ISPE® | Delaware Valley Chapter

January 2017 Program

Case Study - New High Purity Water System Technologies Deliver Reliability & Sustainability for GSK

hargrove
engineers+constructors
controls+automation
life sciences

gsk
do more
feel better
live longer

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AGENDA

Introduction

- Background
- Objectives
- Challenges

Execution

- Design
- Construction
- Qualification

Results

- Benefits
- Lessons Learned
- Summary

INTRODUCTION

Introduction

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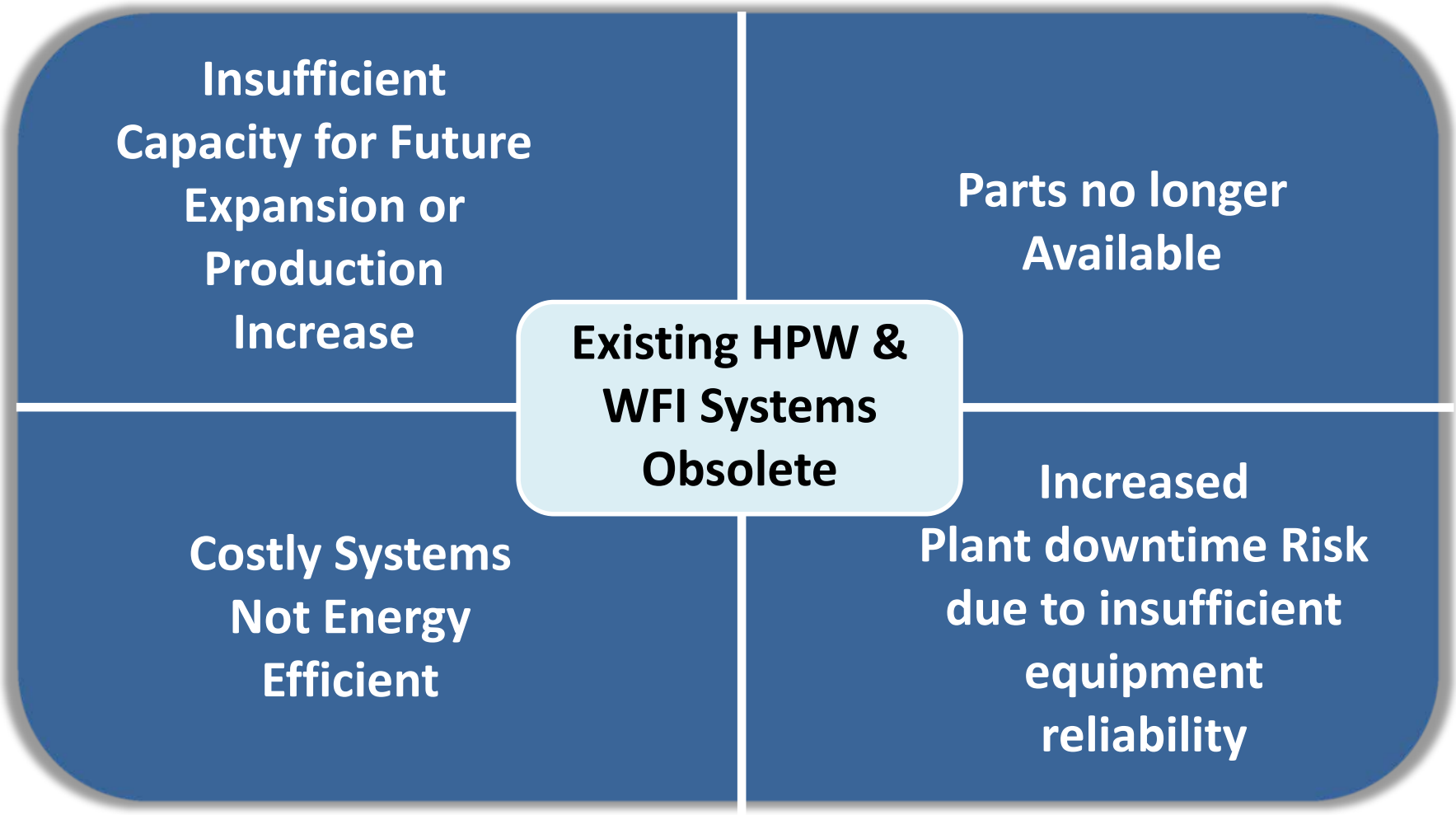
INTRODUCTION: BACKGROUND

gsk do more feel better live longer

CTM (Clinical Trial Materials) Facility

Manufactures purified drug substances for clinical trials worldwide

INTRODUCTION: BACKGROUND



INTRODUCTION: BACKGROUND

Project Scope

Replace 2 Obsolete Water Systems

HPW
High Purity Water

- New Reliable System Design
- Supply HPW to Biopharm Development Pilot Plant

WFI
Water for Injection

- Change System Configuration from 3 to 2 Pumps
- Replace WFI Control Panel
- Install Redundant VC Stills

INTRODUCTION: OBJECTIVES

PROVIDE RELIABILITY THROUGH REDUNDANCY

DELIVER SUSTAINABILITY

REDUCE WATER & ENERGY USAGE

INCREASE SUPPLY & STORAGE CAPACITY

REPLACE OBSOLETE EQUIPMENT

NO IMPACT TO ON-GOING OPERATIONS

INTRODUCTION: OBJECTIVES

RELIABILITY THROUGH REDUNDANCY

HPW

- Multi-Media Filters
- Softeners
- Carbon Filters
- RO/CDI Skid
- Tank Nitrogen Filters
- Distribution Pumps

WFI

- Vapor Compression Stills
- Tank Vent Filters
- Distribution Pumps

re·dun·dant

serving as a duplicate for preventing failure of an entire system

No Unplanned Downtime

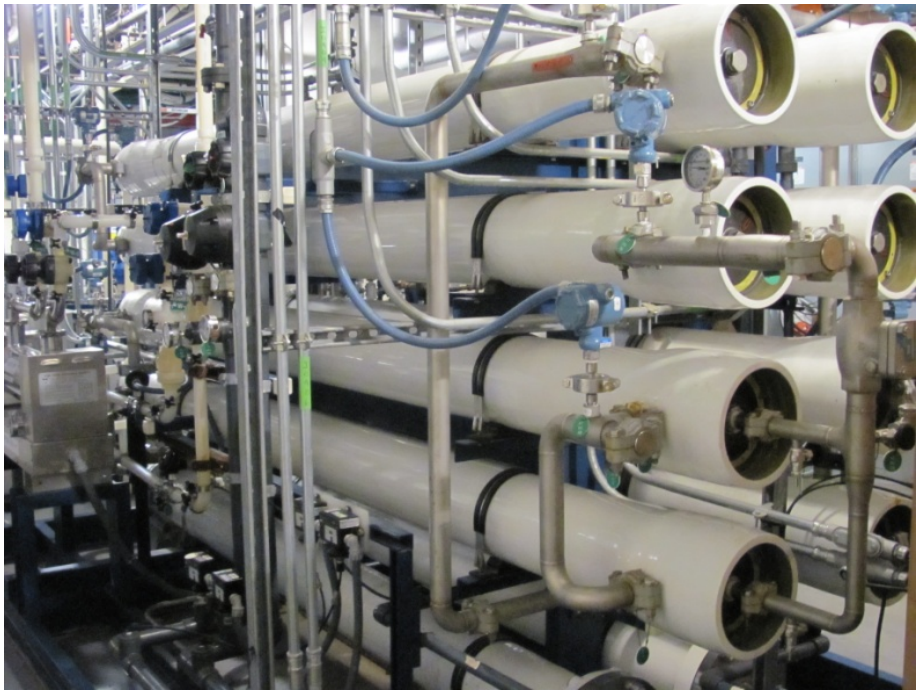
INTRODUCTION: OBJECTIVES

INCREASE SUPPLY & STORAGE CAPACITY

CLINICAL TRIALS	**Need to be Adept & Flexible** **Accommodate Emerging Technologies in Manufacturing**
HPW	**Generation and Storage Capacity** **Insufficient during Maintenance Activities**
WFI	**Generation Capacity Bottlenecked** **Required Daily Water Usage Planning Activities**

INTRODUCTION: OBJECTIVES

OBSOLETE EQUIPMENT



Reverse Osmosis
Pre-Treatment System
(Built c.1987)

FRP High Purity
Water Storage Tank
2000 Gallon (Built c.1987)

INTRODUCTION: OBJECTIVES

OBSOLETE EQUIPMENT

Multi-Effect
WFI Still (5 MEF)
(Built c. 1987)

(3) WFI Distribution Pumps
One pump on each floor
(Spares in Warehouse)

INTRODUCTION: OBJECTIVES

OBSOLETE EQUIPMENT

Softener
Regeneration
Brine Tank

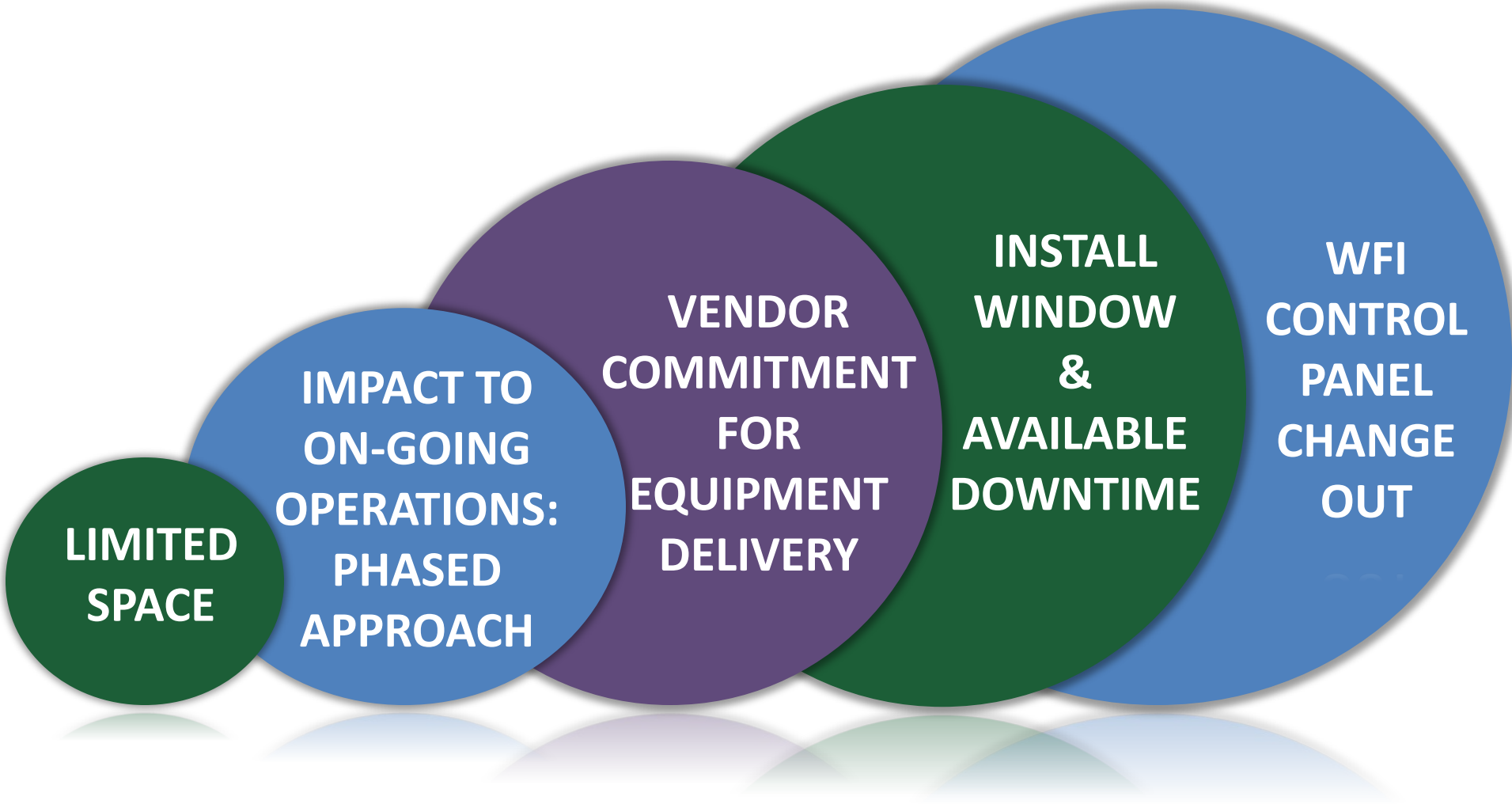
Softener Regeneration
Salt Pellets
Palletized 40 lb bags
Consumed 400-800 lb/day

INTRODUCTION: OBJECTIVES

NO IMPACT TO ON-GOING OPERATIONS

Building 38	Building 5	Building 4
Biopharm GMP Clinical Trial Production Manufacturing	Biopharm Development Pilot Plant	Safety Assessment Manufacturing

INTRODUCTION: CHALLENGES



INTRODUCTION: CHALLENGES

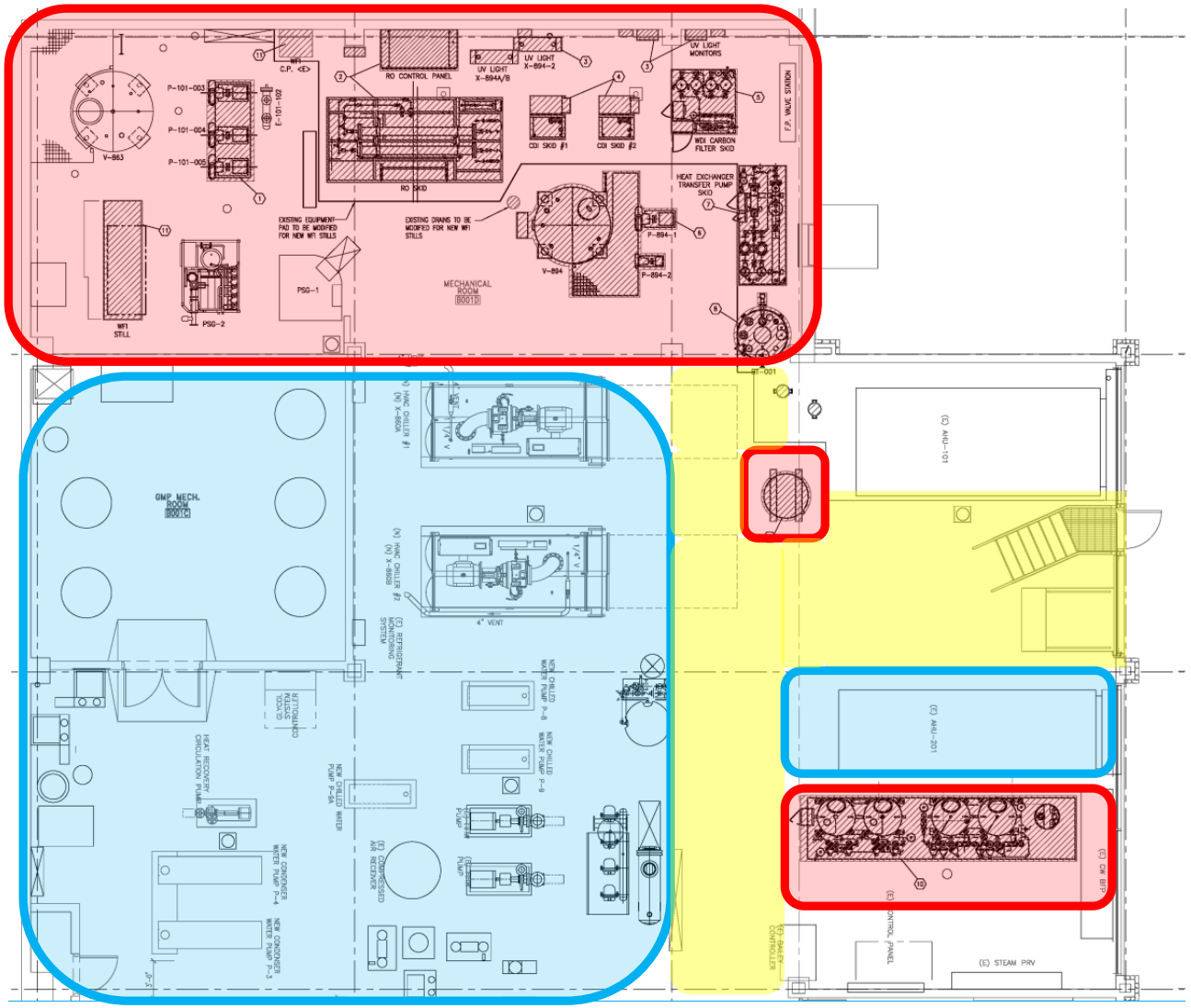
BUILDING 38

EXISTING MECHANICAL ROOM

Generation Equipment

Utilities

Access



EXECUTION

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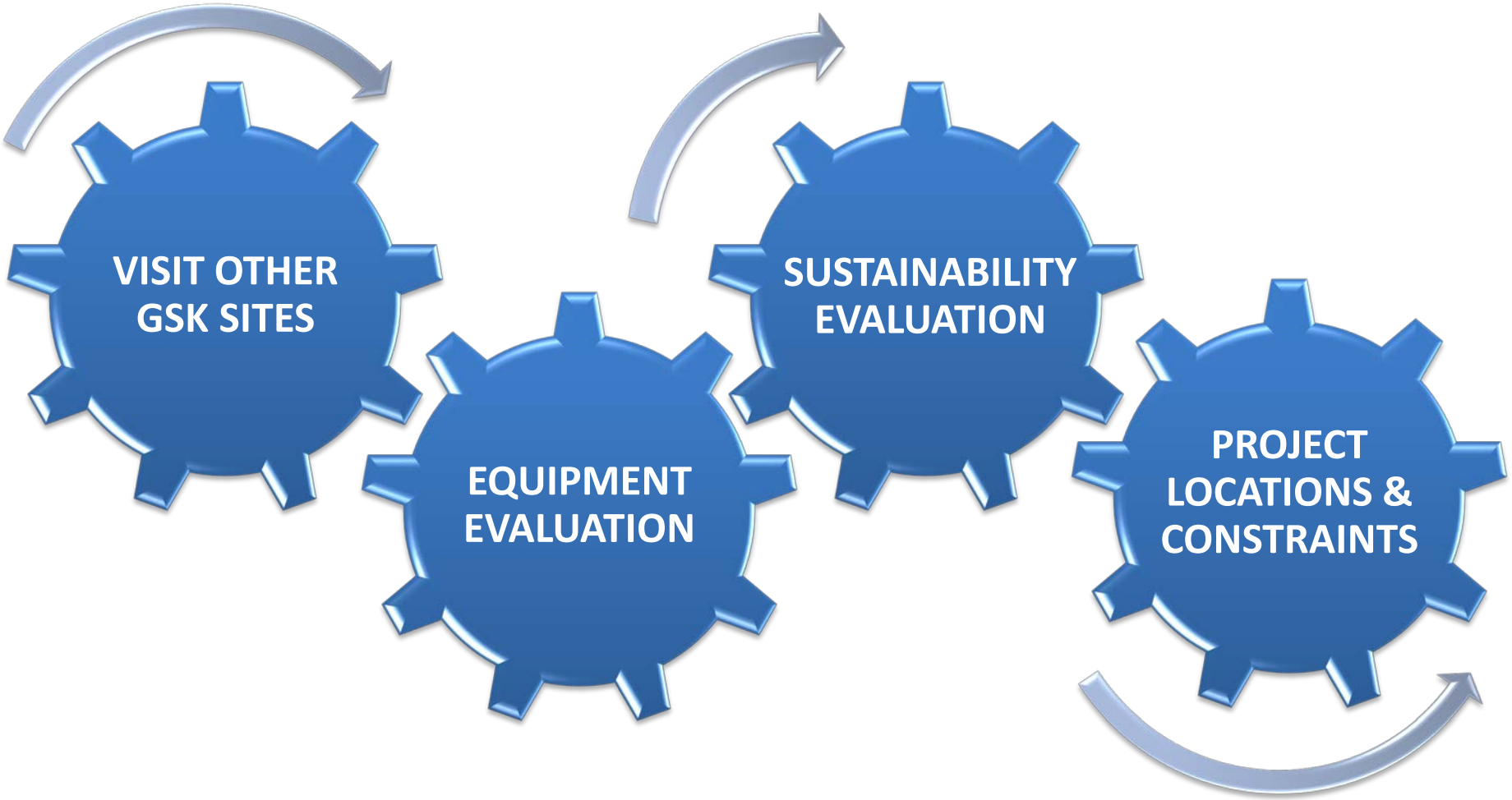
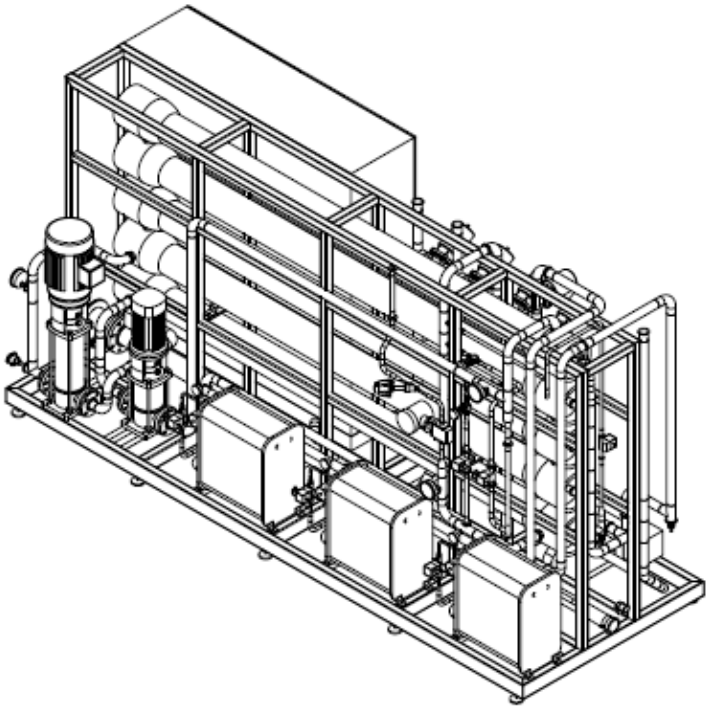
EXECUTION: DESIGN



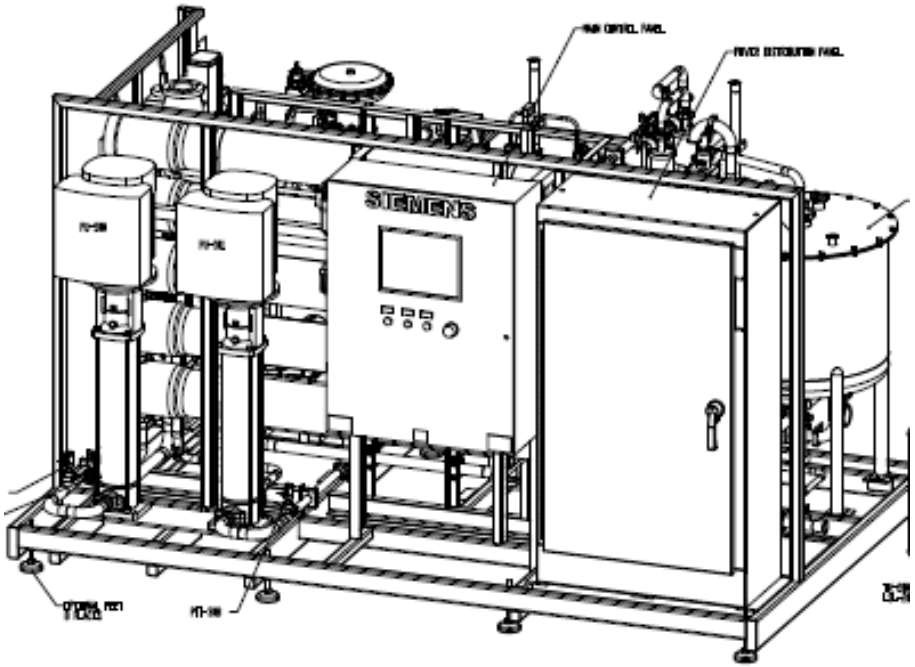
EXECUTION: DESIGN

Other Site Tours (Gemba)

Site 1:
Christ System



Site 2:
Siemens: PreVUE®



EXECUTION: DESIGN

EQUIPMENT EVALUATION

	Options	Decision
HPW	Single Pass vs. Double Pass RO	Single Pass
	Polisher vs. None	Install Polisher
	Carbon vs. Bi-sulfite vs. UV Light Filtration	Carbon Filtration
	Service Type vs. Back Washable Carbon Filters	Back Washable
	Hot Water vs. Chemical Sanitization	Hot Water Sanitization
	FRP vs. SS HPW Storage Tank	SS Tank
	High Recovery RO vs. None	High Recovery RO
	Nitrogen Blanket on Storage Tank vs. None	Nitrogen Blanket
	Bulk Brine vs. Day Tank	Both
	Redundant vs. Single Storage Tank Filters	Redundant Filters

EXECUTION: DESIGN

EQUIPMENT EVALUATION

	Options	Decision
WFI	Vapor Compression vs. Multi Effect	Vapor Compression
	Separate Pump per Floor vs. Redundant Pumps	Redundant Pumps
	Redundant vs. Single Storage Tank Filters	Redundant Filters

EXECUTION: DESIGN

SUSTAINABILITY EVALUATION

	Single Pass RO	Single Pass RO with CDI	Double Pass RO	Double Pass RO with CDI	SPRO/DI followed by VC stills
Equipment Costs, estimated:					
Pretreatment Equipment	$800,000	$1,150,000	$1,200,000	$1,400,000	$804,000
WFI Still	$535,000	$535,000	$535,000	$535,000	$1,071,000
Total Equipment Cost			$1,735,000	$1,935,000	$1,875,000
Operating Costs per day, estimated:					
• **Standard Operation** with recirc and hot water sanitization			$601	$632	
Modified Standard Operation (note 5)			$517	$544	
• **Start/Stop Operation** (Siemens S-3)			$495	$506	
• **Christ Aqua Standard Operation** with high recovery, idle turndown and hot water sanitization					
• **RO/DI with VC Stills** (note 6)					$1020
• **VC Still**	$215	$210	$205	$200	
Wastewater Volume, gal/day:					
• **Standard Op** sanitization	12,624 gals	13,299 gals	1		
Modified Sta	12,624 gals	13,299 gals			
• **Start/Stop C**	16,198 gals	16,900 gals			
• **Christ Aqua** recovery, turn		9,975 gals			
• **RO/DI with**					300 gals
• **VC Still**	3,120 gals	2,200 gals			
Limitations	istivity / short life of polishing bed / pH adjust necessary to eliminate ammonia		resisti necessary to eliminate ammonia		water quality higher than needed for WDI

Systems Design Evaluations

Operating Cost Comparisons

Wastewater Volume Reduction

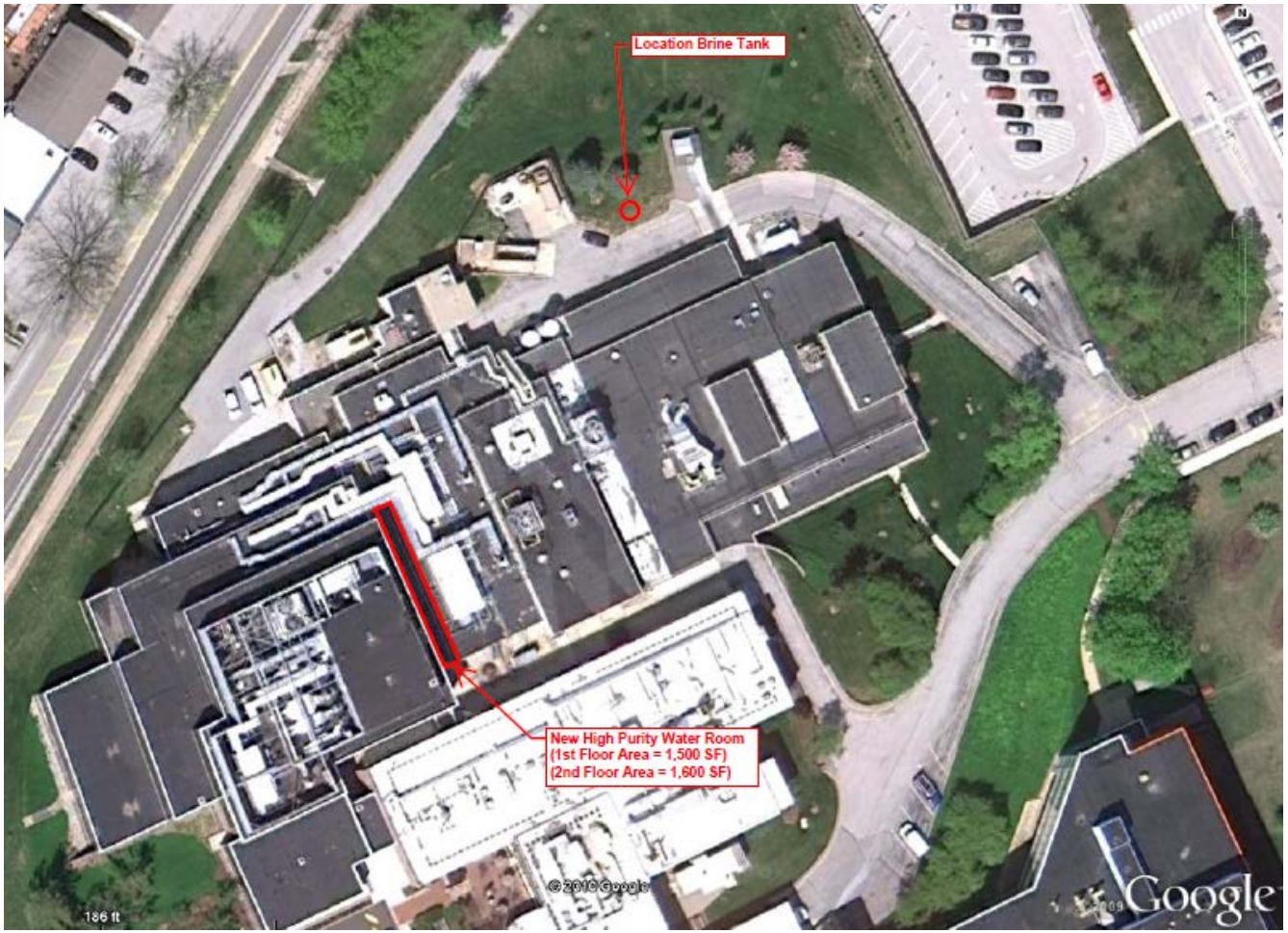
EXECUTION: DESIGN

PROJECT LOCATIONS & CONSTRAINTS

Project Locations Limited

Only Feasible Solution:

Utilize existing Courtyard between B5 & B38 (14’ W x 110’ L)



EXECUTION: DESIGN

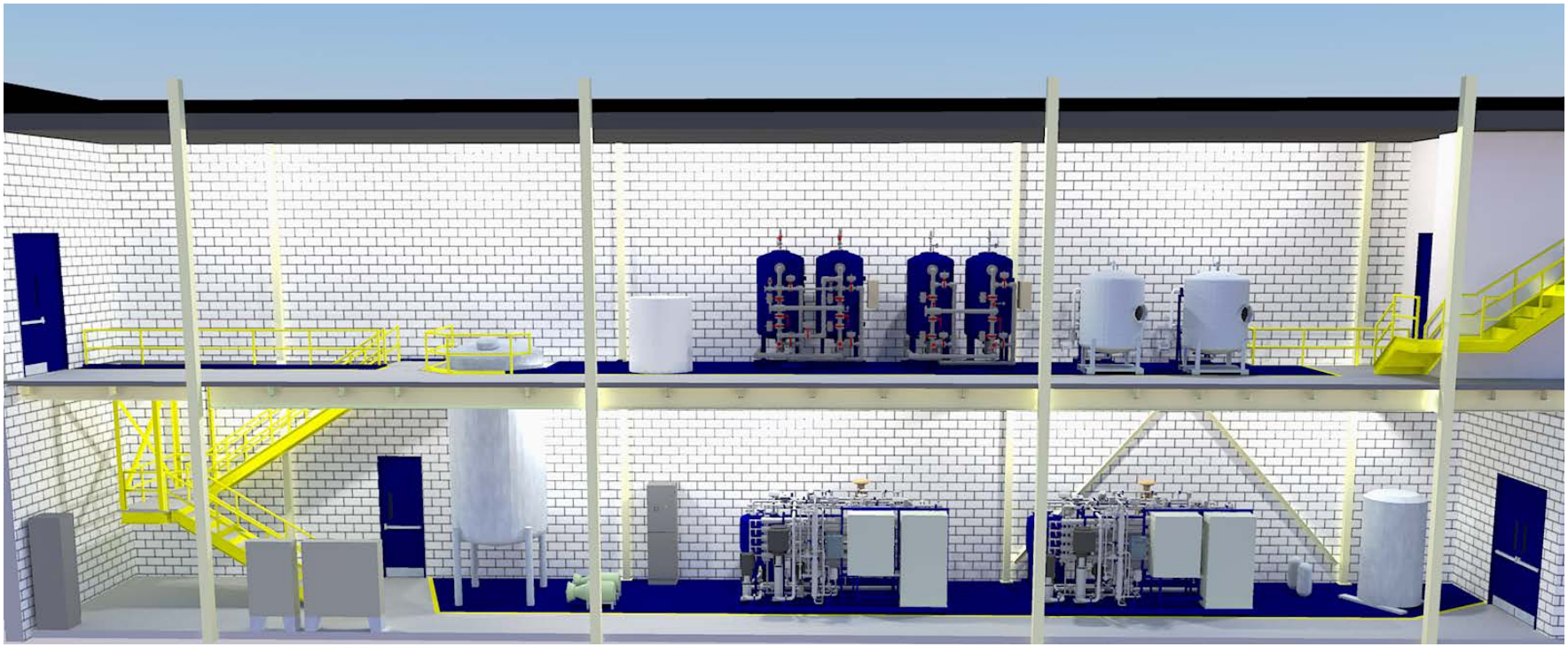
PROJECT LOCATIONS & CONSTRAINTS

Top of Courtyard
Looking NORTH

Bottom of Courtyard
Looking SOUTH

EXECUTION: DESIGN

2-Story Mechanical Room Design



EXECUTION: DESIGN

2-Story Mechanical Room Design

EXECUTION: DESIGN

NO IMPACT TO ON-GOING OPERATIONS

Phased Construction/ Qualification Approach

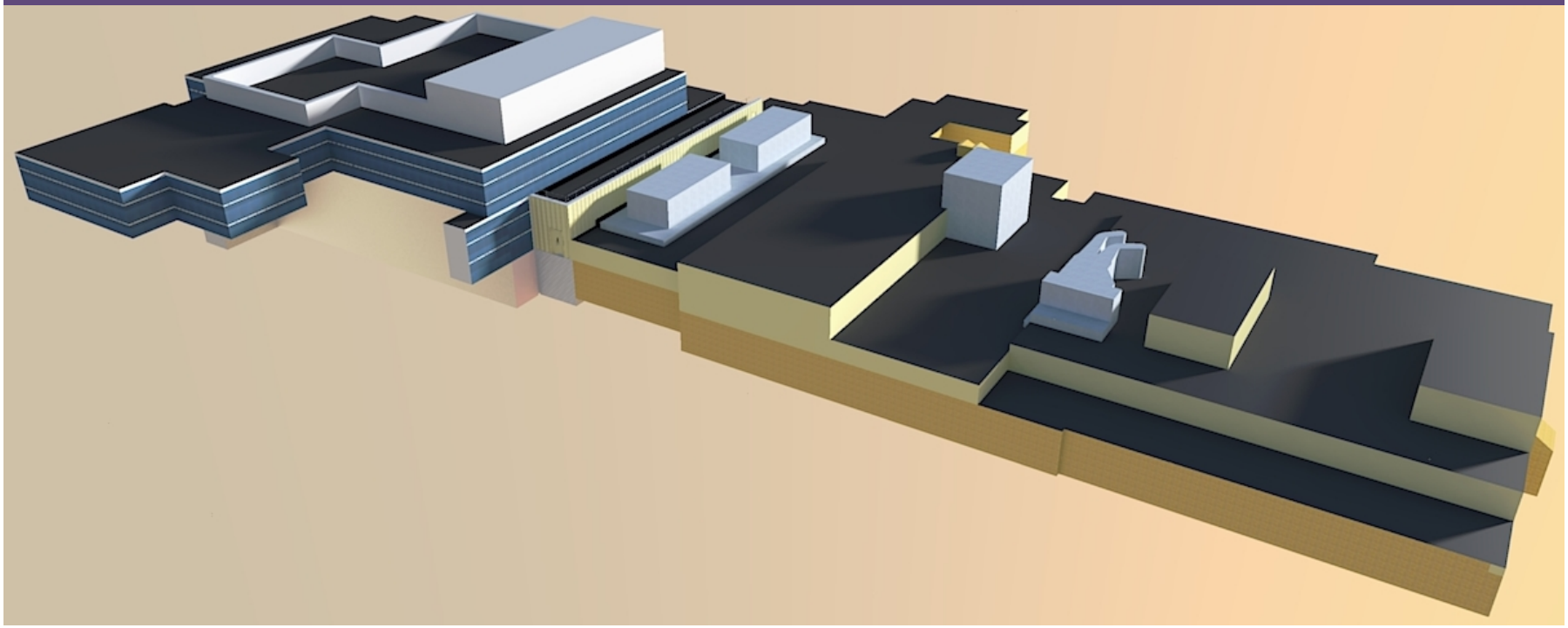
PHASE 1	PHASE 1A	PHASE 2
Construct Addition & Install HPW System	Install WFI Pumps & Control Panel	Demo Old HPW System Install WFI VC Stills Demo Old Still

EXECUTION: DESIGN

PHASE 1

Construct 2-Story Addition for HPW

Between 2 Buildings | Adjacent GMP Operations | Limited Access

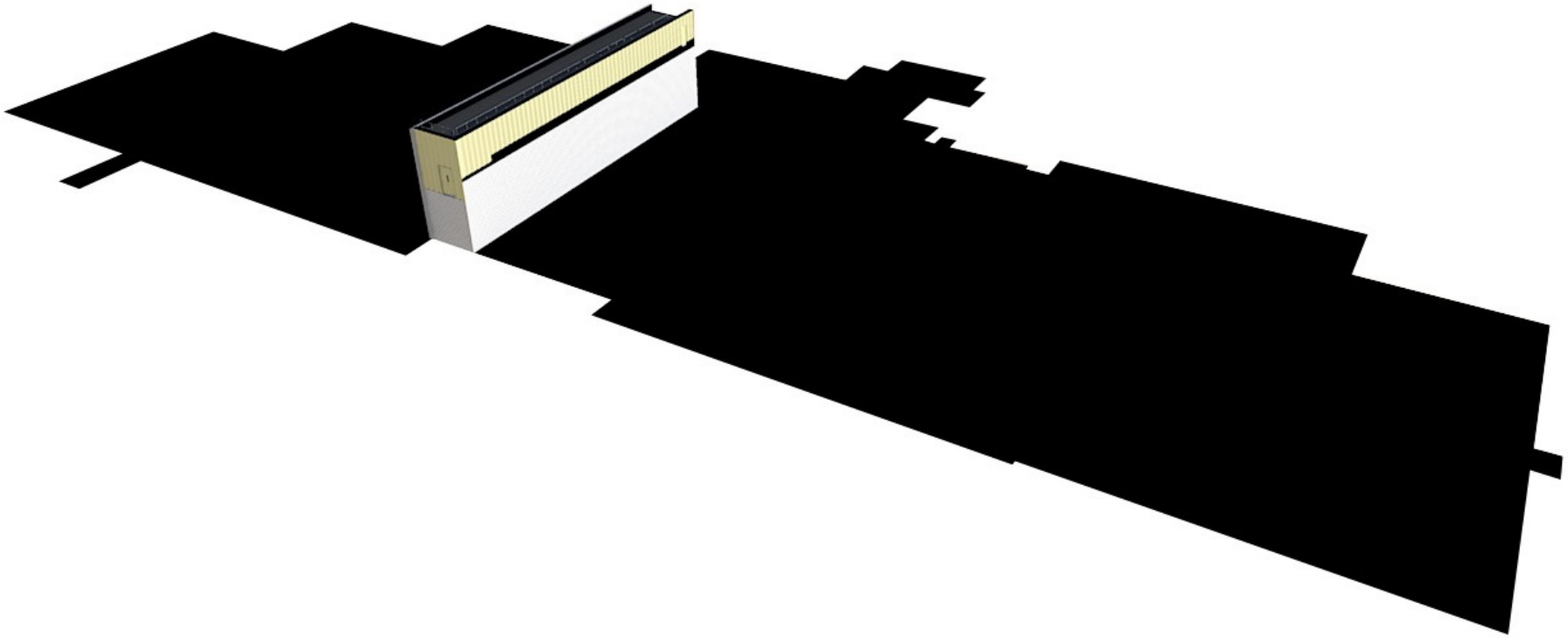


EXECUTION: DESIGN

PHASE 1

Construct 2-Story Addition for HPW

Between 2 Buildings | Adjacent GMP Operations | Limited Access



EXECUTION: DESIGN

SYSTEM CONSIDERATIONS

Energy Efficiency

S3 Technology & Pump VFDs

Reduce Water Usage

S3 Technology & High Recovery RO

Bulk Brine Tank System

WFI: Pump Schemes

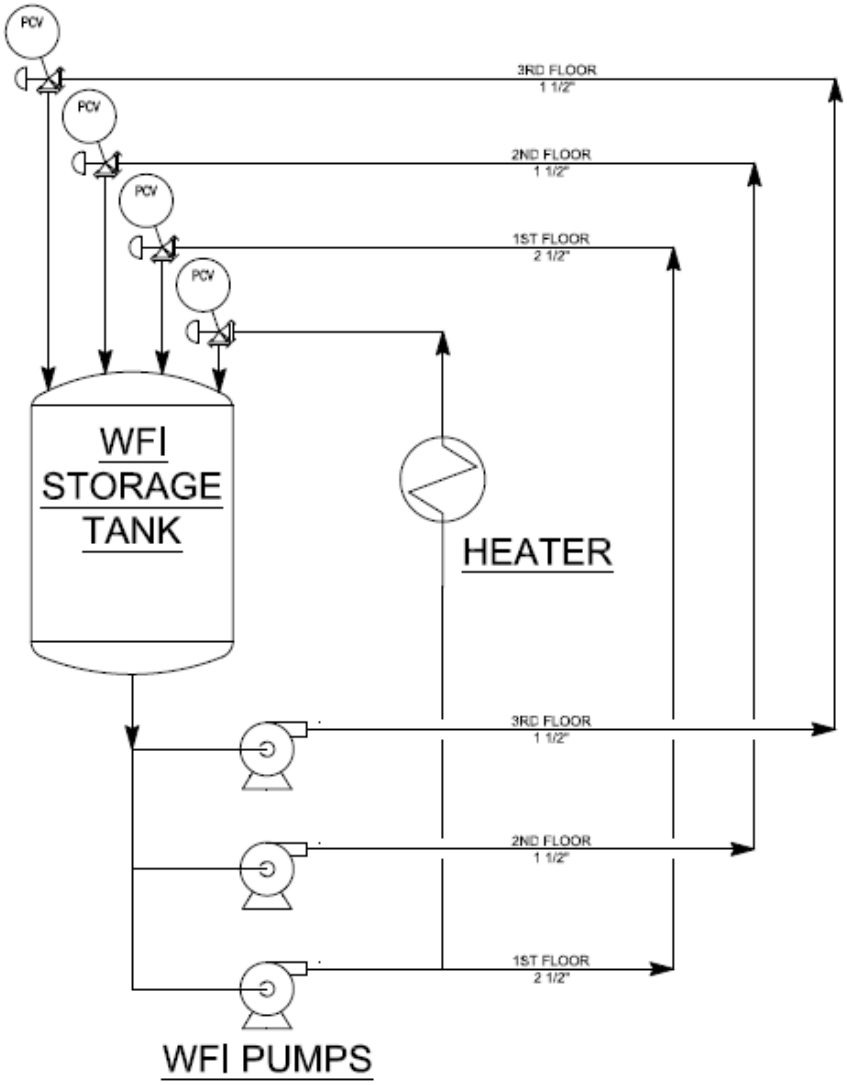
Fathom Software
Complexity of Flows – Multiple Floors

Online TOC, Conductivity & Microbial Detection

Choose Vendor that Supplies Customizable PLC Controllers:

- Normalized Differential Pressure to determine cleaning interval
- Softener Regeneration is based on Hardness
- Softener Regeneration Rinse is based on Conductivity

EXECUTION: DESIGN



PHASE 1A - WFI

OLD SYSTEM

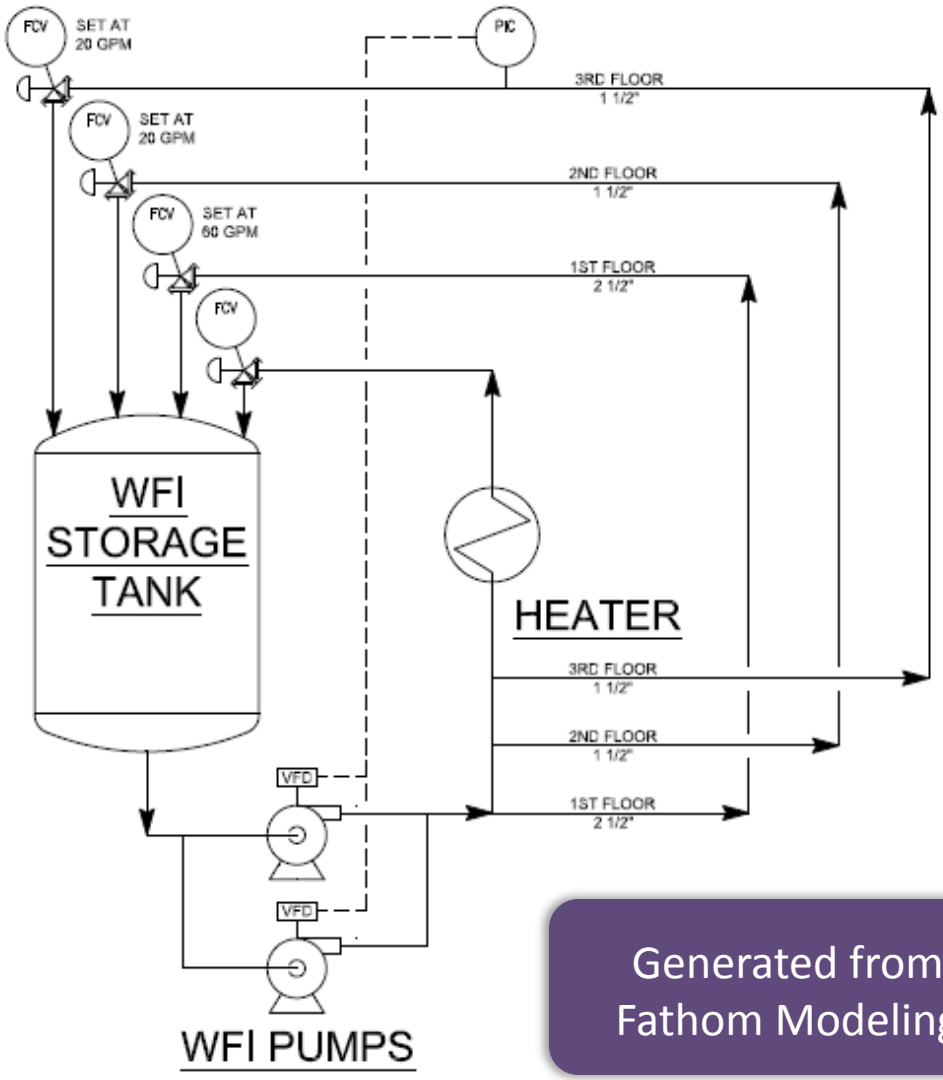
No Redundancy

Difficult to Control Flow

Maintenance requires Shutdown

Single Pump affected Tank Temp and other Floor Availability

EXECUTION: DESIGN



Generated from Fathom Modeling

PHASE 1A - WFI

NEW SYSTEM

- Redundancy
- Control From Worst Case
- Pump Maintenance = No downtime
- VFD's to manage fluctuations
- Individual Loops can be Isolated

EXECUTION: DESIGN

WFI CONTROL PANEL

Extensive Pre-Planning

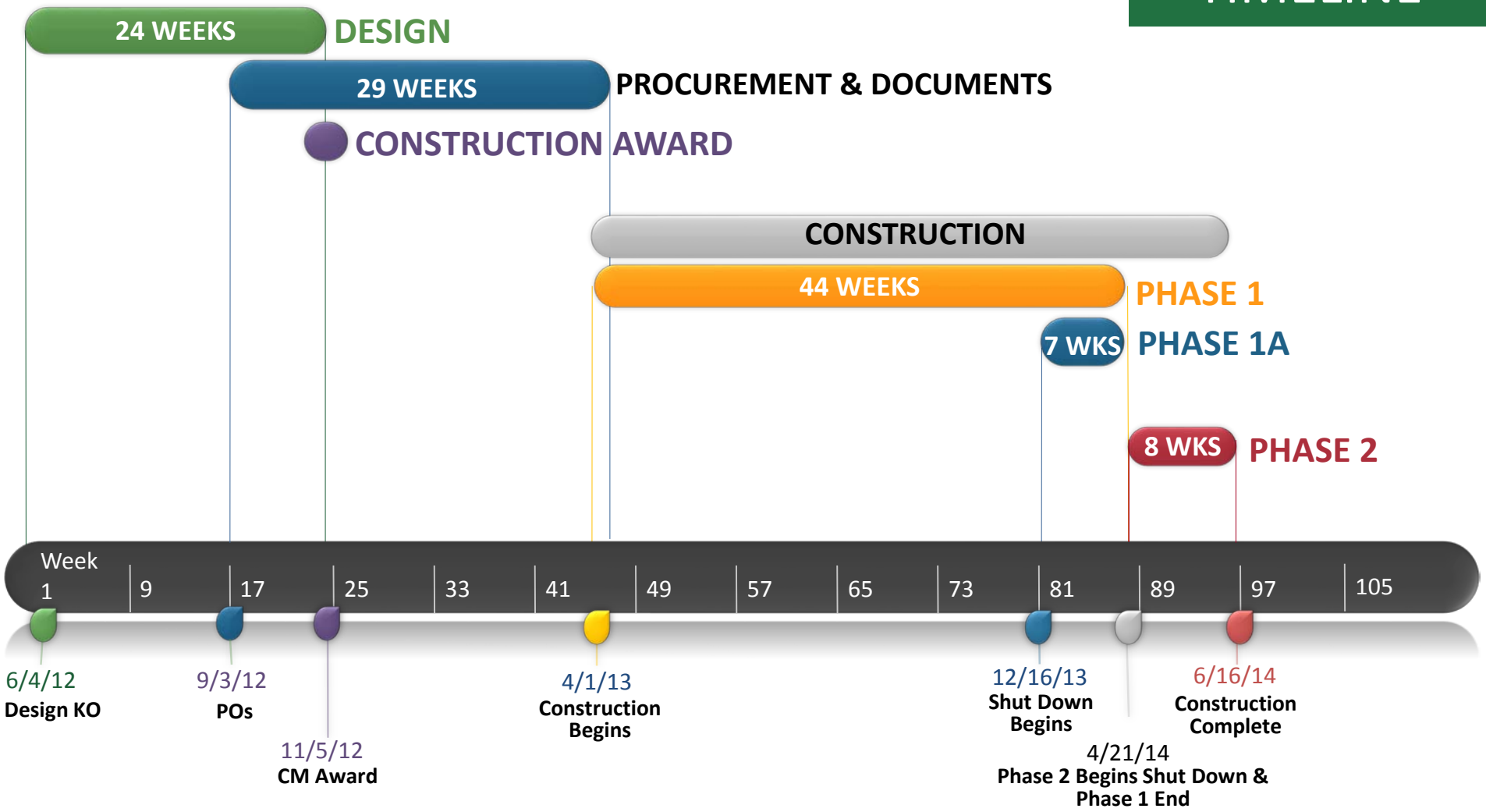
Instruments = 86
I/O Points = 106

EXECUTION: DESIGN

HPW GENERATION SUMMARY

EXECUTION: CONSTRUCTION

TIMELINE



EXECUTION: CONSTRUCTION

PHASE 1

Existing Courtyard

Stone & Soil Excavation

1st Floor Slab Installation

EXECUTION: CONSTRUCTION

TEMPORARY PROTECTIONS

Maintain Building Integrity during Removal of Building Façade

Removal of the façade exposed
Utilities above occupied space inside

Installed Temporary Partition Walls in
Active Areas & Issued Change Control

Updated Qualified Flow Drawings Continually During Construction

EXECUTION: CONSTRUCTION

PHASE 1

Building Structure Construction

Large Crane due to Limited Access

EXECUTION: CONSTRUCTION

PHASE 1

Installation of
HPW Equipment

EXECUTION: CONSTRUCTION

PHASE 1

Outdoor Bulk Brine Tank

2nd Floor HPW

EXECUTION: CONSTRUCTION

PHASE 1

1st Floor
Dual RO Skids

1st Floor
HPW Tanks & Pumps

EXECUTION: CONSTRUCTION

PHASE 1

2nd Floor Dual Softeners & Multi-Media Filters

2nd Floor Dual Carbon Filters

EXECUTION: CONSTRUCTION

PHASE 1A

B38 Mechanical Room
Existing WFI Pumps to Demo

B38 Mechanical Room
New WFI Pumps

EXECUTION: CONSTRUCTION

PHASE 2

B38 Mechanical Room
HPW System to Demo

Access Doors to B38
Mechanical Room

EXECUTION: CONSTRUCTION

PHASE 2

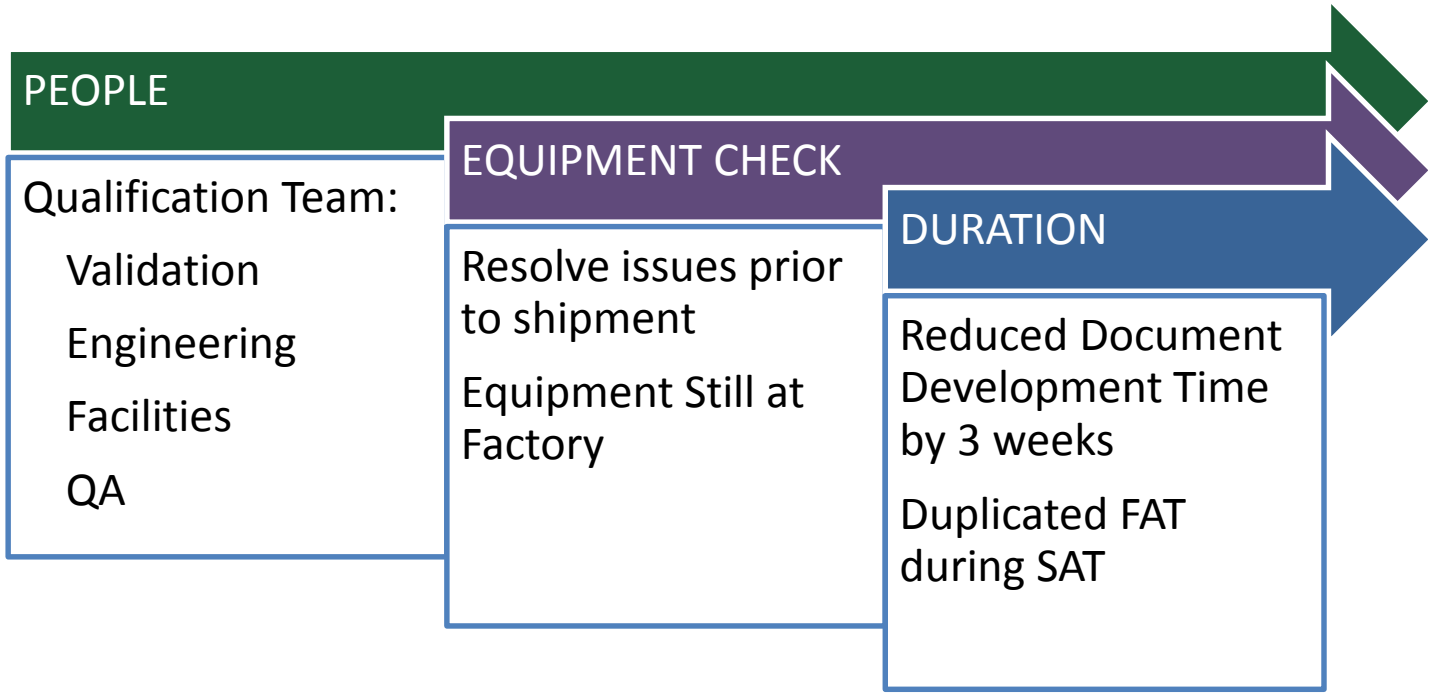
New WFI Stills at FAT
Sugarland, TX

New WFI Stills in
B38 Mechanical Room

EXECUTION: CONSTRUCTION

LEVERAGED QUALIFICATION APPROACH

Vendor Qualification Documents Reformatted to GSK Standards PRIOR to Factory Acceptance Test (FAT)



EXECUTION: CHALLENGES

CONSTRUCTION

- Constrained Area within the Middle of Operating Buildings
- S3 Design Not Turn-Key
- Polisher Tank Delivery
- Sartorius Filter Housings
- Delivery of High Purity Equipment
- Installation of High Purity Equipment
- DI Tank Filters
- Failure of PQ1 Testing (Plan B)

EXECUTION: QUALIFICATION

VALIDATION DOCUMENTATION

EXTENSIVE DOCUMENT MANAGEMENT

1	Validation Master Plan (HPW/WFI) including 3 Validation Interim Reports
5	User Requirement Specs
14	Change Controls
27	Installation Operation Qualification Documents
10	Standard Operating Procedure Updates
22	Functional Design Specifications
3	Factory Acceptance Test / Site Acceptance Test
2	Design Qualifications

RESULTS

Introduction

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RESULTS: BENEFITS

INCREASED SUPPLY & CAPACITY

IMPROVED RELIABILITY & DELIVERED SUSTAINABILITY

LOWER OPERATING EXPENSE

RESULTS: BENEFITS

IMPROVED SUPPLY TO CLINICAL OPERATIONS

Redundant HPW & WFI

B38 B5 B4

Increased Capacity & Reliability

RESULTS: BENEFITS

Water Consumption

- Reduced ~**11,000** gallons per day / ~**4,050,000** gallons per year
- Cost savings of ~**$32K** per year (Water & Sewer)
- Supports GSK's strategic goal to reduce Water Consumption

Electrical Energy

- Pumping operations reduced by 88%
- Cost Savings of ~**$28k** per year

Carbon Emissions

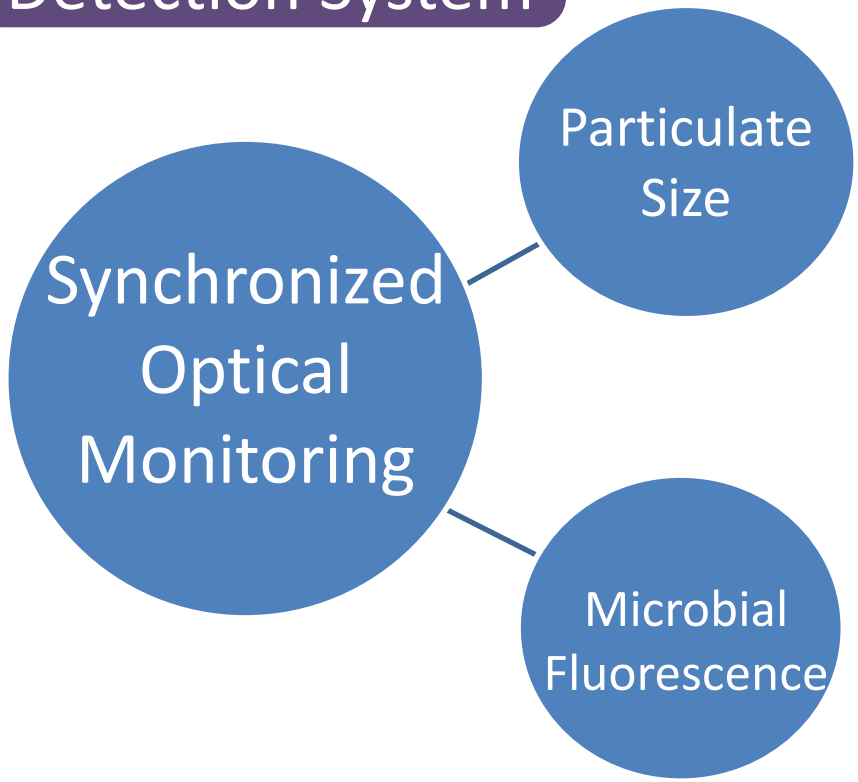
- Annual carbon emissions reduction of **348 TONNES CO2**
- Supports GSK's strategic goal to reduce Carbon Footprint

Operations

- New System supplying HPW to Biopharm Development Pilot Plant
- Eliminated Resin Bed Train Service
- New Bulk Brine & Online Microbial Detection Systems
- Cost Savings of ~**$170,000** per year

RESULTS: BENEFITS

Online Microbial Detection System



FUTURE OPERATING SAVINGS

Reduces Regulatory Sampling

Doesn't Eliminate

Bioburden/Endotoxin

20% (96) Samples/ Year

Only 4th System Installed in US

RESULTS: LESSONS LEARNED

COULD HAVE DONE BETTER

Procurement Management

WFI Batcher Orifices

WFI Still & Clean Steam Supply Pressure

PQ1 Failure / 'Plan B'

WHAT WENT WELL

Full Control Replacement: Demo Simulation of functionality

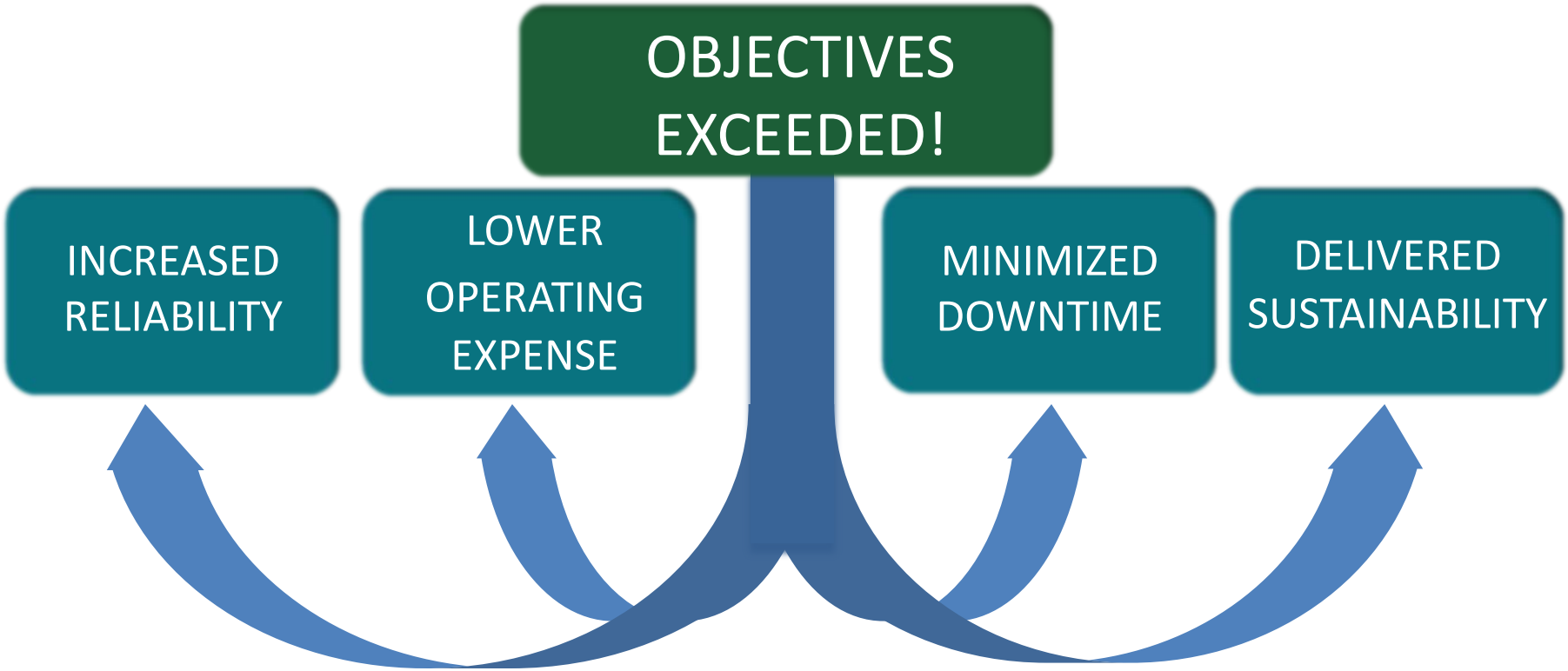
Integration of Automation Contractor

Selection of Construction Contractor

RESULTS: SUMMARY

SUCCESS!

RESULTS: SUMMARY



RESULTS: SUMMARY

OBJECTIVES EXCEEDED!

We kept the Trains on the Tracks

QUESTIONS