USP 797 Pharmacy Cleanrooms - Facility Requirements & Planning

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Technovation Systems, Inc. – an Introduction

- A design/build engineering firm specializing in cleanrooms for Life Sciences, Biotech, Pharmaceutical and Hospital applications.
- A manufacturer of advanced energy efficient filtration/air handling equipment.
- R&D firm with expertise in contamination control, particles science, fluid mechanics and engineering.

Examples of Cleanroom Projects

- Walter Reed Army Medical Center – USP 797 Pharmacies
- LIFENET – Tissue Processing
- Philip Morris – R&D Labs
- Encelle, Inc – Biotech
- Medical College of VA – islet lab - Biotech
- Burlington & TriState – Cleanroom Laundries
- Med Pharmex - Pharmaceutical
- Schwarz-Pharma - Pharmaceutical
- MSHA – US Dept of Labor – Test Lab
- Dow Chemical – Cleanroom Glove packaging
- Beckman Coulter – Medical Devices
- Hollister – Medical Devices
- Universities of Athens & Crete – BSL3 labs for 2004 Olympics
- JM Huber Corporation – Material Science Labs

Technological Innovation for Cleanrooms

- Advanced Energy Efficient Design – by means of Technovation computer models and advanced air handling technology.
- Low bio burden cleanroom technologies.
- Expert DQ/IQ/OQ services for easier cGMP/ GTP/ GxP compliance/USP 797 validation.
- PM with multi disciplinary expertise – including contamination control.
- Expertise in USP 797 Conformance

USP 797 - Guidelines

- Current Status – ISO 8 with anteroom and ISO 5 work benches
- USP 797 – Proposed Revisions (est. 2007), ISO 7 with ISO 8 (ISO 7 for Chemo & Nuclear) anteroom and ISO 5 Zone/work benches

Ref: Dr. Christina Lee, USP

Conclusion – Build for Proposed Revisions

USP 797- Guidelines "Proposed Revisions"

- ISO Class 5 – **Compounded Sterile Products "CSP" Work Area.**
- ISO Class 7 – **Outside CSP Work Area or *compounding room***
  - CSP in general pharmacies requires positive pressure
  - Negative pressure must be present for hazardous/potent materials i.e. Oncology/Nuclear
- ISO Class 7 (Chemo) or 8 (IV) - **Airlock/Gowning room for entry into cleanroom**

USP 797 New Guidelines

- Material pass-thru into ISO Class 7
- Monitoring of temperature, humidity, and pressure differentials is desirable
- Surfaces should be flush & sterilizable
- Protocols for Personnel gowning, washing, etc.

USP 797 Revision …..

ISO Class 5 Environment

- The Class 5 Environment is to be located in a Class 7 Room.
- Personnel must be fully gowned, covered and gloved in the Class 7 area.

USP 797 Revision ….

ISO Class 7 Environment

- Personnel must be fully gowned, covered and gloved.
- Pass-thru or ISO 8- anteroom must be used to access the area.
- No stock can be stored in the area, but material to be processed is allowable.
- Admixture jobs must be set up outside and transferred in through an airlock/pass-thru.

USP 797 Revision ….

Ante Room ISO Class 7 or 8

- Suitable for IV anteroom only, not CSP
- All storage shelves on casters for removal – cleaning/sterilization.
- Refrigeration is allowed in the area, but pass-thru refrigeration is preferred
- Computers are allowed.

Implied USP Bio Burden Requirements

	Class 5 Requirements
Air	■ 0.1 cfu/ft^3
Surface	■ 3 cfu/plate*
Gowns	■ 5 cfu/plate
	Class 7 Requirements
Air	■ 0.5 cfu/ ft^3
Surface	■ 5 cfu/plate
Gowns	■ 10 cfu/plate
	Class 8 Requirements
Air	■ 2.5 cfu/ ft^3
Surface	■ 20 cfu/plate
Gowns	■ 30 cfu/plate

A "Cleanroom" is a Cleanroom …… only if

- Particle, Bio Burden, Temperature, Humidity and Pressure are controlled and preferably, automatically monitored.
- The Air Handling System is Critical to the success of the Cleanroom.
- It is designed, constructed and used in a manner to minimize the introduction, generation, and retention of particles inside the room.

Why a Dedicated Air Handling System is a "*MUST*"

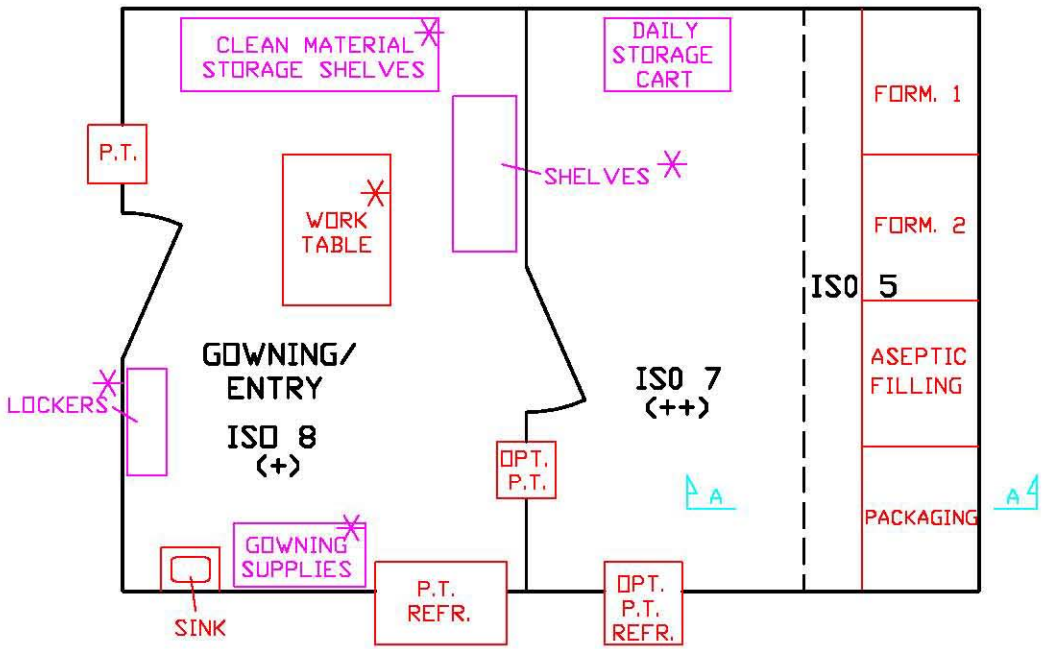
A Shared system *can not meet* the requirements because:

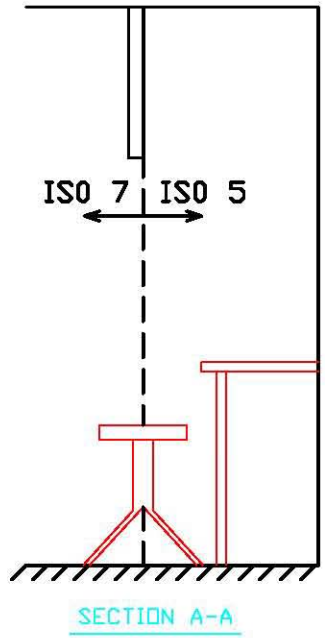
- Typically not enough air changes available
- Lose control of the T, RH & P
- You may disperse Pharmacy chemicals/air throughout the building
- Filters will be filtering more dirty air, less useful life of HEPA's

Technovation's Solution

- Contiguous Class 5 Environmental Zones created in Class 7 Room.
- No Flow Benches are required.
- Bactericidal BioPlus® HEPA Filters.
- Energy Efficient Design.
- No initial cost penalty.

TYPICAL IV PHARMACY





TYPICAL IV PHARMACY LAYOUT

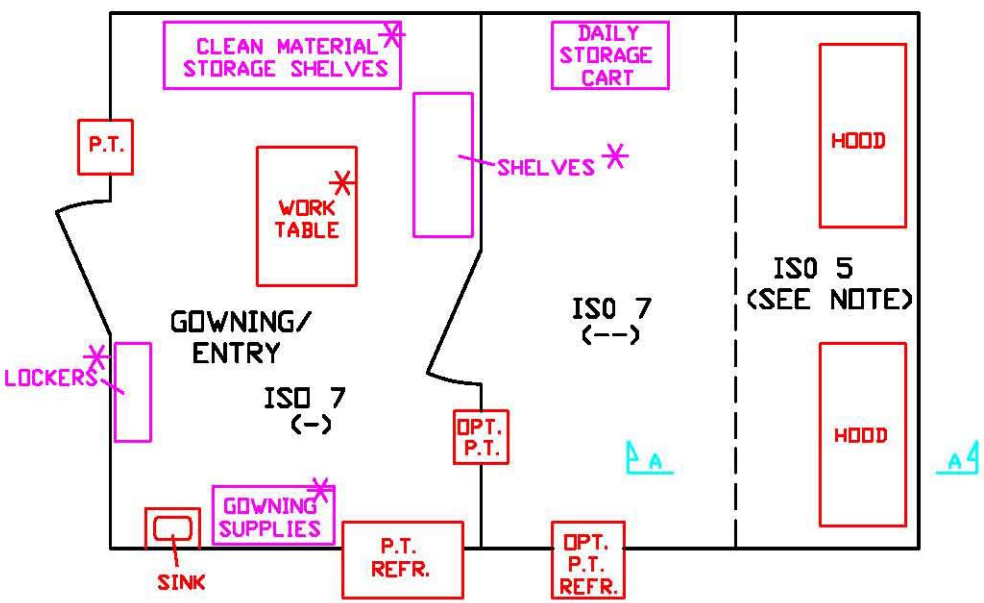
ABBREVIATIONS:

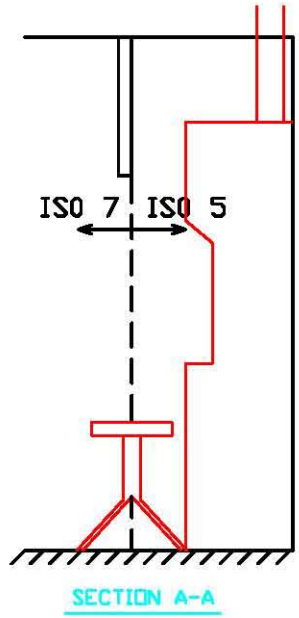
P.T.	PASS THROUGH
P.T. REFR.	PASS THROUGH REFRIGERATOR
OPT.	OPTIONAL
SS	STAINLESS STEEL
FORM.	FORMULATION

SYMBOLS:

REMOVABLE W/CASTERS - SS

TYPICAL NUCLEAR/ONCOLOGY/ CHEMO PHARMACY LAYOUT





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NOTE:

ISO 5 ZONE IS OPTIONAL (NOT CURRENTLY REQUIRED BY USP 797).

Energy Efficient Design achieved via ….

- Air Flow Modeling – 40% of operating costs are due to airflow rates used – hence this must be optimized.
- Re-Heat Minimization – Optimized Bypass Air Handling System – saves up to 25% in operating costs.
- BioPlus® HEPA In Duct filters – Ultra Low Pressure Drop (ULPD) and bactericidal

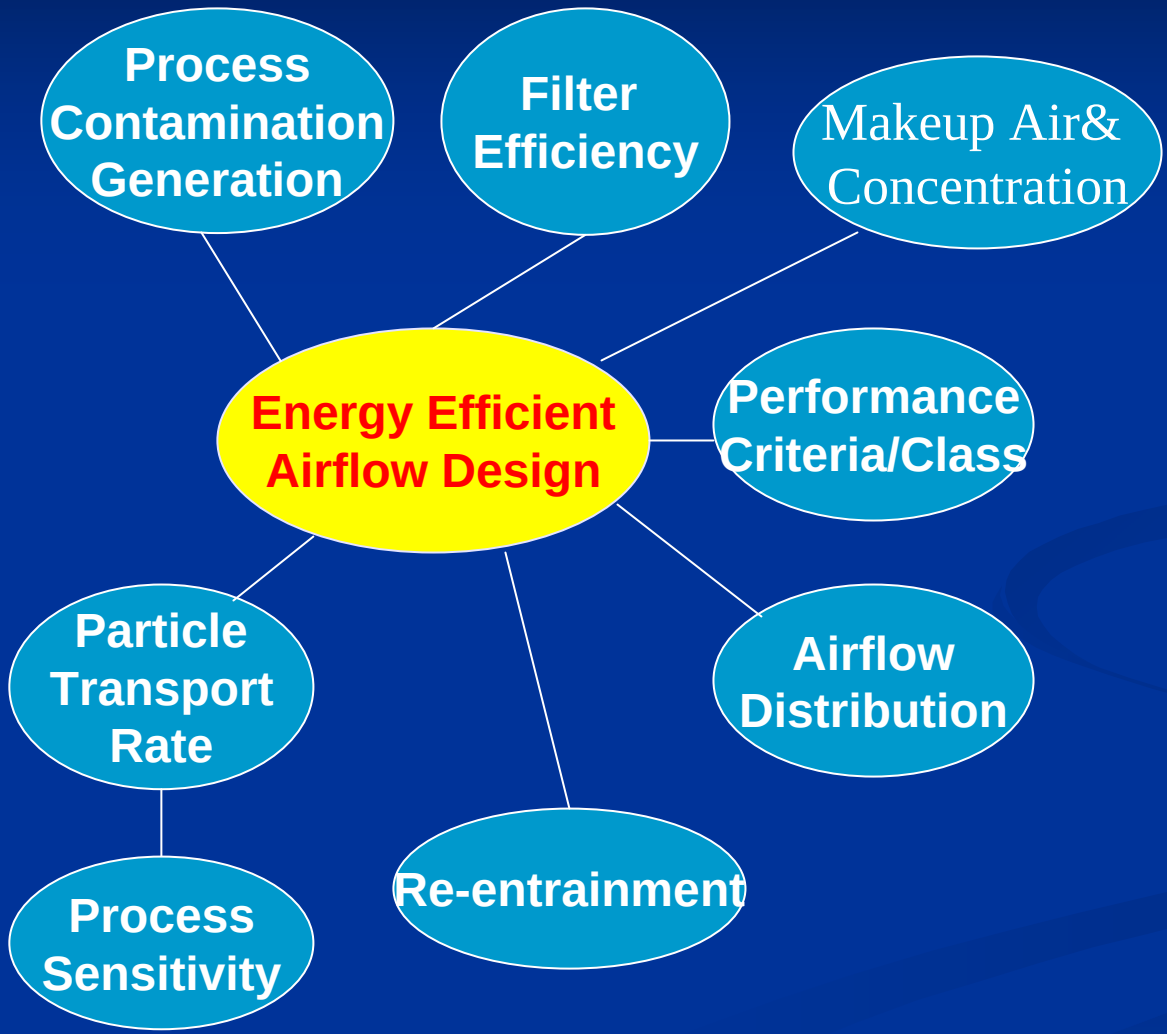
Result = significant Cost savings vs. Conventional AH Systems

Current Airflow Design Methods used by our competition... Charts

Charts recommending Av. Velocity/ Air Changes/hr (ACH) are used. These charts have no technical basis.

ISO Class	Velocity, fpm	ACH
3	60-100	360-540
4	50-90	300-540
5	40-80	240-480
6	25-40	150-240
7	10-15	60-90

Design Variables



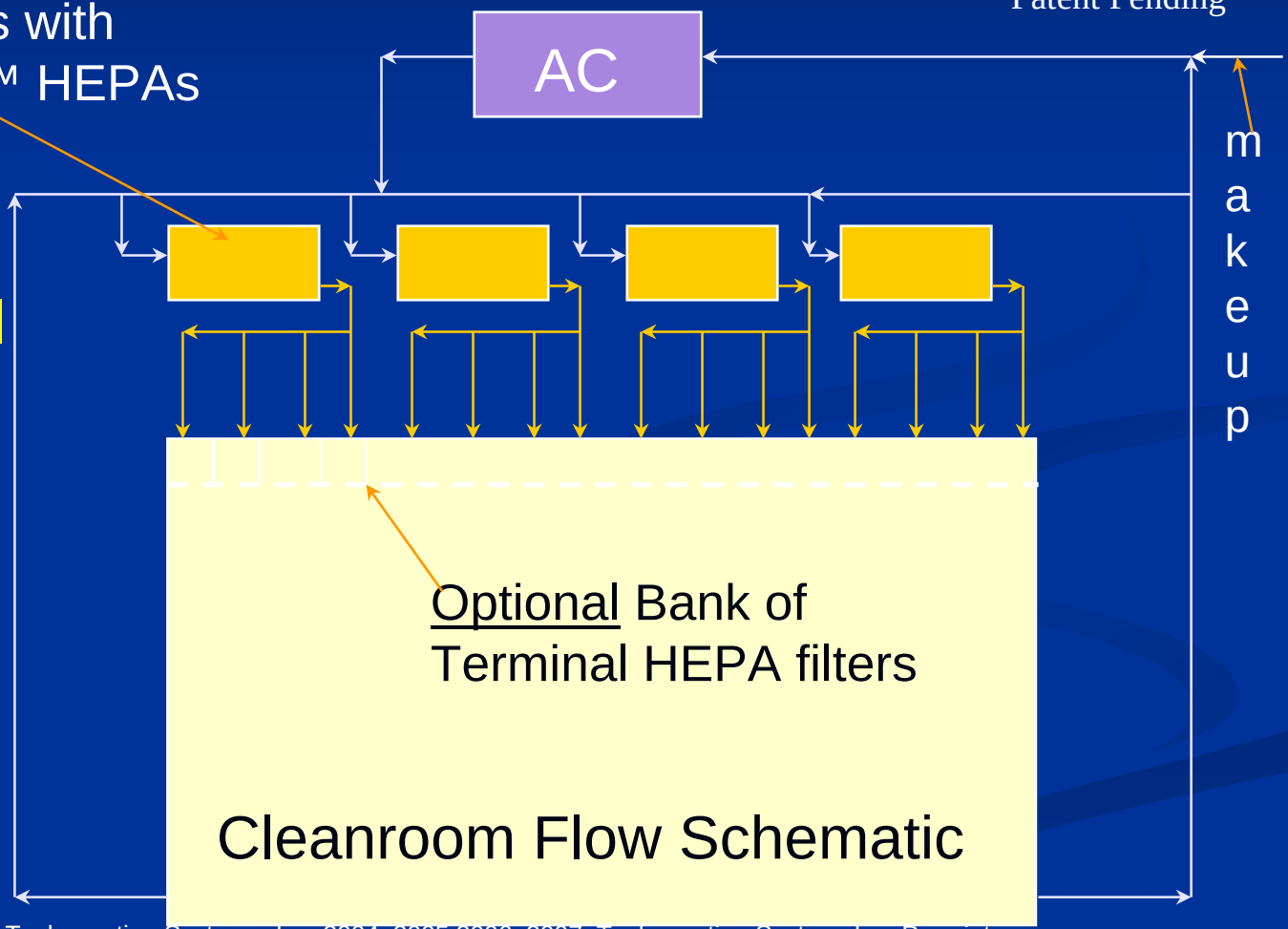
- Airflow design depends on many variables.
- Design charts do not take these variables into account.
- Technovation uses its proprietary Dilution and Transient Analysis Models in conjunction with CFD analysis for Optimum Airflow

Technovation's Optimized Bypass Distributed Air Handling System

Patent Pending

In duct fan units with primary ULPD™ HEPAs

- AC flow is a fraction of total flow
- Flow/ velocity independence



Re-Heat Minimization

- This is accomplished by varying (optimizing) the by-pass flow and AC flow so that the dehumidification exit temperature from the AC unit is also what is required to overcome the sensible heat load due to the fans and the process.
- Reheat then is only used for fine temperature control – thereby saving significant amount of energy.

Technovation's Operating Cost Savings (2003 energy costs)

- Distributed Air System vs. Conventional Air System in a ISO 5/ ISO 7 Work Environment
- Pharmacy areas assumed to be 400 sq.ft

	Mid-Atlantic	Northeast	CA
Savings/yr	$10,345	$15,345	$17,283

* Data on file at Technovation Systems, Inc

Bio Burden / Energy Implications

- EEF bactericidal filters result in significantly lower (negligible) bio burden.
- Pharmacies must achieve USP Standards for maximum allowable airborne bio burden levels.

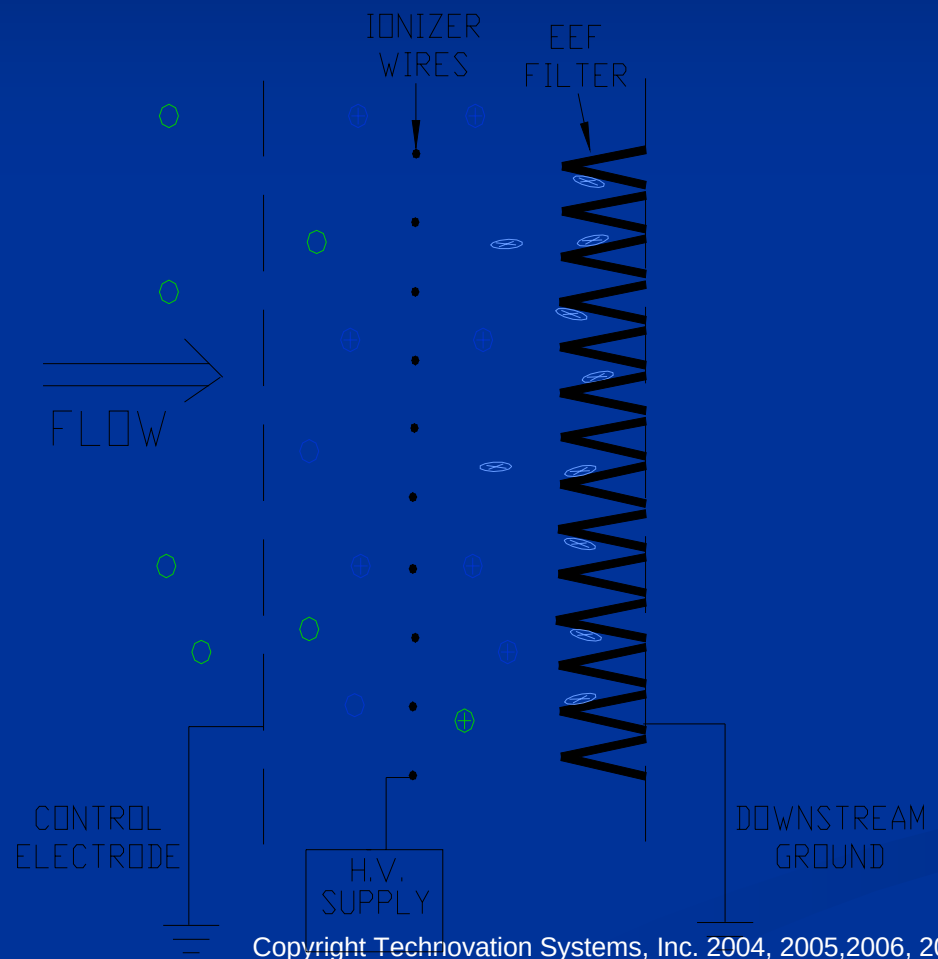
Ultra Low PD (ULPD) BioPlus® HEPAs

Technovation's 1997 R&D 100 Award winning filters are used in our distributed air handling systems.

- 0.6" WC @ 2400 scfm – 2'x2'x12" deep! 40% lower pressure drop than conventional HEPA.
- ~ 3 times higher dust holding capacity due to lower PD and formation of porous dust deposits –lower filter maintenance costs.
- Estimated savings of ~ $900 per year per filter vs conventional HEPAs.
- Used in central and distributed air handling systems.

Electrically Enhanced Filtration (EEF)

Winner of 1997 R&D 100 Award



BioPlus® Filter

A 90-95% DOP filter is electrically enhanced to a 99.99% DOP.
Additionally the filter becomes bactericidal!

Lab Results – Bactericidal Properties of EEF (*Staph. Epi.*)

FILTER	EXPOSURE TIME	AV. CFUs	COMMENT
control or EEF	hours	#/sq inch	
control	4.00	1.00E+06	Baseline
control	4.00	1.02E+05	After 24 Hours
EEF	4.00	0.00E+00	100% KILLED
EEF	4.00	3.44E+02	99.93% KILLED
EEF	4.00	0.00E+00	100% KILLED

Cleanroom w/ EEF - Bio-burden

Design Class 1,000	11/14/99 Av. cfu/ft3	11/30/99 Av. cfu/ft3
Device Testing	0	0
Coating	0	0.057
Formulations	0	0
Device Manufacturing	0.170	0.113
Refrigeration	0	0
Isolation	0.170	0.849
Class 1,000 Av	0.057	0.170

Design Class 1,000	12/13/99 Av. cfu/ft3	1/28/00 Av. cfu/ft3
Device Testing	0.000	0.000
Coating	0.000	0.000
Formulations	0.000	0.000
Device Manufacturing	0.000	0.000
Refrigeration	0.000	0.000
Isolation	0.000	0.000
Class 1,000 Av	0.000	0.000

Validation Related Services During Design/Build

- DQ – Design Qualification
- IQ – Installation Qualification
- Commissioning
- OQ – Operational Qualification

This documentation becomes part of the Master Validation Plan. This is not required by USP 797 however, it ensures high quality design and construction.

Process Integration & Consulting

- Cleanroom design cannot be divorced from the process / process equipment.
- Cleanroom equipment must be carefully selected – Technovation provides consulting utilizing our R&D facility. Examples freezers, refrigerators, filling machines etc.
- Material /chemical compatibility is an important issue for process integration.

Technovation with its strong background in research & process contamination control is able to better provide these services to the end user.

Technovation Project Management

- Establishment of proper Cleanroom Construction Protocols (CCP), will prevent major cost and time overruns. E.g. isolating dust sources and preventing contamination of duct work; utilizing rigid controls when doing dry wall is ridiculous.
- CCPs based on "probability" (requires contamination control expertise) rather than "possibilities", will save dollars$$$. E.g. understanding migration of dust from outer areas; lower level CCPs are sufficient while applying wall finishes / floors.

Successful Design/Build Services

This requires expertise in:

- Basic Engineering – mechanical, HVAC, structural, electrical, plumbing, safety.
- Contamination Control – aerosol science, associated instrumentation and fluid mechanics, process integration.
- Validation related activities– DQ/IQ/OQ.

Further, the Designer must be capable of partnering with End User to translate process requirements into design specifications.

Why Chose Technovation?

- USP 797 Expertise
- Design/Built ~ 100 Cleanrooms
- Specialize in Cleanroom Environments only
- Dedicated Team
- Functional Layout
- Energy Efficient and Functional Design
- Bactericidal BioPlus® HEPA filters
- Expert Design Build Services, DQ,IQ,OQ

Statement of Customer Satisfaction

Technovation prides itself in our record of *100% customer satisfaction* as evidenced by the amount of repeat business we have achieved. References testifying to our unparallel record customer satisfaction are available.

Next Step – Phase I Design

- Technovation will assist your Hospital in the assessment of your pharmacies USP 797 compliance and potential cost.
- Coordinate meeting with Pharmacists to develop design specifications.
- Conduct field survey.
- Develop architectural and equipment layout.
- Define utility requirements.
- Develop budget cost.

sales@technovation.org or call 804-744-0604