

Design and Operation of GMP Cell Therapy Facilities PACT Workshop April 10-11, 2007

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Mayo Clinic Human Cellular Therapy Laboratory

- **332 HPC transplants in 2006**
 - 280 Auto 52 Allo
- **Formerly contract manufacturer for Phase 1-3 cell therapy trials (400 products, 200 pts)**
- **Pancreatic islet cell transplant programs**
 - Allogeneic and Autologous
- **Several Mayo investigator held INDs active and/or in development**
 - Dendritic cells
 - MSC



Mayo Clinic Human Cellular Therapy Laboratory (continued)

- **Approx. 6,000 square foot facility**
- **About 20 FTE -7 development techs**
- **“Uncontrolled” laboratory + suite of clean rooms**
 - **Shared staff throughout**
 - **Much shared space and equipment**

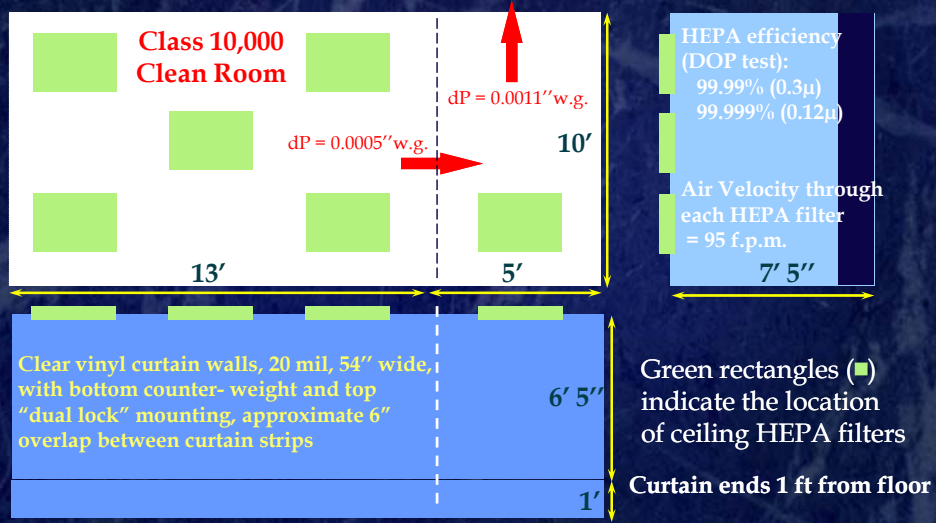


Facility History

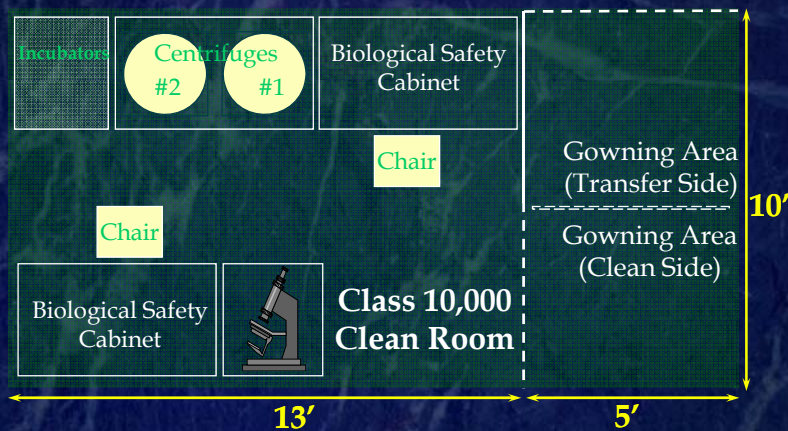
- **Before 1996 standard lab space**
 - **400 SF or less, 2 or fewer LN2 tanks**
- **1997-2002**
 - **1, then 2 200 SF soft walled tents**
- **2002**
 - **About 5,500 SF with clean rooms**
- **2005**
 - **Additional clean room space for islet transplant program**
- **2007**
 - **6000 SF, 13 LN2 tanks**



Soft Sided Clean Room Design & Performance Characteristics



Soft Walled Clean Room



New Facility Planning

- Planning started in 1997
 - At least two sites in two buildings considered before final location
- Initial plans were for clean room tents in large open space
 - Nixed due to potential of cross contamination
- Construction process (6 months) was much shorter than planning
- Post construction task list is long

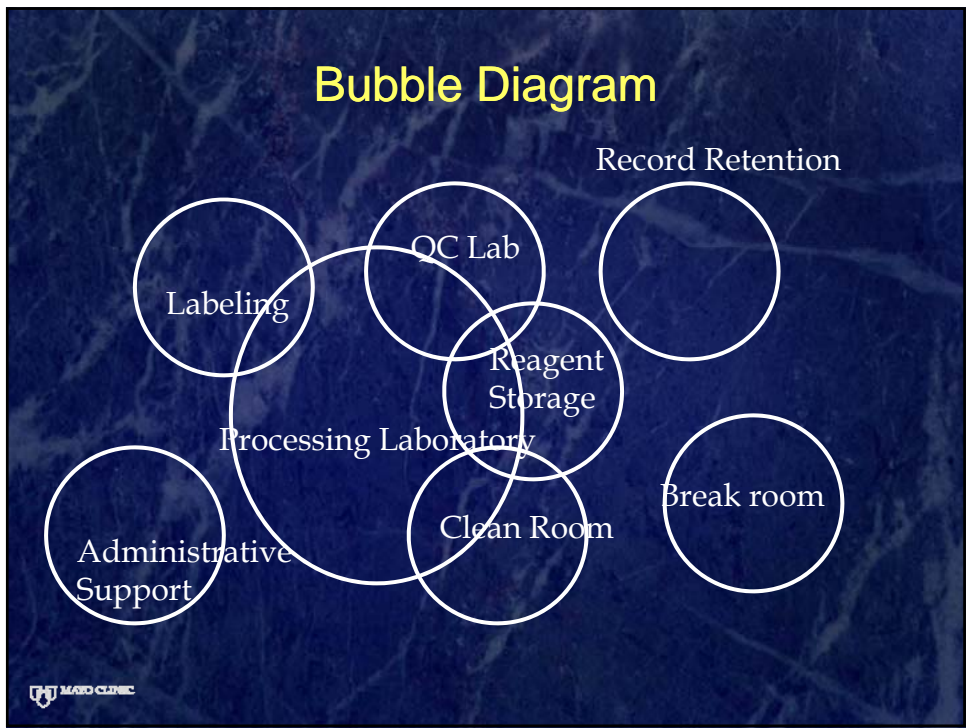


Facility Planning Suggestions

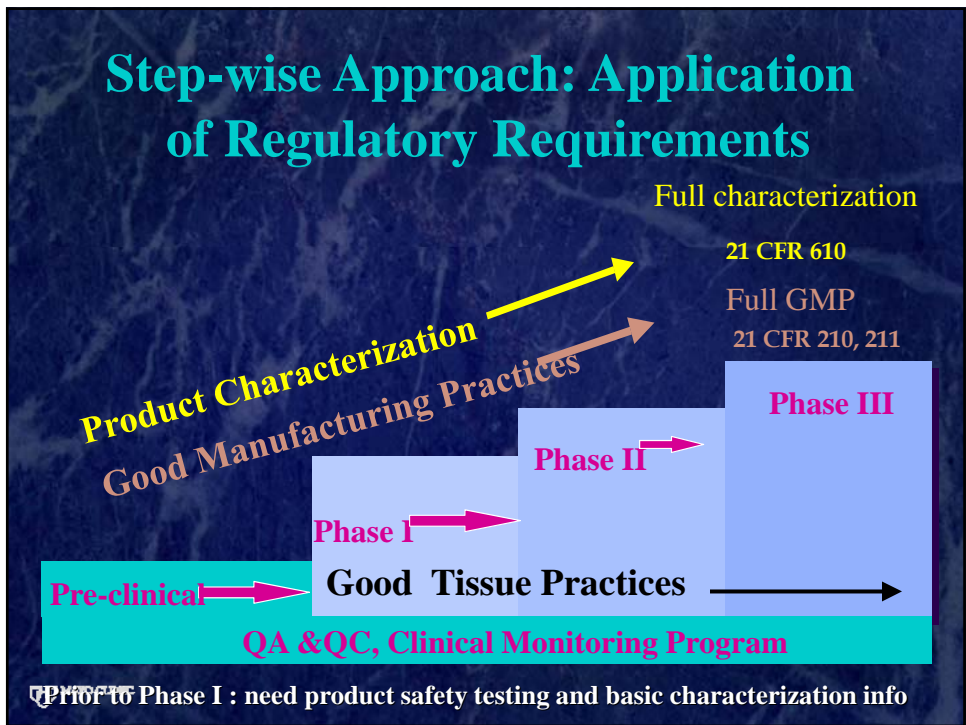
- Planning team should include:
 - Facilities, manufacturing, quality, regulatory, architect & engineers, contractor, (Consultant), Ad Hoc members
- Work with experienced architects, planners and engineers
 - But know what requirements are for the type of manufacturing you will be performing...
 - Which means you should know what you plan on using the facility for.



Bubble Diagram



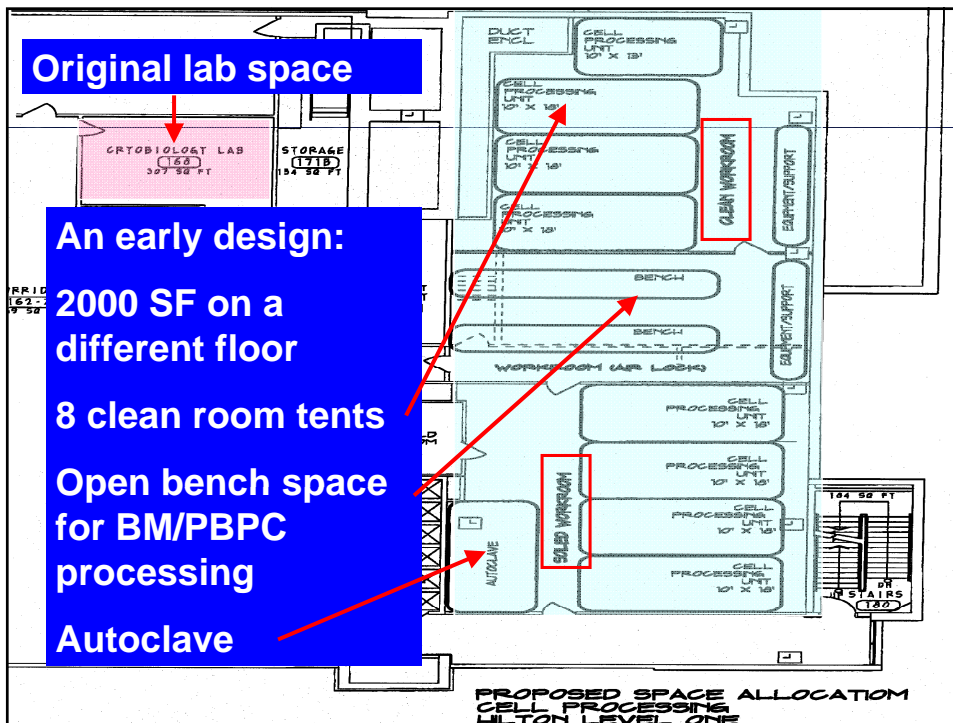
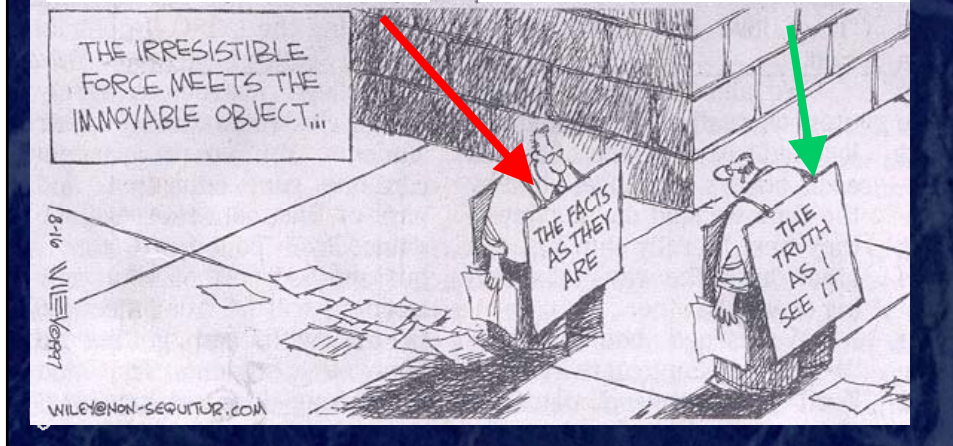
Step-wise Approach: Application of Regulatory Requirements

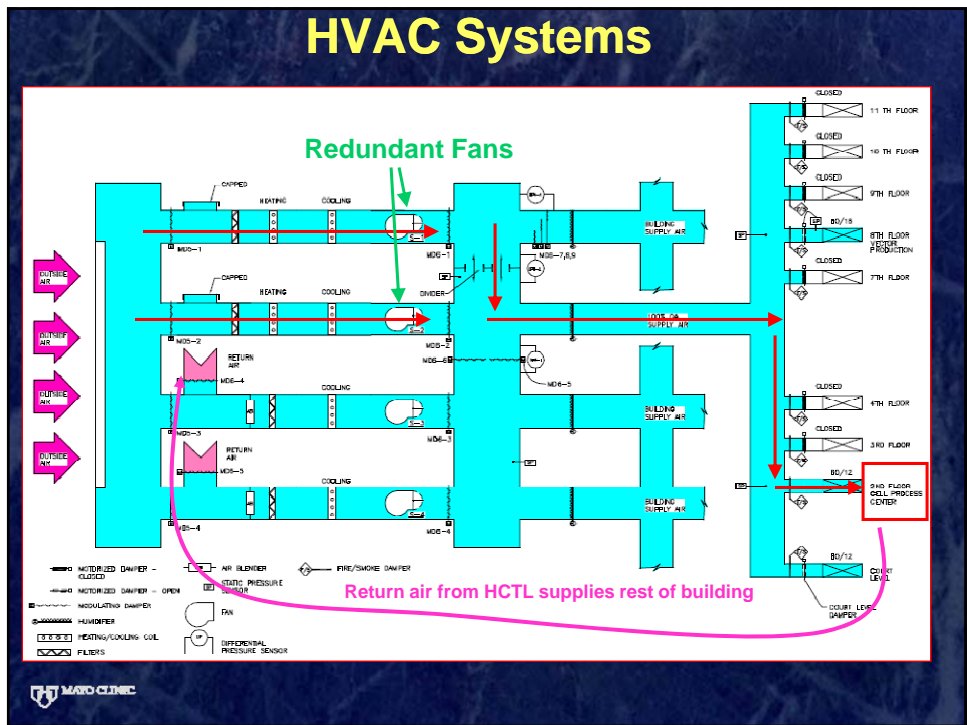
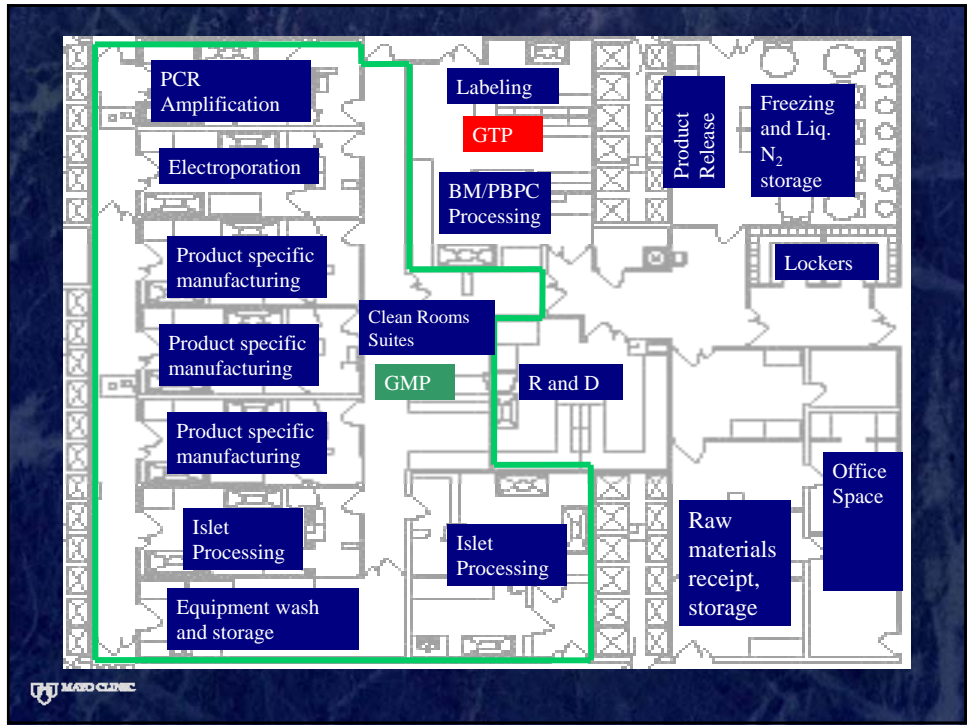


The Art of Compromise

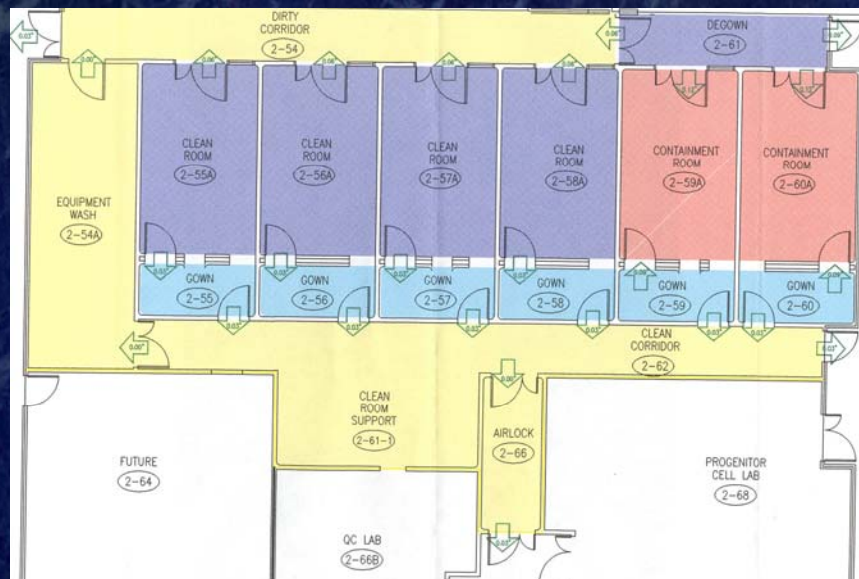
Budget or space limitations

What you think you need

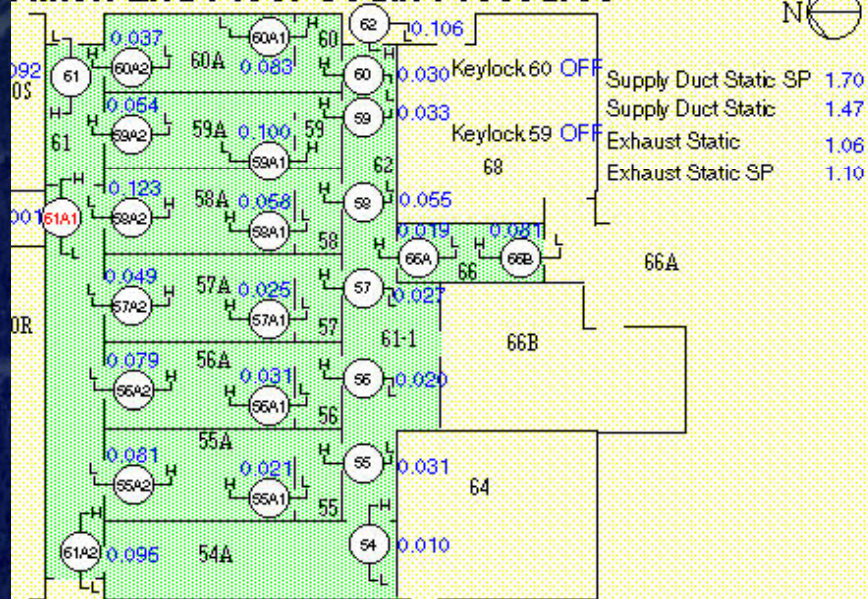




Clean Room Suite- "Final" Design



Hilton 2nd Floor South Pressures



Human Cell Therapy Laboratory Pressure Status Report

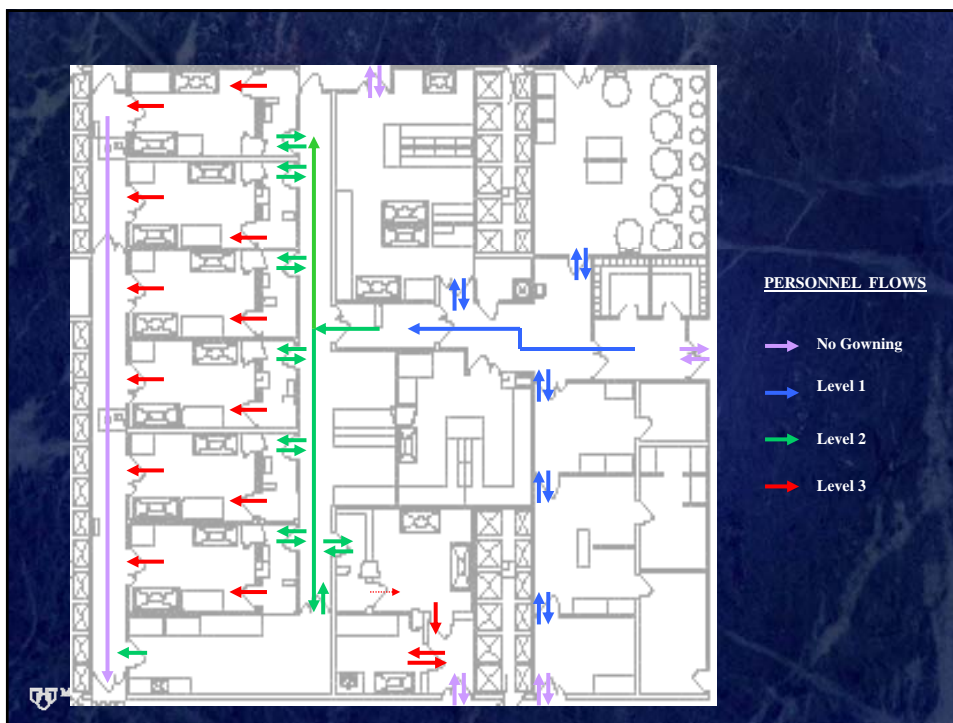
Andover System Date/Time: March 10 2005 10:30:26

Red = Andover Alarm

Purple = Value Disabled

Room Number	Pressure relative to:	Deviation +0.02		Pressure relative to:	Deviation +0.02	
		In. wc.	SP		In. wc.	SP
Clean Room 255A	Gowning 255	0.030	0.030	Exit Hallway 254	0.125	0.060
Gowning 255	Clean Support 262	0.081	0.030			
Clean Room 256A	Gowning 256	0.058	0.030	Exit Hallway 254	0.125	0.060
Gowning 256	Clean Support 262	0.064	0.030			
Clean Room 257A	Gowning 257	0.051	0.030	Exit Hallway 254	0.092	0.060
Gowning 257	Clean Support 262	0.065	0.030			

Reviewed by _____ Date _____



Other Flow Diagrams Exist For:

- Raw materials and reagents
- Equipment
- Waste
- Air pressure differentials for clean rooms



Facility Design and Layout

- In smaller labs segregation can be achieved through procedures and process controls.
- Document where key activities occur and any restrictions or limitations on that process.
 - i.e. Only one product being labeled at a time if the bench top is not large enough for adequate segregation



Facility Construction and Design: Take Home Messages

- Planning is critical
- Learn from others
- Build in flexibility when possible
- Compromise is inevitable
- As soon as you finish start thinking about your next facility



"The best-laid plans of mice and men
Gang aft agley,
And leave us naught but grief and pain,
For promised joy."

To A Mouse, On Turning Her Up In Her Nest With The Plough
Robert Burns

Since 2002 we have made 6 significant
changes to our facility

- Office areas (x2)
- Manufacturing space (x 2)
- More R and D space
- LN2 piping expansion



