PART C: APPROACHES TO THE DESIGN OF CLEAN AIR HANDLING FACILITIES FOR RADIOPHARMACEUTICALS

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1. Introduction

Manufacturing, handling and administering processes of radiopharmaceuticals have to meet the requirements of both the fields viz. "radio" activity and "pharma" activity. Both these fields often dictate conflicting requirements. A step by step analysis of these conflicts can lead to practices reasonably acceptable to both the fields.

2. Engineering concepts of radiation protection

- radiation shielding against direct/reflected streams
- single/multiple containment of the radioactive material
- prevention of escape of radioactivity from the containment to the surroundings
- maintenance of negative pressures within the containment
- air flow from low activity areas to high activity areas
- controlled release from containments to the atmosphere after appropriate treatment

The discharge has to be filtered, cleaned and decontaminated before release.

3. Concepts and practices for pharmaceuticals

Salient engineering features in which the pharmaceutical field differs from radiation field are, as follows

- The product has to be shielded from impact of external surroundings w.r.t. parameters like heat, humidity, dust, microorganisms, viruses or any other contaminants.
- Containment/isolation is also needed for pharmaceuticals, but these have to be at positive pressure.
- The containment has to be kept clean and sterile so that the product does not get contaminated.
- Fresh, filtered, treated, clean and sterile air has to be pumped into the facility.
- Air is allowed to flow from cleanest to cleaner zones and then to clean zones.

4. Toxic/hazardous/biologically unsafe pharmaceutical products/process

- Some pharmaceutical products/processes are considered toxic & hazardous if spread to working area. Research, fermentation, processing of some bacteria/viruses are considered biologically unsafe.
- Biosafe laboratories, cabinets and manufacturing plants and processes have been evolved to meet the needs of such pharmaceutical products.
- * Sterility is important & essential for processing many fermentation processes. At the same time escape of the process constituents to surroundings can be hazardous.
- * Some such arrangements are shown in the slides. These are very close to radioactive labs/hot cells/glove boxes etc.

- These concepts have paved a way towards working out strategies for handling & processing radio/pharmaceuticals.

5. Manufacturing, handling and administering processes for radiopharmaceuticals

- Above processes of radiopharmaceuticals have to meet the requirements of both field viz. radioactivity and pharma activity

- Conflicting requirements of these two fields have already been brought out. Some acceptable engineering solutions to meet the 'conflicting' requirements can be worked out.

- Schemes that could be considered for radiopharmaceutical laboratories, as given in Figs 3-5.

6. Basics to be looked into for framing GRP

- Construction features of R.P. plants can generally follow the GMP for pharmaceuticals, since the requirements of cleanability, washability, disinfection, non-permeability, withstanding the weathering effects, prevention of accumulation and growth of contaminants, microbes, bacteria, etc. are similar.

- Double door/air locked accesses, material hatches, gowning areas, isolation housings etc. should also be similar to pharmaceutical GMP.

- Philosophy of multiple containment may have to be adopted wherever required after incorporating all engineered features which will overcome the 'conflicts' of positive and negative pressures, inward and outward air flow directions, shielding requirements, etc.

- Maintenance of desired class of cleanliness/sterility underlines the need of enveloping the working areas by surroundings of suitable grades.

- This should be considered in the layouts vis-à-vis the flow of materials and personnel and as functionally required by the process demands.

- Detailed flow sheets for the manufacturing process of each radioisotope and radiopharmaceutical right from its loading/unloading into a nuclear reactor or cyclotron, decapping, handling through various plants and hot cells, sterilization, packing and dispatch, reopening and reprocessing at a user's end or hospital, if any, should be available.

- All the nodes where the product can get exposed to atmosphere should be very clearly indicated on the flow sheets.

- While all properties and sterility of fluids and services entering the production process are carefully looked into by manufacturers it is noticed that said nodes, which can cause contamination, are sometimes not identified.

- Sterilization steps also should be mentioned on the flow sheet, with specific

identification of terminal sterilization.

- Requirements of quality of surroundings/services before sterilization are often guided by the functions of the product, hence are normally taken care by the manufacturer himself.

- Processes after sterilization demand aseptic handling and call for more stringent quality control over surroundings. Such exposures are critically important for both the manufacturers and health authorities.

- Austerity and aesthetics would generally demand that last cover should not be below a class 100,000.

- Cosmetic maintenance & landscape development also plays a major role.

- The disciplines and culture of pharmaceutical and other types of clean rooms must be followed for radiopharmaceuticals as well.

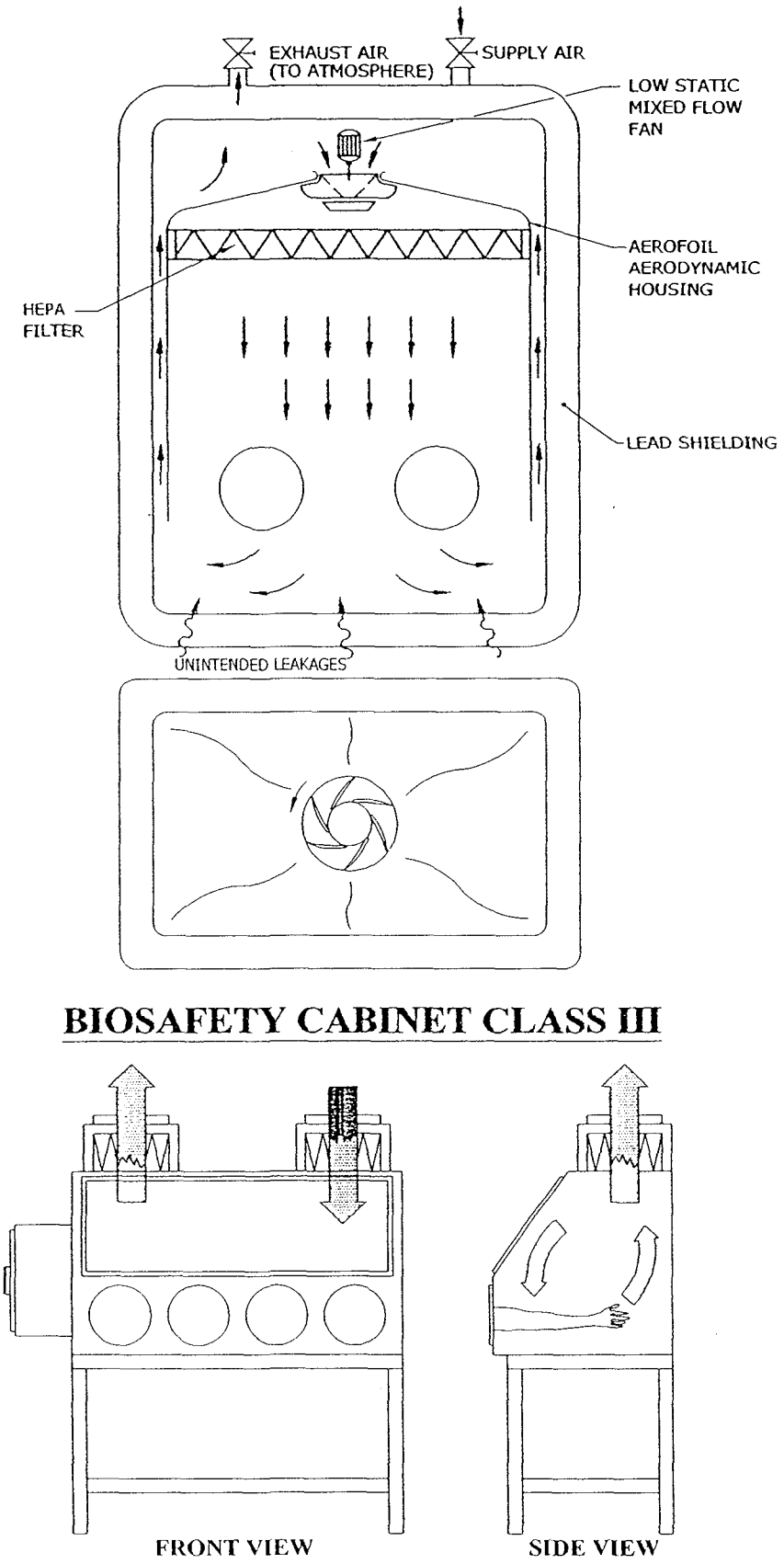
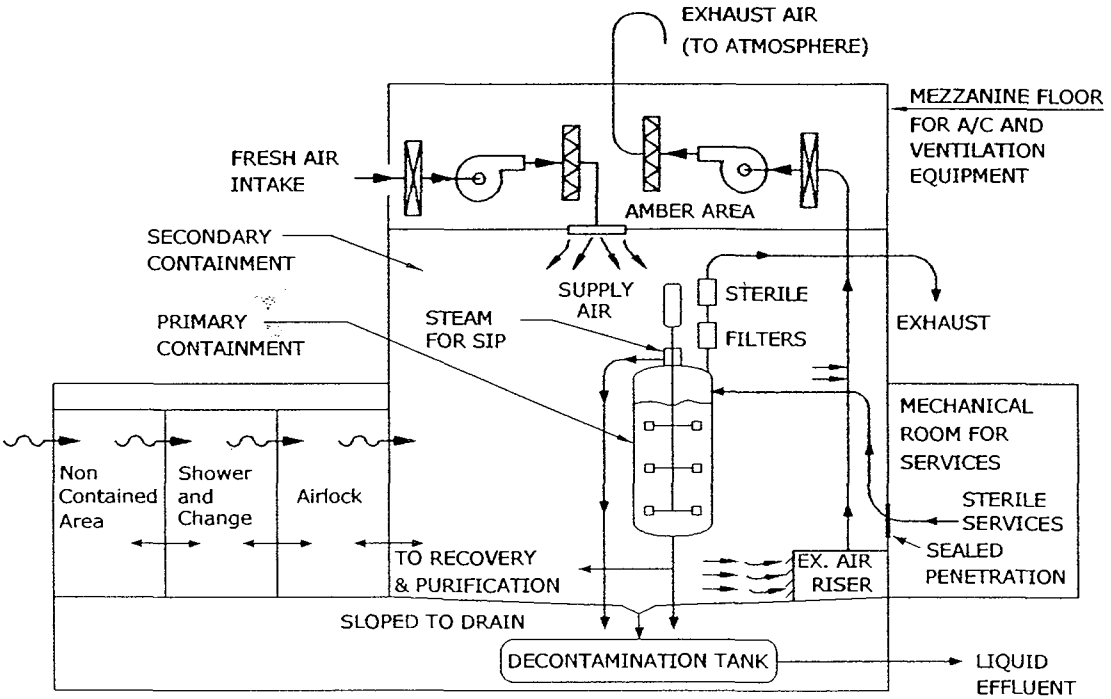
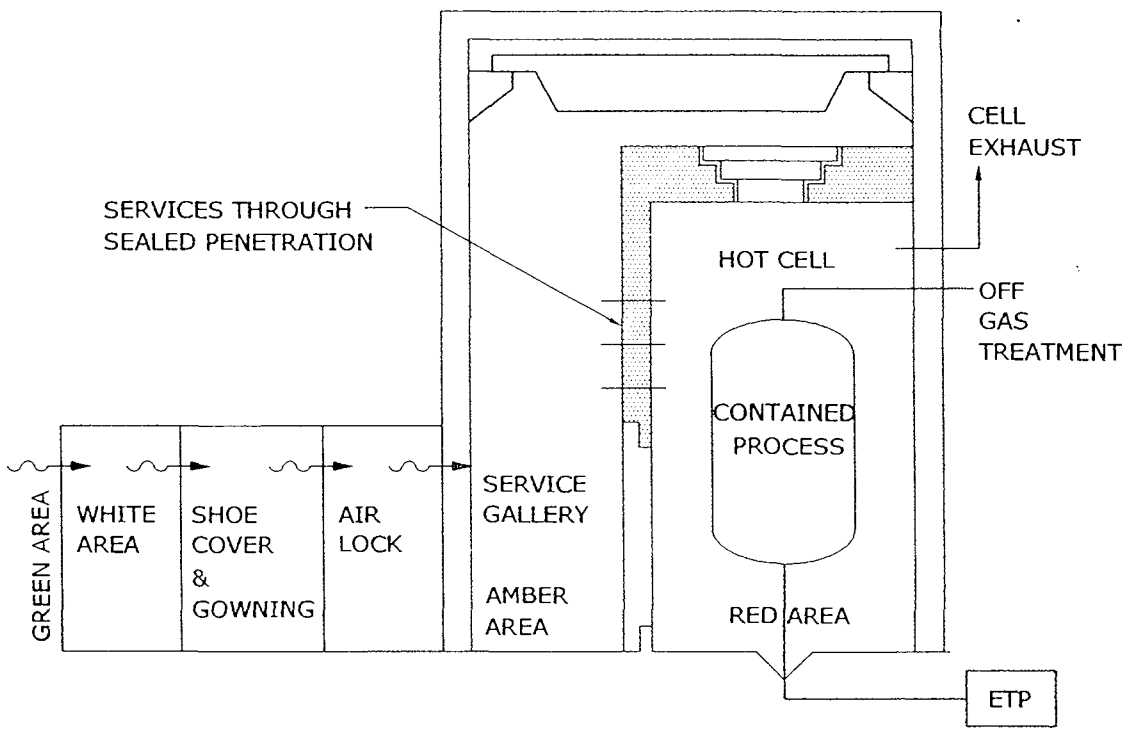


FIG. 3. Air flow schematic for chemistry module.





TYPICAL RADIO-ACTIVE PROCESSING LABORATORY

SEE THE CLOSE COMPARISON WITH BIO CONTAINMENT FACILITY

NOTE THE MAIN DIFFERENCE REGARDING STERILITY REQUIREMENTS

FIG. 4. Comparison of biocontainment and radioactive facilities.

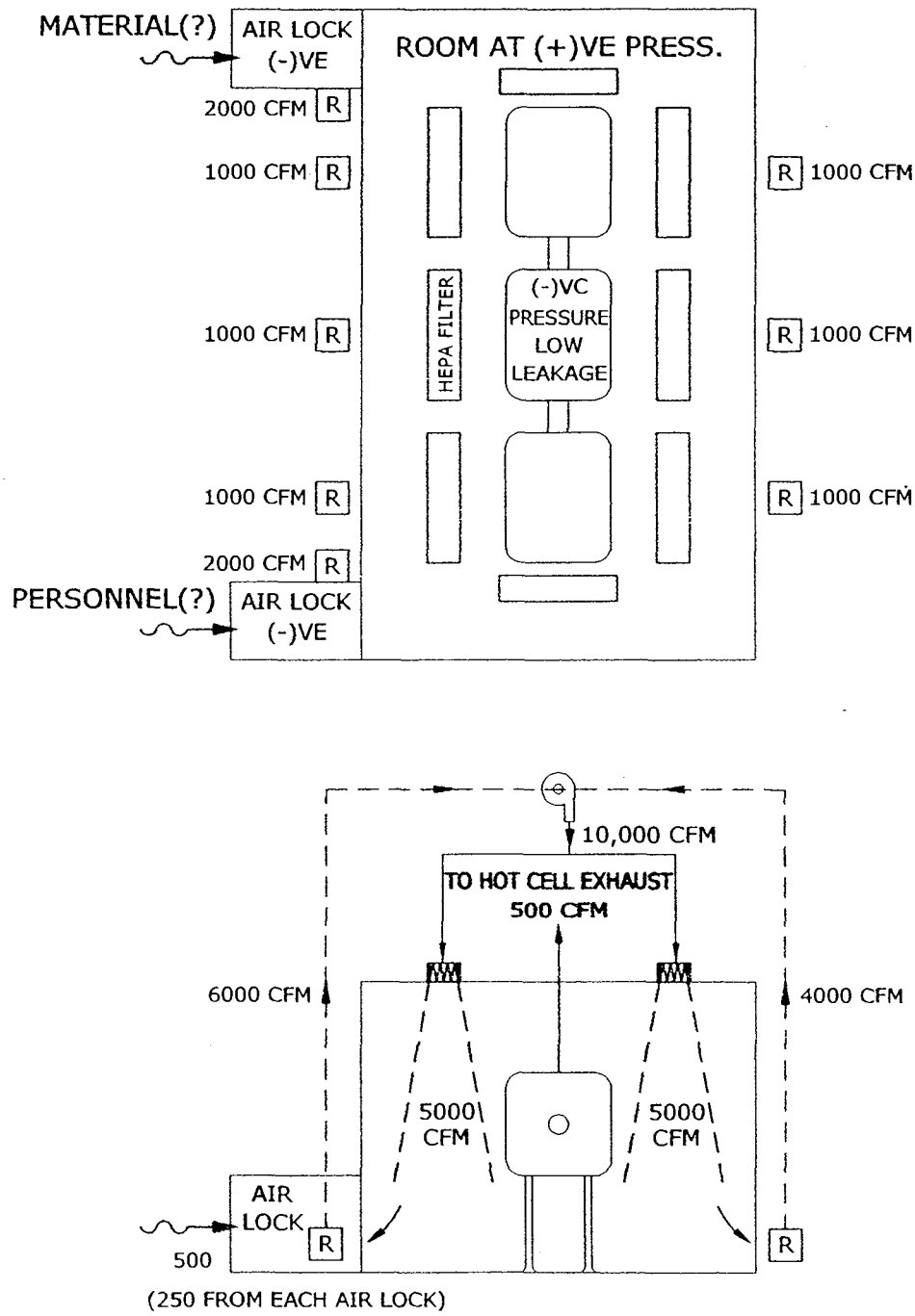


FIG. 5. Suggested lay-out/air flow pattern for radiopharmaceutical production in cells.