

ISPE – Copenhagen Conference

Changing Regulations

Secondary Facility and Laboratory Refurbishment



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ENGINEERING PHARMACEUTICAL INNOVATION



Pythius – An example of a well planned & well executed GMP refurbishment Project

Project X – An example of a well intentioned, less structured but never-the-less well executed GMP refurbishment Project

Pythius

An example of a well planned & well executed GMP refurbishment Project

By Graham Sex

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Project Success Factors

These required:

- An Understanding of Client's operations
- Development of an implementation strategy to take account of the Client's operations
- Clear definition of the Project management process
- Integration with the Client's internal procedures to form a single seamless process

Project Success Factors

These factors meant:

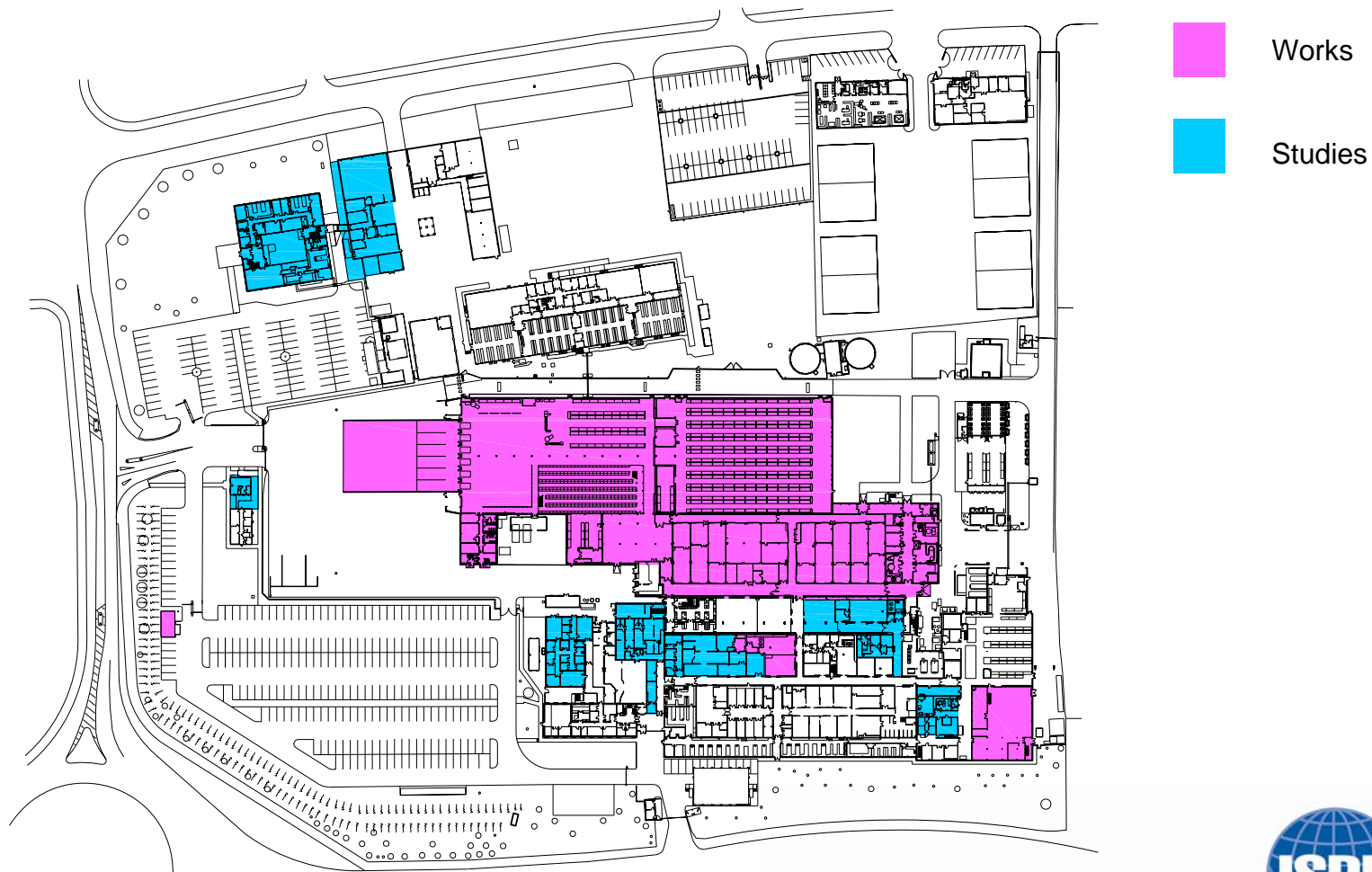
- Undertaking the complete project within - **A single point contact for all work**
- Delivery of the project within the agreed criteria

Project Success Factors

These were met by:-

- Using our experience to understand the Client's:
 - Working practices and procedures
 - User requirements
 - Site rules, safety and security procedures
 - Site's infrastructure and building conditions
- Providing a single Design, Manage and Implementation service
- Proven track record of similar projects, delivered successfully on time and cost

Austin's Experience



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Developing a Solution - Concept

- The solution was initially progressed by implementing a concept study over 4 weeks to confirm:
 - The project was feasible
 - It could be implemented safely whilst adjoining operations continued
 - An outline programme for the works
 - An order of magnitude cost for the works
- This provided the Client with confidence to seek initial financial approval from their management

Developing the Solution

- In order to meet Client's demands a solution had to be developed to deliver and address all the challenges
- Following approval of the Concept study, a preliminary engineering study was undertaken to define more detail

Developing the Solution – Preliminary Study

- This involved close discussions with Client's module managers, users, quality departments and maintenance staff.
- This included an understanding of an Implementation Strategy which dealt with:-
 - How best to maintain operations
 - Safety in particular maintaining escape routes
 - cGMP and cross contamination issues
 - Validation requirements

Developing the Solution – Preliminary Study

- Future maintenance requirements
- Detailed programme
- Preparing an estimate to $\pm 10\%$ accuracy
- Preliminary engineering drawings & specification
- This study was concluded in 8 weeks and allowed client to obtain final Financial Approval
- This then allowed the Client to proceed with the Contract

Design Considerations

These extended to review of:

- Existing finishes and condition of the corridor areas that did not meet cGMP
- Concerns with the wall tiling, timber dado rails and skirting, surface mounted services, deformed and dirty ceiling tiles

Design Considerations

- The design solution had to:
 - Achieve GMP conditions
 - Provide a visually acceptable appearance suitable for a modern Pharmaceutical Manufacturing Facility
 - Encompass construction processes that would limit the amount of dust, noise and vibrations
 - An example of this was to over clad the existing tiled wall rather than removing

Design Considerations

- The design solution had to consider:
 - The best way to work within the first floor Plant room
 - This was essential to prevent any possible risk to operations in the rooms below



Design Considerations

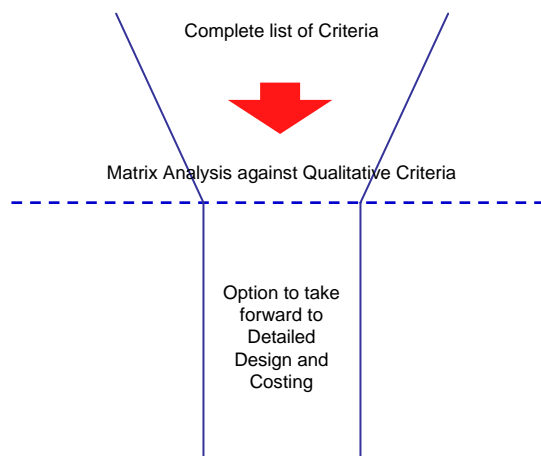
- Choice of major components and materials were undertaken with the client team.
- This was through the use of a “Decision Matrix” which identified key options and compared alternative strategies, leading to a preferred decision

Design Considerations

Four different wall-cladding options have been considered to satisfy 3M Health Care's requirements to improve the cGMP aspects and aesthetics of the main corridor in the Derby Road 'Hanger' building

The four options have been considered against qualitative criteria, in order to select the best option to take forward for detailed design and costing

This approach is shown diagrammatically below



The selection criteria are as follows:-

1. Capital Cost
2. Suitability / Impact resistance
3. Aesthetics
4. cGMP Considerations
5. Programme Implications
6. Customer Impression

The four options considered are:-

- A. 'Clestra' type metal panels
- B. Plasterboard / Stainless Steel / Whiterock
- C. Vinyl cladding on plywood and plasterboard
- D. Vinyl / Plywood and Plasterboard / Stainless Steel

Analysis

Criteria	Options			
	A	B	C	D
Capital Cost	17%	85%	100	56%
Suitability / Impact Resistance	80%	90%	30%	50%
Aesthetics	100	80%	90%	90%
cGMP Considerations	80%	50%	80%	50%
Programme Implications	0%	100	50%	40%
Customer Impression	90%	70%	90%	90%
Total	61%	79%	73%	63%

Taking all the relevant criteria into consideration, it was concluded that the proposed specification of plasterboard cladding with stainless steel dado and skirting, with Whiterock over cladding between dado and skirting was the best solution

Design Considerations



Before

Before



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Pre - Implementation

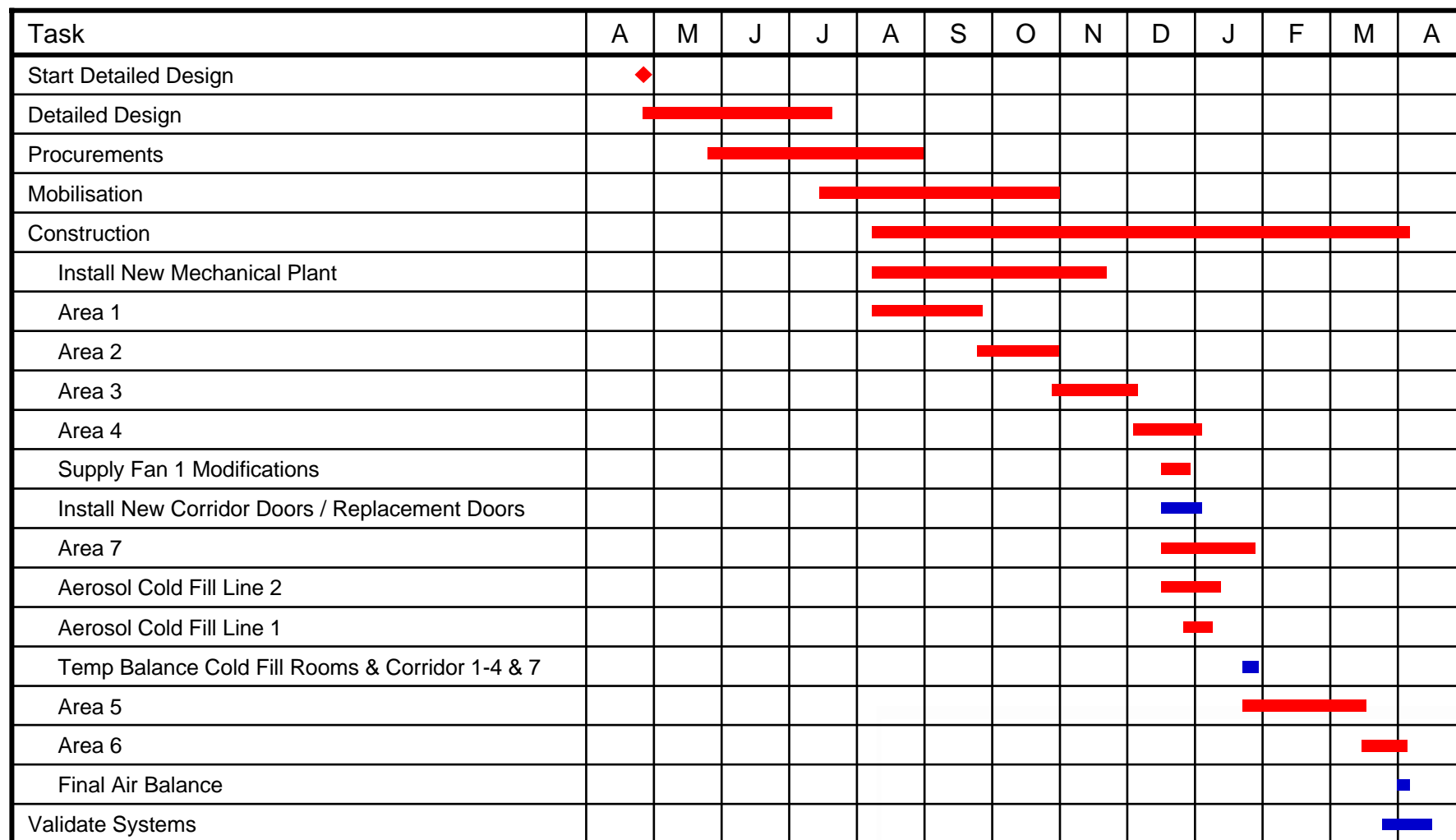
- Project Control documents, included:-
 - Detailed drawings
 - Detail Work Package Specifications
 - Programme and Implementation strategies
 - Health & Safety Plan
 - Procurement Plans
 - Cost Monitoring Document

Pre - Implementation

- The detail design was divided into 12 trade packages- Sub-Contracts
- This strategy was used to obtain greater control over subcontractors
- Pre-selection of tenderers was with the Client

There was continual liaison with the Client to ensure all parties were fully aware of the evolving project requirements

Outline Programme



Project Implementation – Subcontractor Selection

An important aspect to the success of this type of project, is the ability to select the most suitable subcontractors

This required each tenderer to go through a competitive process, this extended to:

- Visiting site during the tender period to ensure understanding of Client's operations, Safety & Security procedures and site constraints
- Post tender meetings with each subcontractor extended to detail review of:-
 - Technical documentation, H&S plans, programme and quality issues - to ensure they were understood
 - Review of resources and establish commitments
 - Obtaining references

Project Implementation – Subcontractor Selection

- Validation of tender sums to ensure they were realistic and appointments were not made just on lowest submissions
- Programmes were reviewed for capability, coordination and quality
- Confirm the need for appropriate working drawings, method statements, risk assessments etc were understood

Project Implementation

- Once subcontractors were appointed, the complete team consisting of Client, Austin project manager / construction manager / designers and subcontractors met on site for a day's workshop to review the project requirements in detail
- The purpose of this was to “walk and talk the job”
- This ensured that there was a total “BUY IN BY ALL PARTICIPANTS” and the risk of misunderstandings reduced to a minimum

Project Implementation – Considerations



- The work area included two process rooms, the central access corridor and first floor plant room within an old aircraft Hangar Building
- These were surrounded by process/support areas and offices that were to remain operational throughout the works

Project Implementation – Planning

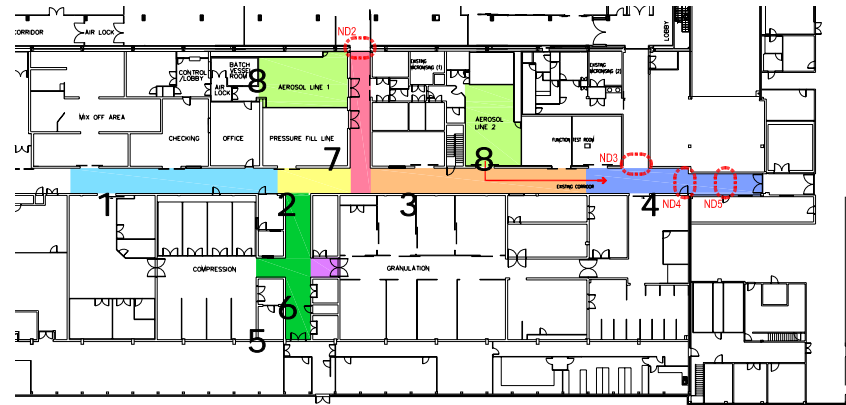


- In order to complete the project and keep all areas operational, the works were phased
- This allowed people/material flow routes and fire escape to be maintained
- Of particular concern was the need to electrically isolate each work area
- Temporary enabling works were undertaken to maintain operations in adjacent areas

Project Implementation – Planning

- Design / construction risk assessments were completed to consider the implications of the works on continuing operations
- Contingency plans were identified, in case the works did not go to plan
- One particular area of study was the planned change over to the new air handling plant during the Christmas shutdown
- The phasing strategy was discussed and agreed early in the design stage with all User Groups
- This determined that the works were best undertaken in eight distinct phases

Project Implementation – Planning

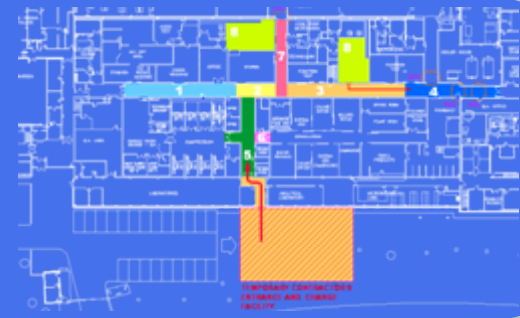


The phasing diagram shows the complexity of the works

- The works were completed in the order – Phases 1, 2, 3, 4, and 7 with phases 5 & 6 being completed together and phase 8 during Christmas period
- The works at the junction of phases 2, 3 and 7 was completed over a weekend shutdown with 4 contractors being involved. It was essential to keep this junction open at all other times
- On the rare occasion when Client's material flows could not be maintained, access for the Client through the construction area was planned.
- To maintain cGMP conditions the work area was cleaned and adhesive backed plastic film was laid on the floor to prevent contaminants being transferred from the work area as materials were brought through

Project Implementation

GMP Considerations



- In order to maintain operations in adjacent areas it was imperative that GMP conditions were maintained
- To achieve this, the following had to be complied with:-
 - To access the work area the construction operatives had to walk through clean areas
 - To enable this an outside change facility with lockers was constructed for operatives to change to GMP clothing
 - All jewellery / watches etc were removed and placed in the lockers
 - Any materials or tools that needed to be transported through the clean corridor were wrapped and sealed in plastic

Project Implementation

GMP Considerations



- The operatives would then proceed directly along the agreed routes to the work area
- The work area itself was separated from the GMP areas by temporary partitions
- The erection of these partitions took place after the Client had completed work for the day or at weekends to minimise disruption
- The partitions were constructed from framing covered with heavy gauge polythene to prevent shedding within the GMP area

Project Implementation

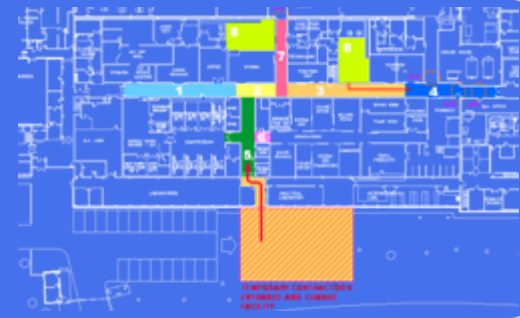
GMP Considerations



- The partitions were sealed at the ceiling and floor junctions to prevent air flow from the construction area to the GMP area
- The entrances to the construction area comprised of a further airlock, also containing lockers to allow the construction operatives to change out of their GMP clothing, into their work attire and PPE
- Every time the operatives exited the work area they would reverse this whole procedure
- To ensure there was no risk of contamination to GMP areas, a temporary extract fan was installed and ducted to the work space to create a slight negative pressure

Project Implementation

GMP Considerations



- The mechanical systems were re-balanced to ensure that the temporary partitions did not affect the air flows in the facility
- The flow of air would always be from the GMP area into the construction area to ensure no contaminants could exit the construction area
- When planning for air flows to be from the GMP area to the work area, it was important to assess the possibility of contamination of the construction work area with product
- To prove that it was safe to work air flow readings were taken at the start of the day

Project Implementation

GMP Considerations



GMP considerations:-

- To ensure the flow was into the construction work area a smoke pencil test was used
- The Client took regular particulate counts and microbial tests in the surrounding areas
- The tests results / air flow readings were regularly monitored to prove that the construction works were not affecting surrounding GMP areas

Project Implementation

Other Important Factors

- Prior to any individual starting on site they had to attend a site induction process to understand how the site was managed with respect to H&S and cGMP
- Everybody was introduced to the cGMP requirements as they had to enter the work area through the double temporary change facility
- Daily reviews with the sub-contractors, Client's project manager and user representatives were implemented to ensure everyone understood what was happening and their obligations
- Weekly programmes and bulletins were posted in the main reception and work areas to keep everyone informed

Project Implementation

Other Important Factors

- Austin's & Client's project managers worked side by side and informed the users of planned activities to ensure everyone knew what was happening – **communication was crucial**
- The Module Managers were separately informed on exactly how the work would affect operatives, material and people flows
- If there were issues, these were resolved almost instantly
- Shut downs were agreed with the Module managers, users, maintenance staff and subcontractors well in advance
- Dedicated access routes were reviewed regularly and changed to suit as the project progressed from phase to phase and from area to area

Project Implementation

Other Important Factors

- Client's operations were always given priority.
- If requirements changed, then modifications were made to the phasing, e.g.:
 - It was identified during construction that the junction between Phase 2, 3 and 7 had to be implemented in a single phase
 - This resulted in a revised implementation strategy
 - Work to Cold Fill lines 1 & 2 was rescheduled to meet changing demand and work was undertaken over weekends
 - Rescheduling this also resulted as beneficial to the Client to undertake their own maintenance work over the Christmas shut down

Project Implementation

Other Important Factors

- Daily reviews of commissioning programmes
- Planned Christmas shut down extended by one week to avoid any major impact on Operations / Production
- Prior to hand over the areas were fully snagged –
aim was to have minimum snags
- Formal hand over of each phase to the Client

Project Implementation

Every two weeks a formal site meeting took place to review:-

- Progress against programme
- Critical issues
- Design
- Construction
- Quality
- Commercial status

Project Implementation

Monthly Project status reports were published to formally report on:

- Critical items needing urgent resolution
- Health & Safety
- Design
- Procurement
- Construction
- Quality
- Cost assessment for each subcontractor
- Overall projected forecast final cost

Lessons Learnt

- Time spent in **pre-planning pays off** tenfold during the construction
- Regular discussion and **communications with users is vital**
- Correction of snagging should not be left to Post Construction stage as this protracts the completion. Any **snags should be resolved as ongoing not at the end**

Lessons Learnt

- Spending more **time up front on selection of critical materials is Vital**
- **Openness by all parties** to resolve challenges on cost, quality, programme, implementation throughout the project lifecycle - **paid off**

Result

- Impact on Client's Operations / Production – **ZERO**
- Quality of Installation – **Overall very good**
- Programme – **Expedited as planned**
- Cost – **Maintained below the 10% accuracy stated**
- Safety – **one incident, not reportable, no lost time**

Result



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Result



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Result

From the Client and Austin's perspective

..... a successful project.



Project X

An example of a well intentioned, less structured but never-the-less well executed GMP refurbishment Project

By John Broomfield

Project Success Factors

The project's success factors required:

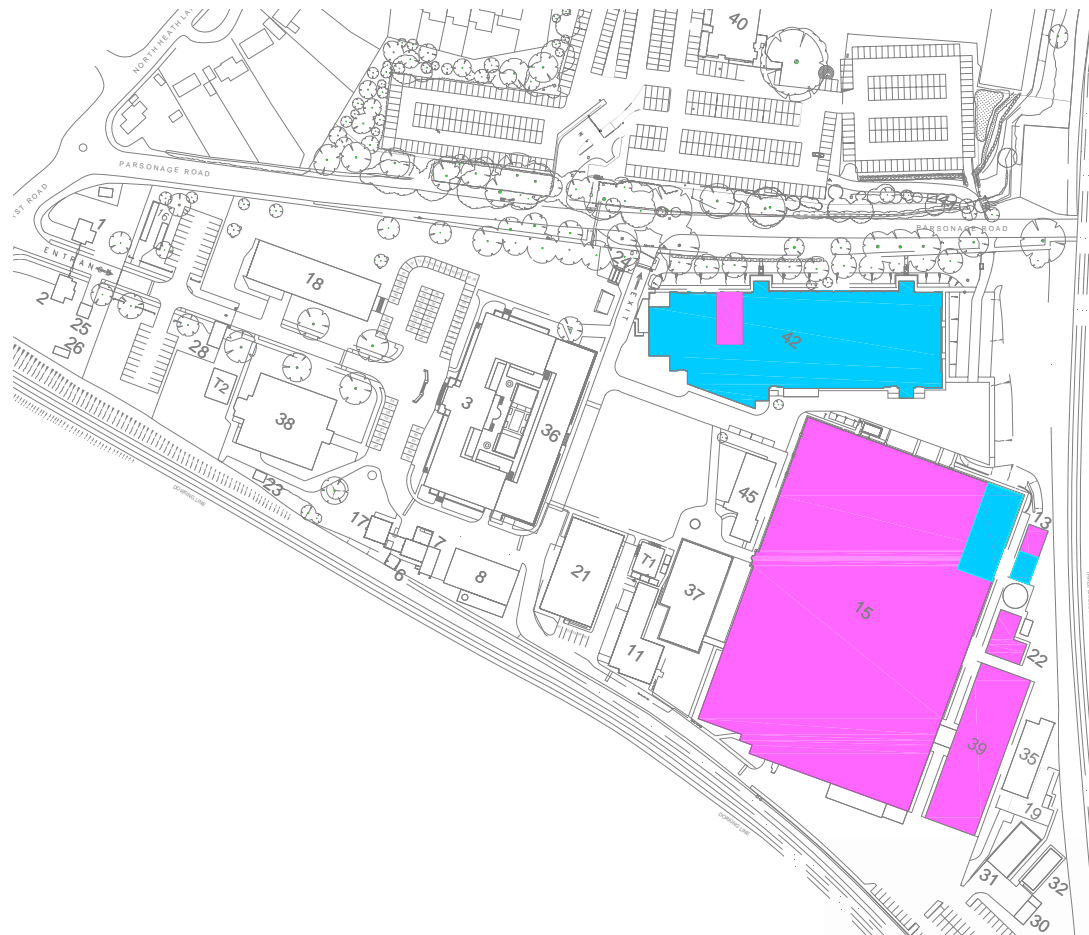
- Broadly the same as Project Pythius with a desire to achieve a project that was on time, in budget and achieved the initial targets set

Project Success Factors

The project success factors were met by:

- Once again, the same broad understanding of the Clients site and working practices and the single point of design & construction responsibility

Austin's Experience on the Site



- Works
- Studies

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Developing the Solution

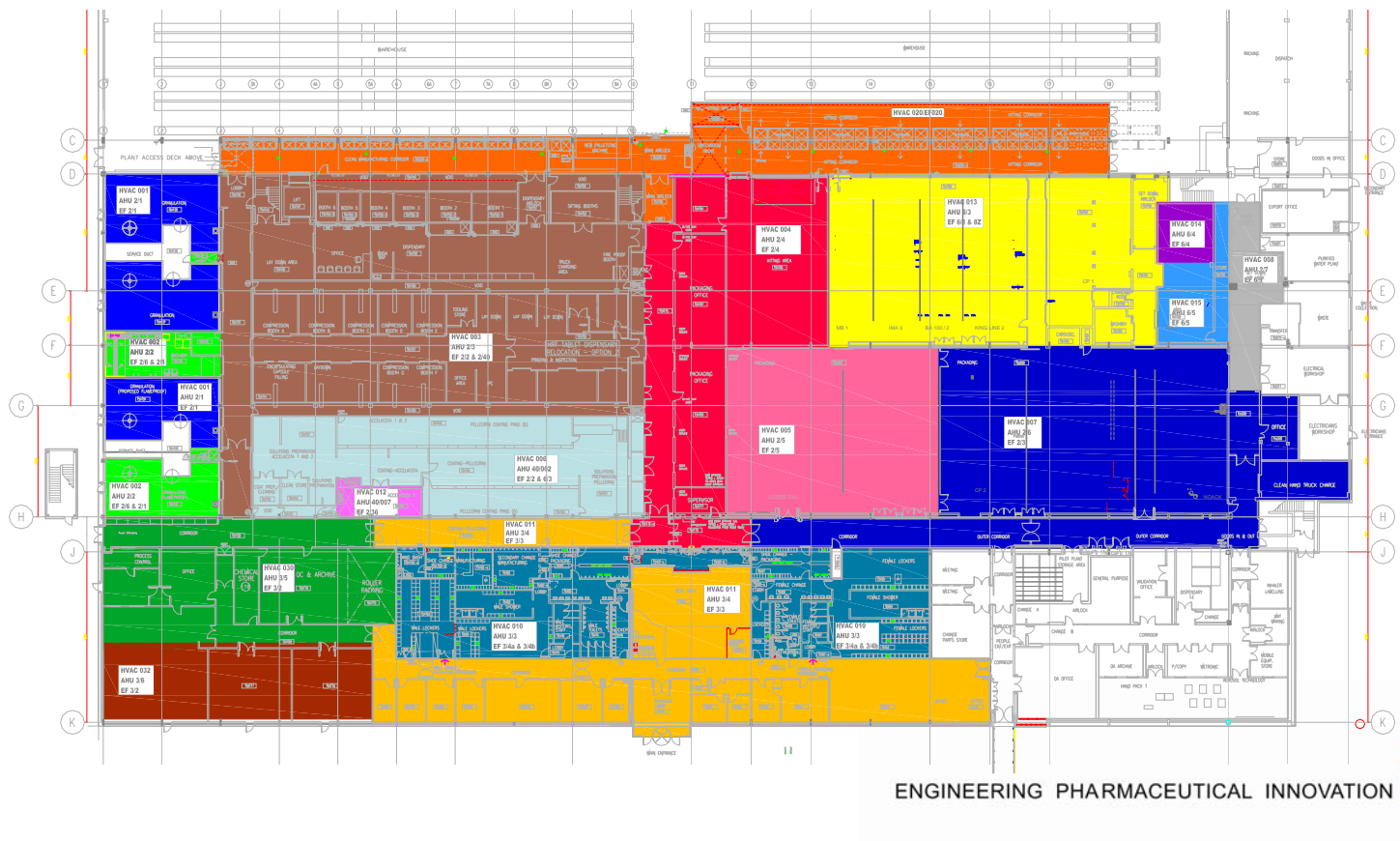
- As with Project Pythius a concept study was developed in liaison with Clients Operations managers
- However, it is at this point where the two projects begin to differ

Developing the Solution

- Project Pythius had a substantial amount of verifiable record documentation relating to the services within the areas being affected by the changes
- Project X on the other hand, had some information but this was either incomplete or non-verifiable

Developing the Solution

In order to meet the Clients demands a solution had to be developed to address all the challenges



Developing the Solution

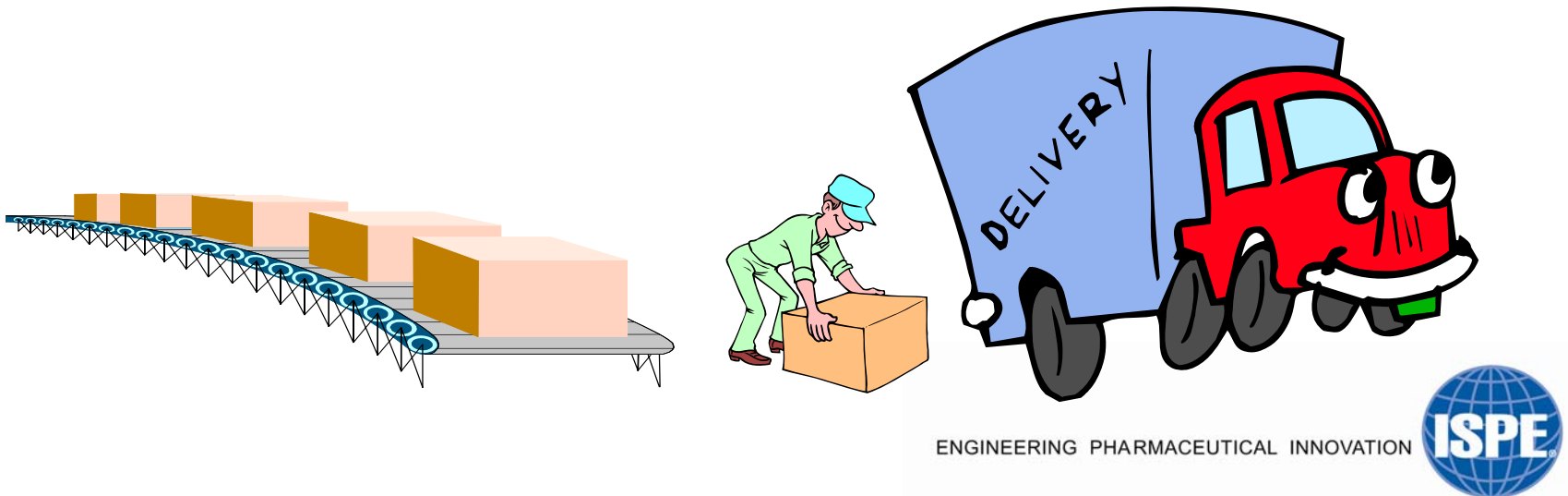
The complexity of the phasing gave rise to its own special challenges:

- Existing AHU's and services fed more than one phase
- Each phase had to be returned to GMP operations before the next phase was undertaken
- This required substantial temporary connections and many rounds of commissioning

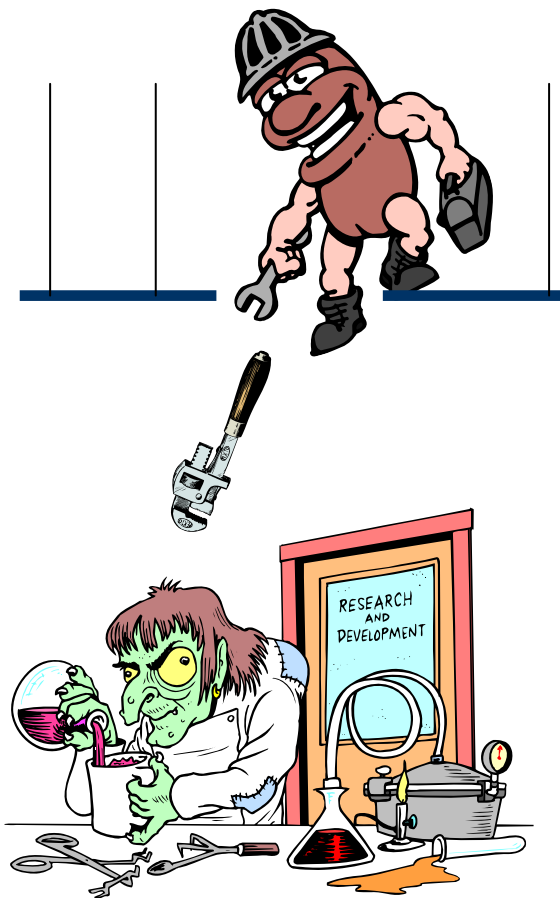
Developing the Solution

The Clients operations also conspired against detailed pre-planning:

- Stockpiling of product was not possible as they were already running on extended shift patterns to meet demand and shutdowns were few and far between



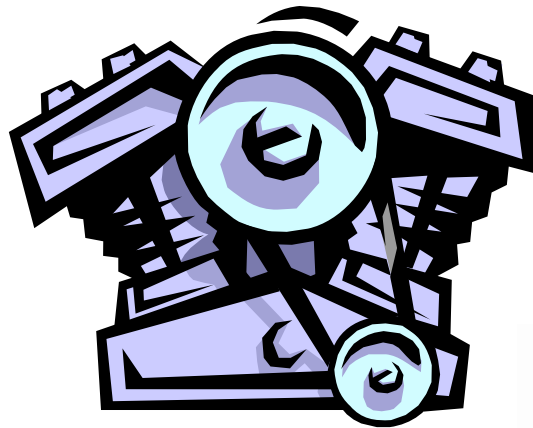
Developing the Solution



- Access to survey ceilings voids above occupied areas was not possible due to Health & Safety restrictions

Developing the Solution

- Identifying the condition of existing equipment was based on visual assessment only



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Design Considerations

These included:

- Re-use existing or replace with new?
Cost and disruption issue
- Increase existing capacity or add new stand alone equipment?
Cost issue
- Were interim GMP conditions acceptable until works on individual systems were complete?
Validation issue

Design Considerations

The design solution had to:

- Make assumptions regarding existing services routes and capacities that could not be surveyed prior to construction
- Allow additional programme time for each construction phase but without over extending the programme. This was required to allow for design adaptation once accurate system routes and performance were revealed

Design Considerations

Planning :

- Design / Construction risk assessments were continually reassessed to ensure the changing requirements were properly dealt with
- Contingency plans were identified, in case the works did not go to plan
i.e failure to complete specific works in a given shut down period

Design Considerations

Planning :

- The phasing strategy was discussed and agreed early in the design stage with the User Groups
- The phasing strategy was reviewed with the User Groups prior to the commencement of each and every phase to ensure that no changes were required to suit the current operations

Project Implementation

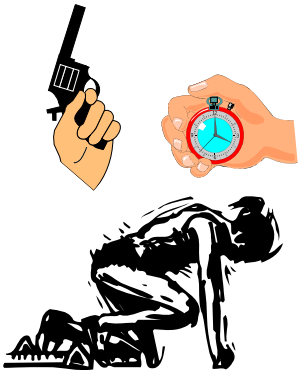
As with Project Pythius there were GMP considerations:-

- To prove that it was safe for work to begin air flow readings were taken within the facility
- To ensure the flow was into the construction work area a smoke pencil test was used
- The tests results / air flow readings were regularly monitored to prove that the construction works were not affecting surrounding GMP areas

Project Implementation

Other important factors:

- The Clients operations were always given priority. If requirements changed, then modifications were made to the phasing, e.g.:



- The “Go / No Go” decision for out of hours working was not able to be made until 4 hours before the work was planned to start.
- This resulted in several revised implementation strategies

Lessons Learnt

- Time spent in pre-planning pays off tenfold during the construction
- Time spent in surveying the existing services to update or verify capacities, duties and equipment is almost invaluable
- Regular discussion and communications with users is vital
- Correction of snagging cannot be left to Post Construction stage when using phased handover for GMP production

Lessons Learnt

- An openness by Austin, Client and subcontractors to resolve all challenges on cost, quality, programme, implementation etc throughout the project lifecycle meant that more time was spent in Achieving than Arguing

Results – Pythius vs. Project X

	Pythius	Project X
Impact on Operations / Production	Zero	Minimal
Quality of Installation	Overall very good	Mainly to Corporate Standards
Programme	Expedited as planned	Overall End Date met but multiple re-programming required during the project
Cost	Maintained below the 10% accuracy stated	Maintained within the 15% accuracy stated
Safety	One incident, not reportable, no lost time	Three incidents, none reportable, no lost time

Result

From the Client and Austin's perspective

**A different way of achieving
a result but, never-the-less,
..... a successful project.**

