



THE UNIVERSITY OF
CHICAGO
MEDICINE

Design, Construction and Commissioning of an Academic Cellular Manufacturing Facility

June 17th 2020

Amittha Wickrema, Ph.D

Director, Advanced Cellular Therapeutics Facility

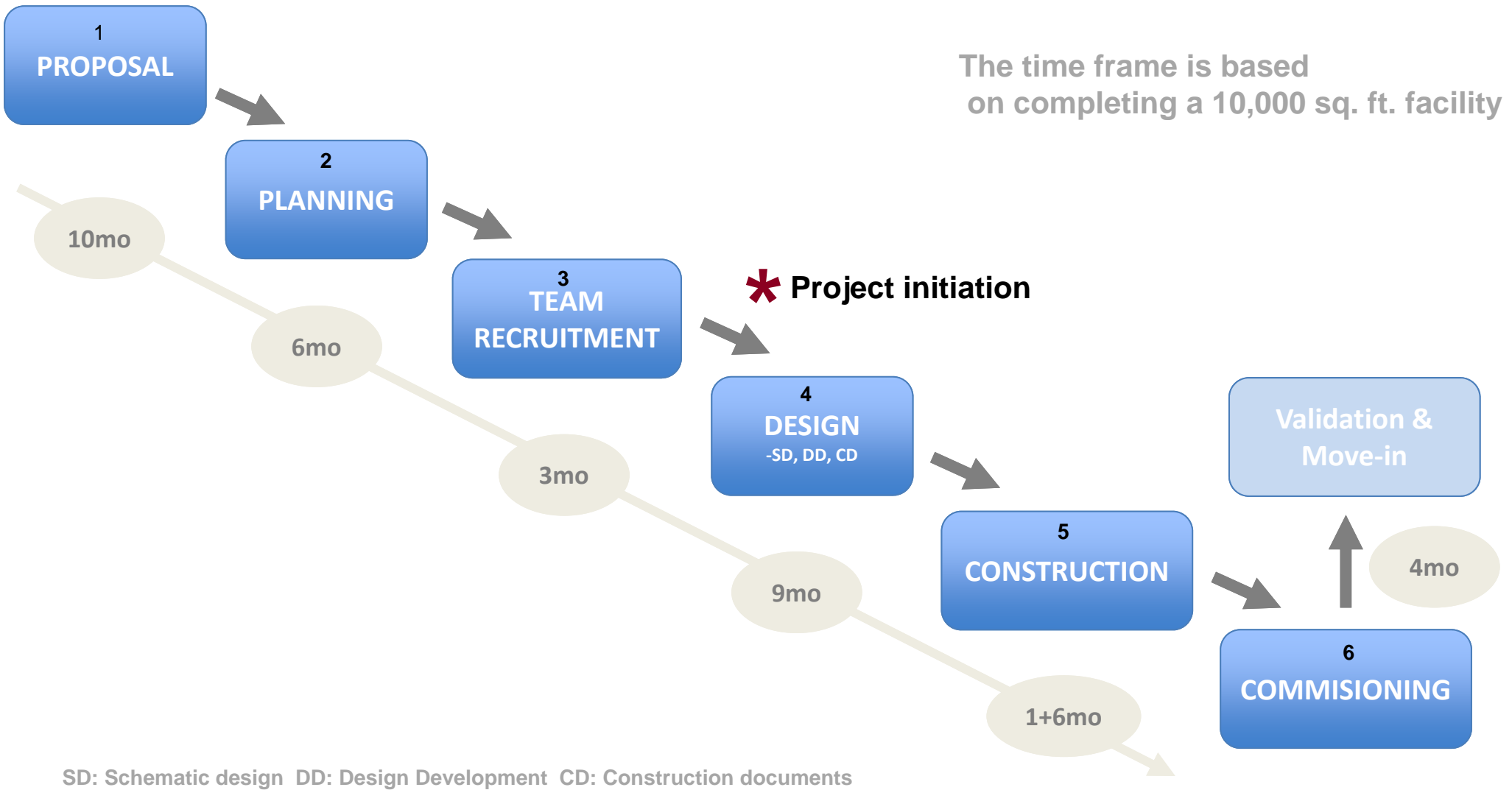
awickrema@uchicago.edu

SCOPE AND GOAL OF THE PROJECT

- Build a hybrid facility capable of manufacturing 361 and 351 categories of cellular therapy products.
- Spaces consisting ISO8 (GTP), ISO7 (cGMP) and other ancillary areas.
- Overall facility that supports a 350 standard of care stem cell transplants per year and approximately 700 cellular therapy products including novel cell therapies for the next 10 years.
- A facility with product development capabilities for IND filings.
- To build a facility consistent with FDA requirements (21CFR 1271, 211,610) for manufacture of human cellular therapy products (HCTPs) that meet basic criteria of cellular potency, viability, sterility and stability.



THE ROAD MAP FOR ACHIEVING GOAL



JUSTIFICATION OF NEED TO THE LEADERSHIP

Need

- Information regarding current volumes and projected growth over 5-10 yrs.
- Information regarding increasing efficiency (new technologies and automation).
- Information regarding the need for developing novel cell therapies.
- Information on potential new revenue.
- Approximate/estimate cost of the new facility (ie: \$ all-in1,000/sq feet).

Method of communication

- A program workshop with hospital leadership on hand.
- A detailed proposal and follow up face-to-face meeting.



ELEMENTS INCLUDED IN THE PLANNING

- ❑ Engage the head of institutional space planner
 - Educate about the type of work, tour the current facility.
 - Provide a hand-drawn space diagram along with approximate square footage of each space needed.
 - Communicate the ideal space will be an existing shell space if the facility will be housed within the medical center/university (an external site is possible).

- ❑ University of Chicago Facility
 - Constructed in an existing empty shell space within 5 min walk from the previous facility.
 - Shell space occupies approximately 10,000 square feet.
 - In a isolated area away from patient traffic.



ENGAGE AN EXTERNAL ARCHITECT FIRM

-For cost estimation and feasibility purposes only – predesign phase

- Select final space together with internal space planner, external architect and the owner (stake holder).
- Architect drawing using owner hand-drawn plan.
- Secure an initial cost estimate from a consultant architect firm.
- Obtain final approval of budget from the leadership.
- Begin recruitment/solicit bids of a qualified company for design and engineering.



MAJOR ELEMENTS OF PROJECT BUDGET

- Not necessarily the highest cost items

- Design and engineering drawings.
- Costs associated with HVAC systems.
- Costs associated with cGMP consultants, permits and regulatory compliance.
- Costs associated with construction and interior finishes.
- Costs associated with commissioning, validation, IQ/OQ.
- Central monitoring systems (ie Johnson control and REES).
- Medical Equipment.

(Note: Medical equipment costs will depend on complete new purchase or using existing equipment)



BUDGET/COST CONTINUED.....

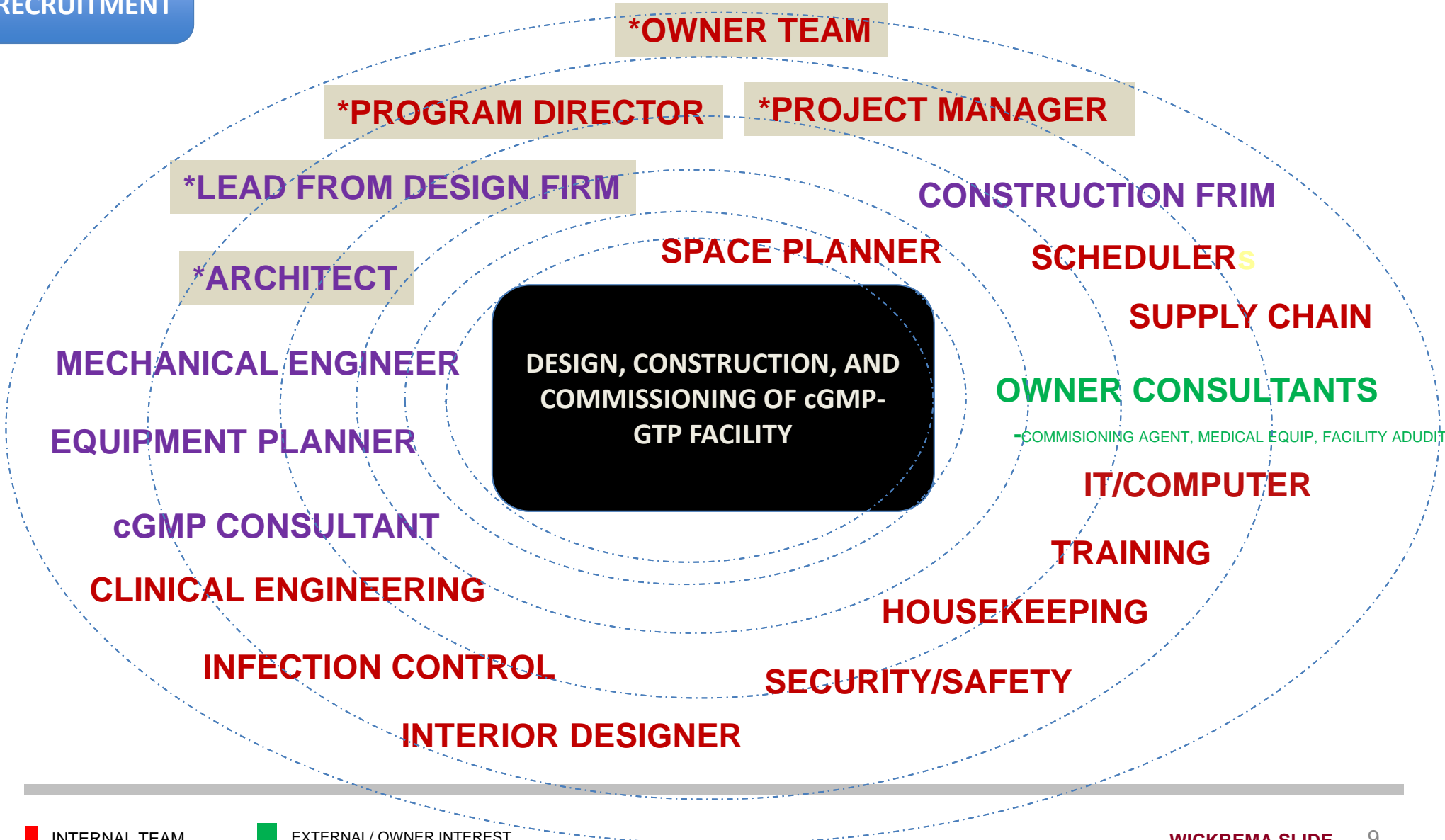
(based on build out of an empty shell space of 10,000 square feet)

- Typical costs of major items: (**Total budget 7.6 million US**)
 - Design, architectural and engineering firm (**\$750K**).
 - Construction/HAVC (**\$ 4.4 million**).
 - Commissioning agent –owner hired (**\$ 80K**).
 - Medical equipment (**\$ 1.1 million**).
 - Contingency (**\$450K**).



**TEAM
RECRUITMENT**

PROJECT TEAM



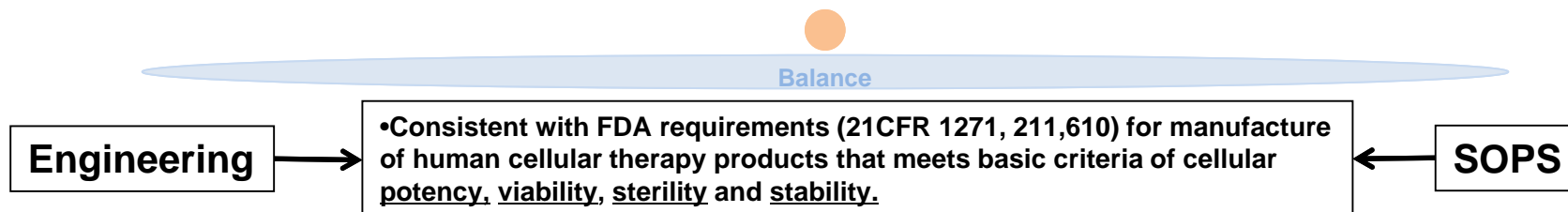
- INTERNAL TEAM
- EXTERNAL TEAM

■ EXTERNAL/ OWNER INTEREST

* * ATTEND EVERY PROJECT MEETING (AROUND 400 HRS.) ----- 17 MONTHS

PRINCIPLES GUIDING DESIGN METRICS

- A hybrid facility that is multifunctional.
- Consistent with FDA guidelines (21CFR parts 1271, 211, 610).
- Manufacture covers steps of recovery, processing, storage, labeling, packaging, distribution and testing/screening (361 & 351 prod).
- Adequate space and segregated areas capable of processing multiple human cell or tissue based products (HCT/Ps).
- Physical facility design aimed at minimizing introduction of microbial contamination (Uni-directional flow, medical grade finishes, workflow segregation).



HVAC AND ENGINEERING METRICS

- 100% redundant two air handlers servicing work spaces. A third handler servicing office area (ISO7-30/50 ACH; ISO8-20 ACH).
- A single air pass setup. 0.05 pressure gradient. No phoenix valves.
- Equipped with HEPA filters both at source and terminal spaces.
- ISO7 spaces have positive and negative pressured suites.
- Piped-in gasses, vacuum and liq N2.
- Redundant remote monitoring and UPS systems for power.
- Connected to building back-up power system.



FACILITY SPACES

- ISO8 GTP cell processing area (4 work stations)---height adjustable BSCs.
- ISO8 QC/product development space.
- ISO7 cGMP cell processing suites (2 +1).
- Uni directional gown-in and gown-out spaces.
- Material storage, Material pass, cGMP cleaning supply room, Locker room.
- Material receipt area, non-cGMP cleaning supply room, Biowaste room.
- Mechanical space, gases and Liquid N2 storage space (within the shell space).
- Offices and document storage, private bathroom, kitchen and conference room, private internal corridors.



OTHER DESIGN FEATURES

- **Comfort, esthetic and non-essential features:**
 - Custom lighting throughout, height adjustable BSCs.
 - See-through glass panels throughout the facility.
 - State of the art automatic doors that slide as well as swing.
 - Unobstructed island work spaces with ceiling plug-ins.
 - 10 feet high ceiling in non-cGMP spaces.
 - Staff amenity space, staff office space, private bathroom, conference room.

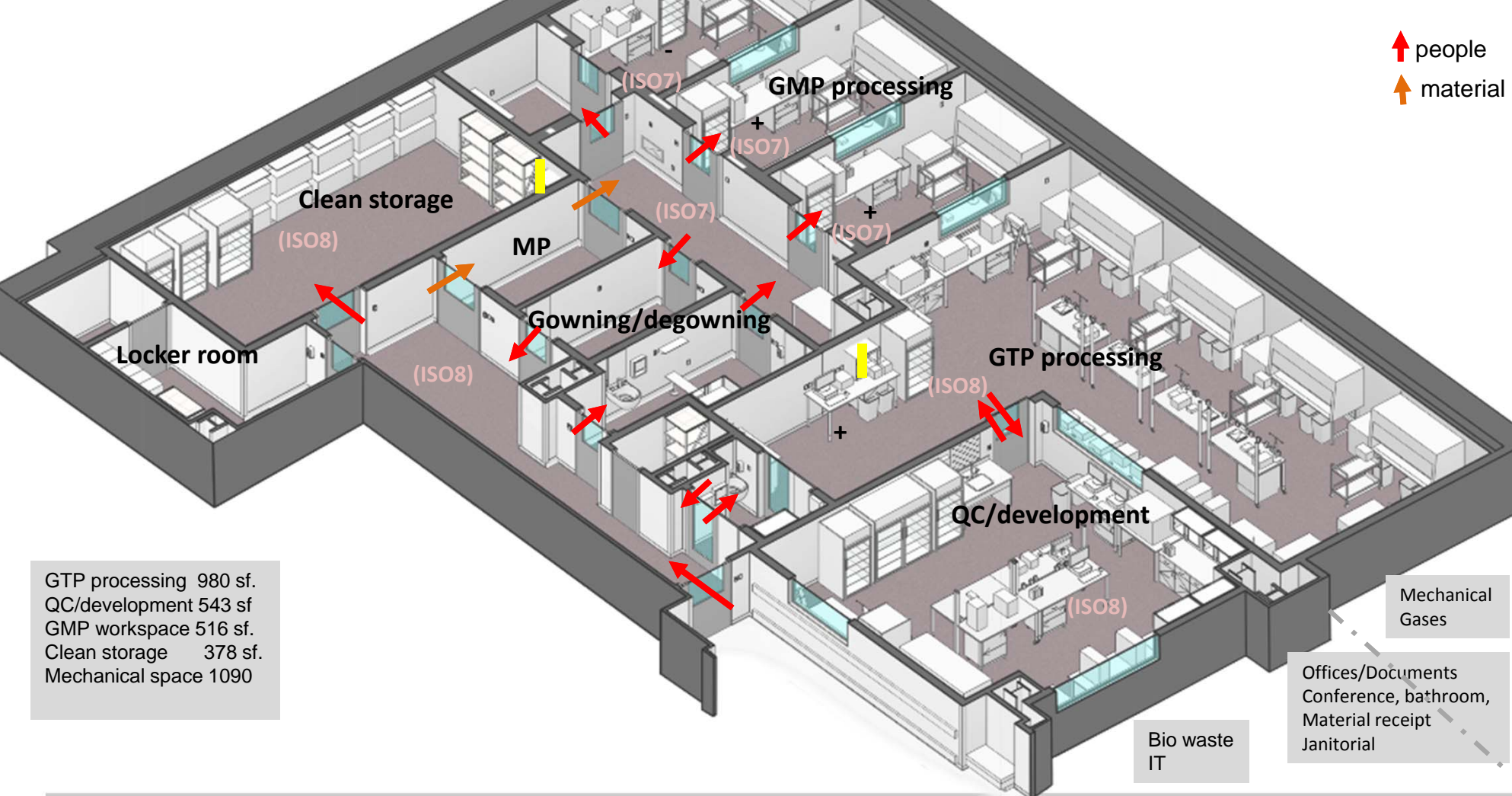


ASPECTS DURING CONSTRUCTION

- Construction phase required very little input of the owner team compared to all other phases (Supervision by design firm and internal project manager).
- Aspects to pay attention:
 - All changes and substitutions of materials and any changes to the layout and HVAC should be pre-approved by owner team.
 - Periodic tour/inspection of the construction space.
 - Opportunity for owner team to try out finishes/materials (flooring, lighting etc.).



HYBRID CELL PROCESSING FACILITY LAYOUT (8000 SQFT. Manufacturing space)



GTP processing 980 sf.
 QC/development 543 sf.
 GMP workspace 516 sf.
 Clean storage 378 sf.
 Mechanical space 1090

Mechanical Gases

Offices/Documents
 Conference, bathroom,
 Material receipt
 Janitorial

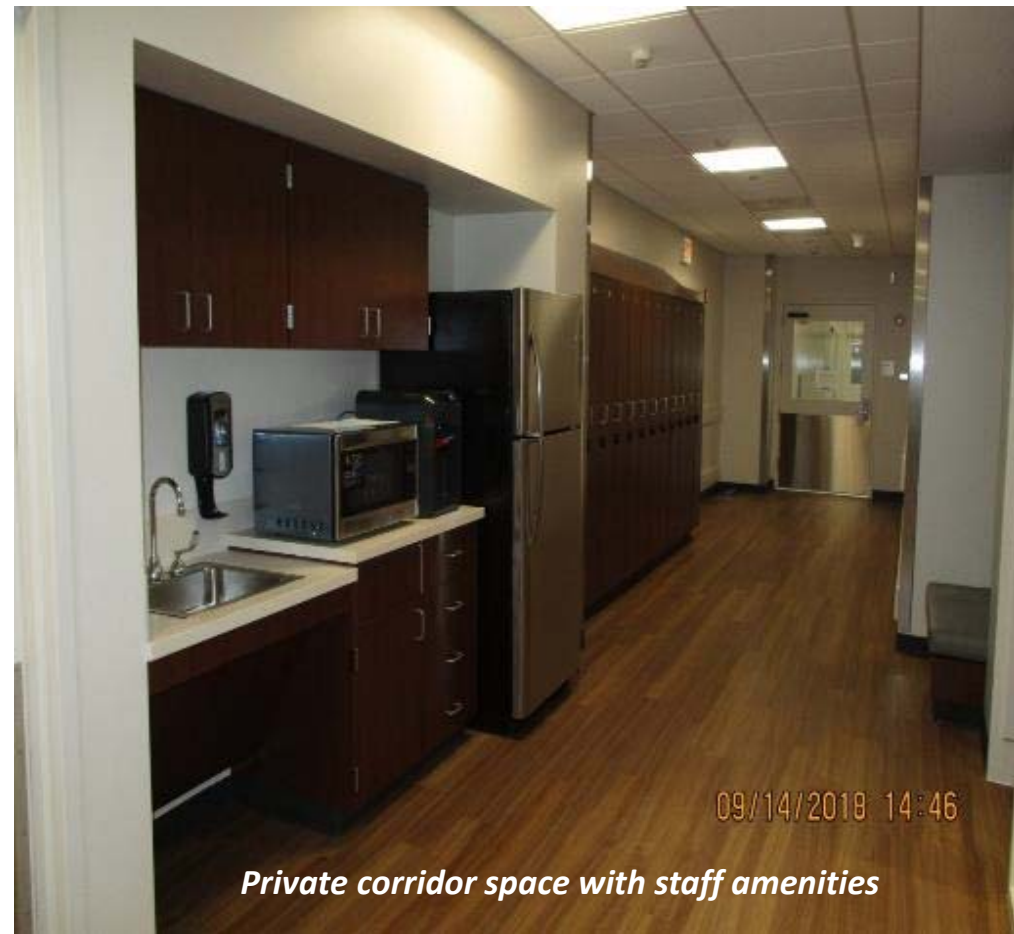
Bio waste
 IT

FULL-SCALE MOCK UP

- 100% Scale mock-up of GTP, QC, and cGMP spaces (extremely valuable)
- An opportunity to adjust layout and design of work spaces and personnel



COMPLETED FACILITY SPACES



COMPLETED ISO7 SPACE



ISO7 negative pressured suite



vestibule to the clean room suites



Mechanical space

TO AVOID SECOND GUESSING AT THE END OF THE PROJECT

- Visit similar facilities that has been commissioned recently.
- Retain and engage an experienced advisor in the field (outside of the design firm) outside of relying on recommendations of the design firm only.
- Entertain multiple bids from design firms. Face-to-face interview prior to hiring. The lowest bid should not be a criterion for selecting a firm.
- Be engaged in all decisions from start to finish as the “owner” (minimize delegation).
- The “owner” or his/her staff member must attend all project meetings (around 400 hrs).
- Do not compromise on HVAC and other engineering features to save money for equipment and/or esthetic aspects.



SUMMARY OF ITEMS POST CONSTRUCTION

- **Initiate commissioning activities end of substantial completion**
 - Independent commissioning agent certify all HVAC and other mechanical metrics as stated in the design plans.
 - Perform IQ/OQ functions for medical and non-medical equipment.
 - Comprehensive walk through by owner and project manager.
- **Initiate pre- move-in validation activities**
 - Follow owner designed *master validation plan*:
 - Include process validations (budgeted US \$50K)
 - Include equipment and space validations.

performed by cell processing staff