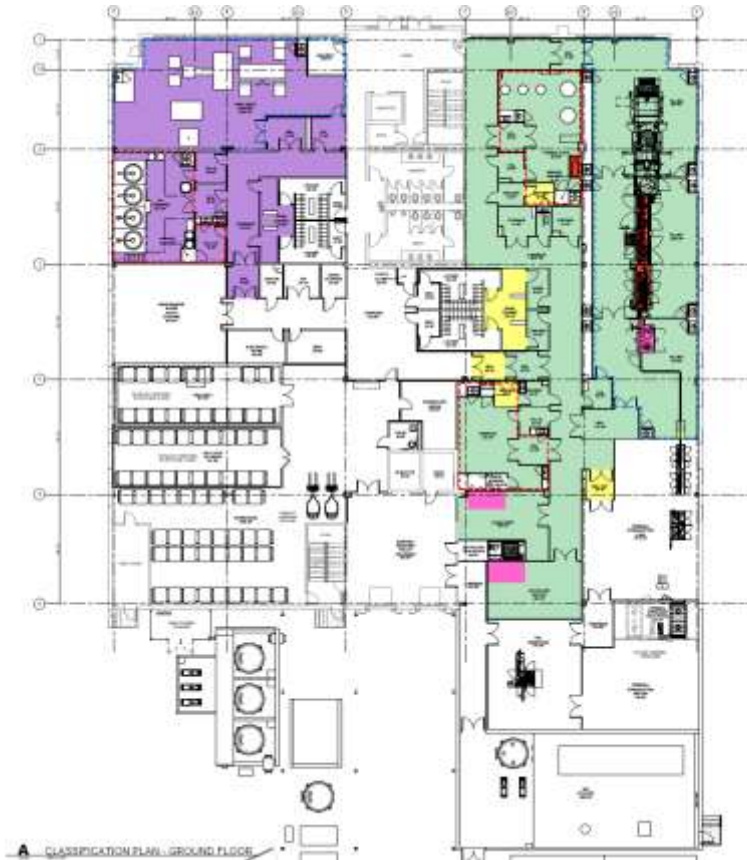
GROUND FLOOR



SECOND FLOOR

Warehouse - JIT

ICM Factory – Floor Plan



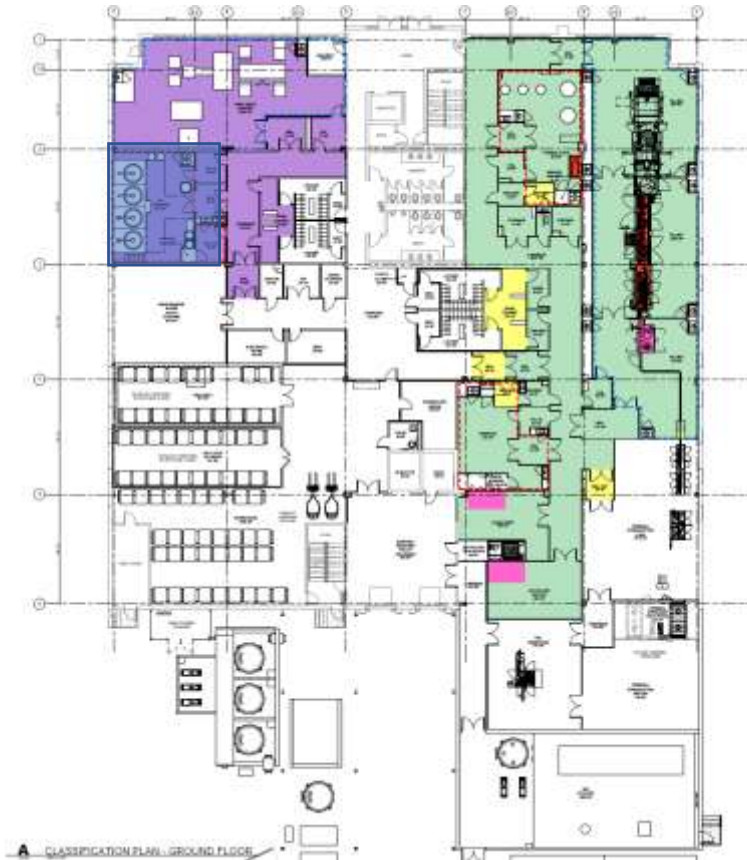
GROUND FLOOR



SECOND FLOOR

Continuous API Production

ICM Factory – Floor Plan



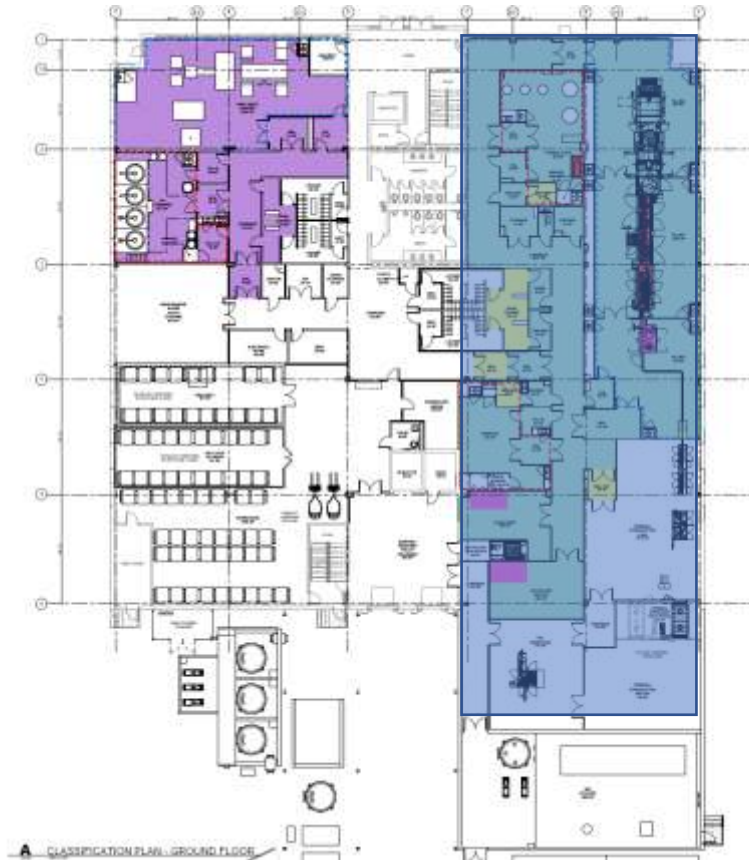
GROUND FLOOR



SECOND FLOOR

API In Process Storage

ICM Factory – Floor Plan



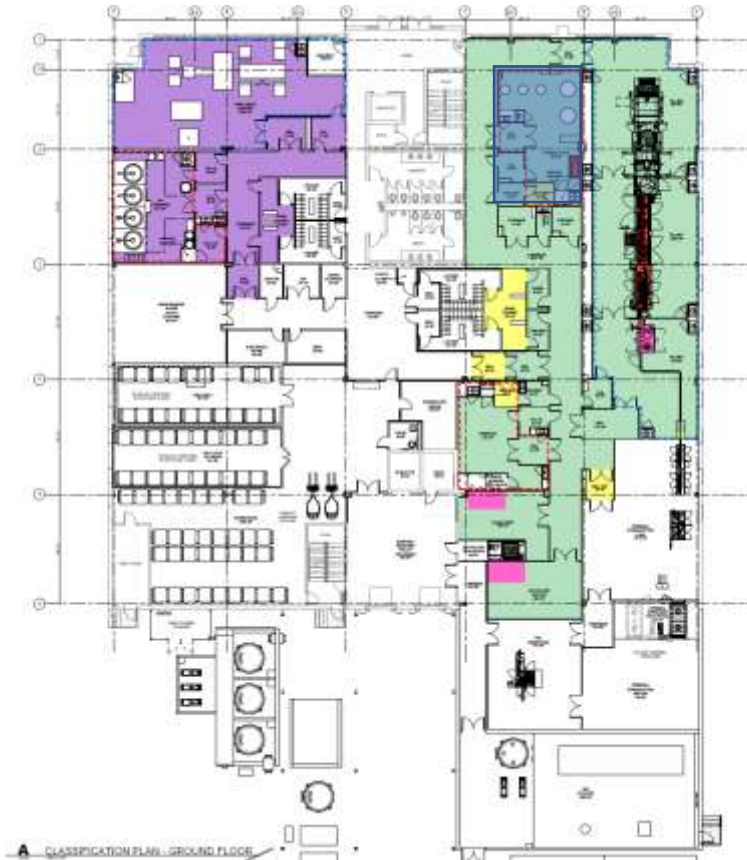
GROUND FLOOR



SECOND FLOOR

Vial Production

ICM Factory – Floor Plan



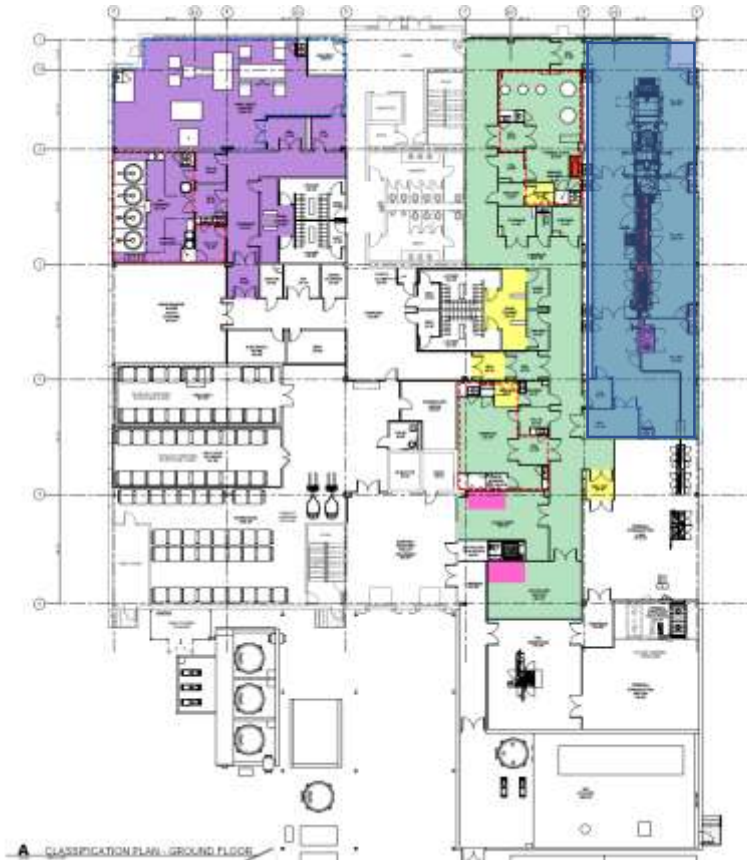
GROUND FLOOR



SECOND FLOOR

Continuous Formulation
Vial Production

ICM Factory – Floor Plan



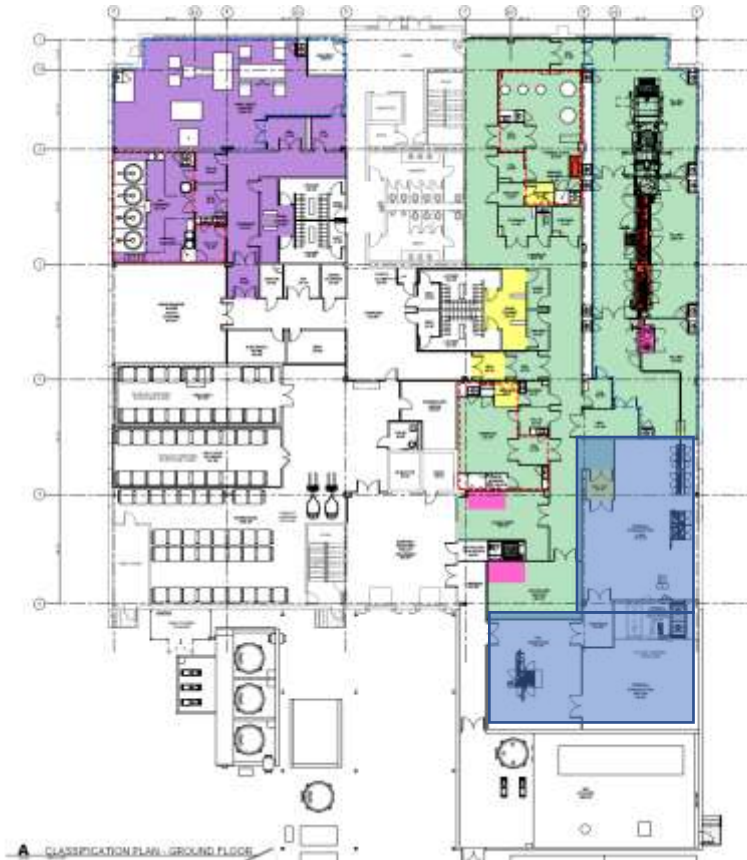
GROUND FLOOR



SECOND FLOOR

Vial Filling Line

ICM Factory – Floor Plan



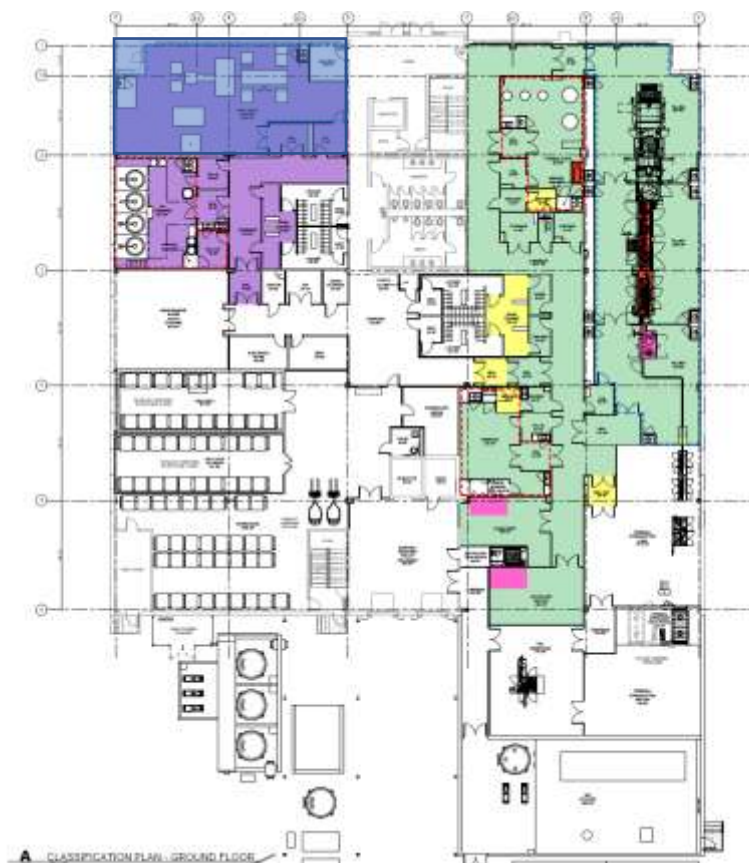
GROUND FLOOR



SECOND FLOOR

Vial Terminal Sterilization & Visual Inspection

ICM Factory – Floor Plan



GROUND FLOOR



SECOND FLOOR

Oral Solid Dosage Form
Production

End to End Continuous Manufacturing Challenges

Lot Definition and Control Strategy



- Quantity of product?
- Quantity of starting material?
- Run time at defined mass flowrate?
- Other?

End to End Continuous Manufacturing Challenges – Lot Definition



Production Time

End to End Continuous Manufacturing Challenges – Lot Definition

Master Lot - Continuous API Production
3,000 kg of API

Month 1

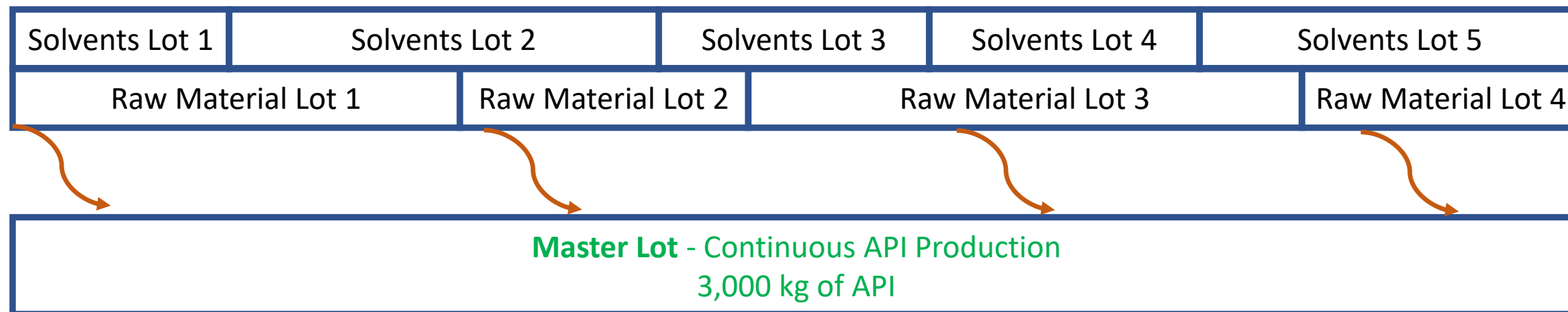
Month 2

Month 3

Month 4

Production Time

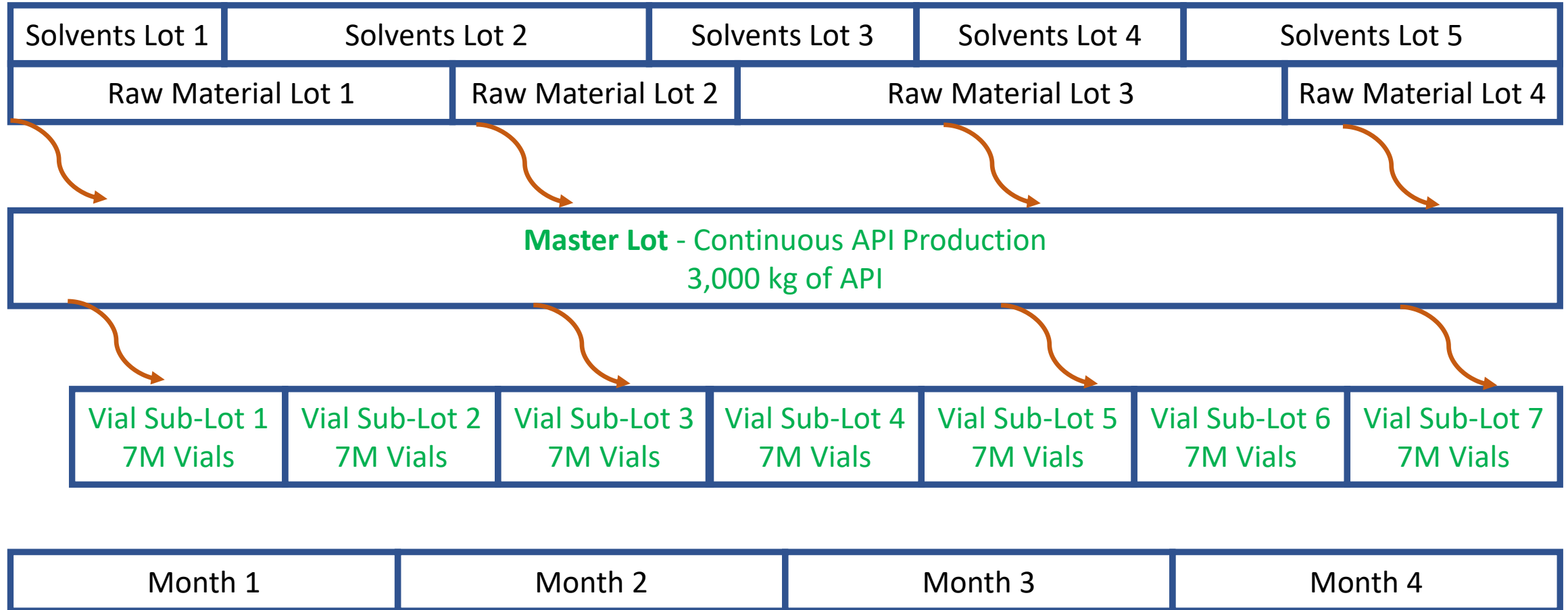
End to End Continuous Manufacturing Challenges – Lot Definition



Production Time

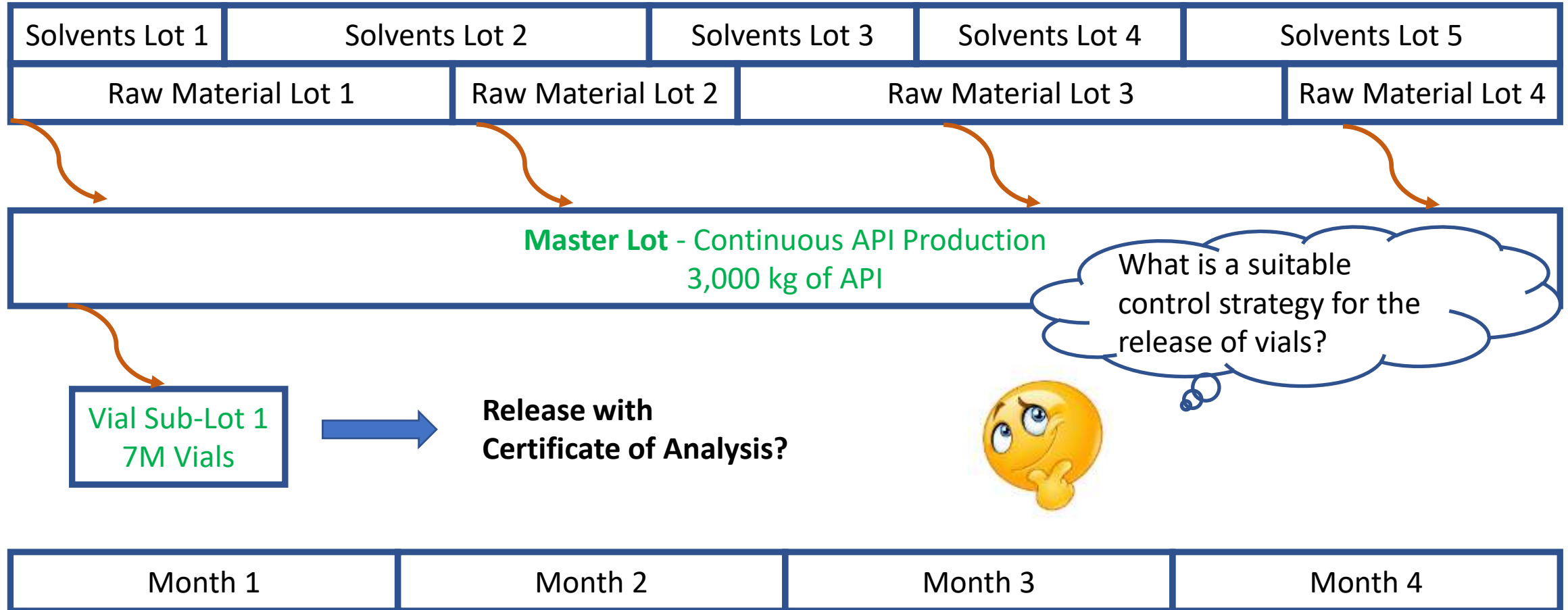
End to End Continuous Manufacturing Challenges

Lot Definition – Master Lot



End to End Continuous Manufacturing Challenges

Lot Definition – Lot Release



End to End Continuous Manufacturing Challenges

Control Strategy Example – Option 1 Drug Substance Sampling

Drug Substance CQA's

- Appearance
- Solubility
- Specific Rotation
- Identity
- Impurities
- Alkalinity
- Residual Solvents
- Water Content

Drug Product CQA's

- Identity
- Assay
- Impurities
- Sterility
- Bacterial Endotoxin
- pH

End to End Continuous Manufacturing Challenges

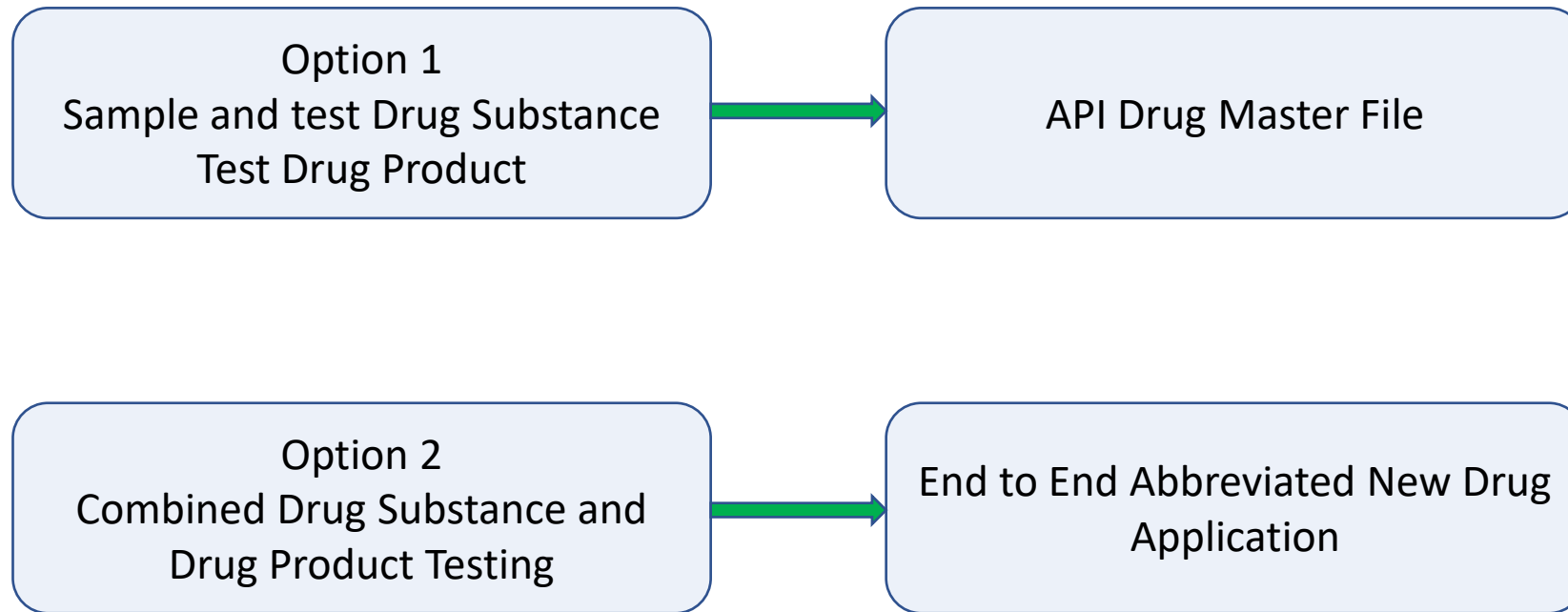
Control Strategy Example – Option 2 All Testing on Drug Product

End to End CQA's

- Identity
- Assay
- Impurities
- Sterility
- Bacterial Endotoxin
- pH
- Residual Solvents
- Water Content

End to End Continuous Manufacturing Challenges

Control Strategy Options



Final Thoughts

Benefits of End-to-End Production

Benefits of Continuous Manufacturing

Solutions to Challenges

Thank you!

The CONTINUUS Pharmaceuticals Team

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