DISSERTATION

Implementation of an Aseptic Service for Radiolabelling of Autologous Blood Cells at the Department of Nuclear Medicine, Dr George Mukhari Hospital

In partial fulfilment of the requirements for the

MSc (Med) (Pharmacy)

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DECLARATION

I, **Ignecious Miyelani Maringa**, hereby declare that the work on which this study is based is original, except where acknowledgements indicate otherwise.

This dissertation is submitted for the degree Master of Science in Medicine (Pharmacy) at the University of Limpopo, Medunsa Campus. Neither the whole work nor any part of it has been submitted before for any degree or examination at this or any other university.

Signed……on the……day of……..

DEDICATION

“I dedicate this work to Eneto Maringa and my parents.”

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ABBREVIATIONS AND ACRONYMS

ACD-A	Anticoagulant Citrate Dextrose Formula A
ASSIG	Aseptic Services Specialist Interest Group
AHU	Air Handling Unit
CEO	Chief Executive Officer
cGRPP	Current Good Radiopharmacy Practice
DCI	Data Collection Instrument
DGMH	Doctor George Mukhari Hospital
DOH	Department of Health
DGMH	Doctor George Mukhari Hospital
EU GMP	European Good Manufacturing Practice
FDG	Fludeoxyglucose
FGD	Focus Group Discussion
Ga	Gallium
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
GrPP	Good Radiopharmacy Practice
HEPA	High Efficiency Particulate Air
HOD	Head of Department
IAEA	International Atomic Energy Agency
ISO	International Standards Organization
ISORBE	International Society of Radiolabelled Blood Elements
LAF	Laminar Air Flow

MCC	Medicines Control Council
MCREC	Medunsa Campus Research, Ethics and Publications Committee
mIBG	Meta-iodobenzyl guanidine
MSc	Masters of Science
NECSA	Nuclear Energy Corporation of South Africa
NHLS	National Health Laboratory Services
NSF/ANSI	National Science Foundation/American National Standards Institute
NSPQAC	National Sciences Pharmaceutical Quality Assurance Committee
OL	Operational Level
PET	Positron Emission Tomography
QA	Quality Assurance
QASIG	Quality Assurance Specialist Interest Group
QC	Quality Control
RBC	Red Blood Cell
Rhe	Rhenium
SAEB	South African Atomic Energy Board
SAPC	South African Pharmacy Council
SOP	Standard Operating Procedures
SREC	School Research and Ethics Committee
Tc	Technetium
^{99m}Tc	metastable Technetium-99m
UL	University of Limpopo
UR LLE	University of Rochester Laboratory for Laser Energetic

UKRG	United Kingdom Radiopharmacy Group
USP	United States Pharmacopeia
VLAF	Vertical Laminar Airflow
WBC	White Blood Cells

ABSTRACT

Introduction:

The Department of Nuclear Medicine at Dr George Mukhari Hospital (DGMH) received a biological safety cabinet (Laminar airflow hood - LAF) as a donation from the International Atomic Energy Agency (IAEA) in 2007, for the specific purpose of preparing radiolabelled blood cells. The laminar airflow hood was installed but has never been commissioned for use. Radiolabelled white blood cells are used in a range of Nuclear Medicine applications related to infection and pyrexia of unknown origin. Correct handling of the blood is essential for both patient and operator safety. A laminar airflow procedure is required for the radiolabelling of autologous blood. Therefore, there was a need to further investigate the guidelines for radiolabelling autologous blood cells with a view to commissioning the LAF and implementing a service for radiolabelling of autologous blood elements.

Objectives:

1. Identify the equipment
2. Identify and development of the SOPs
3. Implement aseptic services to radiolabelling blood cells.

Method:

The study was conducted at the Department of Nuclear Medicine, Dr George Mukhari Hospital. The design of the study was prospective, descriptive and interventional. Data were collected through independent (objective) observation, questionnaires (subjective). In order to involve staff in the implementation of aseptic services in the respective department a focus group discussion (FGD) followed. The International Atomic Energy Agency (IAEA); Operational Guidance on Hospital Radiopharmacy and United Kingdom Radiopharmacy Group (UKRG) Guidelines were consulted to identify equipment and operational standards required.

Permission to conduct the study was obtained from the Head of Department of Nuclear Medicine and Chief Executive Officer (CEO) of the Hospital. The proposal was approved by the Medunsa Campus Research and Ethics Committee (MCREC).

Results:

Premises: The room in which the LAF is situated is not in use as a clean room; hence few of the IAEA infrastructure and LAF requirements were met. Only, three aspects (18.75%) were compliant (type of LAF, lighting and dedicated equipment availability) and thirteen (81.25%) were not. For the hot lab only two (16.67%) of the fourteen items regarding structure and facilities were compliant, twelve (83.33%) were not (e.g. access, layout, cleanliness levels). The short term plan devised is to partition the area in which LAF is currently situated into a clean room and change room, seal the ceiling and windows, paint and ensure that walls, floors and surfaces are smooth and impervious in both the clean room and hot lab. The cost of alterations is (+/-) R50 000. The long term plan is to obtain funds (approximately R960 000) for the full development of the aseptic suite which will comply with local and international standards for radiolabelling of autologous blood cells recommended by ISORBE.

Environment and Personnel: None of the four survey items on environment was compliant for the clean room (e.g. air not filtered, no temperature or humidity monitoring or control). Only in the hot lab was the temperature monitored. The LAF/clean room is not currently in use. In the hot lab, gowns and overshoes are not available. The plan is to have thermometers installed in both the clean room and hot lab and have log books for recording temperature.

Microbial Contamination: In the Department, monitoring of microbial contamination is not performed. The IAEA recommends that surfaces, environment and equipment should be monitored for microbial contamination in an area where sterile products are handled.

Staff Training & Improvement of Aseptic Services: Two staff had been trained in aseptic admixing. All eight respondents agreed that training on aseptic handling of radiopharmaceuticals is necessary.

Hygiene and SOPs: Six respondents rated hygiene as satisfactory and two as not satisfactory. Despite these views, all felt that hygiene should be improved in the hot lab and that standard operating procedures (SOPs) should be developed. A group

was set up to develop SOPs. Four SOPs were developed - cleaning the clean room and LAF, hand washing, gowning/degowning and leukocyte radiolabelling.

Radiolabelling of Autologous Blood Cells: Doctors in the Department want this service to help with the diagnosis of pyrexia of unknown origin (PUO) and infections. Therefore, they were supportive to the researcher in the project set-up the processes and facilities for radiolabelling cells. The short term plan is to train staff in radiolabelling of autologous blood cells. The long term plan is to have the facility to set-up correctly to facilitate service provision and research.

Equipment: Staff mentioned that a centrifuge dedicated to the radiolabelling of blood cells should be obtained to ensure that all the procedures for labelling blood cells are followed. The short term plan is to commission the LAF (Cost: approximately R15 000 including VAT) and obtain a cooled centrifuge with sealable buckets (Cost: approximately R40 000 including VAT) for the purpose of commencing with the radiolabelling of blood cells service in the Department.

Finance: Staff indicated that some of the problems in the department can be solved if they can obtain funding for infrastructure development. The short term plan is to have the budget for the upgrade of the facility included in the Departmental budget. And the long term plan is to obtain funds from the Gauteng Government for the full development of the facility

Conclusion: Required standards and guidelines for radiolabelling of autologous blood cells in a radiopharmacy unit have been identified. Therefore, the upgrading process of the facility should commence and SOPs developed should be implemented.

Recommendations: Necessary structural changes on the facility should be made to meet the local and international standards for radiolabelling blood products. Therefore, funds should be obtained for upgrading the facility and obtain the necessary minimum equipment for radiolabelling of autologous blood cells. It is recommended that a post for a radiopharmacist be created to increase capacity and help improve standards with regards to pharmaceutical services in the Department.

CHAPTER 1
INTRODUCTION

1.1 INTRODUCTION

A radiopharmaceutical is defined as any pharmaceutical preparation that includes a radionuclide in its composition (i.e. a chemical moiety and a suitable radionuclide which acts as signal detector). They can be used for the diagnosis and/or therapeutic treatment of human diseases (Theobald, 2011). Many radiopharmaceuticals are administered parenterally to patients. Their preparation requires that the operator (pharmacist or radiographer) be protected from radiation exposure during their preparation, but also that the product is suitable for intravenous administration (i.e. sterile as well as particle- and pyrogen-free) (ISO, 2000). For some nuclear medicine purposes (e.g. the diagnosis and treatment of inflammation, infection and haematopoietic diseases) blood products are radiolabelled. In the latter case, there is a further requirement that neither the operator nor the blood should become infected through inappropriate handling of the blood samples (Theobald, 2011).

The Department of Nuclear Medicine at Dr George Mukhari Hospital (DGMH) received a biological safety cabinet (Laminar airflow hood - LAF) as a donation from the International Atomic Energy Agency (IAEA) in 2007, for the purpose of preparing radiolabelled blood cells. The laminar airflow hood was installed but has never been commissioned for use.

1.2 PROBLEM STATEMENT AND RATIONALE FOR THE STUDY

A senior consultant at Department of Nuclear Medicine at DGMH was awarded a fellowship to study radiolabelling of autologous blood cells. The staff of Department of Nuclear Medicine would like to perform radiolabelling of blood cells for diagnosis of various diseases. The LAF in the Department is not currently used for labelling of blood cells due to the lack of conditions which comply with the recommended standards (Theobald, 2011) for the aseptic handling of radiopharmaceuticals and blood products. As a result, no radiolabelling of blood cells can be performed. Therefore, there is a need to commission the LAF in order to implement aseptic

services for radiolabelling of autologous blood cells in Nuclear Medicine Department at DGMH.

1.3 AIM OF THE STUDY

To identify the equipment and operational standards required, for commissioning the laminar airflow hood in the Department of Nuclear Medicine at DGMH and then to implement the aseptic services required for radiolabelling of autologous blood cells.

1.4 OBJECTIVES OF THE STUDY

The objectives of the study were as follows:

1. To describe the aseptic equipment and laboratory conditions that are in place at the Department of Nuclear Medicine DGMH in the area where the LAF is currently situated.
2. To identify best practice standards for a situationally-relevant process for radiolabelling of autologous blood cells at the Department.
3. To identify the equipment and laboratory conditions that are required for radiolabelling of autologous blood cells.
4. To produce an action plan and budget for the introduction of the service and to ensure that the required structure and equipment is in place, in order for radiolabelling of autologous blood to be carried out.
5. To monitor microbiological and particulate contamination and ensure that aseptic conditions are achieved within the laminar flow hood.
6. To develop (collaboratively with Nuclear Medicine staff) standard operating procedures (SOPs) for radiolabelling of autologous blood cells.
7. To ensure operator training in blood cell labelling.

CHAPTER 2
LITERATURE REVIEW

2.1 INTRODUCTION

In this chapter, the subheadings that will be discussed are as follow: radiopharmacy and radiolabelling of blood cells and practical considerations for radiolabelling of autologous blood cells.

2.2 RADIOPHARMACY

Radiopharmacy is defined as the science and art of the design, preparation, quality assurance and clinical pharmacy of radioactive medicines called radiopharmaceuticals (Theobald, 2011).

Nuclear pharmacy is also considered to be a speciality that ensures that health is promoted and improved by ensuring the safe and effective use of radiopharmaceuticals. However, today the focus is on pharmaceutical care to monitor the safety of patients for using these products (Ponto & Hung, 2000).

Radiopharmaceuticals are governed by four different sets of regulations in South Africa (SA), i.e. The Nuclear Energy Act (Act No. 49 of 1999), Hazardous Substance Act (Act No.16 of 1973), Medicines and Related Substances Act (Act 101 of 1965, Section 22C, Regulation 19) (Government Gazette, 1999) and also South African Atomic Energy Board (SAEB) regulations (iThemba Laboratories, 2011). The International Atomic Energy Agency (IAEA) is the international body that sets out guidelines to provide best-practice recommendations and guidelines for many aspects of nuclear safety. In the area of health, they provide guidance for Nuclear Medicine and Radiopharmacy practice in an attempt to promote safe and professional handling of these radioactive materials (IAEA, 2008a).

Radiopharmaceuticals find their applications in diagnostic imaging techniques and also for therapeutic purposes in the treatment of various diseases (Theobald, 2011).

The procedures in which radiopharmaceutical products are administered intravenously necessitate the production of radiopharmaceuticals that are sterile and

pyrogen-free as well as appropriately shielded. Therefore, facilities in which these products are handled should be very specific to radiopharmaceuticals in order to comply with these requirements (IAEA, 2008b). Winfield and Richards (2004), recommends that the preparation of sterile and pyrogen-free product should be carried out aseptically in a laminar airflow hood situated in a clean room or isolators (Winfield & Richards, 2004; ISO, 1999; ISO, 2004). In addition, there is a need to protect the operator from the dangers of radiopharmaceutical handling, through the provision of a biological safety cabinet with lead glass shielding (Qatyana, 2011).

There is an attempt to standardise parameters worldwide with regard to the design, environmental conditions and processes for radiopharmacy facilities where autologous blood cells are radiolabelled (Rodrigues *et al.*, 1999; ISO, 2001).

This standardised approach is designed to ensure that personnel responsible for handling blood products follow all the procedures necessary to protect these products since they are re-injected intravenously (Soroa *et al*., 2009)

2.2.1 Operational levels in Radiopharmacy

The IAEA operational levels in hospital radiopharmacy which cover all the processes that are performed in a radio pharmacy unit (IAEA, 2008b) are as follows.

Operational level 1a

This operational level covers the dispensing of radiopharmaceuticals purchased or supplied in their final form. However, radiopharmacies which are recognized and/or authorized manufacturers or centralized radiopharmacies should be sources of these products. Only unit doses or multiple doses should be handled and no compounding is required.

Operational level 1b

This level involves the dispensing of radioiodine and other ready to use radiopharmaceuticals, mainly used for radionuclide therapy or palliative care. Ready to use injections of strontium and samarium for pain palliation are examples included in this level.

Operational level 2a

Operational level covers “closed procedures”, where preparation of radiopharmaceuticals from prepared and approved reagent kits, generators and radionuclides are done. The most common activity in nuclear medicine departments is with the routine use of a technetium generator and reconstitution of pre-sterilized radiopharmaceutical cold kits.

Operation level 2b

The level involves radiolabelling of autologous blood cells widely used for inflammation and infection (i.e. red blood cells, platelets and white blood cells are the most commonly used cells).

Operational level 3a

Involves “open” procedures where compounding of radiopharmaceuticals from ingredients and radionuclides for diagnostic application is performed. For example: modification to existing commercial kits; in-house production of reagent kits from ingredients, including freeze dried operation; related research.

Operational level 3b

This operational level involves the compounding of radiopharmaceuticals for therapeutic purposes from ingredients and radionuclides with related research and development. Some of the examples of these radiopharmaceuticals include radio-iodination of Meta-iodobenzylguanidine and rhenium labelled lipiodol.

Operational level 3c

Operational level 3c covers the synthesis of positron emission tomography (PET) radiopharmaceuticals. This includes the increasingly popular fluorodeoxyglucose (^{18}F) injections (FDG).The compounding of radiopharmaceuticals produced from unauthorized or long lived generators such as gallium (^{68}Ga) or rhenium (^{188}Re) mostly related to research and development.

Hence radiolabelling of autologous blood elements falls under Operational level (OL) 2b. The IAEA recommends that all OL 2b activities should be carried out in a Grade A (Class 100) clean area (i.e. under laminar flow).

2.2.2 Radiopharmacists

Radiopharmacists are pharmacists who have the specialised education and training required to handle radiopharmaceuticals and radioactive material. Responsibilities of radiopharmacists include the following areas: planning and design of radiopharmacy units; preparation and compounding radiopharmaceuticals, quality assurance and quality management. Radiopharmacists also perform radiolabelling of autologous blood cells. (Lagebo, 2009; Rubow & Eiselen, 2009). The South African Pharmacy Council describes scope of practice of the radiopharmacist as follows (SAPC, 2009):

- Perform acts and services specially pertaining to the profession of a pharmacist
- Take a leading pharmaceutical role in protocol and guideline development in nuclear medicine
- Act as a leading pharmaceutical partner within a multi professional health care team in nuclear medicine
- Develop, implement, evaluate and provide strategic leadership for radiopharmacy services
- Appraise information, make informed decisions regarding supply and use of radiopharmaceuticals with the evidence available and be able to justify/defend the decisions
- Develop policies and procedures specifically for the specialty area

- Provide education and training related to radiopharmacy
- Perform research, teach and publish in radiopharmacy

Radiopharmacists have a potentially major role in Quality Control (QC) and Quality Assurance (QA) of radiolabelled blood cells in Nuclear Medicine Departments. Departments with QA programmes in place promote rendering of services that are of high quality since all the services and processes performed are validated (Sharp *et al.*, 2005).

2.3 RADIOLABELLING OF BLOOD CELLS

The most commonly radiolabelled autologous blood cells include erythrocytes, leukocytes, platelets and lymphocytes. However, individual components of the blood may be labelled with various radionuclides (e.g. ^{99m}Tc, ^{131}I, ^{51}Cr and ^{111}In) to help obtain the information which will assist in the diagnosis and treatment of various inflammatory and infectious diseases. The labelling of blood cells should be done in an environment that will eliminate the risk of possible contamination of the blood specimens by the operator or the environment (United Kingdom Radiopharmacy Group, 2009).

2.3.1 Uses

Radiolabelling of autologous blood cells provides a solution in diagnosing infections and inflammatory disorders in Nuclear Medicine Departments. The use of radiopharmaceuticals helps with the visualisation of various steps in inflammatory processes i.e. infectious and non-infectious inflammation. However, scintigraphic imaging of inflammation can be done in two possible ways, (1) utilise the locally enhanced vascular permeability by injecting radiolabelled molecules at the site of infection or inflammation which shows increased extravasation: (2) exploitation of the diapedesis and chemotaxis of leukocytes, either by radiolabelling white blood cells of the patient in vivo or directly targeting leukocytes antigens (Theobald, 2010).

Structural and physiological imaging can be used for diagnosis in Nuclear Medicine Departments, which can assist in detecting underlying conditions at an early stage and thus lead to a more positive prognosis (Society of Nuclear Medicine, 2009).

Examples of indications for radiolabelled autologous white blood cells include (Gutta, 2011; Roca, De Vries, Jamar *et al.*, 2010):

- Inflammatory bowel disease
- Intra-abdominal infection
- Osteomyelitis of the appendicular skeleton
- Diabetic foot
- Infected joint and vascular prostheses
- Neurological infections
- Fever of unknown origin
- Postoperative abscesses and endocarditis

There are two major aspects to be considered in radiolabelling of autologous blood cells: the environment (facility) and radiolabelling methods involved, which are both discussed below (Ramafi, 2012).

2.3.2 Radiolabelling Methods

There are six major methods used to label various individual components of blood, namely (Saha, 2004):

- Isotope exchange
- Introduction of a foreign label
- Labelling with a bifunctional chelating agent
- Biosynthesis
- Recoil
- Excitation labelling

These labelling methods together with the labelled compounds may be affected by many factors such as denaturation of labelled compounds, chemical stability of the radionuclide, and specific method of labelling (Saha, 2004).

The methods are categorised into direct and indirect labelling methods. The direct method involves the formation of either covalent or coordinate bonds between the radioactive atoms and the constituents atoms of the amino acid side-chain, whereas the indirect method relies on an intervening prosthetic moiety which is first conjugated to the protein or peptide (Rubow & Eiselen, 2009).

In South Africa, the most commonly used method is that of labelling with bi-functional chelating agent, which appears in summary below (Rubow & Eiselen, 2009).

Basic Method for radiolabelling of autologous blood cells in SA

1. Obtain blood sample with acid citrate dextrose anticoagulant (ACD-A)
2. Allow red blood cells (RBCs) to sediment
3. Transfer leukocyte-rich plasma into sterile test-tube(s)
4. Centrifuge to obtain leukocyte pellet
5. Remove plasma, re-suspend leukocytes in suitable medium
6. Add radionuclide and incubate
7. Centrifuge. Remove supernatant containing unbound radionuclide
8. Resuspend cells in plasma

2.4 PRACTICAL CONSIDERATIONS FOR RADIOLABELLING OF AUTOLOGOUS BLOOD CELLS

2.4.1 Facility

The facility for preparation of radiopharmaceuticals and radiolabelling of autologous blood cells should meet the standards stipulated in the Good Manufacturing Practice (GMP) and current Good Radiopharmacy Practice (cGRPP), and these standards require that the safety and quality of the products prepared or handled is met (Decristoforo & Penuelas, 2009).

Below are some of the parameters to be considered for a facility where radiolabelling of autologous blood cells is performed.

2.4.1.1. *Layout and design*

Both pharmaceutical manufacturing and radiation security regulations require that access to the radiopharmacy should be restricted only to the staff working in the pharmacy. In addition, access to clean areas should be restricted to personnel working in the clean rooms. The most important aspect is that the layout should allow an orderly flow of work in between the rooms (Ballinger *et al*., 2008). Figure 2.1 presents an example of a well-designed radiopharmacy:

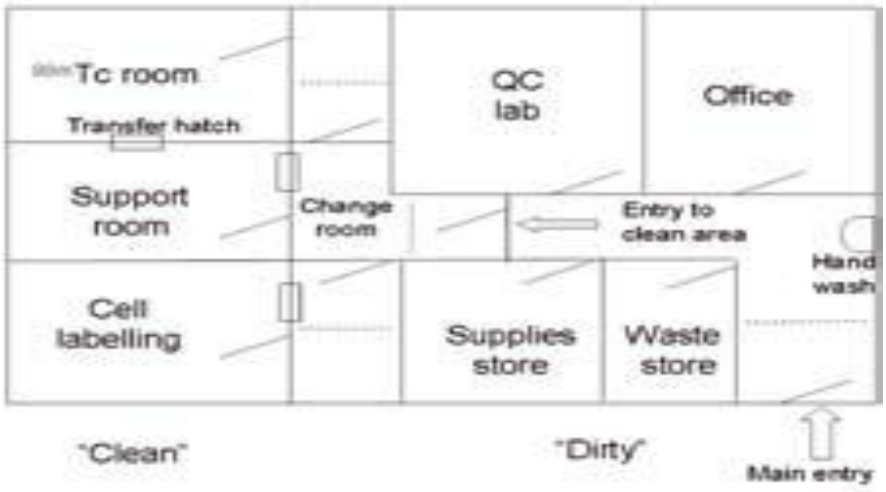

Figure 2.1: Example of a radiopharmacy layout (Ballinger et *al.*, 2008)

2.4.1.2. ***Equipment***

Vertical Laminar Airflow (VLAF) hoods should be installed for manipulation of autologous blood cells. Isolator technology can also be employed in situations where there are no clean rooms in place to render this service. However, the laminar airflow hoods and isolators should be commissioned before they can be used (Furguharson, 2010; Lazarus, 1999; .WHO, 2009).

A LAF or isolator and a cooled centrifuge with sealable buckets are examples of the minimum equipment required for radiolabelling of blood cells (IAEA, 2008a; Rubow & Ozker, 2012).

2.4.1.3. ***Surfaces, materials and services***

Walls, floors and ceilings in the clean rooms should be smooth, impervious and unbroken (i.e. free of cracks and exposed joints). In addition, the material used for surfaces should be easy to clean with cleaning agents and disinfectants. Gases and liquid pipes should be filtered before they can enter the clean rooms (Department of Health, 2005; IAEA, 2008a; ISO, 2001).

ISORBE recommends that the above parameters should be addressed in all facilities where manipulation of blood products is performed (Rodrigues *et al*., 1999).

In addition the IAEA recommends that all the benches in a radiopharmacy unit must be made of special steel with curved edges to contain any spillages in the unit and should be non-absorptive (IAEA, 2008b; ISO, 2001).

2.4.1.4. ***Environmental control and monitoring***

The environment in which radiolabelling of autologous blood cells is done should be carefully controlled as aseptic procedures are employed for the manipulation of these cells (ISO, 2004).

The different grades for clean areas are shown in Table 2.1below (EU Guidelines, 2008; ISO, 2000).

Table 2.1: Clean area standards – cross reference

Standards	Classification					
ISO 14644-1	3	4	5	6	7	8
AS 1386	0.035	0.35	3.5	35	350	3 50
BS 5295	C	D	E/F	G/H	J	K
Federal Standards 209E	1	10	100	1 000	10 000	100 000
EU cGMP	-	-	A/B	-	C	D

Sources: Cockroft, 2012; European Guidelines, 2008; ISO, 1999;

Grade A

- The local zone for high risk operations, e.g. filling zone, stopper bowls, open ampoules and vials, and making aseptic connections.
- LAF work station provides the environment required for the procedures performed in this grade.
- LAF systems should provide a homogeneous air speed in a range of 0.36 – 0.54 m/s (guidance value) at the working position in open clean room applications.
- A uni-directional air flow and lower velocities may be used in closed isolators and glove boxes in a grade A area.

Grade B

- Aseptic operations are carried out in this area e.g. preparation and filling of pharmaceutical products, this is the background environment for grade A zone.

Grade C and D

- Clean areas for carrying out less critical stages in the manufacture of sterile products.

Sources of microbial and particulate matter include inflow of external air, air supply of the room and production of contaminants within the room. Therefore, the contaminants should be minimized by considering the air supply, temperature, humidity, personnel, change room and cleaning in the clean rooms (Winfield and Richards, 2004). Furthermore, the quality of the environment where radiolabelling of these cells is performed should be monitored. Monitoring of aseptic units includes; air quality, air movement, air velocity, and airborne particulate and microbial contamination in the clean rooms (Winfield & Richards, 2004). Settle plates and swabs are used for assessing the level of microbial contamination. In GMP aseptic areas are grade A to D based on levels of microbial and particulate contamination (EU Guidelines, 2008). Table 2.1 below shows microbial contamination limits of an aseptic suite (ISO, 1999).

Table 2.2: Microbial contamination limits

Grade	Microbial contamination limits – operating clean room			
	Viable organisms / m^3 air	**90 mm settle plate / 4 hours**	**55 mm contact plate**	**Glove print (5 fingers)**
A	<1	<1	<1	<1
B	10	5	5	5
C	100	50	25	Not applicable
D	200	100	50	Not applicable

Source: (ISO, 1999)

The airborne particulate classification for these grades is given in Table 2.2 below.

Table 2.2: The airborne particulate classification for grades

Grade	At rest (b)		In operation (b)	
	Maximum permitted number of particles/m³ equal to or above (a)			
	0,5 µm	5 µm	0,5 µm	5 µm
A	3 500	1	3 500	1
B	3 500	1	350 000	2 000
C	350 000	2 000	3 500 000	20 000
D	3 500 000	20 000	not defined (f)	not defined (f)

Source: ISO, (1999)

2.4.1.5. ***Personnel and protection***

Staff working in radiopharmacies are exposed to radiation; hence, precautions to protect and monitor them should be in place. (Brooks, 2009; NECSA, 2006; York, 2002)

Staff radiation doses in the radiopharmacy are normally affected by three fundamental parameters, the distance between the staff member and the source, the time spent manipulating the source and the amount of shielding used to reduce the dose rate from the source. Hence, personal dosimeters (TLD, film badge, electronic dosimeter) and protective clothing (gown, gloves, face masks and goggles) should be worn by all personnel as radiation works (Ballinger *et al*., 2008; Zeissman *et al.*, 2006).

The IAEA states that all departments where radioactive materials are handled should ensure that personnel are protected at all times. This can be achieved by having programmes in place that ensure that the working environment is safe at all times (IAEA, 2007).

2.5 SOPs

SOPs are defined as authorized written procedures which give instructions for the performance of operations. They are not necessarily specific to a given product or material (e.g. equipment operation, maintenance and cleaning; validation; cleaning of premises and environmental control; sampling and inspection) (IAEA, 2010). Labelling of blood cells requires a number of procedures to be followed to ensure that the final products handled are sterile. Therefore, a number of SOPs should be developed prior to implementation of aseptic services. The staff working in this area should be able to write, control, revise and manage SOPs in order to render a service that is of high quality (Siddig, 2011).

CHAPTER 3
METHOD

3.1 INTRODUCTION

This chapter describes the methodology for the data collected on current practices for handling radiopharmaceuticals, aseptic practices and related Standard Operating Procedures (SOPs) in the Department of Nuclear Medicine, Dr George Mukhari Hospital.

3.2 STUDY DESIGN

The study was mixed methods, concurrent, practice research with descriptive and interventional aspects, using a facility checklist/ survey, personnel questionnaire and focus group discussion to collect both quantitative and qualitative data. The questionnaire administered was first completed by two radiopharmacy students to test the reliability of the questionnaire and also to determine the time required to complete the questionnaire.

The quantitative aspects for the facility survey included parameters such as:

- Premises compliance
- Environment control
- Personnel competence and safety

The qualitative aspects included:

- Hygiene status of both the hot lab and Laminar Airflow (LAF) area
- SOPs for admixing of the radiopharmaceuticals
- SOPs in place in the department
- Microbial and particle tests in place

The quantitative aspects for the Focus group discussion (FGD) included:

- aseptic services in the department
- SOPs for admixing radiopharmaceuticals
- aseptic handling of radiopharmaceuticals

The qualitative aspects of the FGD included all the opinions and suggestions made. Below is the overview of the entire study:

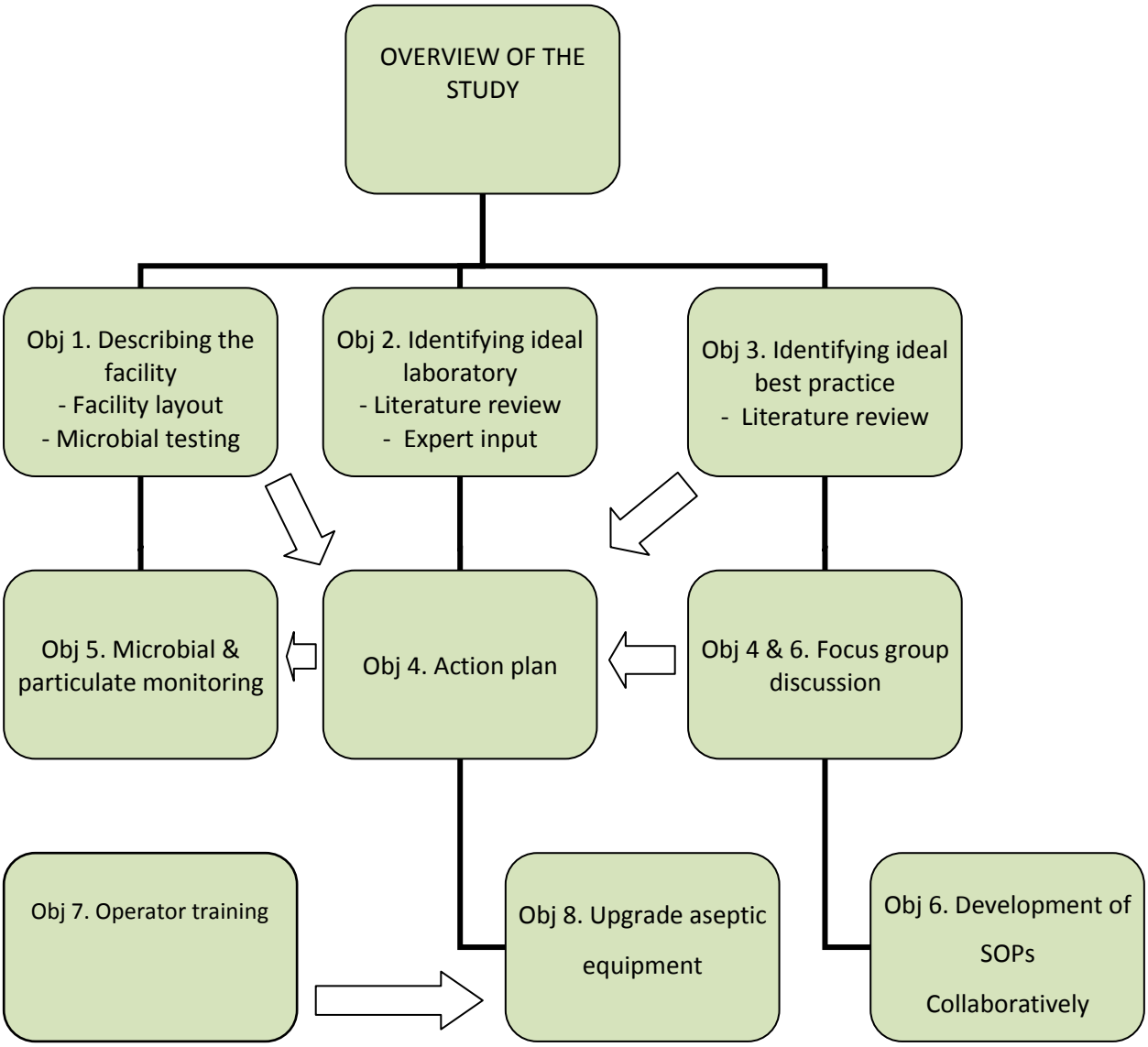

Figure 3.1: Overview of the study

(Refer to section 1.4)

3.3 STUDY SITE

The study was conducted at the Department of Nuclear Medicine, Dr George Mukhari Hospital (DGMH), Ga-Rankuwa, Pretoria, South Africa.

3.4 STUDY POPULATION

For Objective 1, the aseptic area of the Department of Nuclear Medicine DGMH was surveyed according to the Personnel Questionnaire **(**Appendix A).

For Objectives 4 and 6, all staff (one medical physicist, three radiographers and five doctors) involved in aseptic handling of radiopharmaceuticals in the Department, were invited to participate in the focus group discussion to provide the qualitative data.

3.5 SAMPLE SELECTION

For Objectives 4 and 6, no sample selection was done. All doctors, radiographers and the medical physicist working in the Department formed the population.

Inclusion and exclusion criteria

3.5.1 Inclusion criteria

The personnel that were involved in handling of radioactive material were included as participants in the focus group discussion.

3.5.2 Exclusion criteria

Staff that were not involved in aseptic handling of the radioactive material (e.g. Nurses).

3.6 DATA COLLECTION INSTRUMENTS

The data collection instruments (DCIs), facility survey form (see Appendix A) and personnel questionnaire (see Appendix B) were used to collect data in this study. The method of data collection is discussed below.

3.6.1 Survey form

Permission was obtained from the Head of the Department of Nuclear Medicine prior to commencing with the situational analysis in the Department. The situational analysis was intended to assess the compliance of the facility with required standards. The researcher and two colleagues commenced with data collection. The survey form (see Appendix A) with relevant elements to be addressed in the study was used by each researcher as data was collected in triplicate to avoid bias and also to strengthen the findings of the survey. The three data collectors started with the facility survey form on the same day, but rotated through different areas in the Department.

The facility checklist (see Appendix A) was completed in an unobtrusive way by the researcher and two colleagues, who were already familiar with staff of the Department. Hence, their presence was not seen as a threat.

At the end of the survey the other two data collectors handed their survey forms to the main researcher. Consensus was reached on each aspect. The findings of the survey were captured on a Microsoft Excel™ spreadsheet.

Data capture was according to each parameter addressed in the survey form in sequential order. Data were summarized and analyzed to assess the compliance of the Department in rendering radiopharmaceutical services.

3.6.2 Expert consultants

The researcher drew a rough floor plan of the relevant section of the Nuclear Medicine Department. The rough plans as well as the measurements were sent to the architect for a professional drawing to be produced.

Experts in clean rooms and aseptic services were consulted to assess structure and give input on what should be changed as well as the budget for the proposed changes.

The aseptic suite engineer requested the architect’s floor plan (see Figure 4.2) of the premises together with the measurements.

The experts consulted communicated their findings to the researcher as well as the supervisor, via emails. The experts gave comment on the following areas:

- The layout of the premises
- The walls and floors
- Ceiling
- Air quality and monitoring systems

3.6.3 Questionnaire

Once the facility survey was completed, the administration of staff questionnaires (see Appendix B) followed for collection of both qualitative and quantitative data.

The researcher with the aid of the supervisor and the other two researchers coordinated the administration of questionnaires to staff members, who took about an hour. All staff members (five doctors, three radiographers and one medical physicist) who took part in the study granted their permission prior to administration of the self-administered structured questionnaire (see Appendix B) by signing a consent form (see Appendix C). Staff members were then given the questionnaires to complete anonymously. The questionnaire administration session was specially arranged during tea break. After completing the questionnaire staff placed the questionnaire in a sealed box provided to facilitate confidentiality.

The responses were captured in a Microsoft Excel™ spreadsheet.

3.6.4 Microbial contamination

Study baseline microbial contamination in the LAF area was assessed using settle plates and swabs. The following materials were used to assess the level of contamination and type of microorganisms:

- 8 blood agar settle plates
- 8 nutrient broth settle plates
- 6 swabs (3 blood agar and 3 nutrient agar)

The settle plates were place in four different areas in the room, including the working surface of the LAF. They were all left in the room overnight and the following day they were collected, covers replaced and the plates were placed in two different plastic bags. Each plastic bag contained 8 settle plates labelled with the date, type of plate, station and name of the department. The first 8 settle plate (four blood and four nutrient agar) were taken for incubation (temperature = 35^{o} C) for a week at the Department of Virology. The second batch of four settle plates and four swabs (i.e. eight in total) were kept at room temperature for a week.

After a week all the settle plates were collected for reading the type of microorganisms that had grown and also the number of colonies per settle plate. The results were then recorded in the microbial contamination checklist (Appendix E).

3.6.5 Results feedback

Data collected were analysed by the researcher and supervisor prior to giving feedback to staff in the Department. After data analysis was performed, a presentation was prepared with all the findings of the study. The findings of this study were presented to staff in the Department at the appointed date and time before the Focus Group was conducted. The feedback session was coordinated by the researcher and two colleagues. He presented his results and answered questions that arose during the feedback session.

3.6.6 Focus group discussion

The FGD (Appendix D) was conducted by the researcher's supervisor who is experienced in facilitation of such groups. Due to logistical reasons, the FGD followed four weeks after the study findings were presented to staff at the appointed date and time. Staff members from the Department that availed themselves for the FGD were as follows:

- Head of Department (HOD)
- Two specialists
- Two registrars
- Three radiographers

- One medical physicist

The researcher, two colleagues and supervisor also formed part of the FGD.

To refresh the memories of staff members about the project, they were given summary results hand-outs of the project. The proceedings of the FGD were recorded with a digital recorder and summarised in writing.

3.7 DATA ENTRY AND ANALYSIS

3.7.1 Quantitative data from the personnel

A Microsoft Excel Spreadsheet was used to capture the data collected. Data analysis was descriptive, therefore, the results were summarized.

3.7.2 Quantitative data from the facility survey

The Excel® spreadsheet data was classified into categories such as compliant or non-compliant to the results from the survey forms. Due to the small sample sizes in the survey, no descriptive statistics are presented.

3.7.3 Qualitative data

The qualitative responses of the participants from the survey form and the Focus groups was categorized and counted. No detailed qualitative analysis was intended to be performed as that was not the focus of the study.

3.8 RELIABILITY AND VALIDITY

The facility survey forms and focus group topics were sent for expert review prior to administration.

DCIs were validated for face validity by circulating amongst other Master of Science (MSc) students for review and inputs. This allowed the DCIs to be strengthened. Content validity of the DCIs was also strengthened by looking at local and international standards.

The DCIs (facility survey form and questionnaire) were used by the researcher and two other MSc students to collect data. The data collected was compared for consistency to test the reliability of data.

Parallel-forms reliability was enhanced by using multiple data collection approaches i.e. facility survey forms, questionnaires and focus group discussion questions were used to address relevant research questions.

Microbiological samples were taken by a microbiologist to enhance reliability and they were analysed by National Health Laboratory Services (NHLS).

3.9 ETHICAL CONSIDERATIONS

Permission to proceed with the study in the Department of Nuclear Medicine was requested from the Head of Department who signed the MREC forms.

Approval for conduct of the study was obtained from the MEDUNSA Research Ethics Committee (MREC), after protocol review by School of Health Care Science Research Ethics Committee (SRC). The study only took place after approval certificate was granted by MREC.

Participants were given detailed information about the study before participating and written informed consent was obtained from all participants. They had the right to withdraw from the study at any time.

3.10 BIAS

This study may be subject to selection bias for Appendices B and D through volunteer bias.

Observer bias was also present but the observers tried to be impartial. Use of multiple observers minimised this bias.

CHAPTER 4
RESULTS

4.1 INTRODUCTION

This chapter presents the findings of the objective survey (Appendix A, Facility Survey form), the subjective personnel questionnaire (Appendix B) as well as reports from experts' consultation.

4.2 FACILITY

The facility results are presented under the following sub-headings: premises, environment and personnel.

4.2.1 Premises

The survey form (See Appendix A) with relevant elements to be addressed in the study was used to survey the premises in the Department as discussed in Chapter 3.

The results of the survey for the facility (Hot Lab and LAF Area) appear below in Table 4.1.

Table 4.1.: Survey results for premises: DGMH

Premises				
Description	**Hot lab (n = 14)**		**LAF Area (n = 19)**	
	Total	Items	Total	Items
Compliant	2	Lighting and dedicated equipment	3	Type of LAF, lighting and dedicated equipment availability
Non-compliant	12	Layout, staff restriction, protective clothes, safe working environment, ceiling, walls, floor, cleanliness, eyewash facility, decontamination shower & bins	16	Layout, staff restriction, internal environment, ceiling, walls, floor, surfaces, cleanliness, LAF location, LAF functionality, protective clothes, no sinks, eyewash facility, change room, SOPs & step over bench.

The room in which the LAF was situated was not in use as a clean room, Hence few of the IAEA infrastructure and LAF requirements were met. Only, three aspects (18.75%) were compliant (type of LAF, lighting and dedicated equipment availability) and sixteen (84.21%) were not. For the hot lab only two (16.67%) of the fourteen items regarding structure and facilities were compliant, twelve (83.33%) were not (e.g. access, layout, cleanliness levels).

4.2.1.1. ***Discussion***

The IAEA recommends that elution of generators and reconstitution of radiopharmaceuticals in the hot lab should ensure the protection of the operator, the product and the environment (IAEA, 2008a). In the Department some aspects that contribute to ensuring personnel protection as stipulated in IAEA guidelines, are compromised (i.e. no proper protective clothing, eyewash facility, shower and restriction of personnel in the hot lab). The integrity of the products handled in the hot lab is also questionable since reconstitution/admixing of radiopharmaceuticals is not performed in a fume cupboard or LAF hood. There is also a high risk of contaminating the environment with radioactive materials that are volatile (e.g. Technegas) and radioiodine capsules. Hence, it is clear that the hot lab in the Department does not meet most of the IAEA requirements. In order to improve the conditions in the hot lab structural changes must be considered.

The IAEA also requires that the LAF hood should be situated in a clean room with class C background for radiolabelling of autologous blood cells. In the department there is a LAF hood which was installed but never commissioned. The clean room does not meet the standards required for aseptic work (i.e. walls, ceiling, floor and air supply do not comply with IAEA standards). Therefore, before radiolabelling of autologous blood cell can be carried out the clean room needs to be brought up to standards as recommended by IAEA (IAEA, 2008b).

4.2.2 Environment and personnel

The environment in which the LAF is situated was assessed for compliance with IAEA standards for aseptic work. However, not only the LAF area's environment was monitored but hot lab's environment was also assessed. Personnel compliance monitoring in both the LAF area and hot lab was assessed as well.

Table 4.2 below gives the results from the survey.

Table 4.2: Summary of environment and personnel results (Survey)

Description	Compliant? (Yes/No)	
Environment (n = 4)	**Hot lab**	**LAF Area**
Temperature monitoring	N	N
Temperature control	N	N
Filtered air is supplied	N	N
Humidity control and monitoring	N	N/A
Personnel (n = 3)		
Limited number of personnel in hot lab	N	N
Suitable protective clothing used (lint-free gowns, overshoes, mask, gloves-sterile and powder free)	N	N
Personnel adhere to hand washing SOPs	N	N
Totals		
Compliant	0	0
Non-compliant	7	6
Not applicable	0	1

In Table 4.2 above, none of the four survey items on environment was compliant for the clean room (e.g. air not filtered, no temperature control or humidity monitoring or control). In the hot lab there is a thermometer which have been calibrated but the temperature is not recorded.

4.2.2.1. ***Discussion***

Monitoring of the environment and controlling access of personnel in areas where sterile radiopharmaceuticals are handled forms a crucial part in radiopharmacy. These actions reduce the chances of contamination of sterile radiopharmaceuticals by personnel. The parameters mentioned in Table 4.2 do not comply with the IAEA requirements for admixing of these products in the Department. This can lead to possible cross-contamination if these parameters are not corrected.

GMP guidelines state that a minimum number of personnel should be allowed entry into the clean room when processing aseptic products. All movement increases particle counts and the major source of particulate matter is humans. High levels of particulate matter increases the likelihood of microbial contamination in clean rooms (ISO, 2000). Therefore, regulation of personnel entry into the clean room from outside is necessary, to ensure that the recommended standards are met and possible contamination is avoided. Personal hygiene, cleanliness, background of microbial contamination and proper dress code are important elements for staff working in the aseptic area and training should be received in these parameters (DOH, 2010).

EU guidelines recommend that personnel, surfaces and environment in which aseptic handling of pharmaceutical products is performed should be monitored using different methods such as settle plates and swabs to ensure that potential contamination is detected as soon as possible (European Guidelines, 2008).

In addition, the IAEA requires that protective clothing should be worn when handling these products, especially when working in a clean room and for labelling autologous blood cells IAEA (2008a). Table 4.2 above indicates that neither the hot lab nor the LAF area in the Department comply with the IAEA requirements with regards to environment monitoring and personnel access.

It should be acknowledged that the LAF area is not functional, but these issues will need to be corrected in order to carry aseptic work in the clean room. In the hot lab, some of the IAEA requirements could be achieved with a small investment e.g. in special sterile lint-free gowns and overshoes.

4.3 QUESTIONNAIRE

Findings from the questionnaire are discussed below.

4.3.1 Knowledge of the LAF usage

The questionnaire (see Appendix B) was used to assess the knowledge of the LAF usage by staff in the department. (Table 4.3 below gives results of the LAF usage).

Table 4.3: Knowledge of LAF use (Questionnaire)

Description	Occupation (n = 8)	Hot Lab			LAF Area		
		Totals			Totals		
		Yes	No	Unknown	Yes	No	Unknown
LAF hood is used for radiopharmaceuticals	Doctors	1	2	2	1	3	1
	Radiographers	0	2	1	2	0	1
LAF hood is currently in use	Doctors	1	2	2	0	3	2
	Radiographers	0	2	1	0	1	2
LAF hood is in clean room	Doctors	2	1	2	1	1	3
	Radiographers	1	0	2	0	2	1

In Table 4.3 above, four out of eight (50%) staff members stated that the LAF hood is not used for radiopharmaceuticals. They stated that the reason for this is due to the fact that the LAF hood is not situated in the hot lab. Hence, no aseptic admixing (OL2a) is possible there. Four out of eight (50%) staff members stated that the LAF hood is not currently in use in the LAF area. Three out of eight (37.5%) staff members agreed that LAF hood is in a clean room in the hot lab and three out of eight (37.5%) staff members agreed that the LAF hood is not situated in a clean room in the LAF area.

4.3.1.1. ***Discussion***

The use of LAF for radiolabelling of autologous blood cell and fume hoods reconstitution/admixing of radiopharmaceuticals is recommended by the IAEA to ensure that the product is protected from possible contamination from the outside environment and the operator (IAEA, 2008a).

According to Theobald, when designing a radiopharmacy unit, the LAF work station should be situated in a clean room which has an environment that is controlled. Thus, personnel should also be aware of the specifications required for handling aseptic preparations to help in maintaining these requirements (Theobald, 2011).

In areas where aseptic operations are performed to produce pharmaceutical products that are sterile and free from pyrogens, LAF hoods and isolators are used to ensure that the quality of the product is not compromised. In order to achieve this, the attitude, skills and training of staff is decisive. Therefore, personnel working with these products should have skills and adequate training before they can be involved in handling such products. All of this necessitates the need to assess the knowledge of personnel who are directly and indirectly involved in performing aseptic operations (DOH, 2010).

The responses from newly appointed staff showed a lack of awareness of the presence of the LAF, even though they have been in the Department for seven months to a year. If a full orientation briefing had been performed they would have known about the LAF and lack of fume hoods. As explained previously, the LAF is currently not in use. No fume hoods are present in the Department. The ones who said the LAF was not n a clean room were correct as the room is not clean.

4.3.2 Training of staff and improvement of aseptic services

The questionnaire (See Appendix B) was used to assess the knowledge on training of staff and improvement of aseptic services by staff in the department.

Table 4.4 below shows results of the views on staff training.

Table 4.4: Staff training and improvement of aseptic services (Questionnaire)

Description	Occupation (n = 8)	Hot Lab			LAF Area		
		Totals			Totals		
		Yes	No	Unknown	Yes	No	Unknown
Aseptic training received by staff	Doctors	3	2	0	1	1	3
	Radiographers	1	0	2	0	1	2
Aseptic training can improve services in the department	Doctors	5	0	0	2	0	3
	Radiographers	3	0	0	0	1	2

In Table 4.4 above, four out of eight (50%) staff members working in the hot lab stated that they had been trained in aseptic admixing. However, all eight respondents (100%) agreed that training on aseptic handling of radiopharmaceuticals is necessary.

4.3.2.1. ***Discussion***

Training of personnel on aseptic work enhances the chances of improving and maintaining aseptic services that are of good quality in areas where aseptic preparations are processed. The involvement and commitment of staff to producing products that are of high quality contributes to improving aseptic services (DoH, 2010). Therefore, any Department that performs any aseptic work should ensure that personnel are well trained to render such services.

Theobald mentioned that radiation safety and aseptic conditions should be monitored in clean rooms. Neither of the two parameters should be compromised at any time, hence, training of personnel is necessary to ensure that the environment in

which they work in is safe and free from contamination, either from microbes or radioactive material (Theobald, 2011).

In Table 4.4 above, staff indicated that they are keen to receive more training in order to improve aseptic services in the Department.

4.3.3 Hygiene and SOPs for aseptic admixing

The hygiene status of a health facility should be satisfactory so as to avoid spreading infectious diseases. The questionnaire (See Appendix B) was used to assess the knowledge on hygiene and SOPs for aseptic admixing in the Department by staff. Table 4.5 below shows results on this section of the survey.

Table 4.5: Hygiene satisfaction & SOPs for aseptic admixing (Questionnaire)

Description	**Occupation (n = 8)**	**Hot Lab**			**LAF Area**		
		Totals			Totals		
		Yes	No	Unknown	Yes	No	Unknown
Hygiene satisfactory	Doctors	5	0	0	2	2	1
	Radiographers	1	2	0	0	3	0
SOPs for aseptic admixing	Doctors	1	2	2	0	2	3
	Radiographers	2	0	1	0	1	2

In Table 4.5 above, six respondents (75%) rated hygiene as satisfactory and two (25%) as not satisfactory. All felt that hygiene should be improved in the hot lab and SOPs should be developed.

4.3.3.1. *Discussion*

Hygiene is a critical aspect in the prevention of infections. Therefore, it should be addressed at all times in all hospital departments. It is also necessary to have SOPs for aseptic admixing of radiopharmaceuticals to ensure that the sterility of the products is maintained at all times as recommended by IAEA (IAEA, 2008a).

EU Guidelines stipulate that hygiene status of personnel should be of high standards as well as their cleanliness to minimise flaking of possible micro-organisms and particulate matter from their skin while working in the clean room. Avoiding this problem of poor hygiene and cleanliness will help to ensure that sterile products are protected from the operator (European guidelines, 2008).

The Medicines Control Council of South Africa (MCC) recommends that personnel working in an aseptic area should report any condition that leads to shedding of any unusual kind of contaminants and should go for regular health checks for such conditions (DOH, 2012).

In Table 4.5 above, personnel indicated that there is a need to raise awareness about hygiene and also to follow written programmes (SOPs) on how to perform admixing of pharmaceutical products.

4.3.4 Microbial contamination results

Microbial contamination monitoring is recommended by the IAEA for clean rooms where radiolabelling of autologous blood cells is performed. Therefore, before one can commence with radiolabelling of these cells in a radiopharmacy unit, level of microbial contamination should be assessed when setting up a radiopharmacy unit (2008a).

Figure 4.1 below shows the sampling area where settle plates and swabs were placed in the clean room.

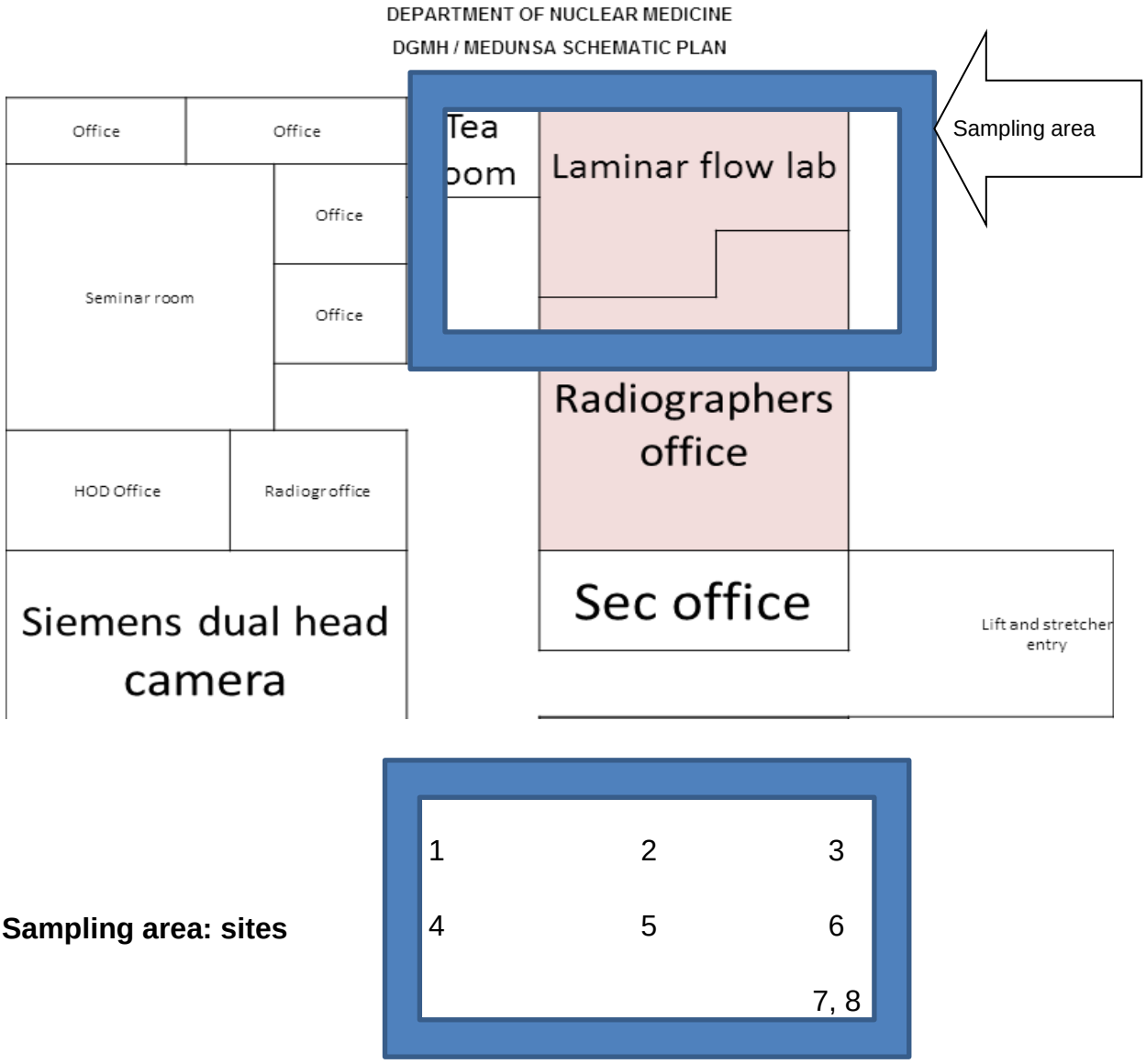

Figure 4.1: Schematic of Dept of Nuclear Medicine and Microbial sampling area

Radiopharmaceuticals should be sterile and pyrogen-free since they are injected intravenously. Therefore, in order to ensure that only sterile and pyrogen-free radiopharmaceuticals are injected, monitoring of the environment in which they are prepared and admixed is necessary. Table 4.6 below shows the baseline results of microbial contamination in the clean room.

Table 4.6: Microbial contamination baseline results

Area	Settle plates and swabs	Bacteria	Mould	Fungi	Total
1	Settle plate agar	✔			1
	Settle plate blood	✔	✔		2
	Swab agar	✔	✔		2
	Swab blood	✔	✔	✔	3
2	Settle plate agar	✔	✔		2
	Settle plate blood	✔	✔	✔	3
	Swab agar	✔	✔		2
	Swab blood	✔	✔	✔	3
3	Settle plate agar	Scanty	Scanty	Scanty	-
	Settle plate blood	Scanty	Scanty	Scanty	-
	Swab agar	Scanty	Scanty	Scanty	-
	Swab blood	Scanty	Scanty	Scanty	-
4	Swab agar	Scanty	Scanty	Scanty	-
	Swab blood	Scanty	Scanty	Scanty	-

Table 4.6 above shows different micro-organisms that grew on the settle plates and swabs. The results are discussed below.

Bacteria

Both blood and nutrient agar settle plates as well as blood and nutrient agar swabs placed in Area 1 showed growth for bacteria.

Blood- and nutrient agar settle plates as well as blood and nutrient agar swabs in Area 2 showed growth.

Mould

Nutrient-agar settle plate in Area 1 did not show any growth of mould. Blood settle plate as well as blood and nutrient agar swabs showed growth of mould in Area 1.

Blood- and nutrient agar settle plates as well as blood and nutrient agar swabs in Area 2 showed growth for both bacteria and mould.

Fungi

Only blood agar swab showed growth of fungi in Area 1.

In Areas 3 and 4 both blood and nutrient agar settle plates and blood and agar swabs did not show growth of any of three types of microorganisms (i.e. bacteria, mould and fungi)

4.3.4.1. *Discussion*

Microbial monitoring is an inherent part of Good Radiopharmacy Practice and enhances the safety of radiopharmaceuticals. In the Department, monitoring of microbial contamination is not performed. The IAEA recommends that surfaces, environment and equipment should be monitored for microbial contamination in an area where sterile products are handled (i.e. clean room for radiolabelling of autologous blood cells) (IAEA, 2008a). Winfield and Richards recommend that staff should master the techniques required to prevent contamination when handling sterile products (Winfield & Richards, 2004).

EU guidelines (2008) state that “in operation” and “at rest” environmental conditions in clean rooms should meet recommended standards for the purpose of handling

sterile products at all times. Therefore, monitoring of the environment and surfaces for contamination should be performed more regularly using settle plates and swabs. Staff involved in day to day handling of sterile products should, therefore, receive adequate training on how to monitor microbial contamination (IAEA, 2008b).

The MCC suggest that in clean areas where aseptic preparations are handled there should be processes in place to control the internal environment to prevent contamination by microbes and particulate matter (DOH, 2010).

Training should be received by staff in order to improve knowledge with regard to the importance of microbial contamination of radiopharmaceuticals and measures to prevent contamination in the Department.

4.4 EXPERT CONSULTANTS: STRUCTURE OF PREMISES: RESULTS AND DISCUSSION

Both of the local aseptic expert consultants emailed their reports to the supervisor and the researcher a week after their visit to the Department. They both recommended that the design, air supply, installation and commissioning of equipment should be considered. Below are parameters that were addressed in their reports:

4.4.1 Structure and layout of the premises

All three experts (including the international engineer who subsequently gave input) recommended the following interventions:

- Cleanroom wall and ceiling requires panelling (sealing)
- Flooring material which is suitable for clean rooms should be used to facilitate cleaning and hence prevent microbial growth
- There must be an interlocked pass-through hatch
- There must be a step over bench in change room
- There must be allowance for laboratory bench style worktops in the premises

- Wet services (sink and associated plumbing) should be available in the change room but not in the clean room area because this can lead to growth of microbes in the sinks since water is an ideal medium for micro-organisms

4.4.2 Air supply system needs

All three experts including the international engineer recommended the following interventions:

- Air handling unit complete with primary, secondary and tertiary HEPA filters must supplying clean air to the clean room
- There must be filtered exhaust for extraction of contaminated air

4.4.3 Installation and commissioning of equipment

All three experts including the international engineer recommended that:

- Wet services (sink and associated plumbing) should be installed
- The LAF should be commissioned and validated

The Figures 4.2, 4.3 & 4.4 below show the progression of the floor plans from the architect's drawing to the recommendations from the aseptic suite engineers.

After the local (SA) aseptic suite engineer requested the floor plan (see Figure 4.2) of the premises together with the measurements as mentioned in Section 3.6.2, the supervisor forwarded the architect's plan (see Figure.4.2) to the engineer. The engineer sent back the proposed radiopharmacy unit floor plan and the cost of the proposed changes – see Figure 4.3 below.

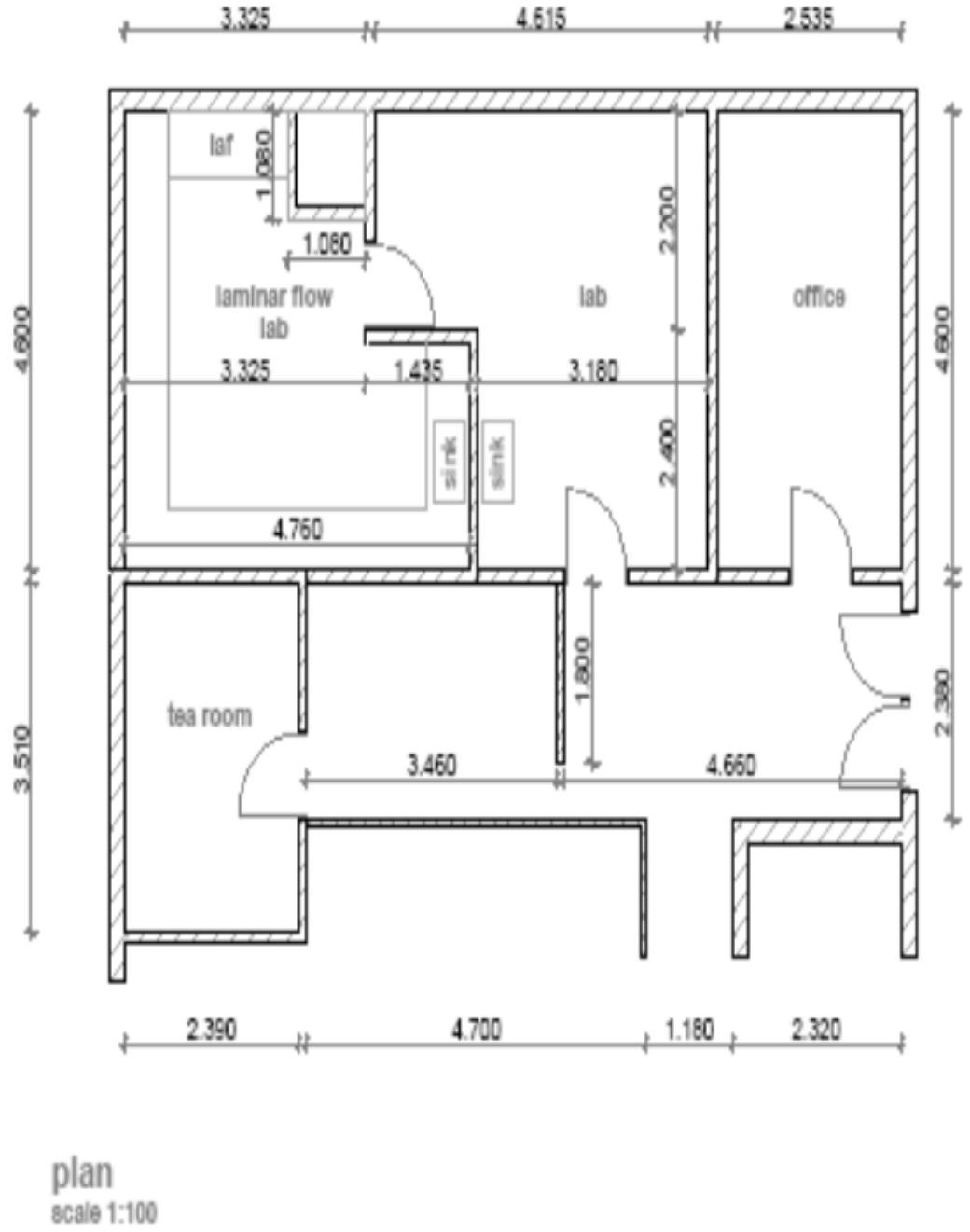

Figure 4.2: Architect's floor plan of part of the Nuclear Medicine Dept, DGMH

Acknowledgements: Katherine Jollye. K-A Architecture and Design

Cost

+/- SA Rands 800,000 = Euros 80,000

31/01/2012

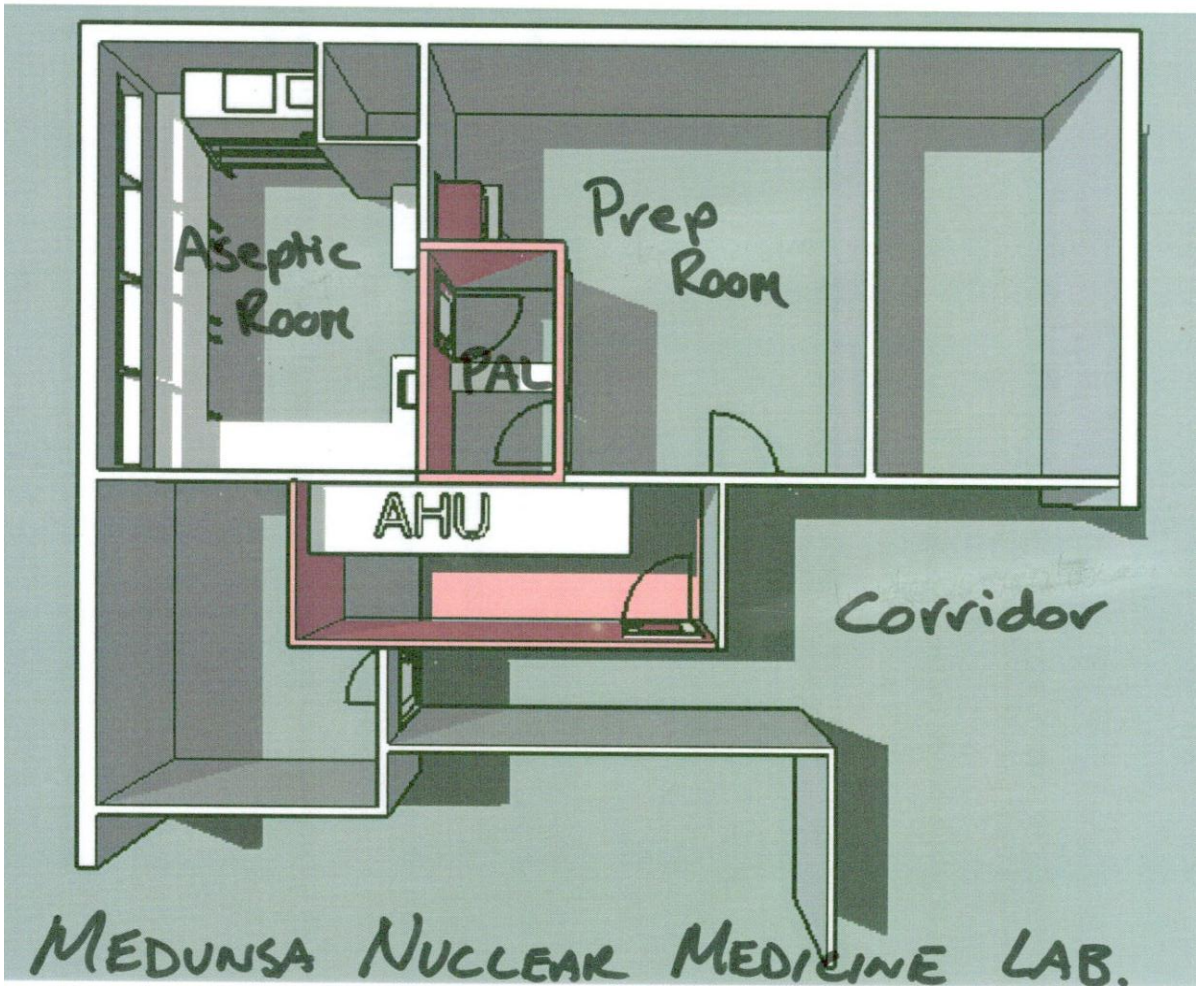

Figure 4.3: Proposed radiopharmacy unit – South African engineers' concept plan

- Acknowledgements: Toby van Reenen, SSI (now Royal Haskoning DHV)

Key: AHU = Air handling unit

PAL = Pass-through air lock

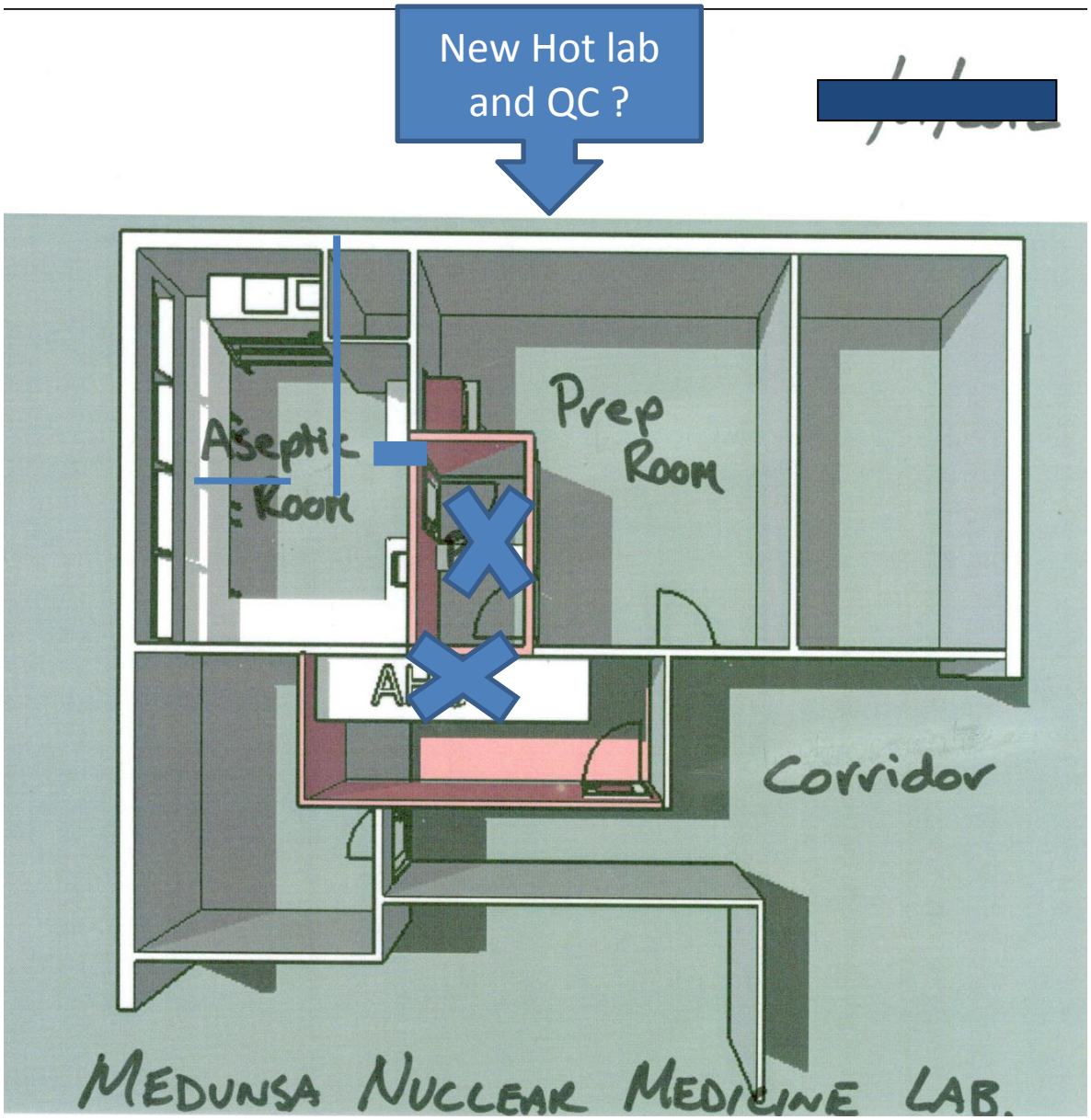

Figure 4.4: Revised radiopharmacy unit floor plan (July, 2012)

Acknowledgements: B Summers & A Cockroft, 2012.

In July, 2012 the postgraduate supervisor attended an IAEA course on “Essentials of end-user testing of radiopharmaceuticals and design/upgrading of a radiopharmacy facility” (IAEA, 2012a).

Information from this course and interaction with two international clean room experts on the course lead to simplification of the proposed structural changes.

Figure 4.3, shows the structural changes recommended by the local clean room engineering expert. Simplification and rationalization of that proposal as a result of the IAEA course experts’ input are shown in Figure 4.4. It can be seen that the clean room area is much smaller in Figure 4.4 than in Figure 4.3 and easier to maintain. The sink unit is no longer in the clean room (which is an improvement in terms of GMP requirements). The gowning/preparation area has been moved into the area adjacent to the clean room and allows for better use of the sink and the existing hatch facility. In addition, the previous preparation area can now be used for QC or even possibly for relocation of the existing hot lab (which is currently too small and not ideally placed).

The recommendation from the IAEA experts was to retain the existing air conditioner (which is new) but to have it recycling air within the unit. Fresh HEPA-filtered (but not air conditioned) air can be introduced via a small filter box from the outside. That arrangement is far less expensive than the special air-conditioned filter unit (AHU) in the budget for Figure 4.3.

The changes as shown in Figure 4.4 can be effected through the use of dry walling and within a much lower budget than those for Figure 4.3.

Figure 4.4 above indicates all the marked areas that the supervisor discussed with the IAEA consultants with regards to structural modifications that should be considered in order to implement aseptic services in the Department at a lower cost.

4.4.4 Cost

The quotation from SA clean room specialists for the full upgrade of the radiopharmacy estimated that the cost of proposed changes would be approximately R852 000.00 excluding VAT to design, install and commission all equipment in the

radiopharmacy unit (See Figure 4.3). The cost for the upgrade is one of the limitations to radiolabelling of autologous blood cells.

The proposed cost included designing the flow pattern of the products and personnel, walls, ceiling, surfaces, doors, access limits, lighting fittings, and room specifications (air supply and pressures).

The cost of Figure 4.4 changes are likely to be a fraction of the price of those shown in Figure 4.3, i.e. approximately R50 000.

That cost covers dry wall partitions, painting, sealing the ceiling and servicing the LAF.

Other costs provided by UK engineers are as follows (Cockcroft, 2012):

- New facilities in the UK cost around £3,200.00 / m^2 excluding equipment. (approx. R 35 836)
- LAF cabinets based on a 1200mm wide unit £5,200.00 (approx. R58 233)
- Class II Safety cabinet £8,300.00 (approx. R92 950)
- Technetium Isolator £26,000.00 (approx. R291 169)

CHAPTER 5

RESULTS AND DISCUSSION
FOCUS GROUP DISCUSSION AND STANDARD OPERATING PROCEDURE DEVELOPMENT

5.1 INTRODUCTION

This chapter presents the findings of the Focus Group Discussion (Appendix D), conducted in this study.

The FGD was conducted by the researcher's supervisor who is experienced in the facilitation of such groups. Refer to Chapter 3 for details on the method for the conduct of the Focus Group

The FGD was held four weeks after presentation of the project results (described in Chapter 4 above) were presented to staff.

Staff present at the FGD was as follows:

- Head of Department (HOD)
- Two Nuclear Medicine specialists
- Two registrars
- Three radiographers
- One medical physicist

5.2 FOCUS GROUP DISCUSSION OUTCOMES

5.2.1 Staff quota and training

5.2.1.1. *Results*

- Staff agreed that there is a need for a departmental induction programme for new staff members.
- Staff suggested that more radiographers should be employed and trained in the Department.
- Potential radiography staff should be encouraged through rotation of radiography students through the Department.
- Staff suggested that there should be programmes in the Department that will ensure that regular health check-ups for personnel working in clean areas to minimise possible contamination by staff is conducted.
- Staff suggested that training in radiation safety and aseptic services should be received at regular planned intervals to ensure that the working environment is safe and aseptic services are not compromised.
- Staff agreed that personnel working in clean areas should receive extra training on hygiene, gowning/degowning and hand washing procedures.
- The radiation safety officer should train staff members on how to handle spillage, generated waste and reporting spillage of radioactive material.

5.2.1.2. *Discussion*

Currently, there are five physicians, three radiographers and one medical physicist employed in Department. Clearly, with the additional help of a radiopharmacist there is enough staff for performing work. What needs to be done is rescheduling of duties in order to organise work properly. Sometimes there is limited staff availability due to poor scheduling of duties, which compromises the quality of the service rendered. Staff are therefore pressurised in the preparation process of the radiopharmaceuticals leading to lapses in safe working procedures.

The Department does not have a radiopharmacist employed for handling pharmaceutical services or radiolabelling of autologous blood cells. It is recommended that they create a post for a radiopharmacist to increase capacity and help promote standards with regards to pharmaceutical services in the Department.

Westcott stated that training is the only tool that can be used to train leaders who can implement strategic planning in the work place to improve the quality of the service being rendered. Therefore, it is necessary for personnel to receive training so that they can perform to their full capacity (Westcott, 2005; EANM, 2007).

The design and conduct of the programme for the training courses offered by the International Society for Radiolabelled Blood Elements (ISORBE) in SA should be adopted to improve training. The society provides guidance on radiolabelling of blood products with regards to the facility, equipment, SOPs and staff training (ISORBE) (IAEA, 2012).

5.2.2 Aseptic suite

5.2.2.1. *Results*

- Staff recommended that the availability of an aseptic suite for the purpose of handling sterile and pyrogen free radiopharmaceuticals would improve aseptic services in the department.
- Staff suggested that funds should be obtained in order to purchase the equipment and upgrade the aseptic suite.
- Staff also suggested that quotations should be obtained from different suppliers in order to establish the suite in a cost-effective manner.
- Measures to protect the suite were also discussed in order to prolong its life-span.
- The use of sterile theatre gowns as protective clothes for working in the aseptic suite was recommended by staff. Such gowns must be non-linting.
- Staff stated that the use of an isolator can be an alternative to a clean room for manipulation of blood products. However, they were fully aware that an isolator

can be very expensive so it is better to use the LAF that is already in the Department.

- Staff suggested that SOPs for cleaning the suite should be developed.

5.2.2.2. *Discussion*

The Departmental budget cannot fund the upgrade of the full new aseptic suite at the moment. An interim plan will have to be implemented if services are to develop (see Chapter 6).

It is recommended that non-linting sterile theatre gowns should be used as protective clothing as they can easily be obtained from the hospital and minimizes the cost for purchasing protective clothing to be used in the clean room. For now minimum equipment to be used in the aseptic suite should be obtained and long-term goals would be to upgrade the facility to meet local and international standards for aseptic suites (ISO, 2001).

5.2.3 Radiolabelling of autologous blood cells

5.2.3.1. *Results*

- Physicians showed interest in having this service implemented in their Department as it will help them with the diagnosis of infectious and inflammatory diseases.
- However, they also seem to understand that the implementation of such services needs team work. Therefore, they showed interest in supporting the researcher to set-up the processes and facilities for radiolabelling of these cells.
- Personnel acknowledge the fact that blood is a good environment for micro-organisms to grow; therefore, they support the setting-up of the laboratory in order to ensure that the facility and equipment in their laboratory protect the cells to be labelled, patients, environment and personnel.
- Staff suggested that the hot lab, QC lab and clean room should be situated next to each other so as to minimise contamination of other sections in the department by radioactive materials.

- Staff emphasised that only personnel trained in aseptic techniques should be allowed entry into the clean room to minimise possible contamination of the clean room.
- Staff wants to produce products that are sterile and free from pyrogens by committing themselves to quality services.
- Staff agreed that only blood products from one patient should be handled at a time to ensure that correct blood samples are re-injected into the right patient.

5.2.3.2. ***Discussion***

There is one specialist physician who specialized in radiolabelling of autologous blood cells in the Department. That physician also has experience in the use of radiolabelled blood elements and could act as a driver of service expansion.

Therefore, it is recommended that the facility be upgraded and staff should receive training in radiolabelling and use of these blood products to increase expertise in the field.

5.2.4 Equipment

5.2.4.1. ***Results***

- Personnel are concerned about the shortage of equipment that is necessary to render the best services and high in quality as well.
- Staff mentioned that the LAF hood in their Department should strictly be used for radiolabelling of autologous blood cells since it will be situated in dedicated clean room with controlled internal environment.
- Staff stated that no cell labelling should be performed on an ordinary work bench to avoid contamination of these blood products.
- Staff also suggested that superfluous items currently stored in the clean room must be taken out of the room to reduce sources of contamination in the clean room.

- It was mentioned that a centrifuge dedicated for radiolabelling of blood cells should be obtained to ensure that all the procedures for labelling blood cells are followed.
- Staff suggested that there should be measures in place to monitor contamination of equipment used in the clean room by radioactive materials as well as micro-organisms.
- Maintenance of equipment in the clean room should be planned in such a way that the specifications of the clean room are not compromised.

5.2.4.2. *Discussion*

There is a Veenstra (QQF-081) shielded LAF biological safety cabinet (not in use) in the Department, but they do not have a cooled centrifuge with sealed buckets to be used specifically for radiolabelling of blood cells. The SA guide to GMP, 2010 stated that equipment should be assembled in such a way that surfaces that come into contact with the product are not reactive, additive or absorptive to ensure that the quality of the radioactive products is not affected (DOH, 2010).

ISORBE, 1999 recommend that the minimum equipment should be obtained prior to rendering services of radiolabelling blood products (ISO, 2007; Rodrigues *et al*., 1999).

5.2.5 Finance

5.2.5.1. *Results*

Staff indicated that some of the problems in the department can be solved if they can obtain funding for infrastructure development.

5.2.5.2. *Discussion*

As mentioned above in Section 4.4.4, cost is one of the limitations to the implementation of aseptic services for radiolabelling of autologous blood cells. The Departmental budget is not large enough to fund the full upgrade project at this stage.

Funding must be obtained from the Gauteng provincial Government but an interim plan must be made in order to introduce the much needed blood labelling service. The approach to this problem is discussed later in this dissertation (see Chapter 6).

5.2.6 SOPs

5.2.6.1. *Results*

- Staff showed interest in the development of SOPs in the Department. The HOD suggested that the researcher plus one registrar and one radiographer should work together to draft SOPs.

5.2.6.2. *Discussion*

There are no SOPs in the Department that are relevant to radiolabelling of autologous blood cells. Therefore, it is necessary to develop them to serve as a tool for guidance for all the aseptic procedures performed when radiolabelling blood products.

SOPs serve as a tool for ensuring a safe working environment; hence, they are used as a checklist for the processes performed and promote consistency in tasks performed (Jain, 2008).

5.3 DEVELOPMENT OF SOPS

The SOP process consists of six steps to be followed when developing an SOP , namely; SOP preparation, review and approval, revisions and reviews, checklist, document control and SOP document tracking and archival.

The process for the development of the SOPs for clean room procedures was as follows:

- Literature was consulted for steps to be followed in the development of SOPs.
- The following guidelines: IAEA, ISORBE, cGRPP, SA guide to GMP, were consulted by the researcher to draft the procedures for each SOP developed.
- The drafted SOPs were then emailed to the supervisor for corrections.

- The corrected draft was then emailed to the key Nuclear Medicine personnel appointed to assist in the development of these SOPs for comments.
- SOPs with comments were emailed back to the researcher and supervisor by the key personnel involved in the development of these SOPs
- All the comments were addressed by both the researcher and supervisor
- They were then finalized by the researcher

Below are the draft SOPs that were developed collaboratively with the core group of staff in the department.

The resources for the compilation of the SOPs were as follows:

- IAEA, 2008a
- IAEA IOG, 2008
- ISORBE, 2000
- EU Guidelines, 2008
- USP<797>,2009
- UR LLE, 2006
- Tygerberg hospital SOPs, 2012
- NHS,2006

The SOPs appear in the following pages, 103-116

CHAPTER 6
SUMMARY, CONCLUSION AND RECOMMENDATIONS

6.1 INTRODUCTION

The aim of the this study was to identify the equipment and operational standards required, for commissioning the laminar airflow hood in the Department of Nuclear Medicine at DGMH and then to implement the aseptic services required for radiolabelling of autologous blood cells.

6.2 SUMMARY

This summary addresses the objectives of the study, method and results.

6.2.1 Objectives of the study

The objectives of the study appear in Chapter 1 but two are reproduced here for ease of reference.

Objective 3

To identify the equipment and laboratory conditions that are required for radiolabelling of autologous blood cells.

SA guide to GMP, EU guidelines, IAEA guidelines and MCC were consulted with regards to identifying equipment, laboratory conditions and OLs of hospital radiopharmacy unit.

Objective 6

To develop (collaboratively with Nuclear Medicine staff) standard operating procedures (SOPs) for radiolabelling of autologous blood cells.

Local and international regulations were consulted in developing the standard operating procedures collaboratively with staff.

6.2.2 Method

The study was conducted at the Department of Nuclear Medicine, Dr George Mukhari Hospital. The design of the study was prospective, descriptive and interventional. Data were collected through independent (objective) observation, questionnaires (subjective). In order to involve staff in the implementation of aseptic services in the respective department a focus group discussion (FGD) followed. The International Atomic Energy Agency (IAEA); Operational Guidance on Hospital Radiopharmacy and United Kingdom Radiopharmacy Group (UKRG) Guidelines were consulted to identify equipment and operational standards required.

Permission to conduct the study was obtained from the Head of Department of Nuclear Medicine and Chief Executive Officer (CEO) of the Hospital. The proposal was approved by the Medunsa Campus Research and Ethics Committee (MCREC).

6.2.3 Results

The key findings of the study are provided below. Results summarized are from the objective survey, the subjective questionnaire and the focus group discussion.

6.2.3.1. *Facility*

The room in which the LAF is situated is not used as a clean room, therefore, walls ceiling, floor, doors, personnel restriction and benches do not meet local and international standards for radiolabelling of autologous blood cells (i.e. they are not made of special material with curved edges to contain any spillages). Hence few of the IAEA infrastructure and LAF requirements were met. Only, three aspects were compliant (type of LAF, lighting and dedicated equipment availability).

The internal environment of the clean room does not comply with the SA Guide to GMP (DOH, 2010) or with the EU guidelines for radiolabelling blood cells (i.e. No HEPA filters for the air, no control or monitoring of relative humidity and temperature, no monitoring of microbial and particulate matter contamination, air circulation is not planned and pressure gradients are not maintained).

None of the four survey items on environment was compliant for the clean room (e.g. air not filtered, no temperature or humidity monitoring or control). Only in the hot lab was the temperature monitored.

For the hot lab only two of the fourteen items regarding structure and facilities were compliant, twelve were not (e.g. access, layout, cleanliness levels).

6.2.3.2. ***Equipment***

In the Department a LAF was installed for the purposed of radiolabelling autologous blood cells several years ago. They do not have key items such as a cooled centrifuge with sealed buckets or an isolator in the Department to use for radiolabelling of blood products as recommended by ISORBE.

Staff mentioned that a centrifuge dedicated for radiolabelling of blood cells should be obtained to ensure that all the procedures for labelling blood cells are followed.

In the hot lab, gowns and overshoes are not available

The equipment mentioned above is considered to be minimum equipment that should be in place in the Department prior to providing services of radiolabelling blood cells.

6.2.3.3. ***Staff and training***

Doctors showed interest in the implementation of radiolabelling WBC service in their Department. This service will help them with the diagnosis of many infectious and inflammatory diseases. Therefore, they showed interest in supporting the researcher to set-up the processes and facilities for radiolabelling of these cells.

There is no radiopharmacist currently employed in the Department for handling of radiopharmaceuticals. At the moment a medical physicist and radiographers are responsible for reconstituting/admixing radiopharmaceuticals. One physician has been trained in radiolabelling of blood cells but there are no aseptic services being rendered currently due to lack of appropriate facilities and equipment. Two staff had been trained in aseptic admixing. All eight respondents agreed that training on aseptic handling of radiopharmaceuticals is necessary.

Staff needs training on aseptic techniques as well as in developing SOPs that are relevant to radiolabelling of blood cells (see Section 6.3.1.5 below).

6.2.3.4. ***Finance***

Staff indicated that some of the problems in the department can be solved if they can obtain funding for infrastructure development.

There are no funds for the upgrade of the radiopharmacy unit at the moment. Therefore, funding should be obtained.

6.2.3.5. ***SOPs***

Six respondents rated hygiene as satisfactory and two as not satisfactory. Despite these views, all felt that hygiene should be improved in the hot lab and SOPs to be developed.

There are no SOPs in place in the Department, relevant to radiolabelling of blood cells, since there is no such service in-house. Staff had to be trained, as part of this study in the development and implementation of SOPs for radiolabelling of blood cells.

The way forward was to develop draft SOPs to be used during radiolabelling of these blood products.

As discussed in Chapter 5 above, a working group was formed to coordinate the development of the SOPs to safeguard tasks performed in the clean room area. The researcher and the team identified the SOPs to be developed by consulting IAEA guidelines, GMP, ISORBE and other relevant resources for clean rooms. SOPs that were developed covered the following areas (see Section 5.3):

- Cleaning and disinfecting procedures
- Hand washing and aseptic hand washing
- Gowning and degowning procedures
- Radiolabelling of autologous blood cells.

6.3 CONCLUSION

6.3.1 Staff and training

6.3.1.1. *Staff*

- HOD of Nuclear Medicine and Senior Specialists are supportive
- Radiographers and medical physicist accept that there is need for change in the Department
- The five pharmacy postgraduates are enthusiastic and will provide practical and theoretical support
- Rescheduling of duties is recommended as there are enough radiographers working in the Department to cover all duties, if properly managed

6.3.1.2. *Training*

It is clear from the results of this study that staff training is a priority. Without training, service implementation cannot progress as neither the skills nor the process knowledge will be adequate to implement appropriate services. Training has already commenced.

IAEA training course Cape Town (SA) December, 2012

Three staff members attended a training course (Regional (AFRA): Training course on radiolabelled blood products including radiolabelled white cell for infection imaging) which was arranged by the IAEA during the first week of December 2012.

The following topics were covered in the training course (IAEA, 2012b):

- Operation of a cell labeling facility: Basic aspects, design of facilities and environmental controls
- Operation of a cell labeling facility: infection control, aseptic procedures and cleaning procedures
- Radiolabelling of WBC
- Radiolabelling of RBC

- Principles of platelet labelling
- WBC labelling demonstration
- Platelet labelling demonstration
- Clinical application of radiolabelled blood cells
- Infection and inflammation imaging
- Safety issues: radiation safety and disposal of byproducts (radioactive and biological waste)
- Practicals in radiolabelling blood products

The design and conduct of the programme for the course was in cooperation with the International Society for Radiolabelled Blood Elements (ISORBE). The society provides guidance on radiolabelling of blood products with regards to the facility, equipment, SOPs and staff training.

6.3.1.3. ***Facility***

Internal environment control

Annex 1: Section 53, 54 and 55 of EU Good Manufacturing Practice Guidelines (EU, 2009) stipulates that air that is supplied into clean rooms should have positive pressure, while ensuring that the air flow relative to adjacent lower grade areas cleanses the area efficiently. The pressure difference of the surrounding grades should be 10 – 15 Pascal lower in order to maintain air flow effectively between the different grades. Patterns of air circulation should be designed in a manner that will prevent contamination between the grades. Hence, monitoring of pressure differences should be in place as well as warning systems that gives warnings to any pressure difference between the grades. Pressure should be logged on daily basis to have record of these pressures for each area (EU guidelines, 2009; ISO, 2001).

Figure 6.1 below is an example which illustrates the complex aspects to be considered when planning air circulation in a GMP-compliant radiopharmacy unit.

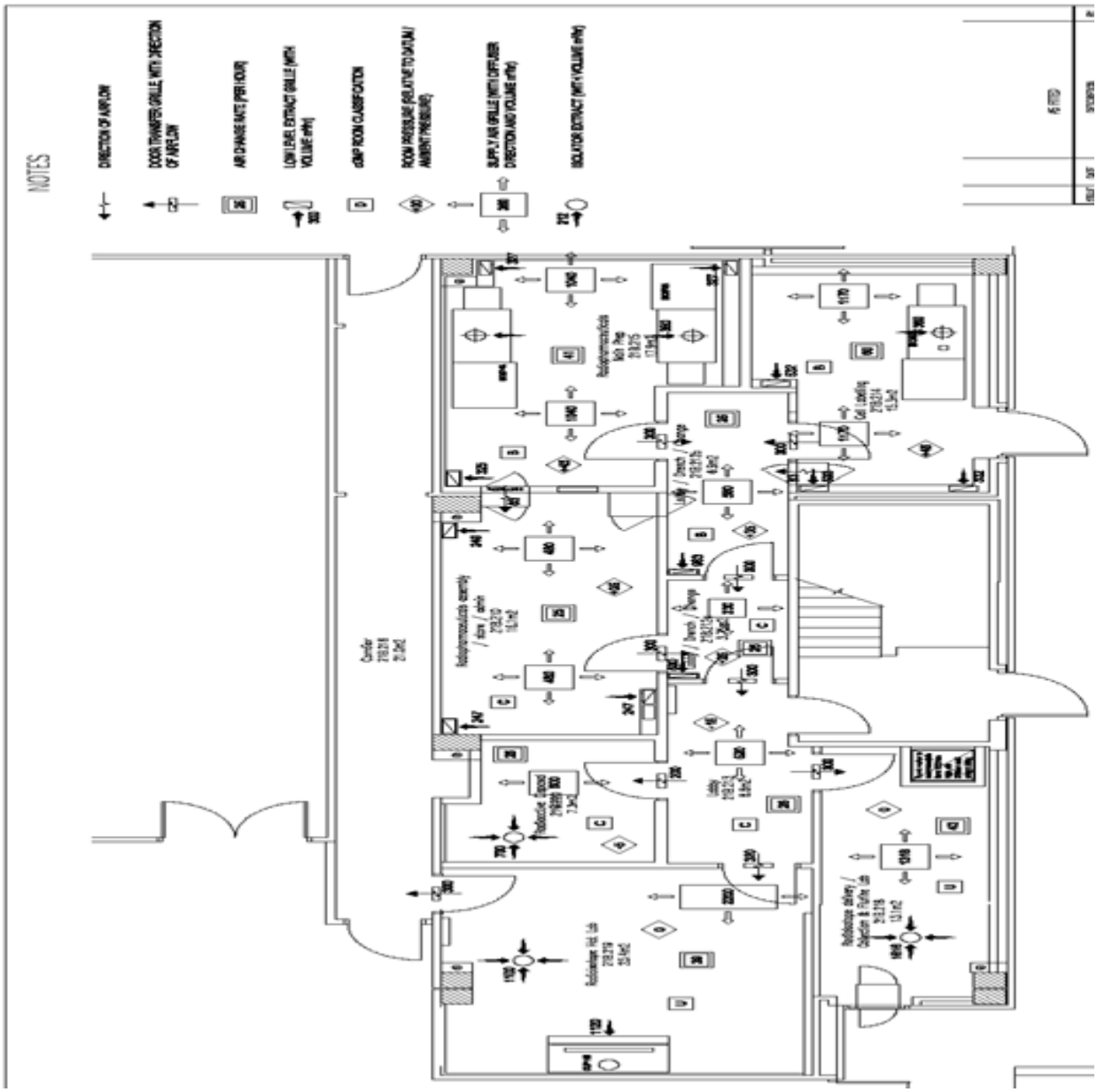

Figure 6.1: Example of airflow and pressure differences in a radiopharmacy unit

Source: (Envair, 2012.)

6.3.1.4. ***Equipment***

The LAF must be commissioned prior to implementation of aseptic services for radiolabelling of blood cells and should only be used for radiolabelling of blood cells. Centrifuge and kits used for radiolabelling should be obtained.

The aseptic suite should also be used for protecting the products handled as well as protecting the operator from the blood products handled since they are highly infectious.

The minimum requirements required with regard to equipment includes the use of a vertical LAF cabinet which is situated in ISO class 5 environment or grade A (or old class 100) environment. Isolators can also be used to provide necessary environment conditions required for radiolabelling of these blood products where it is not possible to work under aseptic environment. It is also recommended that key items such as a cooled centrifuge with, sealable buckets be used for radiolabelling blood. All the equipment should be dedicated to radiolabelling of blood cells and should be stored in a designated area.

Below are examples of suitable equipment that could be installed and commissioned for use for radiolabelling of autologous blood cells. In the Department they have a Veenstra (QQF-081) LAF similar to the one in Figure 6.2.

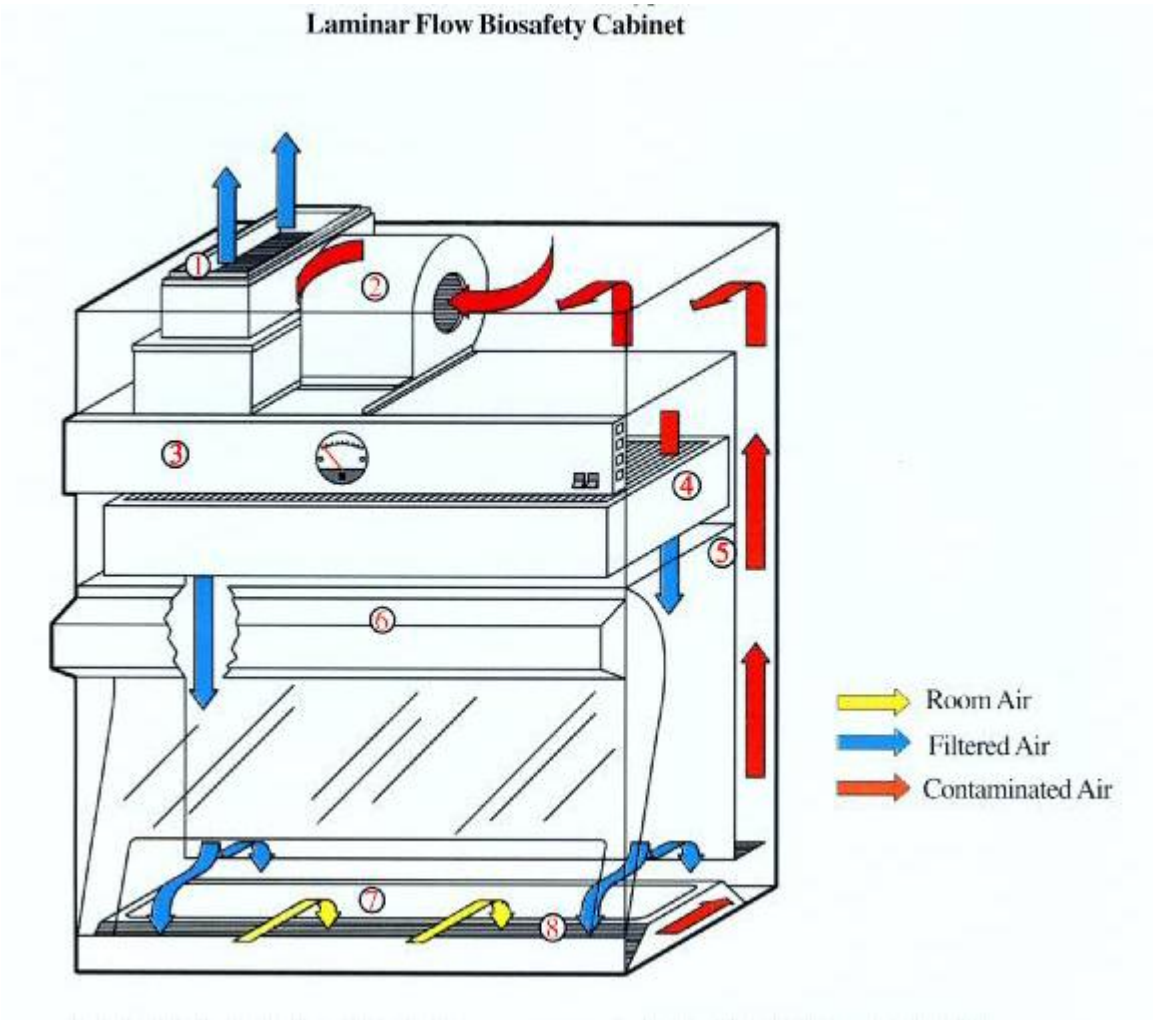

Figure 6.2: Example of a vertical LAF cabinet

Source: (NSF/ANSI-49, 2002)

Figure 6.2 above is an example of an ideal LAF cabinet to be used for manipulation of blood products recommended by SA guide to GMP (MCC, 2010) and ISORBE (Soroa, 2009). It also indicates the circulation of air into and out of the LAF which ensures that the products being handled in the workstation are protected from the operator and the operator protected from the radioactive material.

Figure 6.3: Example of an isolator

Source: (Cockcroft, 2012)

Figure 6.3 above is an example of an ideal isolator to be used for manipulation of blood products recommended by the SA guide to GMP (DOH, 2010) and ISORBE (Soroa, 2009). The internal environment can be adjusted to provide the required requirements for labelling blood products. It also provides protection of the operator from the products being handled in the isolator.

6.3.1.5. ***Finance***

Radiopharmaceuticals should be handled in a controlled manner with each procedure performed in designated area. Therefore, the Department plans to upgrade the radiopharmacy as a whole as well as the clean room/aseptic facility so that it complies with international and local standards for radiolabelling of blood cells. The general layout of the facility has been proposed with all the necessary amendments to be made with regard to the premises and environmental control measures.

However, there are major financial restrictions for the development of the facility as proposed. The Department has limited funds at the moment; therefore, the Department will need financial assistance from Government in order to proceed with the upgrading process of the facility (see Figure 4.3). They cannot only rely on sourcing funds from companies as that can produce conflicts of interest. The university may be able to provide limited funds on the basis that the development of services within a teaching department will promote learning and research. The planning process must proceed and plans will be executed once funds are obtained. The plan therefore is to make small changes to the facility based on available funds and to develop SOPs in order to commence autologous blood labelling services of acceptable quality to patients. The long term goal is to obtain funds from Gauteng DoH, as mentioned above, for a full upgrade of the facility.

6.3.1.6. ***SOPs***

The IAEA promotes the safe use of radioactive materials in Nuclear Medicine Departments by providing advice and guidance to development of these SOPs (ENSREG, 2009). In addition the International Society for Radiolabelling of Blood Elements (ISORBE) has comprehensive guidelines designed to promote international best practice and standardisation of these services (Soroa, 2009).

Making use of clear and concise SOPs for each procedure involved in radiolabelling of blood products will assist in ensuring that all operators work efficiently. The use of SOPs eliminates possible mistakes that can be made if the procedures are not standardized. It is also necessary to document tasks performed in order to keep records for each activity performed on daily basis which will make it easy to review

the procedures followed, should there be any problems arising from the radiolabelled blood products.

These SOPs will form a crucial role in achieving successful quality systems since they are to be used by all personnel (newly employed and old staff) for performing these tasks efficiently. They also assist in excluding any variations for the tasks performed and increase consistency of all the process. As for the newly recruited staff they can also serve as a tool for training staff on how to follow the working procedures as they contain detailed instructions and minimizes miscommunication (USEPA, 2007).

6.3.2 Government's responsibility

In South Africa the Medicines and Related Substance Act (101 of 1965) defines a medicinal product as any substance or mixture of substances used or purporting to be used or manufactured or sold for use in:

a) The diagnosis, treatment, mitigation, modification, or prevention of diseases, abnormal physical or mental state or symptoms thereof in men; or

b) Restoring, correcting or modifying any somatic or psychic or organic function in men, and includes any veterinary medicine.

The Nuclear Energy Act (Act No. 49 of 1999), DOH on Nuclear Medicine inspection (DOH, 2007) and Hazardous Substance Act (Act No.15 of 1973) requires the handling of radioactive materials to be carried out in a facility that is approved and licensed to offer these services (DOH, 1973, 1999 & 2007).

Therefore, based on the requirements stipulated in the Acts above, the government must make sure that facilities under its control comply with the laws of the country. If they do not, the Government is responsible for rectifying the situation.

There are several examples of the Government being taken to task over facilities and services which do not comply with health conditions and patient rights.

Chowdhary, and colleagues conducted a study in 2000 in a state hospital in the Eastern Cape (SA), in order to identify the main causes of neonatal deaths in pediatric patients who received a parenteral nutrition product (ITN 1601t which

contained Nitrogen 0.78g, Glucose 26g, Fat 4g, Na^{+} 4.15 mmol, K 3.70 mmol, Mg 0.12mmol, Cl 8.60mmol, PO4 1.40mmol, Ca^{++} 2.20mmolm Soluvit, Peditrace, and Vitalipid). The findings of the study indicated that many deaths occurred in patients who received the nutritional products that were prepared in-house by simple admixing procedures and did not meet the international aseptic standards for parenteral nutrition compounding. Babies developed different types of infections after receiving these parenteral products which lead to death. The study revealed that in-house preparation of parenteral nutrition products has a high risk of contamination compared to those products that are prepared in designated sterile manufacturing facilities (Chowdhary *et al*., 2000).

Therefore, the state has a big responsibility in ensuring that incidents similar to the one discussed above do not occur.

Medical litigation decisions are starting to hold the state responsible for negligence. Recently, a 30 year old man was awarded R5 million in compensation as he suffered brain damage in 2005 at Charlotte Maxeke Academic Hospital, Johannesburg. A family of a brain damaged child was also awarded R11.6 million in compensation due to staff negligence at birth at Far East Rand Hospital, Johannesburg, in 2004. The Gauteng DOH has paid out more than R44 million in total in 2012 due to negligence claims. These were landmark decisions which highlights that the province is not above the law and that staff are expected to comply with basic service standards (Report, 2012).

The Gauteng provincial government and state officials must take responsibility for the health and well-being of all their patients. Government officials have the authority to make decisions that will help to solve the problems encountered in the province and to implement a strategic plan on how to improve service delivery in public sector.

6.3.3 The way forward

The steps that need to be taken in order to set up services for radiolabelling of autologous blood cells are as follows:

6.3.3.1. ***Short term***

- Future development of protocols based on ISORBE guidelines should be implemented
- Staff training
- Staff should receive training in radiolabelling of autologous blood cells. This have already commenced (see Section 6.3.1.2 above)
- Staff should be accredited for radiolabelling of blood cells with ISORBE
- Facility
- The air conditioner in the clean room should be serviced
- All the windows in the clean room should be sealed
- Partitioning of room to create gowning & preparation area
- Fittings for the change area – hooks, mirror, bins and cupboards for storing protective clothes must be installed
- Access control installed
- Clean whole area thoroughly.
- LAF services and filters checked
- The Department should obtain a reliable cooled centrifuge to be used for radiolabelling of autologous blood cells
- The Hot lab should be moved to the new radiopharmacy unit
- In the new radiopharmacy unit there must be QC lab section for quality control purposes
- As an initial practical step, *in vitro* labelling of red blood cells can be introduced in the cleaned laboratory using the cooled centrifuge mentioned above. This approach will provide staff with the opportunity to practice the process and gain skills in handling autologous blood in a closed procedure that does not need aseptic conditions.

- Practice in aseptic work – gowning, cleaning area, degowning, – followed by *in vivo* labelling of WBC and QC using donor blood that will not be re-injected
- Microbial monitoring of area and of practice WBC products
- Prepare radiolabelled WBC (leukocytes) for administration to volunteers
- Prepare radiolabelled WBC (leukocytes) for administration to patients

6.3.3.2. ***Long term***

- Necessary structural changes on the facility should be made to meet the local and international standards for radiolabelling blood products
- All the necessary equipment should be obtained
- Funds should be obtained for funding the upgrade of the facility
- Full upgrade of the clean room

The budget for achieving all the long term goals is approaching R1 million.

6.4 RECOMMENDATIONS

The following recommendations are made based on the results of the study:

6.4.1 Staff

- It is recommended that the Department motivates for a post for a radiopharmacist to ensure that pharmaceutical services are of high quality
- Staff should receive training in radiolabelling of autologous blood cells and be accredited with ISORBE
- It is recommended that rescheduling of radiographers' duties occurs in order to organise work properly
- There should be programmes in the Department that will ensure that regular health check-ups for personnel working in clean areas are in place to minimise possible contamination by staff and also to monitor their exposure to radiation
- Personnel working in clean areas should receive training on radiolabelling of blood cells, hygiene, gowning/degowning and hand washing procedures

6.4.2 Facility

6.4.2.1. *Short term – clean room*

- The current area with the LAF must be partitioned into a clean room and change room
- The layout of the premises should allow for a logical flow of work
- It is recommended that walls, floors and ceilings in the clean room must be smooth, impervious and unbroken
- Access to the clean room and hot lab must be restricted to authorized personnel only
- All the windows in the clean room must be sealed
- The hatch should be transformed into a suitable and cleanable transfer hatch

- The whole area must be thoroughly cleaned
- The change room must have a sink, full height mirror, hooks for hanging coats, storage space for gowns masks, bins etc.
- Ideally there should be a step over bench in the change room but at least a demarcation line is needed.
- Personnel must wear proper protective clothing prior to entering the clean room
- HEPA filters should be installed for incoming air
- There must be thermometers to monitor temperature in the clean room
- Microbial and particulate matter contamination should be monitored monthly using settle plates and swabs
- All movement should be minimized since it increases particle counts and the major source of particulate matter is humans
- Personal hygiene and cleanliness should be promoted to reduce possible contamination by personnel

6.4.2.2. ***Short term – hot lab***

- It is recommended that walls, floors and ceilings in the hot lab must be smooth, impervious and unbroken.
- Access to the hot lab must be restricted to authorized personnel only
- There must be thermometers to monitor temperature

6.4.2.3. ***Long term – clean room***

- Funds should be obtained for funding the upgrade of the facility
- Aseptic suite should be constructed
- Benches should be made of special stainless steel with curved sealed edges to contain spillages and prevent dust build up

- The air that is supplied into clean rooms should have positive pressure and filtered through HEPA filters, while ensuring that the air flow relative to adjacent lower grade areas cleanses the area efficiently
- Necessary structural changes to the facility should be made to meet the local and international standards for radiolabelling blood products
- It is recommended that there must be an interlocked pass-through hatch in the aseptic suite
- There must be filtered exhaust for extraction of contaminated air
- The must be pressure gauges in the clean room to monitor pressure changes
- The pressure difference of the surrounding grades should be 10 – 15 Pascal lower in order to maintain air flow effectively between the different grades. This will ensure that the internal environment of the clean room is controlled
- Electrical controls should be installed
- There must be an eyewash facility and a shower near the clean room
- All the necessary equipment should be obtained

6.4.2.4. ***Long term – hot lab***

- The hot lab must be moved to the new radiopharmacy unit
- In the hot lab there must be a fume cupboard for volatile radiopharmaceuticals
- There must be an eyewash facility and a shower near the hot lab
- Staff working in the hot lab should have additional film badges, and finger dosimeters since they are involved in the elution of generators and their hands are exposed to high levels of radiation

6.4.3 Equipment (short-term)

- The LAF hood in the Department should be commissioned for use and maintenance plan developed
- LAF services and filters checked

- A cooled centrifuge with sealable buckets dedicated for radiolabelling of blood cells must be obtained
- There should be measures in place to monitor contamination of equipment used in the clean room by radioactive materials as well as micro-organisms
- Equipment should be assembled in such a way that surfaces that come into contact with the product are not reactive, additive or absorptive to ensure that the quality of the radioactive products is not affected

6.4.4 Finance

- Funds should be obtained for upgrading the facility
- Short term funding for clean room: (+/-) R50 000
- Cost for the centrifuge: R40 000 including VAT
- Long term funding for the clean room: R960 000 including VAT

6.4.5 SOPs

- Final SOPs should be developed collaboratively with all the staff in the department

6.5 LIMITATIONS OF THE STUDY

The audit was only done in a single facility. Therefore, this may not reflect the true picture in SA public sector hospitals in general.

6.6 SUMMARY

This chapter described the summary of results, conclusion and recommendations of the study conducted.

6.7 CLOSURE

This investigation has clarified the shortfalls in the facilities and training of staff in the Department with regard to the implementation of a service for radiolabelling of autologous blood cells at DGMH. The study has provided a detailed way forward for the proposed service. Management and staff of the Department have shown a commendable openness and enthusiasm to address the challenges that are present. Medunsa Campus administration has indicated support in principle. It is to be hoped that such support translates into financial support.

An investment in the staff and facilities at the Department of Nuclear Medicine will have considerable spin-off benefits in terms of improved patient care and research.

The Department of Health, Gauteng is bound by the law to provide safe and appropriate care for patients and a safe and appropriate working environment for staff. Failure to do so can have serious repercussion. Hence Gauteng DoH must support the upgrade of the radiopharmacy facility.

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APPENDICES

Appendix A: Facility Survey Form

Description	Compliant	Non-compliant	Non-compliant
Premises			
Access is limited to authorised personnel			
The layout and structure of the radiopharmacy unit ensures a safe and organized workflow			
The lighting is fluorescent globes which are working			
The ceiling is smooth, impervious and unbroken			
The work surfaces material is smooth, impervious and unbroken			
The walls are smooth, impervious and unbroken			
The floor is smooth, impervious and unbroken			
The equipment is dedicated for use in the radiopharmacy unit only			
The hotlab is kept clean			
The LAF cleanroom is kept to Class D standards			
There are no sinks in the clean room			
There is an eyewash facility in the radiopharmacy unit			
There is a decontamination shower next to the radiopharmacy unit			
The laminar airflow hood is situated in a clean room			
The laminar airflow is currently in use			
The laminar airflow is the correct type for compounding of radiopharmaceuticals/radiolabelling of autologous blood cells			
There is a designated change room for de-gowning			
There are bins for waste disposal in the clean room			

Description	Compliant	Non-compliant	
Environment control			
Temperature is monitored			
Temperature control in the facility are kept between 20^{o}C and 25^{o}C			
Air supply is filtered to ensure removal of particulate and microbial contamination			
Humidity is kept between 35-45% and monitored on a daily bases			
Personnel			
The number of personnel in the hot lab at any one time is restricted			
Suitable protective clothing is used by personnel (non-linting gowns, overshoes, masks, gloves (sterile and powder-free)			
Personnel adhere to hand washing SOPs			

Appendix B: Personnel Questionnaire

Date: _____ Occupation: _____

This is a personnel questionnaire developed in order to conduct research on aseptic services at the department of nuclear medicine, DGMH. Your feedback is important to my study. This survey is anonymous and your responses will be held in the strictest confidence. Thank you for your thoughtful feedback.

- This survey will take approximately 10 minutes to complete.

PART A

1. Please answer the questions below:

DESCRIPTION	HOT LAB		LAF AREA	
	YES	NO	YES	NO
Hygiene is satisfactory				
LAF hood is used for manipulation of radiopharmaceuticals				
LAF hood is currently in use				
LAF hood is situated within the cleanroom				
Are there SOPs are valuable for aseptic admixing of radiopharmaceuticals tasks performed?				
A change room i s available?				
Staff members received training in aseptic services				
Training on aseptic handling of radiopharmaceutical can improve aseptic services in the department				
Microbial and particle tests are performed				
Is there an observational checklist for admixing of radiopharmaceuticals				

Please give your suggestions with regards to following:

- The importance of SOPS in the radiopharmacy unit

……
……
……
……
……

- ❖ The importance of staff training in aseptic services and monitoring of staff performance.

……
……
……
……
……
……
……

PART B (Working procedures)

1. Are there SOPs for the following tasks?

	YES	NO	UNKOWN
Hand washing			
Wearing of protective clothing			
Elution of the generator			
Admixing of radiopharmaceuticals			
Record keeping of tasks performed			

Other SOPs, please list

……
……
……
……
……
……

Do you have suggestion(s) with regard to the current SOPs?

……
……
……
……

2. Give suggestions on how to improve current aseptic working procedures in the Department.

……
……
……
……..

Thanks for your time and your valuable input

Appendix C: Consent form for personnel

This study aims to implement aseptic services for radiolabelling of autologous blood cell in the Department of Nuclear Medicine, DGMH. Therefore, participation of personnel working in the department is value in this study. Participants will remain anonymous and their responses will be held in the strictest confidence. .

Name of Study

Implementation of an Aseptic Service for Radiolabelling of Autologous Blood Cells at the Department of Nuclear Medicine, Dr George Mukhari Hospital

I have heard the aims and objectives of the proposed study and was provided the opportunity to ask questions and given adequate time to rethink the issue. The aim and objectives of the study are sufficiently clear to me. I have not been pressurized to participate in any way.

I know that sound recordings will be taken of me. I am aware that this information scientific publications which will be electronically available throughout the world. I consent to this provided that my name is not revealed.

I understand that participation in this Study is completely voluntary and that I may withdraw from it at any time and without supplying reasons.

I know that this Study has been approved by the Medunsa Research Ethics Committee (MREC), University of Limpopo (Medunsa Campus) / Dr George Mukhari Hospital. I am fully aware that the results of these results of this Study will be used for scientific purposes and may be published. I agree to this, provided my privacy is guaranteed.

I hereby give consent to participate in this Study.

....
Name volunteer Signature

....
Place Date Witness

I hereby to agree that I will hold responses given by the respondent in the strictest confidence.

Statement by the Researcher

I provided verbal and/or written information regarding this Study
I agree to answer any future questions concerning the Study as best as I am able.
I will adhere to the approved protocol.

....
Name of Researcher Signature Date Place

Appendix D: Focus group discussion (FGD)

This is a FGD which will allow staff to give their opinion on the current working procedures regarding aseptic handling of the radiopharmaceuticals.

Topics to be discussed during the FGD are as follows:

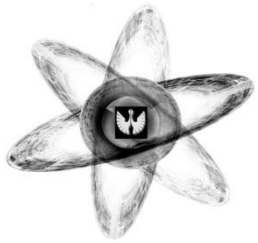
1. Do you have aseptic services in place in the Department?
2. How do you ensure aseptic handling of radiopharmaceuticals?
3. Are there SOPs for admixing radiopharmaceuticals?
    - ❖ If NO, what is needed to develop these SOPs
4. Who develops these SOPs?
    - ❖ If YES, what is covered by the SOPs
    - ❖ Who developed the SOPs and what sources were used to develop these SOPs
5. Would implementation of aseptic services improve aseptic handling of radiopharmaceuticals?
    - ❖ If so, how will it improve the aseptic services and who should be involved in implementing aseptic services
6. In your opinion, how will implementation of aseptic services improve current working conditions in the hot lab and who should be involved?

Appendix E:Microbial contamination data collection form

Date: _____

Station	Settle plates	Type of organism	Number of counts
1			
2			
3			
4			

Appendix F: Standard Operating Procedures (SOPs)

MEDUNSA/DGMH 	**STANDARD OPERATING PROCEDURE**	**SOP NO: CR 2012-01**	Copy: 1/1
	TITLE: CLEANING PROCEDURES		Page 1 of 6
	PURPOSE: The aim of this procedure is to ensure that the clean room in the department is clean and does not exceed the recommended limits for microbial contamination. Compliance will be assured by continuing successful outcomes of microbiological monitoring.		Revision No: 0
	SCOPE: Applies to all staff involved in cleaning and disinfecting in the clean room		Revised Date: N/A
			Effective Date: TBD
DEPARTMENT: Nuclear Medicine	**RESPONSIBILITY:** Radiopharmacist, radiographers and NM Physician		Supersedes no: N/A

This SOP has been designed to be used in a working radiopharmacy environment.

LEAD PAGE: this page will indicate the latest current version in circulation and record any changes made by the any personnel in the SOP.

LEAD PAGE

PROCEDURES FOR SAFE AND EFFECTIVE USE OF THE CLEAN ROOM	SOP NO: CR 2012-01	Attachment No.
Department:	Nuclear Medicine	Page 1 of 6
Effective Date:	TBD	Revision No. 0
		Revision Date:

<table>
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 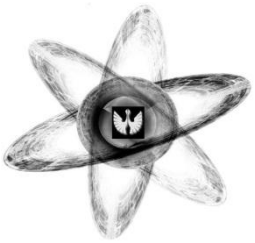 </td><td>STANDARD OPERATING PROCEDURE</td><td>SOP NO:
CR 2012-01</td><td>Copy: 1/1</td></tr>
<tr><td colspan="2">TITLE: CLEANING AND DISINFECTING PROCEDURES</td><td>Page 2 of 6</td></tr>
<tr><td colspan="2">PURPOSE: The aim of this procedure is to ensure that the clean room in the department is clean and does not exceed the recommended limits for microbial contamination. Compliance will be assured by continuing successful outcomes of microbiological monitoring.</td><td>Revision No: 0</td></tr>
<tr><td colspan="2" rowspan="2">SCOPE: Applies to all staff involved in cleaning and disinfecting in the Department</td><td>Revised Date: N/A</td></tr>
<tr><td>Effective Date: TBD</td></tr>
<tr><td>DEPARTMENT:
Nuclear Medicine</td><td colspan="2">RESPONSIBILITY: Radiopharmacist, medical physicist, Radiographer</td><td>Supersedes no: N/A</td></tr>
</table>

This SOP has been designed to be used in a working radiopharmacy environment. Changes should be considered carefully as some processes are based on legislative or good practice requirements.

PROCEDURE 1

Staff responsible for cleaning in the clean room should commence cleaning activities in the clean room to prevent cross contamination of highest grades (i.e. start from grade A towards grade D which may have unclassified internal environment, GMP requirement)

NB: wear protective clothing, and start cleaning the room from the ceiling, walls and floor

Ceiling, walls and floor

- Cleaning must be in the following sequence, ceiling walls and floor as follows: Use a cylinder vacuum to remove any masonry particles attached to surface since they are capable of scratching the ceiling
- Wash the surface using a disposable mop head/sterile cloth, sterile neutral detergent and clean water
- Use of non-ionic surfactants is advisable as they are non-aggressive and produce low foam

- Avoid wetting HEPA filters (if present) as they can be easily be damaged by cleaning agents
- DO NOT use household disinfectants since they are abrasive and leave residues
- Repeat the cleaning process with the detergent until the bucket appears to have no sign of solid particulate matter and the mop head is not looking dirty
- Discard dirty water in the sink outside the clean room after completing the cleaning procedure

NB:

- Minimise the use of aggressive of harsh chemical disinfectants as they can damage the surfaces
- Change the detergents and disinfectants used for cleaning at least every six months to avoid microbial resistance

Benches, hatches and doors

- Cleaning should commence from the benches, hatches and doors in that order
- Chlorine dioxide, hypochlorite or dichloroisocyanurate should be the disinfectants to be used to disinfect benches, hatches and doors
- Spray the disinfectant on benches, hatches and doors and allow at least 15 minutes for the disinfectant to dry
- Spray 70% alcohol on the surfaces sprayed with the disinfectant and wipe by hand using non linting wipes
- Repeat the process at least twice using different wipe
- Avoid contact of used wipes with cleaned areas
- Place the used wipes in the bin outside the clean room after completing the cleaning process

LAF

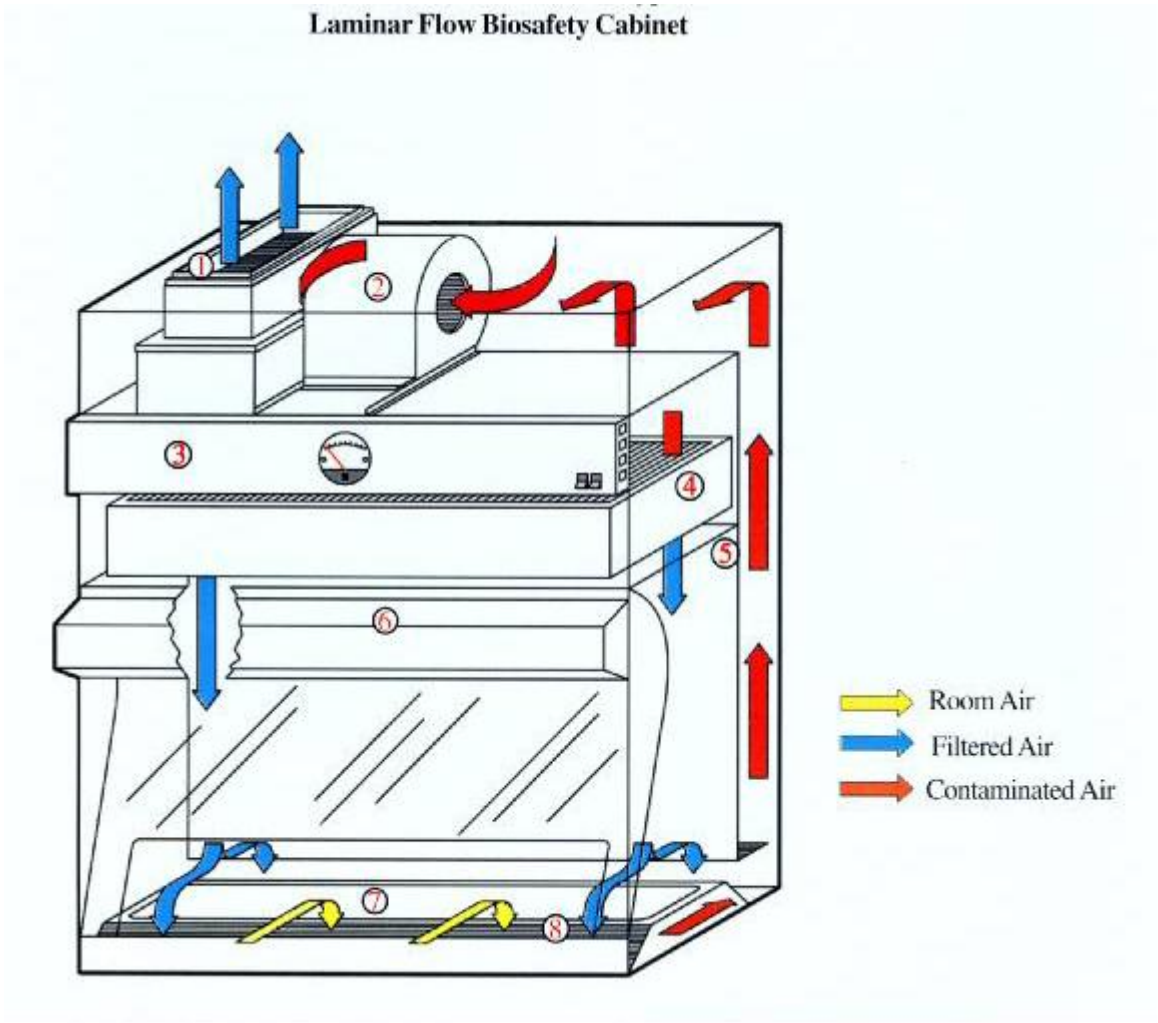

Figure 5.1: Example of a vertical LAF cabinet
Source: (NSF/ANSI-49, 2002.)

- Follow the aseptic procedures for gowning prior to commencing with the cleaning process of the LAF in the clean room
- Gather the following cleaning materials:
- Sterile non-linting wipes
- A spray bottle of 70% isopropyl alcohol (IPA) (Sterile IPA should be used)
- Spray gloved hands with sterile 70% alcohol

- Spray all cleaning materials to be placed in the LAF with sterile 70% alcohol IPA. Make sure that all the sides are sprayed before placing the material in the LAF
- Use the sterile 70% alcohol in a spray bottle and sterile non-linting wipes to clean all surfaces of the LAF
- Cleaning should start from the cleanest area to the dirtiest area (i.e. wipe from the ceiling of the LAF, back, sides and the floor of the LAF in that order)
- Spray the 70% IPA to the ceiling of the LAF and use sterile wipes to wipe. The following procedure should be followed for wiping all the sides of the LAF:
- Wipe in overlapping parallel strokes
- Overlap each stroke by 10-20 %
- The wipe should be a quarter-folded for each wipe stroke
- Use a new sterile wipe for each stroke procedure

  NB: This procedure should be followed for all the sides of the LAF.

- Dispose of all the soiled wipes in the waste bag and remove it from the LAF.
- Place the waste bag in the bin outside the LAF
- Surfaces of the LAF should be allowed to dry before manipulation of blood cells can commence

NB:

- All cleaning material used in the clean room should be stored in a designated area which is free from contamination
- Disinfection should be done weekly
- Sporicidal cleaning should be done only if there is sign of contamination by spores (agents of choice to be used include: chlorine agents, peroxygens, hydrogen peroxide and peracetic acid)

MONITORING OF THE CLEANING PROCESS

- Use contact plates and swabs to monitor level of cleanliness of surfaces, ceiling, walls, floors and buckets used for cleaning in the clean room
- If the level of contamination is above recommended limits the cleaning process should be reviewed
- Monitoring of the cleaning process should be performed at least six monthly
- Record of results should be kept

NB: An inline particle counter and/or settle plates should be used to validate the LAF hood during use. This will help to establish whether the LAF hood complied during use to the Grade A specifications.

END OF PROCEDURE

Compiled by: MARINGA I.M **Adapted from:** IAEA, IAEA IOG, ISORBE, EU Guidelines, USP<797> Guidelines, UR LLE **Date: 01/10/2012**	**Checked by:** **Date:**	**Approved by:** **Date:**

<table>
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 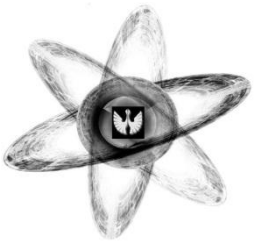 </td><td>STANDARD OPERATING PROCEDURE</td><td>SOP NO:

CR 2012-02</td><td>Copy: 1/1</td></tr>
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<tr><td colspan="2" rowspan="2">SCOPE: Covers procedure that should be followed regardless of which detergent is used.</td><td>Revised Date: N/A</td></tr>
<tr><td>Effective Date: TBD</td></tr>
<tr><td>DEPARTMENT: Nuclear Medicine</td><td colspan="2">RESPONSIBILITY: Radiopharmacist, medical Physicist, Radiographer</td><td>Supersedes No:

N/A</td></tr>
</table>

This SOP has been designed to be used in a working radiopharmacy environment. Changes should be considered carefully as some processes are based on legislative or good practice requirements.

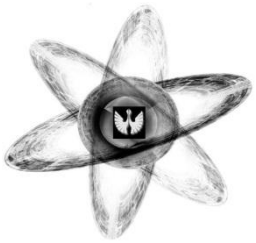
PROCEDURE 2

- Remove any jewellery and wristwatches.
- Securely cover any breaks in your own skin with a waterproof dressing.
- Make sure you are not allergic to the detergent to be used.
- Turn on the taps – adjust the water flow until a comfortably warm temperature is achieved and the splashing of water to surrounding areas is minimized.
- Wet both hands thoroughly.
- Apply the chosen detergent solution and rub the hands together to create a soapy lather.
- Continue to rub hands together briskly, paying particular attention to the area surrounding the nails.

- A nailbrush should only be used if the nails are dirty – it should not be used on the skin.
- Continue to wash hands for a minimum of 15 seconds at least.
- Hands should be rinsed thoroughly under warm water, again being careful not to splash the surrounding area. There should be no visible trace of detergent remaining on the hands.
- Turn off the water using either the elbow or foot depending on the taps. If the taps do not operate this way, leave the water running until drying of the hands is complete, when the taps can be turned off using a clean paper towel.
- Disposable paper towels should be used to pat the hands dry; it is recommended that drying should be initiated at the fingertips and proceed upwards to the wrists.
- Used paper towels should be disposed of according to the local infection control policy.

END OF PROCEDURE

Compiled by: MARINGA I.M **Adapted from:** IAEA;ISORBE;ISO **Date: 01/10/2012**	**Checked by:** **Date:**	**Approved by:** **Date:**

<table>
<tr><td rowspan="5">MEDUNSA/DGMH
  </td><td>STANDARD OPERATING PROCEDURE</td><td>SOP NO:

CR 2012-03</td><td>Copy: 1/1</td></tr>
<tr><td colspan="2">TITLE: Gowning and degowning procedures</td><td>Page 1 of 2</td></tr>
<tr><td colspan="2">PURPOSE: The aim of this procedure is to ensure that all personnel working in the clean room follow the right procedure for gowning/degowning.</td><td>Revision no: 0</td></tr>
<tr><td colspan="2" rowspan="2">SCOPE: Covers procedure that should be followed regardless of the type of aseptic suit used.</td><td>Revised Date: N/A</td></tr>
<tr><td>Effective Date: TBD</td></tr>
<tr><td>DEPARTMENT: Nuclear Medicine</td><td colspan="2">RESPONSIBILITY: Radiopharmacist, Medical Physicist, Radiographer</td><td>Supersedes no:

N/A</td></tr>
</table>

This SOP has been designed to be used in a working radiopharmacy environment. Changes should be considered carefully as some processes are based on legislative or good practice requirements.

PROCEDURE 3

Gowning Procedure

- All jewellery and make-up should be removed before entering the change room.
- Follow SOP 2 for the aseptic technique to wash hands with antiseptic soap and warm water, then dry hands with low lint paper towel
- Put on a pair of disposable shoe covers immediately after entering the change room Move to the clean side of the change room
- Treat hands with sanitizer
- Put a facemask on (disposable). Ensure that there are no gaps around nose or mouth
- Put the first pair of sterile powder-free bulk packaged gloves on.

- Put on a non-linting theatre gown
- Inspect completed gowning in mirror
- Put on a second pair of sterile powder-free bulk packaged gloves on. Make sure glove cuffs are over gown cuffs
- Put head cover on head, make sure that hair and ears are completely covered
- Enter the clean room

END OF PROCEDURE

PROCEDURE 4

Degowning Procedure

- Exit the clean room
- Enter the change room
- Move to the dirty side of the change room and remove the outer gloves and place in Biohazard waste bag
- While still in the dirty side remove the facemask, head cover, theatre gown and overshoes in that order
- Place garments in correct waste or laundry bag
- Exit the change room

END OF PROCEDURE

Compiled by: MARINGA I.M **Adapted from:** IAEA; ISORBE; NHS; UR LLE **Date: 01/10/2012**	**Checked by:** **Date:**	**Approved by:** **Date:**

<table>
<tr><td rowspan="4">MEDUNSA/DGMH</td><td>STANDARD OPERATING PROCEDURE</td><td>SOP NO:

CR 2012-04</td><td>Copy: 1/1</td></tr>
<tr><td colspan="2">TITLE: Radiolabelling of Leukocytes with 99m Tc HMPAO autologous blood cells</td><td>Page 1 of 4</td></tr>
<tr><td colspan="2">PURPOSE: The aim of this procedure is to ensure that all the necessary steps in radiolabelling of autologous blood cells are adhered to by the operator.</td><td>Revision No: 0</td></tr>
<tr><td colspan="2" rowspan="2">SCOPE: Covers procedures that should be followed regardless of the environment in which manipulation of these blood cells is performed</td><td>Revised Date: N/A</td></tr>
<tr><td>Effective Date: TBD</td></tr>
<tr><td>DEPARTMENT: Nuclear Medicine</td><td colspan="2">RESPONSIBILITY: Radiopharmacist, medical Physicist, Radiographer</td><td>Supersedes No:

N/A</td></tr>
</table>

This SOP has been designed to be used in a working radiopharmacy environment. Changes should be considered carefully as some processes are based on legislative or good practice requirements.

PROCEDURE 5

Preparation of the area:

- Preparation should take place 30 minutes prior to use
- Put on protective clothing before commencing with manipulation of blood products
- Wipe the work surface and sides of the LAF with 70% alcohol
- Manipulation of autologous blood cells should only be performed in a LAF
- Ensure that the environment is safe for manipulation of blood products and the operator is protected from the blood product as well as the blood components is protected from the operator

- Ensure that all the apparatus (glassware/plastic ware) and reagents used are sterile
- Blood products from one patient should be handled at a time to avoid cross-contamination
- This procedure should only be performed at room temperature unless stated otherwise
- Check if the LAF fan is on

Preparation of autologous radiolabelled leukocytes:

- Draw 3 ml ACD-A into three 20 ml syringes (syringe A, B and C)
- Use a 19-G Butterfly needle infusion set to withdraw the blood into syringe A, B and C:
    - A: Gently infuse 17 ml of blood in syringe A containing 3 ml of ACD-A
    - B: Gentle infuse17 ml of blood in syringe B containing 3 ml of ACD-A
    - C: Gentle infuse17 ml of blood in syringe C containing 3 ml of ACD-A
- After withdrawing the blood into different syringes, mix the blood gently until mixed thoroughly with ACD-A
- Use sterile hubs to close the syringes with blood
- Syringes containing blood with ACD-A should carefully be wiped with 70% alcohol before placing them in the LAF
- Without a needle, transfer contents of one 20ml into an empty 50 ml conical tube
- Run the blood down the side of the tube to avoid bubbles and frothing
- Centrifuge the tube at 200g (3200rpm) for 10 minutes with balance tube supernatant **A**-(cell free plasma)

- Use a sterile 3-way-stopcock and a syringe to withdraw 4 ml Macrodex into each of the remaining 20ml syringes with blood. Ensure that the tips of each syringe is clean and mix carefully
- Cover syringes containing blood and Macrodex with a clean needle. Use a glass beaker or stand to position the syringes with the needle upwards
- Allow the syringes in the beaker or stand to stand for 30-60 minutes for erythrocytes sedimentation to take place
- Transfer plasma from syringes into two clean tubes using butterfly
- Centrifuge the two tubes at 150g (870 rpm) for 5 minutes to give supernatant platelet rich plasma (PRP) and a pellet of mixed leukocytes in each tube
- Using a pipette or syringe with intracath tip to transfer supernatant from the tubes of the step above into two tubes. Be careful not to disturb the pallet
- Remove the last bit of the supernatant with a 2 ml syringe with Intracath/Jelco plastic tip
- Centrifuge supernatant tubes from the step above at 2000g (3200rpm) for 10 minutes to obtain supernatant **B** (Platelet poor plasma - PPP)
- Loosen the pellets of leukocytes by very gently tapping and swirling the tubes
- Prepare HMPAO with 800-1000 MBq Tc-99m MBq for fractionated kit or 1500-2000 MBq in 5 ml for Ceretec kit and withdraw 2 ml (500 – 650 MBq) in a syringe. Do chromatography immediately
- Carefully wipe syringes with alcohol and place in the LAF
- Add Tc-99m HMPAO drop wise to the cell suspension
- Mix gently and allow to stand for 15 minutes at room temperature
- On completion of incubation, carefully add 5ml cell free plasma **A** to cell suspension. Mix gently.

- Labelled cells should be centrifuged for 5 minutes at 150 (870rpm)
- Remove all the radioactive supernatant and transfer into a clean tube
- Use a syringe with a 19G needle or intracath plastic tip to measure the activity
- Carefully resuspend the labelled cells with 5 ml cell free plasma **A.**
- gently swirl to mix
- carefully draw up the labelled cells into a plastic, non-heparinised syringe and close it with a sterile hub or needle
- keep only a drop in the tube for Trypan Blue test
- measure activity of the syringe
- Calculate the labelling efficiency and do Trypan Blue test
- Administer labelled cells to the patient as soon as possible via a 19G needle/butterly

END OF PROCEDURE

Compiled by: MARINGA I.M **Adapted from:** Tygerberg Hospital SOPs; IAEA; ISORBE. **Date: 01/10/2012**	**Checked by:** **Date:**	**Approved by:** **Date:**