

AZENTA
LIFE SCIENCES

Cryo Intro

Manchester Distributor Meeting
30 Jan 2024

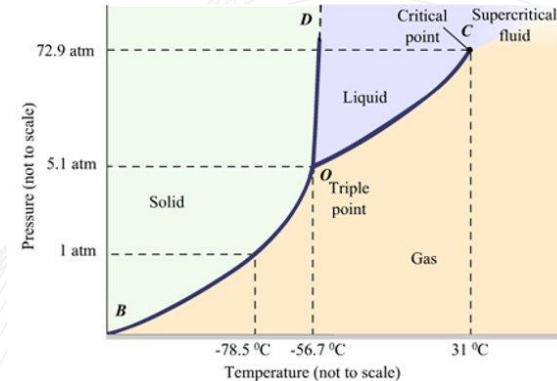
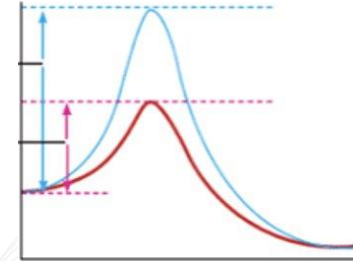
Agenda:



- Why do we cryopreserve?
- LN2 Basics Heat Transfer
- Differentiators
- Products
- Customer Personas
- Channel Partners/Installed Base
- Value Proposition
- Objections to Automation
- Workflow Solutions

Why Do We Cryopreserve Samples?

- **STABILIZE CRITICAL BIOLOGICAL PROPERTIES**
- **SLOW DEGRADATIVE ENZYMATIC ACTIVITY**
 - 15,000 PROTEINS IN PLASMA PROTEOME
 - HUNDREDS ARE DEGRADATIVE & PRESENT IN EVERY CELL
 - REDUCING TEMPERATURE REDUCES ACTIVITY
- **PREVENT WATER FROM MOVING AND REACTING**
 - MULTIPLE PHASE CHANGES AND RE-CRYSTALLIZATIONS
 - GLASS TRANSITION - TG = -135°C
- **LONGTERM PRESERVATION FOR VIABILITY REQUIRES:**
 - DEGRADATIVE ENZYMES SLOWED TO A STOP
 - WATER MOLECULES FULLY SOLIDIFIED



Scientific Basis for Selecting Temperatures

- **STORAGE TEMPERATURE DRIVEN BY:**

- **SAMPLE TYPE**

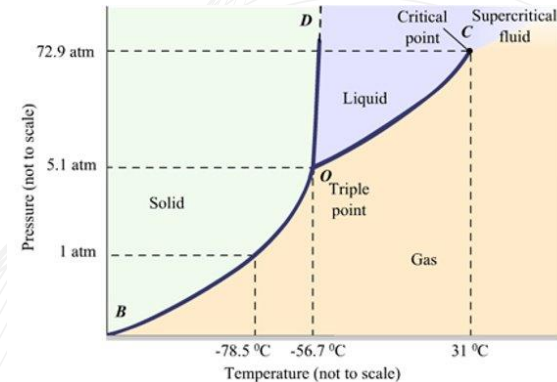
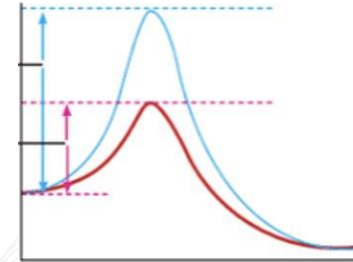
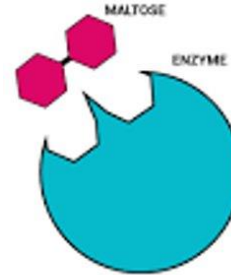
- CELLS, BIOFLUIDS PROTEINS, NUCLEIC ACIDS ETC

- **END USE APPLICATION**

- VIABILITY, FUNCTION, PROTEIN COMPONENT STUDIES, ANTIBODIES, RNA/DNA EXTRACTIONS, ETC

- **DURATION**

- Short term: days to months
 - Long term: years to decades
 - Expiration dates



Liquid Nitrogen (LN₂)

- LN₂ is a consumed refrigerant and must be replenished
- LN₂ is produced industrially through liquefaction of atmospheric air
 - Distillation through repeated pressurizing and supercooling
 - LN₂ is affordable, abundant byproduct at 78% of Earth's atmosphere
 - At 1 atm LN₂ is $-196\text{ }^{\circ}\text{C}$ with an expansion ratio nearly 800:1
- Cannot be a liquid at room temperature
- LN₂ trapped inside lines with no relief device can generate extreme pressures!

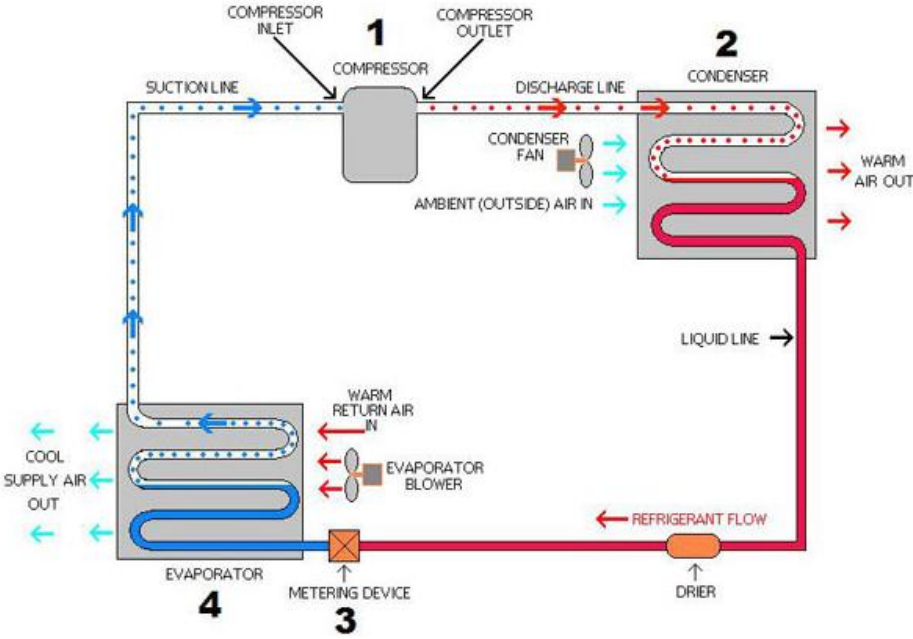


Liquid Nitrogen (LN₂)

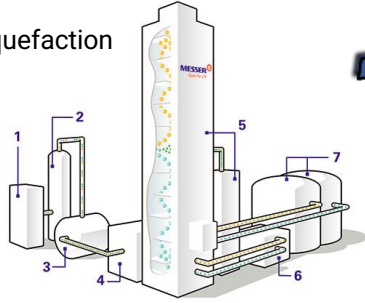
- Total LN₂ Consumption: 100-200 L/week
 - Freezer evaporation
 - 7-15 L/day
 - 5-10% volume/day
 - Supply evaporation
 - 5-10 L/day
 - 3-5% volume/day
 - Transfer losses
 - 10-15 L/week
 - 20% volume/fill



Closed vs Open Loop Refrigeration



Air Liquefaction Plant



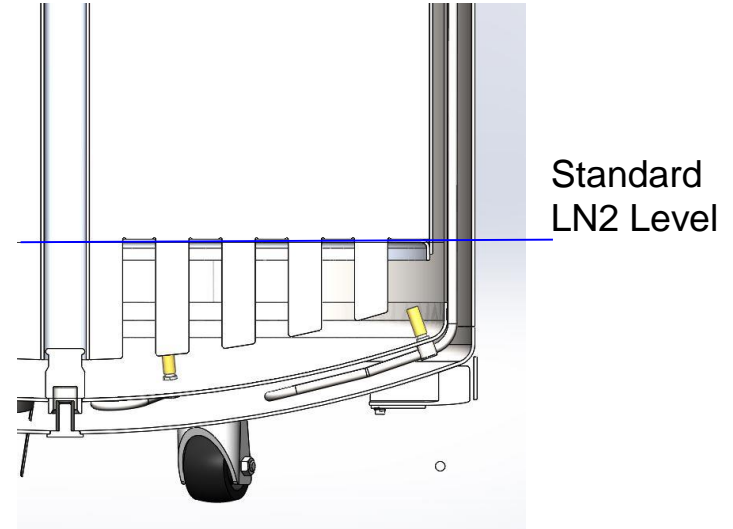
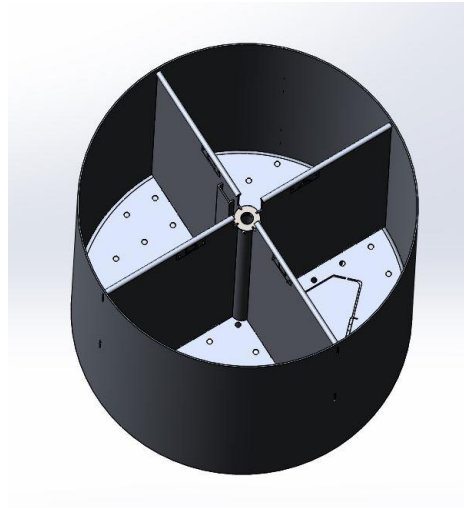
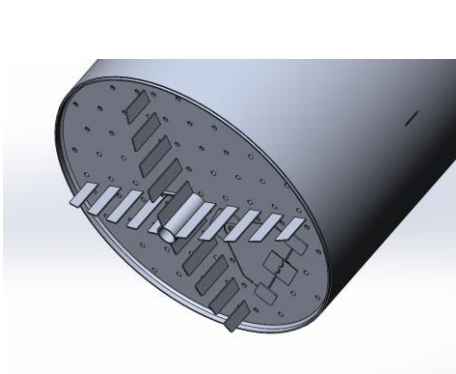
Cryo Freezer is analogous to the evaporator in a closed loop system

Heat Transfer and Insulation

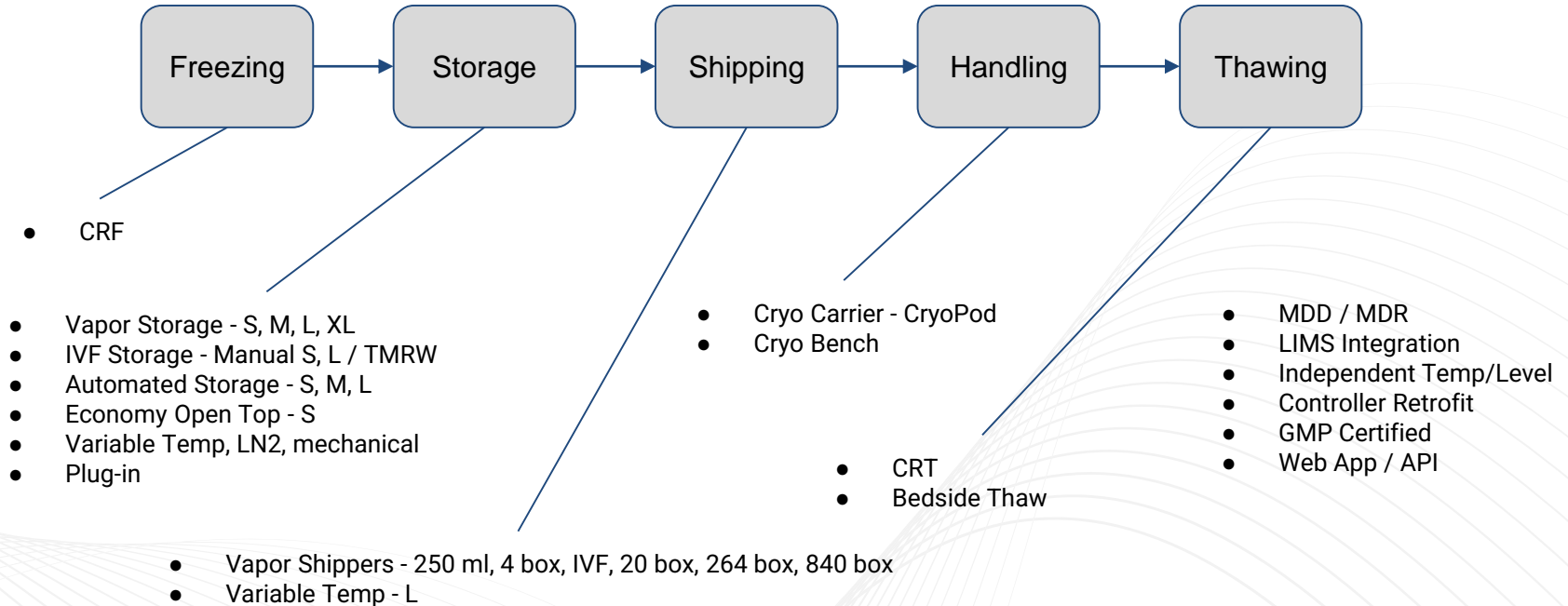
- Goal is to keep as much heat out of the freezer as possible
- Heat is transferred in 3 ways:
 - Conduction
 - Through physical contact; electric burner on a stove heating a pan
 - Minimize metal contact and heat path between inner and outer vessels
 - Convection
 - Through movement of a fluid (gas/liquid); forced-air furnace, weather systems
 - Vacuum between vessels removes molecules and heat path
 - Radiation
 - Sun warming the Earth, microwaves, infrared, body heat
 - Super insulation wrap lengthens heat path from 1" between the vessels to over 1 mile.
 - Heat must follow full length of insulation wrap to reach inner vessel

Turn Tray Fingers

- Extension of aluminum dividers below the turntray floor to carry heat from samples in the turn tray to the LN2.
- Current art has a shell around the outside of the turntray that touches the LN2 but it does not extend into the dish of the bottom head and as such loses contact sooner. This design improves on that by having the extensions reach deeper and also be directly connected to the interior dividers of the turn tray thus pulling heat from the samples and into the LN2



Workflow Solutions



Customer Personas



<i>Personas</i>	<i>Channel Partner</i>	<i>Biobanker</i>	<i>Researcher / Clinician</i>	<i>Lab Manager</i>	<i>Technician</i>
Priorities	Profit	Risk Management	Sample Quality	Workflow	Ease of Use
	Customer Satisfaction	Documentation	Reducing Variables	Sample Quality	Workflow
	Vendor Relationship	Sample Quality	Workflow	Documentation	Sample Quality
Challenges	Bandwidth	Audits / Record Keeping	Audits / Record Keeping	Audits / Record Keeping	Safety
	Competition (Manf & Dist)	SOPs	SOPs	SOPs	Rack ID
	Personnel	Personnel	Personnel	Personnel	Rack removal/replacement
	Coverage	Purchase / Maintenance	Purchase / Maintenance	Purchase / Maintenance	Sample handling
	Service	Redundancy	Redundancy	Redundancy	Documentation

- Pharma / Biotech
 - CGT, R&D, Translational, Reference, Cell Banks, Vaccine
- Clinical
 - Transfusion Medicine, Regenerative, BMT
 - IVF
- Research
 - University, Government, CRO / CMO
- Biorepository

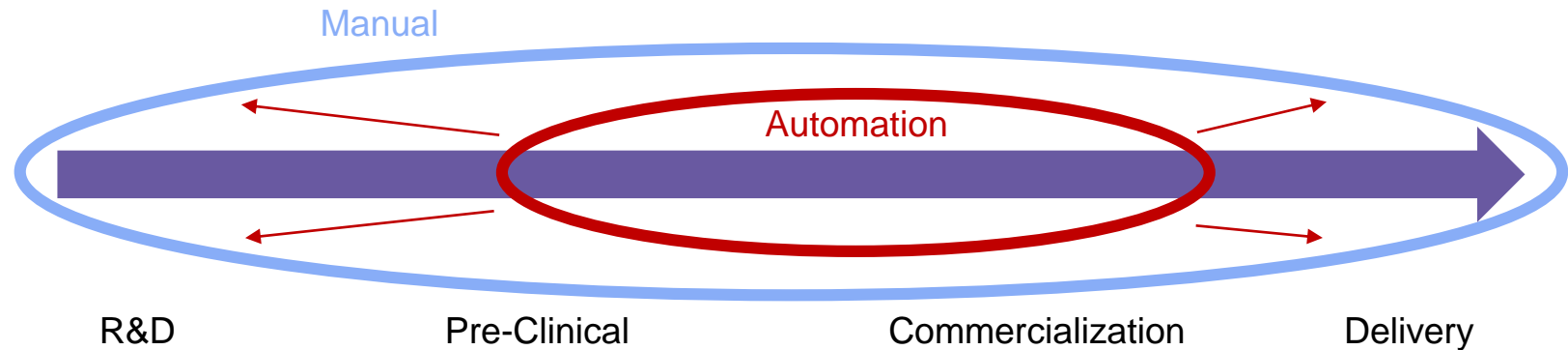
- Market Trends
 - Cold Chain Data
 - Application specific solutions
 - Redundancy
 - Remote Monitoring
 - Automation
 - IVF consolidation

Cryo Freezers

Cryo Freezers	A220	A440	A700	A1000
Outer Diameter - in (mm)	34.0 (864)	45.0 (1143)	55.0 (1397)	65.0 (1651)
Usable Height - in (mm)	30.0 (762)	30.0 (762)	30.0 (762)	30.0 (762)
2 ml Vial Box Capacity - 5-2	220	440	700	1,060
2 ml Vial Box Capacity - 13-2	156	416	676	988
250 ml Blood Bag Capacity	400	848	1,376	2,032
Extended Height Freezers	E264	E528	E840	E1200
Outer Diameter - in (mm)	34.0 (864)	45.0 (1143)	55.0 (1397)	65.0 (1651)
Usable Height - in (mm)	34.0 (864)	34.0 (864)	34.0 (864)	34.0 (864)
2 ml Vial Box Capacity - 6-2	264	528	840	1,272
2 ml Vial Box Capacity - 15-2	180	480	780	1,140
250 ml Blood Bag Capacity	500	1,060	1,720	2,540
Dry Vapor Shipper			S840	



R&D to Delivery



Expand cryo automation through new products, channel partner relationships and market development

Differentiators



Capacity

10-30% More Samples
Highest Storage Density
Lowest LN2 Usage Per Sample



Ergonomics

Cryo LED & Auto Fog Clear
Full Sample Visibility
Low Lifterover Height | Workspace



Connected

Touchscreen with WiFi / LAN
Text & Email Alerts | Cloud Backup
Redundant Remote Monitoring



Differentiators

PERFORMANCE

- Temperature, storage density, LN2 usage

REDUNDANCY & SECURITY

- Redundant valves and sensors
- Secondary temperature and LN2 level monitoring
- Lifecycle testing

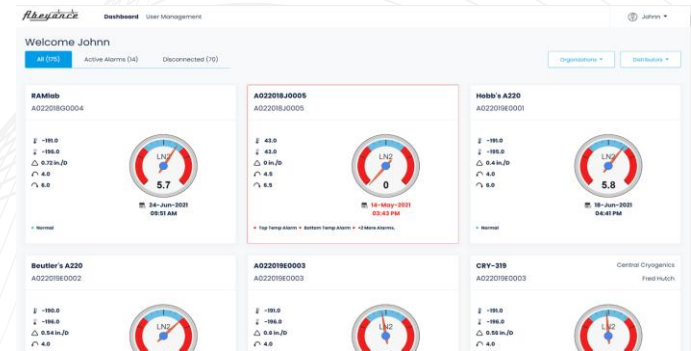
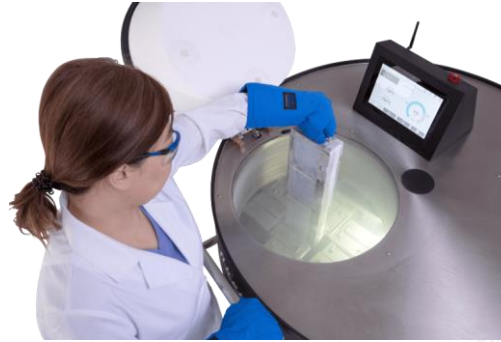
ERGONOMICS & EASE OF USE

- Better sample access with reduced reach and lift
- Full sample visibility with cryo LED and fog clear
- Workspace to maintain cold chain

MONITORING & CONNECTIVITY

- Simple controller with WiFi/LAN
- Text / Email alerts, Cloud backup, Web App

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Value Proposition



- **PREMIUM PRODUCT AT PREMIUM PRICE**

- Fully featured standard product
- Best price and usage per sample
- Industry leading warranty

- **USER FOCUSED FEATURE / BENEFITS**

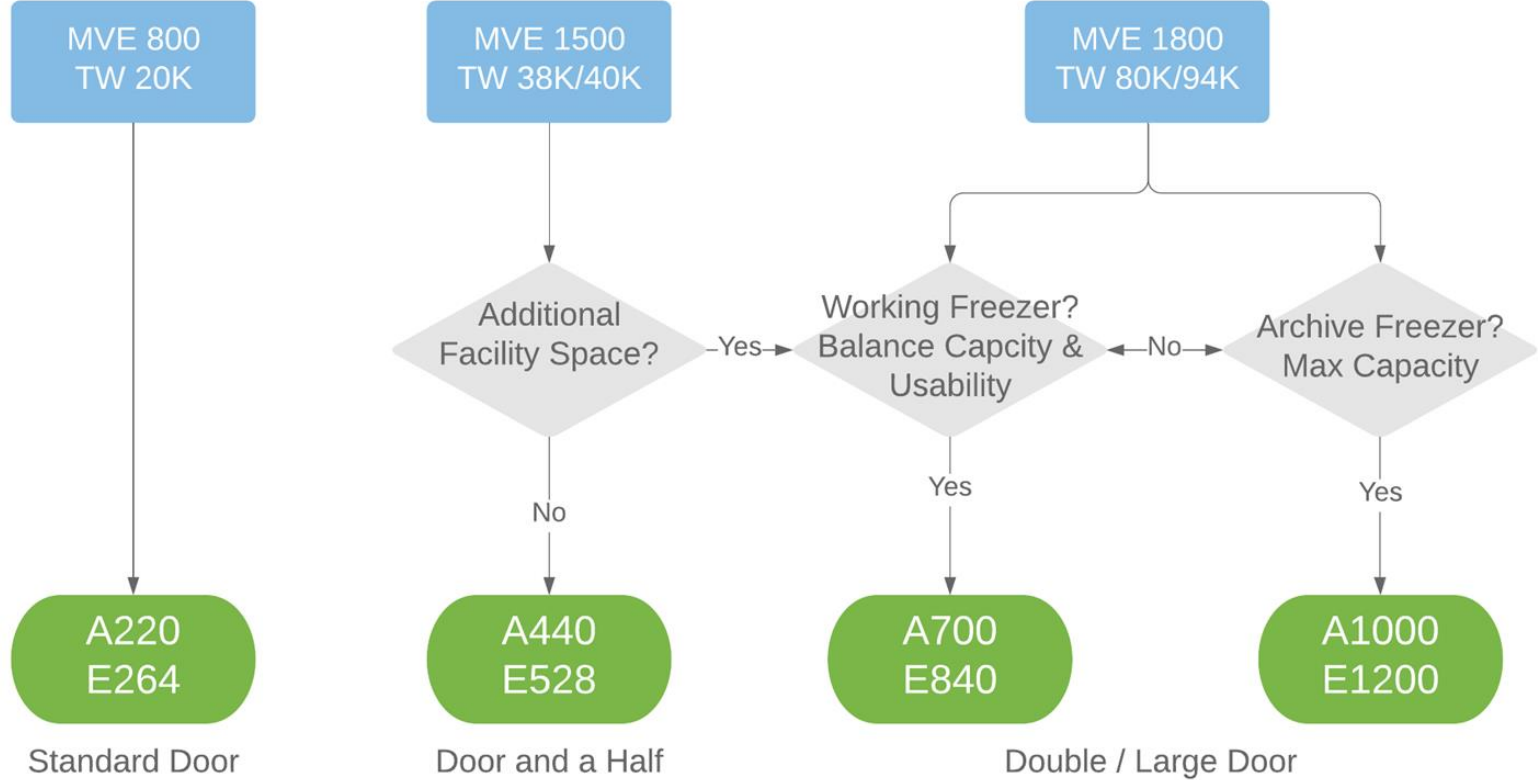
- **LEAD TIME**

- **CUSTOMER SERVICE / TECH SUPPORT**

- Dedicated service personnel at the factory
- Remote monitoring, troubleshooting

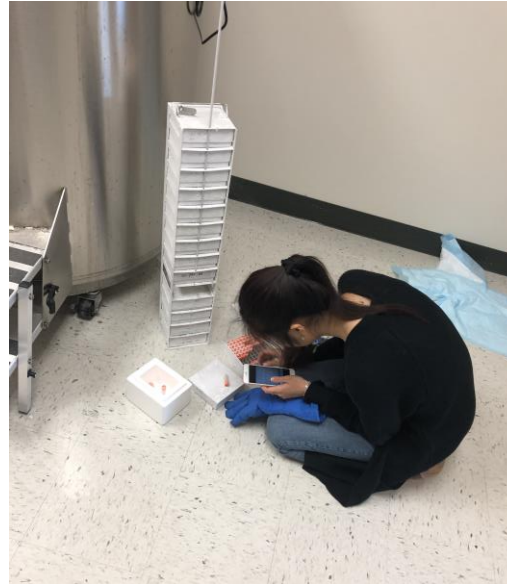
- **CHANNEL PARTNERS**

- 60 professional lab capital equipment reps
- 20+ year relationships
- Open access to customers and facilities



Objections to Automation

- PRICE COMPARISON
- LACK OF FLEXIBILITY
- RELIABILITY CONCERNS
- FACILITY RESTRICTIONS / REMODELING
- ALREADY HAVE WORKFLOW SOLUTIONS
- SOPS IN PLACE



Pharmaceutical & Biotechnology



abbvie



GRIFOLS



Lilly

FUJIFILM
Value from Innovation



moderna



Research & University



Clinical & Biorepository



Cryopreservation Summary

- Goal is to preserve sample potential for successful use in the lab or clinic
- Samples preserved by reducing temperature below where:
 - Enzymatic activity slows to a stop
 - Molecules completely frozen and solidified
- Scientific basis for selecting temperature:
 - Sample type, end-use application, and duration
- Cryo applications in life science research, therapies, diagnostics, and drug development
- Cryo freezers are open loop refrigeration systems
 - LN2 is a consumed refrigerant produced industrially through air separation
 - Cryo freezers cold because of LN2 vaporization inside super insulated vessel
 - Cryo freezers must be refilled to maintain cooling function
- Double-walled, vacuum insulated freezers minimize the 3 forms of heat transfer:
 - Conduction, convection and radiation
 - Maintain low, stable temperature with extended hold times