PC4 laboratory construction: a users' point of view

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The Sydney 2000 Olympic Games was a tremendous event for Australia, bringing the world's best athletes and thousands of visitors to Sydney. As it was a global event with comprehensive media coverage, it also bought to our shores the possibility of terrorist activity. During the period the games were held, the Centre for Infectious Diseases and Microbiology (CIDM) performed laboratory investigations of suspicious substances found at Olympic Games venues and Sydney airport and worked with the Defence Science and Technology Organisation (DSTO) testing air samples, taken at venues, for the presence of bioterrorism agents.

Even though no bioterrorism agent was detected during the period of the games, this work demonstrated the inadequacy of normal physical containment level 3 (PC3) laboratories for the investigation of unknown substances. Targeted dissemination of anthrax spores via mail in the United States in 2001 and subsequent hoax episodes in Australia highlighted the need for specialist laboratories that could safely handle unknown substances that could contain chemical, toxin or infective agents.

Construction and commissioning of a specialised PC4 laboratory, funded by NSW State government and designed for investigation of unknown substances that could contain bioterrorism agents, was completed in 2007 in the Institute for Clinical Pathology and Medical Research (ICPMR). This facility was purpose built using the Australian and New Zealand *Standards for Laboratory design and construction* (AS/NZS 2982.1:1997) and *Safety in laboratories – Part 3: Microbiological aspects and containment facilities* (AS/NZS 2243.3:2002), as the starting point. The Director of CIDM, Professor Lyn Gilbert, and CIDM senior scientists Marion Yuen and Greg James worked very closely with Graeme O'Neill (Graeme O'Neill Consulting) to develop the feasibility assessment for the facility and then with architects and engineers from S2F Pty Ltd during the design phase of the project (Figure 1).

Crucial to the successful outcome of the project was for the scientists to have in depth knowledge of what was required for the laboratory to meet current and future diagnostic challenges including staff numbers needed to perform investigations, safety issues, security concerns, equipment functions and footprints, laboratory procedures and operational demands. These comprehensive requirements gave the architects and engineers clear design briefs, enabled critique of individual elements of the facility and fostered discussion and deeper understanding of both laboratory needs and engineering constraints, resulting in the best possible design for purpose. The design was then reviewed by consultants – Tony Della-Porta of Bio2IC and Neil Walls (Neil Walls Consulting). Their involvement ensured the design met proposed current and future requirements and those of the various Australian Standards (for accreditation), utilities (water, electricity) and building codes (Council).

Features that set the facility apart from traditional PC4 laboratories included a higher negative pressure gradient from –50Pa in the shower, –100Pa in the inner change room and –140Pa in the laboratory than that specified in the Standard (requiring a pressure differential of 25Pa between compartments), providing a greater barrier to the escape of organisms on air currents from the laboratory.

In addition, the total laboratory air volume is replaced every 5 minutes and air flows from supply vents sited above the laboratory entry/ exit to the exhausts vents sited at the opposite end of the laboratory above the area in which specimen processing and follow up examination of cultures is performed. These procedures hold the most risk for staff of being exposed to a chemical, toxin or infective agent in the event of a laboratory accident. Having the exhaust above the work area, combined with high rate of replacement of air volume, limits any potential exposure. Also, potentially contaminated air is distant from the exit, providing the safety of distance for escape of organisms from the laboratory.

The laboratory was constructed using aluminium / polystyrene sandwich panels, used extensively in the construction of cold rooms, for the walls and ceiling. These panels provide an air tight seal and strength to withstand the force placed on panels by the high negative pressures at a relatively low cost and ease of assembly. An exoskeleton of steel beams around the laboratory provide the framework for the panels and enable ease of cleaning of the inside of the laboratory as intrusive internal beams are avoided. Further, the inclusion of a decontamination chamber large enough to place the largest item of laboratory equipment permits sterilisation of faulty equipment without the need to close and fumigate the laboratory (Figure 2).

Processing of samples is performed in cabinets specified for use with chemicals and constructed from plastic polymer that

is resistant to sodium hypochlorite solutions used for surface sterilisation. Two variations of this cabinet are employed. The first is similar to a Biological Safety Cabinet (BSC) Class I with air drawn into the front opening of the cabinet, over the work surface to the rear, through a pre-filter, then two HEPA filters in series and a carbon filter before exhausting directly into the laboratory exhaust system. Air is not recirculated into the laboratory so that, in the event that the sample contained a chemical agent, it would pass through the HEPA filter and, although it may overwhelm the carbon filter, it will be exhausted from the laboratory and not endanger staff.

The second cabinet is similar to a BSC Class III and has added features to those listed above, with an enclosed work area, HEPA filtered inlet air and an entry chamber with two air tight doors for sample delivery (Figure 3). The chamber and cabinet can be fumigated through ports located on the chamber. Samples suspected of containing a Risk Category Group (RCG) 4 infective agent can have nucleic acid extracted in this cabinet for use in diagnostic molecular biology assays.

A combination of flexible film isolators, when installed, will enable culture, isolation and identification of RCG4 viruses. Air enters each isolator through a HEPA filter and is exhausted through a HEPA filter integral to the isolator. Each isolator exhaust is then directly connected to the laboratory exhaust system, providing a second HEPA filter barrier to the escape of infectious aerosols. When the isolators are in use, the laboratory will adopt strict PC4 laboratory procedures that includes showering out of the laboratory for handling RCG4 agents.

Liquid waste treatment conventionally uses large stainless steel tanks in combination with heat, chemical, UV or hydrogen peroxide gas sterilisation. Plastic polymer tanks used in the facility provided a substantially cheaper alternative able to use sodium hypochlorite sterilising agent that is corrosive to metal tanks (Figure 4).

Having the right design is not the end of the story. The facility had to be built to a standard of finish and function. A PC4 facility is a complex structure and small elements of the design needed to be modified during construction due to practicality and future maintenance issues. Again, it was absolutely vital for the scientists to be able to convey to the construction managers prior to the commencement of construction, the purpose of the facility, laboratory work that would be performed, operation requirements and need for laboratory staff to perform aspects of maintenance. During construction, scientists had regular meetings with the builders and designers and sometimes daily site inspections as required for fast evaluation and resolution of issues.

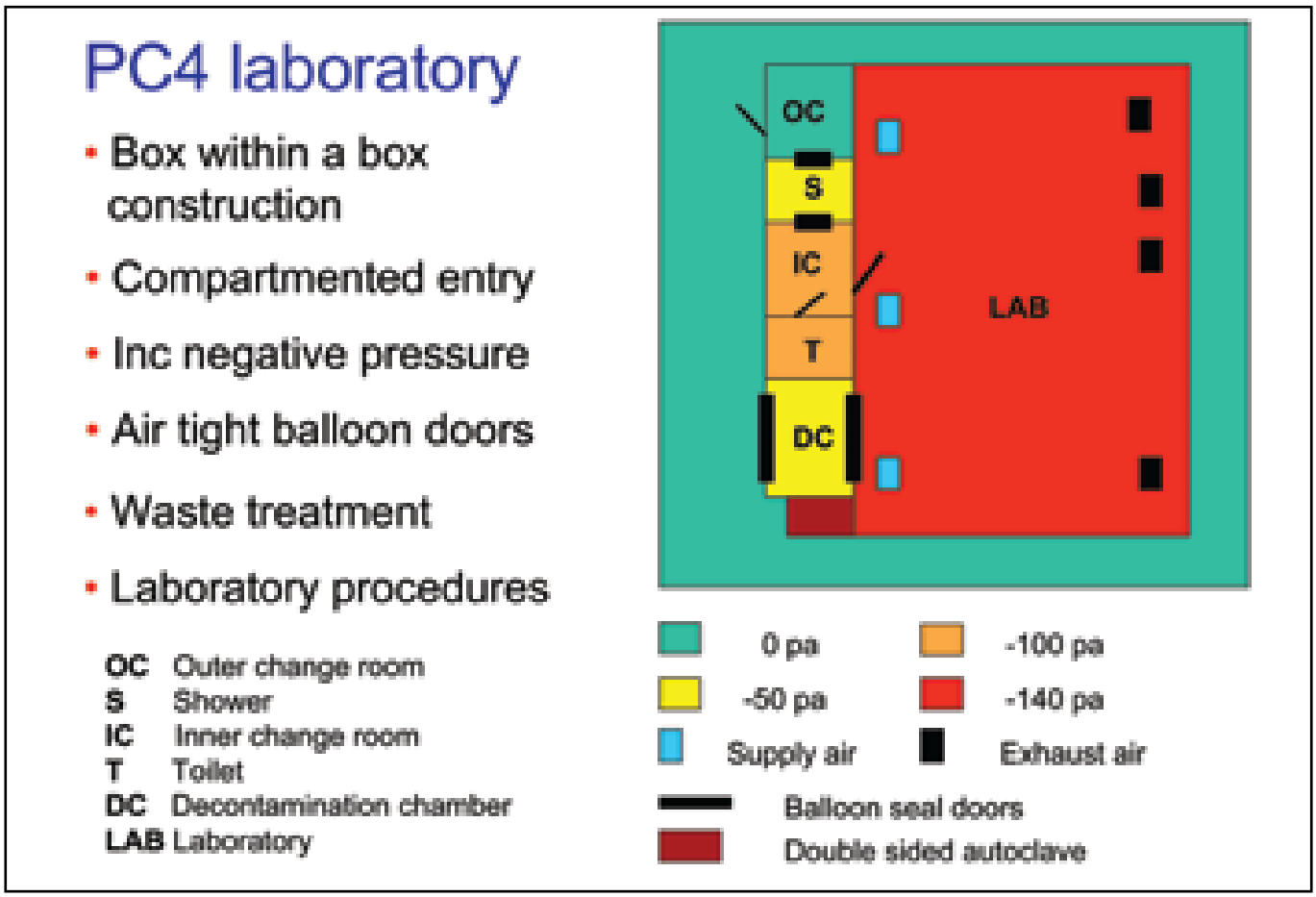

Figure 1. Schematic of PC4 facility laboratory level.

Figure 2. Decontamination chamber outer door.

Figure 3. BSC Class I.

Figure 4. Liquid waste treatment tanks.

During set-up and commissioning of the facility prior to official handover to ICPMR, scientist Jimmy Ng was on site each day with the construction team learning every engineering aspect of the facility. Any issues arising in this period were immediately reviewed by senior scientist Greg James and a solution developed with constructors and designers as needed. Having scientists actively involved in troubleshooting during this start-up phase further enhanced their knowledge of facility engineering and their ability to define and rectify problems. This is important for minimising future laboratory downtime due to an engineering fault.

The brief for the Emerging Infectious Diseases and Biohazard Response Unit (EIBRU) PC4 facility is to provide safe, secure, rapid investigation of potential bioterrorism agents (such as anthrax and ricin toxin) and emerging infectious diseases (such as the SARS coronavirus and H5N1 avian influenza) for New South Wales. Its aim is to also work collaboratively with other Public Health Laboratory Network (PHLN) laboratories in other States as a national resource.

The successful completion of the PC4 facility has been the result of having clear laboratory operational requirements and strong partnerships between scientists, designers, consultants and builders, working together to ensure the facility met all objectives.

Greg James (BSc. MSc. MASM) is a senior scientist in charge of the Reference Laboratories Section (RLS) in the Centre for Infectious Diseases and Microbiology Laboratory Services Department in the Institute for Clinical Pathology and Medical Research at Westmead in NSW. The RLS comprises: NSW State Mycobacterium Reference Laboratory; NSW State Enteric Reference Laboratory; Specialist Bacterial Identification Laboratory; Mycology Laboratory; Parasitology; Molecular Biology; Emerging Infectious Diseases and Biohazard Response Unit; Pneumococcal Reference Laboratory; Culture Collection; and Research Units.

Greg has more than 27 years' experience in medical microbiology specialising in molecular diagnosis of infectious diseases and organism characterisation. He leads a team of 36 scientists in the RLS providing expert microbiology services and consultation to hospitals, institutions, government agencies and other laboratories in NSW and Australasia. The RLS regularly investigates outbreaks of disease in the community, has methods ready to detect and identify emerging infectious disease agents, and performs laboratory investigations on samples from Police Forensic Services for the presence of bioterrorism agents for NSW.