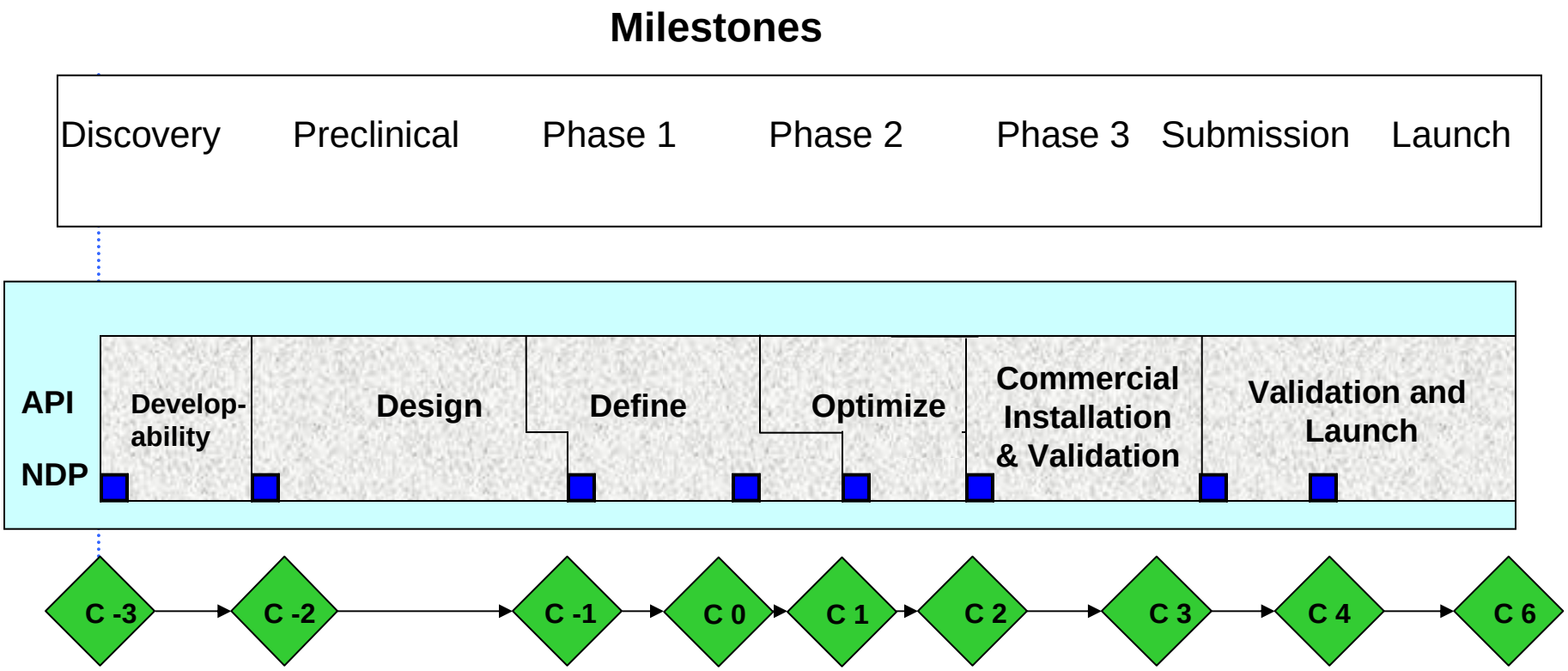
Governance

Single Process Map - Key Milestones and Stages



NOTE: Development involvement from Lead Declaration through 1+ year post launch

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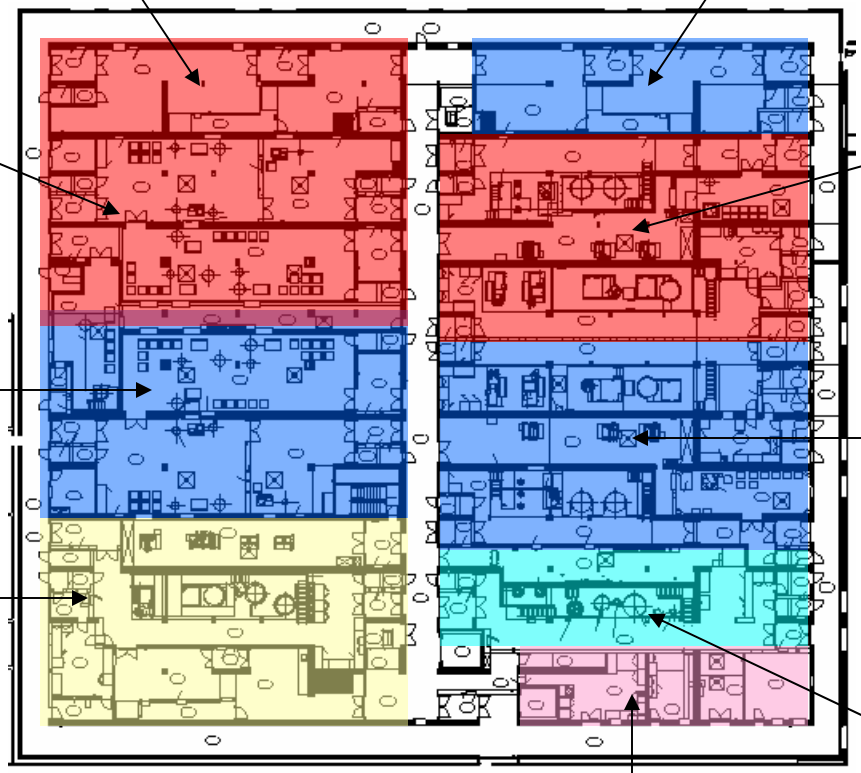
K360 Second Floor – Main Processing



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Unit Ops and Purpose

Overview

Unit operations	Purpose
Cell culture	Biosynthesis of Mab
Centrifuge/filter	Remove cells, clarify broth
Detergent Viral Inactivation	Inactivate lipid enveloped virus using Triton X-100 detergent
Protein A capture	Capture and Purify the Mab, remove MCC components, reduce HCPs, and nucleic acids
Low pH Inactivation and Neutralization	Inactivate Virus using low pH condition
CEX/AEX, ion exchange chromatography	Further purification and reduction of HCP, polymer, leached Protein A, and DNA
FNL polishing chrom – ion exchange or mixed mode	Further purification and reduction of HCP, leached Protein A, nucleic acids and soluble aggregate
Viral Nanofiltration	Removal of viral particles
TFF	Buffer exchange, concentrate
Final API Fill	Dispense final bulk API into containers

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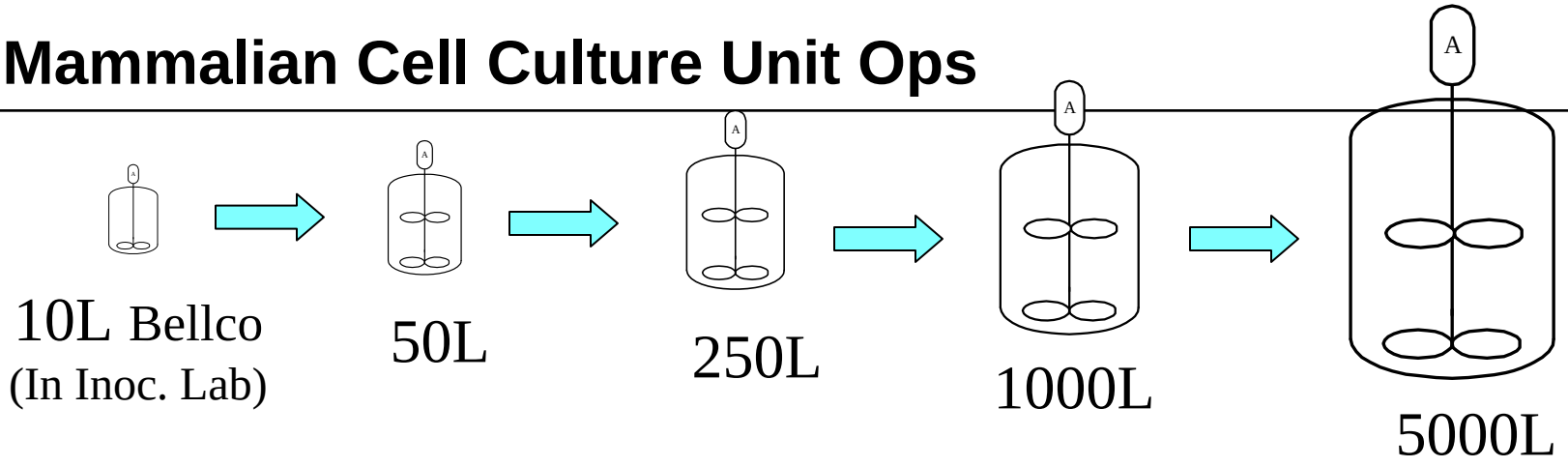
Upstream Operations

Mammalian Cell Culture Unit Ops



Braun Reactor Capabilities:

- Automated CIP and SIP
- 3 Addition ports with scales (Antifoam, Caustic, Nutrients)
- Temperature control with Steam and 0° Glycol
- Sparge and Overlay Gas flow control with Back-pressure control (Air, Oxygen, CO_2 and Nitrogen)
- pH, DO_2 probes with control
- Variable speed agitation with dual A100 marine prop impellors
- Harvest capabilities on the 1000L and 5000L

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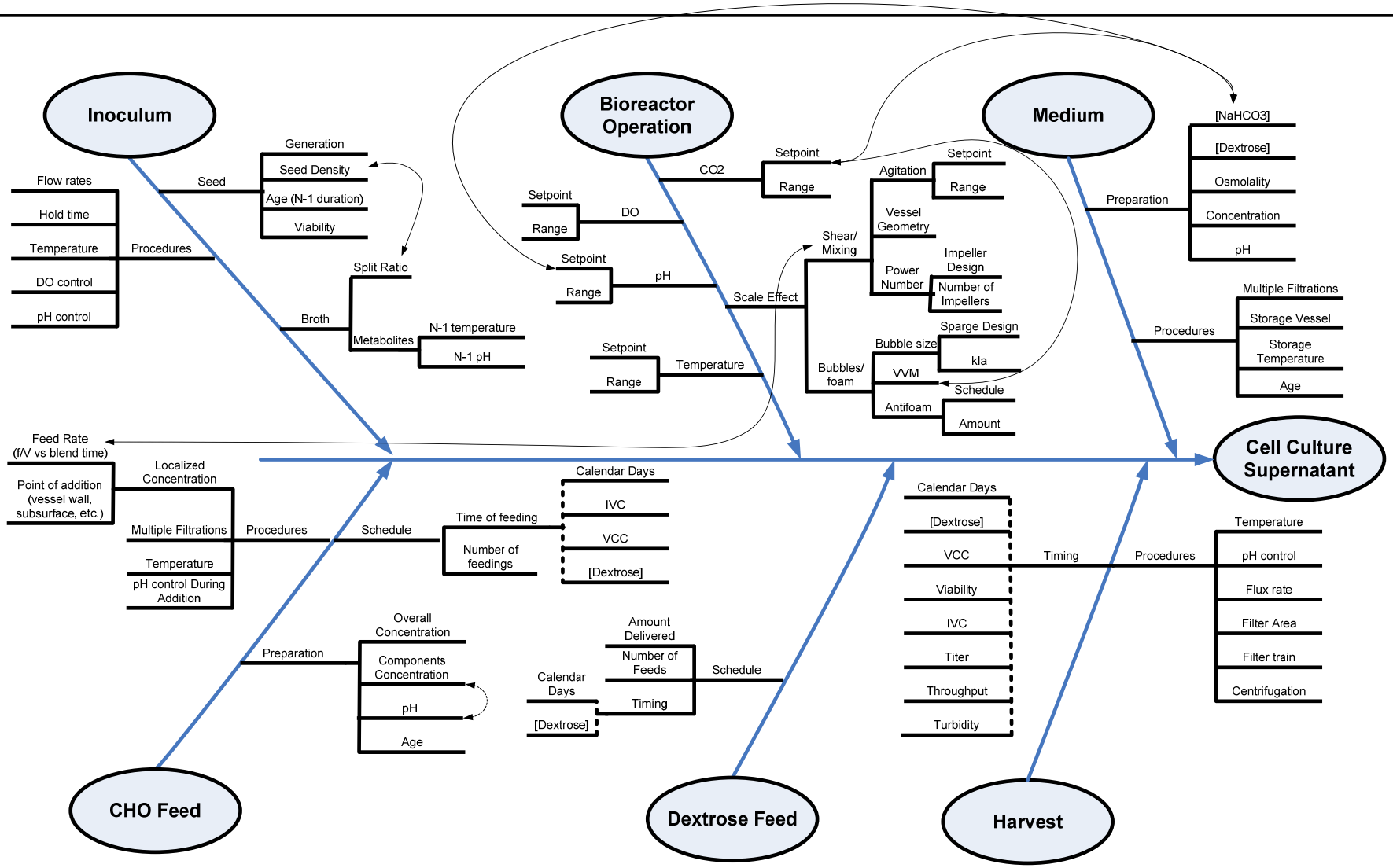
Fishbone diagram

Mammalian Cell Culture Process Flow – DOE Guide



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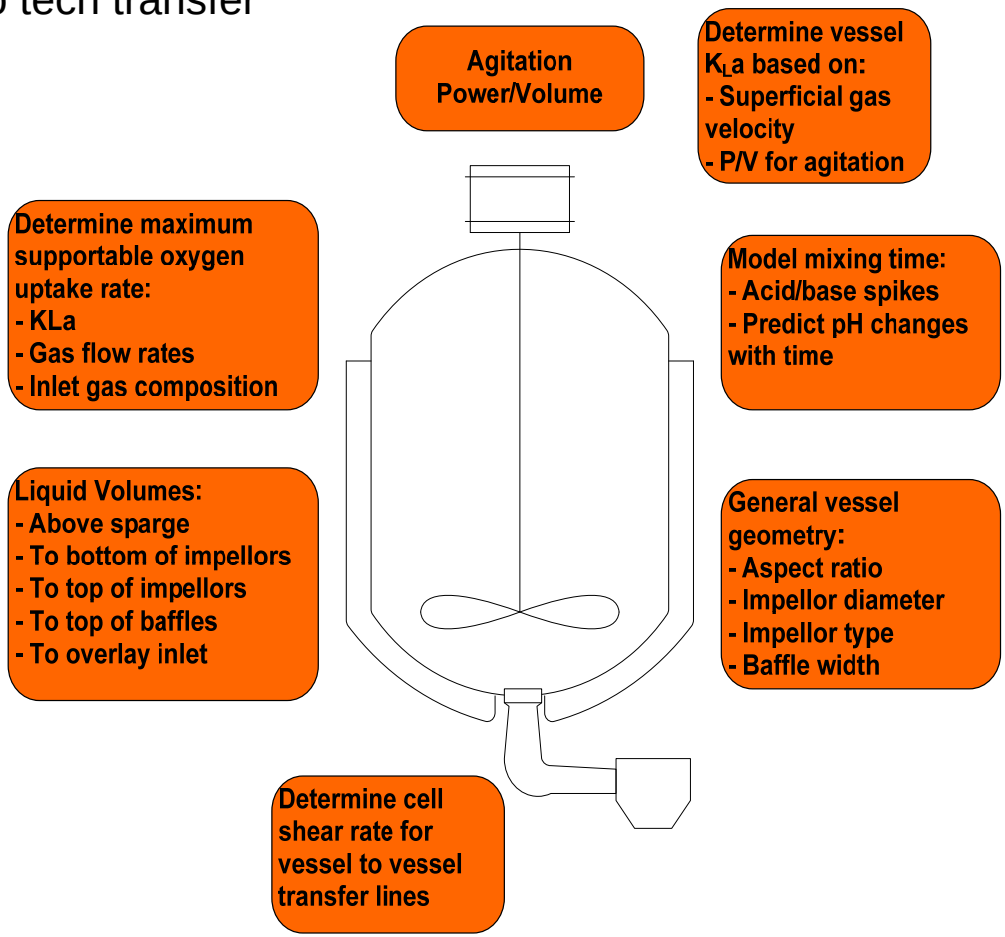
Bioreactor Characterization and Operation

Leveraging Assessment for All Processes

The capability to optimally mix and support O2 and CO2 levels must be demonstrated prior to tech transfer



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Downstream Operations

Purification and Filtration Unit Ops

3 Rooms per Suite

Room	Chrom I	Chrom II	TFF Area
Process Area (ft^2)	1400	1100	700
Portable Equipment Stations	3	2	1
Laminar Flow Hoods	0	0	1

Portable skids and support equipment



Use of Disposables







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Purification

Focus on More Rapid Turnaround

Portable Equipment Benefits

Clean and move out of processing suite or move to cleaning area makes area staging and turnaround simpler

Disposable Product Contact Surfaces

Disposable bags in reusable carts require no product-to-product cleaning verification

Area turnaround has shortened from weeks to 1-2 days

Platform Impact

Risk assessment analysis for bags, tubing, etc can be leveraged across processes (leachables data and vendor choices)

Avoid design or alternation of fixed steel equipment for each process

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