CASE STUDY:

Preparing Weston Park Hospital for Gene Therapy Challenges in the NHS

- A new Advanced Therapy Medicinal Product (ATMP) and Clinical Trials (CT) Aseptic Suite
- A refurbished pharmacy Chemotherapy Aseptic Dispensing Unit
- Design from RIBA Stage 2
- Fully Integrated Solution
- Principal Designer and Principal Contractor
- Fully operational hospital
- Phased approach to project delivery
- Grade C cleanroom areas
- Compliance with HTM, GMP and MHRA standards
- Validation and Qualification Support

Jonathan Morton, engineering director of BES, the specialist in design and construction of sophisticated healthcare, pharmaceutical and biopharma environments, discusses the company's current pharmacy and aseptic suite project at Weston Park Hospital in Sheffield.

In any hospital that treats acute conditions, the pharmacy plays an important role in ensuring that complex and often tailored medication is prepared for patients. With skilled professionals handling potentially hazardous substances, these high-specification environments require a specialist approach to design and construction.

Emerging cell gene therapy treatments mean that there is now a need for such facilities to be constructed within hospital pharmacies to enable the use of viral vectors in targeting advanced medicines to the affected part of the body. Weston Park Hospital, part of the Sheffield Teaching Hospitals NHS Foundation Trust, specialises in cancer treatment. The hospital is in the process of realising a two-phase refurbishment project designed, engineered and constructed by BES, to create a new Advanced Therapy Medicinal Product (ATMP) and Clinical Trials (CT) aseptic suite, along with a refurbished pharmacy Chemotherapy Aseptic Dispensing Unit.

The hospital was already planning a new Chemotherapy Aseptic Dispensing Unit and was able to make a business case for adding the aseptic suite as part of the same project to aid its clinical trial capabilities and enable gene therapy preparations. The pharmacy and aseptic suite project is designed to future-proof the hospital's drug preparation capabilities on site.

Advanced Therapy Medicinal Products

The new gene therapy preparation area being installed at Weston Park Hospital as part of the pharmacy Chemotherapy Aseptic Unit is an ATMP suite. The term denotes an extremely sophisticated field of emerging biopharmaceutical medicines, with preparations tailored to the specific requirements of individual patients. An ATMP classification includes regenerative medicine, personalised treatments and the development of nanomedicines using either a gene therapy medicinal product, a somatic cell therapy medicinal product, or a tissue engineered product.

The exacting science of these preparations requires equally sophisticated storage, reconstitution and handling procedures, specific to each product. Their potentially hazardous nature also demands complex toxicity management to prevent contamination of the medical treatment, or avoid any risk of particle release outside of the controlled area.

Project Scope

BES has been appointed as both principal designer and principal contractor for the project, with responsibility for maintaining BAU (business as usual) within the fully-operational hospital. The BES team will plan and carry out all construction works in the live healthcare environment, considering the needs of clinicians, service users and patients. The avoidance of any interruptions is a critical success factor for the project.

The pharmacy aseptic suite will be developed in two phases. Redundant office area on the 6th floor will be refurbished to create a new, high-specification Chemotherapy aseptic dispensing facility in phase 1. Once this has been fully-validated, the hospital's pharmacy team will move across to the completed accommodation and the former pharmacy will be refurbished as the new aseptic suite with sophisticated clinical trial (CT) and ATMP preparation facilities.

Multidisciplinary Approach

The project will draw on BES' previous healthcare experience and track record in the pharmaceutical sector. The hospital wanted a specialist that understands NHS processes and procurement requirements, but was also keen to benefit from any opportunities to adopt best practice from the pharmaceutical sector and incorporate industry standards.

Due to the project's specialist nature, the hospital needed a partner that was proven across the design and construction requirements. Working with BES as a multidisciplinary team meant that the hospital team could collaborate with a single company for a full turnkey service across design and construction, with a smooth and seamless transition between each discipline. Dealing with one, integrated team ensured every aspect of the project was joined-up, with proven processes and effective information sharing. This has been critical for eliminating the risk of details being overlooked or buildability issues occurring during construction.

Design Development

Working with the hospital's user requirement specification (URS) and engaging with the hospital's estates team and senior pharmacist, BES took the concept design from RIBA Stage 2 to stage 4 in a collaborative process that draws on the company's experience in sophisticated environments.

It was clear to the BES team that there were opportunities to make significant improvements to the design to generate cost, buildability and operational benefits.

Validation of the project also began at design stage, with design qualification ensuring that the project is viable, fit for purpose and meets the URS.

Adding Value

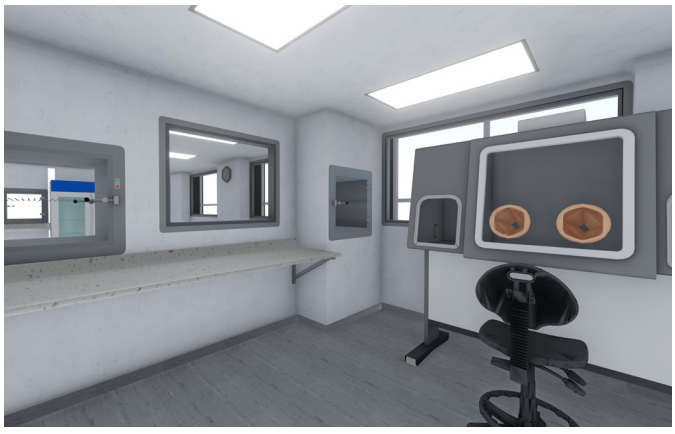
One of the key improvements made during the design process was the relocation of the main corridor used to access the new pharmacy and the aseptic suite entrance. The BES team suggested that this be switched from the north side of the building to the south as this will enable key areas that need to be temperature controlled to the north side of the building where there is less solar gain.

This change to the original layout will reduce the cooling load required for the facility, simplifying the building services and reducing operational cost.

The new pharmacy aseptic suite is arranged from east to west in a linear progression, occupying the entire level of the building. Former nurses' accommodation on the 7th floor was earmarked for refurbishment as a plant room to serve the new facilities and this had to be put in place during phase one of the project to enable the new pharmacy to become operational before construction work commences on phase 2.

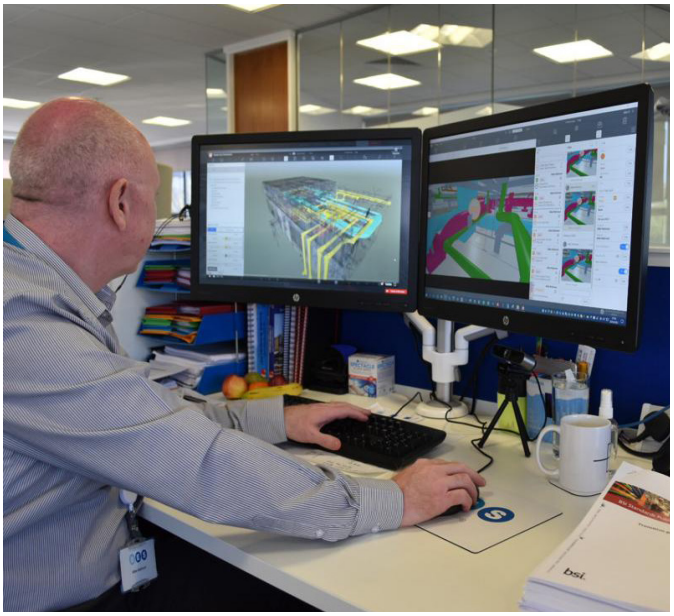
As part of the design development process, BES also had to verify that the existing slab was capable of supporting the loads required for the two air handling units (AHU) needed for the pharmacy and aseptic facility. As the existing slab was constructed using hollow terracotta panels, the BES team had to confirm the load requirements to establish whether a replacement slab would be needed. This addition to the original scope of works was avoided with the use of a screed to provide a suitable base for the AHUs.

Once the load bearing issues with the 7th floor slab had been resolved, it remained clear that service penetrations through this unconventional slab would have to be small in size. This required a greater number of small ducts, adding to the challenges of the congested service void. Once again, close collaboration between BES' design and construction teams was required to ensure the duct routes could be installed within very strict tolerances in the limited void.



Design Compliance

The facilities have been designed to HTM and GMP pharmaceutical requirements, with BES carrying out the design qualification validation process before work began on site and leveraging the team's experience in the pharmaceutical sector. Because ATMP is such a new area of biopharma preparation, the design development process also involved consultation with the MHRA (Medicines and Healthcare Regulatory Authority) to ensure the design of the facility will be compliant with regulatory requirements. Following a consultation with MHRA, the BES team improved the design of the phase 2 facilities, splitting the change areas to avoid any cross-contamination risk. MHRA also confirmed the viability of the design, ensuring that validation can be achieved without any issues following completion of the project,



Digital Design Tools

To aid the design and end-user engagement process, the BES team leveraged a suite of modelling and visualisation software. The facilities were designed using 3D REVIT modelling and Navisworks was utilised for clash detection. This was a vital step in designing the building services for the project around the restrictions of a limited existing ceiling void.

The new pharmacy aseptic suite is heavily serviced and the 500mm void had to accommodate both the new services and a number of existing service routes that needed to remain in place. Lumion software was also used to transfer the model into rendered images to give the client a realistic view of what the facility would look like.

Virtual reality walk throughs then allowed the client to experience the facility and gain a sense of how the space will be laid out. This formed part of a collaborative design development process with regular reviews to tweak the detail of the design in line with client preference, the URS and compliance requirements. Once again, the use of technology as part of detailed design is valuable in supporting a smooth validation process.

The New Pharmacy

Construction of the phase 1 project began with demolition of internal walls, opening up the space and allowing in natural light throughout the facilities with views to both the north and south of the building thanks to vision panels in the internal walls. This will be transformational for pharmacy staff as some areas of the old pharmacy have no aspect to the outdoors.

The internal layout has then been reconfigured to provide the accommodation required for the new pharmacy. On entering the suite from the stair or lift lobby, there is a primary change area and locker room. From here staff will enter the facilities via the perimeter corridor on the south side of the building, which leads to the outer support room at the far side of the facilities. This is an unclassified office area.

From here, pharmacy staff will enter the Grade D inner support room, a lab area that provides the central hub of the new pharmacy, via a grade D first stage change area. They can then access, two Grade C isolator rooms, via a Grade C second stage change area. To maintain compliance with the required clean room grades, the accommodation has been designed with a pressure cascade of highest pressure in the isolator rooms, lower pressure in the secondary change area and lowest pressure in the inner support room.

The multidisciplinary approach provided by BES was central to delivering this effectively because engineered air flows can only be achieved if the architectural design is aligned to the required air leakage paths. Construction of the facility must be meticulous to ensure air gaps are controlled in the built asset, so close collaboration between BES' design and construction teams was vital.

Aseptic Suite

The phase 2 project has been fully-designed and will begin construction when completion of the validation process for the new pharmacy allows the pharmacy team to move across to the new accommodation. Once again, the existing accommodation will be remodelled to enable a completely new layout that enables effective segregation of the Grade C change and isolator rooms and allows air pressure regimes to be maintained.

Access to the aseptic suite will be by one of two routes: through the new pharmacy outer support room or via the perimeter corridor that runs along the south side of the new pharmacy. A corridor will run through the centre of the suite, with access to the CT preparation facilities on the north side of the building and to the ATMP preparation area on the south side.

Storerooms and toilet facilities will be located at the interface between the new Chemotherapy aseptic suite and the CT/ATMP aseptic suite. A clog wash designed specifically for the facilities and the pharmacy team's gowning protocols will also be located in this area, as a change of footwear will be required each time a member of staff moves between a Grade D and Grade C area. Due to the number of clog changes and variation in foot size, the BES team designed a bespoke clog storage system along with clog washing facilities.

The entrance to the ATMP facilities will be at the far end of the central corridor. The outer support room will be accessed first and, from here, operatives must pass through a first stage Grade D change area before entering the Grade D inner support room. They must then prepare for access to the Grade C ATMP isolator room in a Grade C change area before being able to enter. Each stage of travel through the ATMP areas is governed by inter-connecting air-lock doors that are controlled on a traffic light system which enables only one door to open at any given time with a visual colour cue to indicate when the magnetic locking system can be opened.

An important element of the design process for the ATMP facilities was to understand the health and safety implications of working with materials that could be potentially hazardous if allowed to escape from the controlled isolator room environment. After considering the hospital's risk assessment and proposed operating procedures, the BES team designed the airflow to minimise contamination risk while ensuring that accidental spillages in the ATMP isolator room are contained.

By maintaining highest negative pressure in the second stage change room, the design of the facility ensures that any spillage occurred in the isolator room cannot escape to the inner support or first stage change areas, nor even to the outer support area. In this way, any spillage can be dealt with using a spill kit and bagging procedure, before cleaners come in to decontaminate the facilities.

The CT areas will be accessed from the opposite end of the same central corridor, with a similar route through the outer support room to a Grade D first change area into the Grade D inner support room. From here, operatives will enter the Grade C second change area before accessing the Grade C isolator room. These facilities will also be built with traffic-light managed air lock system between each controlled environment. Pressure regimes will be the same differentials as implemented in the new pharmacy.

The air handling provision will follow the model already constructed for the new pharmacy phase of the project with full fresh air supply via the AHUs and a HEPA-filtered air extract, along with individual HEPA-filtered exhausts for each isolator. The BES team considered the COSHH assessment to determine whether local exhaust ventilation (LEV) was required for the CT inner support room. Although LEV was not required for compliance, Nederman Arms have been specified in this location to ensure the comfort and wellbeing of operatives using alcohol spraying equipment.

Clean & Controlled Environment

As the project is being delivered in two phases and there is a need for the hospital to retain a functioning pharmacy at all times, two air handling units have been installed as part of the phase 1 programme.

BES has designed heat recovery into the air handling system to reduce the heat energy required. The fresh air supply will serve both the classified clean room areas and the ancillary rooms and HEPA filters will clean the extracted air before this is released into the atmosphere.

In addition to the general extract, Local Extract Ventilation (LEV) exhaust systems have been designed into the facility where sporicidal and alcohol spraying occur, with the CT and ATMP Isolator room LEV's being filtered through safe change HEPA units before being discharged to atmosphere.

Across all cleanroom-classified areas of the new Chemotherapy Aseptic Suite and CT/ATMP Aseptic Facilities, the environment will have a strict tolerance of the temperature control as well as upper humidity limits being maintained for occupancy comfort. The Grade C areas are maintained at 19°C ±2°C whilst the Grade D rooms are maintained at 19.5°C ±1.5°C, both areas are controlled with an upper limit of 55% relative humidity.

To ensure that these conditions are met consistently, a new BMS has been installed specifically for the Chemotherapy Aseptic Suite and CT/ATMP Aseptic Facilities. This will constantly monitor temperature, humidity and the various air pressure cascades between the different grades (C, D and CNC+) of the rooms. Temperature sensors installed in the return ductwork from each room will monitor the temperature of the air leaving the location enabling automated temperature adjustments by the BMS in line with real time conditions. In this way, the environment will consistently meet temperature and humidity parameters, regardless of occupancy levels, equipment use or outdoor temperatures.

Ease of Maintenance

The BES team worked with the client to consider the logistical and maintenance implications of AHU specification. Often facilities of this kind are specified with some level of redundancy in the AHU installation as standby provision for the controlled environment. The challenges of locating additional standby AHU capacity in the limited 7th floor plant room location, however, led to a an alternative approach to resilience. Fault monitoring has been built into the BMS to ensure fans are repaired or filters are changed before a developing fault can begin to affect the performance of the air handling system.

Indeed, ease of maintenance and the need to ensure the environment remains fit for purpose has influenced all aspects of the design, including the choice of materials and finishes. The inner support and isolator areas are fully vinylled across the walls, floors and ceilings creating a robust and easy to clean environment with no crevices where particles can collect. All work benches and desks have been fabricated using Corian; a smooth impervious material that is compatible with cleaning agents and regimes. The workstations and benches have smooth rounded edges to ensure there are no awkward corners, with every effort made to enable faster, easier and more effective cleaning.

Pioneering Facilities

The new Chemotherapy aseptic dispensing unit has now been completed without disruption to the normal working of the hospital. The BES team has completed the installation qualification process in preparation for the client to carry out the operational qualification and finalise the validation.

Construction will begin on the aseptic facility as soon as the old pharmacy has been vacated, with BES continuing to provide both design and construction services, within social distancing guidelines, during the COVID-19 pandemic.

The co-ordination of architectural design, building services engineering and construction across the multidisciplinary BES team will result a best in class facility that supports the hospital's reputation for excellence in cancer treatment and creates a template for future gene therapy preparation facilities for other NHS Trusts.

Commissioning & Validation

Validation of the new facilities has been embedded in the project design and construction process from the outset. Design reviews commissioned by the Trust were documented to enable design qualification, which considers the validity of the design against the URS and compliance requirements.

Further detailed documentation has also been compiled by the BES team during the construction phase to ensure the Installation Qualification carried out by the Trust, cross-references with the as-built information, detailed design and the URS. The BES team is also responsible for commissioning the new facilities and ensuring accurate information is available for future maintenance or modifications.

Operational and performance qualification of the facilities will be undertaken by the hospital's Chemotherapy aseptic dispensing team, with the support of BES, following completion of each build phase.

BES also carried out airborne particle cleanliness classification tests, recovery (clean up) tests and airflow (smoke) visualisation studies. Because the BES team is familiar with the validation process, all validation requirements have been built into to the design and construction process at every stage. This has reduced validation risk and ensures that all design, installation and compliance documentation is available.

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We provide fully integrated solutions to the highest standards of quality and stringent regulatory compliance.

Our specialist services comprise front end consultancy and site/facility planning, and all aspects of design; we also offer comprehensive range of construction services from new build, refurbishments, conversions to fit outs, project management, commissioning and validation support.

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