DESIGN OF RADIOCHEMICAL LABORATORIES FOR USE IN PHARMACEUTICAL RESEARCH

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During the development of new drugs extensive use is made of labelled compounds to study their absorption, distribution and metabolism. At the Wellcome Research Laboratories, these novel compounds are synthesised in a radiochemical facility that has been incorporated into a modern purpose built medicinal chemistry building. The facility has an area of approximately $10m^2$ and consists of a large laboratory with controlled access and a separate office suite. It has been designed to safely handle up to 9.25 GBq of ^{14}C labelled compound per synthesis and to comply with the UK Ionising Radiations Regulations 1985. Five syntheses can be carried out at any one time.

The laboratory has been designed as a containment area in which the air pressure is always below ambient. Access is through an airlock entry in which there are changing and decontamination facilities. There is a separate entry to the office area which is partitioned off from the laboratory with glazed panels so that continuous observation of the activities in the laboratory is possible. Work surfaces, fume cupboards and unit furniture are of materials capable of resisting the solvent based cleaners used for decontamination. There are 2 'walk-in' safety cabinets for tall apparatus and three fume cupboards. The laboratory floor is bunded 4" below the office and adjacent area to contain any liquid spills. It is covered with a flexible 2mm heavy contact polyvinyl sheet with welded seams, which is impermeable to aqueous solutions but not all organic solvents. The walls are spray painted and finished with polyurethane lacquer to give a wipe clean finish. All joints are sealed with a smooth finish silicone mastic to avoid crevices where contaminants could accumulate.

SYSTEM OF ENTRY AND EXIT

The laboratory is entered through an airlock which has electromagnetic interlocks fitted to the doors to prevent both being open at once as the laboratory is maintained at slight negative pressure to prevent contamination of adjacent areas. Within this airlock there are electronically controlled washing facilities and hand drier so that hands may be cleaned without touching taps or towels. Changing facilities and a radiation monitor are located within this area. A step over bench is placed in the middle of the lobby. It is constructed of melamine covered chipboard and incorporates a shoe rack. In case of a failure of the interlock system or other emergency, breakglass alarm points are present which activate a local alarm/flashing light and relay the alarm state to the Building Management System.

THE WORKBENCHES

The laboratory furniture comprises cantilever framed supports with solid epoxy resin work surfaces, dished to contain any spillage. Flexible metal underbench units are suspended below to facilitate easy floor cleaning. The cupboards and drawers are painted steel for easy cleaning and in extreme situations the paint can be stripped off with the contaminant and cabinets repainted. Similarly the resin tops are impermeable to most chemicals but in exceptional cases of contamination the surfaces can be sanded down and repolished.

THE WASTE DRAINAGE SYSTEM

All sinks discharge into a borosilicate glass drainage system. For ease of maintenance the drains from each half of the laboratory pass to vertical voids on either side of the laboratory. The drainage system has been routed so that it enters the main drain of the building at the lowest practicable point. This maximises the dilution factor for radioactive residues and minimises the risk of reflux into other areas should a blockage occur in the system.

THE SAFETY CABINETS

Each fume cupboard is constructed with a double skin. The outer skin is zinc coated steel finished with an epoxy powder coating. The inner skin is a stainless steel shell produced in one piece with no seams and all curves are smoothed to prevent radioactive materials adhering to sharp edges or corners. There is a glazed top panel with anti-glare lighting giving excellent illumination of the work zone. The work top is heavy gauge stainless steel with reinforcing bars on the underside so that it supports the shielding and equipment with minimum deflection.

The sash is 6mm laminated safety glass with an epoxy coated steel frame. It is counter balanced by weights running in guides and suspended on stainless steel cables over nylon pulleys with a fail-safe device in the event of cable failure. The sash is fitted with an adjustable stop limiting the opening to the optimum height of 500mm, with a warning light on the control panel which indicates when this height has been exceeded. When closed the sash can be locked so that radioactive material can be kept secure in the fume cupboard rather than taken to store every night.

Uniform airflow characteristics at the working area are achieved by streamlining the entrance faces of the cupboard. The design incorporates an automatic by-pass to eliminate high face velocities at lower sash openings. The average face velocity is 0.75m/s at 500mm opening height.

Each fume cupboard is fitted with flow sensors and electrically operated airtight dampers. If the sensors indicate that the extraction has failed the dampers will automatically close to prevent reverse airflow through the

fume cupboard. These dampers will also close in the event of power failure so that radioactivity is contained within the cupboards and the exhaust systems. Each fume cupboard is separately ducted to roof level and thence, through filters and silencer, to the atmosphere.

All the services are controlled from the panels mounted at the side of each cabinet. The services available are electricity, water, steam and most routine gases such as nitrogen, hydrogen, oxygen and helium. Vacuum is generated for each cupboard and is independent of the general vacuum system for the building.

STORAGE OF CHEMICALS

Located between the fume cupboards are vertical steel pull out cupboards ventilated by the fume cupboard extraction system. These vertical cupboards are provided with racking and trays for storage of containers of various sizes and are mounted on pantograph drawer gears. Ventilated lockable flammable solvent storage cupboards are positioned under the fume cupboard work tops.

THE ENVIRONMENTAL CONTROL AND MONITORING SYSTEM

For safety reasons, the air supplied to the laboratories in the medicinal chemistry building cannot be recirculated. To limit the substantial costs of preheating and circulating the air, the environment is controlled by the Building Management System computer and separate air-handling units are dedicated to each laboratory. The air-handling plant is located on each floor to facilitate the distribution of ducts and to minimise the fire risk. The computer is programmed to continuously monitor the air-conditioning demands. Thus, in the radiochemical laboratory, as the number of fume cupboards in use increases or decreases, the computer balances the input air with the rate of extraction. The flow of air in the laboratory is from the ceiling plenum through the perforated steel ceiling tiles and out through the fume cupboards. Although the cupboards can be controlled manually, the computer has overall control which ensures that at all times at least two fume cupboards are operating in order to maintain the negative room pressure.

A series of sensors within the system monitor the performance of the plant and status reports are produced by the Building Management System. An immediate warning is given when plant failure causes loss of negative pressure, failure of fume cupboard extract or failure of the labelled compound cold stores. Further alarm systems monitor the gas supplies to the fume cupboards, the integrity of the fire escape door and the airlock.

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