MICROBIAL CONTAMINATION AND LABELLING OF SELF-PREPARED, MULTI-DOSE PHENYLEPHRINE SOLUTIONS USED AT A TEACHING HOSPITAL

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of

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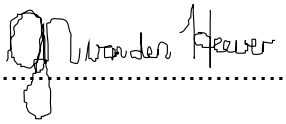
Declaration

I, Zacharias Andreas Neethling van den Heever, declare that this research report is my own work. It is being submitted for the degree of Master of Medicine in the branch of Anaesthesiology in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.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25th day of November, 2013

Dedication

To all the people who believed in me and supported me.

Abstract

Microbial contamination of multi-dose vials is one of the mechanisms by which transmission of pathogens to patients can occur in anaesthesia. Common practice at Chris Hani Baragwanath Academic Hospital (CHBAH) is to use boluses of a self-prepared, multi-dose phenylephrine solution (referred to as the solution) to treat hypotension, due to the vasodilatory effects of a spinal anaesthetic, in stable patients undergoing a caesarean section.

The aims of this study were to determine if there was microbial contamination of the solutions used at CHBAH and to evaluate if appropriate labelling and aspiration practices were adhered to with regard to the solutions.

A sample was collected and the labelling data was documented from the solutions found in the obsteric theatres at CHBAH over a period of three months. The samples were sent to a laboratory for microbial investigation.

Microbial contamination was identified in seven of 110 (6.36%) samples collected from the solutions. The name of the solution was indicated on all 110 (100%) containers and the concentration of the solution was indicated on 106 (96.36%) containers. The date the solution was prepared was indicated on 82 (74.55%) containers and the time the solution was prepared was indicated on 63 (57.27%) containers. Only nine (8.18%) of the healthcare workers that prepared the solutions confirmed it by placing a signature on the container. Labelling data was written directly on all 110 (100%) containers and a spike device was used in 71 (64.54%) containers.

This study demonstrated microbial contamination of the solutions and that safe injection practices were not adhered to when intravenous medications were prepared and administered. This is important at CHBAH since a large proportion of South African patients are immunocompromised and susceptible to opportunistic infections. Inappropriate labelling of medications is a cause of medication administration errors and this may have serious legal implications for the anaesthetist.

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Abbreviations and acronyms

APIC: Association for Professionals in Infection Control and Epidemiology

ASA: American Society of Anesthesiologists

***A. viscosus*:** *Actinomyces viscosus*

***B. anthracis*:** *Bacillus anthracis*

***B. cepacia*:** *Burkholderia cepacia*

***B. cereus*:** *Bacillus cereus*

***B. coagulans*:** *Bacillus coagulans*

BSI: Blood Stream Infection

***B. vesicularis*:** *Brevundimonas vesicularis*

***C. albicans*:** *Candida albicans*

CDC: Centres for Disease Control and Prevention

CHBAH: Chris Hani Baragwanath Academic Hospital

***C. parapsilosis*:** *Candida parapsilosis*

***E. aerogenes*:** *Enterobacter aerogenes*

***E. cloacae*:** *Enterobacter cloacae*

***E. dermatitidis*:** *Exophiala dermatitidis*

***E. gergoviae*:** *Enterobacter gergoviae*

***E. rostratum*:** *Exserohilum rostratum*

HBV: Hepatitis B Virus

HCV: Hepatitis C Virus

HIV: Human Immunodeficiency Virus

HPCSA: Health Professions Council of South Africa

ICU: Intensive Care Unit

KCl: Potassium Chloride

***K. oxytoca*:** *Klebsiella oxytoca*

***K. pneumoniae*:** *Klebsiella pneumoniae*

***M. antarcticus*:** *Micrococcus antarcticus*

***M. cohnii*:** *Micrococcus cohnii*

***M. endophyticus*:** *Micrococcus endophyticus*

***M. flavus*:** *Micrococcus flavus*

mg: Milligram

ml: Millilitre

***M. lactis*:** *Micrococcus lactis*

***M. luteus*:** *Micrococcus luteus*

***M. lylae*:** *Micrococcus lylae*

***M. niistensis*:** *Micrococcus niistensis*

***M. terreus*:** *Micrococcus terreus*

***M. yunnanensis*:** *Micrococcus yunnansis*

NHLS: National Health Laboratory Service

NICU: Neonatal Intensive Care Unit

***P. aeruginosa*:** *Pseudomonas aeriginosa*

***P. alcaligenes*:** *Pseudomonas alcaligenes*

***P. falciparum*:** *Plasmodium falciparum*

***P. fluorescens*:** *Pseudomonas fluorescens*

***P. maltophilia*:** *Pseudomonas maltophilia*

***P. putida*:** *Pseudomonas putida*

PVC: Polyvinyl Chloride

***R. pickettii*:** *Ralstonia pickettii*

SAJAA: South African Journal of Anaesthesia and Analgesia

SANC: South African Nursing Council

SASA: South African Society of Anaesthesiologists

***S. aureus*:** *Staphylococcus aureus*

***S. caprae*:** *Staphylococcus caprae*

***S. epidermidis*:** *Staphylococcus epidermidis*

***S. haemolyticus*:** *Staphylococcus haemolyticus*

***S. hominis*:** *Staphylococcus hominis*

***S. lugdunensis*:** *Staphylococcus lugdunensis*

***S. maltophilia*:** *Stenotrophomonas maltophilia*

***S. marcescens*:** *Serratia marcescens*

***S. pasteuri*:** *Staphylococcus pasteuri*

***S. paucimobilis*:** *Sphingomonas paucimobilis*

***S. saccharolyticus*:** *Staphylococcus saccharolyticus*

***S. salivarius*:** *Streptococcus salivarius*

***S. saprophyticus*:** *Staphylococcus saprophyticus*

***S. maltophilia*:** *Stenotrophomonas maltophilia*

***S. viridans*:** *Streptococcus viridans*

***S. warneri*:** *Staphylococcus warneri*

TH1: Theatre 1

TH2: Theatre 2

TPN: Total Parenteral Nutrition

UK: United Kingdom

USA: United States of America

UTI: Urinary Tract Infection

WHO: World Health Organisation

µg: Microgram

Chapter 1: Overview of the study

1.1 Introduction

In this chapter the background, problem statement, aims and objectives, research assumptions, demarcation of study field, ethical considerations, research methodology, significance, validity and reliability, and study outline will be discussed.

1.2 Background

Anaesthetists are responsible for the safe use of anaesthetic-associated drugs (1). They play an important role in preventing microbial contamination of the drugs they use and preventing nosocomial infections. Failure in this role has a negative impact on the patient and the healthcare system.

Recent studies have implicated anaesthetists in the transmission of pathogens to patients during regional (2, 3) and general (4, 5) anaesthesia. A significant number of anaesthetic-associated medication are contained in multi-dose vials (6). Microbial contamination of multi-dose vials (7-10) and anaesthetic equipment (11-14) are two of the main mechanisms by which patient-to-patient transmission of pathogens can occur in anaesthesia (15).

International guidelines on preventing contamination of anaesthetic-associated medication (16, 17) clearly state that preservative-free vials are single-patient, single-dose items. There is however evidence in the literature that single dose-vials can be used for multiple patients if safe injection practices and aseptic technique are adhered to (18). Uncontaminated multi-dose vials may be used until the manufacturer's expiration date only if aseptic technique is used consistently. Each time a multi-dose vial is entered, aseptic technique should be used, including cleaning the multi-dose vial septum with alcohol and using a sterile needle and syringe (16).

Despite the above guidelines current infection control practices of anaesthetists working in developed countries falls short of accepted recommendations (15, 19-21). A matter of particular concern is the infection risk associated with the use of single-dose vials for multiple patients (22-24) and the use of multi-dose vials (7-10). The infection risk is due to unsafe injection practices. Reasons for non-compliance with regard to basic infection control practices in anaesthesia include ignorance, convenience and economical considerations (25).

From the above it is clear that the use of single-dose vials for multiple patients and the use of multi-dose vials pose a risk for microbial contamination if safe injection practices are not adhered to. Most of the studies done on this subject focused on the anaesthetic community and their practices in developed countries.

A review of the local literature with regards to the use of multi-dose vials in anaesthesia yielded only one study done by Morgan (26) at Chris Hani Baragwanath Academic Hospital (CHBAH). Morgan investigated the microbial contamination of a hyperbaric bupivicaine and fentanyl multi-dose preparation used for administering spinal anaesthetics to patients undergoing caesarean section. The results of this study suggested that the use of this multi-dose preparation for spinal anaesthesia was safe. However, strict aseptic technique was used to prepare and administer the preparation and the bupivicaine used in the preparation has antimicrobial properties (27, 28). This might not reflect everyday practice where strict aseptic technique is not always adhered to (15, 19-21).

The correct labelling of medication in anaesthetic practice is a key element to safe medication administration (29). Inappropriate labelling of medication has been identified as a cause for medication administration errors in general (30, 31) and anaesthetic practice (32-34). Anaesthetists can be held legally accountable for medication administration errors and the administration of contaminated medication (35).

1.3 Problem statement

Common practice at CHBAH is to use boluses of a self-prepared phenylephrine solution (referred to as the solution) to treat hypotension, due to the vasodilatory effects of a spinal anaesthetic, in stable patients undergoing a caesarean section. This solution then acts as a multi-dose vial which is used for multiple patients.

The intravenous fluid vaculitres (normal-saline or Ringer's lactate) used to prepare this solution do not contain any bactericidal or bacteriostatic agents. There is no evidence in the literature or in the package information from the manufacturer that phenylephrine has any anti-bacterial activity.

It has been observed that this solution is often labelled incorrectly, used for more than 12 hours on multiple patients and strict aseptic technique is not always adhered to when using this solution as a multi-dose vial. This solution thus has the potential for microbial contamination.

Currently there is no formal protocol on the use of anaesthetic multi-dose vials in the South African literature or at the Anaesthetic Department at CHBAH.

1.4 Aims and objectives

1.4.1 Aims

The aims of this study were to:

- determine if there was microbial contamination of the solutions used at CHBAH
- evaluate if appropriate labelling and aspiration practices were adhered to with regard to the solutions.

1.4.2 Objectives

The objectives of this study were to:

- determine whether there was any microbial contamination of the solutions and to identify the contaminating microorganisms
- evaluate whether the name and concentration of the solutions were documented on the containers
- evaluate whether the date and time the solutions were prepared was documented on the containers
- evaluate whether the healthcare workers that prepared the solutions confirmed it by placing a signature on the containers
- evaluate the labelling method of the solutions (i.e. written directly on the container or label stuck on container)
- evaluate the aspiration method of the solutions (i.e. puncturing the rubber septum of the container with a needle or using a spike-device).

1.5 Research assumptions

The following definitions were used in this study:

Aseptic technique: Any healthcare procedure in which added precautions, such as use of sterile gloves and instruments, were used to prevent contamination of a person, object or area by microorganisms (36).

Disinfection: The process of destroying pathogenic organisms, or of rendering them inert, especially as applied to the treatment of inanimate materials to reduce or eliminate infectious organisms (37).

Healthcare worker: A healthcare worker refers to an individual that provides healthcare services to a patient . In this study the healthcare worker may be a medical docter or a nurse involved in the anaesthetic management of patients.

Infection control practices: Policies and procedures used to minimise the risk of spreading infections, especially in hospitals and health care facilities (36).

Labelling data: In this study it refers to the labelling information contained on the solution containers which included the name and concentration of the solution, the date and time the solution was prepared, the signature of the person who prepared the solution, the labelling method of the solution and the method of aspirating the solution from the container.

Microbial contamination: Inclusion of microorganisms in or on an item used in the medical care of patients. In this study microbial contamination was considered as the presence of aerobic bacteria in the solutions.

Microorganism: An organism that is microscopic or submicroscopic and cannot be seen by the naked eye. Examples of microorganisms include bacteria, viruses, fungi and protozoa (37).

Multi-dose vial: In this study a multi-dose vial was considered as any kind of medication container that was used more than once and was kept for potential reuse (10).

Multi-dose vial septum: This refers to the rubber stopper used to close the opening of a multi-dose vial and prevent macro-contamination of the vial. The rubber stopper can be penetrated with a needle multiple times.

Pathogen: Any disease-causing microorganism (37).

Safe injection practices: Injection procedures that aim to maintain basic levels of patient safety and provider protection (38). A safe injection does not harm the recipient, does not expose the provider to any avoidable risks and does not result in waste that is dangerous for the community (39).

Spike-device: A device, for example a needle or an intravenous catheter, left in the multi-dose vial septum to facilitate aspiration of medication.

The solution: This is a solution prepared by adding 1 ml of phenylephrine (10 mg/ml) to 199 ml of fluid (normal saline or Ringer's lactate) to produce a phenylephrine solution (50 µg/ml). Boluses of this self-prepared, multi-dose phenylephrine solution are used to treat hypotension, due to the vasodilatory effects of a spinal anaesthetic, in stable patients undergoing a caesarean section. This solution then acts as a multi-dose vial which is used for multiple patients.

1.6 Demarcation of study field

This study was conducted in the two identical obstetric operating theatres at CHBAH (theatre 1 and theatre 2). This hospital is the second largest hospital in the world and occupies 0.70 km² with 3 200 beds and 6 760 staff members (40). It is located in the Soweto area of Johannesburg and it is one of the teaching hospitals for the University of the Witwatersrand. A total of 150 - 180 caesarean sections are performed per week in the obstetric operating theatres (41).

1.7 Ethical considerations

This study was a laboratory-based microbiological and checklist-based study concerning the solutions. No patients or healthcare workers were directly involved in the study. Care was taken to prevent identification of patients who received boluses of the solutions and healthcare workers who prepared and administered these solutions.

Ethics clearance was obtained from the Human Research Ethics Committee (Medical), University of the Witwatersrand (Appendix 1). Approval for the conduction of this study was obtained from the Postgraduate Office, Faculty of Health Sciences, University of the Witwatersrand (Appendix 2). Permission to conduct this study at CHBAH was obtained from the Medical Advisory Committee of CHBAH (Appendix 3). Verbal consent to

conduct this study was obtained from the Head of the Department of Anaesthesiology and the theatre matron of the obstetric operating theatres at CHBAH. This study was conducted in accordance with the Declaration of Helsinki (42) and the South African Good Clinical Practice Guidelines (43).

1.8 Research methodology

1.8.1 Research design

A prospective, descriptive research design was used for this study.

1.8.2 Study population

The study population was the solutions used to treat hypotension, due to the vasodilatory effects of a spinal anaesthetic, in stable patients undergoing a caesarean section, found in the two identical obstetric theatres at CHBAH (theatre 1 and theatre 2)

1.8.3 Study sample

Sample size

Due to financial constraints the sample size of this study was limited to 110 samples.

Sampling method

A convenience sampling method was used for this study.

Inclusion and exclusion criteria

Inclusion criteria for this study were:

- the solutions found in the obstetric theatres at CHBAH.

Exclusion criteria for this study were:

- the solutions with < 10 ml of solution left in the container
- any breach in the aseptic technique used during the collection and transportation of samples by the data collector.

1.8.4 Data collection

Data collected

The following data was collected:

- microbial contamination of the solutions
- microorganisms isolated from the solutions
- name and concentration of the solutions as documented on the containers
- date and time the solutions was prepared as documented on the containers
- if the healthcare workers that prepared the solutions confirmed it by signature on the containers
- type of labelling method used on the solution containers (i.e. written directly on the container or label stuck on container)
- method used to aspirate the solutions (i.e. puncturing the rubber septum of the container with a needle or using a spike-device).

Data collection process

Samples of the solutions were collected, labelled, stored and transported in an aseptic manner. Microbiological investigation of the samples was done by qualified laboratory

personnel using standard microbiological laboratory equipment and procedures. The labelling of the solutions was evaluated using a predetermined checklist.

Data collector

All of the data was collected by the researcher.

Data collection period

Data were collected over a three month period, from October to December 2012.

1.8.5 Data analysis

Data capturing was done using an Excel 2007 spreadsheet (Appendix 3). Descriptive and inferential statistics were used to analyse the data. Statistical analysis was performed using GraphPad InStat, a statistics programme. A p-value of < 0.05 was considered as statistically significant.

1.9 Significance of the study

Patient safety is a global healthcare issue affecting countries at all levels of development. Healthcare-associated infections and adverse events due to medication errors are common causes of preventable harm to patients (44).

The World Health Organisation (WHO) Patient Safety programme identified research as a priority for patient safety (44). An international expert working group set up by the WHO Patient Safety programme produced a list of 50 global research priorities (45). Healthcare-associated infections and safe injection practices are among the top research priority areas (45).

The Helsinki Declaration on Patient Safety in Anaesthesiology has identified syringe labelling and infection control as part of their aims for improving patient safety in Europe (46).

An audit of infection control practices at Charlotte Maxeke Johannesburg Academic Hospital theatres during 2011, identified breaches in anaesthetic infection control practices as a potential source of nosocomial infections (47, 48). Recommendations to improve anaesthetic infection control practices included the adequate labelling of medications and to avoid using multi-dose vials.

It was of importance to investigate whether safe injection practices were adhered to when intravenous medications were prepared and administered. Unsafe injection practices expose patients to potentially harmful microorganisms. It is especially important at CHBAH since a large proportion of South African patients are immunocompromised and susceptible to opportunistic infections (49).

If the results of this study demonstrated that there was microbial contamination of these solutions and that correct labelling practices were not adhered to, it would serve as motivation to change the current practice regarding the use of multi-dose medications in the operating theatres at CHBAH.

1.10 Validity and reliability of the study

The researcher collected, labelled, stored and transported all the samples in an aseptic manner.

All the specimens were analysed at the Infection Control Services Laboratory, Department of Clinical Microbiology and Infectious Diseases, Witwatersrand School of Pathology, University of the Witwatersrand. The processing of the samples and identification of the microorganisms were done by qualified laboratory personnel using standard microbiological laboratory equipment and procedures.

A predetermined checklist was used to collect the labelling information from all of the solution containers.

1.11 Study outline

The chapters in this study include:

- Chapter 1: Overview of the study
- Chapter 2: Literature review
- Chapter 3: Research methodology
- Chapter 4: Results and discussion
- Chapter 5: Study summary, limitations, recommendations and conclusion

1.12 Conclusion

In this chapter the background, problem statement, aims and objectives, research assumptions, demarcation of study field, ethical considerations, research methodology, significance, validity and reliability, and study outline were discussed. The next chapter, chapter 2, will provide a review of the literature.

Chapter 2: Literature review

2.1 Introduction

In this chapter the literature concerning patient safety, anaesthetic infection control practices relating to the use of multi-dose vials, the microbial contamination of multi-dose vials as a mechanism for nosocomial infections, types of multi-dose vials implicated in microbial contamination, microorganisms cultured from contaminated multi-dose vials, the safe use of multi-dose vials, medication administration errors relating to the use of multi-dose vials and the labelling of medication will be discussed.

2.2 Patient safety

2.2.1 General

According to the WHO, tens of millions of patients suffer disabling injuries or death each year due to unsafe medical practices and care (44). Nearly one in ten patients are harmed while receiving healthcare in well-funded and technologically advanced hospital settings. There is however little evidence about the burden of unsafe medical practices and care in developing countries (44).

2.2.2 The National Core Standards for health establishments in South Africa

The National Health Act, 61 of 2003 (50) emphasises the need to foster good quality health services by developing structures to monitor the compliance of health establishments with health care standards. The Office of Standards Compliance developed the National Core Standards for Health Establishments in South Africa (51), which assists in the monitoring of service delivery.

The National Core Standards has identified patient safety as an area where quality or safety might be at risk. Patient safety ensures quality nursing and clinical care, reduce

unintended harm to patients, prevent or manage adverse events which include healthcare associated infections, and support any affected patients or staff.

Infection prevention and control programmes has been identified as key components to reduce healthcare associated infections. It is recommended by the National Core Standards that formal surveillance and reporting systems should be in place to aid this process.

2.2.3 The WHO patient safety programme

In 2004 the WHO launched a patient safety programme (WHO Patient Safety) in response to a World Health Assembly Resolution urging the WHO and member states to prioritize the problem of patient safety and to emphasise that it is a global healthcare issue. The WHO Patient Safety programme aims to coordinate, disseminate and accelerate improvements of patient safety worldwide (44).

The WHO Patient Safety programme identified research as a priority for patient safety. Research concerning patient safety enables an understanding of why adverse events occur, how and to what extent patients are harmed and how to reduce patient harm (44).

2.2.4 Global research priorities

An international expert working group set up by the WHO Patient Safety produced a list of 50 global research priorities (45). These priorities identified areas of knowledge gaps and where knowledge would greatly improve patient safety and reduce harm. Healthcare-associated infections and safe injection practices are among the top six research priority areas in developing countries (45).

A global patient safety campaign launched by the WHO, Clean Care is Safer Care, aims to acknowledge infection control as a solid and essential basis towards patient safety. This campaign supports the reduction of healthcare-associated infections and their consequences (52).

2.3 Anaesthetic infection control practices relating to the use of multi-dose vials

2.3.1 General

The guidelines of the South African Society of Anaesthesiologists (SASA) on the duties of an anaesthetist stipulates that an anaesthetist should take responsibility for the safe use of anaesthetic-associated drugs (1).

Numerous studies investigating the infection control practices of anaesthetists working in developed countries have been done (15, 19-21). Of concern are the hygienic practices of anaesthetists relating to the use of multi-dose vials. This includes hand washing, wearing of gloves, disinfection of anaesthesia working surfaces, re-use of syringes for more than one patient and the disinfection of the multi-dose vial septum. These infection control practices will be briefly discussed with the focus on the use of multi-dose vials.

2.3.2 Hand washing

Hand washing after each patient prevents the contamination of medication and injection equipment (53, 54). No local data is available regarding the hand washing practices of South African anaesthetist.

A survey done by Tait et al (19) investigating the infection control practices of 493 anaesthetists in the United States of America (USA) showed that 95.2% of anaesthetists washed their hands after exposure to Human Immunodeficiency Virus (HIV) positive patients. Following exposure to patients' body fluids, 97.5% washed their hands. Only 58% however admitted to always washing their hands after exposure to low risk patients. A national survey undertaken by Ryan et al (15) describing the current infection control practices relating to 272 New Zealand anaesthetists showed that 5.2% rarely and 1.1% never washed their hands between patients. Mikatti et al (21) did a survey of the hygienic practices of 145 consultant anaesthetists in the North-West region of the United Kingdom (UK). It was found that 14.7% of anaesthetic consultants rarely and 1.4% never washed their hands between patients.

2.3.3 Wearing of gloves

The WHO guidelines advocate the use of gloves to reduce microbial contamination of healthcare equipment and medication as well as preventing patient-to-patient transmission of infections (55). Tait et al (19) showed that in the USA only 49.4% of anaesthetists always and 36.9% frequently used gloves during the administration of anaesthesia. The survey conducted by Ryan et al (15) in New Zealand showed that 30.5% of anaesthetists always and 53.7% frequently wear gloves. It was found however that only 57.1% of New Zealand anaesthetists always and 38.7% rarely changed their gloves if they became contaminated. Mikatti et al's (21) survey of consultant anaesthetists in the UK showed that only 14.5% always and 42.1% rarely used gloves.

2.3.4 Disinfection of anaesthesia working surfaces

The Association for Professionals in Infection Control and Epidemiology (APIC) position paper on safe injection, infusion, and medication vial practices in healthcare (56) recommends that medications should be stored and prepared in a clean area and on a clean surface. Hall (57) demonstrated that there is blood contamination of anaesthesia equipment and monitoring equipment in clinical use in operating theatres. This includes the anaesthesia machine table and the anaesthesia cart table, the main areas where anaesthetists prepare medication. Tait et al (19) found that of the respondents from their survey in the USA, 40.4% rarely and 20.1% never disinfected their anaesthesia working surfaces. This is similar to what Mikatti et al (21) found in their survey of anaesthetic consultants in the UK where 33.1% of respondents rarely and 18.7% never disinfected their anaesthesia working surfaces.

2.3.5 Re-use of syringes for more than one patient

According to the American Society of Anesthesiologists (ASA) Committee on Occupational Health Task Force on Infection Control a total of 33 outbreaks of patient-to-patient transmission of Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) were reported between June 1998 and June 2008 (16). The re-use of syringes and

contamination of medications and flush solutions were found to be the primary cause (16). A disturbing finding by Tait et al (19) was the percentage of anaesthetists in the USA who re-used syringes for more than one patient. In private practice 28% of anaesthetists and 7.3% of anaesthetists in university practice reported frequently or always re-using syringes for more than one patient. Mikatti et al (21) found that 6.9% of anaesthetic consultants in the UK re-used syringes for more than one patient.

2.3.6 Disinfection of the multi-dose vial septum

The APIC position paper (56) also recommends that the septum of multi-dose vials should be cleaned with an alcohol swab or other approved antiseptic swab. The septum of the multi-dose vial should be allowed to dry before inserting a sterile needle into the vial. Tait et al (19) showed that of the anaesthetists in the USA participating in their survey, 26.6% rarely and 7.8% never disinfected the septum of multi-dose vials. Similar results were shown in the survey by Mikatti et al (21). Among consultant anaesthetists in the UK 17.5% never and 21.2% rarely disinfected the septum of multi-dose vials. Ryan et al (15) showed that 54.4% of respondents in their study in New Zealand never disinfected the septum of multi-dose vials.

2.4 Microbial contamination of multi-dose vials as a mechanism for nosocomial infections

2.4.1 General

The use of multi-dose vials in the healthcare setting is controversial. Presently there are conflicting results reported in the literature. Numerous case reports (23, 58, 59) and studies (8, 10) have implicated the use of single-dose vials for multiple patients and multi-dose vials in nosocomial infections. Recent studies investigating safe injection and medication vial usage showed that single-dose vials used for multiple patients and multi-dose vials are safe and without infection risk if safe infection control practices are adhered to (18, 60-62). The contamination rates of multi-dose vials in the literature are

inconsistent, and range from 0% to 27% (63). The differences in these contamination rates of multi-dose vials might partly be due to methodological differences and the types of medications collected (10).

2.4.2 Contamination of multi-dose vials in general practice

Multi-dose vials have been implicated as the source of infection in multiple outbreaks of nosocomial infections locally and internationally.

In May 2005 an outbreak of *Klebsiella pneumoniae* (*K. pneumoniae*) infections in a neonatal unit of a regional hospital in KwaZulu-Natal, South Africa, was attributed to contamminated intravenous glucose preparations (64). The blood cultures of 26 neonates infected with *K. pneumoniae* remained positive despite the administration of appropriate antibiotics. The possible causes for the persistently positive blood cultures were investigated and the organism was found in intravenous glucose preparations being used. Unopened vials of these preparations were sterile. On enquiry the staff volunteered that they had used these preparations for multiple dosing despite the fact that the instructions on the label of the vials advise to the contrary.

An outbreak of *Staphylococcus aureus* (*S. aureus*) joint and soft-tissue infections at a hospital in Tennessee, USA, in August 2001 was associated with injections from a multi-dose lidocaine vial (65). A physician performed intra-articular and soft-tissue injections on 17 patients and five were subsequently hospitalised for infections at the injection site. *S. aureus* was isolated from four of the patients. From the ten patients injected with lidocaine and triamcinolone, five developed infections compared with none of the seven patients injected with triamcinolone only. A multi-dose vial of lidocaine was most likely the source for the transmission of infection in this outbreak. *S. aureus* was however not isolated from the multi-dose lidocaine vial as the vial was unavailable for testing.

In 2008 an outbreak of *K. pneumoniae* and *Enterobacter aerogenes* (*E. aerogenes*) were reported at an outpatient pain management facility in New York, USA (23). Four confirmed patients were identified. Of the four patients, three had positive blood cultures

for *K. pneumoniae* and one patient had a positive blood culture for *E. aerogenes*. All confirmed patients had a sacro-iliac joint steroid injection procedure and one confirmed patient also had a greater trochanter bursa steroid injection procedure. Medications used for pain management procedures in these patients included a single-dose vial of bupivicaine (0.25% and 0.5%), triamcinolone and a contrast dye (iodixanol). The opened 100 ml vial of iodixanol was found to be contaminated with *E. aerogenes*.

Mattner et al (10) did a prevalence study of the bacterial contamination of multi-dose vials at a 1 300-bed tertiary hospital in Hannover, Germany, in 2001. Multi-dose vials were defined as all opened containers that had been used at least once and kept for potential re-use. On a specific day, infection control nurses collected all the opened vials from every ward. Data recorded for each vial included the type of medication, labelling, storage temperature, location and date of opening. Each vial was also tested for microbial contamination. A total of 227 multi-dose vials were collected from 47 wards. Two vials containing a saline solution cultured *Staphylococcus epidermidis* (*S. epidermidis*). This resulted in a contamination prevalence of 0.9% for the multi-dose vials.

Motamedifar et al (7) investigated the prevalence of multi-dose vial contamination by aerobic bacteria in a teaching hospital in Iran in 2006. Multi-dose vials were defined as all opened vials that were used more than once. Infection control nurses collected all multi-dose vials daily from each ward over a four-month period. Data recorded for each vial included drug type, location, opening date, storage conditions and expiration date. Each vial was also tested for microbial contamination. A total of 637 multi-dose vials were collected from 36 wards. Bacterial contamination was identified in 36 of the multi-dose vials. Bacteria cultured from the multi-dose vials included *Pseudomonas maltophilia* (*P. maltophilia*), which is now known as *Stenotrophomonas maltophilia* (*S. maltophilia*)*, Bacillus coagulans* (*B. coagulans*)*, S. epidermidus, α* and *β* haemolytic streptococci*, Actinomyces viscosus* (*A. viscosus*)*, Acinetobacter species, Streptococcus viridans* (*S. viridans*)*, Micrococcus species* and *Serratia marcescens* (*S. marcescens*). This resulted in a contamination prevalence of 5.6% for the multi-dose vials which is considerably higher than what was found in the study of Mattner et al (10).

2.4.3 Contamination of multi-dose vials in anaesthetic practice

Multiple case reports of nosocomial infections due to the microbial contamination of multi-dose vials have been reported in regional (2, 3) and general anaesthesia (4, 66-68).

A review on nosocomial infections and infection control in regional anaesthesia by Schulz-Stübner et al (2) identified the use of contaminated multi-dose vials in the practice of regional anaesthesia as one of the mechanisms of nosocomial infection. A case report by Halaby et al (3) discussing a fatal bacterial meningitis after spinal anaesthesia implicated non-adherence to adequate aseptic precautions during neuraxial anaesthesia as an important factor in the development of iatrogenic bacterial meningitis.

The use of intravenous induction agents and analgesic agents as multi-dose vials for general anaesthesia have been implicated in the patient-to-patient transmission of infections. The induction agent propofol in particular has been identified as the source of contamination in numerous case reports (66-69). Propofol is a lipid containing emulsion with no preservatives and is therefore at high risk of microbial contamination (68). Kuehnert et al (67) reported a *S. aureus* bloodstream infection outbreak amongst psychiatric patients undergoing Electro-Convulsive Therapy at a hospital in Mississippi, USA, due to bacterial contamination of propofol. Out of the nine patients who received Electro-Convulsive Therapy on a specific day, five developed *S. aureus* bloodstream infections as diagnosed on blood cultures. On the epidemic day a 100 ml vial of propofol was used for multiple patients. The propofol vial in question was unavailable for microbiological testing. It was suggested that breaks in infection control, such as the multi-dosing of propofol from a single vial, led to the outbreak.

Tallis et al (70) reported two cases of patient-to-patient transmission of HCV through a contaminated multi-dose fentanyl vial in Victoria, Australia in 2002. In the first case a patient became infected with HCV after a general anaesthetic for an arthroscopy. It was discovered that the preceding patient on the list was an intravenous drug abuser and had HCV infection. The same vial of propofol and fentanyl was used for both patients. Contamination of either the propofol or the fentanyl led to cross-infection of the second

patient. In the second case two patients were infected with HCV after neurolept-anaesthesia for a colonoscopy and gastroscopy respectively. The patient preceding the two newly infected patients was an intravenous drug abuser and it was found that he had HCV infection. A single 20 ml (1000 µg) vial of fentanyl was used for the entire endoscopy list. Contamination of the fentanyl vial with HCV led to the infection of the two patients.

2.5 Types of multi-dose vials implicated in microbial contamination

2.5.1 General

Multi-dose vials have a high risk of contamination due to the use of poor aseptic technique (9, 10, 19). Although some multi-dose vials contain preservatives, it must be noted that preservatives does not always prevent the growth of microorganisms (9, 71). Contaminated multi-dose vials have been implicated in the outbreak of nosocomial infections and the contamination of multi-dose vials in the hospital setting has been the subject of numerous prevalence studies.

2.5.2 Outbreaks associated with specific multi-dose vials

Contaminated multi-dose vials have been identified as the source of nosocomial infections in numerous outbreaks. Table 2.1 gives a comprehensive overview of the multi-dose vials implicated in outbreaks of nosocomial infections form 2000 to 2011. The table was compiled from data found at www.outbreak-database.com and www.pubmed.gov . These databases were searched for articles and case reports where multi-dose medication vials were the source of nosocomial infections. Medications most often involved in outbreaks include fentanyl (4, 70, 72, 73), heparin (74-78), heparin-saline solutions (58, 79-83), propofol (69, 84-86) and saline (22, 87-92). Relevant reports and case studies will be discussed shortly and are highlighted in Table 2.1.

Contaminated vials of fentanyl have been implicated in at least four outbreaks of nosocomial infections. Germain et al (4) reported the patient-to-patient transmission of HCV through the use of multi-dose vials during general anaesthesia at a private surgical clinic in Western France in 2001. A multi-dose fentanyl vial became contaminated after a general anaesthetic to a patient with unknown HCV infection, most likely contracted from getting a tattoo. The same syringe and needle used on the infected source-patient was used to aspirate fentanyl from two different vials. The second contaminated vial was subsequently re-used for three other patients. The contamination could be explained by different factors including repeated aspirations and injections of materials from a common vial, sharing of the same anaesthetic vial among different patients, possible blood reflux in the catheter line, and presence of an infected source-patient at the onset of surgery.

Although multi-dose vials of heparin contain preservatives, it has been implicated as the source of infection in numerous outbreaks of nosocomial infections. Yang et al (75) reported the outbreak of *Burkholderia cepacia* (*B. cepacia*) in a Taiwan hospital in 2007. A contaminated multi-dose vial of heparin, used to prepare a heparin-saline solution in a 20 ml syringe that was used as a flush for central venous catheters, was identified as the source of the nosocomial infection.

The use of a heparin-saline solution as a flush to maintain patency of intravenous catheters is controversial and it is still common practice in some institutions (93, 94). Heparin-saline solutions have also been implicated in nosocomial infections. Prospero et al (79) described the outbreak of *Pseudomonas aeruginosa* (*P. aeruginosa*) catheter-related bloodstream infections in a teaching hospital in Ancona, Italy, in 2004. It was found that the source of the infection was the heparin-saline solution that was used to flush intravenous catheters. This solution was prepared by adding 1 ml of heparin from a vial to 100 ml of saline solution by nursing personnel and was then commonly used as a flush for three to five days until it was finished.

Propofol is a lipid containing emulsion that contains sodium metabisulfate, which is bacteriostatic, but not bacteriocidal. Propofol can still support the growth of

microorganisms as it is not an antimicrobially preserved product under the United States Pharmacopeial standards (68, 95). The use of contaminated propofol has been implicated in the outbreak of nosocomial infections. Muller et al (69) reported the outbreak of *K. pneumoniae* and *S. marcescens* bloodstream infections due to the use of contaminated propofol at a hospital in Rotterdam, Netherlands, in 2008. It was found that lapses in the aseptic preparation, handling and storage of the propofol led to its contamination.

The use of saline solutions has been implicated in numerous outbreaks of nosocomial infections. Greeley et al (22) reported the outbreak of HBV infection at a haematology-oncology practice in New Jersey, USA, in 2009. It was found that a single vaculitre of saline was used as a flush for multiple patients and that it was the most likely source of contamination. Krause et al (89) reported the outbreak of HCV at a hospital in Florida, USA, in 1999. The results of this epidemiologic investigation suggested that a multi-dose saline vial, which might have been contaminated with the blood from another patient, was the source of the outbreak. Yu et al (92) documented the outbreak of nosocomial *Enterobacter cloacae* (*E. cloacae*) in a Neonatal Intensive Care Unit (NICU) in Taiwan, China, in 1997. Although there were multiple modes of transmission, a bottle of contaminated saline was identified as the initial source.

Table 2.1 Multi-dose vials implicated in nosocomial infections 2000 to 2011

Multi-dose vial	Pathogen	Infection	Patients	Death	Evidence for relatedness	Year, reference
Betamethasone	*S.marcescens*	Meningitis Spinal abcess Joint or bursa	5 5 1	3	Microbiologic	2006(96)
Bupivicaine (spinal)	*S.salivarius*	Meningitis	1	1	Epidemiologic	2006(3)
Dextrose- saline solution	*E.gergoviae*	BSI	11		Molecular biological	2003(97)
Distilled water	*Pseudomonas spp*	Endopthalmitis	17		Epidemiologic	2006(98)
Fentanyl	*S.paucimobilis*	BSI	6		Microbiologic	2009(72)
Fentanyl	*S.marcescens* *E.cloacae*	BSI	26		Molecular biological	2002(73)
Fentanyl	HCV	Hepatitis C	2		Epidemiologic	2002(70)
Fentanyl	HCV	Hepatitis C	4		Epidemiologic, molecular biological	2001(4)
Glucose preparation	*K.pneumoniae*	BSI	26	22	Microbiologic	2005(64)
Heparin*	*P.putida* *S.maltophilia*	BSI	32		Microbiologic	2008(74)
Heparin*	*B.cepacia*	BSI UTI	9 2		Microbiologic	2008(75)
Heparin*	HCV	Hepatitis C	18		Epidemiologic	2005(76)
Heparin*	*R.pickettii*	BSI	9		Molecular biological	2003(77)
Heparin*	*P.falciparum*	Malaria	1		Epidemiologic	2000(78)
Heparin-saline solution	*P.aeruginosa*	BSI	4		Microbiologic	2006(79)
Heparin-saline solution	*P.putida*	BSI	2		Molecular biological	2005(80)
Heparin-saline solution	*R.pickettii*	BSI	19		Epidemiologic, molecular biological	2005(81)
Heparin-saline solution	*P.fluorescens*	BSI	36		Epidemiologic, molecular biological	2005(58)
Heparin-saline solution	*S.marcescens*	BSI	12	7	Epidemiologic	2002(82)
Heparin-saline solution	HCV	Hepatitis C	11		Epidemiologic, molecular biological	2002(83)
Insulin*	*S.marcescens*	BSI	8	7	Epidemiologic, molecular biological	2004(99)
Iodixanol	*K.pneumoniae* *E.aerogenes*	BSI BSI	3 1		Microbiologic, molecular biological	2008(23)
Iohexol	*S.marcescens*	BSI	5		Epidemiologic	2005(24)
Lidocaine*	*S.aureus*	Joint	5	1	Epidemiologic, molecular biological	2003(65)

Methylprednisolone	*E. rostratum*	Meningitis	22	8	Microbiologic	2011(100)
Methylprednisolone	*E.dermatitidis*	Meningitits Joint	4 1	1	Epidemiologic, molecular biological	2003(101)
Propofol	*K.pneumoniae* *S.marcescens*	BSI	7	0	Microbiologic	2010(69)
Propofol	*E.cloacae*	BSI	4	2	Epidemiologic, molecular biological	2002(84)
Propofol	HCV	Hepatitis C	2		Epidemiologic	2002(70)
Propofol	*S.marcescens*	BSI Wound infection	5 2	2	Molecular biological	2001(85)
Propofol	HCV	Hepatitis C	5		Epidemiologic, molecular biological	2001(86)
Saline	HBV	Hepatitis B	21		Epidemiologic, molecular biological	2009(22)
Saline	HCV	Hepatitis C	16	2	Epidemiologic	2006(87)
Saline	*K.oxytoca*	BSI	3		Epidemiologic, molecular biological	2004(88)
Saline	HCV	Hepatitis C	5		Epidemiologic, molecular biological	2003(89)
Saline	HCV	Hepatitis C	17		Epidemiological, molecular biological	2003(90)
Saline	HCV	Hepatitis C	2		Molecular biological	2002(91)
Saline	HCV	Hepatitis C	95		Epidemiological, molecular biological	2001(102)
Saline	*E.cloacae*	BSI Meningitits	19 4	3 4	Epidemiologic, molecular biological	2000(92)
Saline	HBV	Hepatitis B	30		Molecular biological	2000(103)
TPN	*C.albicans*	BSI	8		Molecular biological	2006(104)

BSI- Blood Stream Infction; HCV- Hepatitis C Virus; UTI- Urinary Tract Infection; HBV- Hepatitis B Virus; TPN- Total Parenteral Nutrition

* Vial contains preservative

Sources: www.outbreabreak-database.com, Mattner et al (10)

2.5.3 Specific multi-dose vials contaminated in hospitals

The study done by Mattner et al (10) investigating the bacterial contamination of multi-dose vials in a tertiary hospital in Hannover, Germany, showed a contamination prevalence of 0.9%. Of the 227 multi-dose vials collected, 77 vials contained saline solution, 41 vials contained heparin, 16 vials contained glucose, 16 vials contained sterile water for injection, 32 vials contained insulin and 45 vials contained miscellaneous medications (catecholamines, atropine, antibiotics, midazolam, furosemide, potassium chloride, iopromide and some others). About 50% of all the multi-dose vials contained no preservatives. From two vials containing a saline solution, *S. epidermidis* was cultured.

Motamedifar et al (7) investigated the prevalence of multi-dose vial contamination by aerobic bacteria in a major teaching hospital in Shiraz, Iran. The prevalence of multi-dose vial contamination by bacteria was 5.6%, much higher than what was found in the study done by Mattner et al (10). A total of 637 multi-dose vials were collected. The medication types were mainly potassium chloride (KCl), saline, sodium bicarbonate, calcium carbonate, insulin and sterile water for injection. The most frequently contaminated solutions were KCl, sodium bicarbonate and saline (7). The data in Table 2.2 shows the contaminated multi-dose vial and the isolated pathogen. There was no mixed contamination in any of the multi-dose vials.

Table 2.2 Contaminated multi-dose vials and pathogens isolated

Multi-dose vial	Pathogen
KCl	*S. maltophilia, B. coagulans, S. epidermidis, A.viscosus, Acinetobacter sp, S. epidermidis, Micrococcus sp, Corynebacterium sp, S.marcescens,α* haemolytic streptococci*, S. viridans*
Saline	*B.coagulans,S.epidermidis,S.viridans*
Sodium bicarbonate	*S.viridians, S.epidermidis, β* haemolytic streptococci*, Micrococcus sp, Acenitobacter sp, B. coagulans*
Calcium carbonate	*S. epidermidis*
Insulin*	*β* haemolytic streptococci
Sterile water for injection	*α* haemolytic streptococci*, S. epidermidis*

* Vial contains preservative

Source: Motamedifar et al (7)

2.6 Microorganisms cultured from contaminated multi-dose vials

2.6.1 General

Bacterial, viral, fungal and protozoal contamination of multi-dose vials has been reported in the literature (Table 2.1). This is concerning in the South African healthcare setting since a large portion of the patients are immunocompromised and susceptible to opportunistic infections (49).

2.6.2 Bacteria

Bacteria are a common pathogen involved in the contamination of multi-dose vials as Table 2.1 shows. *S. marcescens* is most commonly involved in contamination of multi-dose vials, followed by *Enterobacter cloacae*, *K. pneumoniae*, *Ralstonia pickettii*, *Pseudomonas putida* and *S. aureus*.

The study conducted by Mattner et al (10) showed that cultures from two saline solutions were positive for *S. epidermidis*. The pathogens involved in the contamination of multi-dose vials in the study of Motamedifar et al (7) are shown in Table 2.2.

2.6.3 Viruses

HBV and HCV have been the most common viruses associated with the contamination of multi-dose vials as shown in Table 2.1.

Katzenstein et al (105) investigated the nosocomial transmission of HIV in an outpatient clinic in Copenhagen, Denmark, in 1996. They found that the most likely source of infection was a contaminated multi-dose saline solution. This is of particular concern since there is a high incidence of HIV-infection in the South African population (49, 106).

2.6.4 Fungi

Welbel et al (107) reported on the Candida parapsilosis (*C. parapsilosis*) bloodstream infection outbreak in a Neonatal ICU (NICU) in Louisiana, USA, during 1991. A cohort study identified liquid glycerine multi-dose bottles, which were used to administer suppositories to NICU infants, as a risk factor for *C. parapsilosis* bloodstream infection.

2.6.5 Protozoa

Al-Saigul et al (78) reported a case where a patient developed nosocomial malaria due to the use of a contaminated multi-dose heparin vial in a hospital in Riyadh, Saudi Arabia, in 1997.

2.7 The safe use of multi-dose vials

2.7.1 General

Multiple reports in the literature have implicated multi-dose vials as the source of infection in nosocomial outbreaks. In contrast, recent studies have shown that multi-dose vials, and even single-dose vials used for multiple patients, can be used safely if safe injection and medication vial utilisation practices are adhered to.

2.7.2 Uncontaminated multi-dose vials in general practice

A study done by Manchikanti et al (18) investigated the infection control practices for interventional pain management procedures at a private interventional pain practice in the USA from May 2008 to December 2009. A total of 3 179 patients participated in the study and 18 472 procedures were carried out. Correct precautions and simple infection control measures were adhered to for each procedure. No infections of any significance were noted. It was shown that there is no risk with the use of single-dose vials for multiple patients and multi-dose vials if safe injection practices are adhered to.

Chen et al (61) evaluated the sterility, stability and efficacy of bevacizumab that was stored in multi-dose vials for six months. An aseptic technique was used each time bevacizumab was withdrawn from the multi-dose vial. This included disinfecting the vial septum with 10% povidone-iodine solution and an isopropyl alcohol wipe each time the vial was punctured, using a new needle and syringe each time. No microbial growth was obtained from any of the bevacizumab multi-dose vials.

Lin et al (62) reported on the safety of multi-dose vials after routine clinical use for immunotherapy. Safe injection practices were adhered to when each multi-dose vial was used. A total of 136 multi-dose vials were cultured for aerobic and anaerobic bacteria. No microorganisms were cultured.

2.7.3 Uncontaminated multi-dose vials in anaesthetic practice

Morgan (26) investigated the microbial growth in a self-prepared mixture of hyperbaric bupivicaine and fentanyl in a multi-dose syringe in the operating theatre environment in Johannesburg, South Africa, in 2009. All mixtures were prepared by the researcher using an aseptic technique and contained fentanyl 10 µg/ml, bupivicaine 4 mg/ml and dextrose 64 mg/ml. Syringes were divided into pairs, a control syringe and a multi-dose syringe. Samples were withdrawn aseptically by a single person at the beginning and at the end of a 12-hour period from the control syringe, and hourly from the multi-dose syringe. For each syringe pair, both samples from the control syringe and four of the samples from the multi-dose syringe were submitted for microbial culture. A total of 119 samples were submitted for microbial culture and one sample was positive for microbial growth. The positive sample was taken from a multi-dose syringe at the beginning of the study period (0 hours) and showed *S. aureus* growth. Subsequent samples from the same multi-dose syringe showed no microbial growth. Morgan postulated that the culture medium that yielded the microbial growth might have been contaminated since subsequent samples from the same multi-dose syringe were sterile or that the bupivicaine in the mixture, that has antimicrobial activity against some pathogens, inhibited any further microbial growth and produced subsequent sterile samples. The

researcher used a strict aseptic technique to prepare and aspirate all the samples of the hyperbaric bupivicaine and fentanyl mixture. The results of this study suggest that the aseptic use of multi-dose syringes for spinal anaesthesia could be safe, however it might not reflect the techniques used in everyday practice.

Arrington et al (6) investigated whether an alteration in the medication aspiration technique of anaesthetists could cause a significant difference in the incidence of multi-dose vial contamination in a theatre complex in the USA, in 1990. The control group consisted of multi-dose vials collected from staff anaesthetists at the end of each day. A single needle and syringe were used for a specific multi-dose vial throughout the day in the control group. The case group consisted of multi-dose vials collected from the four investigators at the end of each day. A new needle was used each time a multi-dose vial was punctured and a single syringe was used for a specific multi-dose vial throughout the day in the case group. Guaiac testing, using Hemoccult slides and developer, was performed on each collected multi-dose vial to evaluate for the presence of blood contamination. A multi-dose vial was considered positive for blood contamination if traces of blue appeared on the Hemoccult slide. The control group had a blood contamination rate of 2.24% where as the case group had a blood contamination rate of 0.27%. A chi-square test on the data demonstrated a significant ($p < 0.05$) difference between the control and case groups suggesting that the medication aspiration technique of anaesthetists does influence the incidence of multi-dose vial contamination. The research showed that there was blood contamination of the multi-dose vials suggesting that contaminated medication may then be injected into patients.

2.7.4 Guidelines for the safe use of multi-dose vials

The Centres for Disease Control and Prevention (CDC) (108) and the WHO (53) have made recommendations for the use of multi-dose vials. These recommendations include: (1) Refrigerate multi-dose vials after they are opened if recommended by the manufacturer. (2) Clean the septum of the multi-dose vial with 70% alcohol before inserting a device into the vial. (3) Use a sterile device to access a multi-dose vial and

avoid touch contamination of the device before penetrating the septum. (4) Discard the multi-dose vial if sterility is compromised. (5) A needle or other device should never be left inserted into a medication vial septum for multiple uses as this provides a direct route for microorganisms to enter the vial and contaminate the fluid.

The APIC position paper on safe injection, infusion, and medication vial practices in healthcare (56) strongly supports adherence to the following practices when using multi-dose vials: (1) Perform hand hygiene before manipulating medication. (2) Use aseptic technique when handling medication. (3) Store and prepare medications in a clean area on a clean surface. (4) Follow manufacturer's instructions for storage and use. (5) Always use a new sterile syringe and needle when entering a vial. (6) Clean the vial septum using friction and 70% isopropyl alcohol, ethyl alcohol, iodophor or other approved antiseptic swab. (7) Allow the septum to dry before inserting any device into the vial. (8) Never leave a needle, cannula or spike-device (even if it has a one-way valve) inserted into a medication vial septum because it leaves the vial vulnerable to contamination. (9) Discard the vial if the sterility is in question or according to manufacturer's expiration date.

The ASA Committee on Occupational Health and Infection Control have made recommendations for preventing contamination of medications during the practice of anaesthesia (16). Some of the recommendations for safe injection practices regarding the use of multi-dose vials include: (1) Use appropriate aseptic technique and hand hygiene to avoid contamination of injection equipment. (2) Use a sterile syringe and needle each time any medication or solution is accessed. (3) Disinfect the septum of a multi-dose vial with an alcohol swab or appropriate disinfectant before entering. (4) Store medications and solutions in accordance with the manufacturer's recommendations. (5) Discard multi-dose vial if sterility is compromised.

Facilities should develop a policy and procedure for their institution after reviewing and weighing these recommendations, implement an education and competency evaluation program for staff and consider audits for adherence to the facility's policy (56).

Currently SASA does not have an official standpoint on the use of multi-dose vials but it does not endorse the practice of sharing single-dose vials between multiple patients (109, 110).

2.8 Medication administration errors relating to the use of multi-dose vials

2.8.1 General

Medication errors are a common problem in the health care system and can be harmful to the patient and increase healthcare costs (111). There are two main types of medication errors: medication prescribing errors and medication administration errors (112). The safe administration of medication to a patient is a vital part of anaesthetists' responsibilities (1).

2.8.2 Medication administration errors in general practice

Cousins et al (30) reported on the medication errors in intravenous drug preparation and administration in hospitals in the UK, Germany and France in 2004. Pharmacy staff directly observed the preparation of 824 doses and administration of 798 doses by nurses. Common medication administration errors included the wrong diluents (1%, 49% and 18% of doses administered in the UK, German and French hospitals respectively), preparation not mixed correctly (data not collected, 79%, 1%), wrong dose (1%, 2%, 5%), wrong route (1%, 1%, 1%), wrong infusion rate (48%, 21%, 5%), inadequate aseptic technique (100%, 58%, 19%) and incorrect labelling (43%, 99% and 20%). Lack of appropriate labelling was a frequent error. Labelling errors included name of drug missing, dose missing, name of patient missing, time of preparation missing, and label absent or incomplete.

A study done by Gokhman et al (31) reported on the medication errors during medical emergencies in a large tertiary care, academic medical centre in Pittsburgh, USA, from

March 2009 to February 2010. A pharmacist directly observed the medication use of the Medical Emergency Team treating 50 patients experiencing a medical emergency. A total of 186 doses were observed and 296 errors were identified. Of these, 196 errors (66%) were inappropriate aseptic technique. Of the remaining 100 errors, 46% were prescribing errors, 28% administration technique errors, 14% labelling errors, 10% drug preparation errors and 2% dose errors.

The prevalence study done by Mattner et al (10) investigating the bacterial contamination of multi-dose vials showed that appropriate labelling practices were not adhered to. Of the 227 multi-dose vials collected, 113 (50%) were not dated. The medication type was not indicated on two multi-dose vials and the concentration of the medication was not indicated on seven multi-dose vials. Of the 114 (50%) dated multi-dose vials, 15 (13%) had expired.

2.8.3 Medication administration errors in anaesthetic practice

The risk of medication administration errors might be higher in anaesthesia than in other disciplines due to the large number of drugs administered by anaesthetist during their career (113). Most anaesthetists have been or will be involved in medication administration errors during their career (33).

A study done by Orser et al (114) investigated the medication errors in anaesthetic practice of 687 anaesthetist from Canada from 1995 through to 1997. A self-reporting survey was mailed to members of the Canadian Anaesthesiologists' Society. Surveys from 687 anaesthetists revealed that 85% had experienced at least one drug error or near drug error (event that almost involved the wrongful administration of a drug). The misidentification of a syringe (70.4%) and the misidentification of the label (46.8%) were the most common causes for drug error.

Llewellyn et al (34) investigated the drug administration errors of anaesthetists at three teaching hospitals in South Africa from 2005 to 2006. Anaesthetists working at the three hospitals were asked to complete a self-reporting survey for every anaesthetic

performed during a six-month period. Anaesthetist were asked if a drug error or a near drug error had occurred and the details thereof. A total of 30 412 anaesthetics were performed and survey-forms were completed in 53% of anaesthetics. The combined incidence for drug errors and near drug errors was reported as 1 in 274 anaesthetics. Misidentification of syringes accounted for 21.3% of all errors and drug ampoule misidentification accounted for 36.9% of errors. In the studies done by Orser et al (114) and Llewellyn et al (34) a self-reporting survey was used to assess the prevalence of medication administration errors amongst anaesthetists. Limitations of self-reporting studies include the respondent being too embarrassed to answer a question truthfully.

Strategies suggested to reduce the incidence of medication administration errors in anaesthesia include medication safety education and awareness programs, re-reading labels on medication containers, cross-checking medication labels with a second person or a device, clear labelling of all medication containers, adopting the international colour-coded labelling system and improving the organisation of drug drawers and work space (32-34, 114).

2.9 Labelling of medication

The correct labelling of medication in anaesthetic practice is a key element to safe medication administration (29). The Helsinki Declaration on Patient Safety in Anaesthesiology (46) declared syringe labelling as one of their aims for improving patient safety in Europe.

The labelling of medication is often not done or is incomplete (30, 115). Inappropriate labelling of medication has been identified as a cause for medication administration errors in general (30, 31) and anaesthetic practice (32-34).

Recommendations regarding safe labelling practices have been made by international organisations (115-120) as well as individual researchers (32, 34).

Labelling recommendations for medication containers (syringes, bags, bottles and bowls) include colour coded labels for medication classes, patient name, patient identifier, medication added to the container, amount of medication added (including units), total volume of diluent in container (ml), concentration (units/ml), date and time prepared, prepared by (signature), checked by (signature) and route of administration (29, 120). Labels on fluid bags and bottles should be placed on the front and the name of the fluid, batch number and expiry date should remain visible (120). Labels on syringes should be placed parallel with the long axis of the syringe barrel taking care not to cover the graduations (120).

The Medicines and Related Substances Control Act of South Africa clearly states that the name of the medical practitioner, dentist, pharmacist, pharmacy or hospital that prescribe or prepare medication must be indicated on the label of medicines intended for administration to humans (121).

It is recommended that stick-on, colour-coded labels are used for intravenous anaesthetic medications (122). Writing directly onto the container should be avoided as the ink can leach from the polyvinyl chloride (PVC) container into the intravenous fluid and has been shown to be toxic to animals (123).

A study done by Webster et al (124) assessed a new anaesthetic drug administration system at two tertiary hospitals in New Zealand from 1998 to 2003. Features of the new system included labels with the class and generic name of each drug in clear lettering, a barcode on each drug container and the use of the international colour-code standard for anaesthetic drugs on labels. Fewer medication administration errors occurred with the new system than with conventional methods ($p= 0.002$).

Porat et al (122) investigated the use of colour-coded labels for intravenous high-risk medications and intravenous lines to improve patient safety at a tertiary hospital in Jerusalem, Israel, during 2007. The new colour-coded label method was compared with the current labelling method (adhesive paper with black print on a white background and writing directly on the container with a marker pen). A laboratory simulation imitating an ICU was designed and the safety of medication treatment and overall duration of nurses'

orientation with drugs and intravenous lines were measured. The use of the new colour-coded label method improved identification of intravenous bags ($p< 0.001$), reduced time required for description of medication and intravenous lines ($p= 0.04$), improved identification of medication errors ($p= 0.03$) and reduced the average performance time for overall tasks ($p< 0.0001$).

A research doctorate by Jansen (35) regarding the legal liability arising from medication errors emphasises that healthcare workers can be held legally accountable for errors occurring with the dispensing (which includes the labelling of medication), preparation and administration of medication. Healthcare workers can only administer medication that was appropriately checked by the healthcare worker.

2.10 Summary

From the literature it is clear that the use of multi-dose vials pose a risk of microbial contamination if safe injection practices are not adhered to. Bacterial, viral, protozoal and fungal pathogens have been implicated in the contamination of multi-dose vials. Despite safe injection guidelines the infection control practices of anaesthetists fall short of accepted recommendations. Recent studies have shown that multi-dose vials can be used safely if safe injection practices are adhered to. Safe injection practices include the correct labelling of medication containers.

2.11 Conclusion

This chapter discussed the literature concerning patient safety, anaesthetic infection control practices relating to the use of multi-dose vials, the microbial contamination of multi-dose vials as a mechanism for nosocomial infections, types of multi-dose vials implicated in microbial contamination, microorganisms cultured from contaminated multi-dose vials, safe use of multi-dose vials and medication administration errors relating to the use of multi-dose vials. In the next chapter, chapter 3, the research methodology of this study will be discussed.

Chapter 3: Research methodology

3.1 Introduction

In this chapter the problem statement, aims and objectives, ethical considerations, research methodology and the validity and reliability of this study will be discussed. Discussion of the research methodology will include the research design, study population, study sample, data collection and data analysis of this study.

3.2 Problem statement

Common practice at CHBAH is to use boluses of a self-prepared phenylephrine solution (referred to as the solution) to treat hypotension, due to the vasodilatory effects of a spinal anaesthetic, in stable patients undergoing a caesarean section. This solution then acts as a multi-dose vial which is used for multiple patients.

The intravenous fluid vaculitres (normal-saline or Ringer's lactate) used to prepare this solution do not contain any bacteriocidal or bacteriostatic agents. There is no evidence in the literature or in the package information from the manufacturer that phenylephrine has any anti-bacterial activity.

It has been observed that this solution is often labelled incorrectly, used for more than 12 hours on multiple patients and strict aseptic technique is not always adhered to when using this solution as a multi-dose vial. This solution thus has the potential for microbial contamination.

Currently there is no formal protocol on the use of anaesthetic multi-dose vials in the South African literature or at the Anaesthetic Department at CHBAH.

3.3 Aims and objectives

3.3.1 Aims

The aims of this study were to:

- determine if there was microbial contamination of the solutions used at CHBAH
- evaluate if appropriate labelling and aspiration practices were adhered to with regards to the solutions.

3.3.2 Objectives

The objectives of this study were to:

- determine whether there was any microbial contamination of the solutions and to identify the contaminating microorganisms
- evaluate whether the name and concentration of the solutions were documented on the containers
- evaluate whether the date and time the solutions were prepared was documented on the containers
- evaluate whether the healthcare workers that prepared the solutions confirmed it by placing a signature on the containers
- evaluate the labelling method of the solutions (i.e. written directly on the container or label stuck on container)
- evaluate the aspiration method of the solutions (i.e. puncturing the rubber septum of the container with a needle or using a spike-device).

3.4 Ethical considerations

This study was a laboratory-based microbiological and checklist-based study concerning the solutions. No patients or healthcare workers were directly involved in the study. Care was taken to prevent identification of patients who received boluses of the solutions and healthcare workers who prepared and administered these solutions.

An application to the Human Research Ethics Committee (Medical) of the University of the Witwatersrand for the clearance of this study was submitted (Appendix 1). Approval for the conduction of this study was obtained from the Postgraduate Office, Faculty of Health Sciences, University of the Witwatersrand (Appendix 2). Permission to conduct this study at CHBAH was obtained from the Medical Advisory Committee of CHBAH (Appendix 3). Verbal consent to conduct this study was obtained from the Head of the department of Anaesthesiology and the theatre matron of the obstetric operating theatres at CHBAH. This study was conducted in accordance with the Declaration of Helsinki (42) and the South African Good Clinical Practice Guidelines (43).

3.5 Research methodology

3.5.1 Research design

Burns & Grove (125) described a research design as the blueprint for a study. According to Brink (126) a research design determines the methods by which the researcher obtains subjects, collects data, analyses data and interprets results.

Samples of the solution will undergo microbiological investigation and the labelling data of the solution will also be observed. A prospective, descriptive research design was chosen for this study.

A prospective study design is described by Brink (126) as measuring the variables that will be occurring during the study.

Brink (126) defined a descriptive study as a research study in which phenomena are described or the relationship between variables is examined and no attempt is made to

determine cause-and-effect relationships. The labelling data on each of the solutions from which a sample was taken for microbiological investigation was documented on a data collection form (Appendix 3). A standardised checklist, derived from labelling recommendations made by the Australian Commission on Safety and Quality in Health Care (120), was used to document the labelling data. A checklist is a structured observational technique used to establish whether a behaviour occurred (125).

3.5.2 Study population

The study population was the solutions used to treat hypotension, due to the vasodilatory effects of a spinal anaesthetic, in stable patients undergoing a caesarean section found in the two identical obstetric theatres at CHBAH (theatre 1 and theatre 2).

3.5.3 Study sample

A sample is a part of a population selected by the researcher to participate in a research study (126). The sample size, sampling method, inclusion and exclusion criteria will be discussed.

Sample size

The contamination rates of multi-dose vials in the literature are inconsistent and range from 0% to 27% (63). The sample sizes of studies investigating the microbial contamination of multi-dose vials are between 96 and 637 (7, 9, 10, 26). Due to financial constraints the sample size of this study was limited to 110 samples.

Sampling method

A sampling method is the process of selecting a group of subjects from the population with which to conduct a study (125). Endacott et al (127) emphasises that it is more

important for the sample to accurately represent the population in quantitative research than it is to have a large sample.

A convenience sampling method was used for this study. Brink (126) and Burns & Grove (125) described convenience sampling as choosing readily available subjects for the study until the desired sample size has been reached. The date and time of collection of the samples and labelling data was determined by the convenience for the data collector. This sampling method limited the bias caused by the Hawthorne effect.

Inclusion and exclusion criteria

Inclusion criteria for this study were:

- the solutions found in the obstetric theatres at CHBAH.

Exclusion criteria for this study were:

- the solutions with < 10 ml of solution left in the container
- any breach in the aseptic technique used during the collection and transportation of samples by the data collector.

3.5.4 Data collection

Discussion of the data collection process will include data collected, the data collection process, the data collector and the data collection period.

Data collected

Samples taken from the solutions were sent to the National Health Laboratory Service (NHLS) for microbiological investigation. The labelling data on the solution containers were also documented. The following data were collected:

- microbial contamination of the solutions
- microorganisms isolated from the solutions
- name and concentration of the solutions as documented on the containers
- date and time the solutions was prepared as documented on the containers
- if the healthcare workers that prepared the solutions confirmed it by signature on the containers
- type of labelling method used on the solution containers (i.e. written directly on the container or label stuck on container)
- method used to aspirate the solutions (i.e. puncturing the rubber septum of the container with a needle or using a spike-device).

Data collection process

The discussion on how the data was collected will include sample taking, sample labelling, sample storage and transport, sample processing at the laboratory and documentation of labelling data.

Sample taking: From each solution a sample was taken for microbiological investigation and the labelling data was also documented. All samples were collected and transported in a standardised manner.

In consultation with a microbiologist it was decided that a 10 ml sample would be adequate for microbiological investigation. An aseptic technique was used to collect a 10 ml sample from each solution container. This technique included:

- washing hands before taking the sample
- wearing gloves while collecting the sample
- using a new needle and syringe to aspirate each sample if the rubber septum needed to be punctured
- using a new syringe to aspirate each sample directly from the spike-device if such a device was in situ
- disinfecting the rubber septum or spike of each container with 70% isopropyl alcohol
- waiting two minutes after disinfection to allow for drying of the disinfectant before aspirating the sample.

An aerobic blood culture bottle (BacT/ALERT® SA) that has not past its expiration date, obtained from the National Health Laboratory Service (NHLS), was used to culture the solutions. The BacT/ALERT® SA blood culture bottle contains 40 ml supplemented tryptic soy broth as the culture media. The blood culture bottle was opened taking care not to contaminate the rubber septum. The bottle was then inoculated with the whole 10 ml sample and gently rotated for 30 seconds to mix the sample and culture media.

Sample labelling: After inoculating the blood culture bottle with the sample, a standard NHLS investigation request form was completed for every sample (Appendix 4). Care was taken not to use any patient information.The information was recorded as follows:

- Patient Hospital Number: The study number was written as dd-mm-yyyy-TH1/2. Where dd-mm-yyyy was the format in which the date the sample was taken on was recorded. The theatre from which the sample was taken was recorded as either theatre 1 (TH1) or theatre 2 (TH2).
- Surname: Research
- First name: Dr. A. van den Heever
- Hospital / Clinic: CHBAH
- Ward: Obstetric theatre
- Diagnosis / Reason for request: Research
- Type of specimen: Fluid
- Date taken: dd-mm-yyyy
- Time: hh:mm
- Taken by: Dr. A. van den Heever
- Requesting healthcare worker: Dr. A. van den Heever
- HPCSA / SANC number: MP 0659029
- Contact number: 083 415 4235
- E-mail address: zanvdheever@iburst.co.za
- Specimen Type: Fluid (specify) – Phenylephrine solution
- Investigation required: Microscopy / Culture / Sensitivity

This data as well as the data concerning the labelling of the solutions were documented on a data collection form (Appendix 5).

A unique peel-off barcode label from the NHLS investigation request form was attached to the blood culture bottle and the data collection form to facilitate the recovery of results. A unique peel-off barcode label on the blood culture bottle was attached to the NHLS investigation request form and the bar code number was documented on the data collection form.

After collecting a sample for microbiological investigation and labelling data the relevant solution was discarded to avoid reuse.

Sample storage and transport: An attempt was made to deliver the blood culture bottles to the Infection Control Services Laboratory, Department of Clinical Microbiology and Infectious Diseases, Witwatersrand School of Pathology, University of the Witwatersrand Medical school campus as soon as possible. If there was a delay in transporting the sample to the laboratory, it was stored at room temperature (20 - 25 °C) for not more than 12 hours.

Sample processing at the laboratory: The processing of the samples and identification of the microorganisms were done by qualified laboratory personnel using standard microbiological laboratory equipment and procedures.

The blood culture bottles were loaded into a BacT / ALERT 3D ® automated microbial detection system (manufactured by bioMérieux) as soon as it arrived at the laboratory. The cultures were incubated for five days whereafter the bottles with no microbial growth were deemed negative and were discarded. When a bottle signalled positive for microbial growth, broth from the bottle underwent Gram staining and was also subcultured onto agar plates. The agar plates were then reincubated until bacterial

growth occurred. Laboratory personnel then proceeded with the identification of the microorganism using standard microbiological methods.

Documentation of labelling data: The labelling data on each solution container from which a sample was taken for microbiological investigation, was documented on a data collection form (Appendix 5). A standardised checklist, derived from labelling recommendations made by the Australian Commission on Safety and Quality in Health Care (120) was used to document the labelling data.

Data collector

All of the samples were collected in an aseptic manner and transported by the researcher. Labelling data was collected by the researcher using a predetermined checklist.

Data collection period

Data was collected over a period of three months, from October to December 2012.

3.5.5 Data analysis

Data capturing was done using an Excel 2007 spreadsheet (Appendix 3). Descriptive and inferential statistics were used to analyse the data. Statistical analysis was performed using GraphPad InStat, a statistics programme. A p-value of < 0.05 was considered as statistically significant.

3.6 Validity and reliability of the study

Validity is the ability of an instrument to measure the variable that it is intended to measure (126). The measurement of the truth or accuracy of a claim is an important concern throughout the research process. Validity provides a basis for making decisions about which findings are useful for patient care (125).

Reliability refers to the consistency and dependability of a research instrument to measure a variable (126).The reliability of a measure denotes the consistency of measures obtained from a particular instrument and indicates the extent of random error in the measurement method (125).

The researcher collected, labelled, stored and transported all the samples in an aseptic manner.

All the specimens were analysed at the Infection Control Services Laboratory, Department of Clinical Microbiology and Infectious Diseases, Witwatersrand School of Pathology, University of the Witwatersrand. The processing of the samples and identification of the microorganisms were done by qualified laboratory personnel using standard microbiological laboratory equipment and procedures.

A predetermined, structured checklist was used to collect the labelling information from all of the solution containers.

3.7 Conclusion

In this chapter the problem statement, aims and objectives, ethical considerations, research methodology and the validity and reliability of this study were discussed. Discussion of the research methodology included the research design, study population, study sample, data collection and data analysis. In the next chapter, chapter 4, the results of this study will be discussed.

Chapter 4: Results and discussion

4.1 Introduction

In this chapter the sample realisation, the results of the study according to the objectives and a discussion regarding the results are presented.

4.2 Sample realisation

A total of 111 samples were collected from 1 October to 7 December 2012. One sample was excluded from the study due to a breach in the aseptic technique used during the collection and transportation of the sample by the researcher. The sample size of this study was therefore 110 samples.

4.3 Results

4.3.1 Determining whether there was any microbial contamination of the solutions and to identify the contaminating microorganisms

Microbial contamination was identified in seven of 110 (6.36%) samples collected from the solutions.

The contaminating microorganisms identified included coagulase negative staphylococci (2.72%), *Brevundimonas vesicularis* (0.91%), *Bacillus* species (0.91%), *Micrococcus* species (0.91%) and *Pseudomonas alcaligenes* (0.91%) (Table 4.1).

Table 4.1 Microbial contamination of the solutions

Microorganisms	Number of solutions contaminated (n)	%
Coagulase negative staphylococci	3	2.72%
Brevundimonas vesicularis	1	0.91%
***Bacillus* species**	1	0.91%
***Micrococcus* species**	1	0.91%
Pseudomonas alcaligenes	1	0.91%
Total	7	6.36%

4.3.2 Evaluating whether the name and concentration of the solutions were documented on the containers

The name of the solution was indicated on all (100%) of the containers from which samples were collected (Table 4.2).

The concentration of the solution was indicated on 106 (96.36%) of the containers (Table 4.2).

Table 4.2 Labelling and aspiration practices with regards to the solutions

Labelling and aspiration practice	Number of solutions (n)	%
Name of solution indicated on container	110	100%
Concentration of solution indicated on container	106	96.36%
Date solution was prepared indicated on container	82	74.55%
Time solution was prepared indicated on container	63	57.27%
Healthcare worker that prepared solution confirmed it by placing a signature on the container	9	8.18%
Labelling data written directly on the container	110	100%
Spike-device used to aspirate solution from container	71	64.54%

4.3.3 Evaluating whether the date and time the solutions were prepared was documented on the containers

The date the solution was prepared was indicated on 82 (74.55%) of the 110 containers from which samples were collected (Table 4.2).

The time the solution was prepared was indicated on 63 (57.27%) of the 110 containers from which samples were collected (Table 4.2).

4.3.4 Evaluating whether the healthcare workers that prepared the solutions confirmed it by placing a signature on the containers

The healthcare workers that prepared the solutions confirmed it by placing a signature on nine (8.18%) of the 110 containers from which samples were taken (Table 4.2).

4.3.5 Evaluating the labelling method of the solutions (i.e. written directly on the container or label stuck on container)

The labelling method used on all (100%) of the solutions was to write directly on the container (Table 4.2).

4.3.6 Evaluating the aspiration method of the solutions (i.e. puncturing the rubber septum of the container with a needle or using a spike-device)

A spike-device was used as the method of aspiration of the solution in 71 (64.54%) of the solutions from which samples were collected (Table 4.2). From the solutions that had microbial contamination, 6 (85,71%) had spike-devices in situ. Using Fisher's exact test, the association between the aspiration method of the solution and microbial contamination of the solution was not statistically significant ($p = 0.4178$) (Table 4.3).

Table 4.3 Association between the aspiration method of the solution and microbial contamination of the solution

	Microbial contamination	No microbial contamination	Total
Spike-device	6	65	**71**
No spike-device	1	38	**39**
Total	**7**	**103**	**110**

P = 0.4178

4.4 Discussion

4.4.1 Introduction

The use of multi-dose vials in general and anaesthetic practice remains a controversial topic due to the risk of microbial contamination. Presently there are conflicting results reported in the literature (6, 8, 10, 18, 23, 25, 26, 58-62). The literature review suggested that the use of multi-dose vials does have a risk of microbial contamination if safe injection practices are not adhered to. Safe injection practices include the correct labelling and handling of medication containers (16, 29, 56). Currently SASA does not have an official standpoint on the use of multi-dose vials but it does not endorse the practice of sharing single-dose vials between multiple patients (109, 110).

4.4.2 Microbial contamination of the solutions

From the literature the microbial contamination rates of multi-dose vials range from 0% to 27% (63). Bacterial, viral, fungal and protozoal contamination of multi-dose vials have been reported (Chapter 2, Table 2.1). In contrast, recent studies have shown that multi-

dose vials, and even single-dose vials used for multiple patients, can be used safely if safe injection and medication vial utilisation practices are adhered to (6, 18, 26, 61, 62).

In this study seven of 110 samples (6.36%) were contaminated with microorganisms. This is similar to the results of Motamedifar et al (7) which reported a microbial contamination rate of 5.6%. It is however substantially higher than the microbial contamination rate of 0.9% reported by Mattner et al (10). This might not reflect the true microbial contamination rate since only contamination with aerobic bacteria was investigated in this study. It is clear from this study that safe injection practices with regard to the solution are not adhered to and that there is a relatively high risk for microbial contamination of the solution. This is of concern since patients are at risk of developing nosocomial infections when the solution is used.

It has been shown that bacteria are common pathogens involved in the contamination of multi-dose vials and include *Serratia marcescens*, *Enterobacter cloacae*, *Klebsiella pneumoniae*, *Ralstonia pickettii*, *Pseudomonas putida*, *Staphylococcus aureus* and *Staphylococcus epidermidis* (Chapter 2, Table 2.1). The aerobic bacteria contaminating the solutions in this study include coagulase negative staphylococci (2.73%), *Brevundimonas vesicularis* (0.91%), *Bacillus* species (0.91%), *Micrococcus* species (0.91%) and *Pseudomonas alcaligenes* (0.91%). This is similar to the results of Motamedifar et al (7) and Mattner et al (10).

Coagulase negative staphylococci are a group of microorganisms that are increasingly implicated as a cause of nosocomial infections (128, 129). Staphylococci are Gram-positive cocci and are isolated primarily from mammals. There are 32 coagulase negative staphylococci species, 15 being common commensals in humans (129). Most of the staphylococci isolated from humans belong to the *S. saprophyticus* or the *S. epidermidis* group. The *S. epidermidis* group includes the species *S. epidermidis*, *S. hominis*, *S. haemolyticus*, *S. warneri*, *S. caprae*, *S. saccharolyticus, S. pasteuri* and *S. lugdunensis* (130). *S. epidermidis* is the predominant human species and is isolated from mucous membranes, moist habitats such as the groin and axilla as well as dry, exposed skin surfaces. Specific infections associated with coagulase negative

staphylococci include bacteremia, catheter-related infections, central nervous system shunt infections, endocarditis, urinary tract infection, surgical site infection and endophthalmitis. Due to financial limitations the specific coagulase negative staphylococci species were not identified in this study.

Brevundimonas vesicularis (*B. vesicularis*) is an aerobic, non-fermenting Gram-negative bacillus isolated from various sources including soil, bottled mineral water, hydrotherapy pools, shower hoses and human cervical specimens (131). Human infection with *B. vesicularis* is rare with only a few cases reported in the literature (132). Infections associated with *B. vesicularis* include bacteremia, pneumonia, infective endocarditis and spontaneous bacterial peritonitis. *B. vesicularis* is a pathogen that can cause opportunistic infections in immunocompromised patients (133).

Members of the *Bacillus* species are aerobic, spore-forming, Gram-positive bacilli (134). The *Bacillus* species are commonly found in soil, on inanimate objects and on mucous membranes of humans (135). Over 30 species of *Bacillus* have been identified, with *Bacillus cereus* (*B. cereus*) and *Bacillus anthracis* (*B. anthracis*) being the most common pathogens. *B. cereus* is increasingly being recognised as a pathogen involved in opportunistic infections in hospitalised patients (136). Infections associated with *Bacillus* species include cutaneous infections, pneumonia, gastrointestinal infections, bacteremia, meningitis and endocarditis.

Micrococcus species are catalase-positive, coagulase-negative, Gram-positive, aerobic cocci. Currently there are ten species of micrococci which include *M. luteus*, *M. lylae*, *M. antarcticus*, *M. endophyticus*, *M. flavus*, *M. terreus*, *M. yunnanensis*, *M. lactis*, *M. niistensis* and *M. cohnii* (137, 138). *Micrococcus* species are commonly found in soil, water, dust and the skin of humans and animals. Infections associated with *Micrococcus* species include bacteremia, endocarditis, ventriculitis, peritonitis, pneumonia, endophthalmitis, keratolysis, and septic arthritis (139). Recent studies have shown that *Micrococcus* species can be opportunistic pathogens in immunocompromised patients (140, 141).

Pseudomonas alcaligenes (*P. alcaligenes*) is a Gram-negative, aerobic bacteria that has been placed in the *Pseudomonas aeruginosa* group (142). *P. alcaligenes* is isolated mainly from soil and water, rarely from clinical specimens (143). Infections associated with *P. alcaligenes* include bacteremia, endocarditis, otitis media, meningitis and wound infections. Recent studies have implicated *P. alcaligenes* in opportunistic infections in immunocompromised patients (144, 145).

It is evident from the literature that the contaminating microorganisms identified in this study have been implicated as opportunistic pathogens in immunocompromised patients (133, 136, 140, 141, 144). This is especially important at CHBAH since a large proportion of South African patients are immunocompromised and susceptible to opportunistic infections (49).

4.4.3 Labelling and aspiration practices of the solutions

The literature shows that the inappropriate labelling of medication is a cause of medication administration errors in general (30, 31) and in anaesthetic practice (32-34). Labelling recommendations for medication containers include colour coded labels for different medication classes, patient name, patient hospital number, name of medication added to the container, amount of medication added, total volume of diluent in container, concentration of solution, date and time solution was prepared, solution prepared by, checked by, and route of administration (29, 120)

In this study the name of the solution was indicated on all 110 (100%) containers from which samples were collected. This is similar to the results reported by Mattner et al (10) where the medication type was indicated on 99.12% of multi-dose vials. The concentration of the solution was indicated on 106 (96.36%) of the 110 containers which is similar to the 96.91% reported by Mattner et al (10). The date the solution was prepared was indicated on 82 (74.55%) of the 110 containers which is substantially higher than the 50% reported by Mattner et al (10). The time the solution was prepared was indicated on 63 (57.27%) of the 110 containers. It is clear from the results of the

study that the solutions are inappropriately labelled and that there is risk of an administration error when these solutions are used.

Recommendations for correct medication labelling and administration are that the healthcare worker that prepared the medication should indicate it on the medication container (29, 120). In this study only 9 (8.18%) of the healthcare workers that prepared the solution confirmed it by placing a signature on the container. The majority of the solutions in the study were administered to patients without knowing who prepared the solution. This has medical-legal implications.

Writing directly onto the container should be avoided as the ink can leach from the PVC container into the intravenous fluid and has been shown to be toxic to animals (121, 123, 146). In this study the labelling data was written directly on all 110 (100%) containers from which samples were collected. This result shows that a potentially toxic solution is administered to patients.

The APIC position paper on safe injection, infusion and medication vial practices in health care (56) strongly discourages the use of a spike-device inserted into a medication vial septum because it leaves the vial vulnerable to contamination. In this study a spike-device was used in 71 (64.54%) of the 110 containers from which samples were collected. This is substantially higher than the results reported by Mattner et all (10) where 41.41% of multi-dose vials had spike-devices. Although the association between the aspiration method of the solution and microbial contamination of the solution was not statistically significant ($p = 0.4178$), it must be noted that six of the seven contaminated solutions contained a spike-device.

Medication labelling and administration is an important part of safe injection practices as shown in the literature. The results of this study clearly show that the solutions are inappropriately labelled and that a spike-device is commonly used to aspirate the solution. This is not in keeping with the recommendations for safe injection practices (29, 56, 120).

4.4.4 Legal accountability of medication errors in South Africa

An extensive research doctorate by Jansen (35) that comprehensively addresses various errors that can occur with regard to dispensing, preparation and administration of medication from a legal perspective, emphasises that healthcare workers experience a great deal of uncertainty with regard to their legal position and medication administration. Jansen (35) further concludes that healthcare workers do not view medication administration as the high risk activity that it is.

An important medication error that anaesthetists are legally accountable for is the administration of contaminated medication (35). In this study seven (6.36%) solutions were contaminated and these contaminated solutions were administered to patients. All of the solutions were labelled by writing directly on the containers and therefore a potentially toxic solution was also administered to patients. As previously mentioned, a spike-device was used in 71 (64.54%) solutions, a method that is strongly discouraged as it leaves the vial vulnerable to contamination (56).

Jansen (35) further states that a healthcare worker can only administer medication that was appropriately checked by the healthcare worker. This study did not evaluate if anaesthetists checked the solutions appropriately when it was prepared. However 101 (91.82%) solutions had no signature indicating who had prepared the solution and anaesthetists were aspirating and administrating solutions from these containers.

4.4.5 Significance of findings

It is evident from the results of this study that the solutions used to treat hypotension, due to the vasodilatory effects of a spinal anaesthetic, in stable patients undergoing a caesarean section found in the obstetric theatres at CHBAH are at risk of microbial contamination due to unsafe injection practices when these solutions are prepared and administered. These solutions are also inappropriatly labelled, contributing to the risk of medication administration errors.

Unsafe injection practices expose patients to potentially harmful microorganisms. The contaminating microorganisms identified in this study have been implicated as opportunistic pathogens in immunocompromised patients (133, 136, 140, 141, 144). It is especially important at CHBAH since a large proportion of South African patients are immunocompromised and susceptible to opportunistic infections (49).

Anaesthetists can be held legally accountable for medication errors. The medication errors identified in this study include administration of contaminated medication, administration of potentially toxic solutions and failing to appropriately check all medication prior to administration. Medication was administered without checking the date and time the medication was prepared, the concentration of the medication and verifying the healthcare worker that prepared the medication.

4.5 Conclusion

In this chapter the sample realisation, the results of the study and a discussion regarding the results was presented. In the final chapter, chapter 5, a study summary, the limitations of the study, recommendations and the conclusion of the study are discussed.

Chapter 5: Study summary, limitations, recommendations and conclusion

5.1 Introduction

In this final chapter a study summary, the limitations of the study, recommendations, and conclusion of the study are discussed.

5.2 Study summary

Anaesthetists are responsible for the safe use of anaesthetic-associated drugs (1). The use of multi-dose vials in the health care setting is controversial. The literature review suggested that the use of multi-dose vials poses a risk of microbial contamination if safe injection practices are not adhered to. Safe injection practices include the correct labelling and handling of medication containers.

Common practice at CHBAH is to use boluses of a solution to treat hypotension, due to the vasodilatory effects of a spinal anaesthetic, in stable patients undergoing a caesarean section. This solution then acts as a multi-dose vial which is used for multiple patients. It has been observed that the solutions are often labelled incorrectly and strict aseptic technique is not always adhered to when using this solution as a multi-dose vial. This solution thus has the potential for microbial contamination as seven of the 110 samples were contaminated.

The aims of this study were to determine if there was microbial contamination of the solutions used at CHBAH and to evaluate if appropriate labelling practices were adhered to with regard to the solutions.

Samples were collected from the solutions found in the two obstetric theatres at CHBAH. These samples were then used to inoculate aerobic blood culture bottles and were sent to the NHLS for microbiological investigation. The labelling data on the solutions from which samples were collected was documented on a data collection form.

A total of 111 samples were collected of which 110 met the inclusion criteria for this study. Microbial contamination was identified in seven of the 110 (6.36%) samples collected. Contaminating microorganisms included coagulase negative staphylococci (2.73%), *B. vesicularis* (0.91%), *Bacillus* species (0.91%), *Micrococcus* species (0.91%) and *P. alcaligenes* (0.91%).

The name of the solution was indicated on all 110 (100%) containers from which samples were collected. The concentration of the solution was indicated on 106 (96.36%) containers. The date the solution was prepared was indicated on 82 (74.55%) containers and the time the solution was prepared was indicated on 63 (57.27%) containers. Only nine (8.18%) of the healthcare workers that prepared the solution confirmed it by placing a signature on the container. The labelling data was written directly on all 110 (100%) containers. A spike-device was used in 71 (64.54%) containers from which samples were collected.

5.3 Limitations

This study was contextual and focused on the microbial contamination and labelling of a solution prepared and used by anaesthetists working in the two obstetric theatres at CHBAH. This limits the generalisation of the results.

Due to financial constraints only microbial contamination with aerobic bacteria was investigated. Contamination of the samples with blood and other microorganisms (anaerobic bacteria, viruses, fungi, protozoa) was not assessed.

There was concern that the Hawthorne effect (126) would influence the results of this study. This limitation was avoided by collecting samples and labelling data from the solutions on random days and at random times which were convenient for the researcher. Anaesthetists working at CHBAH were not informed about the study so as to prevent any change in their anaesthetic practice.

Convenience sampling was used to collect samples and data from the solutions. This can introduce bias as certain elements may be overrepresented or underrepresented. This makes generalisation based on such samples extremely risky, although the samples so chosen were convenient for the researcher in terms of time and money.

Only categorical data was collected and therefore the association between the length of time the solution was in use and microbial contamination of the solution could not be investigated.

5.4 Recommendations

5.4.1 Recommendations for practice at the CHBAH theatre complex

The use of multi-dose vials should be strongly discouraged at the CHBAH theatre complex as seven (6.36%) solutions were contaminated.

If multi-dose vials are to be used due to financial or resource constraints, emphasis should be placed on the use of strict aseptic technique and only multi-dose vials containing bacteriostatic or bactericidal preservatives should be used.

Spike-devices should not be left in the rubber septum of multi-dose vials.

Guidelines with regards to the appropriate labelling of these solutions should be drawn up and implemented.

Anaesthetists should prepare their own solutions and discard it at the end of their shifts.

Healthcare workers should be educated about their legal position with regards to medication preparation and administration.

5.4.2 Recommendations for the pharmaceutical industry

Pharmaceutical companies should consider manufacturing affordable, single-dose vials of commonly used medications at suitable concentrations for single use.

The phenylephrine used at the CHBAH theatre complex is packaged in a 1 ml ampoule containing 10 mg/ml of phenylephrine. The phenylephrine needs to be diluted to produce an acceptable concentration that can be given as a bolus to treat hypotension in stable patients due to the vasodilatory effects of a general or regional anaesthetic. Pharmaceutical companies should consider manufacturing pre-filled phenylephrine syringes with an acceptable concentration that can be given as a bolus.

5.4.3 Recommendations for formal guidelines regarding the use of multi-dose vials

Local and international guidelines regarding the use of multi-dose vials in general and anaesthetic practice should be drawn up and implemented.

SASA should consider taking an official standpoint on the use of multi-dose vials. This standpoint should then be published in the South African Journal of Anaesthesia and Analgesia (SAJAA) and implemented in state and private hospitals.

5.4.4 Recommendations for further research

Evaluate the cost-effectiveness of using single-dose vials compared to multi-dose vials.

The financial and social burden of nosocomial infections due to the use of contaminated multi-dose vials should be evaluated.

Evaluate the contamination of multi-dose vials with other microorganisms (anaerobic bacteria, viruses, fungi, protozoa) and blood.

5.5 Conclusion

Common practice at CHBAH is to use boluses of a solution to treat hypotension, due to the vasodilatory effects of a spinal anaesthetic, in stable patients undergoing a caesarean section. This solution then acts as a multi-dose vial which is used for multiple patients. This study demonstrated microbial contamination of the solution and that safe injection practices were not adhered to when intravenous medications were prepared and administrated, which includes correct labelling practices. This is especially important at CHBAH since a large proportion of South African patients are immunocompromised and thus susceptible to opportunistic infections. An important medication error that anaesthetists are legally accountable for is the administration of contaminated medication. Furthermore inappropriate labelling of medications is a cause of medication administration errors and this may have serious legal implications for the anaesthetist.

Appendices

Appendix 1

Ethics clearance obtained from the Human Research Ethics Committee (Medical), University of the Witwatersrand

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG
Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Dr Andreas van der Heever

CLEARANCE CERTIFICATE	**M120114**
PROJECT	Microbial Contamination and Labelling of Self-Prepared, Multi-Dose Phenylephrine Solutions used at a Teaching Hospital
INVESTIGATORS	Dr Andreas van der Heever.
DEPARTMENT	Department of Anaesthesiology
DATE CONSIDERED	27/01/2012
DECISION OF THE COMMITTEE*	Approved unconditionally

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE 27/01/2012 **CHAIRPERSON** .....
(Professor PE Cleaton-Jones)

*Guidelines for written 'informed consent' attached where applicable
cc: Supervisor : Mrs Juan Scribante

DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10004, 10th Floor, Senate House, University.
I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES...

Appendix 2

Approval for the conduction of this study obtained from the Postgraduate Office, Faculty of Health Sciences, University of the Witwatersrand

Faculty of Health Sciences
Medical School, 7 York Road, Parktown, 2193
Fax: (011) 717-2119
Tel: (011) 717-2076

Reference: Ms Salamina Segole
E-mail: salamina.segole@wits.ac.za
12 July 2012
Person No: 598098
PAG

Dr ZA Van Den Heever
P O Box 1145
Bergbron
1712
South Africa

Dear Dr Van Den Heever

Master of Medicine (in the specialty Anaesthesia): Approval of Title

We have pleasure in advising that your proposal entitled "*Microbiology contamination and labelling of self-prepared, multi-dose phenylephrine solutions used at a teaching hospital*" has been approved. Please note that any amendments to this title have to be endorsed by the Faculty's higher degrees committee and formally approved.

Yours sincerely

Mrs Sandra Benn
Faculty Registrar
Faculty of Health Sciences

Appendix 3

Permission to conduct this study at CHBAH obtained from the Medical Advisory Committee CHBAH

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

MEDICAL ADVISORY COMMITTEE
CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL

PERMISSION TO CONDUCT RESEARCH

Date: 28 September 2012

TITLE OF PROJECT: Microbial contamination and labeling of self-prepared, multi-dose phenylephrine solutions used at a teaching hospital

UNIVERSITY: Witwatersrand

Principal Investigator: Dr ZAN van der Heever

Department: Anaesthesiology

Supervisor (If relevant): Ms J Scribante/Dr W Lowman

Permission Head Department (where research conducted):

Date of start of proposed study: October 2012
Date of completion of data collection: November 2012

The Medical Advisory Committee recommends that the said research be conducted at Chris Hani Baragwanath Hospital. The CEO /management of Chris Hani Baragwanath Hospital is accordingly informed and the study is subject to:-

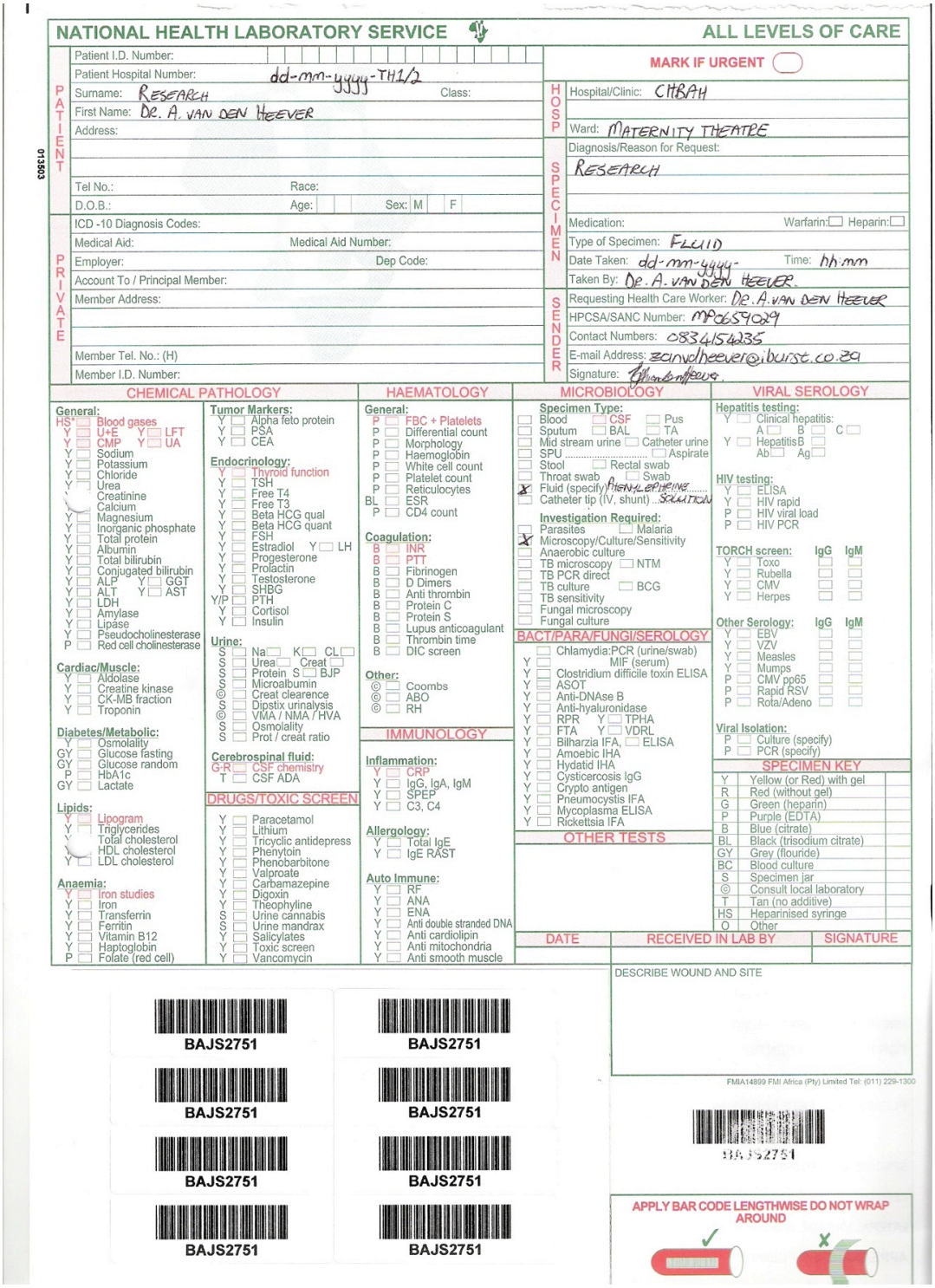
- Permission having been granted by the Committee for Research on Human Subjects of the University of the Witwatersrand.
- the Hospital will not incur extra costs as a result of the research being conducted on its patients within the hospital
- the MAC will be informed of any serious adverse events as soon as they occur
- permission is granted for the duration of the Ethics Committee approval.
- **Costs for the culture analysis from the Infection Control Services Laboratory are to be borne by the researchers and not CHBAH**

.....
Recommended
(On behalf of the MAC)
Date: 28 September 2012

.....
Approved/Not Approved
Hospital Management
Date: 27/10/12

Appendix 4

Standard NHLS investigation request form completed for every sample collected in this study



NATIONAL HEALTH LABORATORY SERVICE — ALL LEVELS OF CARE

PATIENT
Patient I.D. Number:
Patient Hospital Number: dd-mm-yyyy-TH1/2
Surname: RESEARCH Class:
First Name: DR. A. VAN DEN HEEVER
Address:
Tel No.: Race:
D.O.B.: Age: Sex: M F

PRIVATE
ICD -10 Diagnosis Codes:
Medical Aid: Medical Aid Number:
Employer: Dep Code:
Account To / Principal Member:
Member Address:
Member Tel. No.: (H)
Member I.D. Number:

MARK IF URGENT

HOSP
Hospital/Clinic: CHBAH
Ward: MATERNITY THEATRE

SPECIMEN
Diagnosis/Reason for Request: RESEARCH
Medication: Warfarin: Heparin:
Type of Specimen: FLUID
Date Taken: dd-mm-yyyy- Time: hh:mm
Taken By: DR. A. VAN DEN HEEVER.

SENDER
Requesting Health Care Worker: DR. A. VAN DEN HEEVER
HPCSA/SANC Number: MP0659029
Contact Numbers: 0834154235
E-mail Address: zainabheever@iburst.co.za
Signature:

CHEMICAL PATHOLOGY
General:
HS* Blood gases
Y U+E Y LFT
Y CMP Y UA
Y Sodium
Y Potassium
Y Chloride
Y Urea
Creatinine
Calcium
Y Magnesium
Y Inorganic phosphate
Y Total protein
Y Albumin
Y Total bilirubin
Y Conjugated bilirubin
Y ALP Y GGT
Y ALT Y AST
Y LDH
Y Amylase
Y Lipase
Y Pseudocholinesterase
P Red cell cholinesterase

Cardiac/Muscle:
Y Aldolase
Y Creatine kinase
Y CK-MB fraction
Y Troponin

Diabetes/Metabolic:
Y Osmolality
GY Glucose fasting
GY Glucose random
P HbA1c
GY Lactate

Lipids:
Y Lipogram
Y Triglycerides
Total cholesterol
HDL cholesterol
Y LDL cholesterol

Anaemia:
Y Iron studies
Y Iron
Y Transferrin
Y Ferritin
Y Vitamin B12
Y Haptoglobin
P Folate (red cell)

Tumor Markers:
Y Alpha feto protein
Y PSA
Y CEA

Endocrinology:
Y Thyroid function
Y TSH
Y Free T4
Y Free T3
Y Beta HCG qual
Y Beta HCG quant
Y FSH
Y Estradiol Y LH
Y Progesterone
Y Prolactin
Y Testosterone
Y SHBG
Y/P PTH
Y Cortisol
Y Insulin

Urine:
S Na K CL
S Urea Creat
S Protein S BJP
S Microalbumin
© Creat clearance
S Dipstix urinalysis
© VMA / NMA / HVA
S Osmolality
S Prot / creat ratio

Cerebrospinal fluid:
G-R CSF chemistry
T CSF ADA

DRUGS/TOXIC SCREEN
Y Paracetamol
Y Lithium
Y Tricyclic antidepress
Y Phenytoin
Y Phenobarbitone
Y Valproate
Y Carbamazepine
Y Digoxin
Y Theophyline
S Urine cannabis
S Urine mandrax
Y Salicylates
Y Toxic screen
Y Vancomycin

HAEMATOLOGY
General:
P FBC + Platelets
P Differential count
P Morphology
P Haemoglobin
P White cell count
P Platelet count
P Reticulocytes
BL ESR
P CD4 count

Coagulation:
B INR
B PTT
B Fibrinogen
B D Dimers
B Anti thrombin
B Protein C
B Protein S
B Lupus anticoagulant
B Thrombin time
B DIC screen

Other:
© Coombs
© ABO
© RH

IMMUNOLOGY
Inflammation:
Y CRP
Y IgG, IgA, IgM
Y SPEP
Y C3, C4

Allergology:
Y Total IgE
Y IgE RAST

Auto Immune:
Y RF
Y ANA
Y ENA
Y Anti double stranded DNA
Y Anti cardiolipin
Y Anti mitochondria
Y Anti smooth muscle

MICROBIOLOGY
Specimen Type:
Blood CSF Pus
Sputum BAL TA
Mid stream urine Catheter urine
SPU ..... Aspirate
Stool Rectal swab
Throat swab A Swab
X Fluid (specify) PHENYLEPHRINE.....
Catheter tip (IV, shunt) ...SOLUTION

Investigation Required:
Parasites Malaria
X Microscopy/Culture/Sensitivity
Anaerobic culture
TB microscopy NTM
TB PCR direct
TB culture BCG
TB sensitivity
Fungal microscopy
Fungal culture

BACT/PARA/FUNGI/SEROLOGY
Chlamydia:PCR (urine/swab)
Y MIF (serum)
Y Clostridium difficile toxin ELISA
Y ASOT
Y Anti-DNAse B
Y Anti-hyaluronidase
Y RPR Y TPHA
Y FTA Y VDRL
Y Bilharzia IFA, ELISA
Y Amoebic IHA
Y Hydatid IHA
Y Cysticercosis IgG
Y Crypto antigen
Y Pneumocystis IFA
Y Mycoplasma ELISA
Y Rickettsia IFA

OTHER TESTS

VIRAL SEROLOGY
Hepatitis testing:
Y Clinical hepatitis:
A B C
Y Hepatitis B
Ab Ag

HIV testing:
Y ELISA
Y HIV rapid
P HIV viral load
P HIV PCR

TORCH screen: IgG IgM
Y Toxo
Y Rubella
Y CMV
Y Herpes

Other Serology: IgG IgM
Y EBV
Y VZV
Y Measles
Y Mumps
P CMV pp65
P Rapid RSV
P Rota/Adeno

Viral Isolation:
P Culture (specify)
P PCR (specify)

SPECIMEN KEY

Y	Yellow (or Red) with gel
R	Red (without gel)
G	Green (heparin)
P	Purple (EDTA)
B	Blue (citrate)
BL	Black (trisodium citrate)
GY	Grey (flouride)
BC	Blood culture
S	Specimen jar
©	Consult local laboratory
T	Tan (no additive)
HS	Heparinised syringe
O	Other

DATE | RECEIVED IN LAB BY | SIGNATURE

DESCRIBE WOUND AND SITE

BAJS2751 (x8)

FMIA14899 FMI Africa (Pty) Limited Tel: (011) 229-1300

APPLY BAR CODE LENGTHWISE DO NOT WRAP AROUND

Appendix 5

Self-prepared, multi-dose phenylephrine solution data collection form

Sample information

Sample number	
NHLS request bar code number	
Blood culture bottle bar code number	
Date collected	
Time collected	
Theatre collected from	Theatre 1 / Theatre 2

Microbiological information

Bacterial contamination	Yes / No
Organisms isolated	

Labelling information

Name of solution indicated	Yes / No
Concentration of solution indicated	Yes / No
Date solution was prepared indicated	Yes / No
Time solution was prepared indicated	Yes / No
Signature of healthcare worker that prepared solution	Yes / No
Labelling method used	Ink directly on container / Stick-on label / Other
Spike-device	Yes / No

Appendix 6

Example of Excel spreadsheet for data analysis

Sample number	NHLS request bar code number	Blood culture bottle bar code number	Date collected	Time collected	Theatre collected from (Th1/ Th2)	Bacterial contamination (Yes/ No)	Organisms isolated	Name of solution indicated (Yes/ No)	Concentration of solution indicated (Yes/ No)	Date solution was prepared indicated (Yes/ No)	Time solution was prepared indicated (Yes/ No)	Signature of person who prepared solution (Yes/ No)	Labelling method used (Ink directly on container/ Stick-on label/ Other)	Spike device (Yes/ No)
01/10/2012-TH1	BAYM7400B	SAL75G3TB	2012/10/01	6:40	Th 1	No	Nil	Yes	Yes	Yes	No	No	Ink directly on container	Yes
01/10/2012-TH2	BAYM7401B	SAL75HC0B	2012/10/01	6:55	Th 2	No	Nil	Yes	Yes	Yes	No	No	Ink directly on container	Yes
02/10/2012-TH1	BAYM7402B	SAL75G6JB	2012/10/02	6:50	Th 1	No	Nil	Yes	Yes	No	No	No	Ink directly on container	Yes
02/10/2012-TH2	BAYM7403B	SAL75G1HB	2012/10/02	7:05	Th 2	No	Nil	Yes	Yes	Yes	No	No	Ink directly on container	No
03/10/2012-TH1	BAYM7404B	SAL75HB7B	2012/10/03	6:50	Th 1	No	Nil	Yes	Yes	No	No	No	Ink directly on container	No
03/10/2012-TH2	BAYM7405B	SAL75G5HB	2012/10/03	7:00	Th 2	No	Nil	Yes	Yes	No	No	No	Ink directly on container	No
04/10/2012-TH1	BAYM7406B	SAL75DQ6B	2012/10/04	7:00	Th 1	No	Nil	Yes	Yes	Yes	Yes	No	Ink directly on container	No
04/10/2012-TH2	BAYM7407B	SAL75G5M	2012/10/04	7:15	Th 2	No	Nil	Yes	Yes	Yes	Yes	No	Ink directly on container	Yes
05/10/2012-TH1	BAYM7408B	SAL75H9VB	2012/10/05	6:50	Th 1	No	Nil	Yes	Yes	No	No	No	Ink directly on container	No

Appendix 7

Quote for laboratory cost of the study

National Health Laboratory Service
University of the Witwatersrand, Johannesburg
INFECTION CONTROL SERVICES
Department of Clinical Microbiology and Infectious Diseases
Division of Hospital Epidemiology and Infection Control
Medical School Room 3T08, Level 3, Wits Medical School, 7 York Rd Parktown, Johannesburg 2193, Republic of South Africa.
PO Box 2115, Houghton 2041, South Africa Tel: (011) 489 8577 / 8579. Fax: (011) 489 8530

TO: ANDREAS VAN DEN HEEVER

FROM: WARREN LOWMAN
INFECTION CONTROL SERVICES LAB

SUBJECT: QUOTE – MICROBIAL CONTAMINATION OF MULTI-DOSE VIALS

DATE: 28 NOVEMBER 2011

Dear Andreas

The cost of the study, based on consumables to be used, and laboratory time spent in processing the samples will be as follows:

DESCRIPTION	METHOD	PRICE
Blood culture bottles	BacT/Alert	R20.00 per bottle
Biochemical ID Extended	Automated- MicroScan	R300.00
TOTAL per B/C & ID		**R320.00***
Total Estimated Cost	110 blood culture bottles with a 30% positivity rate (i.e. 33 identifications)	**R12 100.00**

*This is an approximate cost per positive sample. Negative samples will only incur the cost of a blood culture bottle

Please contact me if you require any further information.

Regards

Warren Lowman
MBBCh MMed (Micro) FC Path (SA)

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