REPRODUCTIVE HEALTH RISK EVALUATION IN NHLS HISTOPATHOLOGY LABORATORIES

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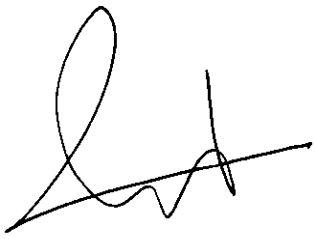
A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Master of Public Health (Occupational Hygiene).

Johannesburg, September 2013

DECLARATION

I, Gabriel Eduardo Mizan, declare that this research report is my own work. It is being submitted for the degree of Master of Public Health (Occupational Hygiene) at 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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ABSTRACT

Introduction

The National Health Laboratory Service (NHLS) is a public health laboratory network consisting of 349 diagnostic pathology laboratories which employ approximately 4200 laboratory personnel. These laboratory workers (the majority of whom are females) may be exposed to various occupational health hazards during the course of their work, including chemical, physical, biological, ergonomic and psychosocial hazards. Some of these hazards may specifically affect the reproductive ability of both male and female workers.

Study Objectives

The aim of this study was to identify and assess, based on field observations, interviews and measurements, the risk to reproductive health from occupational health hazards (focusing on chemical hazards) that might be present in histopathology laboratories of the NHLS.

It was expected that this study could sensitise, raise awareness and improve control strategies and procedures aimed at reducing reproductive health risks to both male and female workers in this particular work environment and in other NHLS laboratories.

Materials and Methods

This was a descriptive, cross-sectional study; the study population included five out of the fifteen existing NHLS histopathology laboratories in the country.

Due to the limited time and resources available for this study four out of the five histopathology laboratories sampled were selected from the Gauteng Province (closest to the researcher) and an additional one from the Northern Cape Province.

Results

The reproductive health risk assessment process detailed in this report, has identified worker's exposure to formaldehyde during specimen cut-up, specimen storage and during the process of disposal and making up of formaldehyde solution, as potentially high risk. It also identified exposure to xylene vapours during the automated staining process (particularly when replacing chemicals in the equipment), as potentially high risk.

Exposure to hazardous biological agents (HBAs) and various other chemical reagents, ergonomic stress and potential exposure to ionising radiation were identified as moderate reproductive health risks when performing specific histopathology laboratory processes.

Discussion

The outcome from the health risk assessment supported the conclusion from researchers reviewed in this study that reproductive health risks in the workplace warrant special consideration and exposure to specific hazards, such as organic solvents, might require the implementation of special measures to protect in particular, but not exclusively, pregnant workers.

Some of the limitations related to this study include: limited research data on reproductive health and the difficulty of inferring from animal studies to human reproduction; another problem relates to the use of occupational exposure limits (OELs) as benchmark for acceptable or over-exposure, as OELs might be determined without sufficient consideration of reproductive health endpoints.

Due to the limited scope of this study only the major chemical hazards identified (formaldehyde and organic solvents, including xylene) could be sampled.

Recommendations

Protection of laboratory workers from reproductive health hazards should follow the standard occupational hygiene hierarchy of control practice, i.e. substitution and engineering methods should get precedence over strategies that rely on personal protective equipment.

Although the substitution of hazardous substances such as formaldehyde and xylene in pathology laboratories appears possible, the health and safety implications of using substitutes must be investigated carefully.

Following observations made during this study it was recommended that local exhaust ventilation (LEV) systems should be maintained in good working order and their performance routinely tested, both by workers and by an external accredited body.

Administrative measures which may include work restrictions and worker transfer should be implemented with caution, and always after thorough consultation with the individual worker. Such measures, when implemented, should be activated even before pregnancy is confirmed to prevent exposure during the crucial period of early foetal growth. It was recommended that the NHLS review the current policy and safe working procedure on pregnancy to include both male and female workers within reproductive age.

In terms of personal protective equipment, it was recommended that when potential short-term, high exposure to formaldehyde or xylene is anticipated a half-mask respirator with the

appropriate filtering media is applied. Workers must be adequately trained and fit tested to ensure that maximum protection is achieved.

Additional information, more research data and detailed survey measurements will be required to substantiate the results of this assessment. In the meantime, the precautionary approach and best control practices should apply, to provide the maximum feasible protection for both males and female laboratory workers in their reproductive age.

ACKNOWLEDGMENTS

- *My Supervisor, Prof David Rees, for his consistent support and valuable comments*
- *My Supervisor, Dr Andrew Swanepoel, for his encouragement and support*
- *Histopathology laboratory managers and staff, for their consent to partake in this study and for their assistance and cooperation during laboratories walkthroughs, information gathering processes and chemical measurements*
- *NIOH Occupational Hygiene team members, for their assistance during laboratory visits and chemical measurements*
- *NHLS Health and Safety Manager, Mr David Jones, for facilitating the visits to the NHLS histopathology laboratories*
- *Mrs Kerry Wilson, for her valuable input during the initial stages of this study*

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ABBREVIATIONS

ACGIH – American Conference of Governmental Industrial Hygienists

AIHA – American Industrial Hygiene Association

CNS – Central Nervous System

CI – Confidence Interval

EI – Exposure Index

EPA – Environmental Protection Agency (USA)

HRA – Health Risk Assessment

HSE – Health and Safety Executive (UK)

HBA – Hazardous Biological Agents

IARC – International Agency for Research on Cancer

LOAEL – Lowest Observed Adverse Effect Level

LTA-OEL - Long-term average occupational exposure limit

mg/m^3 – milligrams per cubic metre

NOAEL – No Observed Adverse Effect Level

NHLS – National Health Laboratory Service

NIOH – National Institute for Occupational Health

NIOSH – National Institute for Occupational Safety and Health (USA)

OR – Odds Ratio

OEL – Occupational Exposure Limit

ORG – Occupational Reproductive Guideline

PPE – Personal Protective Equipment

ppm – Parts per Million

RH – Reproductive Health

SANAS – South African National Accreditation System

TTP – Time to Pregnancy

TLV – Threshold Limit Value

TWA – Time Weighted Average

VOC – Volatile Organic Compound

CHAPTER 1: INTRODUCTION AND LITERATURE REVIEW

The National Health Laboratory Service (NHLS) is a public health agency consisting of 349 diagnostic pathology laboratories. The organisation employs 6826 employees (as of March 2012) of whom about 4200 are laboratory personnel, and it provides services to 80% of the South African population (NHLS, 2012a). These laboratory workers (the majority of whom are females) may be exposed to various occupational health hazards during the course of their work which include: chemical hazards, such as organic solvents and acids; physical hazards, such as noise and radiation; biological hazards, for example blood pathogens and cell cultures; ergonomic hazards, including long periods of standing and manual material handling; psychosocial hazards, such as abnormal working hours, fatigue and stress. Some of these hazards may specifically affect the reproductive ability of both male and female workers.

Human reproduction is a highly complex process requiring coordinated interplay between different anatomic and physiologic factors. During pregnancy foetal tissues migrate, grow, regress and transform at an accelerated rate. These diverse changes in cell and tissue formation make the organism susceptible to adverse health effects, particularly during critical periods in its development (Frazier and Hage, 1998).

Despite the possible detrimental reproductive health effects related to exposure to hazards in the work environment, relatively little research has been devoted to this subject and only a few agents are known to be strongly associated with adverse reproductive health outcomes (Ladou, 2007).

The purpose of this study was to identify, assess and prioritise occupational hazards that may affect both female and male reproductive health, within the NHLS histopathology laboratories. These laboratories were targeted for this study due to the relatively high number of chemical substances utilised while performing routine tasks.

This hazard evaluation study formed part of a larger research project planned by the Epidemiology department of the NIOH to investigate specifically the association between time to pregnancy (TTP) and pregnancy outcomes in relation to self-reported occupational exposures in medical laboratories.

Literature Review

A reproductive health hazard is a chemical, physical, biological, ergonomic, or other type of stressor that alters the ability of a couple to achieve a successful pregnancy. This alteration may include effects on reproductive organs as well as effects on libido, sexual behaviour, hormonal activity or any physiological response that interferes with the capacity to fertilise. A developmental health hazard affects the developing organism, either before birth or postnatally. Such effects may include death, morphological malformations, reduced body weight, altered growth and impaired postnatal physical and mental development. These effects may result from exposure to risk factors of either parent prior to conception or exposure of the offspring in the womb or even postnatally (Frazier and Hage, 1998, Hughes et al., 2009). [1]

The effects of occupational risk factors on reproductive health outcomes have been highlighted in a number of studies although the mechanisms by which these outcomes are produced remain uncertain (Zhu et al., 2006, Figa-Talamanca, 2006, Wennborg et al., 2005, Khattak et al., 1999, Kimmel, 1993, Magnusson et al., 2004);

The research data related to the main reproductive health hazards encountered in laboratories have been reviewed and summarised below.

1.1 Chemical Hazards

Laboratory workers are exposed to a myriad of chemical substances while performing their daily tasks. Some of these chemicals have been found to be mutagenic, genotoxic or teratogenic in experimental animal studies. Occupational exposure of laboratory workers to chemicals has also been associated with cancer, reduced fecundity and other adverse reproductive outcomes (Halliday-Bell et al., 2010).

Strong evidence exists for possible reproductive effects of exposure to specific groups of chemicals, including anaesthetic gases, antineoplastic drugs, toxic metals, solvents and pesticides, while for others the evidence from research is inconclusive (Figa-Talamanca, 2006).

A large nationwide Danish cohort study involving 5425 laboratory workers and 21438 teachers found an increased risk of low birth weight (adjusted odds ratio (OR): 1.27, 95%

[1] *In this study, the term* **reproductive health hazard** *is inclusive and encompasses the term developmental health hazard.*

confidence interval (CI): 1.08-1.45) and small-for-gestational age (adjusted OR: 1.27, 95% CI: 1.02-1.52) for laboratory workers when compared with teachers (Halliday-Bell et al., 2010).

A cohort study followed by a nested case-control study conducted among workers in biomedical research and routine laboratories in Israel (4300 workers, 230 cancer cases) found an increased risk of cancer among female workers in general [risk ratio 2.2 (95% CI: 1.2-4.3)] and of breast cancer in particular [risk ratio 2.3 (1.1-4.70)]. The researchers postulated that the development of breast cancer is related to the effect of carcinogens on female reproductive hormones (Shaham et al., 2003b, Shaham et al., 2003a).

A systematic literature review examined the neurodevelopmental toxicity risks due to occupational exposure to industrial chemicals during pregnancy. The chemical substances studied fell into two major groups, organic solvents and pesticides. The study suggested that, despite the lack of occupational epidemiologic studies in this field, exposures that are not considered to be toxic in adults may still be harmful to foetal neurodevelopment. The researchers concluded, that the overall experimental and epidemiological evidence suggested that the substantial vulnerability of the developing nervous system to low concentrations of neurotoxic chemicals should lead to a strengthened emphasis on protection of pregnant workers (Julvez and Grandjean, 2009).
Due to the fact that the most commonly used chemical substances in the histopathology laboratories investigated are various organic solvents, particularly formalin (aqueous solution of formaldehyde) and xylene, the following sections discuss the scientific evidence found in the literature with regards to the reproductive health risk related to this group of substances.

Organic solvents

Most organic solvents readily cross the lipid barrier of the placenta and, to a lesser degree, the testes. They may also be secreted in breast milk. Thus, excessive occupational solvent exposure can pose a risk to the foetus prenatally and to the infant post-natally (Ladou, 2007, Frazier and Hage, 1998).

Organic solvents have been implicated in the aetiology of spontaneous abortions and malformations since the 1980s (Wennborg et al., 2000). However, evidence for paternal effects is much more limited than for maternal effects (Ladou, 2007).

Spontaneous abortions among women working in laboratories, as well as congenital malformations and birth weights of their children were examined in a retrospective case-referent study in Finland (in the spontaneous abortion study there were 535 women – 206

cases and 329 referents – and in the malformation study 141 women – 36 cases and 105 referents). The study found significant associations between spontaneous abortions and exposure to toluene (OR 4.7, 95% CI: 1.4-15.9), xylene (OR 3.1, CI: 1.3-7.5) and formalin (OR 3.5, CI: 1.1-11.2) among women who were exposed at least 3 days a week during the first trimester of pregnancy (Taskinen et al., 1994).

Pregnancy outcome following gestational exposure to organic solvents was investigated in a prospective study in Toronto, Canada. A total of 125 pregnant women who were exposed occupationally to organic solvents and seen during the first trimester were matched to 125 pregnant women who were exposed to a non-teratogenic agent. The most common occupations among the exposed women were factory worker (n=37) and laboratory technician (n=21). Significantly more major malformations occurred among foetuses of women exposed to organic solvents than controls (13 vs.1, relative risk, 13.0; 95% CI: 1.8-99.5). Twelve of the 13 malformations occurred among women who reported symptoms related to exposure to organic solvents (P<0.001). In addition, more of these exposed women had had a previous miscarriage while working with solvents than the controls (54/117 [46.2%] vs. 24/125 [19.2%]; p<0.001). The study concluded that occupational exposure to organic solvents during pregnancy increases the risk of foetal malformations and that symptomatic exposure appears to predict a higher risk (Khattak et al., 1999).

Pregnancy outcomes of female laboratory personnel working in Swedish biomedical research laboratories were investigated in a questionnaire-based study (n=1052). There was a slightly increased risk for spontaneous abortions among women working with chloroform (OR 2.3, 95% CI: 0.9-5.9), as well as an increase in weight for gestational age (LGA) when the mother had worked with solvents (OR 1.1, 95% CI: 0.3-4.0). The researchers stated that the results may indicate that solvents are not a homogenous group of chemicals but rather have different toxic effects on reproduction in general and on embryonal growth in particular, so that both increased and decreased birth weights can occur (Wennborg et al., 2002).

A retrospective study of solvent exposed women showed an association between occupational exposure during pregnancy and visual deficiencies in offspring, including both colour vision and visual acuity (Ladou, 2007).

Unfortunately, most of the organic solvents in commercial use have not been extensively studied among humans in terms of their potential to cause reproductive harm. Often animal and in vitro studies are the only predictors of potential adverse reproductive outcomes in humans (Frazier and Hage, 1998).

A major problem with the extrapolation from animals to humans is that animal studies typically use high doses of single solvents and a variety of routes of administration, while in the occupational setting, exposure usually occurs to multitude of solvents (mixed exposures) at much lower doses by inhalation (Lindbohm, 1995, Khattak et al., 1999, Frazier and Hage, 1998).

Another important weakness of human studies on solvent exposure is that most studies are retrospective and recall bias may affect the accuracy of assessment of foetal outcome. Moreover, the retrospective design of these studies does not allow validation of crucial details regarding the nature and extent of exposure and this information is often based on workers' own reports or crude estimates inferred from their occupation and/or the industry type (Lindbohm, 1995, Khattak et al., 1999).

A short review of pertinent research related to the two most common substances used in histopathology laboratories – formaldehyde and xylene – is given below.

Formaldehyde

Formaldehyde (CH_2O) is the most simple and reactive of all aldehydes. It has a pungent suffocating odour that is recognised by most human subjects at concentrations below 1 ppm (Viegas et al., 2010).

Since 2006, the International Agency for Research on Cancer classifies formaldehyde as carcinogenic to humans (Group 1), based on sufficient evidence in humans and experimental animals (IARC, 2006).

A study conducted among anatomy and pathology laboratory workers (n=50) in Portugal examined the relationship between occupational exposure to formaldehyde and genotoxic effects. The study found a significant increase in the frequency of micronucleolus (MN) in peripheral blood lymphocytes ($p<0.001$) and in epithelial buccal mucosa cells ($p<0.005$) among the laboratory workers when compared with the control group. (The frequency of MN is used as a sensitive endpoint for the detection of induced formaldehyde genotoxicity.) The study also found a significant positive correlation between MN frequency and duration of exposure to formaldehyde as well as with ceiling (peak) concentrations of exposure (Viegas et al., 2010)

The American Conference of Governmental Industrial Hygienists (ACGIH) reviewed the research related to formaldehyde and concluded that there was a lack of conclusive evidence that exposure to this substance caused adverse reproductive or developmental effects in animals or humans (ACGIH, 2001).

A review on formaldehyde published by the United Nations Environmental Programme (UNEP) concluded that "no specific indications of a specific toxicity of formaldehyde to foetal development and no effects on reproductive organs were observed by chronic oral administration of formaldehyde to male and female rats. Amounts of formaldehyde, which produce marked toxic effects at the portal of entry do not lead to an appreciable systemic dose and thus do not produce systemic toxicity" (UNEP, 2002).

The outcome of several studies reviewed by Frazier and Hage is inconclusive with regards to formaldehyde reproductive toxicity, with a few studies showing a possible adverse effect while others show no significant decrease in reproductive health resulting from exposure. For example in one of the studies quoted by Frazier and Hage, administration of formaldehyde to rats at 10 mg/kg/day for 30 days resulted in a significant fall in sperm motility, viability and count. In another study, conducted on hospital autopsy workers who were intermittently exposed to formaldehyde levels from 3 – 40 ppm, no significant reduction of sperm count, nor any abnormal sperm morphology was found (Frazier and Hage, 1998).

A questionnaire based study conducted in China on wives of 302 male workers occupationally exposed to formaldehyde and 305 referent controls found a significant increased risk of prolonged time to pregnancy (P = 0.034; OR 2.828; 95% CI: 1.081-7.406) and significantly elevated risk of spontaneous abortion (P = 0.021; OR 1.916; 95% CI: 1.103-3.329). It was also observed that reproductive toxicity due to formaldehyde exposure was dose dependent and the researchers concluded that the study strengthen the hypothesis that paternal occupational exposure to formaldehyde has adverse effects on reproductive outcomes (Wang et al., 2012).

Formaldehyde is listed as a <u>suspected</u> reproductive health hazard under the State of California Safe Drinking Water and Toxic Enforcement Act of 1986 (State of California, 2010).

Xylene

Xylene is a clear, flammable liquid with an aromatic hydrocarbon odour that may be detected at thresholds ranging from 0.07 to 40 ppm (0.31 to 176.4 mg/m^3). It occurs in three isometric forms: ortho (o-xylene), meta (m-xylene) and para (p-xylene) (ACGIH, 2001).

The main effect of inhaling xylene vapour is depression of the central nervous system (CNS), with symptoms such as headache, dizziness, nausea and vomiting. It can also cause eye, nose and throat irritation and high or chronic exposure can damage the lung, liver and kidney. Frequent contact with the skin can cause irritation, flaking, cracking and dermatitis

(Kandyala et al., 2010). It has been shown that xylene can cross the placental barrier and that it may be genotoxic and mutagenic (Frazier and Hage, 1998).

IARC reviewed the evidence for the carcinogenicity of xylene and concluded that there is inadequate evidence in both humans and in experimental animals for the carcinogenicity of xylenes. It therefore classifies xylenes in Group 3, i.e. not classifiable as to their carcinogenicity to humans (IARC, 1999).

Frazier and Hage reviewed several animal and human studies related to xylene and reproductive health and found mixed results. The researchers concluded that, although animal studies show that exposure to this substance may cause hormonal changes, there are insufficient data to determine whether women exposed to xylene as a single agent will show menstrual disturbances or reduced fertility. The researchers also state that embryotoxicity was observed in animal studies and quotes the Finnish study (mentioned earlier) that found significant increase in spontaneous abortion among women working with xylene (Frazier and Hage, 1998).

A comprehensive toxicological review of xylene, including reproductive / developmental studies, was undertaken by the US Environmental Protection Agency (EPA). Inhalation reproductive toxicity studies reported no adverse effects in groups of male and female rats exposed to 60, 250 and 500 ppm (264.6, 1102.5 and 2205 mg/m^3 respectively).

A number of inhalation toxicity studies are reported in the same EPA document from which dose-response levels for biologically significant developmental effects, including skeletal, visceral, and external malformations were calculated. Six of these studies were conducted on rats and the calculated dose-response for NOAEL (No Observed Adverse Effect Level) ranged from 230 to 600 ppm (1014 – 2646 mg/m^3) of mixed xylenes, except from one study where 35 ppm (154 mg/m^3) was calculated as the NOAEL for o-xylene with relation to decreased foetal body weight. The dose response for LOAEL (Lowest Observed Adverse Effect Level) that was derived from the same studies ranged from 500 to 1600 ppm (2205 – 7056 mg/m^3). The calculated NOAEL derived from one developmental study on rabbits was 115 ppm (507 mg/m^3); however, exposure to p-xylene level of 230 ppm (1014 mg/m^3) produced severe maternal toxicity and no live foetuses were produced (EPA, 2003). For comparison, the South African occupational exposure limit (OEL) for xylene is 100 ppm (435 mg/m^3) (South Africa Department of Labour, 1995).

Kandyala et al. reviewed the health effects of xylene and its use in histopathology laboratories. They concluded that although the available animal information is insufficient to connect xylene with reproductive effects, inhalation of this substance by the mother can

reach the developing foetus and produce fetotoxic effects such as delayed ossification and behavioural effects. The researchers recommended that pregnant and nursing women minimize their exposure to xylene (Kandyala et al., 2010).

Evaluation of the effects of xylene on reproduction was also carried out by the Health Council of the Netherlands. The Health Council's committee recommended to classify xylene within category 3 chemicals (substances which cause concern for humans owing to possible developmental effects) and to label xylene with the risk phrase R63 (possible risk of harm to the unborn child) according to the Directive 93/21/EEC of the European Union. It further recommended, that due to a lack of appropriate data, xylene should not be classified with regards to effects on fertility and effects during lactation (Health Council of the Netherlands, 2000).

Like formaldehyde, xylene is listed as a suspected reproductive health hazard under the State of California Safe Drinking Water and Toxic Enforcement Act of 1986 (State of California, 2010).

1.2 Ergonomic Factors, Shift Work and Psychosocial Factors

Activities such as lifting, pushing, pulling and bending during pregnancy carry a risk of accidental injury, also due to loss of balance, from slipping or from direct injury by the load. As pregnancy advances, the centre of gravity shifts posteriorly and the protuberant abdomen interferes with lifting objects in front of the body. Awkward twisting or asymmetric movements may be needed to accomplish the lift, and the risk of slipping may be increased. Overexertion may result in acute strain injuries, especially to the back. Moreover, pregnant women tend to tire easily and may alter their work habits to minimize fatigue, placing their back at increased vulnerability to acute and chronic injury. Women with underlying anatomic abnormalities may be particularly vulnerable to pregnancy complications of overexertion (Frazier and Hage, 1998).

Figa-Talamanca, as well as Frazier and Hage, in their review of literature on occupational reproductive risk factors, concluded that, although physical activity in itself may not be considered a proven risk factor for pregnancy, certain ergonomic characteristics of work (e.g. heavy lifting, prolonged standing, long work hours) might increase the risk of negative pregnancy outcome, especially in women with other risk factors or in the presence of other work-related risks (Figa-Talamanca, 2006, Frazier and Hage, 1998).

In a large study conducted in Montreal, the relationship between spontaneous abortion (n=5010), stillbirth without congenital defect, and working conditions was analysed in 22613

previous pregnancies of 56067 women interviewed immediately after termination of their current (latest) pregnancy. Ratios of observed (O) to expected (E) foetal deaths were calculated at four stages of pregnancy in 60 occupational groups and six main sectors for women whose work entailed various physical demands, environmental conditions and exposure to chemicals. Significantly increased O/E ratios for abortion were found in women exposed to various high levels of physical stress, particularly lifting of heavy weights more than 15 times a day (1.45, p<0.01) other physical effort (1.37, p<0.01) and standing more than eight hours a day (1.18, p<0.01). An increased O/E ratios for abortion was also found in relation to working 46 or more hours a week (1.19, p<0.01) and rotating shift work (1.25, p<0.01) (McDonald et al., 1988).

A case-control study conducted in two public hospitals in Spain investigated the effect of physical workload and psychological demand on preterm birth (228 preterm births and 348 controls). The variables that were used to characterise physical workload were standing position, strenuous posture, load carrying (more than 5kg) and an indicator of physical workload which was a combination of the previous ones. The variables that were used to characterise the psychosocial work environment were psychological demand, weekly working hours and daily time spent commuting between home and work. The study concluded that exposure to medium or high level physical workload increases the risk of preterm birth, with an adjusted odds ratio of 1.59 and 2.31, respectively. Psychological demands were not found to be associated with preterm birth (Escriba-Aguir et al., 2001).

When measuring daily physical activity in pregnancy, it is necessary to include the different domains, i.e. occupational, household, leisure and commuting to adequately appreciate their influence on reproductive outcomes. A systematic review study attempting to consider these four domains analysed 22 articles that were selected on methodological quality from an initial list of 52 articles that studied the association between maternal physical activity and low birth weight, preterm birth and intrauterine growth restriction. Only two, of the 22 articles, did not detect a significant association between physical activity and the outcomes studied. The results of the review supported the hypothesis that both excessive and insufficient physical activity impact negatively on pregnancy outcomes. The study, conducted in Brazil, also highlighted that socioeconomic and cultural differences restricted the use of questionnaires published in developed countries (that deal, for example, with recreational sports) by developing countries (low socioeconomic level), that are predominantly occupied with household physical activities (Takito et al., 2009).

Varying work schedules (including rotating shifts and night-work) may present special risks to pregnant women as a result of maternal hormonal disturbances arising from sleep

deprivation or circadian rhythm disruption which might impair foetal growth or lead to complications of pregnancy (Bonzini et al., 2011).

A systematic review of available epidemiological studies (from 1966 to 2010) was conducted to ascertain the association of shift work with preterm delivery (PTD), low birth weight (LBW), small for gestational age (SGA) and pre-eclampsia (gestational hypertension). The findings, after adjusting for confounders and poor methodological quality observed in some studies, suggested only small elevated risks for PTD (RR 1.03, 95% CI 0.93-1.14), LBW (RR 1.27, 95% CI 0.93-1.74) and SGA (RR 1.12, 95% CI 1.03-1.22); only little evidence was found in the literature reviewed on the effects of shift work on pre-eclampsia. Overall, the researchers concluded that the available evidence does not make a compelling case for mandatory restrictions on shift work in pregnancy. However, they postulated that further studies are needed to address the question whether birth outcomes might be related to different types of work schedules (separating, for example, night workers from rotating shift workers). In the meantime, they suggested, that it would be prudent, to permit pregnant women, insofar as job circumstances allow, to reduce their exposure to shift and night work (Bonzini et al., 2011).

A study conducted among females in a semiconductor manufacturing company (n=440) in China found, after controlling for potential confounding factors, that the childbearing rates among women who had consistent daytime work schedules were significantly higher than those of shift workers (OR 1.7, 95% CI 1.01-3.0). The study also found that newborns within the lightest birth weight quintile were significantly more likely to be born to mothers who were on persistent rotating shifts (OR 4.3, 95% CI 1.1-16.8). The study concluded that shift work exposure was significantly associated with both decreased childbearing and lighter birth weight and suggested cautious work scheduling for female workers preparing for pregnancy (Lin et al., 2011).

Some of the problems or weaknesses related to the studies on ergonomic stress and reproductive health have been highlighted by Frazier and Hage. (A) The beneficial effects found in studies of moderate voluntary exercise are in contrast to multiple occupational studies for which an adverse relationship between physically demanding work and reproductive outcome has been reported. The seemingly opposite conclusions from studies of leisure-time versus occupational exertion may have occurred because the two types of exertion are different in some important ways (e.g. activity duration, prolonged standing typical in occupational settings, hydration, etc). (B) There are many sources of bias, such as confounding and selection bias. For example, people employed in physically demanding jobs usually earn less and are from a lower socioeconomic status (which is a reproductive health

risk factor on its own); and recall bias (response bias) which has been often documented in retrospective studies (Frazier and Hage, 1998). The "healthy pregnant worker effect" might also introduce bias to studies. For example, Bonzi et al. postulated that the risks in women who continue to work shifts late in pregnancy might be underestimated as healthier women with uncomplicated pregnancies are less likely to modify their work schedules (Bonzini et al., 2011).

1.3 Hazardous Biological Agents

Infections have been reported to cause spontaneous abortion and foetal death, preterm birth, intrauterine growth restriction and birth defects, including abnormalities of the central nervous system, ophthalmologic manifestations and congenital heart defects. The type of adverse effects may vary with gestational age at the time of infection (Morales-Suarez-Varela et al., 2010). However for many of the infections that can impair reproductive processes, transmission does not occur from occupational exposures (Frazier and Hage, 1998).

Two questionnaire-based studies conducted among female biomedical research laboratory workers in Sweden found a positive association between exposure to bacteria and adverse reproductive outcomes. The first study that investigated possible hazardous effects of laboratory work on reproduction from 1990 to 1994, found an increased **preterm** *birth odds ratio of 2.7 (95% CI 1.2-6.5) for a model that included the use of bacteria as an explanatory variable (Wennborg et al., 2000). The second study compared female university personnel performing laboratory work with non-laboratory female personnel (249 and 613 pregnancies, respectively) and found an increased* **post-term** *births OR of 2.7 (95% CI 1.0-7.4) for laboratory work with bacteria (Wennborg et al., 2002). The number of cases with the observed effect in both studies was relatively small (9 and 19 cases, respectively).*

Frazier and Hage reviewed the available data on reproductive risks from various infectious agents and non-infectious biological products. They postulated that laboratory workers (and other occupational groups) who process specimens may be at increased risk of tuberculosis (TB). However, they also stated that the data suggest that pregnant women infected with TB are at no increased risk of TB progression or extra-pulmonary disease when compared with their non-pregnant counterparts and, therefore, congenital TB is unlikely to occur in mothers with only pulmonary TB (Frazier and Hage, 1998).

In terms of non-infectious biological products, a potential risk for workers in histopathology laboratories is the handling of malignant cells. The researchers concluded that, although some studies have noted alterations in polymorphonuclear function during pregnancy,

pregnancy in itself was not considered to convey clinically threatening immunosuppression in an otherwise healthy person. The researchers recommended that pregnant workers should use similar precautions to all workers to avoid percutaneous exposure to body tissues or blood, and additional restrictions on handling malignant cells are not required (Frazier and Hage, 1998).

1.4 Ionizing Radiation

Ionizing radiation can injure the developing embryo due to cell death or chromosome injury. The most critical exposure period is 8-15 weeks after fertilization. Before implantation, the mammalian embryo is insensitive to the teratogenic and growth-retarding effects of radiation and sensitive to the lethal effects. Permanent growth retardation due to radiation is more severe after mid-gestation. The central nervous system, due to its extended periods of organogenesis and histogenesis, retains the greatest sensitivity of all organ systems to the detrimental effects of ionizing radiation through the later foetal stages (Gilbert-Barness, 2010).

The effects of parental radiation depend on the dose received and the amount delivered to the gonads while the adverse effects on the developing foetus depend on the dose delivered in uterus and on gestational age. In addition, specific types of ionizing radiation (e.g. X-ray, α or β particles) have different routes of exposure and different energy levels, but if sufficient dose reaches a target tissue, a basic profile of toxic effects is thought to occur, regardless of the radiation source. In contrast to other effects, the mutagenic and carcinogenic effects of ionising radiation are not considered to have a threshold (Frazier and Hage, 1998).

Kumar reviewed various studies on occupational exposure associated with reproductive dysfunction and reported that a large number of experimental data were available on the adverse effects of radiation on the reproductive system of both males and females from various animal species. However, only limited data were available from studies on humans with radiation exposure (Kumar, 2004).

Adriaens et al. in a review article on ovarian radiation sensitivity and the genetic hazard of ionizing radiation also noted that human data on the risks of genetically transmissible diseases following exposure of female germ cells to ionizing radiation is scarce and derived mainly from medical or accidental exposure. They found that congenital anomalies have been observed from animal studies after exposure to high radiation doses (1 – 5 Gy), but advised that extrapolation of these data to humans requires caution. They stated that most epidemiological studies found little evidence of genetic diseases at the doses at which medical, occupational or accidental exposure occurred. However, they concluded, that the

fact that genetic effects were observed in irradiated animals suggests that these could also occur in humans. Nonetheless, the probability of such events remains low compared to "spontaneous" risks of genetic effects (Adriaens et al., 2009).

A prospective cohort study conducted in Denmark during 1997-2003 investigated various pregnancy outcomes in female laboratory technicians (n=1025) compared to female teachers (n=8037) as reference subjects. The study found that laboratory technicians working with radioimmunoassay and radiolabelling had an increased risk of preterm birth (OR 2.2, 95% CI 0.8-6.2 for radioimmunoassay and OR 1.9, CI 0.8-4.6 for radiolabelling) as well as increased risk for major malformations (Hazard Ratio, HR 2.1, 95% CI 1.0-4.7 for radioimmunoassay and HR 1.8, 95% CI 0.9-3.7 for radiolabelling). The ORs for preterm birth doubled for women working with these tasks every day or several times a week. However, the researchers noted that the monitoring data on the radioisotopes obtained from the Danish National Institute of Radiation Hygiene did not show excess exposure for the laboratory workers who were at potential risk and they suggested that further investigation is warranted. Nonetheless they also recommended that laboratory technicians should take precautions to protect themselves when working with radioisotopes (Zhu et al., 2006).

A retrospective study conducted in four Swedish universities (1970-1989) compared the offspring of fathers that worked in laboratories (n=2281) with offspring of fathers with no laboratory work (n=1909). The study found an elevated risk for high birth weight in relation to work with radioactive isotopes (OR 1.6, 95% CI 1.0-2.4). Their findings were in contrast with a previous study (Shea and Little, 1997) that observed a weak association between paternal exposure to radiation and **low** *birth weight (Magnusson et al., 2006).*

Frazier and Hage reviewed the studies on radiation and reproductive health and concluded that only limited information was available concerning human reproductive hazards from specific radioisotopes. However, the following were identified as teratogenic: ^{131}I, ^{211}At, ^{144}Cs, ^{137}Cs, ^{252}Cf, ^{3}H, ^{32}P, ^{89}Sr, ^{90}Sr, and ^{233}U. They suggested that any radionuclide should be considered potentially teratogenic if it can be absorbed into the body and is capable of emitting sufficient radiation dose to the embryo or foetus (Frazier and Hage, 1998).

With regards to X-ray radiation, it has been estimated that 1-2 rad (0.01-0.02 Gy) of in uterus exposure increases the risk of childhood leukaemia by 50% – 100%, but not all the studies reviewed supported this (Frazier and Hage, 1998).

Figa-Talamanca, in her review of occupational risk factors and reproductive health of women, stated that exposure to ionizing radiation in prenatal life is a known risk factor for foetal death and congenital defects and that it is widely accepted that women should avoid

all exposure to ionizing radiation in the periconceptional period (i.e. even before the woman is aware of her pregnancy), as well as during gestation. However, she also stated that available evidence suggested that exposure of female health care personnel, prior to conception, within the prescribed limits, did not constitute a risk factor for reproductive health (Figa-Talamanca, 2006).

Table 1.1 summarises the research data obtained on important reproductive health hazards which might be encountered during laboratory work.

Table 1.1: Summary of Reproductive Health Hazards Related to Laboratory Work

Reproductive health hazard	**Main reproductive health effects based on the literature**
Chemicals: organic solvents	*Results from several studies indicate a significant association between exposure to organic solvents and spontaneous abortions, as well as an increased risk of congenital malformations and change in birth weight, although problems exist in extrapolation from animal studies to humans and from single solvent to mixed exposure, as well as general lack of information regarding the nature and extent of worker exposure (Wennborg et al., 2000, Taskinen et al., 1994, Khattak et al., 1999, Wennborg et al., 2002, Frazier and Hage, 1998, Lindbohm, 1995, Ladou, 2007)*
Chemicals: xylene	*Animal studies indicate that xylene might be embryotoxic although there are only few human studies that show direct link between this substance and human reproduction. The most probable effects on humans reproductive health appear to be spontaneous abortion and decreased foetal body weight (Taskinen et al., 1994, Frazier and Hage, 1998, EPA, 2003, Kandyala et al., 2010, Health Council of the Netherlands, 2000, State of California, 2010)*
Chemicals: formaldehyde	*Although earlier studies appear to show inconclusive evidence regarding reproductive health effects of formaldehyde, more recent studies seem to show an increased risk, particularly with regards to spontaneous abortions, prolonged time to pregnancy and genotoxicity; Formaldehyde is classified by IARC as a human carcinogen (Viegas et al., 2010, ACGIH, 2001, UNEP, 2002, Frazier and Hage, 1998, Wang et al., 2012, State of California, 2010)*
Biological agents	*Although biological agents are known to cause detrimental reproductive effects, research data linking exposure to hazardous biological agents at work and reproductive health is scanty. Two studies showed an association between exposure to bacteria and pre or post-term births; another study suggested a possible link between handling of malignant cells and some immunological effects (Morales-Suarez-Varela et al., 2010) (Frazier and Hage, 1998, Wennborg et al., 2000, Wennborg et al., 2002)*
Ergonomic stress	*High levels of physical demand at work (including lifting and prolonged standing) were significantly linked in several studies to adverse reproductive health effects such as abortions and preterm birth (Figa-Talamanca, 2006, Frazier and Hage, 1998, McDonald et al., 1988, Escriba-Aguir et al., 2001, Takito et al., 2009);* *Shift and night work also appear to have a negative impact on reproduction, although the information available is insufficient to substantiate the link (Bonzini et al., 2011, Lin et al., 2011)*

Table 1.1 (cont'd): Summary of Reproductive Health Hazards Related to Laboratory Work

Reproductive health hazard	Main reproductive health effects based on the literature
Ionizing radiation	*A large number of animal studies are available on the adverse effects of radiation on the reproductive system of both male and female species, however only limited data (mainly from accidental and medical exposure) is available from human studies. Two studies conducted in Scandinavian countries suggested a possible association between laboratory work with radionuclides and reproductive effects such as preterm birth, congenital defects and abnormal birth weight; there is also evidence that exposure to X-ray radiation increases the risk of childhood leukaemia; most studies however indicate that effects of ionising radiation appear at higher doses than normally encountered in an occupational environment (Gilbert-Barness, 2010, Frazier and Hage, 1998, Kumar, 2004, Adriaens et al., 2009, Zhu et al., 2006, Magnusson et al., 2006, Figa-Talamanca, 2006)*

In summary, *despite the general paucity of human studies on occupational exposure to hazards in laboratories and the impact on reproductive health, there seems to be sufficient data to elicit concern regarding exposure to organic solvents, including xylene and formaldehyde, ionizing radiation, hazardous biological agents and ergonomic stress.*

1.5 Reproductive Health Risk Assessment

Health risk assessments are a way of using existing toxicity, epidemiology, environmental and exposure information to describe the likely health outcome in terms that are useful to risk managers (Paustenbach, 1990).

The aim of occupational health risk assessments (HRA) is to systematically and proactively identify occupational hazards in the workplace, assess their potential risks to health and determine appropriate control measures to protect the health and wellbeing of workers (ICMM, 2009).

Over the years, various models for HRA have been suggested. A model presented by the US National Research Council incorporates four basic steps: (1) hazard identification / characterization – the presence and quantity of hazards and their effect on human health are determined; (2) dose-response assessment – establishing the relationship between the level or concentration of a contaminant and the incidence of adverse health outcome; (3) exposure assessment – determining the conditions of exposure (who is exposed, routes of exposure and doses); and (4) risk characterization – estimating the likelihood of an adverse

outcome in the exposed population. The four steps are linked with the overall purpose being management and controlling the risk to the workers, as shown schematically below (Sadhra and Rampal, 1999):

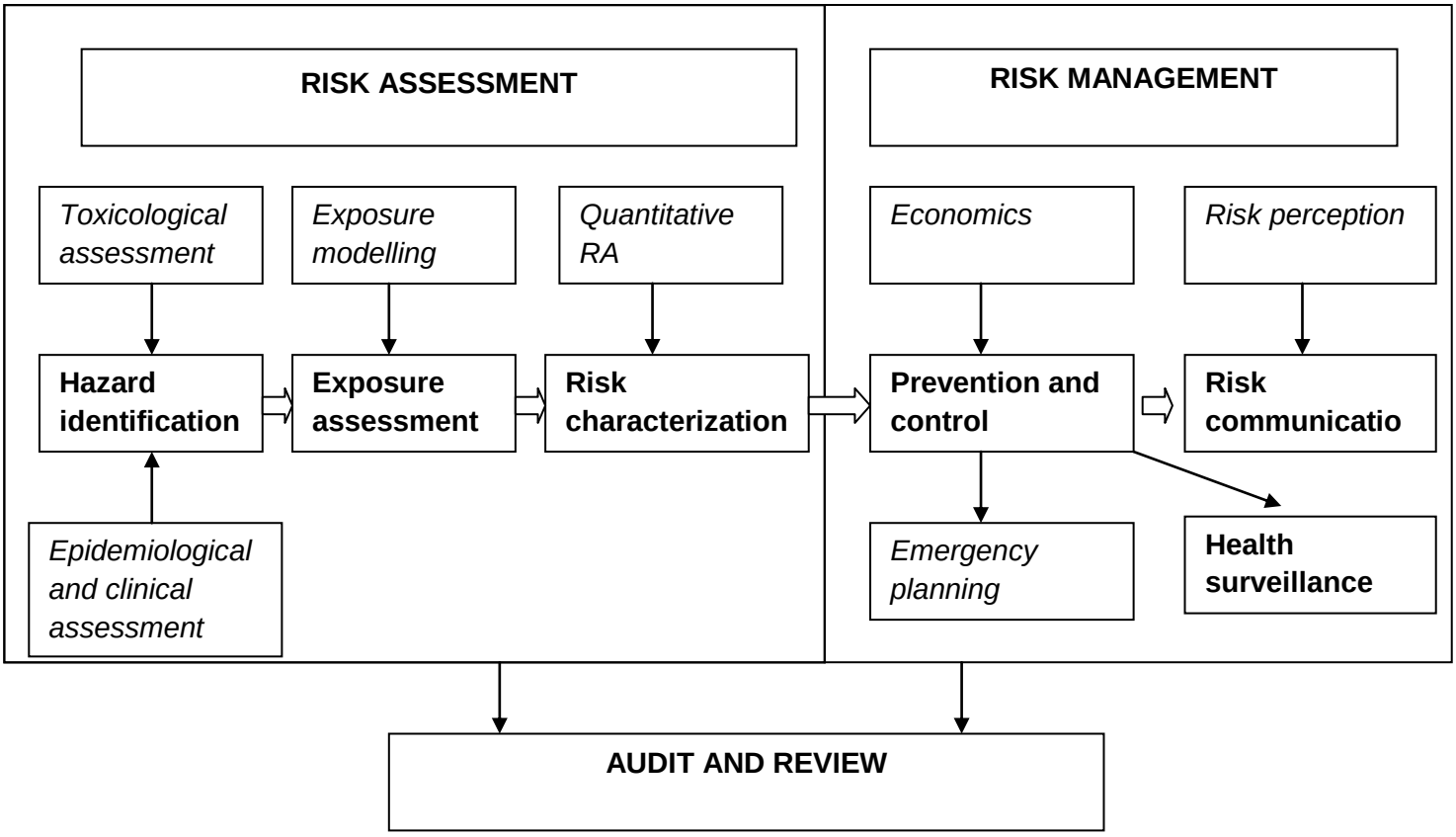


Figure 1.1: Model for risk assessment and management (Sadhra and Rampal, 1999)

Current approaches to risk assessment in reproductive toxicity involve the determination of No Observed Adverse Effect Level (NOAEL), Lowest Observed Adverse Effect Level (LOAEL) and the application of Uncertainty Factors (UF) to account for differences between experimental animals and humans, variability in sensitivity within human populations and other factors (Kimmel, 1993, Jankovic and Drake, 1996).

The European Chemical Agency (ECHA), in its comprehensive guidance document on the implementation of the European REACH Regulations states that reproductive toxicity endpoints should be considered collectively, using the weight of evidence approach to establish the most relevant endpoint and its NOAEL or Critical Effect Dose (CED) to be used in risk assessments. A weight of evidence assessment involves the consideration of all data that are available (including non-human, animal and human data) and may be relevant to reproductive toxicity. There can be no firm rules to the conduct of a weight of evidence assessment as this process involves expert judgment and because of the mix and differing

reliability of information available. Also, the weight of evidence assessment should consider all toxicity endpoints together, and not look at reproductive toxicity in isolation (European Chemicals Agency, 2008).

Very limited information could be found in the literature on reproductive health risk assessment and the existing information relates mostly to chemical hazards. Moreover, there are conflicting points of view about how to determine whether an agent is a reproductive or developmental hazard, on methods to conduct experimentation, on extrapolation of animal data to humans, on how to describe reproductive health risks, and how to reach management decisions that protect reproductive and developmental health (Frazier and Hage, 1998).

The use of Occupational Exposure Limits in the Health Risk Assessment

One major problem related to exposure assessment is the need for an established, well-researched Occupational Exposure Limits (OELs). However, authoritative or regulatory OELs are available for only about 600 of the 70 000 or so chemicals used in industry. The lack of data prompted some organisations to develop in-house OELs were there are no established OELs or when the regulatory or authoritative OEL is outdated. In the absence of a formal OEL from a regulatory, authoritative, or internal source, the occupational hygienist may need to establish a "working OEL", which is an informal limit created during the assessment to enable the hygienist to differentiate acceptable from unacceptable exposures. A working OEL will be based on whatever data are available, including epidemiological or toxicological data, or on another environmental agent for which there is an established OEL. Working OELs might be stated in ranges or include large safety margins to account for the insufficient data (AIHA, 2006).

Also, OELs are set for single substances while workplace exposures are more often than not set for a mixture of substances that may have synergistic effects.

Another problem related specifically to reproductive chemical hazards is that established OELs frequently do not take into consideration reproductive endpoints that occur well below the thresholds established for other toxic effects. An attempt to assign occupational reproductive guideline (ORG) limits to a list of 213 potential reproductive toxins was presented by Jankovic and Drake. The dose-response assessment involved several assumptions, such as that reproductive effects have thresholds (in the case of carcinogens, an additional uncertainty factor of X10 was applied), and that animal data are a reasonable human predictor (an uncertainty factor of X10 was used for animal-to-human extrapolation). The majority of the ORGs generated were based on animal reproductive NOAELs or

LOAELs. The researchers concluded that, for substances with existing Threshold Limit Values (TLVs), 25% (24/95) have established exposure limits equal to or lower than the calculated ORG and were assumed to be adequately protective for reproductive effects, leaving 75% that have established limits greater than the ORG and therefore the existing TLV seems to provide inadequate protection against reproductive effects (Jankovic and Drake, 1996).

Health Risk Prioritization and Hazard Control

The aim of any health risk assessment is to control or mitigate unacceptable occupational exposure risks. Implementing long-term control solutions often requires significant time and capital expenditures. It is therefore important that identified health risks are prioritized with regards to the actions that are required, whether it is implementing immediate controls (when the assessment reveals high and unacceptable exposures) or gathering additional information (when the risk is uncertain and the exposure has not been judged as unacceptable). Occupational hygiene practice advocates the use of a ***hierarchy of control*** *when implementing permanent exposure control strategies. This means that control measures should be implemented according to the following priority (AIHA, 2006):*

- *Elimination of the process, equipment or materials that give rise to exposure;*
- *Substitution with a less hazardous process, equipment or material;*
- *Engineering controls, such as process modification, automation, enclosure, shielding, exhaust ventilation, shielding, insulation;*
- *Work practices and procedures, employee training and other administrative controls;*
- *Proper selection, fitting and use of personal protective equipment (PPE).*

1.6 Aim and Objectives

The study in the NHLS histopathology laboratories was motivated by the fact that no other studies were found in the literature on the nature and extent of reproductive health hazards in South African health laboratories, in general, and in histopathology laboratories, in particular, where exposure to some fairly well established reproductive health hazards was anticipated. The aim of this study was therefore to identify and assess the risk to reproductive health from occupational health hazards present in the histopathology laboratories of the NHLS. The study objectives are listed below:

Study Objectives

1. *To identify potential reproductive health hazards related to various tasks performed in NHLS histopathology laboratories using field observations, interviews and measurements;*
2. *To assess the workers' exposure to some important chemical hazards present in the identified laboratories using air sampling measurements;*
3. *To assess the potential reproductive health risk to workers using a standard occupational health risk assessment tool, and rank the hazards identified taking in consideration the extent and frequency of exposure and the severity of the health effect.*

CHAPTER 2: MATERIALS AND METHODS

2.1 Study Design

This was a descriptive, cross-sectional study.

2.2 Study Population

Five NHLS histopathology laboratories, out of the total 15 existing laboratories, were selected for this study. Due to the limited time and resources available, four of the five histopathology laboratories were from the Gauteng Province (closest to the researcher) and an additional laboratory was from the Northern Cape Province. All five laboratories operated within hospitals and the four from Gauteng were also linked to academic institutions. The fifth laboratory was a smaller, non-academic laboratory.

2.3 Risk Assessment Tool

The risk assessment tool used in this study was adapted from two sources: the American Industrial Hygiene Association (AIHA) strategy for assessing and managing occupational exposures (AIHA, 2006) and the UK Health and Safety Executive monitoring strategies for toxic substances (HSE, 2006). The steps of the assessment are briefly described below.

Information Gathering and Hazard Characterization

The first step in the health risk assessment (HRA) was a thorough gathering of information and characterization of the hazards. The information from the five laboratories that were sampled was collected by means of walkthrough observations and interviews with laboratory managers and workers. The interviews included questions regarding the various processes that are conducted within the laboratory, job categories and tasks performed per job category, chemical substances used and other relevant health and safety information (see Appendix 1 for the standard interview form). A hazard capturing tool was utilised to capture the hazard information collected per task/process performed in a tabulated format. This was therefore a task/process-based risk assessment.

It is important to mention that, although the focus was on potential reproductive health hazards, other occupational health and safety hazards that were encountered, were also recorded.

Assessing the Health Effect – Health Effect Rating

An important component of the HRA is evaluating the health effects (in this case the reproductive outcomes) of an occupational hygiene agent. Several general rating schemes have been suggested by researchers to categorize health effects based on available

toxicological and epidemiological data. The AIHA rating scheme, which has been used in this study, is given in Table 2.1.

Table 2.1: Health Effects Rating Scheme (AIHA, 2006)

Category	Health Effect
4	*Life-threatening or disabling injury or illness*
3	*Irreversible health effects of concern*
2	*Severe, reversible health effects of concern*
1	*Reversible health effects of concern*
0	*Reversible effects of little concern, or no known or suspected adverse health effects*

The AIHA advises that, in the absence of toxicological or epidemiological data, the health effects rating should be based on the agent's chemical or physical properties and its similarity to other agents with known health effects.

Four classes of potential reproductive health hazards were identified during the hazard identification process: hazardous chemical substances, particularly organic solvents, formaldehyde and xylene, hazardous biological agents, ergonomic stress and potential exposure to ionizing radiation. Based on the literature research described earlier in this report, and the AIHA rating scheme given in Table 2.1, the potential reproductive health hazards identified were assessed and rated as follows.

Table 2.2: Health Effects Rating for Reproductive Hazard Assessed in this Study

Reproductive health hazard	Health effect rating	Category
Chemicals: organic solvents, including xylene and formaldehyde	*Life-threatening or disabling injury or illness*	*4*
Biological agents	*Irreversible health effects of concern*	*3*
Ergonomic stress	*Irreversible health effects of concern*	*3*
Ionizing radiation	*Life-threatening or disabling injury or illness*	*4*

Exposure Assessment

Characterizing an exposure profile requires an estimate of the exposure and its variability; it can be quantitative (using measurements and various statistical methods to assess the validity of the data collected) or more qualitative, relying on knowledge, experience and professional judgement – or a combination of both qualitative and quantitative data. Once the exposure profile has been defined, it should be compared with an OEL to determine the acceptability of its risk. An **exposure rating** *is an estimate of the exposure levels relative to the OEL. In this study, the AIHA model of categorization for rating exposures was used and is shown in Table 2.3.*

Table 2.3: Exposure Rating Categorization (AIHA, 2006)

Category	Exposure Assessment
4	*Very High Exposure (levels > LTA-OEL*); frequent contact with stress at very high concentrations / levels*
3	*High Exposure (levels 50% - 100% LTA-OEL); frequent contact with stress at high concentrations / levels*
2	*Moderate Exposure (levels10% - 50% LTA-OEL); frequent contact with stress at low concentrations or infrequent contact with stress at high concentrations / levels*
1	*Low Exposure (levels<10% LTA-OEL); Infrequent contact with stress at low concentrations / levels*

** LTA-OEL: A long-term average occupational exposure limit.*

Health Risk Rating

A health risk may be defined as a combination of the potential health effect caused by an agent and the potential exposure, as given in the equation below (AIHA, 2006):

Equation 2.1: Health Risk Rating = Health Effect Rating X Exposure Rating

Taking into account the health effect rating and exposure rating schemes described earlier, the combined health risk rating can be calculated using the above formulae, or read directly from Table 2.4 or the matrix shown in Figure 2.1.

Table 2.4: Potential Health Risk Rating (AIHA, 2006)

Health Effect Rating					
4	*4*	**8**	**12**	**16**
3	*3*	**6**	**9**	**12**
2	*2*	*4*	**6**	**8**
1	*1*	*2*	*3*	*4*
	1	**2**	**3**	**4**
	Exposure Rating			

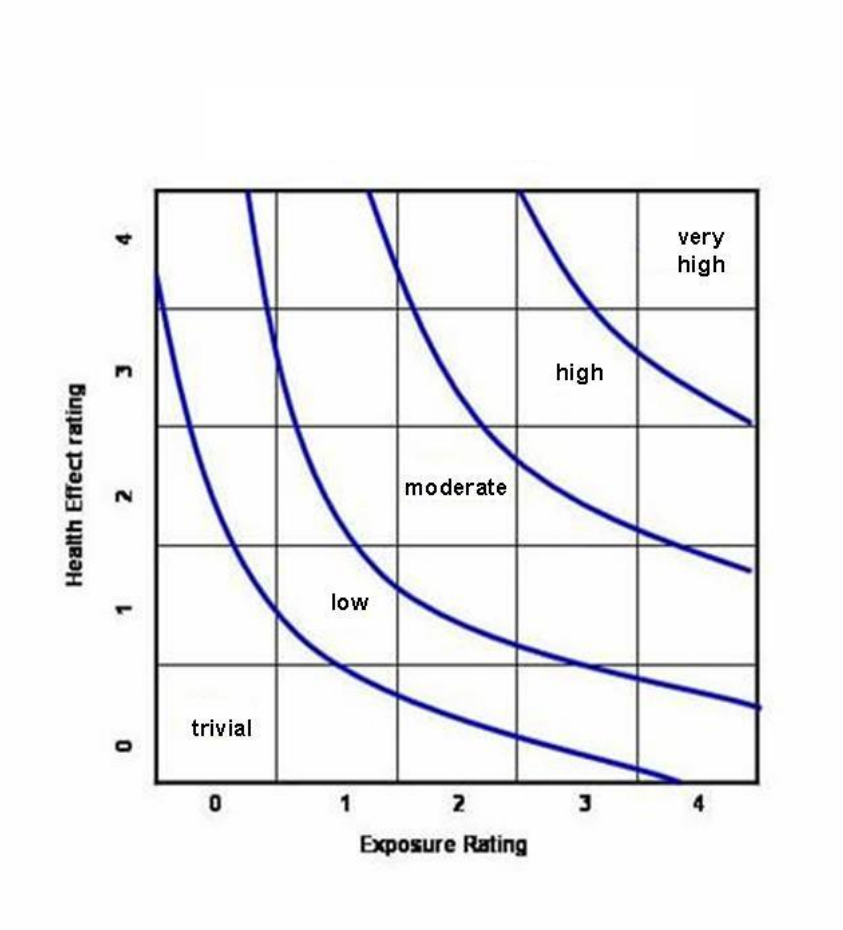


Figure 2.1: Potential health risk rating matrix (Hawkins, 1991)

Uncertainty and Information Gathering Priority Ranking

Uncertainty is a function of the confidence we have in the health effects and the exposure data, as well as the reliability of the existing control measures. Uncertainty was calculated in this study using the AIHA uncertainty rating scheme shown in Table 2.5.

Table 2.5: Uncertainty Rating (AIHA, 2006)

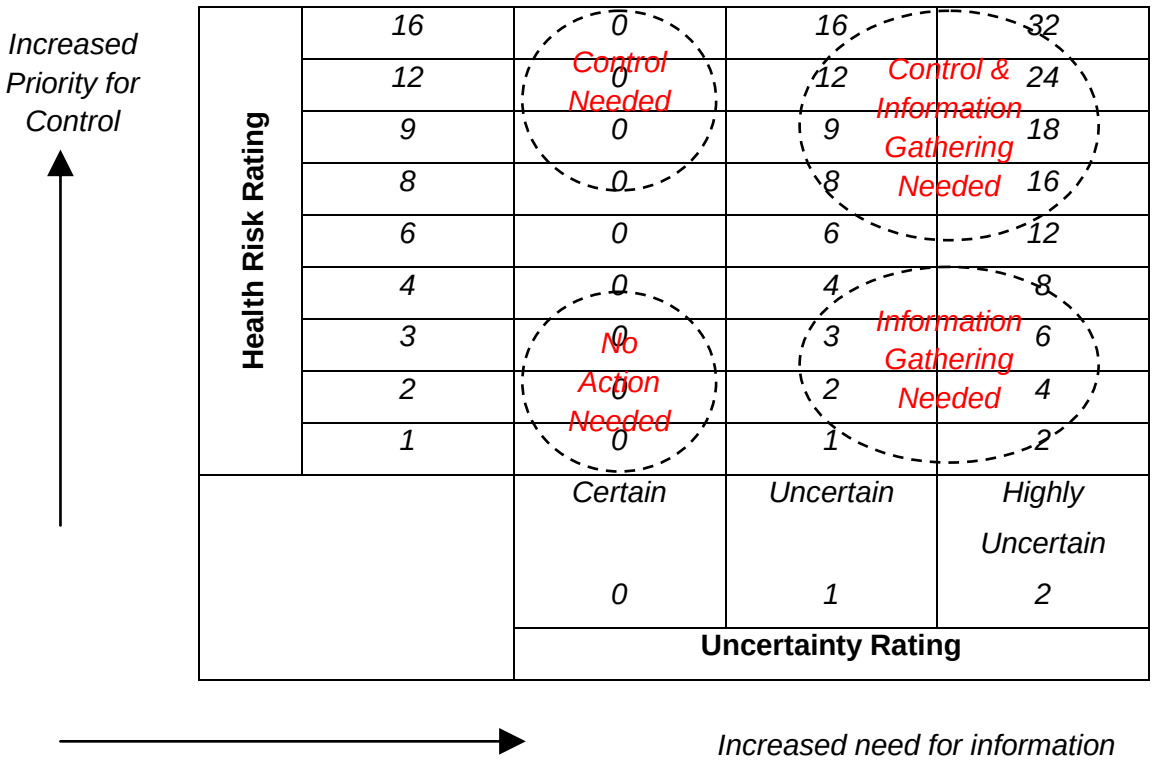
2	*Highly Uncertain*	*The acceptability judgment was made in the absence of significant information on the exposure profile and/or health effects*
1	*Uncertain*	*There is enough information to make a judgment, but further information is required to verify the exposure assessment*
0	*Certain*	*The environmental agent's exposure profile and health effects are well understood. The occupational hygienist has high confidence in the acceptability judgment*

The health risk rating equation (2.1) was combined with the uncertainty rating as follows (AIHA, 2006):

Equation 2.2: **Information Gathering Priority Rating =**
Health Effects Rating X Exposure Rating X Uncertainty Rating

The health risk rating and the uncertainty rating discussed above were combined to produce priorities for action, as illustrated in Table 2.6.

Table 2.6: Priority for Control and Information Gathering Actions (AIHA, 2006)



2.4 Chemical Substances Measurement Methodology

Screening level chemical measurements were carried out as part of the reproductive health study in order to obtain a preliminary quantitative evaluation of the degree of exposure to the most common chemical substances used within the five NHLS histopathology laboratories. During the walkthrough assessment (initial appraisal) and the information gathering process, organic chemical substances, particularly xylene and formaldehyde, presented the most obvious potential risk, from the perspective of the quantities that are used, the frequency of contact with these chemicals and the potential health effects.

Chemical measurement for various volatile organic compounds (including xylene and formaldehyde) was conducted using personal air sampling pumps that were connected by means of flexible tubing to a substance-specific sampling media. The sampling media and pump were attached to a laboratory worker or placed on a work bench or close to a suspected chemical contaminant emission source (e.g. in the cut-up area where formaldehyde is used). The aim was to sample the worst-case scenario, i.e. workers and/or processes that appeared to generate the highest exposures (NIOSH, 1977, HSE, 2006, AIHA, 2006). The selection of these workers or processes was carried out with the aid of the

laboratory managers, and also established from the discussions and task observations performed during the laboratory walkthrough and information gathering process.

The measurement and laboratory analysis methods used in this study were based on the US National Institute for Occupational Safety and Health Manual of Analytical Methods (NIOSH, 2003). An external laboratory accredited by the South African National Accreditation System (SANAS) was contracted to perform the chemical analysis on the sampling media. The sampling equipment (air sampling pumps) was calibrated before and after measurement with a maximum acceptable deviation of ±5% in pump flow rates.

Sampling was conducted over a representative portion of the work shift, typically between 4 and 6 hours. It was assumed that workers' exposure remained similar throughout the shift.

In addition to the time weighted average (TWA) sampling conducted using the "traditional" air pumps, instantaneous ("grab") formaldehyde measurements were also carried out using a direct-reading formaldehyde meter (Formaldemeter™ Htv-m, manufactured by PPM Technology). The aim of these measurements was to obtain a better understanding of the spatial and temporal formaldehyde concentrations emanating from specific work processes or areas within the histopathology laboratory. The instrument draws a sample of air through a built-in electrochemical sensor which produces a reading proportional to the concentration of formaldehyde in the air. This instrument is normally used for screening purposes only and might be susceptible to a small range of interfering substances, such as phenols, some alcohols (ethanol and methanol) as well as aldehydes. The calibration of the instrument was checked before and after measurement using a formaldehyde calibration standard supplied with the instrument.

Due to the abovementioned reasons, where measurements were carried out with both the Formaldemeter and using the NIOSH method', the results from the latter were given more significance in the exposure assessment.

Table 2.7 summarises the methodology that was used for the chemical sampling.

Table 2.7: Chemical Sampling Methodology (NIOSH, 2003)

Chemical sampled	Sampling method used	Collection media	Sampling pump flow rate	Type of laboratory analysis
Volatile organic Compounds (VOCs, including xylene)	*NIOSH methods: 1003/1300/1500/1501; Air sampling pump connected with flexible tubing to the collection media*	*Solid sorbent tube (coconut shell charcoal)*	*0.2 litre / min*	*Gas-chromatography and mass spectrometry (GC-MS)*
Formaldehyde	*NIOSH methods: 2541/2016*	*Solid sorbent tube (XAD-2)*	*0.1 litre / min*	*High-performance liquid chromatography (HLC)*
Formaldehyde	*Direct reading instrument (Formaldemeter)*	*Electrochemical sensor (built-in)*	*N/A*	*N/A*

Table 2.8 gives the exposure limits applicable to the chemical substances that were detected in the air samples taken during this study. Three sets of exposure limits were used for comparison purposes: the South African OELs, The ACGIH TLVs and the occupational exposure guidelines or ORGs suggested by Jankovic and Drake (South Africa Department of Labour, 1995, ACGIH, 2011, Jankovic and Drake, 1996).

Table 2.8: Occupational Exposure Limits for Substances Detected in the Study

	Exposure Limits in mg/m^3 (1)									
Exposure Standard	**Benzene**	**Toluene**	**Ethylbenzene**	**TMB**	**Chloroform**	**Xylene**	**Cyclohexanone**	**Tetrachloroethane**	**2 Butoxythanol**	**Formaldehyde**
OEL (2)	*16*	*188*	*435*	*123*	*9.8*	*435*	*100*	*12.6*	*120*	*2.5*
TLV (3)	*2*	*76.6*	*88.2*	*125*	*50*	*441*	*80*	*7*	*98.2*	*0.37 (4)*
ORG (5)	*0.05*	*9.6*	*---*	*---*	*2.6*	*1.5*	*---*	*---*	*---*	*---*

(1) *mg/m^3 – milligrams per cubic meter*

(2) *SA Department of Labour Occupational Exposure Limits (South Africa Department of Labour, 1995)*

(3) *Threshold Limit Values (ACGIH, 2011); limits stated originally in parts per million (ppm) were converted to mg/m^3 for ease of comparison*

(4) *This is a TLV – **Ceiling** value, i.e. a concentration that, according to ACGIH, should not be exceeded during <u>any part</u> of the working day (ACGIH, 2011)*

(5) *Occupational Reproductive Guidelines (Jankovic and Drake, 1996); ORGs were available only for four of the substances detected during this study*

when comparing with an exposure limit the ACGIH-TLVs were used as a benchmark value as these standards are based solely on health factors as opposed to regulatory standards, where economic and technical feasibility factors are also taken into account (ACGIH, 2011). Reproductive and developmental endpoints were considered in the ACGIH-TLV documentation related to both formaldehyde and xylene (ACGIH, 2001). On the other hand, there is currently insufficient research to substantiate the ORGs and therefore these are not considered in the determination of the Exposure Rating values. The use of PPE is not included in the exposure assessment, although the use of other control measures is considered as a mitigating factor for exposure.

Calculation of Exposure Indices

Workers in a laboratory environment are commonly exposed to a mixture of organic compounds rather than a single substance at any particular time. It is therefore necessary to calculate an "exposure index", i.e. the combined effect of several such substances, as those detected on our samples. In our study we adopted the conservative ACGIH approach that, in the absence of information to the contrary, the toxicological effect of two or more substances should be regarded as <u>additive</u>, i.e. that they affect similar endpoints and target organs in the body (ACGIH, 2011).

The formula that was used to calculate an exposure index (EI) is given below (ACGIH, 2011, South Africa Department of Labour, 1995)

Equation 2.3: $C_1/T_1 + C_2/T_2 + ... C_n/T_n$

Where C_1, C_2, C_n are the measured time weighted average (TWA) concentrations of particular substances and T_1, T_2, T_n, are the corresponding occupational exposure limits for these substances. If the sum of these fractions exceeds unity (above 1.0) this will indicate an overexposure. However, if the sum of these fractions is below 1.0 the exposure to the mixture is regarded as acceptable.

CHAPTER 3: RESULTS

3.1 Hazard Identification

Hazard Identification

During the hazard identification process, it became clear that the majority of processes / tasks were common in all histopathology laboratories. There were very few procedures that were unique to a particular laboratory, and these were generally carried out on a much smaller scale and in addition to the routine work that was common to all. There was also some variability in volume of specimens that were handled and the general layout of the equipment in the laboratory.

Typical work hours in all laboratories are 08:00 – 16:30; on rare occasions work is required outside the routine hours.

The job categories and staff complement for each laboratory studied are given in Table 3.1.

Table 3.1: Job Categories and Staff Complements

Job Category	Lab A	Lab B	Lab C	Lab D	Lab E	TOTAL
Laboratory Manager	*1*	*1*	*1*	*1*	*1*	*5*
Laboratory Supervisor	*---*	*---*	*---*	*1*	*---*	*1*
Pathologist	*10*	*7*	*2*	*3*	*1*	*23*
Pathology Registrar	*16*	*9*	*5*	*3*	*---*	*33*
Medical Technologist	*12*	*8*	*5*	*4*	*2*	*31*
Medical Technician	*2*	*3*	*---*	*2*	*---*	*7*
Medical Scientist	*---*	*1*	*---*	*1*	*---*	*2*
Student Medical Technician	*2*	*2*	*3*	*1*	*1*	*9*
Laboratory Clerk	*3*	*5*	*1*	*1*	*---*	*10*
Laboratory Assistant	*1*	*4*	*---*	*1*	*---*	*5*
TOTAL	*47*	*40*	*17*	*18*	*5*	**127**

The information collected from all five laboratories regarding the various tasks performed and associated health hazards was collated and is presented in the summary table shown below.

Table 3.2: NHLS Histopathology Laboratories – Summary of Process/Task Information and Associated Health Hazards

Task or process performed	Type and nature of hazard	Who might be exposed and how	Hazard quantity / level and frequency of contact	Control measures in place	Comments
Specimen Receiving					
• *Specimens for histopathology examination preserved in formalin were received in closed containers. The specimen and patient's details were captured in a register and the specimen received a unique number and labelled accordingly* • *Used formalin was discarded weekly into 25 litre container using a funnel*	*<u>Chemicals</u>* • *Formalin (formaldehyde)* *<u>Hazardous biological agents (HBAs)</u>* • *Infectious microorganisms (HIV, Hepatitis B, TB, etc.)*	**Lab Technician / Technologist / Clerk** • *Potential inhalation and skin contact with formaldehyde and aerosols containing HBAs, particularly in the event of accidental spillage or container leaking during sorting, labelling and moving specimens* • *High exposure might occur during decanting of waste formalin into 25 litre container*	• *An average of 50-60 specimens were handled daily; 25ml containers were used most commonly, but also 500ml, 1 litre and 5 litres. The containers were kept closed which minimizes potential exposure; formalin is a disinfectant which reduces the potential exposure to HBAs* • *Decanting only lasts few minutes, however relatively large amount of formalin (few litres) are handled during this process*	• *Standard PPE: lab coat; gloves; surgical mask observed in one instance.* • *Ventilation: usually general (through windows, doors)*	• *Surgical mask is inadequate for protecting against organic compounds such as formaldehyde* • *One lab reported that specimens sometimes arrive in plastic bags or containers which are too small and need to be transferred to other containers, hence potential for exposure* • *extractor fan was operating in one lab and an extraction hood (was not working) in another*

Table 3.2 (Cont'd): NHLS Histopathology Laboratories – Summary of Process/task Information and Associated Health Hazards

Task or process performed	Type and nature of hazard	Who might be exposed and how	Hazard quantity / level and frequency of contact	Control measures in place	Comments
Cut-up (Put-through)					
• *Specimens were weighed and measured* • *Representative sections (samples) of the specimen were cut-up (dissected) for analysis using a sharp knife* • *A macroscopic description of the specimen was carried out by the Pathologist / Registrar (by dictation)* • *Sections selected for further processing and analysis were fixated in formalin in special cassettes bearing a unique case number*	*<u>Chemicals</u>* *Formaldehyde, acetone based dye (fixative)* *<u>HBAs</u>* • *Infectious microorganisms* *<u>Safety hazards</u>* • *Sharps injuries (knife)* *<u>Ergonomics</u>* • *Standing for prolonged time*	**Lab Technologist / Technician / Pathology Registrar** *Inhalation and skin contact with formalin and aerosols containing HBAs while handling, cutting specimens and discarding formalin*	*Formalin is a disinfectant which reduces the potential exposure to HBAs (tissue is routinely fixated for 48 hours prior to cut up to ensure sterility);* *Approximately 1.5 litre of formalin was handled;* *Exposure duration per day may vary between 1.5 - 7 hours depending on number of specimens handled and lab;* *Exposure may also vary according to specimen size (specimens were stored in 100ml – 25 litre containers/buckets);* *Registrars rotated and worked at cut-up for one week per month, on average*	• *Downdraft ventilation on cut-up bench (some labs also used an extractor fan)* • *Gloves (cut resistant gloves used in some cases) and sleeve protectors* • *Plastic aprons* • *Goggles* • *Surgical masks*	• *Registrars also carried out post-mortems in mortuary, this might have contributed to their overall exposure burden to chemicals and HBAs* • *Surgical masks are inadequate for chemical protection* • *Not all were using the goggles provided* • *Formalin odour was often noticed in this area*

Table 3.2 (Cont'd): NHLS Histopathology Laboratories – Summary of Process/task Information and Associated Health Hazards

Task or process performed	Type and nature of hazard	Who might be exposed and how	Hazard quantity / level and frequency of contact	Control measures in place	Comments
Tissue Processing					
• *This was an automated process of dewatering the tissue using organic solvents and then impregnating it with paraffin wax* • *The organic solvents used in the processing equipment were replaced periodically (usually weekly); used (waste) chemicals were manually decanted into 20-25 litre containers for disposal*	*Chemicals* • *Formaldehyde, alcohol (ethanol), xylene, paraffin wax* *Ergonomics* • *Lifting 20-25 litre containers, 4-7 drums / week*	**Lab Technologist / Technician / Assistant** *Inhalation and skin contact with process chemicals, particularly during the replacement of used chemicals in the processing machine*	• *Tissue processing is automated and the equipment is enclosed; The process was run overnight which also reduces the risk of exposure to chemicals* • *Exposure to chemicals might have been significant during the decanting and replacement of used chemicals*	• *Enclosed, automated system* *When changing chemicals:* • *Ventilation: usually only general (natural), in one lab extractor fans were operational;* • *PPE: gloves; goggles; in two instances surgical masks were used;* • *Trolley was utilised to move chemical-containers thereby reducing possible ergonomic strain*	• *The main risk of chemical exposure appears to be while decanting used chemicals* • *surgical masks are inadequate for protection against chemicals* • *In one lab a half-mask cartridge respirator was available but rarely used*

Table 3.2 (Cont'd): NHLS Histopathology Laboratories – Summary of Process/task Information and Associated Health Hazards

Task or process performed	Type and nature of hazard	Who might be exposed and how	Hazard quantity / level and frequency of contact	Control measures in place	Comments
Embedding					
Tissue was transferred from cassettes to moulds (blocks) using hot wax	*Chemicals* • *Hot wax* *Safety* • *Molten wax, flame (burns)*	**Lab Technologist / Technician** *Inhalation and accidental skin contact with hot wax*	*Wax is essentially non- toxic, the process took 2-4 hours per day on average*		
Microtomy (sectioning)					
Very thin (few micrometers) tissue slices were cut using a Microtome	*Ergonomics* • *Repetitive hand movement (wrist/hand strain)* • *Sitting for extended time periods* *Safety* • *Sharps injuries: cutting blade, slide edges* *Chemicals* • *Lab chemicals, including xylene and formaldehyde*	**Lab Technologist / Technician** • *While using the Microtome strain may occur to the wrist/ hand (due to a deviated wrist position) and also shoulder/arm* • *Inhalation of chemical vapour present in the general lab air*	• *The duration of this task varied from 30 minutes to 4-5 hours/day* • *Sporadic exposure to chemical vapour*	• *Pacing own work and taking brakes* • *Lockup mechanism to prevent cutting while removing the block from the Microtome*	*In some instances the machine locking mechanism was not applied by staff*

Table 3.2 (Cont'd): NHLS Histopathology Laboratories – Summary of Process/task Information and Associated Health Hazards

Task or process performed	Type and nature of hazard	Who might be exposed and how	Hazard quantity / level and frequency of contact	Control measures in place	Comments
Automated Staining					
• *Colour was applied to the tissue by an automated process of staining* • *Used chemical solutions were replaced regularly in the staining machine: used chemicals were decanted into 25 litre containers using funnel*	*<u>Chemicals</u>* • *Xylene, alcohol (different grades) staining solutions: the most common were Haematoxylin and Eosin (H&E staining), also formaldehyde exposure from the general lab air)*	**Lab Technologist / Technician / Assistant** *Vapour inhalation is possible when opening the machine to mount or take out slides; Inhalation and skin contact may occur during the regular changing of chemical solutions in the staining machine*	*Chemicals were usually changed in the machine once or twice a week (although sometimes more often); it was estimated that approximately 3 litres of each solution were being used up in the machine daily*	• *Mostly automated process with built-in extraction which minimizes exposure to chemicals; exposure mainly occurs during the changing of chemicals* • *PPE: gloves, lab coat*	*Containers with waste chemicals were sometimes left opened which presented a risk of exposure*

Table 3.2 (Cont'd): NHLS Histopathology Laboratories – Summary of Process/task Information and Associated Health Hazards

Task or process performed	**Type and nature of hazard**	**Who might be exposed and how**	**Hazard quantity / level and frequency of contact**	**Control measures in place**	**Comments**
Special Stains (manual staining, including immunochemistry)					
A range of staining chemicals (in liquid and powder form) and different manual techniques (e.g. Reticulin, Zeil-Neelsen) were applied for specialised tests on tissues	*<u>Chemicals</u>* • *Various staining reagents including acids (e.g. acetic, nitric, hydrochloric, sulphuric), ammonia (Reticulin stain), solvents such as: alcohol, xylene (for de-waxing, clearing), formalin, DAB (Diaminobenzidine, possible carcinogen)* • *Antibody solutions*	**Lab Technologist / Technician** *Inhalation and skin contact with chemicals during weighing of powders, mixing, manual pipetting and preparation of stains; Carbol Fuchsin chemical used for the Zeil-Neelsen stain emits phenol when heated on workbench*	*Very small quantities of chemicals were used for the various processes (e.g. DAB: ± 100ml/day); some staining processes were performed infrequently*	• *General ventilation (open windows); safety cabinet (fume hood) used in one lab;* • *PPE: gloves, lab coat, goggles*	• *Safety cabinets provided but not working were observed in two labs;* • *Surgical mask used in another lab is inadequate for protection against chemicals*

Table 3.2 (Cont'd): NHLS Histopathology Laboratories – Summary of Process/task Information and Associated Health Hazards

Task or process performed	Type and nature of hazard	Who might be exposed and how	Hazard quantity / level and frequency of contact	Control measures in place	Comments
Frozen sections (including Immunofluorescence)					
• *Analysis was performed on "fresh" tissue, which had been frozen to about -60^{0}C (in the case of immunofluorescence -22 ^{0}C to -25 ^{0}C);* • *Sectioning and manual staining were carried out prior to analysis*	*<u>Chemicals</u>* • *OCT (optimal cutting temp.) compound, freezing spray, xylene, alcohol* *<u>HBAs</u>* • *Infectious microorganisms* *<u>Safety hazards</u>* • *Sharps injuries (knife)*	**Lab Technologist / Technician / Assistant / Registrar** *Inhalation and skin contact with chemicals and potentially HBAs from fresh tissue;* *The process was mainly enclosed, however, manual staining / pipetting was also performed*	• *Frozen sections were handled only 2-3 times / week* • *Only small quantities of chemicals were used* • *The tissue is frozen which reduces the potential for infections*	*Enclosed, the cutting (sectioning) process is automated*	

Table 3.2 (Cont'd): NHLS Histopathology Laboratories – Summary of Process/task Information and Associated Health Hazards

Task or process performed	Type and nature of hazard	Who might be exposed and how	Hazard quantity / level and frequency of contact	Control measures in place	Comments
Wet Specimen Room / Specimen Storage					
• *Specimen remains were transferred into sealed containers for temporary storage (usually 3 months) and afterwards disposed of* • *Used formalin was decanted into waste containers for disposal*	*<u>Chemicals</u>* • *Formalin (formaldehyde)* *<u>HBAs</u>* • *Infectious microorganisms* *<u>Ergonomics</u>* • *Manual handling of waste chemical and specimen containers; Reaching for, or stowing, specimen containers on top shelves*	**Lab Assistant / Technologist** • *Inhalation and skin contact with formaldehyde and aerosols containing HBAs while handling specimens, particularly in the event of accidental spillage or container leakage;* • *Inhalation and skin contact with formaldehyde during the decanting of waste formalin* • *Possible strain injuries while reaching for / stowing specimen and chemical containers*	• *Specimen containers (1, 2, 4 and 10 litre) were handled about 3 times per day (10-20 containers at a time);* • *The specimen storage area was not occupied continuously therefore the potential for exposure is largely reduced* • *Formalin is a disinfectant which reduces the potential exposure to HBAs*	• *Extractor fans used and in one lab air conditioner* • *PPE: gloves, lab coat, goggles, surgical mask* • *Step ladder assisted in reaching for / stowing containers on high shelves*	• *The main risk of chemical exposure appeared to be while decanting used formalin into 20 litre container for disposal (no respirator used)* • *Surgical mask is inadequate for protection against formaldehyde*

Table 3.2 (Cont'd): NHLS Histopathology Laboratories – Summary of Process/task Information and Associated Health Hazards

Task or process performed	Type and nature of hazard	Who might be exposed and how	Hazard quantity / level and frequency of contact	Control measures in place	Comments
Light Microscopy					
Pathological diagnosis was carried out using light microscopy	*Ergonomics* • *Eye strain as well as ergonomic strain mainly to the back, shoulders and neck due to prolonged sitting at the microscope;*	**Pathologist / Registrar**	*2-4 hours/day (average)*	• *Pathologists and registrars rotated between microscopy work and other tasks (e.g. pathology reports, teaching)* • *Taking breaks*	
Electron Microscopy					
Tissue processing and analysis was done using electron microscope	*Chemicals* • *Osmium tetraoxide in ethanol, alcohol, uranyl acetate* *Radiation* • *Uranyl acetate (low radioactivity)* • *X-ray*	**Lab Technologist** • *Inhalation and skin contact with chemicals* • *Radiation exposure from microscope*	• *Minute quantities of chemicals were used (few ml)* • *Microscope work: 1 hour/day*	• *Safety cabinet* • *Spill kit (sodium sulphite)* • *Radiation source is enclosed*	*No scatter radiation was detected in a survey carried out in April 2010 by Pretoria University*

Table 3.2 (Cont'd): NHLS Histopathology Laboratories – Summary of Process/task Information and Associated Health Hazards

Task or process performed	Type and nature of hazard	Who might be exposed and how	Hazard quantity / level and frequency of contact	Control measures in place	Comments
Making up and Disposal of Formalin / Washing-up					
• *Water was added to dilute formalin from 40% to 10% concentration* • *Ammonia solution (27%) was added to neutralise formalin prior to disposal* • *Containers / buckets containing formalin residue were washed up in basin*	*Chemicals* • *Formaldehyde, Ammonia*	**Lab Assistant/ Technologist Technician** *Inhalation and skin contact with formaldehyde and ammonia*	*These processes were reported in one lab:* • *50 litre of 10% formalin were made once a month; this process took about 20 minutes;* • *60ml of ammonia solution were added to every litre of formalin to be disposed of*	• *General ventilation*	• *No extraction ventilation or respiratory protection were used* • *Purchasing formalin which is already in a diluted form will eliminate the need to perform this process in the lab*

3.2 Chemical Measurements

The results of the screening level chemical measurements conducted in the five histopathology laboratories are summarised in Tables 3.3 and 3.4.

Table 3.3 presents the time weighted average (TWA) chemical concentrations obtained using sorbent tubes and following the NIOSH methods, as described above (Table 2.6). The sample analysis results were compared to three different sets of occupational exposure limits, i.e. the SA – OELs, the ACGIH – TLVs and the occupational reproductive guidelines (ORGs) suggested by Jankovic and Drake.

Different sampling media were used for formaldehyde and for volatile organic compounds (VOCs, including xylene), therefore either VOCs **or** *formaldehyde could be measured on any single sample.*

The volatile organic compounds (VOCs) analysed for were assumed to have an additive effect, therefore the exposure index (EI), i.e. the combined effect of the individual compounds, was calculated using equation 2.3 (page 34). EI values exceeding 1.0 indicated over exposure and are shown in **bold.**

Table 3.3 (a): Air Concentrations of Chemicals Measured at Histopathology Laboratory A, 25 August 2011

Sample #	Person / Position / Task	Time (min)	Sample Type (P / S)[1]	TWA Chemical Concentrations (mg/m^3)					Exposure Index		
				Benzene	Toluene	Ethylbenzene	Xylene	Formaldehyde	SA OELs	ACGIH TLVs	ORG
VK1	*Top of fume hood*	*267*	*S*	*0.02*	*0.15*	*1.80*	*7.94*		*0.02*	*0.05*	**5.63**
VK2	*Section cutting, mounting, staining*	*263*	*P*	*0.02*	*0.17*	*1.98*	*8.52*		*0.03*	*0.05*	**6.02**
FK1	*Cut-up bench*	*264*	*S*					*0.09*	*0.04*	*0.24*	*(2)*
FK2	*Cut-up, section cutting*	*262*	*P*					*0.08*	*0.03*	*0.23*	

(1) P – Personal sample; S – Static sample

(2) No ORG is stipulated for formaldehyde

(3) Figures in **Bold** *denote that one or more of the individual compounds exceeded the respective OEL, TLV or ORG*

Table 3.3 (b): Air Concentrations of Chemicals Measured at Histopathology Laboratory B, 28 October 2011

Sample #	Person / Position / Task	Time (min)	Sample Type (P / S)	TWA Chemical Concentrations (mg/m^3)								Exposure Index		
				Benzene	Toluene	Ethylbenzene	TMB	Chloroform	Xylene	2 Butoxythanol	Formaldehyde	SA OELs	ACGIH TLVs	ORG
CMV1	*Manual staining, Microtoming*	*368*	*P*	*<0.01*	*<0.01*	*0.03*	*0.03*	*ND*[4]	*0.12*	*ND*		*<0.01*	*<0.01*	*0.11*
CMV2	*Slide mounting, specimen handling*	*352*	*P*	*0.03*	*0.05*	*0.09*	*0.02*	*ND*	*4.46*	*0.02*		*0.01*	*0.03*	**3.50**
CMV3	*Tissue processing area*	*348*	*S*	*<0.01*	*0.03*	*0.06*	*0.05*	*0.017*	*2.82*	*0.01*		*0.01*	*0.01*	**1.92**
CMF1	*Cut-up area*	*344*	*S*								*0.06*	*0.03*	*0.17*	
CMF2	*Cut-up area*	*337*	*P*								*0.04*	*0.02*	*0.11*	

[4] *ND – this substance was not detected on the sample media analysed by the laboratory*

Table 3.3 (c): Air Concentrations of Chemicals Measured at Histopathology Laboratory C, 07 November 2011

Sample #	Person / Position / Task	Time (min)	Sample Type (P / S)	TWA Chemical Concentrations (mg/m^3)								Exposure Index		
				Benzene	Toluene	Ethylbenzene	TMB	Tetrachloroethane	Xylene	2 Butoxythanol	Formaldehyde	SA OELs	ACGIH TLVs	ORG
PAV1	*Automated staining*	*252*	*P*	*0.03*	*0.05*	*1.51*	*0.02*	*ND*	*9.45*	*0.02*		*0.03*	*0.06*	**6.96**
PAV2	*On cover slipper machine, next to staining machine*	*240*[5]	*S*	*0.02*	*0.23*	*17.66*	*ND*	*0.16*	*101.19*	*0.26*		*0.29*	*0.47*	**68.15**
PAV3	*Staining*	*108*	*P*	*0.06*	*0.05*	*2.22*	*ND*	*ND*	*10.93*	*0.04*		*0.03*	*0.09*	**8.43**
PAF1	*Cut-up (put through)*	*303*	*P*								*0.04*	*0.02*	*0.11*	
PAF2	*Cut-up area*	*323*	*S*								*0.09*	*0.04*	*0.23*	

[5] *Estimated time – sampling pump stopped*

Table 3.3 (d): Air Concentrations of Chemicals Measured at Histopathology Laboratory D, 02 December 2011

Sample #	Person / Position / Task	Time (min)	Sample Type (P / S)	TWA Chemical Concentrations (mg/m^3)							Exposure Index		
				Benzene	Toluene	Ethylbenzene	TMB	Chloroform	Xylene	Formaldehyde	SA OELs	ACGIH TLVs	ORG
MEV1	*Staining*	*235*	*P*	*ND*	*ND*	*2.81*	*0.01*	*0.12*	*13.18*		*0.05*	*0.07*	**8.86**
MEV2	*Special stains work bench*	*334*	*S*	*0.02*	*0.04*	*3.41*	*0.06*	*0.04*	*19.44*		*0.06*	*0.09*	**13.33**
MEF1	*Staining and cut-up*	*347*	*P*							*0.90*	*0.36*	**2.39**	
MEF2	*Specimen filing and cut-up*	*?* [6]	*P*										
MEF3	*Cut-up, on extraction cabinet*	*319*	*S*							*1.43*	*0.57*	**3.82**	

[6] *No result, the sampling pump stopped and the sample media (tube) was found moist, it might have been dipped accidentally in solution.*

Table 3.3 (e): Air Concentrations of Chemicals Measured at Histopathology Laboratory E, 19 January 2012

Sample #	Person / Position / Task	Time (min)	Sample Type (P / S)	TWA Chemical Concentrations (mg/m^3)							Exposure Index		
				Toluene	Ethylbenzene	TMB	Cyclohexanone	Xylene	2 Butoxythanol	Formaldehyde	SA OELs	ACGIH TLVs	ORG
BV2	*On top of VIP staining machine*	*335*	*S*	*0.04*	*2.10*	*0.07*	*0.02*	*10.20*	*1.40*		*0.04*	*0.06*	**6.83**
BV3	*Special Stains bench*	*333*	*S*	*0.05*	*1.33*	*0.09*	*ND*	*6.05*	*ND*		*0.02*	*0.03*	**4.06**
BF1	*Put through*	*367*	*P*							*<0.01*	*<0.01*	*<0.01*	
BF2	*Specimen archive room*	*335*	*S*							*0.02*	*0.01*	*0.04*	
BF3	*Labelling and receiving specimen*	*303*[(7)]	*P*							*<0.01*	*<0.01*	*<0.01*	

[(7)] *Estimated time – sampling pump stopped*

From the time-weighted-average (TWA) measurements conducted with sorbent tubes followed by a laboratory analysis (NIOSH methods) the following may be concluded:

Organic Volatile Compounds (including xylene)

All the measurements taken for volatile organic compounds (VOCs) were well below the respective statutory SA-OELs and the widely used ACGIH-TLV guidelines for individual compounds as well as combined exposure indices (EI); however 11 out of 12 results (92%) exceeded the ORG for xylene (and consequently the EI for the ORG). This is due to the fact that the ORG for xylene (1.5 mg/m^3) is almost 300 times lower than the SA-OEL and the ACGIH-TLV for this substance (435 and 441 mg/m^3, respectively). This means that a relatively very small amount of xylene that was present in all five laboratories sampled was sufficient to result in the ORG being exceeded.

Formaldehyde

None of the 11 TWA samples taken for formaldehyde exceeded the regulatory SA-OEL of 2.5 mg/m^3 for this substance. However, two of these samples, taken in the same laboratory, exceeded the ACGIH-TLV-C of 0.37mg/m^3, a concentration that should not be exceeded during <u>any part</u> of the working exposure. The TLV-C was exceeded despite the TWA being an average exposure over several hours which flattens peaks and hence probably considerably underestimates peak exposures.

In addition to the formaldehyde samples obtained using sorbent tubes, instantaneous formaldehyde samples were obtained with the direct reading formaldehyde meter (Formaldemeter). The results of this sampling are summarises in Table 3.4. Results that are above the ACGIH TLV exposure limit are shown in **bold***.*

Table 3.4: Instantaneous Formaldehyde Air Concentrations Measured with the Formaldemeter in the Histopathology Laboratories

Position	Formaldehyde concentrations in mg/m^3														
	Lab A			Lab B			Lab C			Lab D			Lab E		
	Range	*Avg.*	*No.*[1]	*Range*	*Avg.*	*No.*	*Range*	*Avg.*	*No.*	*Range*	*Avg.*	*No.*	*Range*	*Avg.*	*No.*
Specimen receiving	---	---	---	*0.05 – 1.14*	*0.37*	*6*	**0.46 – 0.88**	**0.64**	*3*	*0.02 – 0.14*	*0.08*	*3*	*0.01 – 0.02*	*0.01*	*3*
Specimen room	---	---	---	*0.14 –* **0.44**	*0.26*	*6*	*0.22 –* **0.77**	**0.47**	*3*	**1.16 – 2.11**	**1.54**	*3*	**0.55 – 1.18**	**0.93**	*3*
Lab walkway	---	---	---	*0.11 –* **0.63**	*0.24*	*6*	*0.07 – 0.21*	*0.13*	*3*	---	---	---	---	---	---
Cut-up work bench	**0.66 – 0.69**	**0.68**	*2*	*0.14 –* **1.97**	**0.47**	*16*	*0.17 –* **0.50**	*0.31*	*3*	---	---	---	*0.29 –* **0.51**	*0.38*	*3*
Microtomy	---	---	---	*0.10 – 0.35*	*0.17*	*6*	---	---	---	---	---	---	*0.30 –* **0.43**	*0.35*	*3*
Automated staining	---	---	---	---	---	---	**0.42 – 0.98**	**0.64**	*3*	**0.66 – 2.19**	**1.65**	*9*	*0.25 – 0.28*	*0.26*	*4*
Special Stains	**0.55**	**0.55**	*1*	---	---	---	*0.38 –* **0.48**	**0.43**	*3*	**0.84 – 2.12**	**1.62**	*3*	*0.23 –* **0.45**	*0.34*	*6*
Outside lab	---	---	---	*0.00 – 0.12*	*0.03*	*6*	---	---	---	*0.13 – 0.37*	*0.21*	*3*	*0.00 – 0.02*	*0.01*	*3*
Outdoors area	*0.00 – 0.01*	*0.01*	*2*	*0.00 – 0.00*	*0.00*	*4*	---	---	---	*0.00 – 0.01*	*0.00*	*3*	---	---	---
Manager's office	**0.49**	**0.49**	*1*	---	---	---	---	---	---	---	---	---	*0.20 – 0.50*	*0.32*	*3*

[1] *Number of measurements (spot readings) taken*

[2] *Values shown in* **bold** *exceeded the ACGIH-TLV (Ceiling value) of 0.37 mg/m^3*

From the direct-reading formaldehyde meter measurements it may be concluded:

A total of 105 instantaneous spot measurements were taken in various work stations within the five laboratories,using the Formaldemeter. Of these 49 readings (47%) exceeded the ACGIH-TLV-C of 0.37 mg/m^3; none of the readings exceeded the SA-OEL of 2.5 mg/m^3. Formaldehyde concentrations exceeding the TLV were measured at the following working areas: specimen receiving (5), specimen storage room (9), cut-up bench (10), Microtome (1), automated staining (12), special stains (9), Manager's office (2), lab walkway (1). High variability in the measured formaldehyde concentrations was noted among the different laboratories, as well as within laboratories, at different times of the day. This could be attributed to variability in ventilation rates (e.g. due to windows being opened or closed) and temperature fluctuations.

3.3 Reproductive Health Risk Assessment Results

Based on the task observations, interviews, professional judgment and chemical measurements that were carried out during the hazard identification process (Tables 3.1, 3.2 and 3.3) the degree of exposure to the identified reproductive health hazards was assessed and an Exposure Rating assigned (see Table 3.5).

As the tasks performed in the 5 histopathology laboratories were similar, the information gathered for each common task could be collated and summarised under the following headings: reproductive health hazard/s related to the task, the route of exposure to the hazard, a qualitative assessment of the amount/level of exposure, a quantitative assessment of exposure based on the sampling results and existing control measures currently implemented. Based on both the qualitative and quantitative exposure assessment, the exposure rating has been assigned using the AIHA rating scheme shown in Table 2.3.

Lastly, following the AIHA rating scheme shown in Table 2.5, an uncertainty rating value was assigned based on judgment of both the information that was available from the literature on potential reproductive health effect, as well as the certainty that could be placed on qualitative and quantitative exposure assessments generated for this study (AIHA, 2006).

In Table 3.6 the health effect category and exposure ratings are combined (multiplied) to derive at a risk rating value and risk category for each hazard identified in relation to each task performed in the laboratory, using Equation 2.1, Table 2.4 and Figure 2.1.

Lastly, taking into consideration the health risk rating and the uncertainty rating the priority for control value is calculated, using the AIHA method shown in Table 2.6 (AIHA, 2006).

Table 3.5: Reproductive Health (RH) Hazard Exposure Assessment

Task / Process	RH hazard identified	Route of exposure	Hazard quantity / frequency of contact	Exposure measurement results (Average and range), mg/m^3	Control measures in place	Exposure rating [C]	Uncertainty rating [C]
Specimen receiving	*Formaldehyde*	*Inhalation, skin*	*Sporadic, small quantities; potential high exposure during decanting*	*<0.01* [A] *0.31* [B] *(0.01 – 0.64)* [B]	*Gloves, general ventilation*	*1*	*1*
	HBAs	*Inhalation, skin*	*Accidental, formalin is an effective disinfectant*	*Not measured*	*Gloves, general ventilation*	*1*	*1*
Cut-up (Put-through)	*Formaldehyde*	*Inhalation, skin*	*Continuous during task (1.5 – 7 hr/day)*	*0.23* [A] *(<0.01 – 1.43)* [A] *0.46* [B] *(0.14 – 1.97)* [B]	*Downdraft ventilation, gloves, aprons, surgical masks*	*3*	*1*
	HBAs	*Inhalation, skin*	*Accidental, formalin is an effective disinfectant*	*Not measured*		*1*	*1*
Tissue processing	*Formaldehyde*	*Inhalation, skin*	*Sporadic (automated equipment); potential high exposure during chemical replacement (weekly)*	*Not measured*	*Enclosed (automated); gloves, goggles (decanting), general ventilation*	*1*	*1*
	Xylene	*Inhalation, skin*	*Sporadic (automated); Potential high exposure during chemical replacement (weekly)*	*2.82* [A]		*1*	*1*

(A) Chemical concentrations obtained from laboratory analysis using the relevant NIOSH method.

(B) Chemical concentrations obtained from the direct reading formaldehyde meter (Formaldemeter)

(C) Based on the AIHA rating schemes, see Tables 2.2 and 2.4, respectively

Table 3.5 (Cont'd): Reproductive Health Hazard Exposure Assessment

Task / Process	RH hazard identified	Route of exposure	Hazard quantity / frequency of contact	Exposure measurement results (Average and range), mg/m^3	Control measures in place	Exposure rating [C]	Uncertainty rating [C]
Tissue processing	*Ergonomics (lifting and moving containers)*	*Body*	*20-25 litre containers, 4-7 per week*	*Not measured*	*Trolley for moving containers*	*1*	*1*
Sectioning (Microtomy)	*Ergonomics (repetitive hand movement; extended sitting)*	*Body*	*½ – 5 hours/day*	*Not measured*	*Own-pacing, taking breaks*	*1*	*1*
	Xylene	*Inhalation*	*Sporadic*	*Not measured*	*General ventilation*	*1*	*1*
	Formaldehyde	*Inhalation*	*Sporadic*	*0.20 [B] (0.10 – 0.43) [B]*		*1*	*1*
Automated staining	*Xylene*	*Inhalation, skin*	*Sporadic (automated equipment); potential high exposure during chemical replacement in the machine (1-2 times/week)*	*33.48 [A] (9.45 – 101.19)[A]*	*Enclosed, automated process; built-in extraction ventilation; gloves*	*2*	*1*
	Staining solutions	*Inhalation, skin*	*Sporadic (automated equipment); potential high exposure during chemical replacement*	*Not measured*		*1*	*2*
	Formaldehyde	*Inhalation*	*Sporadic (general lab air)*	*1.10 [B] (0.25 – 2.19) [B]*	*General ventilation*	*1*	*1*

Table 3.5 (Cont'd): Reproductive Health Hazard Exposure Assessment

Task / Process	RH hazard identified	Route of exposure	Hazard quantity / frequency of contact	Exposure measurement results (Average and range), mg/m^3	Control measures in place	Exposure rating [C]	Uncertainty rating [C]
Special stains	*Staining reagents and solutions*	*Inhalation, skin*	*Very small quantities are used (few ml/day); some processes performed infrequently*	*Not measured*	*General ventilation; gloves, goggles*	*1*	*2*
	Xylene	*Inhalation, skin*	*Sporadic*	*9.14 [A]* *(0.12 – 19.44) [A]*		*1*	*1*
	Formaldehyde	*Inhalation*	*Sporadic (general lab air)*	*0.65 [B]* *(0.23 – 2.12) [B]*	*General ventilation*	*1*	*1*
Frozen sections	*Xylene*	*Inhalation, skin*	*Frozen sectioning performed infrequently (2-3 times/week); mainly enclosed; small quantities of chemicals used*	*Not measured*	*Mainly enclosed, automated process; general ventilation*	*1*	*1*
	HBAs	*Inhalation, skin*	*Accidental*	*Not measured*	*Frozen sections (-60 ^{0}C), automated*	*1*	*1*
Specimen storage	*Formaldehyde*	*Inhalation, skin*	*Intermittent: closed containers handled about 3 times/day; potential exposure during decanting and accidental spillage*	*0.02 [A]* *0.69 [B]* *(0.14 – 2.11) [B]*	*Closed containers, extractor fan, general ventilation*	*2*	*1*

Table 3.5 (Cont'd): Reproductive Health Hazard Exposure Assessment

Task / Process	RH hazard identified	Route of exposure	Hazard quantity / frequency of contact	Exposure measurement results (Average and range), mg/m^3	Control measures in place	Exposure rating [C]	Uncertainty rating [C]
Light microscopy	*Ergonomics (eye, neck, shoulders and back strain)*	*Body*	*Intermittent (2-4 hours/day)*	*Not measured*	*Job/task rotations; own-pacing*	*1*	*1*
Electron microscopy	*Analysis chemicals*	*Inhalation, skin*	*Minute quantities (few ml)*	*Not measured*	*Safety cabinet*	*1*	*2*
	Radioactive solution (uranyl acetate)	*Inhalation, skin*	*Minute quantities*	*Not measured*	*Safety cabinet*	*1*	*2*
	X-ray source	*Whole body*	*Accidental (if leaking)*	*No scatter radiation detected in 2010 survey*	*Enclosed, shielded radioactive source*	*1*	*1*
Disposal and make up of formalin solution	*Formaldehyde*	*Inhalation, skin*	*Infrequent (task performed ad-hoc)*	*Not measured*	*General ventilation*	*2*	*1*

Table 3.6: Reproductive Health Risk Ratings and Priority for Control

Task / Process	Reproductive health hazard identified	Health effect category [A] (A)	Exposure rating [B] (B)	Risk rating [C] (A)X(B) = (C)	Risk rating category [D]	Uncertainty rating [E] (D)	Priority for control rating [F] (C)X(D) = (E)	Control / information needed [G]
Specimen receiving	*Formaldehyde*	*4*	*1*	*4*	*Moderate*	*1*	*4*	*Information*
	HBAs	*3*	*1*	*3*	*Moderate*	*1*	*3*	*Information*
Cut-up (Put-through)	*Formaldehyde*	*4*	*3*	*12*	*High – Very High*	*1*	*12*	*Control + Info*
	HBAs	*3*	*1*	*3*	*Moderate*	*1*	*3*	*Information*
Tissue processing	*Formaldehyde*	*4*	*1*	*4*	*Moderate*	*1*	*4*	*Information*
	Xylene	*4*	*1*	*4*	*Moderate*	*1*	*4*	*Information*
	Ergonomics	*3*	*1*	*3*	*Moderate*	*1*	*3*	*Information*
Sectioning (Microtomy)	*Ergonomics*	*3*	*1*	*3*	*Moderate*	*1*	*3*	*Information*
	Xylene	*4*	*1*	*4*	*Moderate*	*1*	*4*	*Information*
	Formaldehyde	*4*	*1*	*4*	*Moderate*	*1*	*4*	*Information*
Automated staining	*Xylene*	*4*	*2*	*8*	*High*	*1*	*8*	*Control + Info*
	Staining solutions	*4*	*1*	*4*	*Moderate*	*2*	*8*	*Information*
	Formaldehyde	*4*	*1*	*4*	*Moderate*	*1*	*4*	*Information*
Special stains	*Staining reagents*	*4*	*1*	*4*	*Moderate*	*2*	*8*	*Information*
	Xylene	*4*	*1*	*4*	*Moderate*	*1*	*4*	*Information*
	Formaldehyde	*4*	*1*	*4*	*Moderate*	*1*	*4*	*Information*
Frozen sections	*Xylene*	*4*	*1*	*4*	*Moderate*	*1*	*4*	*Information*
	HBAs	*3*	*1*	*3*	*Moderate*	*1*	*3*	*Information*
Specimen storage	*Formaldehyde*	*4*	*2*	*8*	*High*	*1*	*8*	*Control + Info*

Table 3.6 (Cont'd): Reproductive Health Risk Ratings and Priority for Control

Task / Process	Reproductive health hazard identified	Health effect category [A] (A)	Exposure rating [B] (B)	Risk rating [C] (A)X(B) = (C)	Risk rating category [D]	Uncertainty rating [E] (D)	Priority for control rating [F] (C)X(D) = (E)	Control / information needed [G]
Light microscopy	*Ergonomics*	*3*	*1*	*3*	*Moderate*	*1*	*3*	*Information*
Electron microscopy	*Analysis chemicals*	*4*	*1*	*4*	*Moderate*	*2*	*8*	*Information*
	Radioactive solution	*4*	*1*	*4*	*Moderate*	*2*	*8*	*Information*
	X-ray source	*4*	*1*	*4*	*Moderate*	*1*	*4*	*Information*
Disposal and make up of formalin	*Formaldehyde*	*4*	*2*	*8*	*High*	*1*	*8*	*Control + Info*

[A] *Health Effect Category – based on AIHA rating scheme, Table 2.1*
[B] *Exposure Rating – based on AIHA Exposure Rating Categorization, Table 2.3*
[C] *Health Risk Rating – based on AIHA scheme, Equation 2.1 and Table 2.4*
[D] *Risk Rating Category – read from the Risk Rating Matrix (Figure 2.1)*
[E] *Uncertainty Rating – based on AIHA Uncertainty Rating scheme, Table 2.5*
[F] *Priority for Control – based on AIHA Information Gathering And Priority Rating scheme, Equation 2.2*
[G] *Control / Information Needed – based on AIHA Priority for Control and Information Gathering Actions, Table 2.6*

From the results of the reproductive health risk assessment presented in Table 3.6, the following potential exposures were identified as **High** *risk:*

- *Exposure to formaldehyde during specimen cut-up, specimen storage and during the process of disposal and making up of formaldehyde solution;*
- *Exposure to xylene vapours during the automated staining process (particularly when replacing chemicals in the equipment).*

The following potential exposures were classified as **Moderate** *risk:*

- *Formaldehyde exposure during specimen receiving, tissue processing, sectioning and staining (these potential exposures are mainly due to background levels present in the general lab atmosphere);*
- *Xylene exposure during tissue processing, sectioning, special stains and frozen sections (these potential exposures are mainly due to background levels present in the lab);*
- *HBAs exposure during specimen receiving, cut-up and frozen sections;*
- *Ergonomic stress during tissue processing (lifting chemical containers), sectioning (repetitive movement) and light microscopy;*
- *General exposure to chemical reagents and solutions during various staining processes;*
- *Potential radiation exposure at the electron microscopy from an X-ray source and radionuclide containing solution.*

Due to insufficient and/or inconclusive research data available for the various reproductive health hazards identified in this assessment, combined with only preliminary exposure measurement data, the uncertainty rating for the majority of hazards related to various laboratory tasks and processes was set at 1 (Uncertain); Four processes – which include the use of staining reagents and solutions during the automated and special stains procedures, as well as the use of analysis chemicals and radioactive solution in electron microscopy – were assigned an uncertainty value of 2 (Highly uncertain) as no information was obtained during this study on the possible reproductive health effects of the substances used during these activities.

CHAPTER 4: DISCUSSION, CONCLUSION AND RECOMMENDATIONS

Human reproduction is a very sensitive and intricate process that might be affected by various factors, including factors present at work, home and leisure activities, and it is often difficult to isolate one parameter responsible for a particular health effect. Some factors might act synergistically, for example, exposure to chemicals at work together with alcohol consumption at home. Another example of the complexity of this issue is the assessment of the effect of ergonomic factors on reproduction as studies show that physical activities may have both positive and negative impact on reproductive health.

Although the mechanisms by which reproductive health outcomes are produced often remain uncertain, many of the research reviewed in this study concludes that there is sufficient data to warrant special consideration of reproductive health in the workplace. Specific hazards, such as exposure to chemicals (including organic solvents), heavy physical work and irregular work schedules, might require the implementation of special measures to protect in particular, but not exclusively, pregnant workers (Figa-Talamanca, 2006, Zhu et al., 2006, Julvez and Grandjean, 2009, Khattak et al., 1999, Viegas et al., 2010, Frazier and Hage, 1998, Lindbohm, 1995, Taskinen et al., 1994, Jankovic and Drake, 1996). Several researchers, however, caution against overprotection of women and implementing discriminatory measures that would be disadvantageous to the economic well-being of women (Figa-Talamanca, 2006, Frazier and Hage, 1998, Paul et al., 1989).

The existing research data on reproductive health in general is limited, particularly as far as human studies are concerned. Chemical studies are often conducted using a single substance administered to experimental animals at high doses, while exposure in laboratories is typically to a multitude of substances at relatively lower doses. Most human studies are retrospective and their accuracy might be affected by recall bias and often does not allow validation of crucial details regarding the extent and nature of workers' exposure to various stresses.

Although several researchers found an increased risk of adverse reproductive health outcomes related to chemical exposures in laboratories, very few included results from actual field measurements in their studies. Taskinen et al. reported that in Finland the concentrations of xylene in histopathology laboratories were found to be in the range of 2% to 25% of the Finnish occupational exposure limit of 100 ppm (or 441 mg/m^3, which is similar to the South African OEL and the ACGIH TLV). The concentrations of xylene measured in our study ranged from 0.02% to 23%, which appears comparable to the Finnish study (Taskinen et al., 1994).

The abovementioned researchers also reported ambient air short-term formaldehyde concentrations in histopathology laboratories in Finland of 0.01 mg/m^3 to 9.1 mg/m^3, with a mean of 0.59 mg/m^3 (Taskinen et al., 1994). The short-term concentrations measured in our study using the Formaldemeter ranged from 0.01 mg/m^3 to 2.19 mg/m^3, with a mean of 0.53 mg/m^3, again comparable to the Finnish study. Viegas et al. reported that Pathologists in pathology and anatomy laboratories were exposed to a formaldehyde Ceiling value concentration of 6.52 mg/m^3 while performing macroscopic examination (Viegas et al., 2010). In comparison, we have measured formaldehyde concentrations ranging from 0.14 mg/m^3 to 1.97 mg/m^3 during the macroscopic examination of specimen and cut-up process.

Some of the limitations related to this study are discussed below.

Only five of the fifteen NHLS histopathology laboratories were sampled in this study and, of these, four were located in the Gauteng Province. This could have introduced an element of bias, and, although the main histopathology processes are believed to be similar in all, some of the laboratories perform additional and unique analyses. Also, the specific laboratory set-up, staff complements, work volumes and control measures implemented (such as ventilation system) are varied and this might impact on the exposure.

Due to the limited resources available for this study, only preliminary assessments could be conducted. A large number of samples, taken over many days and using different scenarios, would have been necessary to cater for the large temporal and spatial variability in chemical concentrations, and to obtain a more accurate reflection of the true exposures in these work environments.

The number of chemical substances that could be sampled was limited, therefore we focused our attention on those that, following the information gathering and laboratory walkthrough, appeared to present the most obvious risk to reproductive health, namely organic solvents (particularly xylene) and formaldehyde. It is, however, possible that other toxic substances, which were not measured, might have been present. The histopathology laboratories currently use dozens of different chemicals (some in minute quantities) which could potentially affect reproductive health (a list of histopathology chemicals is given in Appendix 2).

Air sampling only evaluates the exposure risk via inhalation, which is often the most significant route of exposure. However, there is a possibility that exposure could be occur from skin contact with chemical contaminants, for example, skin absorption of organic solvents. A total body burden resulting from exposure via both inhalation and skin contact may be assessed by conducting biological monitoring (e.g. by measuring a metabolite of a chemical contaminant in blood or urine). Although potential skin contact was considered

during the laboratory walkthrough assessment, biological monitoring was outside the scope of this study.

It is also important to note that, compared to the sorbent tube method, the direct reading method, yielded seemingly much higher formaldehyde concentrations. This could be partially explained by possible temporal short-term elevated levels of this substance related to specific work processes. However, this reason alone does not seem to explain the consistent, higher values obtained with the Formaldemeter and it is suspected that the presence of interfering substances, such as ethanol (which is used in histopathology), could have resulted in elevated formaldehyde readings. In general occupational hygiene practice, more confidence is placed in results obtained using the "traditional" method of sorbent tube coupled with laboratory analysis, than in direct reading instruments that are routinely utilised for screening purposes only. Therefore, in this study, the Formaldemeter results were regarded as "indicative" and used more for comparative purposes rather than absolute, exposure values.

It therefore follows that additional information, research data and field measurements will be required in order to further substantiate the results of this health risk assessment.

Another limitation related particularly to chemical hazards is the reliance on existing occupational exposure limits as a benchmark for acceptable or over-exposure. However, OELs are often determined, due to limited research data, without full consideration of reproductive health endpoints.

4.1 Recommendations

The reproductive health risk assessment carried out in this study identified potential exposure to formaldehyde during the cut-up process, specimen storage, as well as the disposal and make up of formalin as high risks in terms of reproductive health; Potential exposure to xylene vapours during the replacement of chemicals in the tissue staining process was also identified as a high risk. All other potential exposures to chemical, biological and ionising radiation were classified as moderate reproductive health risks.

To protect workers from adverse health effects related to exposure, occupational risk factors must be eliminated or, if this is not possible, adequately controlled. Control strategies that include substitution or engineering interventions are generally more effective than administrative control or the provision of personal protective equipment (DiNardi, 2003). In accordance with standard occupational hygiene **hierarchy of control** *practice the*

recommendations listed below are divided into the following categories: substitution, engineering controls, administrative controls and personal protective equipment.

Substitution

Eliminating or substituting a hazardous agent with a less hazardous one is generally the most effective way of control. Although eliminating the source of the hazard may be the preferred solution by the occupational hygienist, it might not always be practical or feasible to do this for various reasons related to process engineering, availability of substitutes, costs, etc. In considering chemical substitution, the health, safety and environmental implications should be carefully considered to ensure that one hazard is not simply exchanged for another. It is sometimes more sensible to put programmes in place to manage a known hazard than to risk mismanaging an unknown hazard (AIHA, 2006).

Kandyala et al. reviewed the health hazards of xylene and preventative measures in histopathology laboratories. They classify xylene substitutes into four groups: limonene reagents, aliphatic hydrocarbon mixtures, aromatic hydrocarbon mixtures and mineral oil mixtures. The researchers state that aliphatic hydrocarbon substitutes of xylene are being used satisfactorily in histopathology laboratories for paraffin tissue processing during clearing and staining as well as for frozen sections although these substitutes generally need more time to obtain the same effect on the tissue and some have much lower flash point which may present a fire hazard. They also claim that mineral oil mixtures, for example isopropanol mixed with molten paraffin, looked promising in eliminating xylene from most procedures. They, however, conclude that most of the less-expensive xylene alternatives do not have the same miscibility with alcohol, wax and resinous mountants and nearly all are sold under trade names without full disclosure of the chemicals of which they are composed (Kandyala et al., 2010).

Zanini et al. evaluated two commercial and three home-made fixatives for the substitution of formalin solution in pathology laboratories, making a strong case for a formaldehyde-free laboratory. They stated that the key problem of fixation without formaldehyde is the modification of the tissues that alter their morphological aspect. However, the researchers have demonstrated that similar, and even better results to formalin fixation, can be achieved by using several alternative fixatives, including patented industrial products as well as reagents easily prepared in the laboratory from readily available chemicals. They mention that, although formalin is relatively cheap and readily available, there are "hidden costs" which include the necessity of using ventilation systems as well as the need for medical surveillance of workers exposed to a human carcinogen (Zanini et al., 2012).

It is therefore clear that chemical substitutes for xylene and formaldehyde are available. It is strongly recommended that such substitutes are investigated by a team, including laboratory managers and health and safety personnel, and, if found to be feasible and safe to use, implemented (after testing), as this could potentially lead to the most significant reduction in reproductive health risk related to histopathology laboratory processes.

Engineering Controls

Engineering controls are directed at modifying process equipment or at capturing emissions to maintain the environmental agent at an acceptable exposure level (AIHA, 2006).

In this study, the most common engineering control method encountered was local exhaust ventilation, either in the form of a fume hood (safety cabinet) or downdraft ventilation, which was utilised mainly on the cut-up work benches. In some instances, extractor fans were installed and windows were opened to increase the flow of air and increase the dilution of chemical contaminants in the work environment. During the laboratory walkthrough observations, it was, however, evident that some of the ventilation systems were either not operational or simply were not switched on. It was also unclear when last these systems were tested and what their efficiency was in terms of capturing the chemical contaminants of concern.

The South African Hazardous Chemical Substances Regulations, promulgated under the Occupational Health and Safety Act of 1993, require that engineering control equipment is maintained in good working order and thoroughly examined and tested by an approved inspection authority at intervals not exceeding 24 months (South Africa Department of Labour, 1995). Examination of local extraction systems may include quantitative measurements, such as face velocity measurement, and qualitative measurements, for example, the use of a smoke tube to indicate the direction and efficiency of air flow.

It is recommended that, in addition to the periodic testing of laboratory extraction systems that is currently carried out annually by an external service provider, in-house qualitative and /or quantitative testing is performed by laboratory personnel, under the guidance of the Occupational Health and Safety team of the NHLS and the Occupational Hygiene Section at the National Institute for Occupational Health (NIOH).

It is also crucial to train and educate all laboratory workers in the importance of using, checking and maintaining their ventilation systems on a regular basis.

Administrative Controls

Administrative controls include measures such as policies and safe work procedures, job rotation, training and education of workers, access control, medical surveillance and wellness programmes.

In a study conducted in Massachusetts corporate practices regarding reproductive hazards were surveyed in 49 chemical companies and 149 electronic companies, whose workforces ranged from 50 to more than 1000 workers. Nearly 20% of the companies excluded certain classes of workers from substances, work areas, or occupations on the basis of reproductive health concerns and another 13% offered voluntary transfers to workers concerned about reproductive risks. However, with one exception, all restrictions and transfers applied to women only, even when scientific evidence supports potential reproductive risk to both sexes. The results of the survey raised important public health concerns about corporate practices that may restrict women's job opportunities on the basis of reproductive status while under-protecting the health of male workers (Paul et al., 1989).

Frazier and Hage reviewed the various aspects of reproductive risk reduction in the workplace. They stated that reducing occupational reproductive hazards should be part of a comprehensive health and safety programme. Programmes to prevent reproductive health risks in the workplace can be divided into three levels: primary prevention – preventing a pathologic process from beginning by applying various control strategies (engineering control, work practices, personal protective equipment, etc); secondary prevention which targets pre-clinical pathologic changes in organ function to prevent these from developing into symptomatic disease; and tertiary prevention programmes which reduce the morbidity and mortality of a clinically apparent illness. The first step in implementing such programmes is a reproductive health risk assessment which includes assessing the hazard, the individual worker and the work environment. Such programmes should cover all employees within reproductive age as interventions that are not activated until pregnancy is confirmed may permit exposure during the crucial period of early foetal growth and development due to the delay between conception and the first prenatal medical visit (Frazier and Hage, 1998).

Various institutions and organizations, such as the International Labour Organisation (ILO) and the US National Institute for Occupational Safety and Health (NIOSH) have issued guidelines relating to reproductive health hazards in the workplace. The guidelines stress the general lack of information and insufficient data with regards to various reproductive hazards and the importance of making workers aware of the potential risks, particularly when working with chemicals or biological agents, when exposed to ionising radiation and when performing physically demanding work or exposed to stressful work conditions. Effective control

measures and sound occupational hygiene practices that eliminate or reduce occupational health risks to all workers, regardless of their reproductive status, will inadvertently also result in reduction of reproductive health risks (ILO, 1996, NIOSH, 1999).

In the current NHLS Safety Health and Environment Policy document and in the Safety Manual a reference is made to pregnant workers. It is stated that the Head of Section or Laboratory Manager must be informed "as soon as the staff member is aware that she is pregnant", particularly with regards to possible detrimental effects resulting from exposure to chemical, radioisotopes, or biological agents. The policy also states that "She (the pregnant worker) must be counselled, advised, and made aware of all possible risks..." (NHLS, 2012b). It is recommended that the NHLS Occupational Health and Safety team, together with the Occupational Hygiene and Occupational Medicine Sections of the NIOH review the current NHLS policy and safe working procedure on pregnancy to include both male and female workers within reproductive age. The policy / procedure must emphasise that potential reproductive risks might be present even before pregnancy is confirmed.

Personal Protective Equipment

The standard PPE used in histopathology laboratories includes lab coat, gloves, goggles and aprons. In some laboratories, workers were observed using surgical masks, mainly during the cut-up process. These masks are inadequate for protection against chemicals, particularly formaldehyde. A half-mask respirator with an appropriate filter for formaldehyde gas should be used. However, it is recognised that the use of such a respirator on a continuous basis might be uncomfortable and impair accurate visual assessment of the specimens being examined and dissected. A disposable formaldehyde respirator is commercially available and should be investigated, as this type of respirator could afford additional comfort to the laboratory worker.

When short-term high exposure to organic solvents, such as xylene, is anticipated, for example, when decanting or changing used solvents in the equipment, it is recommended that a half-mask respirator with an organic vapour filtering cartridge be used.

It is paramount that workers who are required to use a respirator when performing any task are adequately trained and undergo fit testing to ensure that the respirator is used correctly and effectively.

4.2 Conclusion and Future Studies

The reproductive health risk assessment carried out in this study identified potential exposure to formaldehyde and xylene while performing specific histopathology tasks as potentially high risk to reproductive health. Control or mitigating measures, including substitution of hazardous substances, engineering controls (ventilation), personal protective equipment and administrative measures, were recommended.

The assessment conducted during this study may be regarded as a basic survey with screening level measurements performed in order to obtain crude quantitative information with the aim of assessing and controlling exposures that deemed to be unacceptable. The focus of these measurements was on the "worst-case" scenario i.e. employees or tasks that appear to produce the highest exposures; the rational is that by controlling the worst case exposures the less exposed workers would also be invariably protected (Tielemans et al., 2002, HSE, 2006, AIHA, 2006)

Additional information, more research data and detailed survey measurements will be required to substantiate the results of this assessment. Quantitative assessments of other chemical substances, as well as other potential reproductive health hazards, such as ergonomic stress and biological agents could be conducted. In the meantime, the precautionary approach and best control practices should apply, to provide the maximum feasible protection for both males and female laboratory workers in their reproductive age. It must also be recognised that implementing measures to protect workers from other known health hazards (e.g. carcinogens) will invariably also reduce the risk from exposure to reproductive health hazards.

It is hoped that this study will contribute to sensitise, raise awareness and improve control strategies and procedures aimed at reducing reproductive health risks in this particular work environment, and in similar laboratory environments.

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APPENDIX 1: HAZARD INFORMATION GATHERING FORM

INFORMATION COLLECTION FORM

Study number

GENERAL INFORMATION

1. *What is your name, position and contact number?*

Date	**Information obtained from**			**Comments**
	Name	*Position*	*Contact No.*	

2. *What is the laboratory's name and location?*
3. *What is the staff complement of the lab?*
4. *What are the job categories in the lab?*
5. *What are the main tasks or processes performed in this lab?*

Lab name	**Location**	**Manager (name & contact No.)**	**Staff complement and work hours**
Job categories (No. of workers in each category)		**Main processes / tasks**	

HEALTH AND SAFETY INFORMATION

6. *Was there any health and safety training conducted for staff? What type?*
7. *Was there any occupational exposure monitoring conducted? What was measured?*
8. *Is there a medical surveillance programme in place? What tests are performed?*
9. *Was a health risk assessment performed in this lab?*
10. *Are material safety data sheets (MSDS) available for all chemicals used in this lab?*

H&S training	Occupational exposure monitoring	Medical surveillance programme	Health risk assessment	Material safety data sheets

OCCUPATIONAL HEALTH HAZARD INFORMATION

11. In your opinion, what are the most significant occupational health hazards in this lab?

12. For each process / task performed in this lab, specify the following:

a. *In your opinion, what occupational hazards might be associated with this task? (e.g. chemical solvent, noise, ergonomic stress, etc.)*
b. *Who might be exposed?*
c. *What is the nature of the hazard? (e.g. exposure to xylene while staining, or awkward posture while examining slides)*
d. *What is the exposure route? (e.g. inhalation of vapour, skin contact)*
e. *What are the quantities / levels of the hazards? (e.g. 100ml of solvent per day)*
f. *What is the frequency of contact with the hazard? (e.g. ½ hour per day)*

Are there any control measures in place? (e.g. extraction hood, gloves)

HAZARD INFORMATION CAPTURING TABLE

Task or process performed	Type and nature of hazard	Who might be exposed and how	Hazard quantity / level and frequency of contact	Control measures in place	Comments

APPENDIX 2: LIST OF HISTOPATHOLOGY CHEMICALS

(Source: NHLS Histopathology Laboratory Records)

Chemical Name
1. 1,2 Propylene Glycol
2. 221 Alkaline Buffer
3. 3,3 Di-aminobenzidine
4. Abopan
5. Acethythio Choline Iodide
6. Acetic Acid
7. Acetone
8. Acetyl Chloride
9. Acid Alcohol
10. Acid Fuchsin
11. Acid Red
12. Acidun Tri-chlorocetion
13. Adenosine 5Mono-Phosphate
14. Adenosine 5Triphosphate
15. Agar 100 (Resin)
16. Alcian Blue
17. Alcian Green
18. Alcohol – Ethanol
19. Alcohol – Methanol
20. Alcohol Butylicus
21. Alumen Calcium
22. Aluminium chloride
23. Aluminium Chlororatum
24. Aluminium ferric sulphate
25. Aluminium Hydroxide
26. Aluminium Potassium Sulphate
27. Aluminium Potassium Sulphate Dodeco Hydrate
28. Aluminium Sulphate
29. Aluminium Sulphite
30. Ammonia Solution
31. Ammoniac
32. Ammoni-Aluminium-Sulfuricum
33. Ammonium Aluminium Sylphat-12-hydrat
34. Ammonium Eisen III Sulphate crystals
35. Ammonium Oxalate
36. Ammonium Sulphite
37. Aniline
38. Aniline Blue
39. Aniline Oil
40. Antibodies & Diluents
41. Araldite 502 (Resin)
42. Argentum Nitricum

Chemical Name
43. Auramine O
44. Azacarmine G
45. Azur Z
46. Barbital Sodium
47. Basic Fuchsin
48. BDMA (Resin)
49. Benzene
50. Benzoyl Peroxide
51. Biebrich Scarlet
52. Biocide
53. Bismarck Brown
54. Borax Powder
55. Boric acid
56. Brilliant crystal scarlett
57. Cacodylic Acid Sodium salt trihydrate
58. Calcium Chloride
59. Calcium Nitricum
60. Canada Balsam
61. Carbol fuchsin
62. Carmin
63. Celestine Blue
64. Charcoal
65. Charcoal (activated powder)
66. Chloral Hydrate
67. Chloroform
68. Chromic acid
69. Chromic Potassium Sulphate
70. Chromium (VI) oxide
71. Chromium III Oxid
72. Chromium VI Oxid
73. Chromotrope 2R
74. Citric acid
75. Clove Oil
76. Cobalt Chloride
77. Cobalt Nitrate
78. Congo Red
79. Copper Sulphate
80. Crystal Fast Violet
81. Crystal ponceau
82. Crystal Violet
83. Dapo Reagent
84. DDSA (Resin)
85. Di – phosphorous Pentoxide
86. Di Ethyl Ether
87. Diamino Benzidine
88. Di-butyl Phthalate
89. Di-ethylbarbiture Saure
90. Di-Methyl Ferri-amide
91. Di-sodium hydrogen phosphate
92. Di-Sodium Hydrogen Phosphate – 2 – Hydrate

Chemical Name
93. DPX Mountant
94. Eisen III Chlorid
95. Entellan
96. Eosin
97. Eosin Bluishy-yellow
98. Eosin Yellow
99. Erythrosin
100. Ethanol
101. Ethylene glyco mono-athylather (Ethoxyethanol)
102. Ethyl Violet
103. Fast Blue Salt RR
104. Fast Green FCF
105. Fast Red Salt B
106. Ferric Chloride
107. Ferric Chloride (hexahydrate)
108. Ferro Ammonium Sulphuricum
109. Ferrum Sulphuricum Oxydulatum
110. Formaldehyde
111. Formalin (10% buffered)
112. Formalin 42%
113. Formic Acid
114. Fuchsin Acid
115. Fuchsin Diamond Large Crystals
116. Fuchsin Powder
117. Gelatine
118. Giemsa
119. Glacial Acetic Acid
120. Glucose-1-Phosphate
121. Gluteraldehyde
122. Gram's Iodine
123. Glycin
124. Glycogen
125. Glycerine Albumen
126. Gold Chloride
127. Haematoxylin
128. Hankers Yates
129. Haematoxylin
130. Heptahydrate
131. Hexamethylen Tetramin (Hexamine)
132. Hexamine
133. Hyaluronidase
134. Hydrochloric Acid
135. Hydrochloric acid (HCL)
136. Hydrogen Peroxide
137. Hydroquinone
138. Hydroxy Ethyl Metacrylat
139. Hypo (5% solution)
140. Insulin
141. Iodine
142. Iron ferrocyanide

Chemical Name
143. Isopentane
144. Lactic Acid (DL)
145. Lactic Dehydrogen-genase
146. Lead Citrate
147. Lead Nitrate
148. Light green SF yellowish
149. Light Green Yellowish
150. Lithium Carbonate
151. Lugol's Iodine
152. Luxol Fast Blue
153. Magnesium Chloride
154. Magnesium sulphate
155. Marthius Yellow
156. Masson Red
157. Mayers Haematoxylin
158. May-Grünwaldlosung
159. Mercuric Oxide
160. Mercury II Chloride
161. Methanol
162. Methenamine Silver
163. Methyl Blue, Blue B Green, Orange, Violet 6B
164. Methylene blue
165. Millonig's Buffer
166. Mucicarmine
167. Naphtol AS-D Chloro Acetate
168. NaphtolAS-B1 Phosphate
169. Napthyl Acetate
170. Neufuchsin
171. Neutral Red
172. Nicotin Amide Adennine di-Nucleotide
173. Nile Blue A
174. Nitric Acid
175. Nitro Blue Tetrazolium
176. NN Di Methyl-Choline
177. NN Di Methylm-phenyldiamine
178. NN Dimethyl 1-4 Phenelene di-Ammonium di-Chlorid
179. Oil Red O
180. Orange II
181. Orcein
182. Osmium Tetroxide
183. Oxalic Acid
184. Oxalic acid dihydrate
185. Paraldehyde
186. Pararosaniline Chloride
187. Paraffin Wax
188. Periodic Acid
189. Phenol
190. Phenol Extra
191. Phenol Red
192. Phloxine B
193. Phosphomolybdic Acid

Chemical Name
194. Phosphotungstic acid
195. Photo-Rex (4-[Methylamino]phenolsulphate)
196. Picric Acid
197. Pinacyanol
198. Poly Ethylene Glycol 400
199. Poly-L-Lysine
200. Ponceau S.
201. Potassium Acetate Bromide
202. Potassium Aluminium Sulphate
203. Potassium Bromide
204. Potassium Carbonate
205. Potassium Chloride
206. Potassium Di Hydrogen Phosphate
207. Potassium Di-Chromate
208. Potassium Di-hydrogen Phosphate
209. Potassium Di-sulphate
210. Potassium Ferric Cyanide
211. Potassium Ferrocyanide
212. Potassium Hydrogen Phtlate
213. Potassium Hydroxide
214. Potassium Iodate
215. Potassium Iodide
216. Potassium Meta-bisulphite
217. Potassium Nitrate
218. Potassium Permanganate
219. Potassium Phosphate Acid
220. Potassium Sulphate
221. Propandiol
222. Propylene Oxide
223. Protease
224. Pyranin
225. Pyrogalol
226. Quinol (Hydroquinine)
227. Rosaniline Hydrochloride
228. Rubeanic Acid
229. Saffron
230. Safranin
231. Scarlet Red
232. Schiffs Reagent
233. Schwefel Saüre
234. Scotts Tapwater Substitute
235. Silver Nitrate
236. Sodium Acetate
237. Sodium Barbitone
238. Sodium B Glucero Phosphate
239. Sodium Bicarbonate
240. Sodium Bi-Phosphate
241. Sodium Carbonate
242. Sodium Chloride

Chemical Name
243.Sodium Cyadine
244.Sodium Di Hydrogen Phosphate
245.Sodium Dithionite
246.Sodium Hydrogen Carbonate
247.Sodium Hydroxide
248.Sodium Hydroxide Pellets
249.Sodium Iodate
250. Sodium Iodide
251.Sodium Metabisulphite
252.Sodium Nitrate
253.Sodium Sulfite
254.Sodium Sulphate
255.Sodium Tetraborate
256.Sodium Thiosulphate
257.Sodium Thio-Sulphate-5-Hydrate
258.Sodium β Glycerol Phosphate
259.Sta-On
260.Sulphuric Acid
261.Tartic Acid
262.Tartrazine Acid Y
263.Tartrazine O
264.Tetrachloro-Gold III Acid Yellow
265.Thiofavine T
266.Thionin
267.Thymol
268.Toluidine
269.Toluidine blue
270.Toluol
271. Trichloroacetic Acid
272.TRIS Aminomethane
273.Tris Hidroxyl Methyl Amino Methane
274.Trypsin
275.Tungstophos-phoric Acid Hydrate
276.Uranyl Acetate Di-hydrate
277.Virkon
278.Weigerts Haematoxylin
279.Wolframato-Phosphorisive
280.Xylene
281.Xylol
282.Ziehl Neelsen Carbon Fuchsin
283.Ziehl Neelsen Methylene Blue

APPENDIX 3: ETHICS CLEARANCE CERTIFICATE

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

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Mr Gabriel E Mizan

CLEARANCE CERTIFICATE	**M10972**
PROJECT	Reproductive Health Risk Evaluation in the National Health Laboratory Service Histology Laboratories
INVESTIGATORS	Mr Gabriel E Mizan.
DEPARTMENT	National Institute for Occupational Health
DATE CONSIDERED	01/10/2010
DECISION OF THE COMMITTEE*	Approved unconditionally

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

DATE 01/10/2010 **CHAIRPERSON** .....
(Professor PE Cleaton-Jones)

*Guidelines for written 'informed consent' attached where applicable
cc: Supervisor : Prof D Rees

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...