QUALITY ASSURANCE OF RADIOPHARMACY IN SELECTED GAUTENG ACADEMIC HOSPITALS

A dissertation submitted by

Misa Sizipiwe Qatyana

in partial fulfilment of the requirements for the degree

Master of Science in Medicine (Pharmacy)

in the

School of Health Care Sciences

Faculty of Health Science

Supervisor: Dr. B Summers

Co-supervisor: Mr. J Le Roux

Department of Pharmacy

University of Limpopo (Medunsa Campus)

2010

DECLARATION

I, **Misa Sizipiwe Qatyana**, hereby declare that the work on which this study is based is original and is my work in design and execution, 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……..

ACKNOWLEDGEMENTS

I would like to extend my warmest and sincere gratitude to the Almighty God for having given me the strength to carry out this research, through You all things are possible; Also thanks to the following people:

- Dr Beverley Summers, my supervisor, for her guidance, encouragement and endless support throughout my internship. You kept me motivated especially in the darkest hours of this study.
- Mr Jannie le Roux, my co-supervisor, for his input which was invaluable.
- Professor Sietske Rubow for her contribution in this study and for selflessly allowing us to pick her brain and use the Nuclear Medicine Department in Tygerberg Hospital for our pilot study.
- The HODs and the rest of management at Dr George Mukhari Hospital and Steve Biko Academic Hospital; Professor Trevor Mdaka, Dr Ouma Ramafi and Professor Mike Sathekge, for being involved in this study and making it possible for the study to take place.
- The staff at Dr George Mukhari Hospital and Steve Biko Academic Hospital for their help, support, not forgetting their patience during the course of the study.
- The Medical Research Council for supporting this study financially.
- Department of Pharmacy, Medunsa Campus staff, for their continued support throughout my internship.
- Nikki Williamson, for her assistance with the formatting, I could not do what you do even if I try.
- Kate Jollye for lending me a hand with Appendix 6, it might have seemed like a small job, but it is much appreciated.
- Family and friends for their support. Thank you for being there for me.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF APPENDICES

ABBREVIATIONS AND ACRONYMS

Bq	Becquerel
CEO	Chief Executive Officer
Ci	Curie
DCI	Data Collection Instrument
DOH	Department of Health
DPM	Disintergrations per minute
FDA	Food and Drug Administration
FDG	Fluorodeoxyglucose
FGD	Focus Group Discussion
FIP	International Pharmaceutical Federation
GMP	Good Manufacturing Practice
HEPA	High Efficiency Particulate Air
HOD	Head of Department
IAEA	International Atomic Energy Agency
IOG	Operational Guidance on Hospital Radiopharmacy
LAF	Laminar Air Flow
MCC	Medicines Control Council
MIBG	Meta-iodobenzylguanidine
Mo	Molybdenum
mR/h	milliroentgens per hour
OL	Operational Level
PET	Positron Emission Tomography
QA	Quality Assurance

QC	Quality Control
RBC	Red Blood Cells
SAPC	South African Pharmacy Council
SOP	Standard Operating Procedure
Tc	Technetium
UKRG	United Kingdom Radiopharmacy Group

ABSTRACT

Introduction: The aim of this study was to identify and assess compliance with published radiopharmacy procedures in the radiopharmacy units in the Departments of Nuclear Medicine at Steve Biko Academic Hospital, Pretoria and Dr. George Mukhari Hospital, Ga-rankuwa.

Objectives: To identify current written SOPs in use by the selected hospitals and to compare them with the two selected audit documents. To describe the Operational Levels (OLs) according to the IAEA classification, staffing and workload of the selected radiopharmacy units. To assess the two selected radiopharmacy units for compliance with the South African Department of Radiation Control audit criteria and the International Atomic Energy Agency Operational Guidance on Hospital Radiopharmacy (IAEA IOG). To obtain the views of staff at operational, clinical and managerial level regarding constraints in the work situation and the potential implementation of 'best practice' approaches. To identify the elements from the IAEA IOG (IAEA 2008), which are realistically achievable in the South African hospital setting. To compile a comparative report of the assessment and to make recommendations for practice improvement.

Method: Quality assurance audit documents (local and international) for "Hot" Laboratories were sourced and compared. Only three radiopharmacy audit documents could be sourced (namely the South African Department of Radiation Control (DOH, 2007), the International Atomic Energy Agency, Operational Guidance on Hospital Radiopharmacy (IAEA, 2008) and United Kingdom Radiopharmacy Group, Radiopharmacy audit (United Kingdom, 2006). The most stringent of these documents the IAEA IOG was selected and was used to assess the equipment, facilities, practices and work flow in the selected radiopharmacy units. A pilot study was conducted at the Nuclear Medicine Department in Tygerberg Hospital to get a clear understanding of the IOG audit document and to develop a system with which to approach the audit of the two study sites. The numbers and qualifications of staff involved in preparation of radiopharmaceuticals were documented as part of the audit. The IOG audit was conducted in the Nuclear Medicine Departments of the two Gauteng Academic Hospitals. Key informants who included radiopharmacists with international experience, currently working in South Africa and the HODs of the Nuclear Medicine Departments audited. The IOG audit results together with the FGD and Key informant information were used to compile recommendations.

Results: For anonymity, the hospitals are referred to as hospital X and Y in the results. In both hospitals the chief radiographer is responsible for the radiopharmacy unit. In Hospital X

this responsibility is shared with the medical physicist. The radiographers that work in both hospitals have had specific “hot” laboratory training. Neither hospital has a formal system of radiopharmaceutical record keeping, nor do they compile or review their SOPs in any formal or regular way. Neither hospital performs an annual performance review to check the competencies of their staff. Hospital X has equipment that was not in use at the time the research was conducted. Both hospitals are authorised to handle certain radionuclides and radiopharmaceuticals/kits. Hospital Y offers a wider range of Nuclear Medicine services as compared to Hospital X. Hospital Y had already conducted the IAEA Nuclear Medicine IOG Hospital Radiopharmacy audit on their facility, whereas Hospital X had not. Hospital Y, when assessed on verifiable items, met 70 to 100% the required standards for class A items for all components apart from staff at OL2, dispensing protocols and waste management. Hospital X met 70 to 100% of standards only for staff at OL1, facilities and purchasing. In the components of staff at OL2, dispensing, preparation, quality assurance and waste management, the percentages of items where standards were met were much lower at only 12.5 to 55%. In terms of the ease of administration of the IAEA IOG audit, the researcher found that some of the audit items (references) were difficult to interpret because they were presented as multiple questions, some were duplicated, and some lacked clarity.

Conclusion: It can be concluded from the results that the one shortfall that both hospitals share is in terms of documentation and record keeping. Both the hospitals’ waste management procedures need to be documented. Neither hospital has a radiopharmacists in charge of the radiopharmacy unit.

Recommendations: Recommendations are made in terms of staff training, facility upgrades and the introduction of formal standard operating procedures (SOPs) and log books for batch traceability in both Hospitals. Radiopharmacist involvement is recommended. Since there are not enough trained radiopharmacists in South Africa, it could be a part-time function of those qualified or they could share responsibility for more than one radiopharmacy. The audit questions could be revised in order to eliminate factors that were noted by the researcher such as multiple questions, duplication and ambiguity.

The IAEA is commended for its role in the promotion of Nuclear Medicine and Radiopharmacy training and audits. Regional summaries of audit results should be available from the IAEA to aid comparative benchmarking and monitoring of progress over time.

CHAPTER 1
INTRODUCTION

1.1 BACKGROUND AND RATIONALE FOR THE STUDY

Quality Assurance should form part of the routine practice of every institution and department, as it is important that the best possible health care is provided to patients. A Quality Assurance programme should be in place to ensure optimal patient care through the generation of accurate and objective data and adequate records of the processes and services provided (Sharp *et.al.*, 2005).

Nuclear Medicine is an expanding field for the diagnosis and treatment of a wide range of conditions. It is a medical specialty that uses safe, painless and cost-effective techniques for the purpose of imaging a tissue or organ, or to treat disease (Society of Nuclear Medicine, 2009).

The advantage of Nuclear Medicine in diagnostics is that it can combine a range of structural images with functional imaging. It also highlights small areas of abnormality. Hence Nuclear Medicine facilitates accurate and early diagnosis of disease, which can result in a better prognosis. A key component of such imaging is the radiopharmaceutical (Society of Nuclear Medicine, 2009).

Nuclear Medicine, when used as a treatment modality, allows direct radiopharmaceutical targeting of tissues which are hyperproliferative.

The radiopharmaceutical emits energy photons or particles that can be detected and computed into an image of the emission source for diagnostic purposes. If the energy levels are high enough, the radiopharmaceutical can be used to ablate or destroy hyperproliferative tissue.

A radiopharmaceutical is a preparation, intended for *in vivo* use, that contains a radionuclide in the form of a simple salt or a complex. A radiopharmaceutical consists of a radionuclide and a ligand which is organ-specific. It may exist as a solid, liquid, gas, or pseudogas (Remington, 2006).

The radiopharmaceutical when administered is intended to target certain tissues, binding sites, and/or biochemical pathways. Hence the chemical and physical identity and form of a radiopharmaceutical are important (Remington, 2006).

Radiopharmaceuticals are prepared in a radiopharmacy or “Hot” laboratory which is a designated area for their safe and controlled preparation. For the purpose of this study the “Hot” laboratory will be referred to as a radiopharmacy (IAEA, 2008a).

In the South African context, the majority of radiopharmacy units which prepare radiopharmaceuticals for clinical use are operated by technicians, who posses varying qualifications, though many are radiographers (Ramafi, 2008).

The levels of technical procedures and expertise required for the preparation and dispensing of different radiopharmaceuticals are described in the IAEA Operational Guidance as “Operational levels” (IAEA, 2008a).

Internationally it is recognised that a radiopharmacist is required for optimal and safe preparation of radiopharmaceuticals. The role of the radiopharmacist covers the following activities: procurement, compounding, quality assurance, dispensing, distribution, health and safety, provision of information and consultation, monitoring patient outcomes, and research and development (Ponto & Hung, 2000).

Quality assurance (QA) and standard operating procedures (SOPs) are integral to the optimal delivery of radiopharmacy services. Internationally there are guidelines which are recommended for use in the practice of radiopharmacy (UK Radiopharmacy Group, 2006 & IAEA, 2008a).

In Gauteng alone, there are three academic hospitals whose Nuclear Medicine units are operating without a much-needed radiopharmacist (Ramafi, 2008; Sathekge, 2008).

There are no official guidelines for the handling of radiopharmaceuticals in South African hospitals. Radioactivity safety aspects are covered by the Department of Health’s Department of Radiation Control (DOH, 2007).

The researcher performed an online search of academic peer reviewed sites and journals, the International Atomic Energy Agency (IAEA) website and recent editions of radiopharmacy text books. The researcher also consulted experts with local and international experience. This search revealed no published survey of radiopharmacy practice in South African hospitals.

The literature search also covered radiopharmacy audit documents. It was not possible to source radiopharmacy audit documents from the United States of America, despite comprehensive searches. Only two international radiopharmacy audit documents could be sourced, those of the IAEA and UK Radiopharmacy Group. The IAEA audit is in the process

of being introduced internationally but few hospitals in South Africa have undergone the audit (Rubow, 2008). The radiopharmacy at the academic hospital for the university at which the researcher is based had not been audited. In addition, the IAEA has not assessed the audit in terms of the ease of administration for those attempting a self-audit. Hence the researcher identified a need for the radiopharmacy at Dr George Mukhari to undergo the audit. The process would also provide the opportunity to assess the ease of use of the IAEA audit document. For comparison, and because of its accessibility, the radiopharmacy at Steve Biko Academic Hospital was also selected for audit**.**

1.2 PROBLEM STATEMENT

There is a need to define and assess current practices and staff levels in radiopharmacy units which serve Nuclear Medicine departments in South African hospitals, as little information is available on current practices and staff levels in radiopharmacy units in South Africa. In particular, the radiopharmacy at Dr George Mukhari Hospital had not conducted an audit.

1.3 AIM OF THE STUDY

To identify and assess compliance with published radiopharmacy procedures or standards in the radiopharmacy units in the Departments of Nuclear Medicine at Steve Biko Academic Hospital, Pretoria and Dr. George Mukhari Hospital, Ga-rankuwa.

1.4 OBJECTIVES OF THE STUDY

The objectives of the study were as follows:

1. To identify current written Standard Operating Procedures in use by the selected hospitals and to compare them with the two selected audit documents (see note below), i.e. those of the South African Department of Radiation Control (DOH, 2007) and the International Atomic Energy Agency, Operational Guidance on Hospital Radiopharmacy (IAEA, 2008a).

2. To describe the Operational Levels according to the IAEA classification (see Section 2.1 of literature review), staffing and workload of the selected radiopharmacy units in two Gauteng academic hospitals.

3. To assess two radiopharmacy units in Gauteng academic hospitals for compliance with the South African Department of Radiation Control audit criteria and the IAEA Operational Guidance on Hospital Radiopharmacy (IAEA, 2008a).*

4. To obtain the views of staff at operational, clinical and managerial level regarding constraints in the work situation and the potential implementation of 'best practice' approaches.

5. To identify the elements from the IAEA *Operational Guidance on Hospital Radiopharmacy - A safe and Effective Approach* (IAEA, 2008a), which are realistically achievable in the South African hospital setting.

6. To assess the ease of use of the IAEA Operational Guidance on Hospital Radiopharmacy audit document.

7. To compile a comparative report of the assessment and to make recommendations for practice improvement.

*Note: See section 3.5 Study Plan in method for rationale for choice of the two audit documents

1.5 IMPORTANCE OF THE STUDY

The International Atomic Energy Agency (IAEA) has stated that there is a global lack of qualified radiopharmacists and that internationally "hot" laboratories/radiopharmacy units in hospitals are "in a poor state" (IAEA, 2007). The IAEA is concerned that, among current staff, there is a lack of understanding of clean room and aseptic practices, together with poor radiation hygiene and waste management and a lack of staff training (IAEA, 2007).

South Africa (SA) has only two specialist radiopharmacists registered with the SA Pharmacy Council (South African Pharmacy Council, 2008). According to The Pharmacy Act (53 of 1974) registration as a radiopharmacist in South Africa requires an appropriate postgraduate degree and two years work experience in radiopharmacy. Internationally it is recognised that a radiopharmacist is required for optimal and safe preparation of radiopharmaceuticals (Saha, 2004 & Sampson, 1999). Currently the majority of South African hospital radiopharmacy units which prepare radiopharmaceuticals for clinical use are operated by technicians. The qualifications of these technicians vary.

Hence there is a need to assess the safety and practice standards as well as the numbers and categories of staff in South African radiopharmacy units.

CHAPTER 2
LITERATURE REVIEW

2.1 INTRODUCTION

The following topics will be discussed in this chapter: radiopharmaceutical use in Nuclear Medicine, the role of the radiopharmacist, quality assurance and radiopharmaceutical audits.

“A radiopharmacy service in a hospital is provided as either a stand-alone service by a radiopharmacy department or a radiopharmacy section of a nuclear medicine department” (Gross, 2007).

The researcher performed an online search of academic peer reviewed sites and journals, the International Atomic Energy Agency (IAEA), website, and recent editions of revised radiopharmacy text books. Experts in the field with local and international experience were consulted by the researcher. A search of the literature revealed no published survey of radiopharmacy practice in South African hospitals.

2.2 RADIOPHARMACEUTICAL USE IN NUCLEAR MEDICINE

Nuclear Medicine uses small amounts of radioactive materials or radiopharmaceuticals to diagnose or to treat disease. A radiopharmaceutical is a radioactive drug that typically elicits no physiological response from the patient and is based solely on the physiological function of the target organ (Sharp *et al, 2005*).

Radiopharmacy deals with the manufacture, use and monitoring of radiopharmaceuticals for the purpose of diagnosis and treatment. Radiopharmaceuticals allow the measurement of physiological and structural parameters, diagnostic imaging and the treatment of disease (Winfield & Richards, 2004).

A laboratory designed for the safe handling of radioactive materials and which may contain one or more “hot” cells is commonly (though not officially) termed a “hot” laboratory (Wikipedia, 2009)[1]. “Hot” in this case means, having or dealing with dangerously high levels

[1] The researcher is aware that Wikipedia is not a recognised academic reference source, but no other definition of a “hot Laboratory” could be identified.

of radioactivity. A “hot” cell is defined as a heavily radiation-shielded enclosure in which radioactive materials can be handled by persons using remote manipulators and viewing the materials through shielded windows or periscopes. (Wikipedia, 2009)[2]

Facilities required for the production of radiopharmaceuticals are very specific. Since these products are often administered intravenously they must be sterile. The products should therefore be prepared aseptically in a clean room with laminar flow cabinets or isolators (Winfield & Richards, 2004; IAEA, 2008a).

It is important that there is radiation protection in the radiopharmacy which is provided in the form of shielding, distance and time (Winfield & Richards, 2004):

> Shielding – should be around the radioactive source to reduce the radiation by the use of the following materials: plastic, perspex, aluminium, lead and tungsten.
>
> Distance – the radiation dose from a radioactive source is inversely proportional to the square of the distance.
>
> Time – by minimizing the time spent handling a radioactive source radiation exposure is reduced.

2.2.1 Operational levels in hospital radiopharmacy

In hospital radiopharmacy there is a wide range of procedures which are performed. These procedures are classified into three categories or Operational Levels (1, 2 and 3), which are further subdivided and described by the IAEA (IAEA, 2008a) as follows:

Operational level 1a:

This operational level involves the dispensing of radiopharmaceuticals which are purchased or supplied in their final form. Authorised and/or recognized manufacturers or centralized radiopharmacies are the source of these radiopharmaceuticals. No compounding is required since the radiopharmaceuticals are in the form of unit doses or multiple doses.

[2] The researcher is aware that Wikipedia is not a recognised academic reference source, but no other definition of a ‘hot lab’ could be identified.

Operational level 1b

This level involves the dispensing of radioiodine and other ready to use radiopharmaceuticals, which are used in radionuclide therapy or palliative care. Examples of these radiopharmaceuticals include ready to use injections of strontium and samarium for pain palliation.

Operational level 2a

Covers “closed procedures” where the radiopharmaceuticals are prepared from approved reagent kits, generators and radionuclides. In nuclear medicine departments, closed procedures are the most common activity taking place, with routine use of a ^{99}Mo/^{99m}Tc-generator and the reconstitution of pre-sterilised radiopharmaceutical cold kits (i.e. ligands and diluents).

Operational level 2b

This level involves the radiolabelling of autologous blood cells commonly used for infection or inflammation imaging. Red blood cells, platelets and white blood cells are examples of radiolabelled blood components.

Operational level 3a

Involves the compounding of radiopharmaceutials for diagnostic purposes from ingredients and radionuclides. There is also the modification of existing commercial kits, in-house production of reagent kits from ingredients including freeze drying and research and development.

Operational level 3b

Covers the compounding of radiopharmaceuticals for therapeutic purposes from ingredients and radionuclides with related research and development. Examples of these radiopharmaceuticals include radio-iodination of meta-iodobenzyl guanidine (MIBG-iobenguane) and rhenium labeled lipiodol.

Operational level 3c

This operational level involves the synthesis of positron emission tomography (PET) radiopharmaceuticals. Included in this operational level are ^{18}F-fluorodeoxyglucose injections (^{18}FDG), compounding of radiopharmaceuticals produced from unauthorized or long lived

generators such as the gallium-68 (^{68}Ge/^{68}Ga) generator or the rhenium-188 (^{188}W/^{188}Re) generator, mostly related to research and development.

The IAEA Operational Guidance on Hospital Radiopharmacy (IAEA, 2008a) has certain assessment criteria and each criterion indicates the standard of conformance at three levels for Operational Levels 1 and 2:

- "'A' standards are those required by legislation, IAEA technical publications or other external standard bodies. Any failure to reach an 'A' standard is, therefore, regarded as serious and urgent corrective action should be instituted;
- 'B' standards are those that are not compulsory, but are expected to be reached by all departments. In the case of failure, corrective action is recommended;
- 'C' standards are desirable, but not essential. Corrective actions may improve the overall functioning of the department."

2.3 THE ROLE OF THE RADIOPHARMACIST

The role of the pharmacist is described in detail in the Unit Standards for Entry Level Pharmacists from the South African Pharmacy Council and incorporates the following areas of responsibility (SAPC, 2009):

- Organise and control the manufacturing, compounding, and packaging of pharmaceutical products;
- Organise the procurement, storage and distribution of pharmaceutical materials and products;
- Dispense and ensure the optimal use of medicines prescribed to the patient;
- Provide pharmacist initiated care to the patient and ensure the optimal use of medicine;
- Provide education and information on health care and medicine;
- Promote community health and provide related information and advice;
- Participate in research to ensure the optimal use of medicine.

Training of staff is also an area of responsibility of the pharmacist (SAPC, 2009).

The role of the radiopharmacist is also broad and mirrors the South African Pharmacy Council's Unit Standards. It entails the procurement, preparation, quality control and supply

of radiopharmaceuticals as well as monitoring their use, thereby ensuring the safety and efficacy of such products for optimal patient outcomes.

Activities which the radiopharmacist has to perform include all aspects of the management of the production of radiopharmaceuticals. Radiopharmacy has many domains (Ponto & Hung, 2000). Details follow:

- Procurement: The ordering, receipt, storage and inventory control of radiopharmaceuticals, ancillary drugs, supplies and related materials.
- Compounding: Generator elution, kit reconstitution, preparation of products not commercially available, and other radio labelling procedures.
- Quality Assurance: Functional checks of instruments, equipment and devices and determination of radiopharmaceutical quality and purity.
- Dispensing: Dispensing prescriptions by preparing bulk vials or individual patient doses for delivery to the user.
- Distribution: Packaging, labelling and transport of radiopharmaceuticals to the user.
- Health and safety: Radiation protection practices and proper handling of hazardous chemicals and biological specimens.
- Provision of information and consultation: Communication of radiopharmaceutical-related information to others; this information may be of general applicability, of organizational value, or of pertinence to the care of specific patients.
- Monitoring patient outcomes: Activities which help assure optimal outcomes for individual patients, such as assuring that patients receive proper preparation before radiopharmaceutical administration, and assuring that clinical problems are prevented or recognized, investigated and rectified.
- Research and development: Laboratory testing of new radiopharmaceuticals, new compounding procedures, or new quality control methods, and participation in clinical trials of radiopharmaceuticals.

As can be seen from the above list, the radiopharmacist domains compare closely with the South African Pharmacy Council's role of the pharmacist as described in the Unit Standards.

Quality Assurance is paramount when dealing with radiopharmaceuticals and is described in detail in the following section.

2.4 QUALITY ASSURANCE AND RADIOPHARMACEUTICAL AUDITS

2.4.1 Quality Assurance

Organisational and quality audits are an important part of radiopharmacy services. These audits cover the maintenance and monitoring of facilities and equipment (Gross, 2007).

The assessment of quality in the health setting is based on Donabedian's theory which categorizes assessment into structure, process, or outcomes (Donabedian, 1982).

> Structure is defined as the facilities, equipment, types of services, and manpower with the credentials and qualifications of the health professionals involved.
>
> Process refers to the content of care which includes activities which take place between the patient and the provider. Process measures include the procedures or steps followed in providing care.
>
> Outcome refers to the results of care. It encompasses biological changes in disease, ability for self-care, physical functions, and mobility and patient satisfaction.

Donabedian (1982) also describes two components of quality assurance - system design and monitoring.

> "System design includes all measures that an organization uses to safeguard and promote the quality of health care.
>
> Monitoring is the process by which performance is periodically or continuously reviewed and, when found to be deficient, is modified and then evaluated once again.
>
> In both instances, standards of practice are important yardsticks in the assessment of quality".

The true objective of quality assurance and quality control measures is patient care. Benchmarking is a process of identifying best practice and then setting performance standards for the future. Benchmarking has three governing principals and they are maintaining quality, patient/customer satisfaction and continuous improvement (Sathekge & Ellman, 2010).

Quality is an essential component of any service and production process. In order to be accountable, acceptable procedures of evaluation and quality assurance are necessary.

Quality is an important external measure of an institution's performance. (Sathekge & Ellman, 2010)

2.4.2 Radiopharmaceutical Auditing

The auditing of an institution is important in the assurance of quality. The benefits of an audit are that it leads to better quality of care, encourages thorough planning which leads to valid information collection and subsequently to informed decision making. Auditing is also a significant tool in terms of maximizing resources; it is an excellent educational tool, and it is a method that prompts change (Gilroy *et al*, 1993).

Auditing is a way of reviewing and evaluating for conformation and/ or compliance to established procedure and specification requirements (Gilroy *et al*, 1993).

2.5 SUMMARY

This chapter described the role of a radiopharmacist, the importance of quality assurance and auditing as a means of improving the services offered in the hospitals in order to ensure good patient outcomes.

A detailed methodology of the study is to follow in Chapter 3 below.

CHAPTER 3
METHOD

3.1 INTRODUCTION

The IAEA Operational Guidance on Hospital Radiopharmacy (IOG) audit process includes review and evaluation of the facility's compliance with procedures and specification requirements (IAEA, 2008a).

This chapter explains methodology for the conduct of the Operational Guidance on Hospital Radiopharmacy audit. It also describes the supporting process of the focus group discussions and the key informants' interviews.

3.2 STUDY DESIGN

The study was a descriptive, mixed methods (quantitative and qualitative) survey, with a concurrent design. The data comprised a "snap shot" of practice at each site at the time of the study (Tashakorri & Teddlie, 2003).

3.3 STUDY SITE

The focus of the study was radiopharmacy practice for Nuclear Medicine departments in two Gauteng academic hospitals. Sampling of the sites was on an accessibility and convenience basis and was undertaken at the Departments of Nuclear Medicine at Dr George Mukhari Hospital, Ga-Rankuwa and Steve Biko Academic Hospital, Pretoria.

3.4 STUDY POPULATION

Audit population

- Dr George Mukhari Hospital and Steve Biko Academic Hospital.

Inclusion criteria for staff involved in the audit and the focus group discussion:

- Staff involved in the direct handling of radiopharmaceuticals.
- All available full time or part time technical and managerial staff i.e. radiographers, medical physicists.

Inclusion criteria for Key informants' interviews:

- Radiopharmacist with international experience, currently working in South Africa.
- The Heads (HOD) of the Nuclear Medicine Departments audited.

Exclusion criteria:

- Staff not involved in the direct handling of radiopharmaceuticals.

3.5 STUDY PLAN

In the preparation of the protocol for this study, quality assurance audit documents (local and international) for radiopharmacy units were sourced and compared. Only three radiopharmacy audit documents could be sourced (namely the South African Department of Radiation Control (DOH, 2007), the International Atomic Energy Agency, Operational Guidance on Hospital Radiopharmacy (IAEA, 2008a) and United Kingdom Radiopharmacy Group, Radiopharmacy audit (United Kingdom, 2006). The most stringent of these documents was the IAEA Operational Guidance on Hospital Radiopharmacy (IAEA, 2008a) (see Appendix 1). That document together with the only existing official audit document for South Africa i.e. the South African Department of Radiation Control were intended to be used to assess the equipment, facilities, practices and work flow in the two selected radiopharmacy units.

It was anticipated that the radiopharmacy services provided would fall within Operational Levels 1 and 2 only, as no level 3 tasks (PET products or development of new radiopharmaceuticals) are routinely conducted by the two hospitals.

Table 3.1 below compares the two radiopharmacy audit documents; the South African Inspection Procedure (Nuclear Medicine) and the IAEA Operational Guidance (IAEA, 2008a). As can be seen the South African Inspection Procedure (Nuclear Medicine) (DOH, 2007) does not cover purchase, dispensing or quality assurance of radiopharmaceuticals.

Table 3.1 Comparison between the South African Inspection Procedure and the IAEA Operational Guidance audit documents

Topic	S. A. Inspection Procedure (Nuclear Medicine)	IAEA Operational Guidance on Hospital Radiopharmacy
Documentation	×	×
Staff	×	×
Facility	×	×
Purchase of materials		×
Dispensing protocol		×
Preparation protocols		×
Quality Assurance and Quality Control		×
Waste management	×	×

**Topics covered in the documents are marked with an (×)

Due to fact that the South African DOH Department of Radiation Control Inspection Procedure does not cover the processes involved in the daily running of a radiopharmacy unit, the IAEA document was used to conduct the audit aspect of the study.

As the study developed, it became apparent that the IAEA Hospital Radiopharmacy audit document was not always clear and simple to use. Hence and additional outcome of this study was a review of the ease of use of the audit document and identification of ambiguities in the format of the questions/areas covered in the audit.

3.6 PILOT STUDY/ TRAINING SESSION

The Department of Nuclear Medicine at Tygerberg Hospital was chosen for the pilot study because it is run by a radiopharmacist (Professor Sietske Rubow) who is registered as such with the SA Pharmacy Council. In addition, Professor Rubow is a member of the International Atomic Energy Agency's (IAEA's) audit team, so is experienced with the IOG audit process.

The pilot study process was as follows:

- The researcher and together with the researcher's supervisor met the radiopharmacist and were introduced to the rest of the staff of the Department of Nuclear Medicine staff at Tygerberg Hospital. The IOG audit questions were reviewed briefly with Professor Rubow for areas of ambiguity or lack of clarity.
- The researcher together with the researcher's supervisor, over a period of three days, became familiar with the processes that take place in the department by observing the radiographers perform their duties.
- On the fourth day, with the aid of one of the chief radiographers, the researcher and the researcher's supervisor commenced the audit.
- The pilot audit started with the staffing section and carried on sequentially to facilities, purchase of materials, dispensing protocols, preparation protocols, QA and QC and lastly waste. Each audit component was addressed.
- A feedback session with Professor Rubow followed on the fifth day of the pilot study. The feedback session served to clarify any queries with regards to the audit process.

3.7 SAMPLE SELECTION

Audit – convenience sampling based on geographical accessibility and ability to obtain permission to conduct the audit.

Focus group – staff working in radiopharmacy unit.

Key informants – registered radiopharmacists and HODs of Nuclear Medicine departments.

3.8 DATA COLLECTION

3.8.1 The IAEA IOG audit document. (Appendix 1)

The document is intended initially as a self audit, followed by an external independent audit. The audit document (Appendix 1) is divided into seven sections, all of which are further divided to address the first two Operational Levels.

The audit document covers the areas of staff, facilities, purchase of materials, dispensing protocol, preparation protocol, Quality Assurance/Quality Control and waste management for Operational Levels 1 and 2.

The audit document focuses on standards A and B (see Section 3.9 below).

Full ethical clearance was obtained to conduct the audits.

The following steps were undertaken during the study process:

Method at Hospital X

- The Head of the Department of Nuclear Medicine was contacted, and permission was granted to perform the audit.
- The researcher was introduced to the members of staff at the appointed date and time.
- The researcher informed the HOD and members of staff as to when the researcher would commence with the project.
- As the researcher was familiar with processes that took place in the department, the researcher immediately commenced with the data collection.
    - The researcher started with the staffing section and moved on to the facilities section.
    - The researcher then moved on to the preparation protocol section of the document on day three of the audit as the researcher had observed the manner in which the department prepared the radiopharmaceuticals.
    - The researcher then completed the section on dispensing protocols together with the QA and QC. Audit results were based on what the researcher observed.
    - The researcher then approached the section on waste management.
    - The last section the researcher approached was the purchase of materials.
- The researcher did not disturb the routine of the department.
- Once the researcher had completed the audit, the researcher's supervisor checked it and discussed the findings with the researcher.
- The researcher's supervisor then made an appointment with the Head of Department (HOD) at the Nuclear medicine department for a feedback session.
- The researcher presented the results of the audit of both Hospital X and Y, with the permission of the HOD in Hospital Y to Hospital X. The results were presented in table

form (as presented in Chapter 5). The results were presented in two sessions to the HOD and his second in command.

- The researcher, with the permission of the HOD then presented the findings of the audit to the technical staff. This presentation was followed by a FGD, with the technical staff. The researcher's supervisor facilitated the FGD. The presentation of results to the technical staff was a power point presentation, which included results for both hospitals.

Method at Hospital Y

- The HOD was contacted and permission was granted to perform the audit.
- The researcher was assigned to work with one of the chief radiographers by the HOD.
- Before the researcher commenced with the audit, the researcher requested and received the organogram of the department.
- The researcher commenced with the audit aided by the chief radiographer.
- The researcher did not have the opportunity to become familiar with all the processes that take place in the department ahead of the audit.
    - The researcher commenced with the audit and began with the facilities section. Audit of this section required the researcher to play a passive role and observe what happened in the sections to be audited.
    - The researcher then moved on to the preparation protocol; the dispensing protocols together with the QA and QC sections. These were completed according to what the researcher observed and what the researcher was told.
    - The researcher then audited waste management processes.
    - The researcher audited approached the purchase of materials following an appointment to discuss this section with the appropriate person.
    - The researcher did not want to disturb any of the daily activities that took place in the department.
- Finally, the researcher was able to complete the first section of the audit; the staffing section, as by this time the researcher was familiar with, and to, the staff of the department.
- Once the researcher had completed the audit, the researcher's supervisor checked it and discussed the findings with the researcher.

- The researcher's supervisor then made an appointment with the Head of Department (HOD) for a feedback session.
- The researcher presented the results of the audit of both hospital X and Y, with the permission of the HOD in hospital X to hospital Y. The results were presented in table form (as presented in chapter 5). The researcher emailed the results to the HOD of hospital Y.
- The researcher with the permission of the HOD then presented the findings of the audit to the technical staff, this presentation was followed by FGD, with the technical staff. The researcher's supervisor facilitated the FGD. The presentation of results to the technical staff was a power point presentation, which only included results for hospital Y.

3.8.2 Focus group discussion outline and consent form (Appendices 2, 3 and 4)

The main purpose of this study was the IOG audit. The qualitative aspects i.e. focus group discussions and key informant interviews were intended purely to aid the formulation of the recommendations for improved practice.

Prior to the focus group discussions, the results of the audit were made available to the two Heads of the Nuclear Medicine Departments.

Focus group discussions (FGDs) (see Appendix 2) were held with all available technical staff members after the audits. The FGDs were to identify current practices, constraints in the work situation and to obtain radiopharmacy staffs views on the feasibility of the implementation of 'best practice' radiopharmacy approaches.

Consent forms were signed by all participants in the FGD. The discussions were recorded digitally and the researcher made the necessary notes while listening to the discussion.

Feedback was given to the radiopharmacy staff of the units involved in the study in the form of summaries of a Powerpoint presentation of the key results. The FGDs followed the feedback sessions.

3.8.3 Key informant interview outline (Appendix 5)

Key informants (Heads of the Departments and radiopharmacists with international experience, currently working in South Africa) were interviewed with questions from Appendix 5. The emphasis was on how international 'best practice' approaches could reasonably be introduced into South African academic hospital radiopharmacies.

3.9 DATA ANALYSIS

Results from Appendix 1 (IAEA, 2008) for each facility were quantified in terms of the number of components achieved within each standard of conformance (A to C - see below for the relevant Operational Levels). Elements from the IAEA document (IAEA, 2008a) which are realistically achievable in the South African tertiary hospital radiopharmacy setting were identified.

Responses from the Focus Group Discussions and interviews with key informants were summarised, and used to aid formulate recommendations as to how 'best practice' approaches could realistically be introduced into South African radiopharmacy units.

3.10 STATISTICAL ANALYSIS

As this was a descriptive study with a small population sample (n=2), no comparisons were envisaged, hence no statistical analysis was performed.

3.11 RELIABILITY AND VALIDITY

Quantitative

- The audit Data Collection Instrument (DCI) was designed and is used by existing authorities (IAEA) therefore both internal and external validity should have already been determined.
- The data for both hospital audits were crossed-checked by the researcher's supervisor.
- There was internal consistency in the DCIs as the questions were grouped, though some sections were repeated under the two Operational Levels.
- The DCI covers the structure, process and outcome criteria described by Donabedian (1982).
- A pilot study was conducted under the supervision of an experienced auditor, to aid validity of data collection.

Qualitative

- A role play session for the focus group discussion facilitation was conducted on the researcher's colleagues.

- The researcher together with the researcher's supervisor collected data and once the discussion was over, they then compared the data collected to determine the accuracy and consistency of the data collected.
- The discussions were recorded.
- The views of the staff were taken separately from that of management.

3.12 BIAS

Quantitative

- The researcher was an impartial observer.
- The DCI was designed and piloted by experts internationally, for use in a wide range of countries; hence it should be universally applicable.

Qualitative

- The researcher was an impartial observer with the motive only to assess practice.
- The questions were designed with little knowledge of specific practices at both the study sites.
- For further minimization of bias, the researcher rehearsed the interview technique during the role play.

3.13 ETHICAL CONSIDERATIONS

Permission was sought from both HODs of the Nuclear Medicine departments in Dr George Mukhari Hospital and Steve Biko Academic Hospital. Ethical approval and permission was sought from the School of Health Sciences Research Committee of Medunsa Campus (University of Limpopo) and the Medunsa Campus Research and Ethics Committee (MCREC), the University of Pretoria, and the CEOs of Dr George Mukhari Hospital, Ga-rankuwa and Steve Biko Academic Hospital, Pretoria.

Results are coded so that the respective institutions are not identified individually.

Participation in the study was on a voluntary basis. Individual participants could withdraw at any time during the conduct of the study without providing reasons.

For the focus group discussions consent forms were signed prior to enrolment in the study by all those who participated in the focus group discussions and interviews. Participants were assured of confidentiality and their responses remained anonymous.

The researcher strove for integrity at all times and was guided by ethical principles that include respecting the rights of the participants, and reporting results as they are found.

3.14 SUMMARY

This chapter has described the methodology for the IOG audit, the FGDs and the interviews with key informants.

The results and discussion of the IOG audit will be presented in Chapter 4. The FGD and key informant responses appear in Chapter 5.

CHAPTER 4
RESULTS AND DISCUSSION

OPERATIONAL GUIDANCE ON HOSPITAL RADIOPHARMACY (IOG) AUDIT

4.1 INTRODUCTION

This chapter presents the findings of the IOG audit conducted in this study.

A secondary objective that developed from the audit process was a review of ease of use of the audit document itself (see Section 3.5 above). Audit reference items that required clarification in terms of the secondary objective are highlighted in the tables thus and will be discussed at the end of this chapter.

Hospital Y had already conducted an IOG radiopharmacy self-audit in January, 2010.

There are three (3) Operational Levels (OLs) of technical procedures required for the different radiopharmaceuticals. They are described in the IAEA Operational Guidance as follows:

- Operational Level 1a – dispensing of radioiodine or other radiopharmaceuticals which have been supplied in their final form.
- Operational Level 1b – dispensing of radioiodine or other radiopharmaceuticals which have been supplied in their final form for therapy and palliation.
- Operational Level 2a – preparation of radiopharmaceutical from kits, or generators.
- Operational Level 2b - radiolabelling of autologous blood cells commonly used for infection and inflammation imaging.
- Operational Level 3a – entails the compounding of radiopharmaceutical for diagnostic purposes.
- Operational Level 3b – entails the compounding of radiopharmaceutical for therapeutic purposes it also encompasses research and development.
- Operational Level 3c – involves the synthesis of positron emission tomography (PET) radiopharmaceuticals plus research and development.

The institutions audited did not carry out Level 3 functions and the IOG audit does not cover OL3, hence only data for OLs 1 and 2 are presented.

Table 4.1 below summarises the audit components (main areas of the audit) at the two Operational Levels (1 and 2).

Table 4.1 Summary of IOG audit components at Operational Levels 1 and 2

AUDIT COMPONENT	LEVEL 1	LEVEL 2
Staff	✓	✓
Facilities	✓	✓
Purchase of Materials	✓	✓
Dispensing Protocols	✓	✓
Preparation Protocols	×	✓
Quality assurance and Quality control	✓	✓
Waste Management	✓	×

The IAEA audit covers Operational Level 1 under each component (topic) heading and then deals with OL2 under similar headings. For clarity and ease of discussion, the results for each audit component for the two OLs will be dealt with together in the same chapter section.

The reference numbers of each Audit Component in the IOG, indicate to which OL the component refers. OL1 components are prefixed by the number ‘1.’ and components for OL2 by the number ‘2.’. This approach is followed in all the tables below.

In the tables below, the data are reported as observed or as the answers were given to the researcher. Where an audit component was reported but no proof was available, the response in the tables below is marked with an asterisk (*). As the researcher was junior in status and a guest in the departments, it was not always appropriate to insist on the provision of proof for a particular statement.

In the sections below, comment will only be made on the outcomes of the audit in cases where the Hospital radiopharmacies did not comply with the ideal requirements or where discussion or explanation is deemed necessary.

4.2 STAFF

4.2.1 Results

The staffing organograms as supplied by each of the Hospitals appear below.

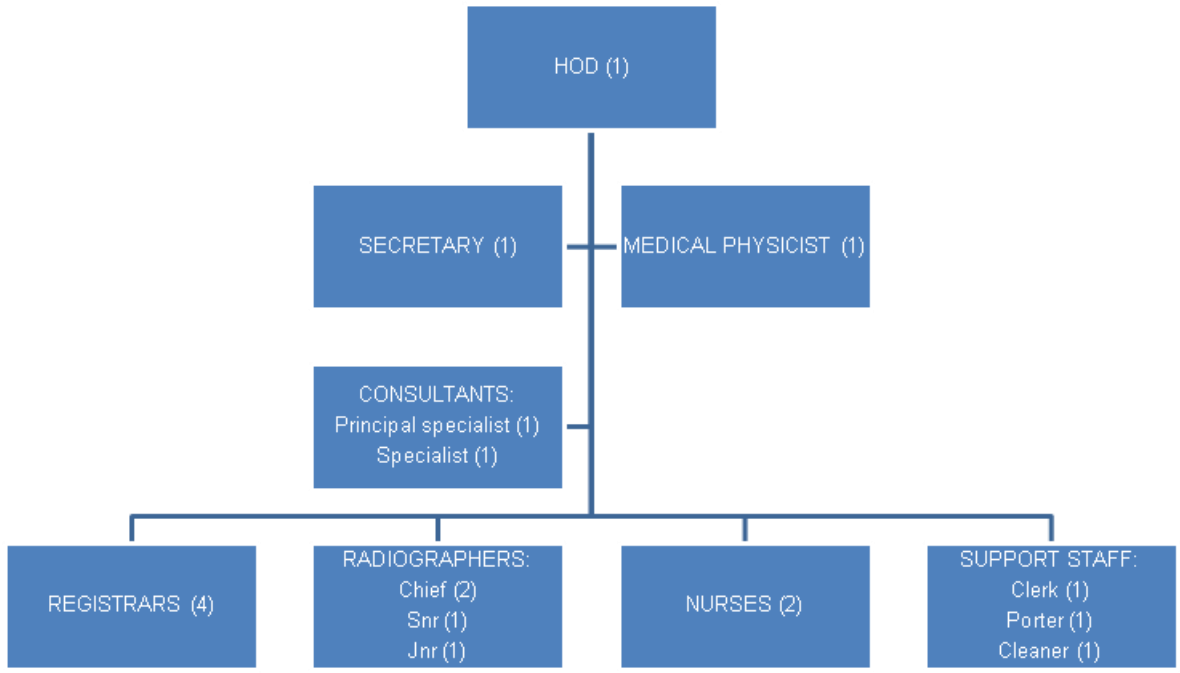


Figure 4.1 Hospital X staff organogram

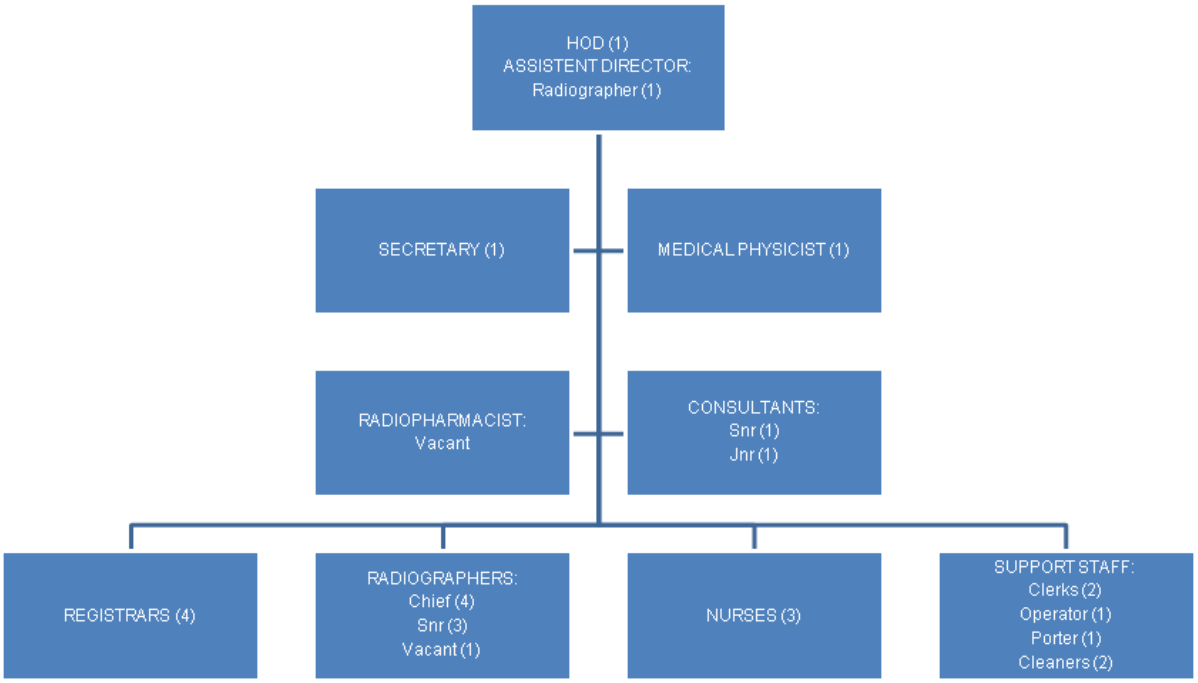


Figure 4.2 Hospital Y staff organogram

The results of the audit for the staffing of each hospital radiopharmacy for OL1 and 2 appear below in Table 4.2.

Table 4.2 Staffing results for Hospital X and Y.

Audit Ref. #	Component Detail	Class	Hospital X	Hospital Y
1.1	Is there a responsible professional for the radiopharmacy? Provide details.	A	Yes Chief radiographer and Medical physicist	Yes Chief radiographer
1.2	Is the radiopharmacy unit operated under the direction of a person with appropriate training as defined by local or national regulations?	A	Yes They are all qualified Nuclear Medicine radiographers	Yes They are all qualified Nuclear Medicine radiographers
1.3[a]	Are there written staff training manuals for all grades of staff?	B	Yes*	Yes*

[a] Shaded audit references are those for which the IAEA audit document requires to be clarified and/or edited.

Audit Ref. #	Component Detail	Class	Hospital X	Hospital Y
2.1[a]	Have all staff working at OL2 received specific staff training on the following:	A		
2.1a	Calibration of equipment	A	Yes*	Yes*
2.1b	Working practices in the Radiopharmacy	A	Yes*	Yes*
2.1c	Preparation of individual doses	A	Yes*	Yes*
2.1d	QC and analytical techniques	A	Yes*	Yes*
2.1 e	Dose release	A	Yes*	Yes*
2.1 f	Record keeping	A	Yes*	Yes*
2.1g	Cleaning	A	Yes*	Yes*
2.2	Is there a system for formal approval of all documentation including radiopharmaceutical preparation, QC and formal release to patient?	B	No	No
2.3	What training is provided to staff performing the final checks on all products prepared before release for patient use?	A	2.1 Covers the training that staff have undergone	2.1 Covers the training that staff have undergone
2.4	Are there training records for all staff performing cell labelling, e.g. RBC, WBC?	B	Yes* It forms part of the theory they learn in their undergraduate and postgraduate education	Yes* It forms part of the theory they learn in their undergraduate and postgraduate education
2.5	Is there an annual performance review to check the competencies of radiopharmacy staff?	B	No	No

4.2.2 Discussion

Responsible professional (Audit ref 1.1 and 1.2)

At OL3, it is a requirement that the person in charge of the radiopharmacy is a radiopharmacist (IAEA, 2008), but that is not deemed necessary for OLs 1 and 2, where a medical physicist or chief radiographer can be in charge. The latter situation exists in both of the hospitals. In Hospital X there is joint responsibility; the radiographer handles the

[a] Shaded audit references are those for which the IAEA audit document requires to be clarified and/or edited.

radiopharmaceutical kits, and the medical physicist handles radionuclides. In hospital Y the chief radiographer is responsible for the radiopharmacy unit as a whole.

In Hospital Y there is a vacant post for a radiopharmacist but Hospital X has no such post on the staff complement.

Hospital Y has a much larger Nuclear Medicine Department, which is reflected in the staffing levels for that department.

Staff training (Audit ref 1.3 and 2.1)

“All personnel on whom [radiation] protection and safety depend must have the appropriate qualifications and training so that they understand their responsibilities and perform their duties with proper judgement and according to defined procedures” (IAEA, 2006a).

The following are staff considered to be qualified to work in the nuclear medicine department (IAEA, 2006b):

- Medical practitioners working with radionuclides (e.g. nuclear medicine physicians and other appropriately trained clinical specialists);
- Radiopharmacists working in the nuclear medicine facility;
- Medical physicists working in nuclear medicine (qualified experts in nuclear medicine physics);
- Other health professionals involved in the clinical use of radionuclides (e.g. nuclear medicine technologists);
- Radiation protection officers;
- Staff performing special tasks (e.g. type testing of equipment, Quality Control tests).

The radiographers that work in both hospitals have had specific hot” laboratory training (i.e. in handling radioactive substances), but not radiopharmacy training in its broader sense. Neither of the hospitals has a radiopharmacist. The role of a radiation protection officer is played by the medical physicist in both hospitals.

To obtain personal accreditation, the staff listed above must have the following qualifications and training, as applicable (IAEA, 2006b):

- A university degree or academic qualification relevant to the profession, issued by the competent education authorities as required in the country.

- Accreditation to practise the profession granted by the competent authorities or other institutions as required in the country.
- A course on radiation protection whose contents, methodology and teaching institution are approved by the regulatory authority. This course may be part of the curriculum of the professional education above.
- On-the-job training supervised by professionals with accreditation by the regulatory authority. This training must include the full range of tasks and professional activities in which the individual will be engaged.

Record keeping system (Audit ref. 2.2)

The main objective of any documentation is to provide an audit trail. The records that the department keeps must cover details such as staff, patients, radiopharmaceuticals, reagent kits, radioisotopes, facilities, equipment, radiation safety and fire safety, it is important that these records are comprehensive (IAEA, 2008a). Neither hospital has a formal system of radiopharmaceutical record keeping, as described in audit reference 2.2.

Competence assessment (Audit ref. 2.5)

The practical training must include competence assessments and must be documented by other qualified personnel. The laboratory needs to ensure that staff is aware of (IAEA, 2006b):

- The conditions, including limits, of the license (or registration) authorising possession and use of radioactive materials;
- Reviews and analysis of incidents and accidents that have occurred in the institution or elsewhere;
- The institution’s QA programme and QC procedures;
- The proper use and operation of equipment;
- All relevant radiation safety procedures.

Neither hospital performs an annual performance review to check the competencies of their staff.

Records of any training by radiopharmacy staff is to be kept by the department for at least five (5) years (IAEA, 2006b).

4.3 FACILITIES

The floor plans for the Nuclear Medicine Departments of Hospitals X and Y appear as Appendices 6 and 7 respectively.

4.3.1 Results

The results of the audit for the facilities of each hospital radiopharmacy for OLs 1 and 2 appear below in Tables 4.3 and 4.4

Table 4.3 Facilities results for Hospital X and Y

Audit Ref. #	Component Detail	Class	Hospital X	Hospital Y
1.4[a]	Does the unit have appropriately finished rooms including:	A		
1.4 a	Adequate lighting	A	Yes	Yes
1.4 b	Appropriate finishes to walls	A	Yes	Yes
1.4 c	Floors	A	Yes	Yes
1.4 d	Ceilings	A	Yes	Yes
1.4 e	Ventilation	A	Yes Extraction fan	Yes Air conditioning system
1.4 f	A shielded dispensing station?	A	Yes	Yes
1.5	Is there a shielded dispensing station available?	A	Yes	Yes
1.6a	For operational level 1b: Is there a shielded dispensing station and/or a fume hood available?	A	Yes The dispensing station is shielded but there is no fume hood available.	Yes The dispensing station is shielded and there is a fume hood available
1.6 b	For operational level 1b: Is there a fume cupboard with suitable filters for volatile radioactive materials such as ^{131}I solutions?	A	No No fume hood	Yes
1.6c	If only radioiodine capsules are handled, is the package opened in a well-ventilated area?	A	No	Yes*

[a] Shaded audit references are those for which the IAEA audit document requires to be clarified and/or edited.

Audit Ref. #	Component Detail	Class	Hospital X	Hospital Y
1.7	Is there a validated (annual check on air flow, safety and challenge testing) fume hood with suitable filters for handling radioiodine solutions?	A	No	Yes*
1.8	Are there records and logs kept for all equipment irrespective of whether maintenance and calibration is performed in-house or by external contractors??	B	Yes*	Yes*
2.6	For Operational Level 2: Are there regular checks on validated Class II type B microbiological safety cabinets located in a dedicated room?	A	N/A The LAF cabinet is not in use	Yes* The LAF is maintained by external contractor
2.7	Are manometer readings of pressure differentials across HEPA filters recorded daily?	B	N/A	Yes*
2.8	Are there periodic records of air velocity determination for LAF cabinets or isolators?	B	N/A	Yes*
2.9	Is challenge testing of the HEPA filters in LAFs and isolators carried out annually?	B	N/A	Yes*
2.10	For negative pressure isolators: Before preparation takes place, are gloves or gauntlets visually inspected and integrity tests carried out and recorded?	B	N/A	N/A
2.11	Is there a system and record of planned preventative maintenance for all equipment in the radiopharmacy including the refrigerator?	B	No	No
2.12	When clean rooms are used, are the over-pressure gauges monitored and recorded daily?	B	N/A No clean rooms	N/A No clean rooms

Table 4.4 below lists the equipment in both the hospitals.

Table 4.4 List of equipment in each hospital radiopharmacy

Equipment	Hospital X	Hospital Y
Biohazard II A (LAF cabinet)	✓*	✓
Well counter system	✓	✓
Area radiation monitor	✓	✓
Printer for well counter		✓
Centrifuge	✓*	✓
Trolley ECG		✓
Cobra auto – gamma detector	✓*	✓
Fridge	✓	✓
Technigas® generator	✓	
Lead multi-syringe carrier	✓	✓
Lead bench shield large	✓	✓
Lead dustbin	✓	✓
Water bath	✓	✓
Laboratory scale	✓	✓
Trolley		✓
White board writing		✓

*Not in use.

4.3.2 Discussion

Aims of radiopharmacy design are to protect: (Lazarus, 1999)

- the product from the environment, operator and other products.
- the operator from radioactivity and pathogenic organisms.
- the environment, including equipment, from radioactive and microbial contamination

The radiopharmacy should be adapted to suit the radioactive nature of the products as well as the activities carried out in the radiopharmacy. The IAEA also stresses that it is important that the radiopharmacy (“hot” laboratory) offers protection to the operator, the product and the environment (IAEA, 2008a).

Ideally the radiopharmacy should consist of (Saha, 2004):

- workbenches made of stainless steel or wood covered with laminated plastic;
- stainless steel sinks deep enough to prevent splashing, with foot control;

- exhaust fume hoods fitted with filters to absorb gaseous and particulate radioactive substances;
- a laminar flow hood in the shielded dispensing area, so as to maintain a sterile environment.

Equipment needed for the operation of a radiopharmacy laboratory are as follows (Saha, 2004):

- dose calibrator, capable of measuring a variety of radioactivity;
- chromatography equipment;
- radiation survey meters;
- an area monitor;
- a pH meter;
- a light microscope for particle size determination;
- a NaI or Ge detector*;
- a well-type NaI counter
- a hot water bath;
- dry heat oven;
- lead-lined refrigerators;
- lead containers and syringe covers.

*Note: It is very rare that a radiopharmacy will actually have a NaI or GE detector, it is normally used to detect low amounts of radioactivity and long-lived isotopes.

Appropriately finished rooms (Audit ref. 1.4 and 1.5)

Both hospitals have appropriately finished rooms, together with a shielded dispensing station. Both hospitals are adequately lit, with the walls, floors and ceilings appropriate for the work carried out in the hospital. Work bench surfaces are made of stainless steel. The walls and floors are smooth and impermeable allowing easy cleaning and decontamination. Neither hospital has work benches are made of steel or are curved upwards to contain spills but this could be attributed to the fact that small quantities of liquids are handled. Hospital X has an extraction fan as compared to the air conditioning system at Hospital Y.

Fume hood (Audit ref 1.6 and 1.7)

Hospital X does not have a fume hood; Hospital Y does and uses the fume hood for the reconstitution/admixing of kits. Hospital X only handles I^{131} capsules and not I^{131} solutions, therefore with regards to OL1b they stated that they can operate without a fume hood. The fume hood in Hospital Y is validated by an external contractor.

Equipment records (Audit ref. 1.8)

Both hospitals have records of their equipment (for asset purposes) irrespective of whether they are maintained. In both hospitals the equipment records are in the form of a list, with an allocated asset number and the serial number. The importance of record keeping is so that traceability is maintained. This is to ensure that the equipment listed matches what the hospital has in stock, as a security measure and to ensure that the equipment are safe and accurate for the duties that are performed in the radiopharmacy.

Planned preventative maintenance (Audit ref. 2.6 to 2.10)

Planned preventative maintenance on the biological safety cabinet is an essential component of quality assurance and is a necessary control requirement by good manufacturing practice (GMP); this is to ensure that the medicinal products are sterile and of consistently high quality can be prepared. Documented evidence is required to show that all equipment involved in the production of radiopharmaceuticals continue to perform within the manufacturer's specification (Sharp *et al.*, 2005).

A maintenance strategy should be established at the time of purchase of equipment, this is important in achieving and maintaining short downtimes, high quality examinations, patient and staff safety, measurement accuracy and accident prevention (IAEA, 2006b).

Ideally, maintenance procedures will include consideration of the following points (IAEA, 2006b):

- Overall management of the maintenance programme should be provided by a qualified expert in nuclear medicine physics;
- Service records should be maintained throughout the lifetime of the equipment;
- A service contract, including preventive maintenance, provided by the manufacturer;
- Measures to prevent the use of equipment that is undergoing maintenance or repair are implemented.

Neither of the hospitals has planned preventative maintenance for their refrigerators.

Clean rooms (Audit ref. 2.11 and 2.12)

In order to provide the aseptic conditions necessary for the production of sterile radiopharmaceutical injection a clean room suite is advisable. There are different classes/grades of clean rooms, and they are as represented in Table 4.5 below (ISO, 2010):

Table 4.5 ISO cleanroom standards

EU cGMP classifications Grade	Maximum concentration limits (particles/m^3) for particles ≥ sizes shown			
	At rest		In operation	
	≥ 0.5µm	≥ 5.0µm	≥ 0.5µm	≥ 5.0 µm
A	3500	0	3500	0
B	3500	0	350000	2000
C	350000	2000	3500000	20000
D	3500000	20000	not defined	not defined

Neither of the hospitals has a clean room. Strictly speaking since they do not produce radiopharmaceuticals but only reconstitute them in closed systems (i.e. no open vials), a clean room is not necessary (Elliot, 1998).

From the list of equipment in Table 4.4 it is clear that Hospital Y has more equipment. Hospital Y is a larger and more modern facility than Hospital X. Hospital X has a few items which are not in use (due to their equipment not being commissioned yet) i.e. the Laminar Air Flow (LAF) cabinet, centrifuge, and Cobra auto gamma counter. The LAF in Hospital Y was used for generators but not for the reconstitution of the radiopharmaceuticals.

The researcher did not observe the use of the area radiation monitor in either hospitals. The area radiation monitor is specific and pertains to levels of radioactivity at predefined positions in the room, it is not usually moved from the predestined positions.

4.4 PURCHASE OF MATERIALS

4.4.1 Results

The results of the audit for the purchase of materials of each hospital radiopharmacy for OL1 appear below in Tables 4.6 and 4.7.

Table 4.6 Purchase of materials results for Hospital X and Y

Audit Ref. #	Component Detail	Class	Hospital X	Hospital Y
1.9[a]	Are there suitable protocols and trained staff for the purchase of approved or marketing-authorized radiopharmaceuticals?	A	Yes*	Yes*
1.10	Are all goods received checked and recorded against the order for correctness of delivery?	B	Yes*	Yes*
1.11	Are records of batch numbers and quantities received kept?	B	Yes	Yes
1.12	Are visual inspections and label checks carried out prior to acceptance?	B	Yes*	Yes*
2.13	Do all products, kits and generators have product approval, marketing authorization or bear a product licence number?	A	Yes (but not necessarily in South Africa)	Yes (but not necessarily in South Africa)
2.14	How many unlicensed or unapproved products are used each year and is there a record of them?	A	Number not determined Yes - recorded Section 21 products are registered in other countries but not in SA by the MCC	Number not determined Yes – recorded Section 21 products are registered in other countries but not in SA by the MCC
2.15	For all unlicensed kits, radiopharmaceuticals or radiochemicals, are the prescribers or responsible medical doctors made aware of their responsibilities?	A	Yes The medical doctors are the ones responsible for informing the patients about the unlicensed products.	Yes The medical doctors are the ones responsible for informing the patients about the unlicensed products.
2.16	Do the suppliers of reagents and unapproved products provide a “certificate of analysis”?	B	N/A	Yes*

[a] Shaded audit references are those for which the IAEA audit document requires to be clarified and/or edited.

Table 4.7 Products unauthorised in South Africa (i.e. Section 21) utilised in each hospital

Unauthorised products*	Hospital X	Hospital Y
DISIDA (Diisopropyl Iminodiacetic Acid)		✓
DTPA (Diethylene triamine pentaacetic acid)		✓
^{131}I(Iodine)DIAG CAPS		✓
^{131}I(Iodine)THERAPY CAPS		✓
^{123}I(Iodine) CAPS		✓
^{123}I MIBG (Iodine-123-meta-iodobenzylguanidine)		✓
MAA (Macroaggregated Albumin)		✓
MDP (Methylene-diphosphonate)		✓
RBC (Red Blood Cell)		✓
TIN COLLOID		✓
DMSA (Dimercapto succinic acid)	✓	✓
^{67}GA (Gallium)		✓
FDG (Fluorodeoxyglucose)		✓
MIBI (methoxyisobutylisonitrile)CARDIOLITE®		✓
MAG-3 (Mercapto acetyl tri glycine)	✓	✓
NANO COLLOID	✓	✓
^{201}TI (Thallium)	✓	✓
^{51}Cr (Chromium)		✓
^{90}Y(Yttrium)		✓
HMPAO (hexamethylpropyleneamine oxime)	✓	✓

* Note – abbreviated terms are used commonly for many radiopharmaceuticals, hence the above list uses the abbreviation first followed by a descriptor.

4.4.2 Discussion

Both hospitals are authorised to handle certain radionuclides and radiopharmaceuticals. This license is granted by the Department of Health: Radiation Control. The wider range of Nuclear Medicine services offered in Hospital Y is reflected in the radiopharmaceuticals stocked.

Purchase of radiopharmaceuticals (Audit ref. 1.9 to 1.12)

In both hospitals the purchase of products is performed by the responsible person as mentioned above under Section 4.2. Those staff members are trained individuals. Only licensed products are purchased, though they may not necessarily be licensed in South Africa. If the product is not registered by the South African Medicines Control Council (MCC)

it is the responsibility of the hospital to cover the use of that product with a Section 21 form as specified by the Medicine and Related Substances Control Act (Act 101 of 1965).

The IAEA (2008a) recommends that from the delivery note, the date, name of the radiopharmaceutical or radionuclide, radioactivity, lot number, person receiving, surface radiation, and transport index, should be recorded. Following administration, these should correspond to the patient's name and details. These records should be kept for at least five (5) years. The researcher did not establish how long the hospitals keep their records.

According to Saha (2004), when goods are received, the individual receiving the goods should monitor the radioactivity level of the package within 3 hours of delivery or within 3 hours the beginning of the following day if the goods are delivered after hours. This monitoring must be done on the surface of the packages using a Geiger Mueller counter at a distance of 1 metre, the reading of which should not exceed 200mR/hr the same day as delivery or 10mR/hr the day after delivery. A wipe test should be performed on the delivered goods, the limit of which is 0.003µCi (6600 dpm or 111Bq) per 300 cm^2. All the achieved readings should be recorded into a log for the receipt of the goods. None of the hospitals have this log.

Radiopharmaceuticals are considered to be consignment stock, due to their relatively short shelf-life and therefore in terms of payment the invoice is attached to the VA2 form.

Stock records

In South Africa the purchase and storage of radiopharmaceuticals is governed by a range of legislation. The medicinal control falls under the Medicine and Related Substances Control Act (Act 101 of 1965). Permission to hold radioactive substances falls under the Group IV of the Hazardous Substances Act (Act 15 of 1973).

According to the Hazardous Substances Act (Act 15 of 1973), the hospital to which authority is granted to have in their possession Group IV (radionuclides and/ or radiopharmaceuticals) is required to keep a permanent stock record containing the following information:

- the name and activity of the substance;
- the date of acquiring or gaining control over the substance;
- the purpose for which the substance is or is to be used;

- whether the substance is in the form of a sealed or unsealed source, and in the case of a sealed source, the serial number, the date of and the specific action which was carried out with the substance.

Both hospitals have a record of the radiopharmaceuticals they are permitted to have in their possession.

Unlicensed products (Audit ref. 2.13 to 2.16)

Under Section 21, the medical doctors are the ones responsible for informing the patients about the use of unlicensed products. The use of that product is to be covered by a patient consent form and Section 21 form.

Interpretation of audit ref. 2.14 was not easy. It can be interpreted as the total number of unlicensed products that the department utilizes or the different products such as that listed in table 4.6 above.

There are very few radiopharmaceutical manufacturing companies in South Africa. Section 21 products are those which are not registered by the Medicines Control Council (MCC) in South Africa, but are registered in other countries and imported.

4.5 DISPENSING PROTOCOLS

4.5.1 Results

The results of the audit for the dispensing protocols of each hospital radiopharmacy for OLs 1 and 2 appear below in Table 4.8.

Table 4.8 Dispensing protocol results for Hospital X and Y

Audit Ref. #	Component Detail	Class	Hospital X	Hospital Y
1.13	Are there specific written radiopharmacy procedures for dispensing operations undertaken in the radiopharmacy?	B	Yes	Yes
1.14[a]	Under operational level 1a: Are there written procedures for the aseptic dispensing and labelling of unit doses of ready to use radiopharmaceuticals?	B	N/A In the context of level 1a the question is ambiguous	N/A In the context of level 1a the question is ambiguous
1.15	Is there a system for labels which assesses quality, number produced and number applied to dispensed doses?	A	No	Yes
1.16	For operational level 1b: Do the written procedures contain clear safety and monitoring instructions for dispensing radioiodine solutions or capsules?	A	Yes*	Yes*
1.17	Under operational level 1b: Are there written procedures for calibration assays, and preparation and dispensing of individual patient radionuclide therapy?	A	No	Yes*
1.18	Can the audit and documentation for each radiopharmaceutical batch be traced from the prescription to the actual administration of individual patient doses?	A	No	Yes

4.5.2 Discussion

SOPs for dispensing (Audit ref. 1.13)

Both hospitals have written dispensing procedures, but they are not detailed or formal SOPs.

[a] Shaded audit references are those for which the IAEA audit document requires to be clarified and/or edited.

SOPs for radiopharmaceuticals and radionuclides (Audit ref. 1.14, 1.16 and 1.17)

Audit reference 1.14 is unclear and confusing. OL1a refers to ready-prepared patient doses, hence aseptic preparation of those would not be applicable in the hospital radiopharmacy setting as they would arrive ready for administration to the patient.

Audit reference 1.16 and 1.17, both hospitals have written SOPs for the handling of radioiodine but Hospital X has no written procedures for the calibration assays of radioiodine.

System for labels (Audit ref. 1.15)

Hospital X has no system in place for labels while Hospital Y does. As these labels are generated by the hospital's patient administration software they should comply with current legal requirements. The label should contain the following information: the product, product identification number, activity at the time it is administered to the patient, the volume time of dispensing, name of the patient, date, the operator and the checker (IAEA, 2008a).

Batch traceability (Audit ref. 1.18)

Hospital X: there is no batch traceability for each radiopharmaceutical from the prescription.

Hospital Y: there is batch traceability from the prescription.

4.6 PREPARATION PROTOCOL

4.6.1 Results

The results of the audit for the preparation protocol of each hospital radiopharmacy for OL2 appear below in Table 4.9.

Table 4.9 Preparation protocol results for Hospital X and Y

Audit Ref. #	Component Detail	Class	Hospital X	Hospital Y
2.17	Are there written and approved procedures for the use of generators and reconstitution of each radiopharmaceutical kit used?	A	Yes	Yes
2.18	Are SOPs independently reviewed and approved at specified intervals?	B	No	No
2.19	Is the preparation of ^{99m}Tc radiopharmaceuticals from kits and generators carried out in an LAF cabinet?	A	No	No
2.20a	Are there set criteria before release for preparation for patient use?	B	Yes	Yes
2.20b	Are these undertaken by the same operator or a different individual?	B	Done by the same operator	Done by the same operator
2.21a[a]	Can each individual patient's dose be traced to a specific generator?	A	Yes	Yes
2.21b	Can each individual patient's dose be traced to a kit batch number?	A	No	Yes
2.22	Under operational level 2b: Do the written procedures for any autologous preparation, e.g. red and white blood cells, include clear instructions on safety, cleaning and decontamination	A	Yes For RBC only	Yes for RBC only
2.23	Are there written procedures for the preparation and dispensing of approved kit formulations of radiolabelled biologicals, e.g. monoclonal antibodies, peptides?	A	N/A	Yes*

4.6.2 Discussion

[a] Shaded audit references are those for which the IAEA audit document requires to be clarified and/or edited.

SOPs (Audit ref. 2.17, 2.18, 2.22 and 2.23)

Both hospitals have approved written procedures for the use of generators and the reconstitution of each radiopharmaceutical kit. These written procedures are provided by the manufacturer but no formal SOPs have been developed.

Neither of the hospitals reviews their SOPs in any formal or regular way.

Due to the fact that neither of the hospitals has suitable facilities (no cleanrooms), neither performs white blood cell labelling. Red blood cell labelling is performed at both hospitals. Written procedures for red blood cell labeling are available for both hospitals. Both hospitals use the *in vitro* method of labelling red blood cells. Since hospital X has no centrifuge, they use the modified cell labelling that does not require a centrifuge whereas hospital Y uses the method requiring a centrifuge.

Records are essential for the traceability of products prepared in the radiopharmaceutical.

The IAEA IOG on hospital radiopharmacy states that “Preparation records such as the description of the product, including the radionuclide, product identification number, activity at the time of patient administration, volume, time of dispensing, patient name, operator and checker identification should be kept” (IAEA, 2008a).

Preparation (Audit ref. 2.19 and 2.20)

The preparation of radiopharmaceuticals in Hospital X is not performed in a LAF. Hospital X does have a LAF but it is not in use at the moment.

In Hospital Y admixing is performed in a fume hood and not in the LAF, the generators are eluted in the LAF. The reason for the latter practice is unclear.

In both hospitals the individual who prepares the radiopharmaceuticals is the same individual who dispenses them. This leaves room for errors to go undetected. It is better to have one person preparing and another checking in order to eliminate the potential of errors.

Traceability (Audit ref. 2.21)

Hospital X: the radiopharmaceutical dose can be traced to the generator since the generator lot number is recorded on a daily basis when it is eluted, but the dose cannot be traced to the kit batch number. The lack of batch traceability for the kits, poses a potential problem should kits prove to be faulty or recalled.

Hospital Y: the dose can be traced to both the generator and the kit batch number.

Saha (2004), states that the preparation of radiopharmaceuticals should be carried out in a LAF under aseptic conditions. Information such as control number, product name, concentration, date, time of calibration and expiry date should be furnished on a label, which should be pasted on the lead container which holds the radiopharmaceutical. IAEA (2008a) Operational guidance recommends that a class II vertical LAF in a grade C background or an isolator cabinet in a grade D background be used for the preparation of the radiopharmaceuticals, and that the integrity of the LAF filter should be checked at regular intervals and according to the manufacture's guidelines.

4.7 QUALITY ASSURANCE AND QUALITY CONTROL

4.7.1 Results

The results of the audit for quality assurance and quality control of each hospital radiopharmacy for OLs 1 and 2 appear below in Table 4.10.

The aim of quality control of radiopharmaceuticals is to ensure the purity, potency, product identity, biological safety, and efficacy of radiopharmaceuticals. There are two (2) categories of quality control test a) physicochemical tests, indicate the level of radiochemical and radionuclidic purity b) biological tests, determine product sterility, apyrogenicity, and toxicity. (Saha, 2004)

Radiochemical purity is defined as that fraction of the total radioactivity in the desired chemical form in the radiopharmaceutical. Poor-quality images are due to the presence radiochemical impurities, these impurities arise from decomposition either due to the action of a solvent, change in temperature or pH, light, presence of oxidizing or reducing agents, or radiolysis (Saha, 2004).

Radionuclidic purity is defined as that fraction of the total radioactivity in the form of the desired radionuclide present in a radiopharmaceutical (Saha, 2004).

Biological safety is necessary to ensure that the product is sterile, that is, a total absence of viable microorganisms, also that the product is apyrogenic and does not contain any particles or particulate matter that might cause fever when injected. The product must be free of any toxins.

Efficacy of the product is determined in three (3) ways, namely, chromatography, biodistribution and clinical evaluation.

Table 4.10 Quality assurance and quality control results for Hospital X and Y

Audit Ref. #	Component Detail	Class	Hospital X	Hospital Y
1.19	Are daily QC checks performed on radionuclide calibrators?	A	Yes	Yes
1.20	What quality checks are undertaken on a supplier before purchase?	B	The MCC is the one that inspects the suppliers, no inspection is undertaken by the department	The MCC is the one that inspects the suppliers, no inspection is undertaken by the department
1.21[a]	Are periodic quality checks on radiopharmaceuticals performed?	B	No	Yes for HMPAO
1.22	Is there a written procedure for dealing with products failing to meet the required standard?	B	No	No
1.23	Is there a record of complaints and any associated follow-up and investigation?	B	No	No
1.24	Are there written procedures and records for regular contamination surveys of the radiopharmacy unit?	A	No	Yes For spills only

[a] Shaded audit references are those for which the IAEA audit document requires to be clarified and/or edited.

Audit Ref. #	Component Detail	Class	Hospital X	Hospital Y
2.24	For operational level 2: Are there **records** for the following:	B		
2.24 a	Purchase of radioactive products and ingredients	B	Yes	Yes
2.24b	Generator elution, yield, ^{99}Mo breakthrough and aluminium ion breakthrough	B	Yes	Yes
2.24c	Product preparation, QC and Release	B	No	Yes
2.24d	Environmental and microbiological monitoring;	B	No	No
2.24[e]	Aseptic process, aseptic operator validation and trend analysis;	B	No	No
2.24f	Laboratory cleaning and Maintenance	B	No	No
2.24g	Equipment and plant calibration and maintenance	B	No	No
2.24h	Radioactive contamination monitoring and radioactive waste disposal;	B	No	No
2.24i	Product defects and SOPs nonconformance, i.e. when a procedure is performed in a manner other than that described in the relevant SOP;	B	No	No
2.24j	Independent inspection and audit	B	No	No
2.25	In line with the IAEA Operational Guidance on Hospital Radiopharmacy publication, are there records of routine microbiological monitoring of the preparation area in the radiopharmacy?	A	No	No
2.26	Are there calibration and linearity checks of the dose calibrator response over the complete range of activities measured at least annually?	A	Yes	Yes
2.27	Is there a set programme for checking the quality of radiopharmaceuticals?	B	No	Yes*

Audit Ref. #	Component Detail	Class	Hospital X	Hospital Y
2.28	Considering patient safety, are certain simple checks performed on prepared radiopharmaceuticals, e.g. minichromatography?	A	No	Yes for HMPAO
2.29	For operational level 2: Is a ^{99}Mo breakthrough measurement performed on the first eluate from each ^{99m}Tc generator and repeated when the generator is moved?	A	Yes but they do not move the generator	Yes but they do not move the generator
2.30	Is aluminium ion breakthrough checked on the first eluate from a ^{99m}Tc generator?	A	Yes	Yes
2.31	Are changes in the source of any kits, diluents or vehicle used, needles, syringes, swabs and sterile containers used within radiopharmacy recorded?	B	No	No
2.32	On first use of a new batch or first new delivery of radiopharmaceutical kits, is radiochemical purity performed?	B	No	Yes When there is a need to use that kit
2.33	Are rapid alternative methods employed for swift prospective QC for critical radiopharmaceuticals, e.g. the determination of RCP for ^{99m}Tc HMPAO?	A	No	Yes
2.34	Is there regular pH testing of radiopharmaceuticals carried out?	B	No Do not have a pH meter	No Do not have a pH meter
2.35	Prior to release for patients, is each individual radioactivity dose checked?	A	Yes	Yes
2.36	Is there a record of the formal approval/release by an authorized person before a product is administered to a patient?	A	No	No
2.37	Are there written procedures for the recall of defective products?	A	No	No
2.38	Is there a record of complaints and any associated follow-up and investigation?	B	No	No

Audit Ref. #	Component Detail	Class	Hospital X	Hospital Y
2.39	Is there a system of recorded **self inspection** and reports evaluation?	B	No	Yes
2.40	Is there a system for an external audit or peer review process?	B	Yes* But only the DOH inspection	Yes* But only the DOH inspection

4.7.2 Discussion

Quality control checks and records (Audit ref. 1.19 to 1.22)

Both hospitals perform daily QC checks on the dose calibrator and record the process accordingly.

Neither hospital performs checks on the supplier. The suppliers are inspected by the MCC.

Hospital X does not perform QC checks on their prepared radiopharmaceuticals, whereas Hospital Y does.

According to the IAEA Operational Guidance (2008a), the pH, clarity, radiochemical purity and sterility should be checked at least for the first and last generator eluate. Because the eluate's sterility cannot be guaranteed if the generator is used for longer than two weeks, the sterility needs to be checked at least once a week.

Neither hospital has written procedures for dealing with products that fail to meet the required standards.

Audit ref. 1.21 is not clear regarding which quality checks are referred to here. Only hospital Y is equipped to perform some quality checks. The only quality checks they perform on these products is the labelling efficiency.

Record of complaints (Audit ref. 1.23)

As part of the management systems, records of complaints are necessary. The radiopharmacy/nuclear medicine department must have a policy and procedure for the resolution of complaints received. Records need to be maintained of all product-related complaints and of the investigations and corrective actions taken by the laboratory (IAEA, 2006b).

Neither hospital has a record of complaints.

It is not clear from the audit question whether the complaints are about the product or are related to do with product use.

[Radiation] Contamination surveys (Audit ref. 1.24)

As microbiological checks are dealt with under Audit ref 2.24d it was assumed by the researcher that audit Ref 1.24 related to radiation contamination.

Neither hospital has written procedures and records for regular contamination surveys, but Hospital Y has written procedures for the management of spills only.

Records (Audit ref.2.24)

Neither hospital has records of environmental and microbiological monitoring, laboratory cleaning and maintenance, equipment and plant calibration, radioactive contamination monitoring, product defects, SOP non-conformance, and an independent inspection/audit. The sterility of the generator eluate is also not checked.

Self inspection (Audit ref. 2.39)

Hospital Y had already conducted the IAEA Nuclear Medicine IOG Hospital Radiopharmacy audit on their facility in January, 2010 and therefore had been able to address some of the areas where there was a lack of compliance. Unfortunately it is not within the scope of this project to review the self-audit results for Hospital Y.

“The laboratory must aim at maintaining biological sterility, a dust free environment and a steady electricity supply, and due attention must be paid to environmental conditions such as electromagnetic disturbances, other sources of radiation, humidity and temperature. Tests and calibrations must be stopped when the environmental conditions jeopardize the results of the tests and/or calibrations. The laboratory must be designed so as to limit the spread of surface or airborne contamination by the radioactive material as well as unnecessarily high background radiation” (IAEA, 2006b).

4.8 WASTE MANAGEMENT

4.8.1 Results

The results of the audit for the management of waste of each hospital radiopharmacy for OL1 appear below in Table 4.11.

Table 4.11 Waste management results for Hospital X and Y

Audit Ref. #	Component detail	Class	Hospital X	Hospital Y
1.25	Are there written procedures for the disposal of radioactive and non-radioactive waste specific to the radiopharmacy?	A	No	No
1.26a	Is there a periodic review/audit of arrival and use of all radioactive materials?	A	Yes*	Yes*
1.26b	Is there a periodic review/audit of disposal of all radioactive materials?	A	No	No
1.27a	Are there written logs for each solid source that indicate usage and transfer of the source?	A	Yes	Yes
1.27b	Are there written logs for each solid source that indicate disposal of the source?	A	No	No

4.8.2 Discussion

Neither hospital has a record keeping system in place for waste management.

Hospital X – places their waste in a “decay box”, separate from the “hot” laboratory. They then keep this box for approximately 2 weeks (see Chapter 5 for additional information). Then the delegated staff from the hospital collect the waste, which is discarded as standard medical waste. The “sharps” are not separated from the rest of the waste and placed in a container that will not allow the content to cause harm to the environment. Sharps include needles and vials that when broken can cause an injury due to them being made of glass.

Hospital Y - Within the “hot” laboratory there is a dedicated area for waste which is labelled accordingly and is kept closed at all times. The waste is segregated into sharps and other waste. Hospital staff delegated to remove the waste do so at specific intervals. By the time the waste is disposed of, the hazardous label has been removed.

It is suggested that the radioactive waste be segregated into short- and long-lived waste, with the sharps in the sharps container and the rest of the waste in another separate container (IAEA, 2008a).

With regards to $^{99}Mo/^{99m}Tc$ generators it is best to return them to the vendors (Saha, 2004), who will dispose of them once they have decayed, this out of use generator should be

placed in its original packaging before being collected by the vendor when they deliver a new generator. Both hospitals practice this procedure, which is done every two weeks.

4.9 COMMENT ON THE IOG AUDIT DOCUMENT *PER SE*

4.9.1 Multiple questions in one audit reference

Several audit references deal with multiple items (e.g. in 2.1, 1.4 and 2.24), or ask more than one question (e.g. 1.6, 1.9, 2.20, 1.26 and 1.27).

The audit references mentioned above need to be broken down into smaller units, for clarity and to aid in the accuracy of the response. The tables (above) in this chapter show how those references were split for accuracy and clarity.

4.9.2 Duplication

There was some duplication of items (e.g. 1.4f and 1.5). Presumably, when the audit was compiled, there was a different intention for these duplicate sections, but that purpose was not clear from the audit document and accompanying information.

4.9.3 Lack of clarity/ambiguity of questions

Audit reference 1.3 deals with training manuals for all grades of staff but the audit does not give guidance as to the areas of training required for different cadres of staff.

Audit reference 2.9 deals with challenge testing of LAF. It is not specified what kind of challenge test is required, be it a smoke test or the introduction of microbes to test the effectiveness of the LAF HEPA filters.

Audit reference 1.9 “Are there suitable protocols and trained staff for the purchase of approved or marketing-authorized radiopharmaceuticals?” The audit notes are not specific regarding what is required in terms of training of the staff for the purchase of products.

Audit reference 2.14 “How many unlicensed or unapproved products are used each year and is there a record of them?” It is not clear whether this statement refers to the total number of unauthorised (unregistered) products items used or the number of different Section 21 products.

Audit reference 1.24 contamination surveys of the radiopharmacy unit - It is assumed that the contamination mentioned is that of radiation, as microbiological contamination is mentioned under OL2 of the quality control aspect of the study.

Audit reference 1.23 refers to complaints. It is not clear from the question whether the complaints are about the product quality as received or related to product use or both.

Audit reference 1.14 is unclear and confusing. Under operational level 1a: “Are there written procedures for the aseptic dispensing and labelling of unit doses of ready to use radiopharmaceuticals?” Our interpretation of ready to use products would mean that no aseptic dispensing is required.

Audit reference 1.21 “Are periodic quality checks on radiopharmaceuticals performed?” This reference covers a huge area. The required quality checks are not specified. Also, it is not clear whether the quality checks mentioned are meant to be performed before or after preparation.

In summary – the audit is comprehensive and valuable. It is not always easy to interpret and a clear set of accompanying guidelines would be helpful for those who are attempting a self-audit.

CHAPTER 5
RESULTS AND DISCUSSION

FOCUS GROUPS AND KEY INFORMANTS

5.1 INTRODUCTION

This chapter presents the results of the focus group discussions carried out in both Hospital X and Hospital Y. This chapter starts with a brief discussion on the manner in which the focus group discussion was carried out. All participants signed consent forms before the discussions commenced.

As described in Chapter 3, the focus group discussion was conducted in each hospital once the audit was completed. Staff involved in the direct handling of radiopharmaceuticals participated in the discussion. The researcher presented the findings of the audit to the technical staff of both hospitals. Once the findings were reported the researcher's supervisor then facilitated the focus group discussion, whilst the researcher took notes. The discussions were taped with the consent of all participants.

The topics for discussion from Appendix 4, the FGD guidelines were as follows:

- Whether the hospital had undergone a recent audit.
- Whether the hospital has SOPs.
- The person who develops these SOPs.
- Whether there is room for improvement and their feelings towards the environment they work in.
- Their feelings about the audit and the way forward.

5.2 HOSPITAL X

In hospital X eight (8) staff members participated in the discussion and they consisted of radiographers, medical physicists, and physicians.

5.2.1 Surveys/Audits

No survey or audit has been conducted on the Nuclear Medicine department in the past few years.

5.2.2 Standard Operating Procedures

The staff stated that there are few in-house SOPs

For radiation safety and equipment such as the dose calibrator, Hospital X uses the IAEA technical document on quality control of nuclear medicine instruments (TECDOC 602:, IAEA, 1991) as a guideline.

Radiopharmaceutical reconstitution is conducted according to the manufacturer's instructions. Summary procedures were typed and placed on the wall of the preparation area in 2006 but these have not been reviewed since. The summary procedure includes the manner in which the radiopharmaceutical should be prepared, the incubation period and the activity/amount of ^{99m}Tc to be added to the kit.

5.2.3 Room for improvement

When asked where the participants felt there was room for improvement, lack of **batch-traceability** was raised as an issue. Participants felt that, they could improve on this factor by recording the batch number of the kits they use in the patient's prescription. At the moment the kit batch numbers can only be traced loosely, by reference to a time period over which the batch was used.

The hospital performs molybdenum breakthrough but does not perform **QC checks** such as radiochemical purity or aluminium breakthrough, nor do they check the labelling efficiency of the reconstituted products. This gap is attributed to the fact that the hospital does not have the equipment/resources such as chromatography strips and a multichannel analyser.

The hospital has no **fume hood** for the handling of radioiodine, but they do handle radioiodine in the form of capsules for therapeutic use. Since the release of ^{133}Xenon (^{133}Xe) gas is not that significant staff felt that a fume hood is not a necessity.

Microbiological testing is not performed in the hospital. Operator technique is not checked and there are no environmental tests performed on the "hot" laboratory. As noted in Chapter 4 the LAF cabinet is not in use at the moment, lack of funds are a constraint. The commissioning of the LAF cabinet is fund-dependent.

Senior staff agreed that settle plates could be placed in the radiopharmacy laboratory to check the environment. In addition they stated that they do try to keep procedures as aseptic as possible.

They ensure that the **waste,** when disposed of, is within the radiation limits as can be found in Chapter 4. The waste is taken away by the hospital staff after approximately a week or two of it being in the department. Since they deal mainly with ^{99m}Tc based products which has a half-life of 6 hours, by the time the waste leaves their premises it poses no risk. They did not have an idea of how waste is handled once it has left their premises.

They do not separate their waste. The sharps (such as vials and needles) are not separated from gloves and neither are the short-lived radiopharmaceuticals separated from the long-lived radiopharmaceuticals but non radioactive waste such as biological waste and is separated from radioactive waste.

The hospital has been having problems with the supply of ^{99}Mo/^{99m}Tc generators as their account has been suspended; this is due to problems with the payment of **accounts** by the DOH Gauteng.

There are major budget problems in terms of insufficient initial funding as well as on-going payment of accounts. The financial administration at the Hospital is a major stumbling block.

5.2.4 Views on the survey

The staff expressed the opinion that the survey was beneficial. The survey was a way in which they would learn to work better. Their response was very positive. The survey was seen as a tool to aid in improving the services of the hospital. The opinion was expressed that it should be done on a continuous basis as they want to ‘grow’ and be on a par with other departments around the country.

The staff did not appear to have felt threatened by the survey.

5.2.5 Way forward

The staff felt that the way forward is for them to upgrade their “hot” laboratory and this is already in the planning stages.

5.3 HOSPITAL Y

In Hospital Y six (6) staff members participated in the discussion. They were radiographers and one medical physicist.

5.3.1 Surveys/Audits

Hospital Y conducted a self audit in the past year, using the IAEA Operational Guidance on Hospital Radiopharmacy audit document, but none of the focus group participants was involved in that survey.

5.3.2 Standard Operating Procedures

The staff voiced that the DOH Inspection procedure (Nuclear Medicine) (DOH, 2007) - Radiation control audit is conducted routinely and that they use the recommendations that emanate from that report.

SOPs are driven ‘top-down’. The hospital doctors use the IAEA website to source and draw up SOPs. The HOD is the one responsible for the implementation of new procedures, though he is open to staff suggestions.

5.3.3 Room for improvement

The staff were content with the manner in which the hospital operates, they felt that in terms of **QC** from the feedback session, that the addition of a pH meter would be welcomed.

Microbiology tests – when prompted, staff felt strongly that these could be introduced – but they needed some equipment and also guidelines.

5.3.4 Views on the survey

The question was asked as to whether staff were familiar with the IAEA Nuclear Medicine Department audit (IAEA, 2006a). Staff were familiar with it and were enthusiastic about the positive impact of its use.

The staff mentioned that the survey was a way in which they would learn to work better. The response was positive; it was seen as a tool to aid in improving the services of the hospital.

5.4 KEY INFORMANTS INTERVIEW OUTLINE

As mentioned in Chapter 3, key informants were the different HODs of Nuclear Medicine departments and specialist radiopharmacists. Unfortunately the views from key informants C and D were not received in time for inclusion in the study. Below are the views given by the key informants A and B to the following questions:

- Radiopharmacy practice in South Africa
- South African Department of Radiation Control audit document
- Views about the IAEA Operational Guidance on Hospital Radiopharmacy
- Changes needed for South African tertiary hospitals to achieve the standards set out in the IAEA Operational Guidance on Hospital Radiopharmacy

5.4.1 Radiopharmacy practice in South Africa

Key informant A

"Radiopharmaceuticals are regarded as medicines and are thus subject to regulations for production and importing of medicines. Production/manufacturing of radionuclides and radiopharmaceuticals is done at correctly licensed sites.

"In hospitals and Nuclear Medicine practices, radiopharmacy is not yet fully recognised as "pharmacy". The place where radiopharmaceuticals are prepared and dispensed is regarded as a laboratory rather than a pharmacy, and with a few exceptions, pharmacists are not involved in hospital preparation and dispensing of radiopharmaceuticals.

"Some of the radiographers performing the day to day operations in radiopharmaceutical laboratories in hospitals have been well trained regarding radiation safety and quality control of radiopharmaceuticals. Training is however not the same at all training institutions."

Key informant B

"Radiopharmacy in key informant B's opinion is still in its infancy in the South African environment. Except for the one state hospital and maybe one or two private institutions, radiopharmacy is not practiced to its fullest. Academic institutions, such as training hospitals where nuclear medicine is practiced, should all have an adequately staffed and equipped radiopharmacy."

5.4.2 South African Department of Radiation Control audit document

Key informant A

Key informant A has not seen such an audit document. Key informant A knows that Radiation Control uses a check list when they inspect nuclear medicine facilities. This document is not freely available to nuclear medicine practitioners.

Key informant B

To the knowledge of key informant B the audit document that is being referred to only addresses the radiation safety aspect of a facility. This document does not make provision for setting of standards and auditing radiopharmacy from a pharmaceutical point of view and can therefore not be used to evaluate a radiopharmacy from that perspective. From a pharmaceutical point of view, the Medicines Control Council and/or South African Pharmacy Council should be much more involved in this process.

5.4.3 International audit documents

Key informant A

Key informant A has extensively used the self-assessment forms provided in the IAEA Operational Guidance on Hospital Radiopharmacy.

Key informant A has read the audit document of the British Nuclear Medicine Society.

Key informant B

“The FDA and European Association for Nuclear Medicine (EANM) have guidelines available for good radiopharmacy practice for both kit based radiopharmaceuticals and PET produced radiopharmaceuticals. These guidelines, if adapted can be used as basis for an auditing document.

“The United Kingdom Radiopharmacy Group (UKRG) has formal auditing documents that are utilized by all radiopharmacies and regulatory bodies in order to audit a radiopharmacy. These auditing document are extensively used throughout the UK by inspectors when auditing radiopharmacies. These auditing documents are of a high standard and although it specifically addresses UK requirements, it can (should!) be extensively used as reference document in auditing radiopharmacies.”

5.4.4 South African Department of Radiation Control audit document in comparison to international audit documents

Key informant A

"Radiation Control only considers radiation safety aspects of the facility. Not the sterility, quality and safety of the radiopharmaceuticals."

"It is an important aspect of radiopharmacy, but by no means sufficient to ensure that radiopharmaceuticals are safe and effective."

Key informant B

"As mentioned by key informant A, the South African Department of Radiation Control audit document only addresses the facility in which radiopharmacy is practised. It does not address any pharmaceutical aspects of radiopharmacy".

5.4.5 Views about the IAEA Operational Guidance on Hospital Radiopharmacy

Key informant A

"The Operational Guidance is based on recommendations for radiation safety and for preparation of injectable pharmaceuticals. It is a very comprehensive document.

"At this stage, probably no South African hospital radiopharmacy meets all requirements described in the IAEA Operational Guidance. There are not enough trained radiopharmacists to supervise all radiopharmacies (this could be a part-time function or a shared responsibility for more than on radiopharmacy). Radiographers performing daily preparation and dispensing functions probably need further training regarding pharmaceutical quality of products, aseptic technique, and quality assurance. Facilities are inadequate, especially regarding clean air provision."

Key informant A thinks the requirements are achievable in the long run. It may take up to 10 years to upgrade all radiopharmacies and train the required number of persons to the necessary levels.

Key informant B

"The IAEA Operational Guidance on Hospital Radiopharmacy is an international accepted reference document that can be utilized as a basis for practicing good radiopharmacy. It addresses all the keys aspects of proper radiopharmacy practice, from the basic layout and requirements for the facility to staffing, training and administrative tasks."

5.4.6 Changes needed for South African tertiary hospitals to achieve the standards set out in the IAEA Operational Guidance on Hospital Radiopharmacy

Key informant A

"Quality assurance should receive the necessary attention. This means that staff needs to be trained in the required quality control procedures as well as documentation systems. The syllabi for Nuclear medicine radiographers may have to be reviewed to incorporate more information and hands-on training in quality control procedures, proper record keeping and pharmaceutical aspects such as microbiological safety of products and environments."

"Facilities need to be upgraded to provide better air quality."

"Each nuclear medicine unit should have a qualified radiopharmacist to advise and supervise radiopharmacy staff. This could be part-time services. The necessary posts need to be created for specialised radiopharmacists."

"In the long run, there should be a move to regard radiopharmaceutical laboratories as pharmacies rather than laboratories."

"Care must be taken not to enforce pharmacy regulations on radiopharmacies without providing adequate budgets and time to allow improvements of facilities and procedures, and training of the required number of supervisory staff (radiopharmacists/qualified persons). There should be a long term plan to improve radiopharmacy, and all nuclear physicians should be encouraged to cooperate to achieve these changes. Authorities should at least initially provide guidance rather than enforce regulations."

Key informant B

"A concerted effort should be made by all heads of Nuclear Medicine departments and other key role players to establish radiopharmacy in their departments. This effort should include the following:

- creating posts for radiopharmacy personnel (radiopharmacists, nuclear medicine technologists, etc)
- adequate training (internal and external) of personnel
- adequate equipment necessary

- establishing opportunities for the radiopharmacy team to become involved in research projects in line with the key focusing areas of the nuclear medicine department.
- Ongoing training and development of radiopharmacy staff."

5.5 SUMMARY

This chapter presented the findings of the FGD together with the key informants interviews.

CHAPTER 6
SUMMARY, CONCLUSION AND RECOMMENDATIONS

6.1 INTRODUCTION

The aim of this study was to identify and assess compliance with published radiopharmacy procedures or standards, in the radiopharmacy units in the Departments of Nuclear Medicine at Steve Biko Academic Hospital, Pretoria and Dr. George Mukhari Hospital, Ga-rankuwa.

The purpose of setting standards is to optimize patient outcomes through the judicious, safe, efficacious and appropriate use of medicines (FIP, 2009).

Before this study Hospital X had not had an audit of radiopharmacy services. Hospital Y had performed the IOG hospital radiopharmacy audit in the beginning of the year and had time to make subsequent improvements.

6.2 SUMMARY

This summary addresses the objectives of the study.

Objective 1

To identify current written Standard Operating Procedures in use by the selected hospitals and to compare them with the two selected audit documents.

A comparison of the only available South African radiopharmacy audit document with the IAEA audit document was reported in Chapter 3 (see Table 3.1).

It was apparent that the South African Department of Health document was concerned only with radiation safety and not radiopharmacy services. The results of the IAEA/IOG audit revealed that the two hospitals had few formal SOPs. This shortcoming needs to be addressed, as up to date SOPs are central to controlled processes of good quality.

Objective 2

To describe the OLs of hospital radiopharmacy services according to the IAEA classification (see Section 1.1 of the Literature Review), staffing and workload of the selected radiopharmacy units.

The two (2) radiopharmacy units conducted services at Operational Levels 1 and 2 only. Both hospitals perform autologous labelling of RBC only.

Objective 3

To assess the two units for compliance with the IAEA/IOG audit.

Chapter 4 deals at length with the findings of the audit and discusses the need for compliance with each reference item of each component.

Tables 6.1 and 6.2 below summarise the degree of compliance with the audit components for Hospital X and Y. The totals possible for classes A and B for each OL are shown in the third and fourth columns. The scores for each component and class are shown in the fifth and seventh columns for Hospital X, and the ninth and eleventh columns for Hospital Y. Where a component was not applicable (N/A – see Tables 4.2, 4.3, 4.6 and 4.8 to 4.11), the percentage score is calculated from the number of components that were applicable (numbers shown in brackets in the score columns).

Table 6.1 below shows a summary of compliance with the audit components, based on observed or reported responses (i.e. not all responses were able to be verified). The numbers do not include components that were not applicable (N/A) in Tables 4.2, 4.3, 4.6 and 4.8 to 4.11 from Chapter 4.

Table 6.1 Summary of compliance with IOG audit components (not verified)

Component	OL	TOTAL possible)		Hospital X				Hospital Y			
		Class A	Class B	Class A		Class B		Class A		Class B	
(1)	(2)	(3)	(4)	Score (5)	% (6)	Score (7)	% (8)	Score (9)	% (10)	Score (11)	% (12)
Staff	1	2	1	2	100	1	100	2	100	1	100
	2	8	3	8	100	1	33	8	100	1	33
Facilities	1	11	1	8	73	1	100	11	100	1	100
	2	1	6	0(/0)	-	0(/1)	0	1(/1)	100	3(/4)	75
Purchase of materials	1	1	3	1	100	3	100	1	100	3	100
	2	3	1	3	100	0(/0)	-	3	100	1(/1)	100
Dispensing protocol	1	4	2	1	25	1(/1)	100	4	100	1(/1)	100
Preparation protocol	2	6	3	3(/5)	60	1	33	5	83	1	33
Quality assurance and quality control	1	2	4	1	50	0	0	2	100	1	25
	2	9	17	4	44	3	18	6	67	7	41
Waste management	1	5	0	2	40	-	-	2	40	-	-

Table 6.1 shows that Hospital Y met 100% of the required standards for class A items for the components of staff, facilities, purchasing and dispensing as well as quality assurance at OL1, when assessed on a combination of observed and stated outcomes. Only waste management fell below the 50% level.

Hospital X (see Table 6.1) met 100% of the required standards in the class A category for staff and purchasing only, based on a combination of observed and stated outcomes. Facilities and preparation protocols were above the 50% score but dispensing, quality assurance and waste management were below the 50% score.

Table 6.2 below shows the degree of compliance with the IAEA audit, based on observed **(i.e. verifiable)** responses.

Table 6.2 Summary of IOG audit components (verified)

Component	OL	TOTAL possible)		Hospital X				Hospital Y			
		Class A	Class B	Class A		Class B		Class A		Class B	
(1)	(2)	(3)	(4)	Score (5)	% (6)	Score (7)	% (8)	Score (9)	% (10)	Score (11)	% (12)
Staff	1	2	1	2	100	0	0	2	100	0	0
	2	8	3	1	13	0	0	1	13	0	0
Facilities	1	11	1	8	73	0	0	9	82	0	0
	2	1	6	0(/0)	-	0(/1)	0	0(/1)	0	0(/4)	0
Purchase of materials	1	1	3	0	0	1	33	0	0	1	33
	2	3	1	3	100	0(/0)	-	3	100	0(/1)	0
Dispensing protocol	1	4	2	0	0	1(/1)	100	2	50	1(/1)	100
Preparation protocol	2	6	3	3(/5)	60	1	33	3(/4)	75	1	33
Quality assurance and quality control	1	2	4	1	50	0	0	2	100	1	25
	2	9	17	4	44	2	13	7	78	5	31
Waste management	1	5	0	1	20	-	-	1	20	-	-

As can be seen, Hospital Y, when assessed on verifiable items, met 100% of the required standards for class A items only for staff al OL1, purchase at OL2 and quality assurance at OL1. Facilities at OL1, dispensing protocol at OL1 and quality assurance at OL2 were above the 50% score but staff at OL2 and waste management were well below the 50% score.

Hospital X, when assessed on verifiable items, met 100% of the required standards for class A items only for staff at OL1 and purchase of materials at OL2. Facilities at OL1, preparation and quality assurance at OL1 were above the 50% score. Purchase of materials at OL1, dispensing, quality assurance at OL2 and waste management were all below the 50% score.

Hospital Y had already conducted a self-audit according to the IOG which contributes to some of the difference in terms of the results presented in this chapter.

The reason for the huge gap in facilities between the two hospitals is historical. Hospital Y was, during the Apartheid regime, a hospital for white South Africans only. It was previously, in fact, worse off in terms of Nuclear Medicine facilities than Hospital X. In 1991 it was decided by the Cabinet of South Africa to upgrade Hospital Y (Taylor, 2003). Hospital X catered for the previously disadvantaged black population and is located in a township.

Hospital X was scheduled to be rebuilt in the 1990s but this project was stopped at about the same time Hospital Y was upgraded. Hence there is a historical legacy that has not been properly addressed even since the change of government in 1992.

6.2.1 Staff

Neither hospital has a radiopharmacist responsible for the radiopharmacy but rather radiographers. The radiographers are trained in aspects of radiation safety and some aspects of quality control of radiopharmaceuticals. They apparently require more training on aseptic techniques and SOP development.

Neither hospital has a formal system of radiopharmaceutical record keeping. The main objective of any documentation is to provide an audit trail, it is important that the records are comprehensive.

Neither hospital performs an annual performance review to check the competencies of their staff.

6.2.2 Facilities

Neither hospital has the special steel benches with curved sealed edges to contain spills. These benches would be the ideal in order to protect staff from radiation contaminations.

Hospital X has an extraction fan as compared to the air conditioning system in Hospital Y.

Hospital X does not have a fume hood. Hospital Y does, but uses the fume hood for the reconstitution/admixing of kits.

Neither of the hospitals have planned preventative maintenance on the refrigerator.

Hospital X has a few key items, such as a Laminar Flow unit, that are not in use due to the lack of suitability of the areas in which they are situated and the lack of trained staff to operate them.

The radiopharmacy/“hot” laboratory in Hospital X is too small, essential equipment such as the LAF have no place in the “hot” laboratory due to its size. It is not indicated on the door that it is a radiopharmacy / radiation area, and the door should be closed at all times.

Access to the radiopharmacy/“hot” laboratory is not restricted to the staff member that is destined to work there for that particular period in both hospitals.

There are no dedicated laboratory coats for the radiopharmacy/“hot” laboratory in Hospital X. Those in Hospital Y appear to be re-used indefinitely and often staff do not wear the laboratory coats at all.

Staff working in the radiopharmacy/“hot” laboratory only have film badges to monitor radiation exposure. Their hands are mainly in contact with the radiation, hence finger dosimeters should be worn.

Neither hospital measures and/or records the temperature of the fridges or the ambient temperature of the radiopharmacy.

6.2.3 Purchase of materials

The purchase of materials should be done in accordance with set criteria from approved vendors/suppliers. The Government tender system is designed to cover such requirements Approved vendors in this case does mean approved vendors as stipulated by the finance department of the hospital but rather from reputable suppliers which supply quality products.

In terms of continuity of supply, there has been a problem with the payment of accounts by the Gauteng DOH and as a result Hospital X has been experiencing problems with interruptions in their supply of generators. This matter is not within the scope of the audit, but it has affected patient care detrimentally.

6.2.4 Dispensing protocol

Hospital X has no system in place for issue and monitoring of labels while Hospital Y does.

Hospital X: there is no kit batch traceability for each radiopharmaceutical from the prescription.

Hospital Y: has batch traceability from the prescription.

The main objective of any documentation is to provide an audit trail and it is important that these records are comprehensive (IAEA, 2008a).

6.2.5 Preparation protocol

Neither hospital independently reviews their SOPs. SOPs are of importance in the training of new staff members, SOPs are essential for insuring effectiveness and efficiency of an organization. The quality assurance of any product relies on the validity of the SOPs in the

production of the product, and microbiological validation of SOPs is to ensure that during the aseptic preparation of products the sterility of the product is maintained (Beaney, 2006).

Hospital X: the radiopharmaceutical dose can be traced to the generator since the generator lot number is recorded on a daily basis when it is eluted, but the dose cannot be traced to the kit batch number. Hospital Y: the dose can be traced to both the generator and the kit batch number. Ideally doses should be traced back to whether it is the first, second or third elution from the same generator.

6.2.6 Quality assurance and Quality control

In terms of quality checks, Hospital X only performs ^{99}Mo breakthrough but no other QA checks are performed routinely.

Neither hospital has a record of complaints.

Neither hospital has written procedures and records for the regular contamination surveys, but hospital Y has written procedures for the management of spills only.

Hospital Y had already conducted the IAEA Nuclear Medicine IOG Hospital Radiopharmacy audit on their facility in January, 2010 whereas hospital Y has not conducted an audit.

6.2.7 Waste management

Hospital X does not separate waste. The staff ensures that the waste disposed of is within the radiation dose limitations. The radioactive waste is kept in a lead lined decay box before it is removed from the premises. The waste is not separated into sharps and non-sharps.

Hospital Y have a dedicated area for waste and is kept closed at all times. Their sharps are separated from the non-sharps.

Objective 4

To obtain the views of staff at operational, clinical and managerial level regarding constraints in the work situation.

No audit has been recently conducted in Hospital X. Hospital Y has conducted the IOG hospital radiopharmacy earlier in the year.

For radiation safety and equipment such as the dose calibrator, Hospital X uses the IAEA, 1991 technical document (TECDOC 602 - Quality control of nuclear medicine instruments) as a guideline. In Hospital Y SOPs are driven ‘top-down’. The hospital doctors use the IAEA

website to source and draw up SOPs. The HOD is the one responsible for the implementation of new procedures, though he is open to staff suggestions.

Staff from Hospital X felt that, they could improve on batch traceability by recording the batch number of the kits they use in the patient's prescription. Staff from both hospitals felt that microbiological monitoring tests should be introduced.

The staff in Hospital X felt that the way forward is for them to upgrade their "hot" laboratory which is already in the planning stages. Hospital Y is happy with the way things are at the moment in their facility.

The staff at both hospitals mentioned that the survey was a way in which they would learn to work better. The response was positive; they felt that the audit was a tool that could aid in improving the services of the hospitals.

The South African Radiation Control document which is used to asses Nuclear Medicine departments is not sufficient to audit the processes that take place in the radiopharmacy. International audit documents such as the IOG hospital radiopharmacy and the UKRG audit are good references and should be used locally to audit radiopharmacies. The IOG is a comprehensive document and the goals can be achieved in time in the South African public radiopharmacy setting.

Objective 5

To identify the elements from the IOG audit on Hospital Radiopharmacy which are realistically achievable in the South African hospital setting.

Both hospitals lack SOPs. There are many benefits to having and following SOPs; these include: (Jain, 2008)

- to provide staff with the safety, health, environmental and operational information necessary to perform a job properly;
- to maintain quality control of processes and products;
- to serve as a training document for teaching users about the process for which the SOP was written;
- to serve as a checklist for co-workers who observe job performance to reinforce proper performance;
- to serve as a checklist for auditors;

- to serve as an historical record of the 'how, why and when' of steps in an existing process so there is a factual basis for revising those steps when a process or equipment are changed.

Legal status of radiopharmacies/"hot" laboratorys in South Africa.

According to the IOG a radiopharmaceutical is defined as a radioactive pharmaceutical/medicinal product for clinical use (diagnostic or therapeutic) (IAEA, 2008a).

According to the Medicines and Related Substances Act (101 of 1965) a medicine is defined as any substance or mixture of substances used or purporting to be suitable for use or manufactured or sold for use in-

(a) The diagnosis, treatment, mitigation, modification or prevention of disease, abnormal physical or mental state or the symptoms thereof in man; or

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

According to the IOG a radiopharmacy (nuclear pharmacy) is defined as "a clinical service that procures, prepares or compounds, dispenses radiopharmaceuticals, and assures quality for diagnostic or therapeutic use in patients referred to the nuclear medicine service of a hospital."

From the above information, it is clear that the functions performed in a radiopharmacy unit are in fact part of the dispensing of medicines. Hence the question arises - are "hot" laboratorys actually performing the role of satellite pharmacies (i.e. dispensing)? South African legislation is currently unclear on the subject of the handling of radiopharmaceuticals (Osman, 2010). The fact that radiopharmacy is a specialisation of pharmacy which is registered by the SA Pharmacy Council puts radiopharmacy firmly within the scope of practice of pharmacy.

Except for registration with the DOH's Radiation Safety section, it is not clear whether radiopharmacies are required to register with Pharmacy Council. Privately owned centralized radiopharmacies must register with pharmacy either as a "community pharmacy" or as a manufacturing pharmacy when manufacturing PET-radiopharmaceuticals. Radiopharmacies or "hot" laboratorys may resort under the registration of the main pharmacy of the academic hospital. (le Roux, 2010)

6.3 CONCLUSION

The assessment of quality in the health care setting is based on Donabedian's theory which categorizes assessment into structure, process, or outcomes (Donabedian, 1982): Structure involves the facilities, equipment, types of services, and manpower with the credentials and qualifications of the health professionals involved. Process refers to the content of care which includes activities which take place between the patient and the provider. Outcome refers to the results of care. It encompasses biological changes in disease, ability for self-care, physical functions, and mobility and patient satisfaction.

Quality assurance should be based upon optimizing patient care, ensuring that there is an improvement in the quality of life of the patient. If the structure and processes are of good standards then the outcome should match.

It can be concluded from the results of this study that the one shortfall that both hospitals share is in terms of documentation and record keeping, the main objective of which is to provide an audit trail. Some of the time the researcher had to rely on observation and 'hear say' rather than documented evidence. For both hospitals the waste management procedures need to be documented.

Neither hospital has a cleanroom. There is a drive that all radiopharmaceuticals should be prepared in either isolators situated in a grade D background or a LAF in a grade B background (le Roux, 2010), hence a cleanroom is an objective for the future for both units.

In Hospital Y there is a vacant post for a radiopharmacist but Hospital X has no such post on the staff complement. "It is abundantly clear that there is a national need for radiochemists, radiobiologists, medical physicists and radiopharmacists" (Jarvis, 2009).

The role of the radiopharmacist is broad and it entails the procurement, compounding, dispensing, distribution, provision of information and consultation, preparation, quality assurance and quality control the supply of radiopharmaceuticals as well as monitoring their use, thereby ensuring the safety and efficacy of such products for optimal patient outcomes and research and development (Ponto & Hung, 2000). As can be seen from the above list, the role of a radiopharmacist compares closely with the South African Pharmacy Council's role of the pharmacist as described in the Unit Standards for Entry Level Pharmacists (SAPC, 2009). Some of the shortcomings of the procedures in the radiopharmacies audited are core pharmacist functions. Bringing a pharmacist on board would aid in the handling of radiopharmaceuticals in the correct manner. For example neither hospital unit ensured that the cold chain was maintained, which is an essential approach for product integrity. The

dispensing process, compounding and aseptic admixing are other basic pharmacy functions which require to be addressed. Furthermore, involvement in the quality issues of clinical services is an area that is an internationally recognised role of the pharmacist, as delineated in the Basel Statements on Hospital Pharmacy (FIP, 2009).

Although the legal situation regarding radiopharmaceutical dispensing in South Africa remains a grey area, the application of basic legal reasoning indicates that the process falls within scope of practice of a pharmacist.

Hence, whilst radiographers are fulfilling a much-needed function in South Africa, there is room for the complementary role of a radiopharmacist in the hospital radiopharmacies studied.

Since there are not enough trained radiopharmacists in the South African setting, it could be a part-time function of those qualified or they could share responsibility for more than one radiopharmacy. Certainly more radiopharmacists should be trained for South Africa.

The IAEA provides valuable assistance to hospital Nuclear Medicine Departments in many countries through their on-going promotion of training and audits. Unfortunately there is little published on the results of these audits, so comparative progress is difficult for departments to assess. One of the difficulties in the conduct of this project was the scarcity of published material on radiopharmacy audits. Only one published audit report was sourced (Kiondo, 2010). Regional summaries of audit results should be made available from the IAEA to aid comparative benchmarking and monitoring of progress over time.

The IAEA is a prestigious and respected international organisation. Its involvement in the audit process of hospital radiopharmacies and Nuclear Medicine Departments adds external weight to local and regional attempts to obtain support from their health authorities in the process of improved quality of care. Such support is often critical to the upgrading of existing services. Quality processes assurance can only be achieved through a consolidated and concerted effort at all levels. In addition there needs to be a ‘critical mass’ before progress can be made. South Africa is at the start of such a process.

6.4 RECOMMENDATIONS

Table 6.3 below lists the recommendations for each hospital, based on the results of the study:

Table 6.3 Recommendations of the study

Audit component	Recommendations	Hospital X	Hospital Y
Staff	The post for the radiopharmacist should be filled.		✓
	A radiopharmacist post should be created	✓	
	The competency of radiopharmacy staff should be checked initially and at least annually thereafter.	✓	✓
	The training of radiographers should be standardised in all institutions.	✓	✓
Facilities	Hospital X has only one waiting area. It would be preferable to separate the “cold” and “hot” waiting areas to reduce the amount of radiation exposure to the staff and the patients’ family members.	✓	
	The radiopharmacy/‘‘hot” laboratory needs to be upgraded; it is too small, essential equipment such as the LAF have no place in the “hot” laboratory due to its size. It needs to be identified and the door needs to be closed at all times.	✓	
	Access to the “hot” laboratory needs to be restricted to the staff member that is destined to work there for that particular period.	✓	✓
	The staff need to separate laboratory coats for the “hot” laboratory and the rest of the department.	✓	
	Staff working in the “hot” laboratory should have in addition to the film badges, finger dosimeters because the hands are at risk to receive the highest radiation dose, therefore tongs must be used to handle all radioactive sources.	✓	✓
	The following equipment needs to be put to use: namely the LAF cabinet, the centrifuge and the gamma detector, to ensure product integrity.	✓	
	The walls need to be repainted and the work surfaces need to be slightly curved up so as to contain the spills.	✓	✓
	A thermometer needs to be installed in the fridge and the minimum and maximum temperature recorded on a temperature log twice a day, this is to maintain the cold chain.	✓	✓
	The ambient temperature in the radiopharmacy needs to be checked and recorded to not only for the comfort of the staff but also to maintain the integrity of the products.	✓	✓
	The sealed sources need to be kept in a lead lined safe at the moment they are kept in a safe within the “hot” laboratory.	✓	
	Funding for upgrades	✓	✓

Table 6.3 Recommendations of the study continued

Audit component	Recommendations	Hospital X	Hospital Y
Purchase of Materials	In terms of continuity of supply, there has been a problem with the payment of accounts by the Gauteng DOH and as a result there has been interruptions in the supply of generators. This matter is not within the scope of the audit, but it has affected patient care detrimentally. The manner in which the provincial budget is managed should be reveiwed.	✓	
Dispensing Protocols	A system for labels should be established in order to assess the quality, the number of labels produced and the number of labels applied to the dispensed doses. These labels should comply with legislation as per the Medicines and Related Substances Act 101 of 1965.	✓	
Preparation Protocols	Introduce SOPs and log books for batch traceability for each radiopharmaceutical batch so that it is traced from, prescription to the actual, administration of individual patient doses and individual patient dose has to be traced to a specific generator and kit batch number. Ideally it should be traced back to whether it is the first, second,or third elution from the same generator.	✓	
Quality assurance and Quality control	All reconstituted radiopharmaceutical kits should undergo appropriate QC tests such as radiochemical purity on HMPAO, before release to the patients.	✓	
Waste Management	Sharp items (such as vials and needles) should be separated from non-sharps (such as gloves).	✓	
	The short-lived radiopharmaceuticals separated from the long-lived radiopharmaceuticals.	✓	✓
	There should be a dedicated waste store room until the waste is taken out of the premises.	✓	

REFERENCES

Beaney AM. 2006. Quality Assurance of Aseptic Preparation Services. 4th Ed. Pharmaceutical Press:London

Department of Health. 1973. The Hazardous Substances Act (Act 15 of 1973). Pretoria: Government Printers.

Department of Health. 2007. Inspection procedures: Nuclear Medicine. Pretoria: Government Printers.

Department of Health. 1965. Medicines and Related Substances Control Act (Act 101 of 1965). Pretoria: Government Printers.

Department of Health. 1974. Pharmacy Act (Act 53 of 1974). Pretoria: Government Printers.

Donabedian A. 1982. The definition of Quality and Approaches to its Assessment: Explorations in Quality Assessment and Monitoring. Volume 1. Health Administration Press. Ann Arbor, Michigan

Elliot A. T. 1998. Quality Assurance. In: Sharp P. F. Gemmell H. G. and Smith F. W. Practical Nuclear Medicine. 2nd Ed. New York: Oxford University Press; 1998. pp 49

FIP. 2009. International Pharmaceutical Federation. The Basel Statements on the Future of Hospital Pharmacy. American Journal of Health-Systems Pharmacy, March 2009;66 (Suppl. 3):S61-6

Gilroy L, Hesketh A, Kelly C, Laidlaw JM, Groves RL, Mason-Duff J, and Phillips S. 1993. Moving to Audit: What every Pharmacist needs to know about Professional Audit. Scotland, United Kingdom: Ninewells Hospital and Medical School

Gross, Z, 2007. Hospital careers sector: A career as a specialist radiopharmacist, in Pharmaceutical Journal. January 2007:18-20. [Accessed 2 February 2009]. Available from World Wide Web: <http://www.pharmj.com/students/tp2007/p18radiopharmacist.html>

IAEA. 1991. International Atomic Energy Agency. TECDOC 602: Quality Control of Nuclear Medicine Instruments. Austria: Vienna

IAEA. 2006a. International Atomic Energy Agency. Nuclear Medicine Resources Manual. Austria: Vienna

IAEA. 2006b. International Atomic Energy Agency. Quality Assurance for Radioactivity Measurement in Nuclear Medicine. Austria: Vienna

IAEA. 2007. International Atomic Energy Agency. National Training Course on Hospital Radiopharmacy, [Accessed 18 September, 2008]. Available from World Wide Web: <http://www.siteground182.com/>

IAEA. 2008a. International Atomic Energy Agency. Operational Guidance on Hospital Radiopharmacy: A Safe and Effective Approach. Austria: Vienna

IAEA. 2008b. International Atomic Energy Agency. Quality Management Audits in Nuclear Medicine Practices. Austria: Vienna

ISO. 2006. International Organization for Standardization. ISO Cleanroom Classification, [Accessed 6 December, 2010]. Available from World Wide Web: < http://www.iso.org/>

Jain SK. 2008. Standard Operating Procedures (SOP) - Back bone of Pharmaceutical Industry, [Accessed 15 December 2010] Available from World Wide Web: http://www.pharmainfo.net

Jarvis N. 2009. Nuclear Technologies in Medicine and the Biosciences Initiative (NTemBI): Report on NTeMBI stakeholder workshops, May 2009. Pellindaba. NECSA

Kiondo P. 2010. The First African Radiopharmacy External Audit Mugalo Hospital, Kampala, Uganda 7th – 9th December 2009. World Journal of Nuclear Medicine. September 2010: 9(Suppl. 1):S77

Lazarus CR. 1999. Design of Hospital Radiopharmacy Laboratories. In: Sampson CB. Textbook of radiopharmacy: Theory and Practice. 3rd Ed. The Netherlands: Gordon and Breach; 1999. Pp51 - 58

Le Roux J. 2010. Personal communication. Registered Specialist Radiopharmacist (SA Pharmacy Council)

Norenburg, JP and Hladik III, WB. 2006. Fundamentals of Medical Radionuclides. In Beringer, P, DerMarderosian, A, Felton, L, Gelone, S, Gennaro, AR, Gupta, PK, Hoover, JE,

Popovick, NG, Reilly, Jr, WJ and Hendrickson, R. 2006. Remington: The Science and Practice of Pharmacy. 25th Ed. Philadelphia College of Pharmacy and Science: Lippincott Williams and Wilkins

Osman L. 2010. Personal communication. Vice President of the SA Pharmacy Council and Editor of the SA Pharmaceutical Journal.

Ponto, JA and Hung, JC. 2000. Nuclear Pharmacy, Part II: Nuclear Pharmacy Practice Today in Journal of Nuclear Medicine Technology. 2000; 28:76-81

Ramafi O. 2008. Personal communication. Acting Head of the Department of Nuclear Medicine. University of Limpopo (MEDUNSA Campus) and George Mukhari Hospital

Rubow SM. 2008. Personal communication. Professor; Department of Nuclear Medicine. University of Stellenbosch and Tygerberg Hopital

Saha GB. 2004. Chapter 9: Nuclear Pharmacy. In: Saha GB. Fundamentals of Nuclear Pharmacy. 5th Ed. New York: Springer.

Sabra, K. Chapter 27: Specialised Services. In: Winfield, A. J. Richards R. M. E. 2004. Pharmaceutical Practice. 3rd Ed. Edinburgh: Churchill Livingstone.

Sampson CB, Sharpe S. 1999. The role of the pharmacist as a member of the nuclear medicine team, and ethics, responsibility, standards of practice and audit. In: Sampson CB. Textbook of radiopharmacy: Theory and Practice. 3rd Ed. The Netherlands: Gordon and Breach; 1999. pp271-81

SAPC. 2008. Personal communication. Registration section. South African Pharmacy Council

SAPC. 2009. Intern and Tutor Manual for the Pre-Registration Experience of Pharmacist Interns: Community Pharmacy Interns, Hospital Pharmacy Interns and Academic Interns. Pretoria: South African Pharmacy Council

Sathekge M & Ellman A. 2010. Benchmarking Quality. World Journal of Nuclear Medicine. September 2010:9 (Suppl. 1):S1

Sathekge M. 2008. Personal communication. Professor and Head of the Department of Nuclear Medicine. University of Pretoria and Steve Biko Academic Hospital

Sharp PF, Gemmell HG & Murray AD. 2005. Practical Nuclear Medicine. 3rd Ed. Singapore: Springer-Verlag London Limited

Society of Nuclear Medicine. 2009. Advancing Molecular Imaging and Therapy. [Accessed 9th February 2009]. Available from World Wide Web: <http:interactive.snm.org/docs/whatisnucmed.pdf>

Tashakkori A and Teddlie C. 2003. Handbook of mixed methods in social and behavioral research. Sage Publications. [Accessed 9 October 2009]. Available on World Wide Web: <http://scholar.google.co.za>

Taylor P. (percyt@worldonline.co.za). (13 July 2003). *RE: Pretoria Academic Hospital.* E-mail to Loots M. (mloots@medic.up.ac.za)

United Kingdom Radiopharmacy Group. 2006. Radiopharmacy audit. [Accessed 2 February 2009]. Available from World Wide Web: <http://www.ukrg.org.uk/>

Wikipedia. 2009. Hot Cell. [Accessed 9th February 2009]. Available from World Wide Web: < en.wikipedia.org/wiki/Hot_cell>

Wiktionary. 2009. Hot Laboratory. [Accessed 9th February 2009]. Available from World Wide Web: <en.wiktionary.org/wiki/hot_laboratory>

Winfield, A. J. Richards R. M. E. 2004. Pharmaceutical Practice, 3rd Edition. Churchill Livingstone.

APPENDICES

Appendix 1: The IAEA IOG Audit Document

Staffing

This checklist is based on IAEA Guidance on Hospital Radiopharmacy - A safe and Effective Approach.

Please note: units operating at Operational Level 1 should complete the first checklist -Self Assessment for Operational Level 1.
However those units operating at Operational Level 2 should complete both checklists - Self Assessment for Operational Level 1 & Additional Self Assessment for Operational Level 2.

Self Assessment for Operational Level 1

No	Component	Class	Y/N	Verifiable – Manual, Reference documents, SOP, QC data, file record etc.	Comments/ Planned Action	Date achieved.
1.1	Is there a professional responsible for the radiopharmacy? Provide details.	A				
1.2	Is the radiopharmacy unit operated under the direction of a person with appropriate training as defined by local or national regulations?	A				
1.3	Are there written staff training manuals for all grades of staff?	B				

Additional Self Assessment for Operational Level 2

No	Component	Class	Y/N	Verifiable – Manual, Reference documents, SOP, QC data, file record etc.	Comments/ Planned Action	Date achieved.
2.1	Have all staff working at operational level 2 received specific staff training on the following:	A				
2.1a	Calibration of equipment- please provide details and training records	A				
2.1b	Working practices in the radiopharmacy - please provide details and training records	A				

2.1c	Preparation of individual doses - please provide details and training records	A				
2.1d	Quality control and analytical techniques - please provide details and training records	A				
2.1e	Dose release - please provide details and training details	A				
2.1f	Record keeping - please provide details and training records	A				
2.1g	Cleaning - please provide details and training records	A				
2.2	Is there a system for formal approvals of all documentations including radiopharmaceutical (RP) preparation, QC and formal release to patient?	B				
2.3	What training is provided to staff performing final checks on all products prepared before release for patient use?	A				
2.4	Are there training records for all staff performing cell labelling, e.g. RBC, WBC?	B				
2.5	Is there an annual performance review to check the competencies of radiopharmacy staff?	B				

Facilities

This checklist is based on IAEA Guidance on Hospital Radiopharmacy - A safe and Effective Approach.

Please note: units operating at Operational Level 1 should complete the first checklist -Self Assessment for Operational Level 1.
However those units operating at Operational Level 2 should complete both checklists - Self Assessment for Operational Level 1 & Additional Self Assessment for Operational Level 2.

Self Assessment for Operational Level 1

No	Component	Class	Y/N	Verifiable – Manual, Reference documents, SOP, QC data, file record etc.	Comments/ Planned Action	Date achieved.
1.4	Does the unit have appropriately finished rooms (including adequate lighting, appropriate finishes to walls, floors, ceilings and ventilation) and a shielded dispensing station?	A				
1.5	Is there a shielded dispensing station available?	A				
1.6 a	For operational level 1b is there a shielded dispensing station and/or a fume hood available? [Is there a fume cupboard with suitable filters for volatile radioactive materials such as 131I solutions?]	A				
1.6 b	[If only radioiodine capsules are handled is the package opened in a well ventilated area?]	A				
1.7	Is there a validated (annual check on air-flow, safety and challenge testing) fume hood with suitable filters for handling radioiodine solutions?	A				
1.8	Are there records and logs kept for all equipment irrespective of whether maintenance and calibration is performed 'in-house' or by external contractors?	B				

Additional Self Assessment for Operational Level 2

No	Component	Class	Y/N	Verifiable – Manual, Reference documents, SOP, QC data, file record etc.	Comments/ Planned Action	Date achieved.
2.6	For operational level 2: Are there regular checks on validated Class II type B microbiological safety cabinets located in a dedicated room?	A				
2.7	Are monometer readings of pressure differentials across HEPA filters recorded daily?	B				
2.8	Are there periodic records of air velocities determination for LAF cabinets or isolators?	B				
2.9	Is challenge testing of the HEPA filters in LAFs and isolators carried out annually?	B				
2. 10	For negative pressure isolators: Before preparation takes place, are gloves or gauntlets visually inspected and integrity tests carried out and recorded?	B				
2.11	Is there a system and record of planned preventative maintenance for all equipment in the radiopharmacy including the refrigerator?	B				

2.12	When clean rooms are used, are the over-pressures gauges monitored and recorded daily?	B			

Puchase of materials

This checklist is based on IAEA Guidance on Hospital Radiopharmacy - A safe and Effective Approach.

Please note: units operating at Operational Level 1 should complete the first checklist -Self Assessment for Operational Level 1.
However those units operating at Operational Level 2 should complete both checklists - Self Assessment for Operational Level 1 & Additional Self Assessment for Operational Level 2.

Self Assessment for Operational Level 1

No	Component	Class	Y/N	Verifiable – Manual, Reference documents, SOP, QC data, file record etc.	Comments/ Planned Action	Date achieved.
1.9	Are there suitable protocols and trained staff for the purchase of approved or Marketing Authorized radiopharmaceuticals?	A				
1. 10	Are all goods received checked and recorded against the order for correctness of delivery?	B				
1.11	Are records kept for batch numbers and quantities received?	B				
1.12	Are visual inspections and label checks carried out prior to acceptance?	B				

Additional Self Assessment for Operational Level 2

No	Component	Class	Y/N	Verifiable – Manual, Reference documents, SOP, QC data, file record etc.	Comments/ Planned Action	Date achieved.

2.13	Do all products, kits and generators have product approval, marketing authorisation, or bear a product licence number?	A				
2.14	How many unlicensed or unapproved products are used each year and is there a record of them?	A				
2.15	For all unlicensed kits, radiopharmaceuticals or radio-chemicals are the prescribers or responsible medical doctors made aware of his/her responsibilities?	A				
2.16	Do the suppliers or reagents and unapproved products provide a "Certificate of Analysis"?	B				

Dispensing protocols

This checklist is based on IAEA Guidance on Hospital Radiopharmacy - A safe and Effective Approach.

Please note: that units operating at Operational Level 1, using pre-prepared pharmaceutical products, should complete the first checklist- Self Assessment for Operational Level 1 & 2.
Units operating at Operational Level 2 and preparing own pharmaceuticals should also complete the checklist with regards to dispensing protocols - Self Assessment for Operational Level 1 & 2.

Self Assessment for Operational Level 1 & 2

No	Component	Class	Y/N	Verifiable – Manual, Reference documents, SOP, QC data, file record etc.	Comments/ Planned Action	Date achieved.
1.13	Are there specific written radiopharmacy procedures for dispensing operations undertaken in the radiopharmacy?	B				
1.14	Under operational level 1a: Are there written procedures for the aseptic dispensing and labelling of unit doses of ready-to-use radiopharmaceuticals?	B				
1.15	Is there a system for labels which assesses quality, number produced and number applied to dispensed doses?	A				

1.16	For operational level 1b: Do the written procedures contain clear safety and monitoring instruction for dispensing radioiodine solutions or capsules?	A				
1.17	Under operational level 1b are there written procedures for calibration assay, preparation and dispensing of individual patient radionuclide therapy?	A				
1.18	Can the audit and documentation for each RP batch be traced from the prescription to the actual administration of individual patient doses?	A				

Preparation Protocols

This checklist is based on IAEA Guidance on Hospital Radiopharmacy - A safe and Effective Approach.

All units operating at Operational Level 2 and preparing own pharmaceuticals must also complete the checklist below with regards to preparation protocols (Self Assessment for Operational Level 1 & 2).

Additional Self Assessment for Operational Level 2

No	Component	Class	Y/N	Verifiable – Manual, Reference documents, SOP, QC data, file record etc.	Comments/ Planned Action	Date achieved.
2.17	Are there written and approved procedures for the use of generators and reconstitution of each radiopharmaceutical kit used?	A				
2.18	Are SOPs independently reviewed and approved at specified intervals?	B				
2.19	Is the preparation of 99mTc radiopharmaceuticals from kits and generators carried out in a LAF cabinet?	A				
2. 20	Are there set criteria before release for preparation for patients use? Is this undertaken by the same operator or a different individual?	B				
2.21	Can each individual patient dose be traced to a specific generator and kit batch number?	A				

2.22	Under operational level 2b: Do the written procedures for any autologous preparation, e.g. red and white blood cells, include a clear instructions on safety, cleaning and decontamination?	A				
2.23	Are there written procedures for the preparation and dispensing of approved kit formulations of radio-labelled biological e.g. monoclonal antibodies, peptides?	A				

QA & QC

This checklist is based on IAEA Guidance on Hospital Radiopharmacy - A safe and Effective Approach.

Please note: units operating at Operational Level 1 should complete the first checklist -Self Assessment for Operational Level 1.
However those units operating at Operational Level 2 should complete both checklists - Self Assessment for Operational Level 1 & Additional Self Assessment for Operational Level 2.

Self Assessment for Operational Level 1

No	Component	Class	Y/N	Verifiable – Manual, Reference documents, SOP, QC data, file record etc.	Comments/ Planned Action	Date achieved.
1.19	Are daily QC checks performed on radionuclide calibrators?	A				
1. 20	What quality checks are undertaken on a supplier before purchase?	B				
1.21	Are periodic quality checks on radiopharmaceuticals (RP) performed?	B				
1.22	Is there a written procedure for dealing with product/s failing to meet the required standard?	B				
1.23	Is there a record of complaint/s and any associated follow-up and investigation?	B				
1.24	Are there written procedures and records for regular contamination surveys of the radiopharmacy unit?	A				

Additional Self Assessment for Operational Level 2

No	Component	Class	Y/N	Verifiable – Manual, Reference documents, SOP, QC data, file record etc.	Comments/ Planned Action	Date achieved.

2.24	For operational level 2 are there records for the following:	B				
2.24 a	Purchase of radioactive products and ingredients					
2.24 b	Generator elution, yield, [^{99}Mo] molybdenum breakthrough and aluminium ion breakthrough					
2.24 c	Product preparation, QC and release					
2.24 d	Environmental and microbiological monitoring					
2.24 e	Aseptic process, aseptic operator validation and trend analysis					
2.24 f	Laboratory cleaning and maintenance					
2.24 g	Equipment and plant calibration and maintenance					
2.24 h	Radioactive contamination monitoring and radioactive waste disposal					
2.24 i	Product defects and SOPs non-conformance, i.e. when a procedure is performed in a manner other than that described in the relevant SOP					
2.24 j	Independent inspection and audit					

2.25	In line with the IAEA "Operational guidance on Hospital Radiopharmacy" document, are there records of routine microbiological monitoring of the preparation area in the radiopharmacy?	**A**				
2.26	Are there calibration and linearity checks of the dose calibrator response over the complete range of activities measured at least annually?	A				
2.27	Is there set programme for checking the quality of radiopharmaceuticals (RP)?	**B**				
2.28	Considering patient safety, are certain simple checks performed on prepared radiopharmaceutical, e.g. mini-chromatography?	**A**				
2.29	For operational level 2 is a [^{99}Mo] Molybdenum breakthrough measurement performed on the first eluate from each [^{99m}Tc] Technetium generator and repeated when the generator is moved?	**A**				
2. 30	Is aluminium ion breakthrough checked on the first eluate from a [^{99m}Tc] Technetium generator?	A				
2.31	Are changes in the source of any kits, diluents or vehicle used, needles, syringes, swabs and sterile containers used within radiopharmacy recorded?	**B**				

2.32	On first use of a new batch or first new delivery of RP kits is radiochemical purity performed?	B				
2.33	Are rapid alternative methods employed for swift prospective QC for critical RP e.g. the determination of RCP for [^{99m}Tc] HMPAO)?	**A**				
2.34	Is there regular pH testing of RP carried out?	**B**				
2.35	Prior to release for patients is each individual radioactivity dose checked?	A				
2.36	Is there a record of the formal approval/release by an authorized person before a product is administered to a patient?	**A**				
2.37	Are there written procedures for the recall of defective products?	**A**				
2.38	Is there a record of complaints and any associated follow-up and investigation?	**B**				
2.39	Is there a system of recorded self-inspection and reports evaluation?	B				
2. 40	Is there a system for external audit or peer review process?	**B**				

Waste

This checklist is based on IAEA Guidance on Hospital Radiopharmacy - A safe and Effective Approach.

Please note: units operating at Operational Level 1 should complete the first checklist -Self Assessment for Operational Level 1.

Self Assessment for Operational Level 1

No	Component	Class	Y/N	Verifiable – Manual, Reference documents, SOP, QC data, file record etc.	Comments/ Planned Action	Date achieved.
1.25	Are there written procedures for the disposal of radioactive and non-active waste specific to the radiopharmacy?	A				
1.26	Is there a periodic review/audit of arrival, use and disposal of all radioactive materials?	A				
1.27	Are there written logs for each solid sources that indicate usage, transfer, disposal of solid sources?	A				

Audit Summary

This checklist is based on IAEA Guidance on Hospital Radiopharmacy - A safe and Effective Approach.

The audit summary below should be completed by all units in order to prioritise needs.
Critical priorities have the highest importance.
Major priorities are second to critical priorities however they should still be addressed in a timely manner
Minor priorities are areas which need addressing but do not require such urgent attention as the above two categories.

Critical priority

No:	Class	Comment/action	Time frame	Date achieved

Major priority

No:	Class	Comment/action	Time frame	Date achieved

Minor priority

No:	Class	Comment/action	Time frame	Date achieved

Appendix 2: Focus Group Discussion Outline

You are aware that we have been conducting a survey of the radiopharmacy at this hospital. Thank you to those of you who helped with this and thank you for agreeing to participate in this discussion. We would like to explore some aspects of work in the unit as part of this discussion.

1. Have you had any surveys or audits in the past year?

2. One of the aspects covered in this survey was quality standards/Standard Operating Procedures (SOPs). Could you name the quality standards that you have access to and use regularly?

3. Who develops these quality standards?

4. Which guidelines are these quality standards based on?

5. In your opinion, do you think there is room for improvement of the current guidelines?

6. How do you feel about the environment you work in? Are there any constraints to your job?

7. a) Would you have conducted this survey any differently?

7. b) How did you feel about this survey and the items covered? Are they achievable/ realistic?

8. What changes are needed for you to achieve the standards set out in the survey?

Appendix 3: Consent Form (Medunsa)

Statement concerning participation in a Research Project.

Quality Assurance of Radiopharmacy in Selected Gauteng Academic Hospitals

I have read the information and 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 understand that participation in this Project is completely voluntary and that I may withdraw from it at any time and without supplying reasons.

I know that this Project has been approved by the Medunsa Research and Ethics (MREC), University of Limpopo (Medunsa Campus). I am fully aware that the results of this results of this Project 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 Project.

....

Name of volunteer Signature of patient volunteer.

....

Place. Date. Witness

Statement by the Researcher

I provided verbal and/or written information regarding this Project

I agree to answer any future questions concerning the Project* as best as I am able.

I will adhere to the approved protocol.

....

Name of Researcher Signature Date Place

Appendix 4: Consent Form (University of Pretoria)

TITLE OF STUDY: Quality Assurance of Radiopharmacy in selected Gauteng Academic Hospitals

Dear Participant

1) INTRODUCTION

We invite you to participate in a research study. This information leaflet will help you to decide if you want to participate. Before you agree to take part you should fully understand what is involved. If you have any questions that this leaflet does not fully explain, please do not hesitate to ask the investigator

2) THE NATURE AND PURPOSE OF THIS STUDY

The aim of this study is to get an overview of what you felt about the survey which was conducted earlier on. You as a participant are a very important source of information on this survey

3) EXPLANATION OF PROCEDURES TO BE FOLLOWED

This study involves us asking you, as part of a group, a few questions about the survey. We will explore the experience you had about the survey and whether the survey met your expectations.

4) RISK AND DISCOMFORT INVOLVED

There are no risks in participating in the study. Some of the questions we are going to ask you may make you feel uncomfortable, but you need not answer them if you don't want to. The interview will take about 30 minutes of your time and will be recorded.

5) POSSIBLE BENEFITS OF THIS STUDY

Although you will not benefit directly from the study, the results of the study will enable us to make recommendations which might result in the improvement of the facility in future.

6) WHAT ARE YOUR RIGHTS AS A PARTICIPANT?

Your participation in this study is entirely voluntary. You can refuse to participate or stop at any time during the interview without giving any reason.

7) HAS THE STUDY RECEIVED ETHICAL APPROVAL?

This study has received written approval from the Research Ethics Committee of the Faculty of Health Sciences at the University of Pretoria and University of Limpopo (Medunsa Campus). Copies of the approval letters are available if you wish to have one.

8) INFORMATION AND CONTACT PERSON

The contact person for the study is Misa Qatyana. If you have any questions about the study please contact her at tel. 012 521 5058. Alternatively you may contact my supervisor Dr. Beverley Summers at Tel. 012 251 4673

9) COMPENSATION

Your participation is voluntary. No compensation will be given for your participation.

10) CONFIDENTIALITY

All information that you give will be kept strictly confidential. Once we have analysed the information no one will be able to identify you. Research reports and articles in scientific journals will not include any information that may identify you or your hospital.

CONSENT TO PARTICIPATE IN THIS STUDY

I confirm that the person asking my consent to take part in this study has told me about nature, process, risks, discomforts and benefits of the study. I have also received, read and understood the above written information (Information Leaflet and Informed Consent) regarding the study. I am aware that the results of the study, including personal details, will be anonymously processed into research reports. I am participating willingly. I have had time to ask questions and have no objection to participate in the study. I understand that there is no penalty should I wish to discontinue with the study and my withdrawal will not affect in any way. I have received a signed copy of this informed consent agreement.

Participant's name …….....(Please print)

Participant's signature: .....…… Date.....

Investigator’s name .....……...(Please print)

Investigator’s signature .....…… Date.….....

Witness's Name .....…….....(Please print)

Witness's signature .....…….. Date.….....

VERBAL INFORMED CONSENT

I, the undersigned, have read and have fully explained the participant information leaflet, which explains the nature, process, risks, discomforts and benefits of the study to the participant whom I have asked to participate in the study.. The participant indicates that s/he understands that the results of the study, including personal details regarding the interview will be anonymously processed into a research report. The participant indicates that s/he has had time to ask questions and has no objection to participate in the interview. S/he understands that there is no penalty should s/he wish to discontinue with the study and his/her withdrawal will not affect me in any way. I hereby certify that the client has agreed to participate in this study.

Participant's Name .....……...(Please print)

Person seeking consent .....…….....(Please print)

Signature .....…….....Date.....

Witness's name .....……..….....(Please print)

Signature .....……Date.….....

Appendix 5: Key Informant Interview Outline

You may be aware that we have been conducting a survey of the radiopharmacy at this hospital. Thank you for your help with this and thank you for agreeing to participate in this interview. We would like to explore some aspects of work in the radiopharmacy as part of this discussion.

1. What are your thoughts on the practice of radiopharmacy in South Africa?

2. Are you familiar with the South African Department of Radiation Control audit document?

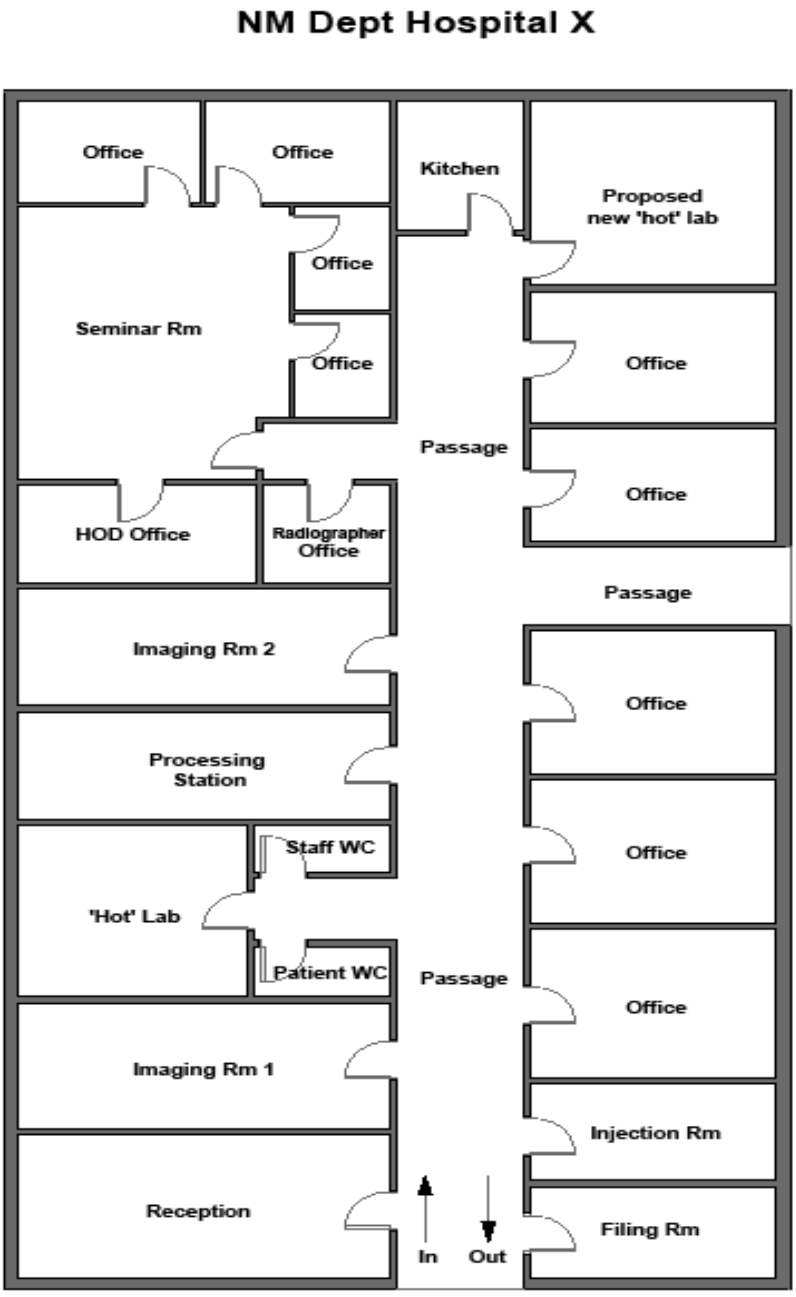
3. What international audit documents are you aware of?

4. How do you think the South African Department of Radiation Control audit document compares with international audit documents, in terms of scope?

5. How do you feel about the IAEA Operational Guidance on Hospital Radiopharmacy and the items covered? Are they practical and achievable in the South African setting?

6. What changes are needed for South African tertiary hospitals to achieve the standards set out in the IAEA Operational Guidance on Hospital Radiopharmacy?

Appendix 6: Hospital X Floor Plan



Appendix 7: Hospital Y Floor Plan