	STANDARD OPERATING PROCEDURE Qualification of Subject Matter Experts	Document No. TEC-010	
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1 Subject Matter Experts

Subject Matter Experts (SMEs) will have primary responsibility for specification, design and verification of the manufacturing systems (E 2500 §6.7.3). Subject matter experts are individuals with specific expertise in a particular area or field. Subject matter experts are individuals with a combination of the following qualifications:

1.1 Experience

- >10 y system manufacturing facility and equipment experience
- Prior experience with design and implementation implemented of systems

1.2 Expertise

- In-depth knowledge of the system or subject, design elements, risk factors
- Knowledge of GMP and compliance aspects
- Knowledge of engineering design principles, system sizing & specification

1.3 Methodology Expertise

Proficient in standard methodologies for design and implementation, such as ICH Quality Guidelines (Q8, Q9, Q10), FDA Guidance Documents, US CFRs, EC Directives, ASME Standards (BPE, E 2500), ISPE Guides (GAMP, Baseline)

1.4 Recognized Credentials

- Professional credentials, license
- Academic institution degree and training
- Formal training course

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WFI SYSTEM USER REQUIREMENTS SPECIFICATION

Spec #	Requirement	Risk Potential
1 Operational Requirements		
1.1 Capacity		
1.1.1	The WFI system shall provide water that meets current USP/EP/JP WFI quality requirements	Critical
1.2 Availability		
1.2.1	RODI must be available 24/7 except for maintenance	Non-critical
1.3 Process Requirements		
1.3.1	Temperature \geq 80 degrees C	Critical
1.3.2	Circulation at turbulent flow regime	Critical
1.3.3	If two or more WFI storage tanks are to be used, they should be connected such that they are not stagnant.	Non-critical
1.3.4	WFI storage tanks are to be blanketed with nitrogen	Non-critical
1.3.5	USP <1231>/EP maximum action level: 10 CFU/100 mL	Critical
1.3.6	Total Organic Carbon (TOC) (USP <643> & EP) < 500 ppb (0.5 mg/L)	Critical
1.3.7	WFI Water conductivity USP <645> : Stage 1 Conductivity \leq 1.1 μ S/cm @ 20 C	Critical
1.3.8	Endotoxins (EP) < 0.25 EU/mL	Critical
1.3.9	Nitrates (EP): <0.2 ppm	Critical
1.3.10	Automated operation is required	Non-critical
1.4 Sanitization		
1.4.1	Sanitization at \geq 80° C for 130 minutes.	Critical
1.5 Environment		
1.5.1	Operation in unclassified areas.	Non-critical
2 Capacity		
2.1.1	Storage tank 20,000 L	Non-critical
2.1.2	Generation 500 kg/h	Critical
3 Design		
3.1 Mechanical Systems		
3.1.1	316 L stainless steel construction	Critical
3.2 Electrical Systems		
3.2.1	Panels UL listed	Non-critical
4. Control Systems		
4.1 Software		
4.1.1	N/A	N/A
4.2 Control Platform		
4.2.1	PLC	Non-critical
4.3 Functions		

COP - critical operating parameter
 NCOP - non-critical opr. parameter
 CPP - critical physical parameter
 NCPP - non-critical phys. parameter

WFI SYSTEM USER REQUIREMENTS SPECIFICATION

Spec #	Requirement	Risk Potential
4.3.1	Alarms for Hot and Cold WFI	Non-critical
4.3.2	Alarms for high and low storage tank levels	Non-critical
4.4 Data, Interface and Security		
4.4.1	21 CFR part 11 compliant	Critical
5 Other		
5.1 Maintenance and Spare Parts		
5.1.1	Supplier shall provide (at minimum) the maintenance and operation manuals for all purchased equipment and software.	NCPP

MILLIPORE

BIOPROCESS ENGINEERED PRODUCTS
 BILLERICA, MASSACHUSETTS 01821
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HX-01
 COOLER/HEATER
 MANUF: EXERGY
 TYPE: SANITARY, SINGLE-PASS
 MAT'L: 316L SST
 DESIGN: 2.18 sq ft

F-01
 AIR INTEGRITY FILTER
 MANUF: MILLIPORE
 MODEL: OPTISEAL
 MAT'L: 316L SST

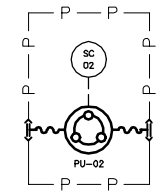
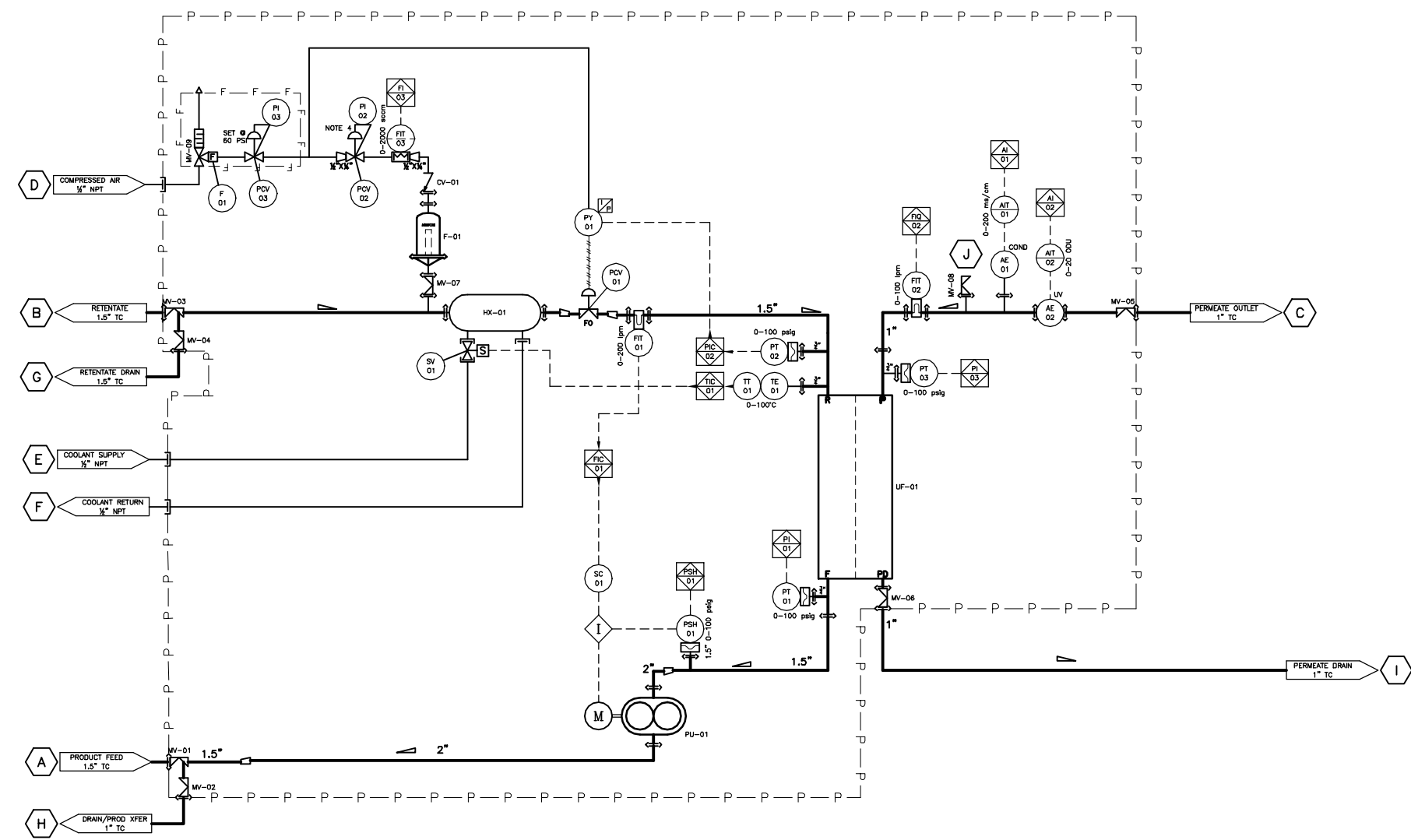
PU-01
 FEED PUMP
 MANUF: VIKING
 MODEL: S3S
 MAT'L: 316 SST
 RATING: 100 lpm @ 60 psig
 MOTOR: 5HP

UF-01
 DIAFL/COAG
 MANUF: MILLIPORE
 MODEL: CUF 1
 MAT'L: 316L SST
 DESIGN: 200 sq ft

PU-02
 FILL/DE PUMP
 MANUF: MASTERFLEX
 MODEL: L77601-10
 RATING: 13 lpm @ 10 psig
 MOTOR: 1/5HP

EXTERNAL PROCESS INPUT/OUTPUT SIGNALS
 NONE

- 1) SYMBOLS ARE IN ACCORDANCE WITH:
 ANSI/ISA-5.1-1984 (R1992) - REFER TO MILLIPORE P&ID LEAD SHEET (D36608) FOR ADDITIONAL DETAILS
- 2) ALL AUTOMATED VALVES FAIL CLOSED UNLESS INDICATED OTHERWISE
- 3) "/>" SYMBOL INDICATES A MINIMUM SLOPE OF 1/8" PER FOOT.
- 4) INTEGRITY TEST PRESSURE DETERMINED BY MEMBRANE TYPE.



SYSTEM CONNECTIONS		
A	1-1/2" TRI-CLAMP	PRODUCT FEED
B	1-1/2" TRI-CLAMP	RETENTATE
C	1" TRI-CLAMP	PERMEATE OUTLET
D	1/2" NPT	COMPRESSED AIR
E	1/2" NPT	COOLANT SUPPLY
F	1/2" NPT	COOLANT RETURN
G	1-1/2" TRI-CLAMP	RETENTATE DRAIN
H	1" TRI-CLAMP	DRAIN/PROD XFER
I	1" TRI-CLAMP	PERMEATE DRAIN
J	1/4" BARB	SAMPLE/INTEGRITY TEST

REV	DESCRIPTION	DATE	INIT
CUSTOMER			
		11-Mar-03	
JOB NUMBER	STANDARD		
CUF-1 CASSETTE SYSTEM PROCESS SCALE MANUAL			
SIZE	DWG NO.	REV	
D	37424	-	

WFI SYSTEM VERIFICATION PLAN TRACEABILITY MATRIX

Spec #	Requirement	Test Plan				
		Risk Level (RPN)	Test	Qualify	Vendor Site	Owner Site
1 Operational Requirements						
1.1 Capacity						
1.1.1	The WFI system shall provide water that meets current USP/EP/JP WFI quality requirements	N/A	See 1.3			
1.2 Availability						
1.2.1	RODI must be available 24/7 except for maintenance	N/A	None	No		
1.3 Process Requirements						
1.3.1	Temperature ≥ 80 degrees C	125	Temp mapping	Yes		TEST
1.3.2	Circulation at turbulent flow regime	75	Check flowrate	No		TEST
1.3.3	If two or more WFI storage tanks are to be used, they should be connected	50	Install verification	No		DOC
1.3.4	WFI storage tanks are to be blanketed with nitrogen	75	As built verification	No		DOC
1.3.5	USP <1231>/EP maximum action level: 10 CFU/100 mL	144	Sample use points	Yes		TEST
1.3.6	Total Organic Carbon (TOC) (USP <643> & EP) < 500 ppb (0.5 mg/L)	144	Sample use points	Yes		TEST
1.3.7	WFI Water conductivity USP <645> : Stage 1 Conductivity ≤ 1.1 μS/cm @ 20 C	144	Sample use points	Yes		TEST
1.3.8	Endotoxins (EP) < 0.25 EU/mL	144	Sample use points	Yes		TEST
1.3.9	Nitrates (EP): <0.2 ppm	144	Sample use points	Yes		TEST
1.3.10	Automated operation is required	75	Install verification	No	DOC	
1.4 Sanitization						
1.4.1	Sanitization at ≥ 80° C for 130 minutes.	256	Temp/Time map	Yes		Test
1.5 Environment						
1.5.1	Operation in unclassified areas.	6	None			
2 Capacity						
2.1.1	Storage tank 20,000 L	75	As built verification	No	DOC	
2.1.2	Generation 500 kg/h	150	Measure output	Yes	TEST	
3 Design						
3.1 Mechanical Systems						
3.1.1	316 L stainless steel construction	125	Verify metalurgy	Yes	TEST	
3.2 Electrical Systems						
3.2.1	Panels UL listed	6	As built verification	No	DOC	
4. Control Systems						
4.1 Software						
4.1.1	N/A	N/A				
4.2 Control Platform						
4.2.1	PLC	25	As built verification	No	DOC	
4.3 Functions						
4.3.1	Alarms for Hot and Cold WFI	125	Dynamic function test	No		TEST
4.3.2	Alarms for high and low storage tank levels	125	Dynamic function test	No		TEST
4.4 Data, Interface and Security						
4.4.1	21 CFR part 11 compliant	108	Verify password	Yes	TEST	
5 Other						
5.1 Maintenance and Spare Parts						
5.1.1	Supplier shall provide maintenance and operation manuals for equipment and	12	Verify in ETOP	No	DOC	

VERIFICATION QUALIFICATION OF THE WATER-FOR-INJECTION SYSTEM

Equipment Manufacturer	Christ Aqua
Equipment Model	Multitron
Installed Location	B68 San Francisco, CA
System Number	W-78497
Customer	Acme Therapeutics, Inc
Address	555 Biopharm Ave, San Francisco, CA

Report Review Approval	
Subject Matter Expert:	
Signature: _____	Date: _
Print Name: _____	
Job Title: _____	Firm: Hyde Engineering + Consulting, Inc.
System Owner:	
Signature: _____	Date: _
Print Name: _____	
Job Title: _____ Firm Acme Therapeutics, Inc.	
Quality Assurance:	
Signature: _____	Date: _
Print Name: _____	
Job Title: _____ Firm: Acme Therapeutics, Inc.	