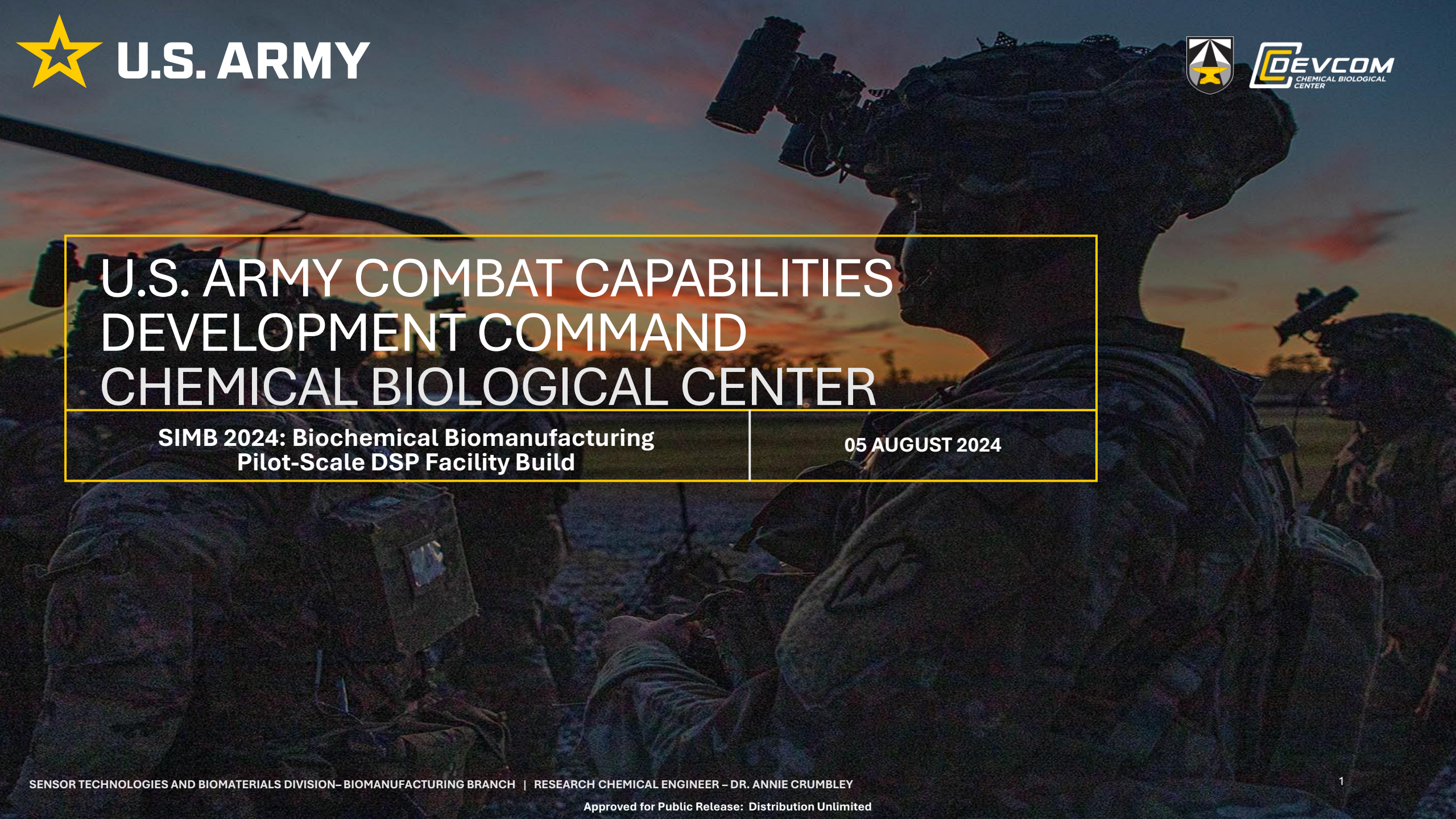


U.S. ARMY

DEVCOM CHEMICAL BIOLOGICAL CENTER

U.S. ARMY COMBAT CAPABILITIES DEVELOPMENT COMMAND CHEMICAL BIOLOGICAL CENTER

SIMB 2024: Biochemical Biomanufacturing Pilot-Scale DSP Facility Build

05 AUGUST 2024

DEVCOM CHEMICAL BIOLOGICAL CENTER (DEVCOM CBC)

Cum Scientia Defendimus (With Science We Defend) statue at Aberdeen Proving Ground, MD

MISSION

Provide innovative chemical, biological, radiological, nuclear and explosive (CBRNE) defense capabilities to enable the Joint Warfighters' dominance on the battlefield and interagency defense of the homeland

VISION

Be the premier provider of innovative CBRNE solutions for the Army, DOD, the Nation and our allies

APPROACH

Research, development and engineering combined with testing, training and field operations to create new, effective chemical biological defense solutions

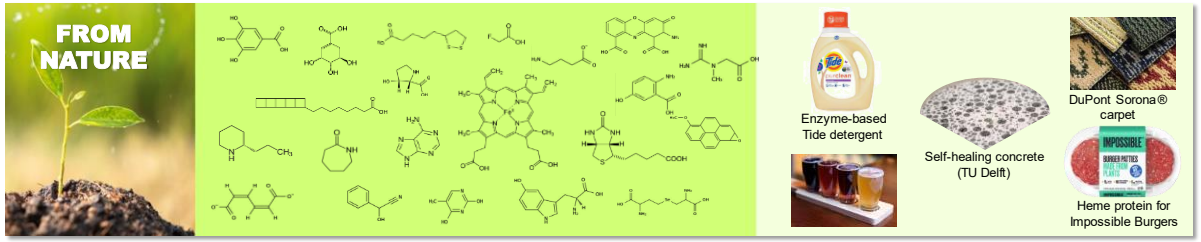
DEVCOM CBC is the Army's principal research and development center for chemical and biological defense technology, engineering, and field operations. DEVCOM CBC is headquartered at Aberdeen Proving Ground, Maryland, with additional locations at Pine Bluff Arsenal, Arkansas, and Rock Island Arsenal, Illinois.

WHY BIOMANUFACTURING?
THE NEXT FRONTIER FOR CHEMISTRY.

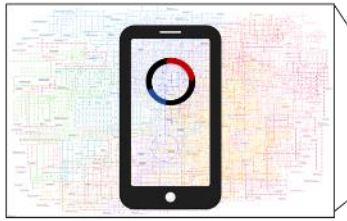
DEVCOM CHEMICAL BIOLOGICAL CENTER

SYNTHETIC BIOLOGY OFFERS CONTROL AND INTENTIONAL ENGINEERING FOR SPECIFIC MATERIAL SYNTHESIS

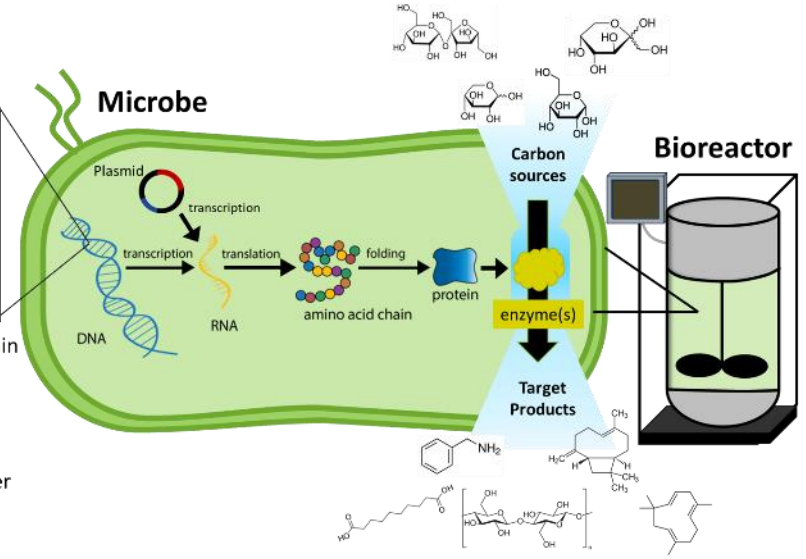
BIOLOGY PROVIDES ENDLESS MOLECULAR DIVERSITY:



A Plasmid is like a molecular "App"



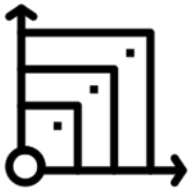
- Small, circular piece of DNA within a bacteria that self-replicates independently from the host's chromosomal DNA
- **Synthetic biology:** Allows transfer of DNA into more tractable organisms for accessible routine synthesis



ADVANTAGES OF BIO-MANUFACTURING BEYOND MOLECULAR DIVERSITY

Flexible & re-usable infrastructure

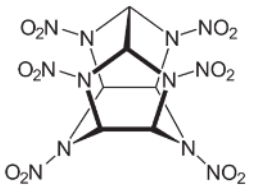
Scalable manufacturing



Environmentally non-destructive

Small capital expenditures

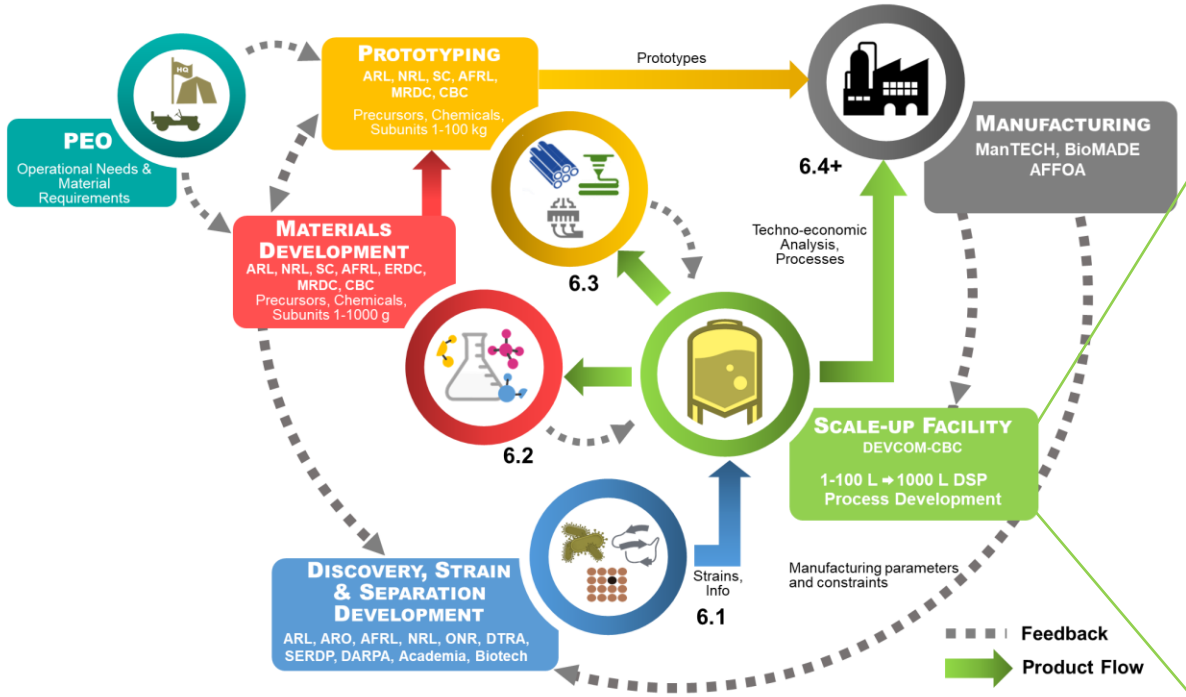
Control of molecular structure



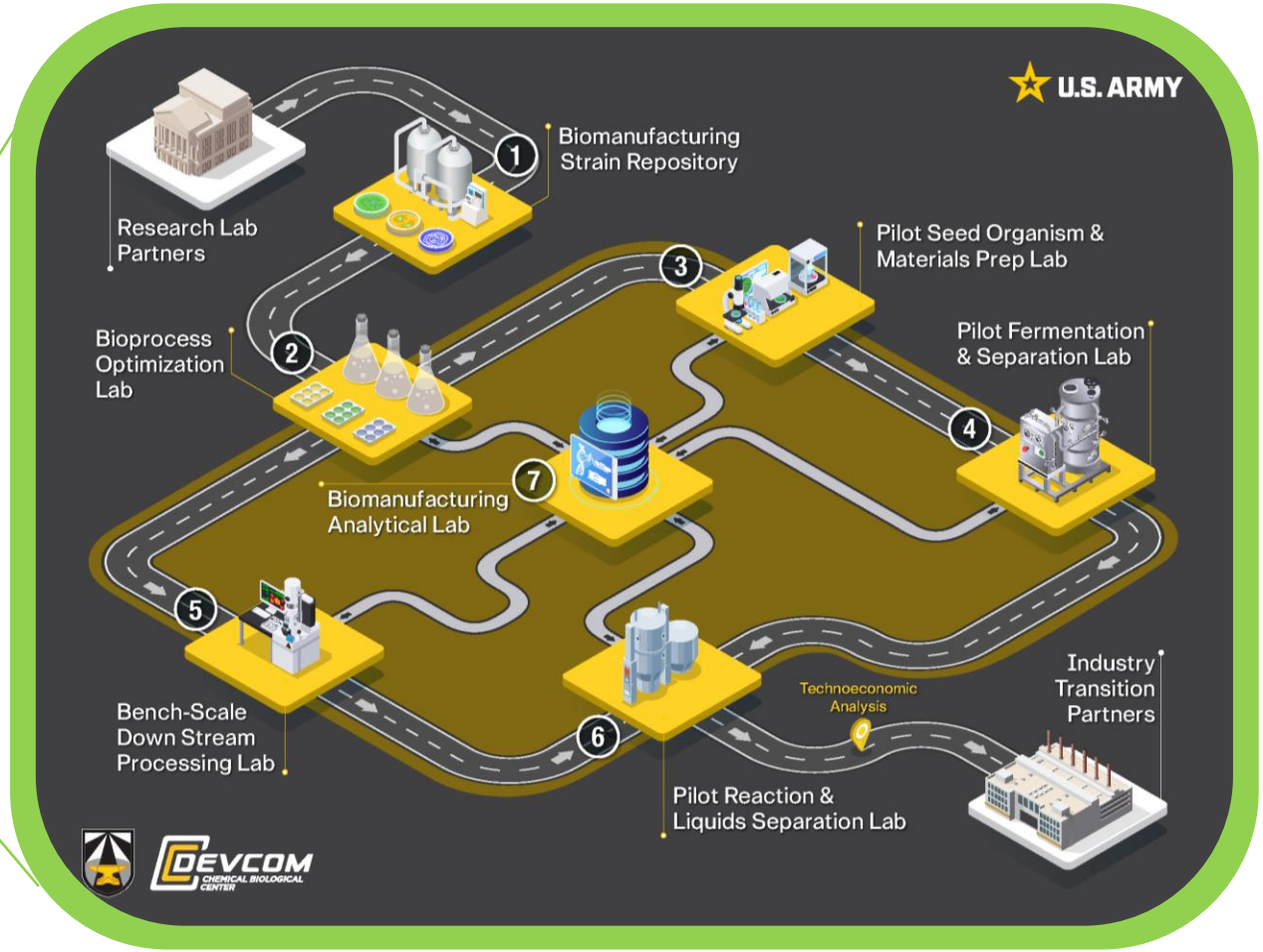
Ambient temperature & pressure production

BIG PICTURE: DEVCOM CBC BIOMANUFACTURING FACILITY SUPPORTS DOD BIOMATERIALS PROTOTYPING ECOSYSTEM

DOD BIOMATERIALS DEVELOPMENT PIPELINE

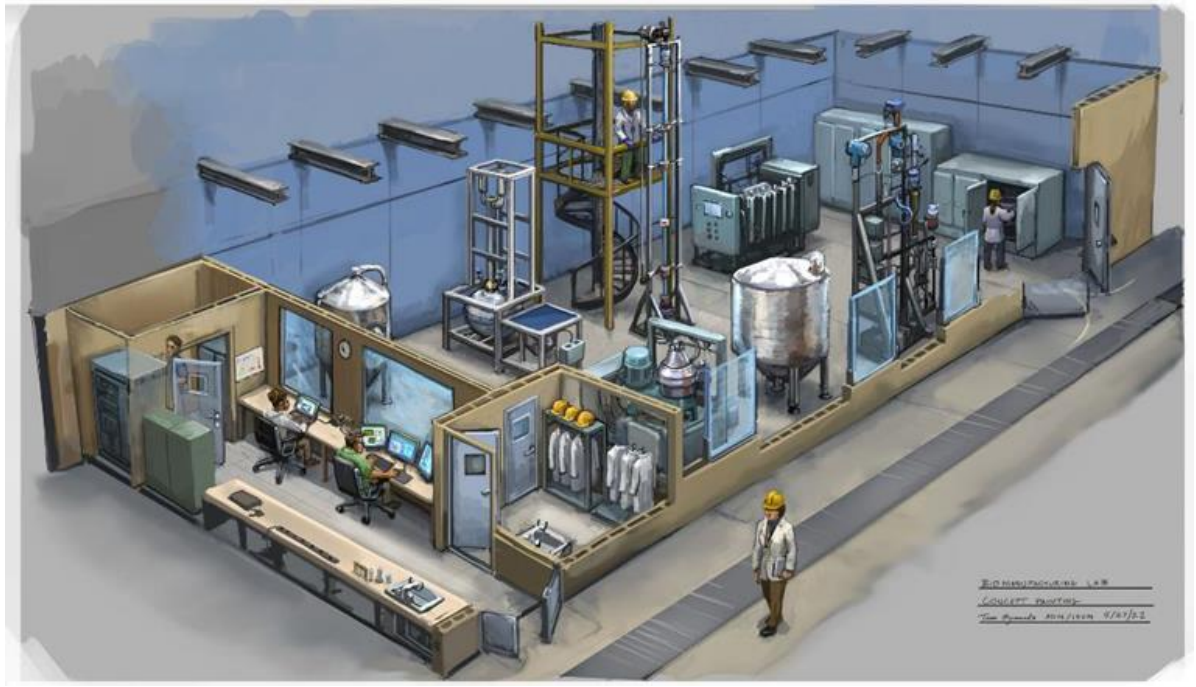


DEVCOM CBC BIOMANUFACTURING WORKFLOW



Anna M. Crumbley, Henry S. Gibbons. (2024). “Accelerating Transition of Biotechnology Products for Military Supply Chains.” *Joint Force Quarterly*: Vol. 113, Article 21.

PIPELINE CAPABILITY: PILOT-SCALE FERMENTATION & DOWNSTREAM PROCESS DEVELOPMENT LAB (PDL)



Summary: DEVCOM CBC is expanding its Biomanufacturing Scale-up Facility to accommodate expanded roles in the DOD biotechnology ecosystem. There has been a $25M+ investment in the modernization of the Army Biomanufacturing Facility. DEVCOM CBC is modernizing its biomanufacturing facility to produce high-value, military-critical chemicals and materials.

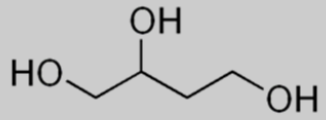
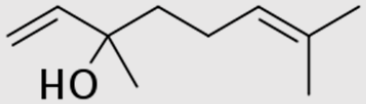
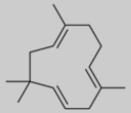
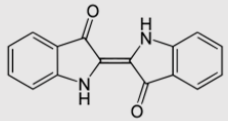
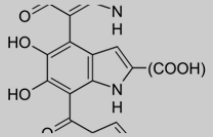
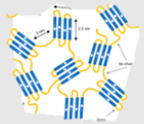
Expansion Plans:	CURRENT CAPABILITY	FUTURE ADDITIONAL CAPABILITIES
Product Profile	• Enzyme, antibodies • Bacteriophage • Whole cell products • BW simulants	• Small molecules • High-value specialty chemicals (energetics, optics, armor) • Polymers and precursors
Infrastructure Required	• Centrifuges • Tangential flow filtration, ultrafiltration • Spray dryer, jet mill • Tube furnace	• Solvent extraction • Distillation • Evaporation and drying • Chromatography • Crystallization

Focus Areas

- Energetics
- Armor
- Textiles & coatings
- Optical Materials
- CBRNE solutions

NEW CAPABILITIES ENABLE NEW PRODUCTS

Potential molecules for biomanufacturing:

Compound	Structure	Military Use	Agency
1,2,4-butanetriol		BTTN Precursor (Propellant)	ONR, SERDP
Linalool		High-density missile fuel	ONR
Caryophyllene		Binder for solid rocket motors, solid fuel ramjets	DARPA
Indigo		Conductive polymers	DARPA
Melanins		Supercapacitors, batteries, corrosion coatings, obscurants	Army
Tandem Repeat Proteins		Self-healing fabrics, coatings	Army


FOOD


FUEL


FITNESS

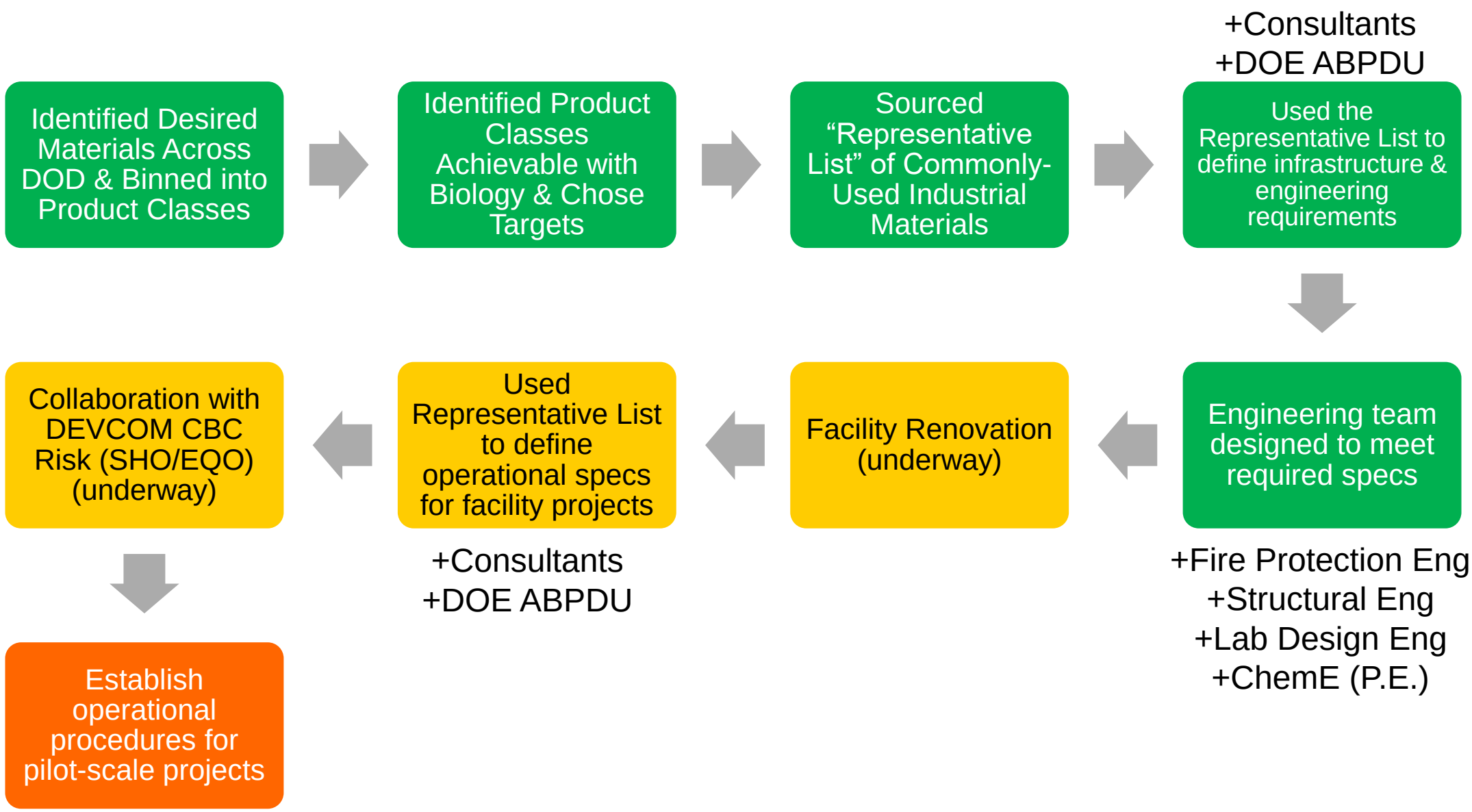

FABRICATION


FIREPOWER

DESIGN REQUIREMENT BOUNDARIES

1. Accommodate multiple as-yet-unknown products requiring different to-be-determined unit operation configurations, including fermentation and enzymatic synthesis
2. Utilize modular and movable unit operations and connections where feasible to allow for DSP reconfiguration as required
3. Accommodate denser-than-air flammable and combustible materials
4. Accommodate the use and processing of microbial organisms and materials originating from microbial organisms (proteins, enzymes, chemicals in bulk aqueous) in organic chemical operations, including the use of hazardous chemical materials as microbial feedstocks and fermentation additives
5. Achieve high-quality, reproducible, data-driven product batches for reproducible and realistic prototyping
6. Operate facility at a scale that would allow for kilogram-scale production of materials within a feasible timescale (est. 2 weeks/batch)
7. Observe all relevant laws, Army Regulations, and DEVCOM CBC Risk policies

PROCESS FOR MEETING THE DESIGN REQUIREMENTS



APPLYING DESIGN CRITERIA

Operating in the Electrically-classified space

Unit Operations List

Process	Unit Operation
DSP Capabilities Expansion - Equipment	
Data management	Process control and data management hardware & software upgrades
Cell rupture	Microfluidizer
Distillation	Packed column pot still
Solvent/Solid/Liquid Extractions	3-phase continuous centrifuge
Solvent Extraction	Podbielniak Contactor Horizontal Centrifuge
Ion Exchange Separations	Simulated Moving Bed Chromatography
Enzymatic Rxns & Reactive Extraction	5L & 10L & 100L Jacketed Glass Reaction Vessels
Holding & Mixing	Angle-agitated holding tank (SS316)
Solvent-Overlay Fermentation	Retrofit angle-agitated holding tank
Material Management	Dispensing & Collection Units
Solid/Liquid Separations & Drying	Filter Press

Representative Chemicals list

Name	Flash Point (°F)	Boiling Point (°F)	NFPA 30 / IBC Flammable / Combustible Liquid Classification
2-Ethylhexanol	170.6	363.2	IIIA
Acetone	1.4	133	IB
Acetonitrile	55	177.8	IB
Butanol	95	243.7	IC
Butyraldehyde	23	167	IB
Carbon Tetrachloride	NA	168.8	NA
Chloroform	NA	140.9	NA
Cyclohexane	-0.4	177.8	IB
Dichloromethane	NA	102.2	NA
Diisopropyl Ether	-20.2	154.4	IB
Dimethyl Sulfoxide	188.6	372.2	IIIA
Dimethylformamide	136.4	307.4	II
Ethanol	57	170.8	IB
Ethyl Acetate	26.6	170.6	IB
Ethylene Bromide	NA	267.8	NA
Ethylene Chloride	55.4	177.8	IB
Hexane	-14.8	156	IB
Isobutanol	82.4	226.4	IC
Isopropanol	53.6	177.8	IB
Mesityl Oxide	82.4	264.2	IC
Methanol	53.6	148.5	IB
Methyl Ethyl Ketone	19.4	176	IB
Methyl Isobutyl Ketone	57.2	243.3	IB
Methyl Isopropyl Ketone	42.8	201.2	IB
Propanol	59	206.6	IB
Propylene Glycol	210.2	368.6	IIIB
Pyridine	62.6	239	IB
Tert-Butyl Methyl Ether	-18.4	129.2	IB
Tetrachloroethylene	NA	248	NA
Toluene	39.2	230	IB
Trichloroethylene	NA	188.6	NA
Xylene	87.8	289.4	IC

REF: IBC (2018); NFPA 30 (2021); NFPA 407 (2017)

EQUIPMENT: THEORETICAL MAX. QUANTITIES (*8-10 HR DAY)

Equipment	Theoretical Max. Flow rates [units]	Anticipated Max. Usage Volumes per Day	Theoretical Max. Waste Volumes per Day (based on 8-10 h operating day)	Solvent volume if a Portion
Centrifuge	9.5 L / min	1500 L	Up to 1400 L	150 L per 1000 L
Distillation	35 L / h	200 L	Up to 150 L	61 L per 20 L
SMB Chromatograph	Eluent IN : 1 L / min Feed IN: 400 mL/min	600 L 250 L	Up to 620 L	
Filter Press	80 L	80 L	Up to 70 L	
Podbielniek Centrifuge (LLE)	Will be less than above centrifuge		Up to 1400 L	150 L per 1000 L

REF: Equipment vendors literature

EQUIPMENT: UNIT OPERATIONS


200 L Distillation Column


3-Phase Continuous Centrifuge

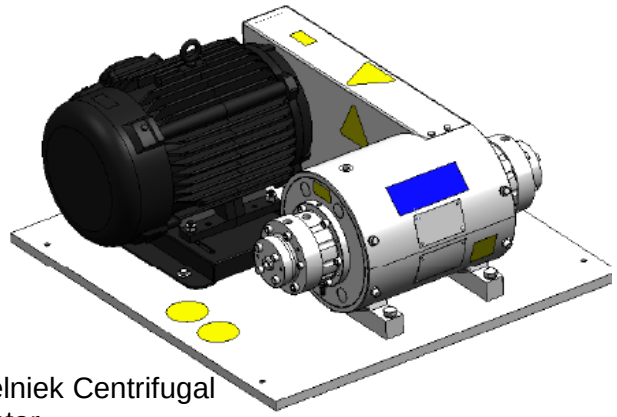

Simulated Moving Bed Chromatography (SMBC)

100 L “squatty” Jacketed Reactor

10 L “squatty” Jacketed Reactor

5 L “squatty” Jacketed Reactor

(Benchtop)


Podbielniek Centrifugal Contactor


Drum Dispensing Cabinet


Tote Collection Cabinet

EQUIPMENT: INFRASTRUCTURE MATERIAL COMPATIBILITIES

- Impacts choices for seals, gaskets, O-rings, etc.

Material	Ethanol	Butanol	2-Ethylhexanol	Isobutanol (CAS 78-83-1)	Isopropanol (2-Propanol)	Methanol	Propanol (1-Propanol)	Propylene glycol	Dimethylformamide	Pyridine	Cyclohexane	Hexane	Acetone	Methyl ethyl ketone	Methyl isobutyl ketone	Methyl isopropyl ketone	Mesityl oxide	Trichloroethylene	Diisopropyl ether (CAS 108-20-3)	Tetrahydrofuran	tert- Butyl methyl ether	Acetonitrile	Water	Ethylene bromide	Chloroform	Ethylene chloride	Dichloromethane (Methylene chloride)	Tetrachloroethylene	Carbon tetrachloride	Dimethyl sulfoxide (DMSO)	Ethyl acetate	Toluene	Xylene	Heptane	2-MeTHF	Butyl acetate	(Ethyl) Hexyl acetate	1-heptanol	1-octanol	1-decanol	1-dodecanol	Oleyl alcohol	2-tridecanone	1,2,4-butanetriol	cyclohexanone	Amberlyst-15	Diethyl ether	Magnesium sulfate	Sea Water	Tap Water	%A	%B	%C & D
PTFE	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	-	-	-	A	A	A	A	-	A	A	-	A	A	A	A	A	A	A	A	A	A	A	-	-	-	A	-	A	A	A	A	84%	0%	0%
304 Stainless	A	A	A	A	A	A	A	B	A	A	A	A	A	A	B	A	A	B	-	-	-	A	A	A	A	B	-	A	B	-	B	A	B	A	A	B	-	A	-	-	A	-	-	-	A	-	B	A	C	A	57%	19%	2%
Hastelloy C	A	B	A	A	A	A	A	B	-	B	B	A	A	A	A	-	A	A	-	-	-	B	A	B	A	B	-	-	A	-	A	A	A	A	A	A	-	A	-	-	A	-	-	-	A	-	B	B	A	A	53%	19%	0%
Kalez	A	A	A	A	A	A	A	A	A	A	A	A	A	-	A	-	-	A	-	A	A	A	A	A	A	A	A	A	A	A	A	A	-	A	A	-	-	-	-	-	A	-	-	D	-	A	A	A	A	73%		
Nylon	A	B	-	-	-	B	-	A	A	C	A	B	A	A	B	A	-	C	-	-	-	A	A	-	A	A	-	A	D	-	A	A	A	A	A	A	-	A	-	-	-	-	-	-	A	-	A	A	A	A	49%	8%	6%
Chemraz	A	A	-	A	A	A	A	A	-	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	A	A	A	A	A	A	A	A	-	A	A	A	-	-	A	-	A	A	A	A	86%		
Acetal	A	A	-	-	A	A	-	B	D	B	A	A	A	C	A	A	-	D	-	-	-	A	-	-	A	A	-	A	B	-	A	C	A	A	A	A	-	A	-	-	-	-	-	-	A	-	A	B	A	A	47%	8%	9%
PVDF (Kynar)	A	A	-	A	A	A	-	A	D	D	A	A	D	D	D	A	-	B	-	-	-	A	A	A	A	-	A	A	-	D	A	A	A	B	B	-	B	-	-	-	-	-	-	D	-	A	A	A	A	47%	8%	15%
316 Stainless	A	A	-	-	-	A	-	B	B	A	A	A	A	A	B	A	A	B	-	-	-	-	A	A	A	B	-	A	B	-	B	A	B	A	A	A	-	A	-	-	-	-	-	-	A	-	B	B	C	A	43%	21%	2%
Aluminum	B	B	A	B	A	A	A	B	A	B	A	A	A	B	B	A	A	D	-	-	-	A	A	B	B	B	-	D	D	-	A	A	A	A	-	A	-	-	-	-	A	-	-	-	A	-	B	B	B	B	39%	27%	6%
Cast/Ductile Iron	B	B	A	-	A	A	A	A	A	A	B	A	A	A	C	C	A	C	-	-	-	A	D	-	B	C	-	A	D	-	A	A	B	A	-	A	-	-	-	-	A	-	-	-	B	-	B	A	D	D	39%	13%	17%
Fluoroelastomer (Viton)	A	A	-	-	A	C	D	A	C	D	A	A	D	D	D	D	D	A	-	-	-	D	A	A	A	B	-	A	A	-	D	C	B	A	D	D	D	D	D	B	B	-	-	-	D	-	D	A	A	A	33%	8%	40%
Polypropylene	A	A	-	-	A	A	-	A	A	A	D	B	A	B	A	C	-	C	-	-	-	B	A	D	C	C	-	D	D	-	A	C	B	C	C	B	-	C	-	-	-	-	-	-	D	-	A	A	A	A	31%	10%	28%
EPR, EPDM	A	A	-	-	A	A	A	A	B	B	D	D	A	A	B	C	B	D	-	-	-	A	A	C	D	D	-	D	D	-	B	D	D	D	D	B	-	D	-	-	-	-	-	-	B	-	D	A	A	A	27%	15%	32%
UHMWPE	A	A	-	A	-	A	-	A	-	D	A	A	A	D	-	C	-	D	-	-	-	-	-	C	C	-	-	B	D	-	B	D	D	A	B	B	-	B	-	-	A	-	-	-	B	-	D	A	A	A	27%	13%	21%
Carbon Steel	B	-	-	-	-	A	-	A	-	A	B	A	A	A	C	C	-	C	-	-	-	-	D	-	B	-	-	A	D	-	A	A	B	A	-	A	-	-	-	-	-	-	-	-	B	-	-	A	D	D	24%	8%	15%
Buna-N (Nitrile TS)	C	A	A	C	A	A	D	A	D	D	B	A	D	D	D	D	D	D	-	-	-	D	A	D	D	D	-	D	D	-	D	D	D	A	D	D	D	D	D	B	A	-	-	-	D	-	D	A	A	A	24%	4%	55%
Fluorocarbon (FKM)	-	-	B	A	-	-	D	A	-	D	A	-	D	D	D	D	D	C	-	-	-	D	-	-	A	-	-	D	B	A	A	D	D	-	D	-	B	B	-	-	-	-	-	-	D	-	D	A	A	A	20%	8%	32%
Santoprene (EPDM & Polypropylene)	A	B	-	A	B	A	-	A	-	A	C	C	B	B	C	C	C	D	-	-	-	A	-	-	D	D	-	C	D	D	C	B	B	-	B	-	-	A	-	-	-	-	-	-	D	-	B	A	A	A	20%	17%	32%
Nitrile (TPE)	A	B	-	-	A	A	-	A	-	-	A	B	D	B	-	D	D	D	-	-	-	D	-	-	C	D	-	D	D	-	D	C	C	B	D	B	-	D	-	-	-	-	-	-	D	-	D	A	A	A	16%	10%	34%
CSM (Hypalon)	A	A	-	-	-	A	-	A	D	D	D	B	C	D	D	D	-	D	-	-	-	A	C	D	D	-	D	D	-	D	D	B	D	D	-	D	-	-	-	-	-	-	-	-	D	A	A	-	14%	4%	43%
Geolast (Buna & Polypropylene)	-	-	-	-	-	-	-	-	D	D	A	A	D	D	D	D	D	D	-	-	-	D	A	-	D	D	-	D	D	-	D	D	D	A	D	D	-	D	-	-	-	-	-	-	D	-	B	A	A	A	14%	2%	43%
Natural Rubber	A	A	-	-	-	A	-	A	C	D	D	D	C	D	D	D	-	D	-	-	-	A	C	D	D	-	D	D	-	D	D	C	D	D	D	D	-	D	-	-	-	-	-	-	D	-	D	B	A	A	14%	2%	49%
Polychloroprene (Neoprene)	A	A	-	A	B	A	D	C	D	D	D	B	C	D	D	D	D	D	-	-	-	D	A	C	D	D	-	D	D	-	D	D	D	B	D	D	-	D	-	D	-	-	-	-	D	-	D	A	B	A	14%	8%	55%
Hytrel (TPE)	A	B	-	-	A	B	-	-	-	C	A	A	B	B	B	-	-	C	-	-	-	-	-	-	D	C	-	-	D	-	B	B	B	B	B	B	D	B	D	-	-	-	-	-	D	-	C	-	A	A	12%	25%	19%
Urethane	D	D	-	-	B	D	D	B	-	D	B	B	D	D	-	D	D	D	-	-	-	B	-	-	D	D	-	D	A	-	D	D	D	B	D	D	-	D	-	D	D	-	-	-	D	-	A	-	A	A	8%	13%	43%
17-4 Stainless	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0%	0%	0%
Leather	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0%	0%	0%

A	Excelle
B	Good
C	Poor
D	Not Re

- Of note – there are 30+ variants of Kalrez – all with different levels of chemical tolerance
- Deep-vacuum (distillation) systems often use copper seals

Material	% A	% B	% A+B
Chemraz	86%		86%
PTFE	84%	0%	84%
304 Stainless	57%	19%	76%
Kalez	73%		73%
Hastelloy C	53%	19%	72%
Aluminum	39%	27%	66%
316 Stainless	43%	21%	64%

REF: https://www.graco.com/us/en/in-plant-manufacturing/support/tools/chemical-compatibility.html

SAFETY & ENVIRONMENTAL: MITIGATING RISKS

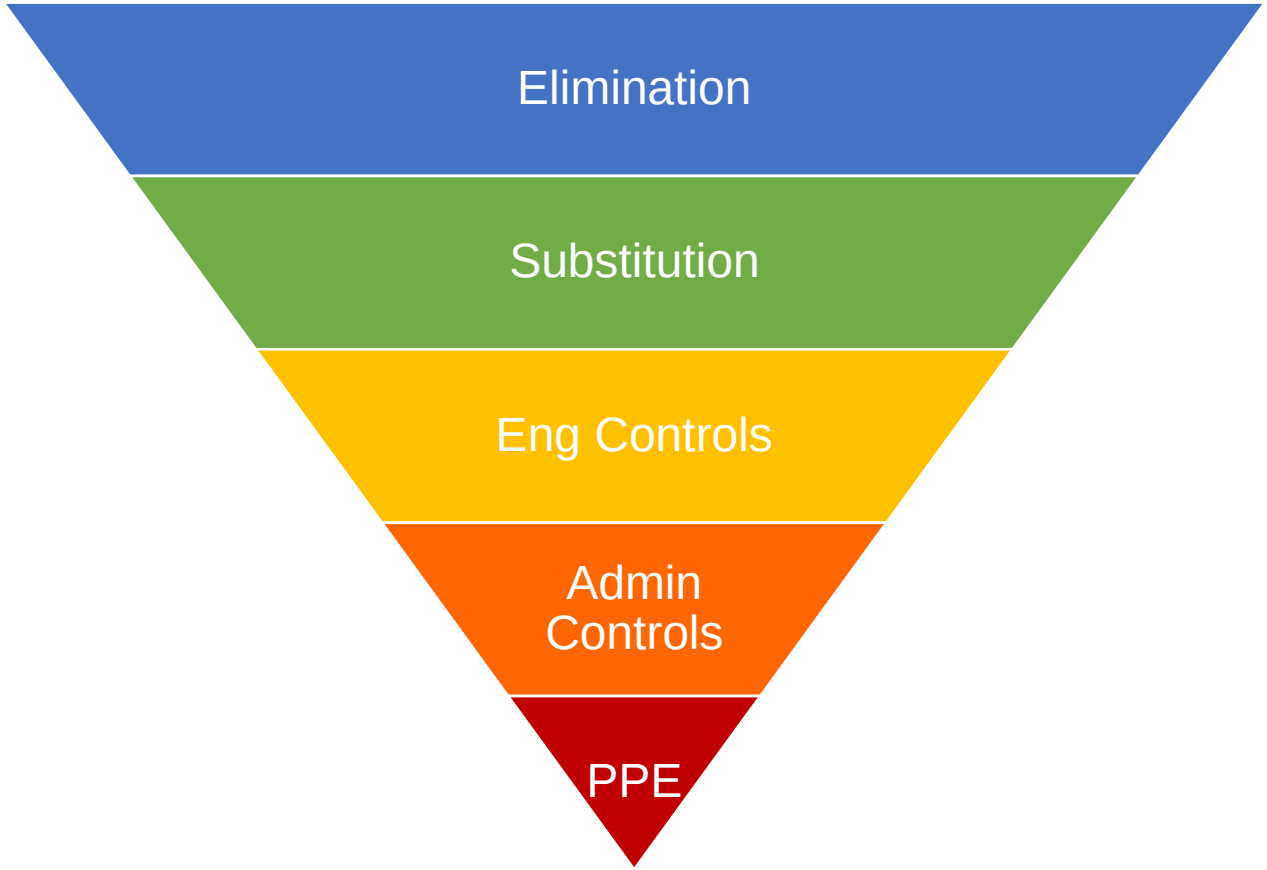
Engineering Controls
- Fire Protection
- Ventilation
- Utilities
- Flooring
- Piping & Tubing

Administrative Controls
- Management of Change (MOC) Procedure

Personal Controls: PPE
- Grounding
- Steel-toed safety shoes
- Eye protection
- Hearing protection
- Gloves
- Protective clothing
- Respiratory

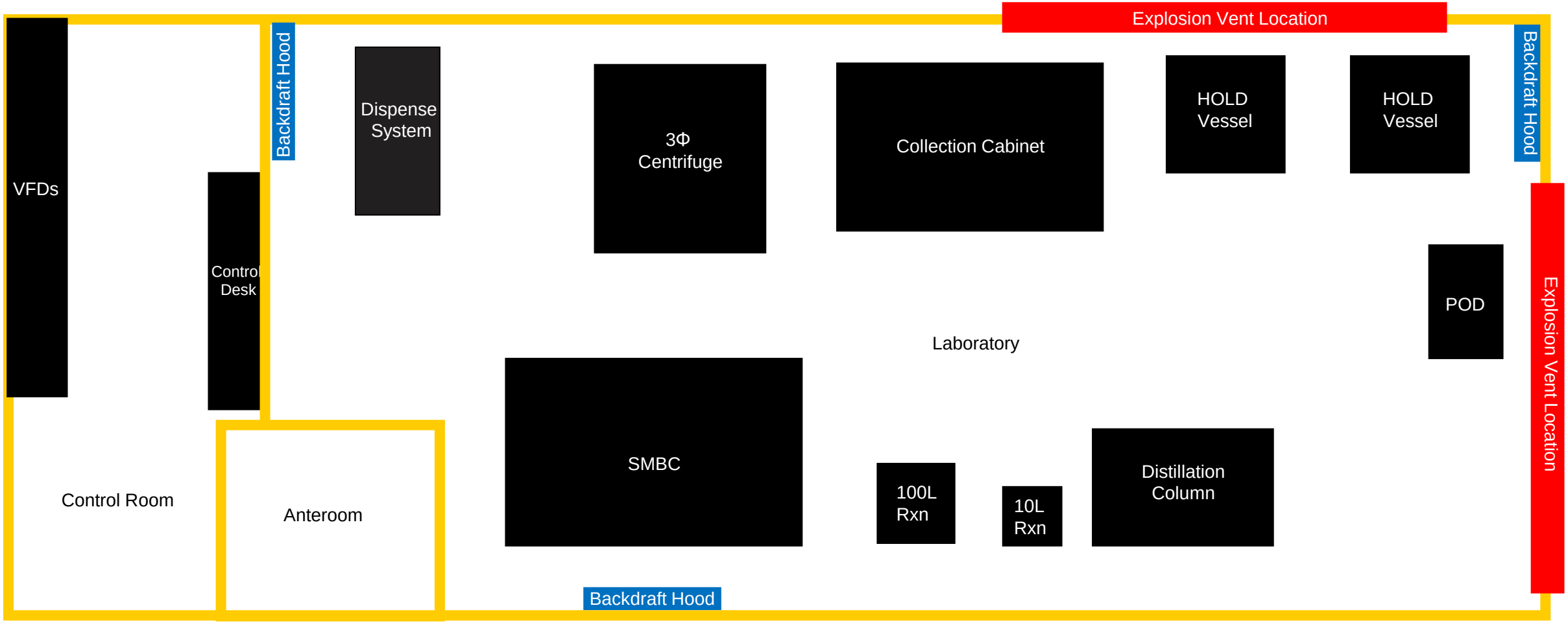
Environmental Controls
- Waste Catchment System and Disposal

Dismantling and Cleaning Procedures
- (Solvent) Reflux cleaning (distillation)
- Multi-step rinsing procedure
  - Aqueous pre-rinse
  - Heated caustic wash
  - Acid wash
  - Intermediate rinse
  - Final wash
  - Sanitizing rinse
  - Air blow



REF: UFC 1-200-01 (Oct 2020); UFC 3-600-01 (May 2021); UFC 4-021-01 (Jan 2020); UFC 4-010-01 (Aug 2020); BC (2018); NFPA 10 (2018); NFPA 13 (2019); NFPA 20 (2019); NFPA 25 (2020); NFPA 30 (2021); NFPA 45 (2019); NFPA 70 (2020); NFPA 72 (2019); NFPA 90A (2021); NFPA 101 (2021); NFPA 110 (2019); DA PAM 385-10; DA PAM 385-69; *NIH Guidelines* (App K) (2024); *Guidelines for Process Safety Fundamentals in General Plant Operations* (CCPS/AICHE, 1995); DEVCOM CBC *Biosafety Manual* (2024)

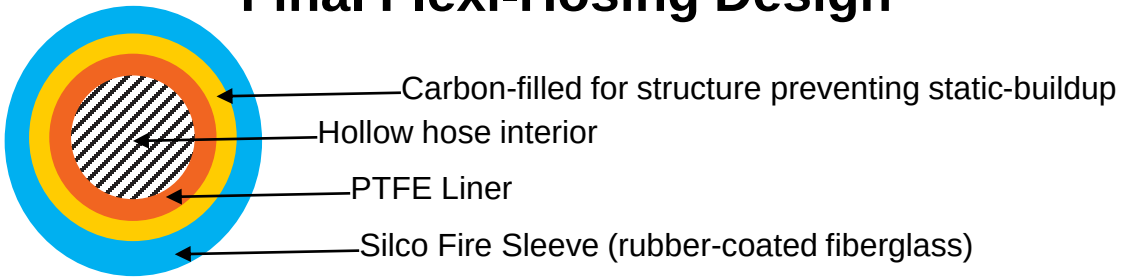
EQUIPMENT: FACILITY LAYOUT & LOGISTICS



- Not pictured (in support space):
  - Air compressor
  - N_2 generator
  - RO water generator

SAFETY & ENVIRONMENTAL: ENGINEERING CONTROLS – E.G., PIPING & TUBING – CLOSED FLOW PATHS

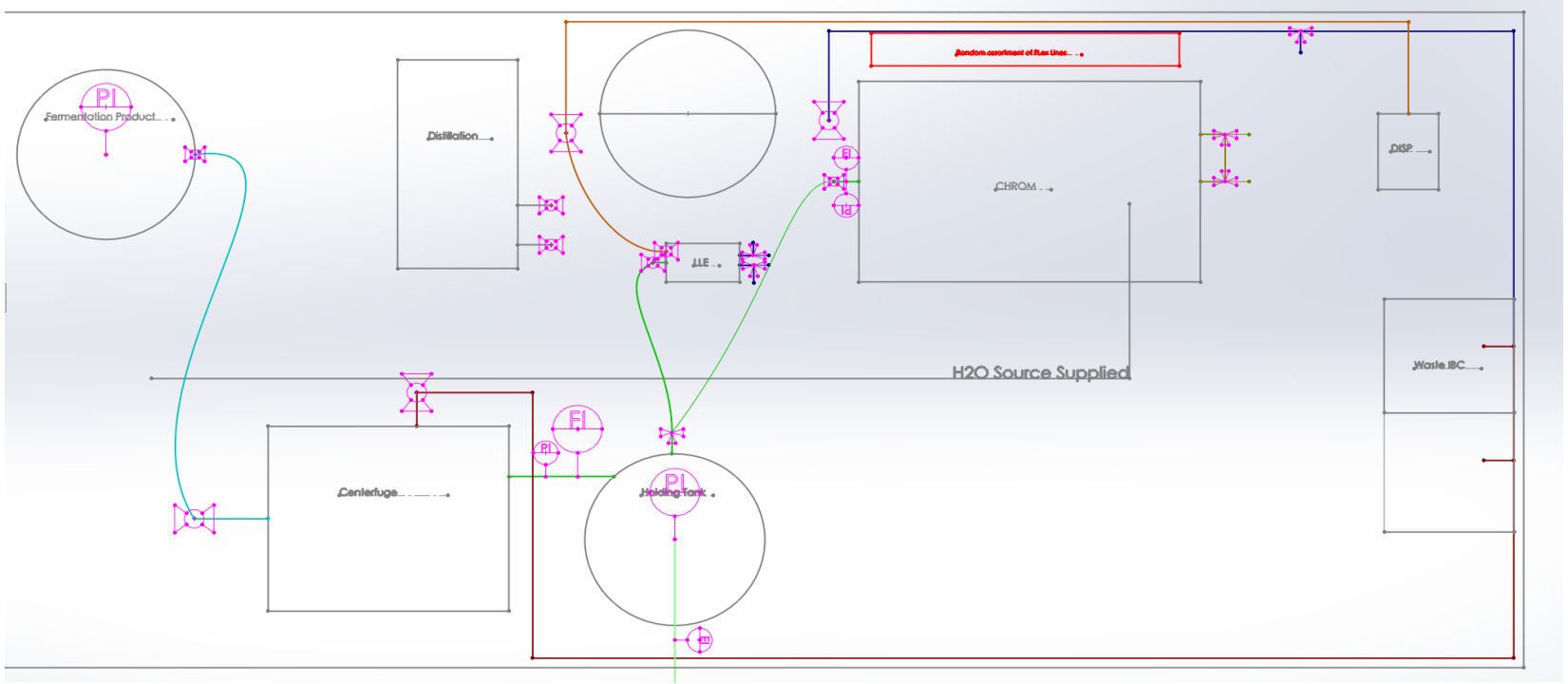
Final Flexi-Hosing Design



- **Piping/Tubing considerations:**
  - Wide range of material compatibility required
  - Cleanability, including disconnection for bio-cleanability as required
  - Grounded (to prevent charge accumulation during flow)
  - Reconfigurability for modularity purposes
  - Low risk of line breakage due to kinking or personnel stepping on lines
  - Eliminate burr accumulation (sharps risk) observed with hoses in use elsewhere in facility
- **Majority of tubing used throughout the facility will be ½ inch ridged 316 stainless steel**
- **<u>Some facility modularity required</u>: PTFE-lined flexible tubing <u>alone</u> cannot meet the NFPA 30 requirements for flexible connectors – requires strengthening support & fire protection**
  - NFPA 30 Section 27.5.2 required flexible connectors comply with UL 2039
  - UL2039 *Standard for Flexible Connector Pipe for Fuels* does not meet purity and cleanliness standards required for this facility (lacks PTFE liner)
  - Identified [vendor] Sanitary TSC-C Silicone Covered Smooth Bore flexible tubing
    - Stainless-steel braided flexible tubing with PTFE liner and hygienic fittings
    - Added a [vendor] Fire Sleeve as exterior line protection from flame/heat to meet the UL 2039 requirement

SAFETY & ENVIRONMENTAL: ENGINEERING CONTROLS – E.G., PIPING & TUBING – CLOSED FLOW PATHS

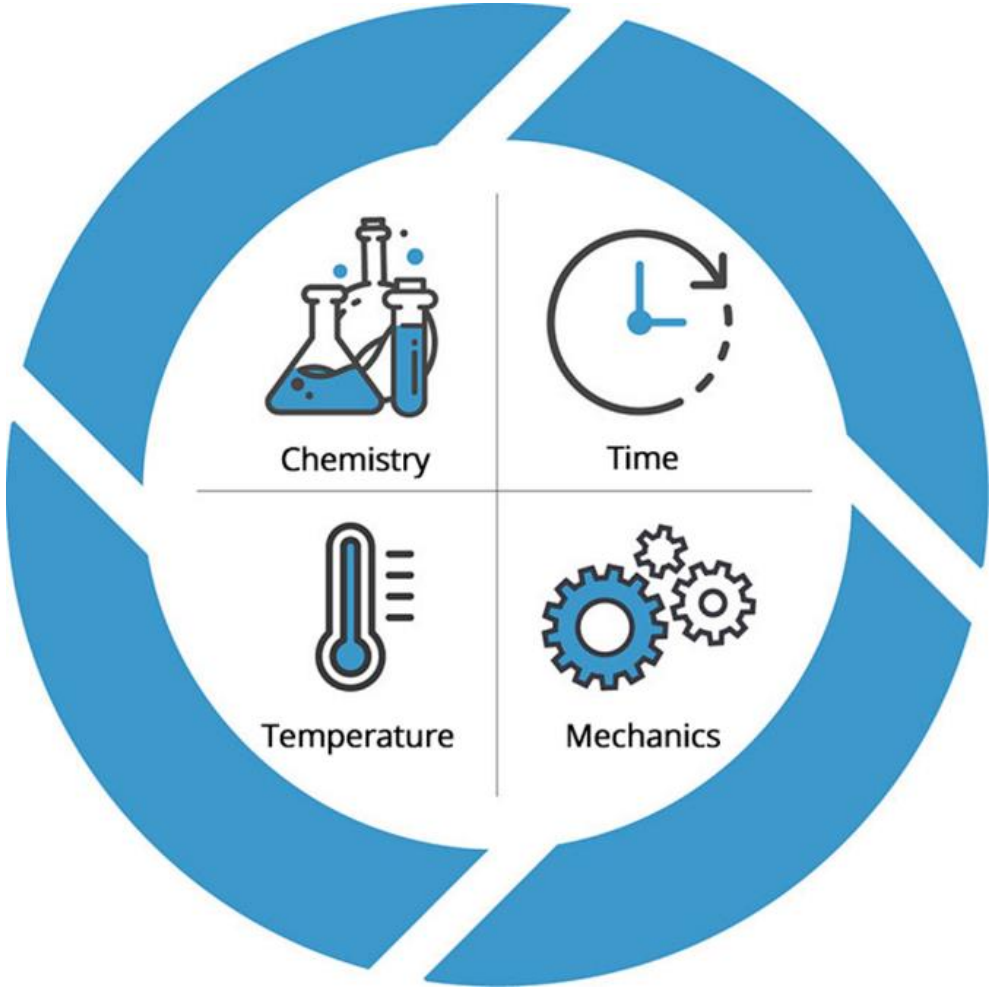
- Recommended hard tubing running off each piece of equipment
  - Centrifuge to holding vessel, centrifuge to collection cabinet, fermentation transfer will be hard tubing
  - All other process connections will be flex lines
  - Rack for flex lines installed behind chromatography operation
  - Collection lines and solvent dispense = hard tubing, terminated with sanitary ball valves



- Straight lines = hard-piped
- Curved lines = flexible hoses

DISMANTLING AND CLEANING PROCEDURES

- Standard methods in the literature for biological operations include SIP and CIP/COP cleaning
  - Steam-in-place (SIP) is not compatible with solvents, not an option
  - COP (manual) = trying to avoid to limit personnel exposure to chemicals & work in C1D1 operational state
  - CIP = best remaining option
    - Two approaches
      - (Solvent) Reflux cleaning (distillation)
      - Multi-step rinsing procedure
        1. Aqueous pre-rinse
        2. Heated caustic wash
        3. Acid wash
        4. Intermediate rinse
        5. Final wash
        6. Sanitizing rinse
        7. Air blow



Herbert "Sinner's Circle" of Cleaning Procedures

Image Ref: https://reitec-online.de/en/cleaning-technique/cleaning-technology/cleaning-process/

DISMANTLING AND CLEANING PROCEDURES

Take-away from analysis of chemical compatibility for cleaning purposes:
will require case-by-case cleaning procedure development

Decontamination solutions:
- 10% bleach, prepared fresh

Ascetic sanitizing solution:
- 70% ethanol or isopropanol
- Acids: 1N - 5N phosphoric acid, 1N - 5N citric acid
- Bases: 1N - 5N NaOH, 1N - 5N KOH

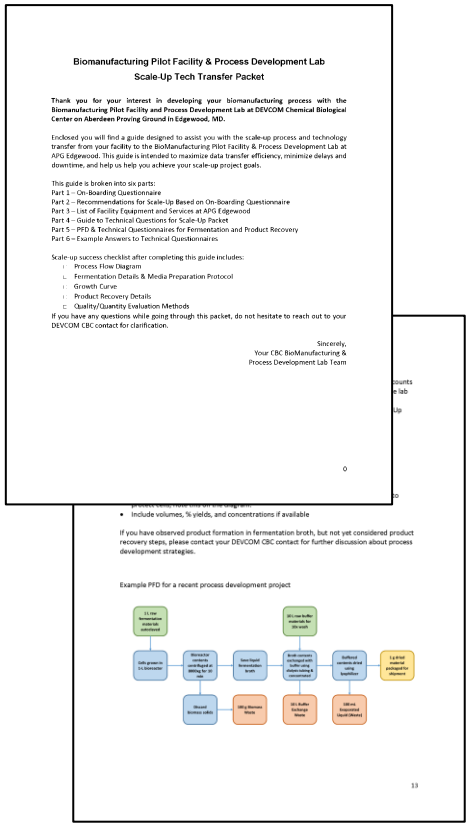
		Group 1 (Inorganic acids)	Group 6 (Alcohols)	Group 1 (Inorganic acids)	Group 2 (Organic acids)	Group 3 (Caustics)	Group 3 (Caustics)
	Compatibility Group (Fisher)	10% Bleach	70% Ethanol	Phosphoric acid	Citric acid	NaOH	KOH
Hexane	9	No reaction	No reaction	No reaction	No reaction	No reaction	No reaction
Diisopropyl ether (CAS 108-20-3)	21	UNSAFE	No reaction	UNSAFE	No reaction	No reaction	No reaction
3utyl methyl ether	6	UNSAFE	No reaction	UNSAFE	No reaction	No reaction	No reaction
Cyclohexane	9	No reaction	No reaction	No reaction	No reaction	No reaction	No reaction
Acetonitrile	14	UNSAFE	UNSAFE	UNSAFE	UNSAFE	UNSAFE	UNSAFE
Isopropanol (2-Propanol)	6	UNSAFE	No reaction	UNSAFE	No reaction	No reaction	No reaction
Ethanol	6	UNSAFE	No reaction	UNSAFE	No reaction	No reaction	No reaction
Acetone	8	UNSAFE	No reaction	UNSAFE	No reaction	UNSAFE	UNSAFE
Methanol	6	UNSAFE	No reaction	UNSAFE	No reaction	No reaction	No reaction
Methyl isobutyl ketone (MEBK)	8	UNSAFE	No reaction	UNSAFE	No reaction	UNSAFE	UNSAFE
Isobutanol (CAS 78-83-1)	6	UNSAFE	No reaction	UNSAFE	No reaction	No reaction	No reaction
Methyl isopropyl ketone (MIPK)	8	UNSAFE	No reaction	UNSAFE	No reaction	UNSAFE	UNSAFE
Propanol (1-Propanol)	6	UNSAFE	No reaction	UNSAFE	No reaction	No reaction	No reaction
Methyl ethyl ketone (MEK)	8	UNSAFE	No reaction	UNSAFE	No reaction	UNSAFE	UNSAFE
n-Butanol	6	UNSAFE	No reaction	UNSAFE	No reaction	No reaction	No reaction
2-Ethylhexanol	6	UNSAFE	No reaction	UNSAFE	No reaction	No reaction	No reaction
Mesityl oxide	8	UNSAFE	No reaction	UNSAFE	No reaction	UNSAFE	UNSAFE
Xylene, Para	10	UNSAFE	No reaction	UNSAFE	No reaction	No reaction	No reaction
Xylene, Meta	10	UNSAFE	No reaction	UNSAFE	No reaction	No reaction	No reaction
Toluene	10	UNSAFE	No reaction	UNSAFE	No reaction	No reaction	No reaction
Xylene, Ortho	10	UNSAFE	No reaction	UNSAFE	No reaction	No reaction	No reaction
Ethyl acetate	13	UNSAFE	No reaction	UNSAFE	No reaction	UNSAFE	UNSAFE
Dimethylformamide (DMF)	7	UNSAFE	UNSAFE	UNSAFE	UNSAFE	UNSAFE	UNSAFE
Pyridine	4	UNSAFE	No reaction	UNSAFE	UNSAFE	No reaction	No reaction
Water	-	-	-	-	-	-	-
Propylene glycol, 1,2	6	UNSAFE	No reaction	UNSAFE	No reaction	No reaction	No reaction
Propylene glycol, 1,3	6	UNSAFE	No reaction	UNSAFE	No reaction	No reaction	No reaction
Dimethyl sulfoxide	-	UNSAFE	UNSAFE	UNSAFE	UNSAFE	UNSAFE	UNSAFE
1,2-dichloroethane	5	UNSAFE	No reaction	UNSAFE	No reaction	UNSAFE	UNSAFE
Dichloromethane	5	UNSAFE	No reaction	UNSAFE	No reaction	UNSAFE	UNSAFE
Trichloroethylene	5	UNSAFE	No reaction	UNSAFE	No reaction	UNSAFE	UNSAFE
Chloroform	5	UNSAFE	No reaction	UNSAFE	No reaction	UNSAFE	UNSAFE
Carbon tetrachloride	5	UNSAFE	No reaction	UNSAFE	No reaction	UNSAFE	UNSAFE
Tetrachloroethylene	5	UNSAFE	No reaction	UNSAFE	No reaction	UNSAFE	UNSAFE
entation Broth (*E. coli* representative)	-	-	-	-	-	-	-
Sea water	-	-	-	-	-	-	-

References:
https://www.coleparmer.com/chemical-resistance
https://www.amherst.edu/system/files/media/Bleach%2520Incompatibility.pdf
https://www.wisconsin.edu/ehs/download/Fisher-Scientific-Chemical-Compatibility-Chart.pdf

TECH TRANSFER: METHODS & BEST PRACTICES

At a minimum, scale-up of a project requires the following from bench-scale researchers:

1. A list of all materials added to the process, including technical grade and amounts
2. Information on order of material addition, including pauses for stirring, separate preparation details for stock solutions, etc.
3. Operating conditions for each of the discrete steps in the operation, e.g.
4. Desired end-product specifications, including chemical composition and purity requirements with applicable analytical methods
5. Commentary on any “surprising, tricky, or unexpected” findings during the research


Biomanufacturing Pilot Facility & Process Development Lab

Scale-Up Tech Transfer Packet

Thank you for your interest in developing your biomanufacturing process with the Biomanufacturing Pilot Facility and Process Development Lab at DEVCOM Chemical Biological Center on Aberdeen Proving Ground in Edgewood, MD.

Enclosed you will find a guide designed to assist you with the scale-up process and technology transfer from your facility to the BioManufacturing Pilot Facility & Process Development Lab at APG Edgewood. This guide is intended to maximize data transfer efficiency, minimize delays and downtime, and help us help you achieve your scale-up project goals.

This guide is broken into six parts:
Part 1 – On-Boarding Questionnaire
Part 2 – Recommendations for Scale-Up Based on On-Boarding Questionnaire
Part 3 – List of Facility Equipment and Services at APG Edgewood
Part 4 – Guide to Technical Questions for Scale-Up Packet
Part 5 – PFD & Technical Questionnaires for Fermentation and Product Recovery
Part 6 – Example Answers to Technical Questionnaires

Scale-up success checklist after completing this guide includes:
- Process Flow Diagram
- Fermentation Details & Media Preparation Protocol
- Growth Curve
- Product Recovery Details
- Quality/Quantity Evaluation Methods

If you have any questions while going through this packet, do not hesitate to reach out to your DEVCOM CBC contact for clarification.

Sincerely,
Your CBC BioManufacturing &
Process Development Lab Team

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- Include volumes, % yields, and concentrations if available

If you have observed product formation in fermentation broth, but not yet considered product recovery steps, please contact your DEVCOM CBC contact for further discussion about process development strategies.

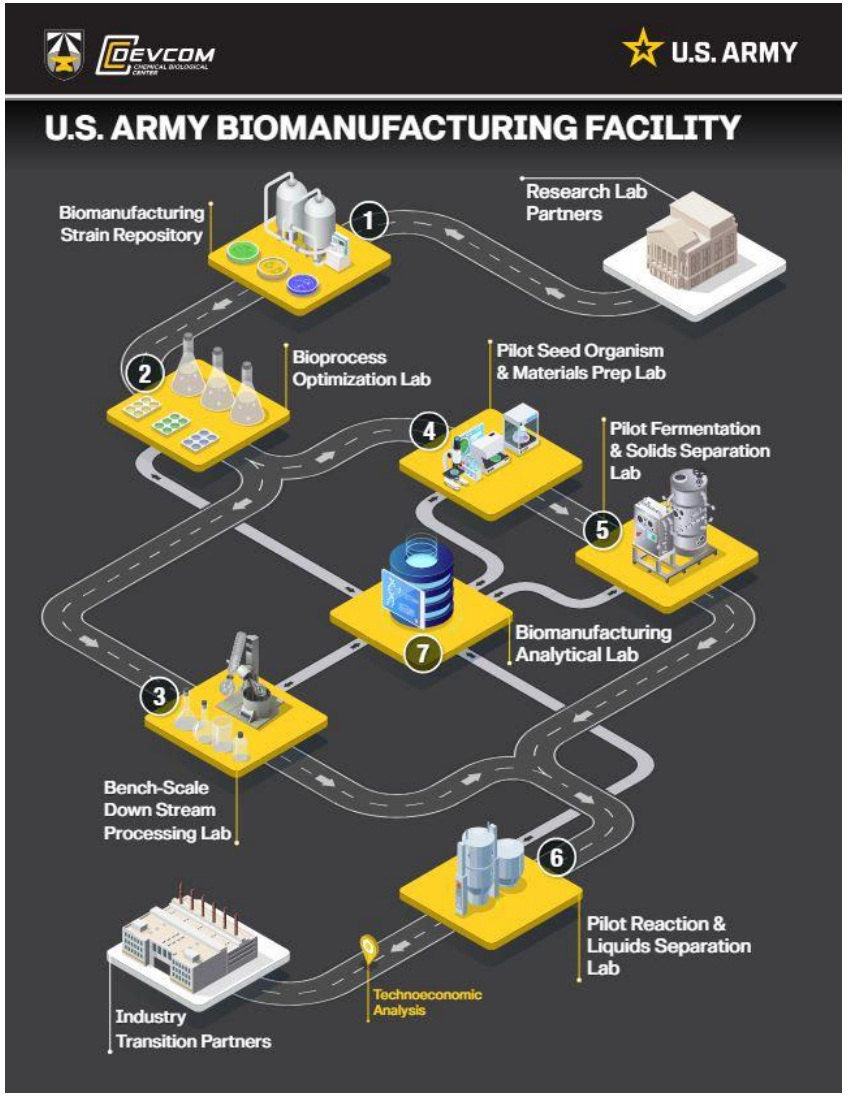
Example PFD for a recent process development project

13

Specific methods and available data should be collected IAW the bench-scale researcher’s best practices and discussed with the tech transfer team during MOC document development.

BIOCHEMICAL BIOMANUFACTURING PILOT-SCALE DSP FACILITY BUILD: IN SUMMARY

- Biomaterials are the next frontier, and the DOD is working to develop and integrate novel and drop-in biomaterials to strengthen materiel supply chains and enhance defense capabilities
- DEVCOM CBC supports the DOD pipeline by producing small-scale to pilot-scale quantities of biomaterials for materiel prototyping.
- Pursuing the “new” classes of biochemical materials now accessible through synthetic biology requires facilities with additional design considerations for safe operation



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- Technical Support: Brooke Simmons

Downstream Process Small Scale
- PI: Dr. Michael Lichstrahl

Fermentation Scale-up
- PI: Dr. Annie Crumbley
- Technical Support: Frank (Joe) Kragl, Hal Royce, Vinita Daniel

Downstream Process Scale-up
- PIs: Dr. Annie Crumbley & Michael Lichstrahl
- Technical Support: Frank (Joe) Kragl

Program Management
Dr. Kelly Basi

Dr. Jeff Noble (Booz Allen)

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- PI: Dr. Michael Lichstrahl
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Techno-Economic Analysis
- Dr. Annie Crumbley

Consulting, Strategic Lead
- Dr. Henry (Sandy) Gibbons

Strain Repository
- PIs: Dr. Edward (Randy) Hofmann & Melody Zacharko
- Technical Support: Vinita Daniel

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BIOMANUFACTURING SENIOR SCIENTIST
FOCUS: PILOT-SCALE BIOCHEMICAL DSP

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