Cape Peninsula
University of Technology

# AN APPROACH TO THE IMPROVEMENT OF THE SELENIUM ANALYSIS PROCESS OF THE WESTERN CAPE PROVINCIAL VETERINARY LABORATORY

**VOLUME I**

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by

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**Cape Town**
November 2011

**DECLARATION**

By

**Bronwyn Claudia Cloete**

"I Bronwyn Claudia Cloete, hereby declare that the contents of this dissertation submitted for the degree (Magister Technologiae: Quality) at the Cape Peninsula University of Technology, represents my own original unaided work and has not previously been submitted for any other institution of higher education. I further declare that all sources cited or quoted indicated or acknowledge by means of a comprehensive list of references. Furthermore, it represents my own opinion and not necessarily those of the Cape Peninsula University of Technology"

Name: Bronwyn Claudia Cloete
November 2011

Signature:

## DEDICATION

To my femeli-yum

With insurmountable love and appreciation. You know that I couldn't do it without you. If we were a car, I'd be the bright pink paint, while you guys would be the powerful fuel injected engine, the GPS navigation, the wiper blades, the air conditioner and the two pretty fragrant air fresheners hanging from the rear view mirror. I know that there is no destination that we couldn't reach....together.

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# ABSTRACT

Reliable analytical results represent the pinnacle assessment of the quality of an analytical laboratory. Variability associated with the analytical method, or process known as selenium analysis which is being used at Western Cape Provincial Veterinary Laboratory (WC PVL), presents a critical quality problem. This is due to the narrow margin of safety between toxic and deficient doses for animal health. In addition, control features of this selenium process, were found to be limited. Limited control features represent 'process waste'. To overcome the adverse impact of variation and limited control, steps towards process improvement present the best solution.

The primary research objective of the research study is: "To establish an alternative accurate and safer digestion procedure within the 'selenium analysis process, in order to attain quality improvement of the process".

The scientific method was employed to accomplish the research objective. The research design and methodology selected was based on the scientific PDCA cycle, and is known as Lean Six Sigma. A research hypothesis was set as $\mathbf{H_0}$ : Variation in process, time and control procedures have a direct impact on the disparity in selenium testing results. Research was able to test the hypothesis using scientific methodology which was empirical, inductive and deductive, systematic, relied on data and was fact based.

Implementation of an alternative, more reliable and safer selenium analysis process is believed to result in reduced risks associated to the digestion procedure, while optimising selenium yield and ultimately translating into improved quality in terms of accuracy and precision, thus confidence in results.



**Key words:** Selenium Analysis, Process Improvement, The Scientific Method, Lean Six Sigma, Quality

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Note: Due to the voluminous nature of the annexures in this research study, for ease of reference, all the annexures referred to herein are contained within Volume II of this dissertation, bound under separate cover.

## GLOSSARY OF TERMS

**Adsorption:** Adsorption is the adhesion of atoms, ions, bio molecules or molecules of a gas, liquid or dissolved solids to a surface.

**Analyte:** A substance or chemical constituent that is undergoing analysis.

**Analytical Bias:** Consistent deviation of analytical results from the "true value". Analytical Bias is caused by systematic error of an analytical process.

**Analytical Sensitivity:** The rate of change in instrument response, observed over that change in concentration, in the analytical measurement apparatus when measuring an analyte.

**Assignable Cause Variation:** Considered to be Random Process Error. See Random Process Error.

**Atomic Absorption Spectrophotometer (AAS):** Analytical laboratory equipment which is widely used to assess the concentration of a variety of elements. It uses the principle that atoms of a particular element absorb light of a characteristic wavelength unique to the element being measured.

**Blank Sample:** The purpose of a blank sample is 'zero' or cancel out the absorbance of all other components in the sample, except the component being analysed.

**Chelate:** A ring shaped molecular complex in which a metal is held at two or more points. Chelating agents include disodium edentate and calcium disodium edentate.

**Chemical Oxidation:** Chemical oxidation is the chemical reaction between oxygen molecules and other substances. When oxygen is added to a substance, oxidation takes place, and an oxide is formed. Oxidation is the loss of electrons.

**Chemical Reduction:** Chemical reduction is the loss of oxygen molecules from a substance. Reduction and Oxidation always takes place simultaneously. Reduction is the gain of electrons.

**Common Cause Variation:** Considered to be Systematic Process Error. See Systematic Process Error.

**Confidence Limits:** A statistical range with a specified probability that a given parameter lies within the range. The extent of the range is known as a Confidence Interval.

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| **Control Limits:** | Also known as Process Specification Limits are defined as the standard deviation (3σ) of a process taken over a long period of time. This is a pure statistical parameter and associated to the uncertainty prevalent in an analytical chemistry method. |
| **Control Sample:** | Part of a study or experiment against which an experimental procedure can be compared, and its effects judged. |
| **Correlation Coefficient:** | This coefficient represents the "goodness to fit" of a regression line. |
| **$C_p$:** | Process Capability Indicator. |
| **$C_{pk}$:** | Process Performance Indicator. |
| **CRM:** | Certified Reference Material. |
| **CSIR:** | Council for Scientific and Industrial Research. |
| **DAN:** | 2,3-Diaminonaphthalene is a photosensitive molecule which is decomposed in the presence of light The principle of fluorimetric detection of selenium is the measurement of DAN in an analyte, which is attached to the trace element selenium. |
| **Fluorimeter:** | Analytical apparatus used to analyse trace elements. Uses the same principle as AAS. |
| **FMEA:** | Reliability analysis tool or methodology to make process designs more reliable. |
| **Ishikawa Diagram:** | Also known as Root Cause Analysis Diagram or Fishbone chart. Causal diagrams used to show the causes of certain events. |
| **Heijunka:** | Japanese term which refers to a technique to reduce process wastes. |
| **Horwitz Ratio:** | Horwitz function or ratio is an index to measure process performance with respect to precision, in analytical chemistry. |
| **Hydride Generator:** | Analytical apparatus facilitates and enables the analysis of certain trace elements on AAS. |
| **Kaizen:** | Japanese term for Improvement. Kaizen Analysis involves the assessment of improvement opportunities. |

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| **Lean:** | Methodology focussed on reduction of waste. |
| **LOD:** | Lowest level of analyte in a sample which elicits a response from the measuring instrument. |
| **LOQ:** | Lowest level of analyte in a sample which elicits a response from the measuring instrument considered to be of reasonable reliability. |
| **Muda:** | Japanese term for an activity that is wasteful. |
| **Mura:** | Japanese term for an activity that is irregular, inconsistent or uneven. |
| **Muri:** | Japanese term for an activity that is unreasonable or causes overburden. |
| **Natural Tolerance Limits:** | These limits are commonly set by the customer of a process. These are not the same as control limits, which are a pure statistical parameter, determined by process standard deviation. |
| **Nitric Acid:** | $HNO_3$. Also known as Aqua Fortis is a highly corrosive strong acid, commonly used for sample digestion in analytical chemistry. |
| **Normal Reference Range:** | Normal biological reference range used by pathologists to make a diagnosis. |
| **Open Heat-block:** | Apparatus used in the chemistry laboratory which serves the purpose of heating multiple samples at the same time. This heating mechanism is regarded as an open heating system. |
| **Oxidation State:** | In chemistry the oxidation state is an indicator of the degree of oxidation of an atom in a chemical compound. |
| **Pareto Diagram:** | A chart used to identify and prioritise problems to be solved. |
| **PDCA Cycle:** | Acronym for Plan, Do, Check and Act. Cycle which consist of these phases and is used for process improvement. |
| **Perchoric Acid:** | $HClO_4$ is a strong corrosive mineral acid, commonly used for sample digestion in analytical chemistry. |
| **ppb:** | Parts Per Billion. Common use in chemistry to express concentration of an analyte. |

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| **ppm:** | Parts Per Million. Common use in chemistry to express concentration of an analyte. |
| **Process Capability Analysis:** | Process Capability statistically describes the ability of any process to perform within specification. It is a means to determine process performance and proficiency. |
| **Process Precision:** | The extent of 'repeatability' demonstrated by a process. A process with little variation is said to be precise. |
| **Process Variation:** | The extent of variability demonstrated by a process. |
| **Random Process Error:** | Variation or error which is as a result of sources outside of the process. |
| **Sample Digestion:** | In order for samples to the analysed by analytical chemistry techniques, it is necessary for the sample to be in a matrix or from that is suitable for analysis. Organic samples are commonly digested using acid to permit further analytical testing. |
| **Six Sigma:** | Methodology or approach for improving quality. The principle behind Six Sigma is the reduction of variation. Six Sigma requires the process standard deviation be no more than one sixth of the total allowable spread. |
| **Statistical Process Control (SPC):** | Application of statistical method to the measurement and analysis of variation in a process. It is commonly used in Six Sigma implementations. |
| **Speciation:** | The distribution of a chemical element among defined chemical species in a system. |
| **Standard Sample:** | A sample containing a specified, determined concentration of analyte. |
| **Standard Calibration Curve:** | Consists of range of standard samples. This standard method permits regression analysis and enables the determination of the unknown concentration of analyte. |
| **Systematic Process Error:** | Variation or error present due to the inherent nature of a process. Such variation cannot be altered without changing the process itself. |
| **Total Regression Uncertainty Analysis:** | A method to determine the total uncertainty associated to an analytical chemistry process with the use of calibration curve and CRM data. |
| **Value Stream Map:** | Flow chart use in process improvement. |

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# CHAPTER ONE

# SCOPE OF THE RESEARCH

## 1.1 INTRODUCTION AND BACKGROUND

Accuracy, precision and reliability play critical roles in every laboratory environment and WC PVL is no exception. Accuracy can be defined as the extent to which measurements agree with the true value of the quantity being measured. Reproducibility of measurement is known as precision, while reliability is the ability of a method to be both accurate and precise.

In order to ensure quality service delivery from the laboratory thereby assuring accuracy and precision of result output, it is an important requirement that all processes employed at the WC PVL be managed using total quality systems management. Total Quality Management (TQM) is a comprehensive and structured approach to organizational management that seeks to improve the quality of products and services. TQM dictates that processes are divided into four sequential categories namely Plan, Do, Check, and Act (PDCA).

The PDCA cycle is asserted to have originated during a lecture presented by Dr. W. Edwards Demings in Japan in 1950 (Moen & Norman, 2011:1). Furthermore, the PDCA is described as a 'model for improvement'. This model is widely applicable and easy to learn to use, yet it supports the full range of improvement efforts, from very informal to the most complex. The PDCA cycle is, by nature, firmly rooted in the scientific method, and the philosophy of science that has evolved over more than 400 years. This evolution saw the integration of the scientific method into the 'science of improvement'. The pragmatic result of this evolution is believed to be the birth of the PDCA cycle and TQM.

An objective of TQM is to eliminate variation and achieve process control. The current selenium analysis process, employed at WC PVL, lacks control. Research is embarked upon to ensure process requirements are met, resulting in process results which are more accurate and precise. Trustworthy, accurate and precise process

results reflected in final customer laboratory reports are the final depiction of the quality of service rendered by WC PVL in the critical diagnostic role they fulfil in South Africa.

## 1.2 RESEARCH PROCESS

The research process to be followed in this dissertation will be based on steps followed according to the Scientific method. According to Shuttleworth (2008a:**Online**), "...whilst there are minor variations between different scientific disciplines, they all follow the same basic path. Fundamental phases in the research are listed below:

- **Phase 1:** Formulate a general question about the area of research and start the defining the research process.
- **Phase 2:** Through a process of elimination, narrow and focus the research area. This leads to the arrival of one fundamental hypothesis around which the experiment can be designed.
- **Phase 3:** Design steps that will test and evaluate the hypothesis, manipulating one or more variables to generate analysable data.
- **Phase 4:** Considered the midpoint of the scientific method, and involves observing and recording the results of research. This stage involves looking at the effect of the manipulated variables.
- **Phase 5:** Broadens the scope of the research again, when statistical analyses are performed on the data, and it is organised into an understandable form.
- **Phase 6:** 'Conclusions and publishing' is technically the phase where the hypothesis is stated as proved or disproved. In this phase, interesting results can be earmarked for further research and adaptation of the initial hypothesis. If the initial hypothesis is proved to be incorrect in this phase, it leads to considering that the experiment had a flaw in design or implementation. Results are usually published, allowing verification of the findings.
- **Phase 7:** 'Cycles' is not the final phase of the scientific method, as the scientific method generates data and ideas to recycle into the first stage."

## 1.3 BACKGROUND TO RESEARCH HYPOTHESIS

Trace mineral status analysis of livestock is one of the crucial diagnostic services rendered by the WC PVL. The most common reason to assess the trace mineral status of livestock is to determine the prevalence of nutrient deficiencies or toxicities within livestock populations. The process of selenium analysis requires highly sensitive, specific and reliable analytical approaches, involving a sample digestion procedure as part of the selenium analysis process occurring, before the actual selenium determination.

The current process for selenium analysis involves the use of an open heat-block for sample digestion. Although results obtained using this method, are considered relatively accurate and precise, the method is believed to lack control. A significant increase in incidents in recent months, where results were either delayed or completely unavailable due to problems associated with sample digestion, prompted the call for research to be carried out in order to ascertain root causes of shortfalls in process control.

This research study was conducted to investigate alternatives to open heat-block digestion. An alternative to open heat-block digestion process is the closed-vessel microwave digestion process. Microwave digestion is believed to lead to augmented digestion in terms of selenium yield and recovery. Furthermore, under microwave conditions the oxidising power of acid is amplified, increasing the rate of digestion reaction and the efficiency of acid decomposition, by significantly improving chemical reaction velocity. It thus reduces digestion time from hours, to minutes. Oxidizing conditions are stably maintained throughout the digestion procedure, and complete digestion can be achieved with one acid, eliminating the need to mix acids consequently reducing the risk of contamination.

A quality management mélange comprising of a combination of three different but complementary quality management approaches namely, ‘Six sigma’, ‘Lean’ and ‘Failure mode and effects analysis’, is believed to be the quality tool which has the ability to accomplish the desired process quality improvement. This dissertation will

attempt to demonstrate the successfulness of the implementation of this quality tool, on the pedestal of a scientific method research process.

## 1.4 HYPOTHESIS TESTING

Leedy and Omrod (2001:60), explain that research hypotheses are nothing more than tentative propositions set out to assist in guiding the investigation of a problem, or to provide possible explanations for observations made by an author. Moreover, Leedy and Ormrod (2001:60), define the term 'hypotheses' as a "logical supposition, a reasonable guess, and educated conjecture".

Collis and Hussey (2003:126), explain that a formulated research hypothesis must identify an 'independent value' and a 'dependent value', and the actual relationship between them. For this study, the two general variables selected are 'the selenium analysis method' and 'result quality improvement'.

According to Leedy and Ormrod (2001:6), hypotheses are never proved or disproved. When findings run contrary to a particular hypothesis, the research either rejects that hypothesis or turns to another as being more likely to explain a phenomenon. Also, over time, as a hypothesis is supported by a growing body of data, it evolves into a theory.

## 1.5 STATEMENT OF THE RESEARCH HYPOTHESIS

Within the WC PVL Biochemistry research environment the following one-tailed hypothesis was identified, and provides a primary focus for the research to be conducted:

**$H_0$** : Variation in process, time and control procedures have a direct impact on the disparity in selenium testing results.

In the above hypothesis 'variation in process, time and control' will serve as the 'dependent' variable, and the 'disparity in selenium testing results' will serve as the 'independent' variable.

## 1.6 INVESTIGATIVE QUESTIONS

The following will serve as investigative questions in support of the research hypothesis:

- Can a modified process design, focussed on digestion procedure be established with better control features, in order to overcome variation within the process?
- Will a modified digestion process result in reduction of associated biohazard and other risks associated to the selenium analysis process?
- Will a modified digestion process result in optimising selenium yield?
- Will a modified process design ultimately translate into an improvement in quality, in terms of the reliability of results?

## 1.7 KEY RESEARCH OBJECTIVES

### 1.7.1 Primary research objective

The primary research objective of the research study is: "To establish an alternative more accurate and safer digestion procedure within the 'selenium analysis process', in order to attain quality improvement of the process".

### 1.7.2 Secondary research objectives

The secondary key research objectives of the research study are:

- To determine if a modification of the existing hot plate digestion method to microwave digestion method is capable of reducing the risks associated with the digestion procedure.
- To determine if a modification of the existing digestion method to the microwave digestion method will result in optimising selenium yield of the process.
- To determine if a modification of the existing digestion method will ultimately translate into an improvement in quality in terms of reliability of results.

## 1.8 RESEARCH DESIGN AND METHODOLOGY

In order to achieve the research objectives, it is deemed necessary that research be conducted according to the scientific method. Shuttleworth (2008b:**Online**), states "The scientific method, as defined by various scientists and philosophers, has a fairly rigorous structure. In reality, apart from a few strictly defined physical sciences, most scientific disciplines have to bend and adapt these rules, especially sciences involving the unpredictability of natural organisms and humans." In agreement with this, Carpi and Egger (2003:**Online**), are of the opinion that "The classical description of the scientific method as a linear or circular process does not adequately capture the dynamic, yet rigorous, nature of the practice".

According to Shuttleworth (2008b:**Online**), the scientific method can be considered to be empirical by nature. In addition to this, the scientific method can be described as 'systematic and methodical', which ensures that researchers do not make mistakes or purposefully manipulate evidence. Results from experiments are therefore retested and repeated until a solid body of evidence is built up.

Quoting Shuttleworth (2008b:**Online**): "Science requires vision, and the ability to observe the implications of results". Induction is thus a very important aspect of the scientific method. Inductive reasoning or induction is the process of relating findings to the 'real world'. Shuttleworth (2008b:**Online**), explains that the visionary part of sciences lies in relating findings back to the 'real world'. Collection of data, as well as data analysis and the interpretation of data form an integral part of this process. Therefore a characteristic of the scientific method is that it uses some type of measurement to obtain and analyse the resultant data. Data is obtained through the two major methods, namely, observation and measurement, which were described as the two fundamentals around which science is purely based. Observation provides qualitative data, while measurement provides quantitative data.

Shuttleworth (2008b:**Online**), was found to contend that, "The process of induction and generalization allows scientists to make predictions about how they think that something should behave, and design an experiment to test it. This experiment does

not always mean setting up rows of test tubes in the lab or designing surveys. It can also mean taking measurements and observing the natural world".

Capri and Egger (2003:**Online**), mentions that "Scientific research is a robust and dynamic practice that employs multiple methods toward investigating phenomena, including experimentation, description, comparison and modelling". Furthermore, these authors contend that, even though the scientific research methods can be separately described, many of these methods overlap, or are used in combination.

Therefore, a scientific research method was required for this dissertation. In alignment with the phases of the research process as discussed in section 1.2, the PDCA cycle is described as methodology to advance scientific knowledge through the 'science of improvement' (Moen & Norman, 2011:9).

The authors state the PDCA cycle does the following:

- Encourages planning to be based on theory.
- The theory leads to appropriate questions which provide the basis for learning.
- Questions lead to predictions which guide the user in identifying necessary data, methods and tools to answer the questions relative to the theory in use.
- Emphasizes and encourages the iterative learning process of deductive and inductive learning.

A 'unit of analysis' has been defined by the Research Methods Knowledge Base as, "...the major entity being analysed in a particular study" (Research Methods Knowledge Base, 2006:**Online**). The primary unit of analysis for this research project is biological samples, on which replicate tests are performed. A known control sample, as well a certified international standard reference sample are also included.

The term 'population' is defined by Ross and Chadwick (1999: **Online**), as, "...all the members or objects of any defined group which might be taken, or about which information might be given." A research population refers to the entire group to which the research results apply e.g., a relevant age group, or equipment group. The

research conducted for this research study, as required by this dissertation, required data collection from population of biological laboratory samples. Quantitative analytical data obtained through the measurement of samples by the process, and is able to be statistically analysed. With the use of a hypothesis the research study is able to ultimately conclude whether or not process modification can be seen as an improvement.

A sample is defined as a finite part of a statistical population whose properties are studied to gain information about the whole, (Merriam-Webster, 2011:**Online**), while sampling is defined as the method of selecting a certain number of units from a total population. (Ross & Chadwick, 1999:Online).

According to Collis and Hussey (2003:155-160), two main categories of sampling can be identified, namely 'probability sampling' and 'non-probability sampling'. This research will make use of the non-probability sampling category. Citing Collis and Hussey (2003), Watkins (2008:54), states that 'non-probability sampling' is considered "...a sampling technique where the researcher has no way of forecasting or guaranteeing that each element of the population will be represented in the sample".

Through the method of non-probability purposive sampling, a sample population of 10 different biological samples, as well as an internal laboratory reference sample, is analysed in 13 replicates, using the current selenium analysis process to determine process capability. A certified reference sample is analysed concurrently with the sample population in 6 replicates, to evaluate accuracy and precision of the process.

## 1.9 DATA COLLECTION AND DESIGN

As data collection methodology plays a critical role in engineering analysis, it must be carefully selected and applied accordingly. To accomplish process improvement on an analytical laboratory process, it is necessary for more than one data collection methodology to be employed. In order to accomplish the objective of this dissertation, 'experimentation' and 'comparison' are the two scientific methods used for data collection.

'Experimentation' is defined by Capri and Egger (2003:**Online**), as a "...research method in which one or more variables are consciously manipulated, and the outcome of the effect of that manipulation on other variables is observed". Thus experimental methods are commonly applied to quantify the magnitude of the response of a variable, or to determine causal relationships. In order to detect any sources of error in experimental designs, 'controls' which provide a measure of the variability within a system, are used. Moen and Norman (2011:2), stated that "Conducting designed experiments are a cornerstone of science and the scientific method".

Capri and Egger (2003:**Online**), state that the research method 'comparison' includes both prospective studies which examine variables from the present forward, as well as retrospective studies, which look at events that have already occurred. Moen and Norman (2011:3), argue that the generation of scientific knowledge may be accomplished through the interplay of 'deductive data analysis', to interpret 'nature', proceeded by 'inductive reasoning', to 'advance scientific knowledge from observations to axiom to law'.

Carpi and Egger (2003:**Online**), regards data collection for the scientific method to be the systematic recording of information, while data analysis involves working to uncover trends and patterns in data sets. An explanation of those patterns and trends is provided via data interpretation. Different scientists can interpret the same data in different ways, as data interpretation is done based on the scientist's background knowledge and experience. By publishing their data and their techniques used to

analyse and interpret data, scientists give the scientific community the opportunity to review the data and use it in future research (Capri & Egger, 2003:**Online**).

## 1.10 RESEARCH ASSUMPTIONS

The research will be conducted on the basis that the following are assumed:

- Researchers performing the analysis are competent to perform analytical work required for research.
- Research takes place under normal working laboratory conditions.

## 1.11 RESEARCH CONSTRAINTS

### 1.11.1 Limitations

Results from this research are reflective of normal operating conditions of WC PVL and will not include process operations during emergency situations, which might potentially occur (e.g. an outbreak of a controlled disease such as African Horse Sickness or Avian Influenza) or laboratory equipment breakdown.

### 1.11.2 De-Limitations

Research will only be conducted on one sample type, namely liver tissue samples.

## 1.12 CHAPTER AND CONTENT ANALYSIS

The following chapters, with reflection of their content, were proposed for inclusion in the research study:

**Chapter 1:** The Scope of the Research:

This chapter sets the scene for research contained within the ambit of the thesis. The chapter provides a brief introduction, with key factors which highlight the importance of quality processes and the need to control and manage them. The research process will be explained, followed by the development of the research

problem, research hypothesis and supporting investigative questions. This chapter identifies research objectives and provides an overview of dissertation structure.

**Chapter 2:** Elemental Selenium: Background, importance and detection, a holistic perspective:

The chapter provides background considerations relating to the research environment. Additionally, this chapter includes specific literature review on selenium to provide insight into the chemical element selenium, upon which research is focussed.

**Chapter 3:** Quality Process Improvement Literature Review:

In this chapter a comprehensive literature review gives an insight into the key academic drivers of the research. This chapter equips the reader with the necessary background and information to understand why quality is critical in the research environment, and how quality methodologies are used to impact a valuable improvement on the research environment.

**Chapter 4:** An approach to the improvement of Selenium Analysis process of Western Cape Provincial Veterinary Laboratory:

In this chapter the survey environment, in which research is conducted will be described, as well as the parameters associated with the data collection. This chapter provides detailed explanations of the scientific method research methodology used, as well as the rules pertaining to the validity and reliability of data.

**Chapter 5:** Data analysis and Interpretation of Results:

This chapter offers an explanation on the way data which was collected, is analysed and interpreted.

**Chapter 6:** Conclusion and Recommendations:

This chapter re-visits the relevant factors pertaining to research problem which were explored in Chapter 1. Analogies are drawn from literature review and data analysis. Key findings are stated, and conclusions and recommendations are made to mitigate the research problem.

## 1.13 SIGNIFICANCE OF RESEARCH

The significant benefit to be gained from the research would be the practical value secured from the improvement of a critical biochemistry process and an overall quality improvement of the service rendered by WCPVL.

## 1.14 CONCLUSION

Despite the fact that it has been historically and traditionally accepted that the current selenium analysis process at WC PVL produces sound results of good quality, there is a growing opinion that there are procedures within this process which can be improved upon. It is believed that modifications to improve the current process will translate into an improvement in the quality of the resultant service delivered by WC PVL.

The first step in mitigation of the problem is understanding the complex nature of the trace element selenium, which is at the core of the analytical process being researched. Only with a concrete understanding of selenium's properties within the context of process dynamics, can any further research be done. In addition, research needs to perform the exercise of holistically and thoroughly examining the process and all factors contributing to the quality of the process outcome. This is seen as a means to accomplish the direction for further research in order to solve the research hypothesis and to accomplish research objectives.

# CHAPTER TWO

# ELEMENTAL SELENIUM: BACKGROUND, IMPORTANCE AND DETECTION, A HOLISTIC PERSPECTIVE

## 2.1 INTRODUCTION

In order to make any meaningful quality improvement in the Biochemistry Section of WC PVL, an extensive and thorough examination into the element selenium, is required, including properties and behaviour within the research environment. Furthermore the actual research environment where quality improvement is desired must also be examined in order to identify the chief requirements of the research area, thereby identifying where improvement will have the most valuable practical impact.

The secondary objective is to establish the broad framework, and identify the guideline parameters in which research will take place. This is done by holistically extrapolating the factors or variables which have an effect on the research environment, specifically related to the selenium analysis method.

## 2.2 RESEARCH ENVIRONMENT ASSUMPTIONS AND LIMITATIONS

The research deemed necessary for this dissertation is based solely on the operation of one specific process, namely the selenium analysis process, within the system of processes which occur during the overall WC PVL service provision. It is thus necessary to assume that all other operating practices which surround any other processes which operate in conjunction with the selenium analysis process – including prior- and post-analysis processes, will not have a significant effect on the topic of research, namely result quality.

According to Huber (2011:**Online**), Good Laboratory Practices (GLP) are a set of published regulations and guidelines, which have a significant effect on the daily operation of an analytical laboratory. This author provides the explanation that

"GLP deals with the organisation, process and conditions under which laboratory studies are planned, performed, monitored, reported and recorded. GLP practices are intended to promote the quality and validity of test data" (Huber, 2011:**Online**). Systems International Inc. (2011:**Online**), state that TIS 17025 (ISO/IEC 17025) is the international standard which specifies general requirements for competence of laboratories to carry out tests and/or calibrations. Further to this, the author states that if testing and/or calibration laboratories comply with TIS 17025 (ISO/IEC 17025), they will operate a quality system for their testing and/or calibration activities that also meet the requirements of ISO 9001 series.

For the purpose of this research it is assumed that standard Good laboratory practices (GLP) are followed in all the peripheral areas affecting the Biochemistry section, as well as suitable quality management system practices, according to ISO 17025 are in place.

Limitations which have a prevalent effect in the Biochemistry section includes availability of analytical equipment. Research can only be carried out with the resources available in the section. An additional limitation includes laboratory operating hours. Although much of the research is conducted outside of normal operating hours of the laboratory, the research being conducted is for improvement on a process which is routinely performed within operating hours. Thus, any recommendations for improvements which are made, should accommodate process operation in normal laboratory operating hours.

Furthermore, research on the selenium analysis process is also only being conducted on a single sample type. However, it is anticipated that slight modifications can be made to accommodate further sample types if necessary, once a process improvement has been established and validated.

## 2.3 ELEMENTAL SELENIUM

Selenium is one of the rarest chemical elements. It is known as an essential trace element, since it is vital for healthy body function. Selenium, however, differs from most other trace elements because of the narrow margin between selenium toxic levels and deficient levels in living organisms. Selenium's atomic number is 34 and it has an atomic weight of 78,96. Selenium's position in the periodic table and electronic configuration, places selenium in the important group of half metals known as metalloids, which are neither fully metallic nor non-metals (Radiochemistry Society, 2003:**Online**).

Research conducted by Tarin (2006:28), found that selenium is known to exist in both inorganic and organic forms, and in four different chemical oxidation states (0, -2, +4 and +6): elemental selenium, selenide, selenite and selenate respectively. In biological samples, selenium is reported to occur in the selenide species. The selenide species of selenium has insoluble properties, whereas the selenite or selenate species have more soluble properties. Between the selenite and selenate species, selenite is more strongly adsorbed than selenate.

Tarin (2006:31), states the adsorption of selenium anions is highly dependent on pH conditions. The presence of other types of anions may also affect the adsorption of selenite. Certain other anions decrease selenite and selenate adsorption, by competing for adsorption sites.

In addition, selenium is known as a redox sensitive element. Thus selenium behaviour is influenced by the presence of other elemental redox species. The availability of certain other elements during sample preparation has an effect on selenium mobility, as they result in oxidation and/or reduction processes taking place of selenium (Tarin, 2006:32). The complex redox behaviour of selenium is therefore an important factor for consideration in the development of any new analytical method for selenium analysis.

## 2.4 PREVALANCE OF SELENIUM

Bem (1981:183), contends that selenium has found broad technological applications, among others in electronics (for production of semiconductors, photocells, rectifiers and printer cartridges), machine industry (for obtaining high-grade steel), glass industry (for staining of glass), chemical industry (as a catalyst), rubber industry (for acceleration of vulcanization), pharmaceutics (veterinary selenium preparations in treatment of diseases due to selenium deficiency) and in agriculture, organoselenium compounds are used as bactericides, fungicides and herbicides.

According to Habeck (1989:**Online**), selenium is a naturally occurring substance that is widely, but unevenly spread across the earth's crust. Selenium is not often found in pure form, but is usually combined with other substances. With the natural degradation of rocks into soil, selenium is released and combines with oxygen to form several substances, the most common of which are sodium selenate and sodium selenite. Thus selenium occurs naturally in soil, from which it permeates the surrounding atmosphere and water.

Furthermore plants easily take up selenate compounds from water, and change them to organic selenium compounds such as selenomethionine. (Habeck, 1989:**Online**). The author's contention is supported by Kurkova, Skrypnik and Zalieckiene (2008:40), who assert that people and animals mainly receive selenium in the form of selenium-bearing amino acids, selenomethanione and selenocysteine of vegetative origin.

## 2.5 IMPORTANCE OF SELENIUM

Kurkova , Skrypnik and Zalieckiene (2008:40), state that the significance of selenium was first recognised in the 1930s, when it was discovered that some well studied and economically significant diseases of agricultural animals, occurred as a result of chronic selenium poisoning. Until the 1950s, scientists regarded selenium exclusively as a toxic element.

Selenium toxicity (selenosis) in animals, as pointed out by Elis (2008:10), is characterised by general dullness, lack of vitality, emaciation, stiffness and lameness. Cattle lose hair from the switch, while in horses hair is lost from their tail and mane. Hooves become loose and often sloughed off. Reduction of reproductive performance and teratogenic effects in animals, have also been reported. Alkali disease (also known as blind staggers), is also regarded as an effect of selenosis. This disease occurs in differing degrees, from a mild chronic condition to an acute form resulting in death, sometimes within a few hours of consuming plants containing toxic levels of selenium (Elis 2008:10).

Habeck (1989:**Online**), maintains a similar point of view to that of Elis (2008:10), by stating selenium is toxic, when eaten in amounts larger than what is needed for good nutrition. Some plants can build up selenium to levels that are harmful to livestock feeding on them. Exposure to high levels of inorganic selenium causes birth defects. Clinical signs of selenium poisoning include weight loss, poor growth rate, lameness, defective hoof growth (horizontal ridges or cracks in hoof wall), hair loss, and acute deaths - especially when errors are made when mixing selenium into animal feed, or overdosing injectable selenium products. It has also been found that a certain form of selenium (selenium sulphide - used in anti-dandruff shampoos) is carcinogenic to animals.

The 1973 discovery that selenium activates the antioxidant enzyme glutathione peroxidise, led to the realisation of the importance of selenium. As a component of the glutathione peroxidise enzyme, together with vitamin E, selenium prevents cell destruction by peroxides, which are generated in the process of metabolism. Thus it plays an important role by protecting non-membranous proteins and biological membranes, explain Kurkova, Skrypnik and Zalieckiene (2008:40).

Both Habeck (1989:**Online**), and Khanal and Knight (2010:101), state that regardless of selenium's toxicity in large enough doses, selenium is also found to be an essential requirement for animals for growth and fertility. Khanal and Knight (2010:101), state that selenium plays a role in neutrophil and lymphocyte, as well as antibody production. Clinical signs of selenium deficiency include reduced appetite, liver necrosis, predisposition to exudates (fluid containing a high content of protein

or cellular debris escaping from blood vessels, and being deposited in tissues), embryonic mortality, poor antigen response as well as pancreatic fibrosis in birds and white muscle disease in ruminants.

Khanal and Knight (2010:101), refer to the problem of selenium deficiency as being more of a geographical problem than selenium toxicity, due to seleniferous soils (soils containing selenium). Kurkova, Skrypnik and Zalieckiene (2008:43), share the same opinion and emphasize that selenium content in vegetative food differs considerably depending on the region of its growth. They elaborate by stating the number of regions in the world with an excess of this microelement is smaller than the number of regions with insufficient selenium content. These statements illustrate the necessity of supplementation in livestock in certain geographical regions.

Thus, this demonstration of the importance of selenium in animal health illustrates why the application of the most accurate and precise analytic methods of detection is critical. This importance is motivated by Campbell (1984:645), who argues that "Although it would appear to be an essential trace element, it also shows toxicity at levels which are regarded as normal for many trace elements". This is supported by Janz, DeForest, Brooks, Chapman, Gilron, Hoff, Hopkins, McIntyre, Mebane, Palace, Skorupa and Wayland's (2010:143), who contend that the margin between essential level and toxic level of selenium is extremely narrow.

Selenium analysis processes have, however, traditionally posed several challenges, due to selenium's complex chemical properties. As a result, many diagnostic and research laboratories decided not to offer the service due to uncertainty surrounding the reliability of their results. It is only with a concrete understanding of selenium's complex chemical properties and the multifaceted principles associated with various detection methods to measure this chemical, that any improvement can be made on the process of selenium analysis.

## 2.6 SELENIUM ANALYSIS

Western Cape Provincial Veterinary Laboratory is currently one of only five testing laboratories country wide offering the service of selenium analysis. Others are Council of Scientific and Industrial Research (CSIR) (Stellenbosch), Allerton Provincial Veterinary Laboratory (KZN), Nutrilab (University of Pretoria), and Bemlab (Strand, Western Cape). Investigations revealed that there are some private laboratories who offer the service of selenium analysis, but analysis of samples is sub-contracted to one of the above-mentioned laboratories.

Ducros, Ruffieux, Belin, and Favier, (1994:1715), state that many techniques have been developed for selenium analysis including fluorimetry, electrothermal atomic absorption spectrophotometry (ET-AAS), hydride-generation atomic absorption spectrophotometry (HG-AAS), neutron activation analysis (NAA) and different mass spectrophotometry methods: gas chromatography-mass spectrophotometry (GC-MS), thermal ionization mass spectrophotometry and, more recently, inductively coupled plasma mass spectrophometry (ICP-MS). All of these methods (except NAA and ET-AAS for some types of samples) require a prior sample digestion to decompose organic matter before detection can occur.

Tarin (2006:28), expresses the opinion that the technique of choice depends on sample matrix, sample concentration and the type of information required (e.g. isotope or species of selenium). The selenium analysis process thus predominantly involves two main sequential steps, namely, digestion of samples (sample preparation for detection), and thereafter, detection of the selenium in samples. Any changes to improve any one part of this process cannot be made without consideration for the other, due to the complex chemical nature of the element selenium.

During the digestion stage, a total decomposition of organic material is essential as selenium values cannot be analytically detected and measured without the release of selenium from the prevalent protein form (selenomethionine and selenocysteine) in biological samples. Furthermore, some of the detection techniques used, (GC-MS,

fluorimetry, or HG-AAS and HG-ICP-MS) require chelate or hydride formation, which are convenient only in total digestion (Tarin, 2006:36).

Kurkova, Skrypnik and Zalieckiene (2008:40), state the main difficulty with selenium analysis process is sample mineralization. As the organic forms of selenium (dimethylselenide and dimethyldiselenide) volatilize from a sample at a temperature exceeding 70$^{o}$C, a loss in selenium yield can occur, and thus cede inaccurate analytical results. Moreover, at different mineralization stages, other volatile selenium compounds may be generated. It is thus important that any laboratory analyst performing sample digestion for subsequent selenium analysis is aware of these factors, so as to take steps to prevent any loss of the selenium yield during the process.

## 2.7 SELENIUM DETECTION: FLUORIMETRY

Campbell (1984:647), contends that the determination of selenium in biological material with the fluorimetric method is widely accepted as a technique for routine analysis. Selenium(IV) reacts quantitatively with aromatic 1,2-diamines in acid solution yielding piazselenols which are measured fluorimetrically following extraction into hydro-carbon solution. The amount of manipulation required in this manual method is considerable, however, the sensitivity is accurate in the 0-100ng per sample range.

Unfortunately 2,3-Diaminonaphthalene (DAN) is a photosensitive molecule, thus decomposed in the presence of light. It is also essential to recrystallise the molecule with hydrochloric acid before use. Extraction with cyclohexane immediately before use, gives a reagent with low and acceptable blank fluorescence (Campbell, 1984:647).

The reaction with 1,2 diamino compounds is however specific for selenium(IV) specie. As sample preparation is normally performed under oxidising conditions it yields a selenium(VI) specie of selenium. Therefore it is essential to effect a reduction of selenium(VI) to selenium(IV) before analysis. Heating with hydrochloric acid is a common reduction method utilised. If all the nitric acid is not

removed before the addition of hydrochloric acid, this may result in poor recoveries, as nitric ions compete in parallel with selenium(VI) for an adsorption site on DAN.

Although selenium(IV) reacts with DAN in both neutral and acidic solutions, the rate of this reaction decreases with acidity. Campbell (1984:647), states that the optimum conditions for analytical work is therefore a pH of between 1 to 2, at a temperature of between 40$^{o}$C to 50$^{o}$C. The addition of EDTA to samples, has the purpose of being a chelating agent, which attaches to other elements present in the samples, which could potentially interfere with selenium-DAN reaction.

## 2.8 SELENIUM DETECTION: HYDRIDE GENERATION

To overcome challenges associated with fluorimetry as a detection method for selenium analysis, a practical alternative detection method is considered to be the hydride generator method, as it does not require the use of DAN. The simplicity of the hydride generator apparatus, which allows the method to be used with a conventional atomic absorption spectrophotometer (AAS), is seen as an advantage and attraction. An atomic absorption spectrophotometer is widely used to assess the concentration of variety of elements. It uses the principle that atoms of a particular element absorb light of a characteristic wavelength unique to the element, being passed through an atomic vapour layer of the element. Most biochemistry laboratories incorporate the use of an AAS in their routine analytical work.

The principle of operation of hydride generators, involves the generation of a hydride vapour. This vapour generation method increases the sensitivity of the routine atomic absorption technique. Campbell (1992:228), maintains that hydride generation atomic absorption spectrophotometry (HG-AAS) is a measurement technique, applied in the determination of selenium, which makes use of a separation principle. Selenium is separated from the sample matrix by converting it to a volatile hydride gas which is analysed with the AAS, onto which the hydride generator unit is mounted. This analytical technique comprises of three basic but distinct processes, namely hydride generation, hydride collection and thereafter atomisation via AAS. There are however many variations of each of these components reported upon in literature.

GBC Scientific Equipment Pty Ltd (1995:1), supports Campbell (1992:228), by stating that integrating the use of hydride generator apparatus enables the quantitative detection selenium based on a chemical separation technique. A gaseous hydride is produced by chemical reaction of the selenium sample to an acidified solution. The resultant gaseous hydride, known as hydrogen selenide, which is formed is not stable is at high temperatures, and thus separates from the liquid immediately after formation. The hydride vapour is then transported by the flow of an inert gas, to a heated quartz tube where thermal decomposition occurs. The light absorbed by selenium atoms is then determined in the normal manner with an AAS.

This explanation of HG-AAS mechanism is elaborated upon by Tarin (2006:36), stating that during HG-AAS, selenite selenium(VI), the only reactive selenium specie, in an aqueous solution, reacts with a reducing agent sodium borohydride ($NaBH_4$), in the presence of hydrochloric acid to generate gaseous selenium hydride ($H_2Se$). The $H_2Se$ is stripped by $N_2$ in a gas-liquid separator, passing through a drying tube into a quartz tube furnace mounted in the light-path of an AAS running on a selenium hollow cathode lamp. The $H_2Se$ is thermally decomposed into selenium atoms, which absorb light at 196.0nm.

Campbell (1992:228), reported that inter-laboratory trials on the determination of selenium in biological materials by hydride generation, obtained results demonstrating excellent agreement between laboratories, with regard to sample measurement values. These were established by following rigorous and precisely defined decomposition regimes, despite using different independent techniques. Campbell (1992:228), states the key to this success is regarded to be establishing an effective digestion regime, to be able to employ the hydride generation technique, with less consideration for the hydride generation analytical technique itself, which is deemed sound.

Galgan and Frank (s.a.), argue that determination of selenium in biological samples by HG-AAS assumes the complete destruction of organic matter. This is regarded as further evidence of the vital importance to exercise concern during sample digestion,

as the process of digestion is indicated as critical to avoid selenium loss and optimise selenium yield, in order to obtain the most accurate results.

The accuracy of results is, however, are also equally heavily reliant on the chemical conversion of selenium to the appropriate speciation, in order for analytical detection of selenium to occur. If chemical conversion does not take place, it is impossible to accurately, quantitatively measure selenium values in samples.

## 2.9 SELENIUM DETECTION: COMPARISON BETWEEN FLUORIMETRY AND HYDRIDE GENERATOR

Evidence is presented of the similarity between fluorimetry and hydride generation methods when Kurkova, Skrypnik and Zalieckiene (2008:41), point out that the stage of 'selenium(IV) reduction' is necessary to achieve accurate results in both analytic techniques. The authors state that, when taking into account that only the species selenium(IV) enters into the reaction with sodium tetrahydroborate (in atomic absorptive estimation) and with 2,3-diaminonaphthalene (in fluorimetric estimation), the transformation of selenate selenium(VI) into selenite selenium(IV) is required. Thus it is of crucial importance in both detection methods, that selenium reduction takes place. This is commonly done either by the use of hydrochloric acid during the sample digestion, or a step immediately after sample digestion involving the addition of hydrochloric acid and heat.

Another similarity found was both fluorimetry and hydride generator techniques are susceptible to interference from other elemental ions in samples. Campbell (1984:646), reports that interference from other elements, such as copper, lead, iron and nitrate can be troublesome and affect the accuracy of analytical methods. The presence of nitrate significantly impedes both atomic absorptive and fluorimetric determinations of selenium analysis. Thus, the removal of these ions is an important element in the preparation of samples for analysis. Several methods of nitrate ion removal from a mineralisate are mentioned in scientific literature, including stripping with water, addition of chloric acid and treatment of samples with hydrogen peroxide. The most preferential method, however, is the application of amidosulforic acid. Amidosulforic acid is less dangerous to work with than chloric

acid, and more effective in the removal of nitrate ions when compared to hydrogen peroxide (Kurkova, Skrypnik & Zalieckiene, 2008:41).

The difference between results of fluorimetric and atomic absorption methods used are statistically negligible, and both methods enable adequate determination of selenium in samples, and thus are equally accurate, according to Kurkova, Skrypnik and Zalieckiene (2008:41). The authors do, however, also express the opinion, that the atomic absorption method is more expressive, as it enables selenium determination to be carried out without any preliminary extraction. This supplements the preference of this method for routine analysis, as it significantly reduces the analysis time.

Furthermore, Campbell (1984:646), maintained that, although an extensive range of analytical methods is available for selenium analysis, two methods in particular, namely, molecular fluorescence and atomic absorption spectrophotometry can be considered to surpass others. The attraction to employ these methods as routine diagnostic methods, lies in the fact that they possess adequate sensitivity, and require only readily available laboratory apparatus and thus are quite suitable for routine survey work. Campbell (1984:646), elaborates on this by stating that, although it has been reported that the difference between the two methods is insignificant, it is his contention that the hydride generation technique, coupled with AAS, may have an advantage at selenium levels below 100ng g-1. He does however, also proffer the opinion that there is no doubt that the technical skill of the analyst as well as the availability of equipment, are also very important factors (Campbell, 1984:646).

## 2.10 RESEARCH ENVIRONMENT PROCESS MAP

A process map of the research environment enabled research to establish the parameters for research, and identify the area where process improvement will add the most value practical value in the Biochemistry laboratory at WC PVL.

Data relating to the current selenium analysis process is depicted in Figure 2.1.

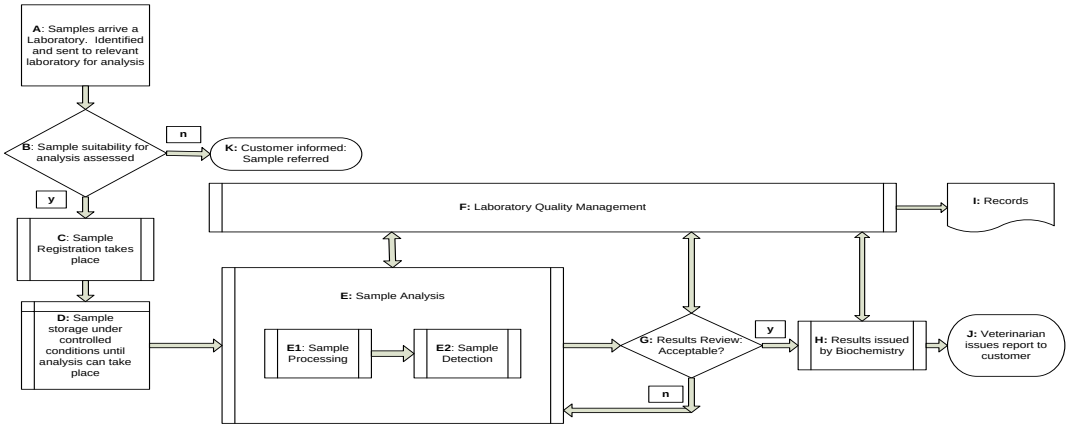


**Figure 2.1:** Workflow Process. (**Source:** Own source)

## 2.11 INITIATION OF QUALITY IMPROVEMENT

Initial data collection on the current selenium analysis directed the focus of research to the digestion process part of the overall selenium analysis process. An Ishikawa diagram seen in Figure 2.2 was constructed to identify root causes of the problematic result quality of selenium analysis, for this dissertation.

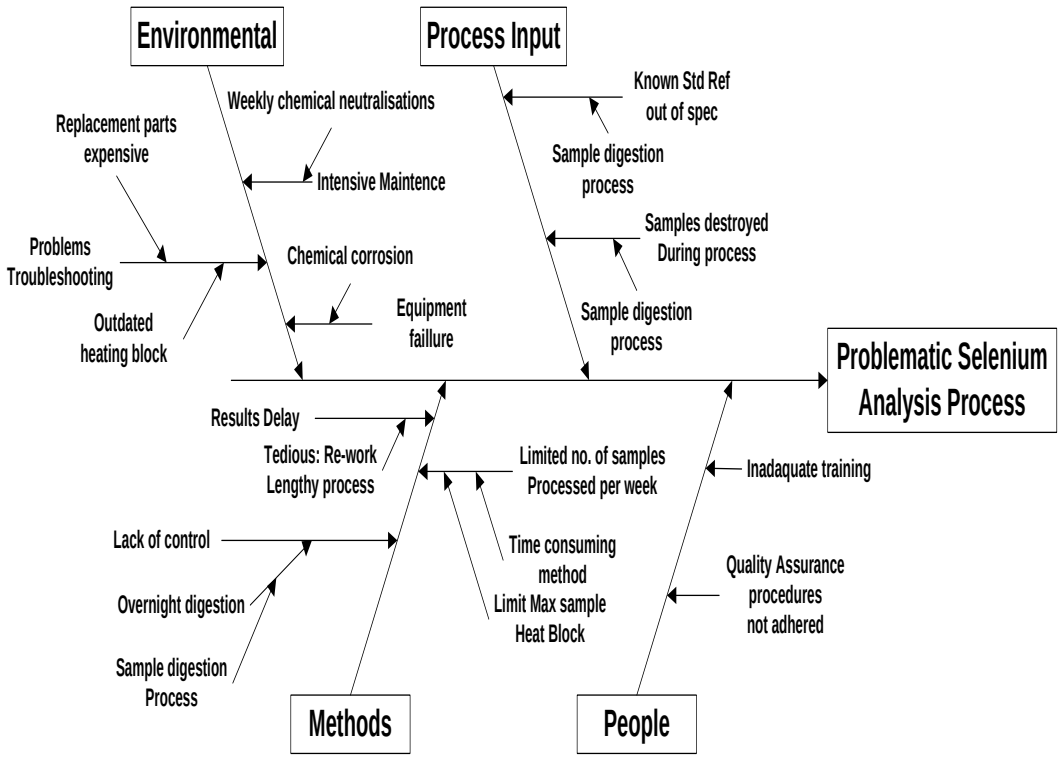


**Figure 2.2**: Ishikawa Root Cause Analysis (**Source:** Own source)

Foster (2007:310), maintains the belief that the Ishikawa cause and effect diagram (also known as fishbone or Ishikawa diagram), is a "...good tool to help us move from lower levels of abstraction into solving problems". With the use of an Ishikawa Root Cause Analysis tool, the four most relevant factors, believed to affect the quality of analysis process, thus with the effect, the quality of result too, were extrapolated on. Major sources were identified, and all smaller causes feeding these major sources could be identified and examined with the use of this quality tool.

The Ishikawa Diagram identified factors that could be investigated around the result quality of the selenium analysis process in an attempt to improve it. The factors are listed as follows:

- **Environment:** All environmental aspects pertain to factors inextricably linked to the research environment or its nature, such as equipment used or the Biochemistry weekly routine, which can only be altered with major modification of the system.
- **Process Input:** Inputs pertaining to any requirement of the process such as samples or reagents.
- **Methods:** Standard operating procedures (SOPs).
- **People:** Personnel factors such as training and implementation of quality control measures in the laboratory.

Evaluation of the Ishikawa yielded the results that, with regard to the selenium analysis process, it appeared that the digestion method required attention in the form of significant modification for overall process quality improvement.

## 2.12 UNIQUE CRITERIA ASSOCIATED TO SELENIUM ANALYIS PROCESS

To achieve successful selenium analysis process improvement, it is essential to take into consideration the unique chemical nature, as explained by Tarin (2006:36), Campbell (1984:647), Kurkova, Skrypnik and Zalieckiene (2008:40), and Galgan and Frank (s.a.), in earlier literature reviewed, on this metalloid chemical element. It was determined that any attempts to attain process improvement would be futile,

unless these unique factors were taken into account, in an endeavour to modify the digestion process as part of the overall selenium analysis process.

Besides the complete organic decomposition of organic material in samples, which was found to be necessary, according to Galgan and Frank (s.a.), Campbell (1992:228), and (Tarin, 2006:36), who indicated that all laboratory digestion procedures need to be capable of accomplishing this, there are further obligatory unique criteria to consider. It is necessary for selenium digestion to include the chemical oxidation and reduction of selenium in samples during digestion, as found to be explained by Kurkova, Skrypnik and Zalieckiene (2008:41), and Tarin (2006:36), as well as inimitable chemical preparation of samples due to ion interference and pH considerations, in order for detection to take place. This was elaborated upon by Campbell (1984:646-647), Tarin (2006:28-36), and Kurkova, Skrypnik and Zalieckiene (2008:40-41). Furthermore, there were also practical laboratory considerations, which would normally vary from one testing laboratory to another, such as the routine amount of samples processed during a weekly test run, the type of glassware used, and the type of apparatus available to perform certain parts of testing procedure, such as laboratory shakers, water baths etc. The practical considerations also required consideration, within reason.

Microwave digestion was identified as an attractive option. Based on literature findings of Campbell (1992:228), Galgan and Frank (s.a.), Kurkova, Skrypnik and Zalieckiene (2008:40-41) and (Tarin, 2006:36), microwave digestion was indicated as capable of meeting all the above-mentioned requirements. This belief was supported by the fact that laboratory microwave was available for sample digestion in the Biochemistry Section. An additional factor motivating in favour of the use of microwave digestion is that literature suggests microwave power is able to digest samples without the use of perchloric acid. Perchloric acid is identified as a seriously hazardous chemical.

The Desert Research Institute (2004:**Online**), states that perchloric acid is a strong mineral acid which is a clear colourless liquid. This author offers that in addition to being a corrosive acid, when heated above $150^{o}$C it becomes unstable, acts as an oxidiser and presents a high explosive hazard. The author states that organic

materials are especially susceptible to spontaneous combustion if mixed in contact with perchloric acid. The author recommends that "...because of its reactivity hazard, perchloric acid digestions of any size must always be performed under a chemical hood".

The Department of Environmental Health and Safety of the University of Alberta (2011:7), is of the similar opinion that perchloric acid is known to be hazardous to operator health, and equally hazardous when released into the environment via open block digestions, even in small quantities. In addition to the harsh corrosive hazard it poses to both the operator and environment, the routine use of perchloric acid promotes the formation of explosive perchloric acid crystals within the fume cabinet where routine open block digestions take place. Perchloric acid crystal formation necessitates additional labour intensive maintenance, in the form of frequent chemical neutralizations. Dry perchloric acid crystals are unstable, and when subject to shock or vibration can explode (University of Alberta, Department of Environmental Health and Safety, 2011:7).

## 2.13 TESTING THE FEASIBILITY OF MICROWAVE DIGESTION

Research proceeded in an attempt to optimise an analytical microwave digestion method for the selenium analysis process, by identifying the process requirements and research variables in order to establish the improved process. The variables were tested accordingly, and resultant data collected and analysed.

### 2.13.1 Test Research Variable 1: Perchloric Acid ($HClO_4$)

Perchloric Acid is an inorganic compound with the chemical formula $HClO_4$, and most commonly occurs in an aqueous form. It is highly corrosive and a very strong oxidization agent commonly used in biological sample digestions in laboratories. The University of Alberta, Department of Environmental Health and Safety (2011:7), confirms the highly corrosive nature and tendency to form explosive peroxides. Steps to eliminate the use of perchloric acid from the selenium analysis process would thus translate into definite process improvement. It was found that various acids being used by other analytical laboratories, including nitric acid and

combinations of nitric and hydrogen peroxide or nitric and hydrochloric acid, were sufficient to completely decompose organic samples during digestions.

### 2.13.2 Test Research Variable 2: Selenium oxidation state

In order for the accurate detection of all selenium present in a biological samples, by the detection apparatus, the selenium in samples must be present in a chemical tetravalent state - selenium(IV). Any proposed change to the current digestion process must make provision for the chemistry requirements during sample processing and extraction process, in order to successfully perform the quantitative measurement of selenium during the actual detection process part of the overall selenium analysis process. It is essential that each and every modification made, be made with consideration for the selenium oxidation requirements of every other stages of the overall process, as indicated by Tarin (2006:28), and Kurkova, Skrypnik and Zalieckiene (2008:41).

### 2.13.3 Test Research Variable 3: Digest volume

A practical consideration specific to fluorimetric determination was the final volume of digested sample material processed could not exceed 5ml. This was due to other practical aspects associated with the test method, such as glassware used and shaker equipment etc. used during sample handling. This variable was tested by establishing if the sensitivity of the fluorimeter was sufficient to overcome any dilutions of samples. Research set out to establish if the fluorometric method was capable of selenium detection, as well as the accuracy of that detection, if sample digests were diluted to a ratio of 1:3.

### 2.13.4 Test Research Variable 4: Selenium-DAN Complex

Fluorimetric determination of selenium is dependent on the formation of a Selenium-DAN complex. This is due to operating mechanism of the fluorimeter apparatus i.e. the detection of fluorescence. Since elemental selenium is not a fluorescencing molecule, in order to be detected, selenium must complex to a 2,3-diaminonaphthalene molecule (DAN). This important variable has a direct

relationship with the accuracy of using a fluorimetric method for selenium analysis. Particular discernment must thus be given when making any modifications to the digestion process, to ensure that Selenium-DAN complexing is enabled.

### 2.13.5 Results of testing variables

Duplicate samples, microwave digested at WC PVL, with a strong nitric acid and hydrochloric acid mix (Aqua Regia), were able to be analysed at CSIR (Stellenbosch). These results are attached as Annexure 1. This provides evidence that complete microwave biological sample digestion is possible. Furthermore, the results of CSIR's analysis provided evidence that the trial runs of the microwave digestion procedure provided a reliable selenium yield between 75 - 80%, based of control reference standards prepared and digested with samples, despite sample digests being diluted at a ratio of 1:3. These samples were however not able to be detected fluorimetrically at WC PVL. It is assumed the reason for this is due to the sample dilution factor and fluorimeter sensitivity.

Trials to determine the sensitivity of the fluorimeter involved preparation of standards without digestion procedure. The results of these trials demonstrated the fluorimeter was in fact capable of accurately detecting selenium without chemical reduction, at concentrations from 100ppb to 500ppb, but not at lower concentrations of 1ppb, 10ppb and 50ppb. Expected normal values for selenium in liver samples can range from 20ppb. It is anticipated that chemical reduction of selenium, enables adequate DAN complexing, which will result in much more accurate fluorimetric detection.

Trials were conducted to determine whether chemical reduction with hydrochloric acid would be sufficient to chemically prepare selenium in order for adequate Selenium-DAN complexing to take place. The fluorimeter apparatus was, however, unable to detect any selenium in these samples. This provides evidence that fluorimetric detection of selenium cannot take place without the selenium in samples firstly being present in the appropriate chemical oxidisation state, before reduction. Chemical reduction can only occur on selenium(VI) and, only after reduction, can

complexing with DAN finally take place. Sample digestion must therefore yield selenium in samples in the selenium(VI) oxidation state.

A laboratory trial was conducted whereby samples were microwave digested with only nitric acid, thereafter chemically reduced with hydrochloric acid using the open heated block. Thereafter samples from this trial were handled according to the existing process method. The results of this trial were inconsistent readings obtained, and a calibration curve could not be established. It is assumed that this was due to interference from the nitrate ions remaining in the sample after digestion. Regardless of required selenium chemical reduction, which is believed to have taken place, while microwave digestion prevented the loss of volatile selenium through evaporation, it also prevented nitric acid from being evaporated during digestion. Literature reviewed revealed that remaining nitric acid in sample digests possibly interfered with selenium-DAN complexing. Since selenium-DAN complexing is critical for sample detection on a fluorimeter, fluorimetric detection of these samples thus yielded inconsistent results.

Simultaneously, in order to eliminate to possibility of operator error, the same samples were analysed by a more experienced operator, and the same inconsistent results were obtained.

As results from the external laboratory (CSIR), provided evidence that selenium was in fact present in sample digests, in order to overcome the fluorimeter's sensitivity range, a laboratory trial was commenced, whereby less digestion acid used to during the microwave digestion. Literature review on the kinetic reaction of selenium(IV) with DAN indicated the potential negative effect of pH on this reaction. Optimal selenium-DAN comlexing takes place at a pH value between 1 and 2. Literature review led to the belief that the presence of nitric acid in samples when selenium-DAN complexing occurs, lowers the pH, and therefore optimal selenium-DAN complexing is inhibited.

As it was anticipated that the pH value of the sample digests would be very low, a sodium acetate buffer with a pH value 4 was prepared beforehand. The average pH value of undiluted sample digests was found to extremely low acidic with a pH value

of -0.08. Even after the addition of 6ml sodium acetate buffer the pH value remained in the negative range at -0.03. Further attempts with increase the pH of samples, using two different buffers made up with the strong alkaline sodium hydroxide at pH values exceeding 13, were unsuccessful. Even after the addition of 6ml of each of these, the pH value of the sample digest never exceeded 0.2. A further possibility involved the use of fuming ammonia as a buffer. However based on literature review, it was decided that the toxic properties of this alkaline base, was in a similar range to perchloric acid and thus should not be used.

Further research indicated that besides to the pH influence, nitrite ions from nitric acid used during digestion, also compete in parallel with selenium for adsorption site on DAN. Investigations revealed amidosulforic acid had been used in previous studies to overcome the influence of nitrate ions. However, various concentrations were attempted with unsuccessful results. Although it is theoretically possible to overcome nitrate ion interference, enabling adequate selenium-DAN complexing for detection, suitable practical measures to overcome both the effect of pH and nitrite ion interference could not be found.

Based on the results of the various laboratory trials conducted to test process variables, it was determined that no suitable microwave digestion method could not be established for a selenium analysis process, to be used in conjunction with the fluorimetry detection method. Research then started to focus on establishing an alternative detection method, in addition to alternative digestion. Of the known available selenium detection methods, there were three possibilities based on apparatus available to WC PVL Biochemistry section. Data was collected on reliability, operating expense and ease of operation on each of the available detection methods. Hydride generator as was selected as a detection method for ultimate improvement of the selenium analysis process.

## 2.14 RESEARCH EXTENDED: MODIFIED ISHIKAWA DIAGRAM

The development of the research problem thus led to the need of drafting a modified Ishikawa diagram. All initial considerations had focussed on possible improvement considerations related to the general selenium analysis process affecting the quality of its results. Thus, all aspects which were identified as problem sources in the general process were investigated.

The exercise of initial root cause investigations, focussed attention on all potential sources of problematic result quality of the selenium analysis process and highlighted one source as the major root cause. The process of brainstorming and elimination had revealed that the digestion procedure within the process was the major contributing source. The subsequent experimental investigation led to the elevation of the research problem due to the deduction that problematic digestion procedure could not be addressed in isolation. The original Ishikawa diagram was adapted accordingly. All original problems highlighted in the initial Ishikawa as 'research environment problems' (specific to the WC PVL Biochemistry section), appeared, at that stage, to be directly related to the sample digestion procedure.

It was deemed appropriate, when drafting the modified Ishikawa, to combine method and environmental factors, or problem root causes affecting result quality into digestion procedure factors, and the detection procedure factors of the general selenium analysis process. The remaining root causes, other than the environment factor and method root causes, were found to be the same for both digestion and detection procedure of the selenium analysis process. Thus, the process input factors and people factors on the quality of results, remain the same in the modified Ishikawa diagram. Irrespective of digestion or detection method, these remain the same in the modified Ishikawa diagram.

The modified Ishikawa diagram is seen in Figure 2.3.

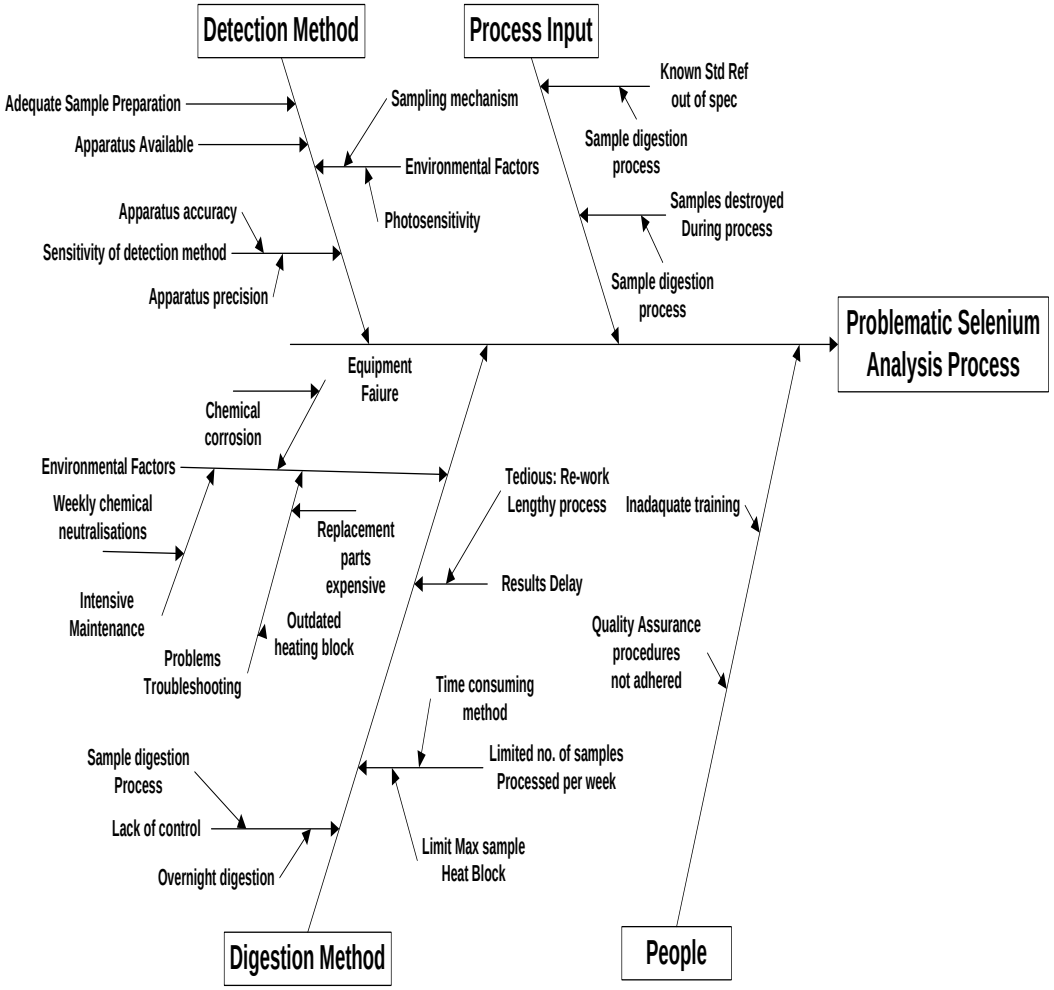


**Figure 2.3**: Modified Ishikawa Root Cause Analysis (**Source:** Own source)

With the use of hydride generation as a detection method, research anticipates the new modified microwave digestion process will provide:

- An improved selenium yield.
- Adequate decomposition of organic material for detection.
- Adequate conversion of selenium to required state for detection.
- Increased safety in use.
- Time cycle reduction.
- Improved process control.
- Less costly maintenance.

Using hydride generator (HG-AAS) is believed to overcome problems associated with detection when fluorometric methods were used, and validation of this method

will set out to prove if it is overall improved method for detection. Reliability of results can then be achieved.

## 2.15 CONCLUSION

It is impossible to implement process quality improvement in the laboratory setting without a proper understanding of the main constituent of laboratory process for which improvement is desired. Furthermore, it is deemed as essentially necessary, that an extensive and thorough examination of the research environment, from a holistic perspective, be conducted, to yield a framework providing the direction research should take in order to obtain the most meaningful quality improvement in the current selenium process. This examination highlighted the need for major modification of both the digestion and detection processes of the selenium analysis process.

The quality of analytical results is seen as a primary objective of any diagnostic service laboratory. The appropriate use of suitable quality tools provides a mechanism to modify and improve the current selenium process, thus adding value to the organisation. Quality tools provide a valuable vehicle and a SMART (specific, measurable, attainable, realistic and timely) means to identify, categorize and then assimilate complicated variables which require attention during process improvement of the selenium analysis laboratory process. The use of quality methodology and tools in the design of the new process is thus a mechanism to ensure quality outcome of the resultant process and consequently an overall laboratory quality improvement.

# CHAPTER THREE

# QUALITY PROCESS IMPROVEMENT LITERATURE REVIEW

## 3.1 INTRODUCTION

A literature review was conducted within the ambit of this dissertation as a requirement to understand the current state of knowledge pertaining to the proposed research. A review of available literature was conducted on the following topics:

- Service Quality and Quality Processes.
- Importance of Quality in Laboratories.
- Quality Improvement on Laboratory Processes.
- Use of Quality Tools in Laboratory Environment.
- Six Sigma.
- Lean.
- Lean Six Sigma.
- Process Analytical Technology.
- Statistical Process Control.
- Process Capability.
- Failure Mode Effect Analysis.

## 3.2. SERVICE QUALITY AND QUALITY PROCESSES

Foster (2007:231), contends for service industries, “High-quality service is essential for competiveness and can even improve employee satisfaction”. Foster elaborates on this by adding that, besides this being an imperative for competitiveness, it is also a sign of quality maturity. He expresses the view that in order to provide a high-quality service, the service provider needs to have a profound understanding of who the customer is, in addition to knowing what the customer “needs, wants and desires” are. Foster states that in order to know how to satisfy your customers, it is important that customer requirements be translated into functional product or service ‘process’ designs (Foster, 2007:203).

Award (1994:**Online**), states that "...Total Quality Management (TQM) is a commitment to the continuous improvement of work processes with the goal of satisfying internal and external customers". According to Brecker Associates (2003:**Online**), in order to attain process improvement, the general focus of improving quality in the service industry lies with improving process productivity and cycle time, thus the quality of processes. Performance of the service must be evaluated and critical success factors (CSF) are identified. The process is mapped and quality issues are examined. The exercise of brainstorming is used to eliminate non-value added activities, and thereby reduce cycle times. Action plans are then developed for high priority recommendations (Brecker Associates, 2003:**Online**).

## 3.3 IMPORTANCE OF QUALITY IN LABORATORIES

Nevalainen (1999:**Online**), expresses an opinion that, in the face of competition in the world economy, the health care services needs to understand, as well as improve, their processes to ensure that the right work is being done in a high quality manner, at a competitive price. This is similar to the evolution experienced by the manufacturing industry and other service industries. The traditional management approach involves following a 'slash-and-burn' tactic to manage costs. However, this method inevitably runs out of fuel. The traditional approach then resorts to changing organisational structure by merging with other organisations to overcome competition. These traditional approaches do not, however, fix the root causes of the existing problems within the organisation. Nevalainen (1999:**Online**), states that "Process improvement is the only real solution". By improving supporting systems and processes, the health care service industry can accomplish the goal of maintaining the focus on quality patient outcomes at a competitive price.

Westgard (2010:**Online**), advocates that managing quality begins with the understanding of the meaning of quality itself. Westgard (2010:**Online**), citing The Centre for Disease Control (CDC) Institute of Critical Issues in Health Laboratory Practice (1986), recommends that the following definition for laboratory quality be adopted: "The quality of a laboratory testing service depends on providing the totality of features and characteristics that conform to the stated or implied needs of its users or customers".

Westgard (2010:**Online**), therefore avers that achieving quality improvement can only be attained by adequately managing quality. Westgard (2010:**Online**), argues that even the management of quality can be viewed as a 'process', centred on quality goals, requirements and objectives, and despite the fact that there are a plethora of different quality programs to manage quality, all these different programs fit into an overall process representing a basic scientific method known as the Plan, Do, Check and Act or PDCA Cycle. The Centre for Health Informatics, University of South Wales (2008:15), states the PDCA cycle is "...an iterative four-step problem-solving process based on the scientific method, developed from the work of Francis Bacon (1620).", while the research of Moen and Norman (2011:**Online**), claims that the PDCA cycle evolved from the scientific method, as depicted in Figure 3.1.

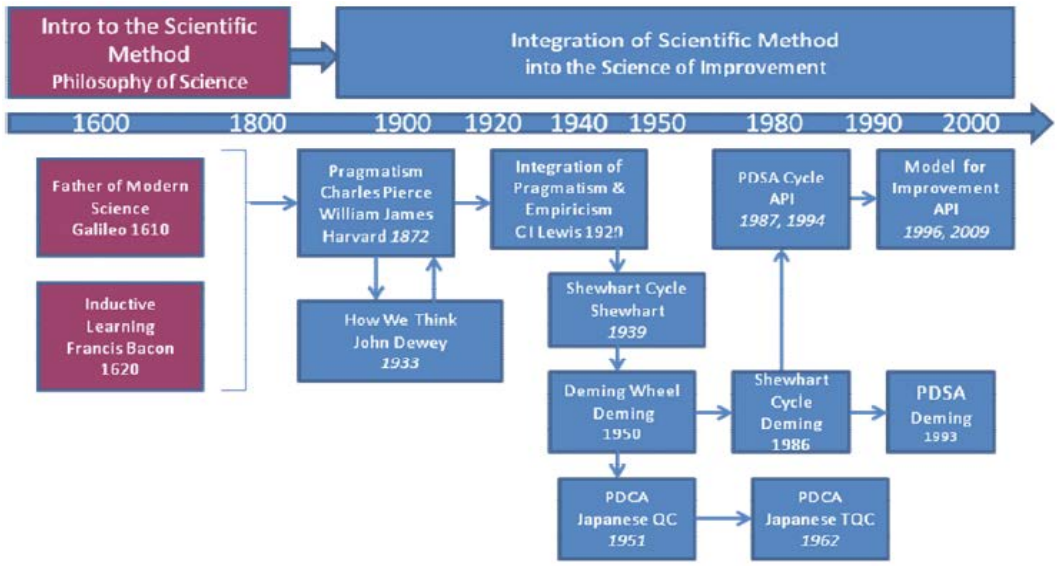


**Figure 3.1**: Evolution of the Scientific Method (**Source:** Moen and Norman, 2011:**Online**)

Sciocovelli, Kane, Skaik, Caciagli, Pellegrini, Da Rin, Ivanov, Ghys, and Plebani (2011:9), assert that, "as quality is not a static entity, it is important that the moving targets of quality be defined, and process measurements should be a critical focal point of quality efforts." Sciocovelli *et al.* (2011:9), support the view that benchmarking in laboratory medicine, as well as accreditation requirements should be accomplished by standardised laboratory approaches to the measurement of laboratory quality. For this purpose quality tools can be successfully utilised to control and monitor pre-, intra- and post-analytical activities.

Moglia (2006:**Online**), states that an actively involved and strong management presence is an essential for continuous process improvement within a laboratory. This statement is underpinned by section 4.2 and section 4.10. of ISO/IEC 17025: 2005 Standard: General Requirements, for the competence and testing and calibration laboratories.

## 3.4 QUALITY IMPROVEMENT ON LABORATORY PROCESSES

In support of an analytical test method being described as a service process, the American Association for Clinical Chemistry (AACC) (2011:**Online**), describes an analytical method as "...a science professionally conducted with rigorous statistical analysis, quality controls, and extensive oversight". AACC (2011:**Online**), elaborates on this description by providing that the laboratory test process is most reliable when used in conjunction with other meaningful data.

Wang (2008:287), deliberates that quality process improvement starts with a diagnostic journey, where problems are identified. The initial common activities, taken in the diagnostic journey, are analysing symptoms, formulating hypothesis, testing hypothesis and identifying causes. Thereafter, remedial activity will be taken and afterwards the process will be continuously monitored.

Plebani, Cerriotti, Messeri, Ottomano, Pansini, and Bonini (2006:150), discuss 'laboratory services' or analytical test methods provided by a service laboratory as a "Total Testing Process (TTP)". Plebani *et al.* (2006:158), argues that indicators and related quality specifications be identified for each phase of a laboratory activity which is part of the analytical process. Plebani *et al.* (2006:150), state that such indicators may be defined as "a measure to assess a particular process or outcome", and are tools, for producing a quantitative measurement of quality.

Llopis, Trujillo, Llovet, Tarres, Ibarz, Biosca, Ruiz, Kirchner, Alvarez, Busquets, Domenech, Figueres, Minchinela, Pastor, Parich, Ricos, Sansalvador, and Palmada (2011:**Online**), state that quality indicators are essential elements in the quality management systems of clinical laboratories, and are used to control the quality of processes. Llopis *et al.* (2011:**Online**), explain that quality indicators for processes

should be designed to monitor and provide data which can be used for continuous improvement of these processes. It is imperative that the design of indicators should enable rapid detection of deviations during the proper functioning of the processes for which they are designed.. Furthermore, Llopis *et al.* (2011:**Online**), believe that the use of indicators should not burden the organisation, and they should be simple to implement.

Performance specifications known as 'limits of acceptability' must be predefined for the quality indicators to be used, in order to measure the quality of processes requiring control. Performance specifications should serve as a reference to compare with results obtained from processes being measured. The studies conducted by Llopis *et al.* (2011:**Online**), over a five year period demonstrated the use of Six Sigma statistic provides value, enabling the detection of processes requiring improvement. In the studies conducted by Llopis *et al.* (2011:**Online**), the results of the indicators used demonstrated that processes were stable and well controlled.

In order to improve analytical confidence and capability in laboratory processes, Cawley (2000:**Online**), is of the opinion that Statistical Quality Control (SQC) techniques can be employed with great success, and they benefit continuous process improvement efforts. Furthermore Cawley (2000:**Online**), believes that "....a shift in approach requires laboratory managers to understand:

- There is an underlying process in generating analytical results,
- this process can be managed, and
- the process must evolve through a program of continuous improvement."

Cawley (2000:**Online**), draws the analogy that laboratories must not only maintain and demonstrate analytical method stability to effectively use SQC for process improvement, but must also maintain the capability to produce analytical results within the expected limits of method performance, thereby demonstrate proficiency.

A statistical technique called 'process capability analysis' is considered by Cawley (2000:**Online**), to be the best method of determining proficiency. Although it was originally developed for industrial quality management, this method fits well within the requirements of demonstrating and managing laboratory proficiency. Process

capability statistically describes the ability of any process to produce results within specification.

## 3.5 USE OF QUALITY TOOLS FOR ANALYTICAL LABORATORY PROCESSES

Scott (2007:1), contends that a plethora of process improvement approaches exist and "...continuous process improvement methods include define, measure, analyse, improve and control, plan-do-study-act, Six Sigma and total quality management"

The author explains all of them contain "...one or more of the following steps:

- Identify the problem or improvement opportunity.
- Identify the root cause.
- Identify data related to the problem and the root cause.
- Identify the potential solutions.
- Select the best solution.
- Implement the best solution.
- Make sure it worked.
- Update your QMS and start over."

HCi information development organisation (2011:**Online**), suggests that process quality improvement can be accomplished through the use of quality tools employed within the framework of the PDCA cycle.

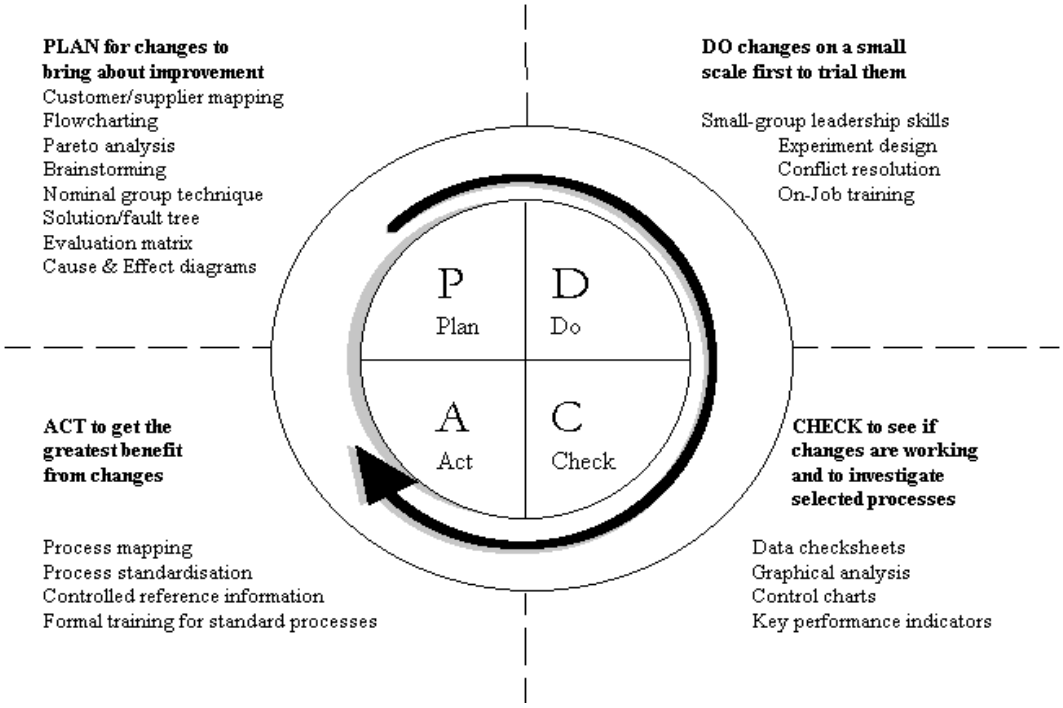


**Figure 3.2**: PDCA Cycle Quality Tools (**Source:** HCi information development organisation, 2011:Online)

HCi information development organisation (2011:**Online**), however, highlights that the classification of tools into sections of the PDCA cycle as seen in Figure 3.2, is not meant to be strictly applied. It should rather be regarded as a useful prompt to assist with making a decision as to what to do at each critical stage, during improvement efforts.

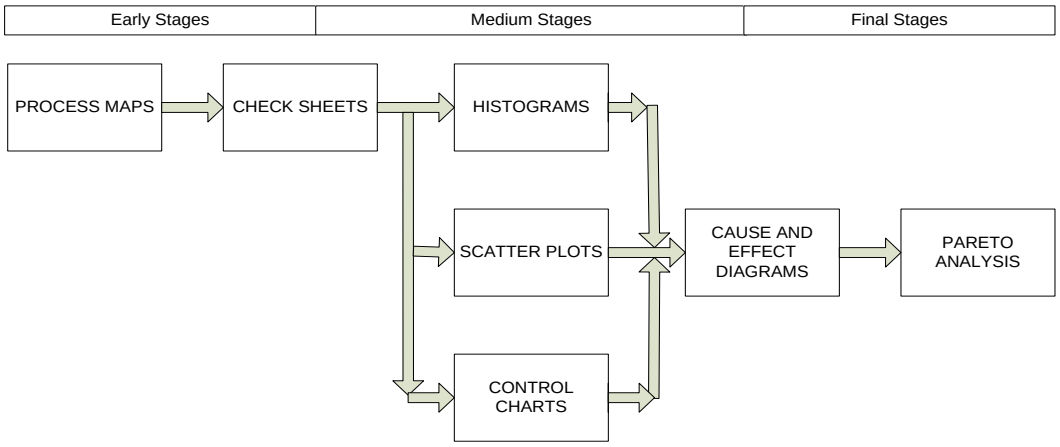


**Figure 3.3**: Logical Map : Order for the Basic Seven (B7) Tools (**Source**: Foster, 2007:297)

Foster (2007:296), asserts that the 'seven basic tools of quality (B7)' are simple to use in continuous improvement efforts as seen in Figure 3.3. According to this

author, the seven basic tools are typically used in a logical order; however they may be used in any order. In addition to the seven basic tools, Foster (2007:296), points out that there are also the 'new seven quality tools (N7)', also referred to as the 'managerial tools'. The tools are often used by teams or by individuals. They are useful at all levels of the organisation, and can be applied by people of different educational levels.

Wang (2008:288), avers that quality process improvement can itself be considered a process which is comprised of three sequential phases namely:

- Diagnosing a process.
- Stabilising and improving a process.
- Improving the performance of a process.

Wang (2008:288), visits the basic quality improvement tools which are applied during the three individual quality process improvement phases, by describing the tools used in each and suggests the approach for their application. As previously explained by this author, process diagnosis involves analysing symptoms, formulating hypothesis, testing hypothesis and indentifying causes. Wang (2008:288), provides a matrix, (refer to Table 3.1), which illustrates the basic quality tools which are believed to most suitable for use in each of the above-mentioned phases.

**Table 3.1:** Basic Tools in Process Diagnosis. (**Source**: Wang, 2008:288)

| | Basic Tools for Quality Process Improvement | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Common Activities to Diagnose Cause | Cause–Effect Diagram | Pareto Chart | Histogram | Scatter Diagram | Normal Probability Plot | Flow Diagrams | Data Collection | Box Plot | Stratification |
| Analyzing symptoms | • | • | • | • | • | • | ○ | • | ○ |
| Formulating hypotheses | • | ○ | • | ○ | • | ○ | ○ | • | ○ |
| Testing hypotheses | • | • | ○ | • | • | ○ | • | ○ | • |
| Identifying cause(s) | • | • | • | • | ○ | ○ | ○ | ○ | • |

*Note*: (•) major; (○) minor.

During the ‘stabilising and improving a process phase’, the author highlights that use application of control charts plays an essential and critical role. The statement was found to be made by Wang (2008:292), that “The control chart is one of the main tools for quality process improvement. It is used to assess the nature of variation in a process and to facilitate the forecasting and management of a process”. There are several types of control charts available for use during this phase of process improvement; however the chart type(s) selected for application should suit the purpose for which the control chart(s) are intended. The purpose is dependent on the process in which improvement is being desired, as well as the objectives desired by quality improvement effort being conducted. This author also explains that control charts serve the function of directing attention toward special causes of variation which appear in a process, as the critical evaluation of control charts enables the identification of ‘symptoms’ which could indicate that a process is out-of control. Wang (2008:293), asserts that out-of-control symptoms include the following:

- **Outliers**: defined as one or more points that fell outside the control limits.
- **Run**: defined as a series of plotted points above or below the centreline.
- **Trend**: defined as a continual rise or fall of plotted points.
- **Cyclicity**: defined as a pattern that repeats itself over time.

Ultimately Wang (2008:293), offers the opinion that the following steps can be used as a guideline, and are usually followed in a control chart’s development and application:

- Determine a ‘base period’ for initial chart development.
- Collect sample data from the base period.
- Calculate the parameters for the control chart, that is, centreline and control limits.
- Plot collected sample points on the chart with the centreline and control limits.
- Determine whether the chart parameters can be used to monitor the process; revise parameters if necessary.
- Collect ongoing samples and continue monitoring the process using the developed control chart.
- Conduct periodic audits on the parameters of the control chart.

Wang's (2008:303), discussion on tools used for process improvement progresses as he details recommendations for after the process has been diagnosed, corrected and brought into statistical control. The author continues that the next critical question which needs be asked by quality managers and process engineers is "What can be done to improve the performance of a process?" The author expands on this, explaining that the solution to this question is obtained first through measuring the present process performance, and thereafter the evaluation and interpretation of process performance results.

Wang (2008:303), offers the opinion that initial measurement of process performance is obtained via a 'process capability study', which gauges the ability of a process to produce according to specifications. Furthermore, the author elaborates that the follow-up step to the 'process capability study' tool is the 'interpretation and improvement of process capability' which involves conclusions being drawn regarding the performance of a process, upon which process improvements are made (Wang, 2008:308).

Berte (2007:281), is of the opinion that a means of improving laboratory test processes at bench level, is accomplished by quality improvement programs. These include the use of statistical quality tools which provide a visual means to understand quality control data, so that timely action can be taken when method problems are detected. Berte (2007:785), explains that quality tools from the non-medical manufacturing arena have been adapted - including Failure Modes and Effects Analysis, Lean and Six Sigma - to be used to improve health care processes.

## 3.6 SIX SIGMA

According to MiC Quality (2011a:**Online**), process variation is the main cause of quality problems. Thus, the main task of statistical process improvement methods, such as the Taguchi approach to experimental design, measurement systems analysis, statistical process control and Six Sigma, is to control and reduce process variation. This author contends that process variation and process precision are closely related, as explained by stating "A process with little variation is said to be 'precise'". Therefore it is important to make a clear distinction between process accuracy and

process precision when studying process variation, as a process which is accurate might not be precise and visa versa (MiC Quality, 2011a:**Online**).

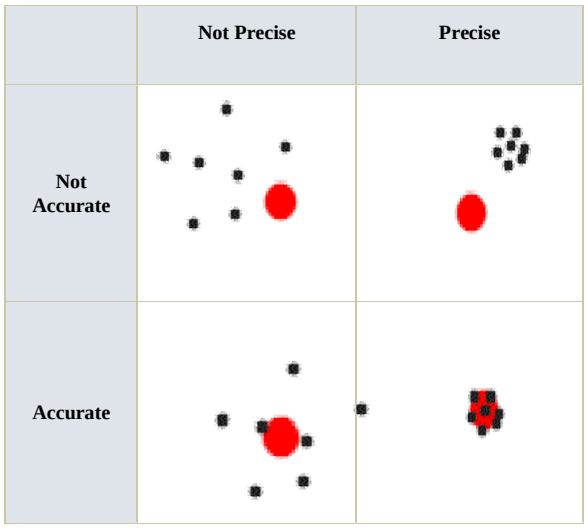


**Figure 3.4:** Process Accuracy and Process Precision (**Source**: MiC Quality, 2011a:**Online**)

The process mean can be adjusted due to most processes being designed with controls which enable process adjustment. However, reducing the amount of variation within a process usually poses a more challenging task. A schematic illustration of accuracy compared to precision is depicted in Figure 3.4. (MiC Quality, 2011a:**Online**).

Foster (2007:437), avers that Six Sigma is a very popular approach to improving quality and there a several distinctions which differentiate it from traditional quality improvement. He explains this by offering that "First, Six Sigma presents a well-thought-out packaging of quality tools and philosophies in an honest effort to provide rigor and repeatability to quality improvement efforts". Additionally he also purports that "Second, Six Sigma is much more cost reduction orientated than traditional continuous improvement" and "The third fundamental nuance of Six Sigma is the way it is organised". The latter is said with reference to Six Sigma belt structure. (Foster, 2007:437).

Pyzdek (2000:140), states that the number 'six' in the name Six Sigma refers to the number of standard deviations from specification limit to the mean of a process, while the 'sigma' in the name Six Sigma refers to the Greek symbol 'σ', which

designates a standard deviation in statistics. Thus a Six Sigma process is considered a highly capable process.

The Six Sigma quality approach differs from the traditional Three Sigma quality in terms of the standard deviation allowable of a capable Three Sigma process which is no more than one-sixth of the total allowable spread, while Six Sigma requires the process standard deviation to be no more than one-twelfth of the total allowable spread (Pyzdek, 2000:140). This author points out that 'Six Sigma' is basically a 'process quality goal' where standard deviation within the process is a statistical measure of variability in the process. As a result of this, Six Sigma is considered to fall within the quality tool category of 'process capability technique'.

Pyzdek (2000:140), elaborates on this explanation by stating "The traditional quality paradigm defined a process as capable if the process natural spread, plus minus Three Sigma, was less than the engineering tolerance". 'Engineering tolerance' is defined as "the permissible limit or limits of variation" (Dictionary3.0, 2011:**Online**). Therefore if variation in a particular process is controlled at the Three Sigma quality level, it translates in a process yield of 99.73% under normal conditions. Six Sigma quality level is considered a refinement of Three Sigma. Six Sigma quality considers the process location as well the process spread, and tightens the minimum acceptance criterion for variation in a process. Thus, Six Sigma requires that the variation in process be more strictly controlled, resulting in nearest 'limit of variation' being at least Six Sigma away from the process mean (Pyzdek, 2000:140).

Buck (2006:**Online**), contends that Six Sigma is an error reduction methodology, which represents both a management discipline, as well as a standardized approach to problem solving and process optimization. Six Sigma means having no more than 3.4 defects per million opportunity in any process, product or service, and the goal of Six Sigma is to redesign a given process to Six Sigma specifications to insure that the process is 99.99975% error free. Six Sigma uses basic quality tools to reduce error through quantitative methods of benchmarking, design of experiments and analysis of variation. (Buck, 2006:**Online**).

Coskun (2006:770), states that "New quality assessment (QA) systems such as Six Sigma have become more popular because they offer a different approach to problems in the clinical laboratory". Coskun (2006:770), is of the opinion that clinical laboratories producing calculated results are in a position to take full advantage of Six Sigma, which this author describes as "In quality management, Six Sigma is accepted as 'world class quality'". As the Six Sigma 'strategy' measures the degree to which any process deviates from the goal, any process producing calculated values can be evaluated in terms of the six sigma metric, which describes how many sigma fall within the tolerance limits. The author does, however, concede that Six Sigma 'world class quality' level, may be difficult to obtain for calculated tests, as calculated tests traditionally have lower precision levels than measured test methods (Coskun 2006:771).

According to Foster (2007:441), Six Sigma follows the DMAIC project methodology. The steps of the DMAIC process are:

- **Define**: Define the project goals.
- **Measure**: Measure the process to determine current performance.
- **Analyse**: Analyse and determine the root cause of defects.
- **Improve**: Improve the process by eliminating defects.
- **Control**: Control future process performance.

Process Management International (2009:5.5), discusses the importance of recognising the type of measures which are needed when gathering data for a Six Sigma project. This author contends that "In order to improve processes you need to know what has been done and how to do it. The first type of measure, called a result measure, allows you to actually compare what is actually accomplished with what your customers require. The second type of measure, called a process measure, indicates where the process needs to be improved".

Furthermore, the author offered the following identifiable characteristics for result measures as being:

- Also known as R criteria.
- They are tied to the end results or outcomes of the process.
- They are overall useful performance measures.

- They are useful to prioritise and monitor process improvement efforts.
- They give a common understanding of present state.
- They are more directly linked to customer requirements.
- They are fairly easy to identify.
- They may not lead to improvement.

In addition, Process Management International (2009:5.5), returned the following identifiable characteristics for process measures:

- Also known as P Criteria.
- They measure factors found within a process.
- They are tied to the process, and correlated with the output.
- They indicate elements of the process, which if done consistently and successfully should ensure results.
- They may be difficult to identify at the beginning.
- They do not yield immediate results.
- They focus on the long term.
- They indicate where action to improve needs to be taken.
- They are manageable by people in the process.

## 3.7 LEAN

'Lean Quality Management', also known as 'Lean Manufacturing', 'Lean Production' or simply just 'Lean' is a production practice that considers any resource expenditure towards a goal - other than the creation of value for the end customer - to be wasteful, and thus such an expenditure should be a target for elimination (Anvari, Ismail & Hojjati, 2011:1585). These authors contend that, when put in simpler terms, 'Lean' may be defined as "...more value with less work".

Originally derived from the Toyota Production System (TPS), Lean is considered a generic process management philosophy. Lean is renowned for its focus on the reduction of waste, as well as its ability to be successfully implemented with certain TQM tools such as Kaizen (tool for continuous work), Statistical control and Process mapping as a complimentary approach. There are, however, fundamental differences between certain TQM approaches and Lean, such as the Lean focus on

improving entire value streams, whereas other improvement approaches tend to focus on individual processes. Another fundamental difference between Lean and other TQM approaches is that Lean emphasizes the elimination or reduction of non-value-adding activities (waste) in contrast to the focus being placed on the improvement of efficiency or productivity of major value-adding processes (Anvari, Ismail & Hojjati, 2011:1586).

Reynolds (2009:**Online**), is of the opinion that laboratories are typically faced with more volatility and variation in the work that they are required to perform, when compared to manufacturing operations. Furthermore, the life science industry is faced with an additional layer of 'Good Laboratory Practice'(GLP) and 'Good Management Practice'(GMP) complexity. From the perspective of this author, however, there should be no inherent conflict between efficiency and compliance, and thus Lean processes in a laboratory have the capacity to achieve regulatory compliance in the most efficient and productive manner possible (Reynolds, 2009:**Online**).

Cogdill (2008:318), contends "...while quality management systems are concerned with process analysis of quality variation, Lean flow path management is concerned with process analysis of production time variation" This author provides an explanation by adding process efficiency can be secured with the use of the technology platform provided by core concepts of the Lean manufacturing. This author states 'Lean manufacturing' or 'Lean' is often misunderstood, as 'Lean' business initiatives are understood by many people as 'slash-and-burn' management tactics, to shut down or reduce workforce levels of low-productivity operations.

Cogdill (2008:318), reports that Lean should instead be characterised as "an amalgam of methodologies including industrial engineering, just-in-time (JIT) (Osadas's) 5-S's, TQC, continuous quality improvement (CQI), Visual Control, Total Productive Maintenance (TPM), Quality Circles, and Kaizen".

Cogdill (2008:319), argues that "As a discipline of manufacturing science, lean manufacturing is a technical philosophy focused on the reduction of seven types of waste, or 'muda'", and the transformation of a process to lean operation is

accomplished through the use of many tools and strategies. This author, however, concedes that when compared to manufacturing industries, service industries, such as the pharmaceutical industry conducting analytical chemical testing, have been relatively late to adopt 'Lean', and consequently cycle times are extremely long when compared with other industries (Cogdill, 2008:319).

Velaction Continuous Improvement (2011:**Online**), offers "Waste reduction is one of the central principles of continuous improvement". Hubbard (2010:**Online**), was offered the following Japanese terms for the types of wastes which can be encountered in a process:

- **Muda**: The Japanese term refers to all wasteful activities or procedures in a process. Muda focuses on the total reduction of non-value added activities in the process.
- **Mura**: This is the Japanese term for unevenness or inconsistency. In practice an example of this type of waste is regarded to be volatile workloads, which are a common source of waste in laboratories. Mura can be avoided by the implementation of "Just-in-time" systems.
- **Muri**: This is the Japanese term for overburden, unreasonableness or absurdity. In practice, this type of waste in a process, is an example of a source of process variation. Muri can be avoided through standardised work.

Hubbard (2010:**Online**), in addition avers that Muda has traditionally been given much more prominence, as compared to Mura and Muri. The author states his opinion that while Lean practitioners focus on getting a process under statistical control by eliminating and reducing Muda, they do not give enough time to 'process improvement by redesign'. A similar view was found to be expressed by Velaction Continuous Improvement (2011:**Online**), when stating "Mura and Muri are particularly bad, as they are not commonly addressed as sources of waste. Most people can see scrap in a bin, or bad parts, common forms of Muda, as wasteful. Fewer people can conceptualize how daily shifts in demand, or speeding up processes to hit deadlines drive waste into an organization".

Rosenthal (2008:**Online**), maintains that the purpose of a lean technique known as heijunka, is to level the workload. The author points out that in a production

environment, this is easiest done by levelling the product mix. The author concedes that in situations where this cannot be done, heijunka should be focused at processes. Heijunka which is focused at processes is considered to be a form of process standardisation. Furthermore, the author offers that heijunka is a technique of dampening variation by means of addressing jidoka. Jidoka is considered to be any obstacle which reduces process effectivity and efficiency.

With reference to the analytical chemistry industry, Cogdill (2008:319), stated that "...admittedly, there are some constraints intrinsic to the industry". The author argues that this may ultimately prevent these industries from attaining world-class Lean quality, and presents the industry with a unique challenge. Data suggests that most Lean methodologies were developed for high volume production processes for uniform products, thus traditional Lean methods are difficult to manage in a complex service process environment. The author additionally holds that the effectiveness of Lean is considered to be limited by variability in cycle time in a laboratory environment (Cogdill, 2008:319).

## 3.8 LEAN SIX SIGMA

Research done by Khalil, Khan and Mahmood (2006:2), found that Lean Six Sigma is, "...a combination of certain tools and techniques to provide Six Sigma practitioners another philosophy to reduce process and production times, while minimizing the variation and reducing waste at the same time". These authors contend that this relatively new approach that incorporates the use of the Six Sigma methodology, which inherently focuses on gathering data; analysing the collected data, and thereafter improving the process yield by using statistical tool which identifies key areas of variation. Six Sigma is, however, unable to address waste and speed issues in the processes, thus the simultaneous application of Lean tools is employed to attain overall process improvement and waste reduction. Combining these two complementary quality philosophies, results in a powerful problem solving tool which reduces waste and increases process efficiency and yield. In addition, when compared to Six Sigma projects, Lean events or projects are relatively easy to implement in a shorter amount of time, and thus can provide quicker results in process improvement (Khalil, Khan & Mahmood, 2006:3).

Khalil, Khan and Mahmood, (2006:2), state that there are many benefits which result from the integration of Lean tools into the Six Sigma process map. Table 3.2 provides an illustration of the strengths that each individual philosophy brings to the merger, and also provides a comparison of the two methodologies.

**Table 3.2:** Comparison of Lean and Six Sigma (**Source:** Khalil, Khan & Mahmood, 2006:2)

| | **LEAN** | **SIX SIGMA** |
|---|---|---|
| **Focus and Objective** | Waste reduction and flow improvement | Process improvement and variation reduction |
| **Applicability** | Predominantly manufacturing and supply chain management | All types of processes |
| **Process Approach** | Speedy and focussed | Discipline of steps |
| **Execution Focus** | Predominantly team focus | Customer focus |
| **Data Driven Style** | Quantitative and qualitative | Predominantly quantitative |
| **Cost of Implementation** | Relatively low | Relatively higher |
| **Solution Approach** | Process orientated | Statistical orientated |

The authors point out that an uncomplicated integration of Lean and Six Sigma is enabled by the fact that there are several Lean tools which can be mapped directly into Six Sigma's DMAIC process map as illustrated in the Table 3.3 below:

**Table 3.3:** Tools of Six Sigma and Lean (**Source**: Khalil, Khan & Mahmood, 2006:2)

| **Process Map Phase** | **Six Sigma Tools** | **Lean Tools** |
|---|---|---|
| **Define/Measure** | Problem Definition, Capability Analysis, QFD | Value Stream Mapping (VSM), TAKT Time, Demand Flow |
| **Analyse** | Pareto, ANOVA, Regression | TAKT Time |
| **Improve (Optimise)** | DOE, Simulations | Jidoka, VSM, MUDA, Project Smoothing (Heijunka) |
| **Control** | Poke-Yoke, Control Charts | Visual Management, 5S, Lean Assessment |

## 3.9 PROCESS ANALYTICAL TECHNOLOGY

Although Process Analytical Technology (PAT) is traditionally used by chemical manufacturing organisations, the principles of PAT are applicable to other

organisations concerned with quality surrounding their chemical processes, as illustrated by Mettler-Toledo International Inc. (2011:**Online**), who states that PAT has been implemented by chemical industry for the control of chemical processes. PAT tools are focussed on the design, monitoring and control of these processes.

GEA Process Engineering Inc. (2011:**Online**), asserts that the goal of PAT is to understand and control a process where quality cannot be tested (as traditional manufactured products are). Thus quality needs to be built-in, or should be, by design. GEA Process Engineering Inc. (2011:**Online**), proposes that within the PAT framework, the following can be categorized as tools:

- Multivariate data acquisition and analysis tools.
- Modern process analysers and process analytical chemical tools.
- Process and endpoint monitoring and control tools.
- Continuous improvement and monitoring tools.

The Institute of Validation Technology (2006:**Online**), mentions that "Process Understanding and Process Control" is one of the critical aspects of PAT implementation. This author states that included in the PAT toolbox are tools for process characterisation including some well known quality tools namely:

- Focus Interviews.
- Database Design.
- $C_{pk}$ and Control charts.
- Bivariate Analysis.
- Multivariate Regression Analysis.
- Table of Effects.
- Confirmatory Trials.
- Screening and Optimisation DoEs.

An opinion which is expressed is that, many quality management strategies and methodologies, including Six Sigma, QFD, TQM, ISO, the Malcolm Baldridge National Quality Award and PAT are related to the principles of Shewhart, Deming, Juran, Crosby and Taguchi in that "...they are based on systematic methods for understanding the sources of variability in processes and minimizing their impact on quality" (Cogdill, 2008:316).

## 3.10 STATISTICAL PROCESS CONTROL

Statistical Process Control (SPC) is defined as "...the application of statistical methods to the measurement and analysis of variation in a process", while a process is defined as "...a collection of activities that converts into outputs, or results" (Gryna, Chua & DeFeo, 2007:667). These authors contend that any process can be considered to be a unique combination of methods, materials, machine, tools and people that attain a specific output. This output may take on the form of goods, services or even software.

Woodall (2000,341), suggests that statistical methods encompassed by the SPC methodology, play a vital role in the quality improvement process of both the manufacturing and service industries. This author is of the opinion that, in addition to the generalised differences in opinion in all areas of statistical science, due to the diversity of those working in the quality field, disagreements tend to be more common and more intense. Woodall (2000,341), describes SPC as "...a sub-area of Statistical Quality Control (SQC), consisting of methods for understanding, monitoring and improving process performance over time", and stresses that there are some basic concepts encompassed by SPC which essentially needs to be understood by practitioners in order to improve the 'use of methods' in practice.

Woodall (2000:341), further expresses the view that it is of primary importance to understand the concept that, 'quality characteristics' are affected by two types of variation: 'Common cause' variation is considered to be variation present due to the inherent nature of the process, and thus such variation cannot be altered without changing the process itself. 'Assignable (or special) causes' variation are uncharacteristic, unusual shocks or other disruptions to the process, and the source of these can, and should, be removed. A featured tool of SPC is known to be control charting, and this author asserts that one purpose of control charting is to distinguish between these two types of variation in order to prevent over-reaction and under-reaction to a process. Furthermore Woodall (2000:342), highlights that the distinction between common and assignable causes is context dependent, and offers the explanation that what is considered a common cause today, can be an assignable cause tomorrow. A change in the designation of the cause could also possibly be as

a result of certain intentional changes made to the process, such as change in a sampling scheme. Thus, any reaction to a cause of variation should only take place if the cause of variation has sufficient impact on the process, and it is practical and economic to remove it in order to improve quality (Woodall, 2000:342).

In support of Woodall (2000:341), Hare (2002:78), was found to opine that understanding variation is key to SPC. This author is of the opinion that, prior to the installation of a control chart with the expectation of positive results, it is critical to foremost understand process variation, how to sample in order to quantify that variation, as well as how to use SPC to guide the reduction in variation. This author states "SPC is not a tool to steer the process; it is a means of gaining process understanding to aid in process improvement".

In contrast to the opinion of Woodall (2000:341), however, Hare (2002:78), maintains the view that there are three basic kinds of variation as seen in Figure 3.5, namely: common cause variation, structural variation and assignable cause variation.

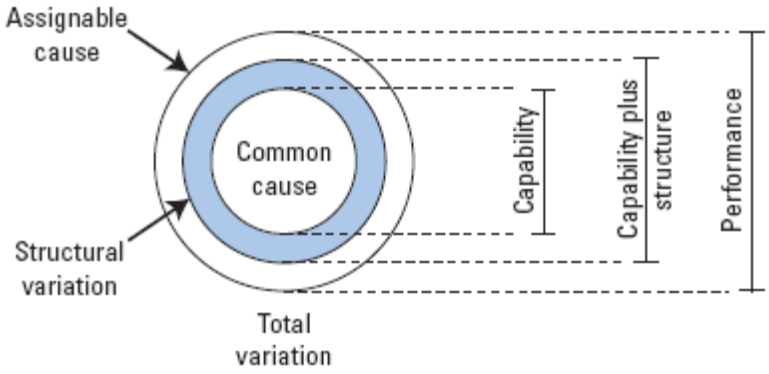


**Figure 3.5:** Understanding Variation (**Source:** Hare, 2001:78)

Despite Hare (2001:78), being simpatico with Woodall (2000:341), on common cause variation as being variation inherent to a process, and assignable cause variation referring to variation which is as a result of sources outside of the process such as shock, this author adds that an additional type of variation exists. This type of variation may be listed as 'structural' variation. Structural variation is considered to be variation as a result of the different parallel parts of a process. Hare (2001:78), conceded, however, that structural variation can be considered a type of assignable variation, and states this as a reason why some quality experts do not make a distinction between the two. This author nevertheless maintains a belief that such a

distinction should in fact be made, due to the reason that the modes of reducing each of these differing types of variability is different (Hare, 2001:78).

A further point of view expressed by Hare (2001:78), is that, in the absence of assignable variation and structural variation, resulting in the effect that only common cause variation is present, a process operation should be consistent with its capability. She makes a case for process improvement through SPC by arguing "But in the real world, all three kinds of variation persist, meaning performance is the sum of all three kinds. Further, the difference between performance and capability is opportunity" (Hare, 2001:78).

Jiang, Murphy and Tsui (2006:174), state that the objective of statistical process control is to identify and remove special cause variation as quickly as possible. The portrayal offered by them is that "...the basic idea in statistical process control is a binary view of the state of the process" which, when paraphrased, can be said to be 'either a process is running satisfactorily or not'. These authors also make reference to two possible types of process variation, namely 'common cause' and 'assignable or special cause' variation, and state that "A process that is subject only to common cause variation is 'statistically' in control" (Jiang, Murphy & Tsui, 2006:174).

The contention of these authors is that SPC charts essentially mimic a sequential hypothesis test. The authors elaborate by explaining that $X_t=\eta_t+Y_t$ is a basic mathematical model behind SPC methods for detecting change, where $X_t$ is the measurement of the process variable at time t, $\eta_t$ is the process mean at that time, and $Y_t$ represents variation from the common cause system. In this manner SPC is used to distinguish assignable cause variation from common cause variation (Jiang, Murphy & Tsui, 2006:174).

The statistical goal of SPC control charts is to detect a 'change point' in processes as quickly as possible, and then trigger corrective action to bring the process back to quality target. The assertion is made that, among others the Shewhart control chart, the Exponentially-weighted Moving Average (EWMA) control chart and the Cumulative Sum (CUSUM) control chart are three of the most important and widely used control charts (Jiang, Murphy & Tsui, 2006:175). The explanation offered by

the authors is that Shewhart control charts are employed to monitor process observations directly, and EWMA control charts provide a control charting algorithm based on exponentially weighted moving averages of the observations, while CUSUM control charts are used as a sequential probability test tool, is offered by these authors. The authors extrapolate on this by stating that Shewhart control charts are sensitive for detecting large shifts in process variation, while EWMA and CUSUM charts are sensitive to small shifts in process variation (Jiang, Murphy & Tsui, 2006:175).

Woodall (2000:342), states that control charts are tools used to monitor processes, in order to determine whether or not the process can be said to be 'in statistical control'. The author proffers successful 'statistical control' to be the probability distribution representing a quality characteristic of a process remains constant over time. Specification limits are used in practice to determine continuous quality characteristics of a process. Woodall (2000:342), makes reference to the type chart that was originally introduced by Shewhart, which provides an out-of-control signal as soon as the statistic calculated from a sample falls outside specification limits. The author states that "...these limits are usually set ± 3 standard errors of plotted statistic from a centreline at its historical average value". Thus, the function of a control chart may be understood to be, the provision of practical value through its use when samples are taken over a period of time, and measurements of a predetermined quality statistic obtained from these samples, are plotted when using the relevant control charts, such as the $\bar{x}$-chart which is used to monitor the process mean, or the R-chart which is used to monitor variability (Woodall, 2000:342).

It may be said that Woodall's (2000:342), point of view is comparable to the views of Jiang, Murphy and Tsui (2006:175), when considering the latter authors' assertion that a superficial perspective of control chart testing is similar to testing hypothesis. According to Woodall (2000:342), (citing Juran, 1997), a contention is offered that, one view of a control chart is that it can be considered a "perpetual test of significance". Furthermore, (citing Box & Kramer, 1992), this author stated that another perspective for consideration is that "Process monitoring resembles a system of continuous statistical hypothesis testing". The author then offers his opinion that not all professionals in the quality field are in agreement, as contradictory views

exist, such as (citing Deming 1986), “Rules for detection of special causes and for action on them are not tests of a hypothesis that a system is in a stable state”. Woodall (2000:343), does however draw attention to the fact that there appears to be a ‘middle ground’ on this matter, by citing Shewhart’s (1939), opinion, “As a background for the development of the operation of statistical control, the formal mathematical theory of testing a statistical hypothesis is of outstanding importance, but it would seem that we must continually keep in mind the fundamental difference between the formal theory of testing hypotheses employed in the operation of statistical control”.

When comparing statistical process control and formal hypothesis testing, Bakker, Kent, Derry, Noss and Hoyles (2008:138), concurred that:

- Both were statistically inferential in nature, thus are both excellent tools for process improvement.
- The construct of both has to be measured, thus samples are used by both to predict some feature of the population or process.
- Both approaches aim to detect differences.
- The equivalent of a null hypothesis in SPC is ‘the process is stable’, with the alternate hypothesis being ‘there is a change in the process’.
- In SPC, probability-based rules are used, such as ‘seven points on either side of the mean may point to a special cause’.
- Possible errors in SPC resemble type I and type II errors, thus non-conforming points might be due to chance, and special causes might still not be detected by probability-based rules.

Consequently it appears apparent that these authors offer an opinion that the above comparison provides an illustration of how the two types of inference are subject to different norms. Whereas SPC is considered to be pragmatic, formal hypothesis testing is traditionally considered to be independent of specific features of the situation i.e. contextual ‘noise’ is not included during the calculations. Thus, hypothesis testing is considered to have become standardised, whereas SPC can be used in more liberal ways and often in non-standard ways (Bakker *et al*. 2008:139).

According to Foster (2007:405), other statistical techniques in addition to hypothesis testing and process control charts can be particularly useful for improving quality as part of the SPC methodology, such as correlation and regression, especially in services. Foster's (2007:405) belief is, however, that it is almost never appropriate to use regression on process data used in developing control charts, as there are other types of data available that can be correlated and regressed. This technique provides the user with a graphic demonstration on whether variables are significantly and positively related. The $R^2$ value obtained shows the strength of relationships between variables for linear and nonlinear (quadratic) models. This author states that such correlation is known as 'interlinking' and is useful in helping to identify casual relationships between variables (Foster, 2007:405).

## 3.11 PROCESS CAPABILITY

Wu, Pearn and Kotz (2009:339), considers Process Capability to be "...an important and well-defined tool in applications of statistical process control (SPC) to a continuous improvement of quality and productivity". They state that the relationship between the specification limits, or tolerance, of a process and the actual process performance may be quantified using suitable process capability indices (Wu, Pearn & Kotz, 2009:339).

An opinion is offered by Foster (2007:403), that there are two purposes of process capability studies namely:

- To determine whether a process is able to consistently deliver results that meet specifications.
- To determine whether a process is in need of monitoring through the use of permanent process charts.

Gryna, Chua and DeFeo (2007:693), were moreover found to contend that "...a concept of process capability has emerged to provide a quantified prediction of process adequacy. The authors state that the ability to predict quantitatively has resulted in widespread adoption of this concept as a major element of 'quality planning'. The statement is also made that the most widely adopted formula for process is "Process capability ($C_p$) = $\pm 3\sigma$ (a total of $6\sigma$)", where $\sigma$ is the standard

deviation of a process under a state of statistical control, and thus this author states the statistical formula process capability is traditionally expressed as:

$C_p = \frac{USL-LSL}{6s}$ . These authors highlight that a process which meets the minimum specification limits has a $C_p$ index of 1.0.

Gryna, Chua and DeFeo (2007:693), also mention that "Process capability, as measured by $C_p$, only refers to the variation in a process about the average value", thus the $C_p$ index is considered only a measure of 'potential' capability assuming that the process is operating in statistical control and that the process average is equal to the midpoint of the specification limits. In practice, however, the process average is often not at the midpoint, and thus it is useful to employ a capability index, which reflects both variation as well as the process average location. Such an index is known to be a process performance index, denoted as $C_{pk}$ (Gryna, Chua & DeFeo, 2007:693). These authors assert that "$C_{pk}$ reflects the current process's mean proximity to either USL or LSL. The statistical formula for process performance is traditionally expressed as $C_{pk} = min\left[\frac{\bar{x}-LSL}{3s}, \frac{USL-\bar{x}}{3s}\right]$. In addition these authors make note of the fact that the higher the value for either of these indices, the lower the amount of resultant product of the process will fall outside of the specification limits and, ultimately, the more capable the process will be. They also highlight that when the actual process mean is equal to the midpoint of the specification range, then $C_p = C_{pk}$ (Gryna, Chua & DeFeo, 2007:694).

Foster (2007:403), maintains that an important step in performing process capability studies is to compare natural tolerance limits with specification limits. The author provides the explanation that natural tolerance limits are three standard deviations for the population distribution. The final step of process capability studies is said to be making a decision as to what is an acceptable benchmark is,regarding which value is an acceptable $C_p$ or $C_{pk}$ value. It is this author's contention that "...processes that achieve capability indexes ($C_{pk}$) of 1.25 are capable, 1.33 are highly capable, and 2.0 are world –class capable (Six Sigma)" (Foster, 2007:403).

Furthermore the author holds the opinion that a process can be considered capable if individual results consistently meet specification, however, it is important to note that a process is considered stable if only common variation is present in the process. Thus it is possible to have a process where random variation present is very high. However, due to its ability to meet specifications, the process is stable but not consistently capable. A less common phenomenon is a process which is stable, yet incapable (Foster, 2007:405). The illustration as seen in Figure 3.6 is an example of the relationship between $C_p$ and $C_{pk}$.

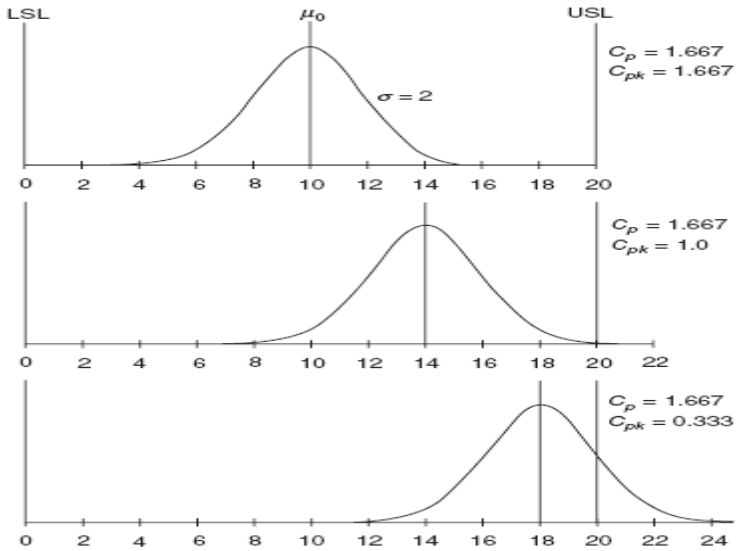


**Figure 3.6:** The relationship between $C_p$ and $C_{pk}$. (**Source**: Wang, 2008:307)

Wang (2008:305), maintained that, in order to conduct a process capability study, it is important to make a distinction between 'specification limits', 'control limits' and 'natural tolerance limits'. The author further states that the general understanding is that the 'specification limits' of a process are given by customers (or in-house design engineers before process operation). Furthermore Wang (2008:305), asserts that 'control limits' are said to be those limits determined by samples collected for processing during a base period. Therefore, should a single sample point fall out of the region indicated by these limits, and consequently trigger an 'out-of-control' state, it should be noted that a sample value produced in the out-of-control state, is not necessarily a non-conforming item. Ultimately a single sample which falls out of the 'control limits' even during a routine process run, will neither cause the process to be out-of-control nor necessarily be nonconforming (Wang, 2008:305). This author attests that 'natural tolerance levels' of a process are those limits which

generally describe the variability of measurements obtained by the process, and it is commonly acceptable that these are ±3 standard deviations from the process mean. Thus, 'natural tolerance levels' will be indicated by variability around the process mean.

The Encyclopedia of Business (2011:**Online**), provides a detailed explanation on the relationship between natural tolerance levels of a process and process specification limits. This source states that natural tolerance levels are traditionally expressed as the process mean plus or minus z standard deviation units. Unless stated otherwise, z is considered to be three standard deviations. Natural tolerance limits are thus normally the limits between which the process is capable of producing parts.

There are three possible situations, as described by the Encyclopedia of Business (2011:**Online**), which may exist, pertaining to the relationship of natural tolerance limits and specifications limits, namely:

- Specification limits are wider than natural tolerance limits. This situation accommodates, to a certain degree, a change in process variability, or shift in process mean, despite this situation essentially not being desirable. This situation does, however, represent a process which is capable of meeting the required specifications.
- Specification limits are equal to process natural tolerance levels. This situation represents a critical process only capable of meeting specifications if no change in variability takes place and no shift in process mean.
- Specification limits are narrower than process natural tolerance levels. This situation guarantees that the process will be unable to meet desired specifications, and thus warrants urgent attention, or action to be taken, in order to widen specification limits by either a change in design or control of the process, such that is variability is reduced.

This source refers to a solution to the latter situation as being "…to look for a different process altogether" (Encyclopedia of Business, 2011:**Online**).

The terminology used to describe measurement parameters by the authors previously referred to in this literature review, namely Gryna, Chua and DeFeo (2007:693),

Foster (2007:403), Wang (2008:305), and Encyclopedia for Business (2011:**Online**), contrasts with the terminology used by a number of other leading authors such as Westgard and Westgard (2006), and Marquis (2011), in the field of quality improvement in clinical laboratories, when describing the above-mentioned limits in the context of analytical chemistry processes. It is accepted, however, the establishment of understanding between concepts referred to can be illustrated, despite the terms being different, through the definitions provided by Marquis (2011a:**Online**). The direct definitions, provided by this author, establish that the concepts referred to by differing terms are related and directly comparable. Marquis (2011a,**Online**), purports that the term 'tolerance levels' in a laboratory context, theoretically identifies the 'maximum deviation or 'breach from' the true analytical concentration of a sample, which will not have an effect on diagnostic value'. 'Diagnostic value' of any laboratory result enables the correct diagnosis to be made, proper treatment to be provided and adequate patient follow-up followed, all based on the analytical result. This author states that the acceptable standard is defined by the clinical value which the result provides to pathologists who require it, in order to make a diagnosis based on it. 'Tolerance limits' are defined by consensus between pathologists (Marquis, 2011b:**Online**). Cappello, King, Marcum and Stanley (2011:**Online**), returned that the normal reference values of selenium in healthy bovine is between 0.25ppm as a lower limit, and 0.50ppm as an upper limit.

Furthermore Marquis (2011b:**Online**), argues that a clinical chemist must ensure that the uncertainty of all analytical processes is compatible to the tolerance required by medical needs. The author's contention is that "...therein lies the objective of process capability analysis, with the use of a capability index, to ensure and monitor the quality of clinical laboratory process".

Chesher and Burnett (1997:1100), contend that the concept of process capability has been used by the manufacturing industry to quantify the relationship between the measured process performance and product specifications and various indices and ratios have been developed to describe this relationship. These authors report that a simple application is considered to be the capability index (or ratio) applied as $C_p$

defined as $C_p = \frac{USL-LSL}{6\sigma}$, where USL and LSL are the upper and lower specification limits of an analytical process and σ is the standard deviation of the process.

Chesher and Burnett (1997:1100), argue, however, that this relation can be described differently for the purpose of a clinical chemistry process. The authors tender that the use of medically important critical system error or uncertainty ($\Delta SE_c$) and critical random error ($\Delta RE_c$) may be used to determine process capability. A promulgation suggested by fellow authors (citing Westgard & Burnett:1990), describes the relation between $C_p$ and $\Delta SE_c$ can be described as $\Delta SE_c = 3C_p - z$, where zero bias is assumed, and where z is a factor for a one-tail test of significance (usually set at 1.65 for 95% confidence, assuming guassian distribution) (Chesher & Burnett, 1997:1100).

Furthermore Chesher and Burnett (1997:1101), express the belief that a limitation of the use of $C_p$, is that it does not consider any bias present within an analytical process. The authors therefore believe a more suitable process capability index would be $C_{pk}$, which considers bias in addition to imprecision. The authors propose the equation $C_{pk} = \frac{\Delta REc \times Z2}{3}$ after demonstrating the mathematical equivalence of $\Delta SE_c$, $\Delta RE_c$ and $C_{pk}$, and vie that this relationship permits a unification of approaches around process capability. Chesher and Burnett (1997:1101) purport that, based on the relation presented, a common language is available between clinical chemistry and quality professionals in the manufacturing industry. Thus, the authors are found to offer the following formula which can be used to measure process capability: $C_{pk} = \min[\frac{\Delta TE + \bar{x} - LSL}{3s}, \frac{\Delta TE + USL - \bar{x}}{3s}]$,which takes total analytical error (ΔTE) or uncertainty of analytical procedure, into account.

The work of Marquis (2011c:**Online**), returned that process capability relates tolerance, defined as "spread allowable by medical customers", to uncertainty, defined as "unavoidable spread of an analytical method". This author is of the opinion that the capability index ($C_p$), is the ratio of the former to the latter and can be expressed as $C_p = \frac{Customer's\ tolerance}{Analytical\ uncertainty}$ (Marquis, 2011c:**Online**). The author provides the explanation that an analytical process can be considered capable if the analytical uncertainty is less than customer tolerance given for the process, whereas

an analytical process should be considered incapable if the analytical uncertainty of the process exceeds the measurement provided by customer tolerance. Furthermore this author offers the following formula which is be derived directly from an example calculation, $C_p = \frac{Upper\ Tolerance\ Level - Lower\ Tolerance\ Level}{3 \times CV\ (specific\ to\ CRM) \times \bar{X}(mean)}$ to determine capability, as presented in his work.

Gaines (2003:**Online**), offers that the coefficient of variance (CV) of a process, which reflects the accuracy or bias of the process, is best established through the analysis of certified reference material (CRM). In addition Gaines (2003:**Online**), explains that if CRM is not available, then the next best approach is comparison studies with an independent validated method can be used. However, if such a method is not available, the third approach would be to conduct an inter-laboratory study with accredited (ISO 17025) laboratories to obtain process CV. A final resort if all of the above methods are not available, would be to establish recovery through spike recovery experiments and/or the use of standard additions (Gaines, 2003:**Online**).

MiC Quality (2011b:**Online**), provides a graphic illustration (see Figure 3.7), as well as the glossary definition for the term 'bias' as "In measurement – the difference between an observed measurement and the true value (according to reference standard). Essentially the same thing as accuracy".

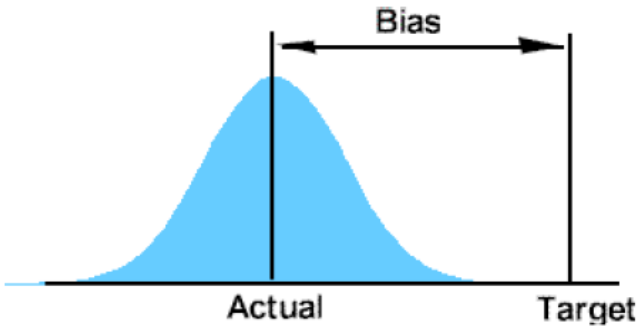


**Figure 3.7** Process Bias (**Source**: MiC Quality, 2011b:Online)

The term 'bias' in analytical chemistry was found to be defined by McGraw Hill Science and Technology Dictionary (2011: **Online**), as "A systematic error containing a chemical measurement that is inherent in the method itself or caused by

some artefact in the system, such a temperature effect". Furthermore, in statistical terms the definition for 'bias' is given by McGraw-Hill Science and Technology Dictionary (2011:**Online**), as "In estimating the value of a parameter of a probability distribution, the difference between the expected value of the estimator and the true value of the parameter".

Ndlovu (2005:**Online**), discusses the laboratory concept of 'method validation processes', which is construed to be used as part of process capability testing in a clinical laboratory. In support of this argument, this author offers that method characterisation is an essential element, whereby the laboratory translates customer requirements into verifiable analytical or statistical data. This data should be checked to see if the laboratory method is capable of meeting the given requirements. This author states "...the actual performance check against these requirements is called a method validation process" (Ndluvo, 2005:**Online**).

The author avers that performance characteristics of an analytical process or laboratory method are factors which, in practice, demonstrate how well a method performs and is capable to achieving the required results. These include accuracy, precision, recovery, detection limit, limit of quantitation, interference and linearity test. The statement is made by this author that "Performance characteristic judgements are based on statistical validation techniques" (Ndluvo, 2005:**Online**).

It was found that Gaines (2003:**Online**), is of the opinion that 'capable analytical processes' are simpatico to 'reliable analytical processes' and therefore process capability is not confirmed without the critical aspect of confirming basic process performance criteria. Gaines (2003:**Online**), expresses the view that the following criteria are typically evaluated in order to validate, and are reflective of an analytical process's capability:

- Specificity.
- Accuracy or Bias.
- Repeatability.
- Limit of Detection.
- Sensitivity.
- Limit of Quantitation.

- Linearity or Range.

Gaines (2003:**Online**), explains 'Specificity' as the confirmation that process interferences are not significant. The author explains that a comparison of results obtained a straight calibration curve gives information regarding process drift, process stability and factors influencing stability. Gaines (2003:**Online**), also offers that 'accuracy or bias', innate to all analytical processes, is established through CRM. Additionally, this author states that an expression of analytical 'repeatability', also referred to as 'single laboratory precision' is the standard deviation of a process.

Furthermore Gaines (2003:**Online**), holds that 'limit of detection' is a criterion establish by analysing known concentrations of the analyte. 'Sensitivity' reflects the standard deviation from the measurement midpoint of interest of a process, while 'linearity' or 'range' is a property that is between the limit of quantitation and the point where a 'plot of concentration versus response' goes non-linear.

Striking resonance seems apparent between the view of Gaines (2003:**Online**), and that expressed by Chan (2008:730), who offers insight into the practical application of the important process capability limits, (namely control limits and tolerance or specification limits), which are required to perform process capability studies, is based on the foundation of validation of some analytical process characteristics namely:

- Accuracy.
- Precision.
- Specificity.
- Detection Limit.
- Quantitation limit.
- Linearity.
- Range.
- Robustness.

Chan (2008:730), argues that the accuracy of an analytical process is the closeness of agreement between the values that are accepted as either conventional true values or accepted reference, and the actual process measurement value of a certified standard

sample analysed. Accuracy is reported as the concentration recovered of a known added amount of analyte in sample during the application of an analytical method, or, as the difference between the mean of the method and accepted true value, together with the confidence intervals.

Furthermore, the contention of Chan (2008:730), is that the "...precision of an analytical method process expresses the closeness of agreement (degree of scatter) between a series of measurements obtained from multiple samples of the same homogeneous sample under prescribed conditions. Specificity is considered by Chan (2008:731), (citing ICH, 2005) to be "...the ability to unequivocally access an analyte in the presence of components that may be expected to be present", while detection limit (DL) is a characteristic referring to the lowest amount of analyte in a sample, that can detected. It is common to compare measured signals from samples with low concentrations of analyte with those of the blank samples, for instrumental procedures that exhibits background noise, enabling this minimum concentration of the analyte to be reliably detected, using an acceptable signal-to-noise ratio (Chan, 2008:733).

Quantitation limit (QL) is defined by Chan (2008:734), as the "...concentration of related substance in a sample that will give a signal-to-noise ratio of 10:1", and furthermore states that the QL of a method is affected by both the detector sensitivity and the accuracy of sample preparation. Chan (2008:734), (citing ICH, 2005), defines linearity of an analytical process as "...the ability (within a given range) to obtain test results of variable data (e.g. absorbance and area under the curve) which are directly proportional to the concentration (amount of analyte) in the sample". Finally Chan (2008:735) explains 'range' to be the interval between the upper and lower concentration of analyte in a sample, and 'robustness' is described to be the measure of the analytical method process to remain unaffected by small, but deliberate variations in method parameters.

Thus process capability studies are seen to arguably be the most fundamental toolset available for quality improvement purposes on a process. This is highlighted by the research offered by several authors, and it is found that this is especially relevant pertaining to clinical laboratory processes. It is thus believed that it may be

summarised as Marquis (2011), was found to do, as "The clinical chemist must check whether the uncertainty of all his analytical methods is compatible with the tolerance required by medical needs. It is the aim of the capability index. If the uncertainty interval of a method is greater than the tolerance interval, the analytical method must be discarded or improved" (Marquis, 2011:Personal Email).

## 3.12 FAILURE MODE EFFECT ANALYSIS

Foster (2007:219), describes 'Failure modes and effects analysis'(FMEA) as a reliability analysis tool or a methodology to make process designs more reliable. According to this author, FMEA is a systematic consideration of each component in a system. The exercise involves the identification, analysing and documentation of the possible failure modes within the system, as well as the effects of each failure mode on the system. As analysis is initiated from the lowest level of detail and progresses upward, it is considered a 'bottom-up' analysis. The result of FMEA provides a detailed description of how failures influence system performance, as well as personnel safety (Foster, 2007:220).

Foster (2007:220), lists some of the benefits that can be derived from FMEA as:

- Improvement of the safety, quality, and the reliability of product.
- Improvement of a company's image and its competitiveness.
- Increased satisfaction from a user standpoint.
- Reduction in product development cost.
- Record of actions taken to reduce a product risk.

Gryna, Chua and DeFeo (2007:330), contend that a methodical method of examining and determining a design for potential shortfalls in which failures can occur is known as Failure mode effect analysis (FMEA). FMEA is described to be the exercise of examining the product of a process at process level, for all the ways in which a failure might occur. An estimate is made of the effect of the each potential failure on the total system as well as the seriousness of the failure event. The next phase of this technique involves a review being conducted of the action, or planned action, which can be taken to minimize the effect of the failure (Gryna, Chua & DeFeo, 2007:330).

These authors advise that a ranking procedure be applied to assign priorities to potential failure modes which warrant further investigation. The ranking procedure takes a twofold format, namely:

- Ranking according to the probability of occurrence of the failure, and
- ranking according to the severity of the effect.

Gryna, Chua and DeFeo's (2007:330), contention draws a parallel to Foster's (2007:220), more detailed description of the FMEA procedure namely:

- Assign each component in system a unique identifier.
- List all functions performed by each part of the system. A block diagram may be used.
- List one or two failure modes for each function listed in the previous step. The best description of a failure mode is a short description of how a function may fail to be performed.
- Describe the effects each failure mode of a component will have. Analysis of effects should follow a hierarchical order, because any effect should be detailed so that the severity of each effect can be judged.
- Determine whether the failure will result in a potential hazard to personnel or the system, and categorise how severe each hazard will be. Four basic hazard categories are: catastrophic, critical, marginal and negligible.
- Estimate relative likelihood of occurrence for each failure using a 10-point scale, ranging from unlikely (1) to very likely (10).
- Estimate the ease with which a failure may be detected.
- Identify highest risks in the system based on information provided by the previous three steps.
- Decide what action will be taken to eliminate or reduce the highest risks in the system.

Foster (2007:220), proffers a graphic depiction of the description of the FMEA procedure which can be seen in Figure 3.8

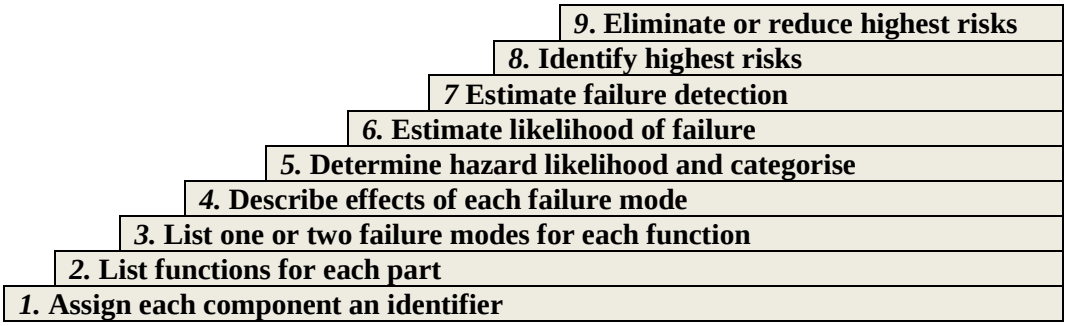


**Figure 3.8:** Failure Mode Effect Analysis (FMEA) Steps (**Source**: Foster, 2007:221)

Another technique highlighted by Gryna, Chua and DeFeo (2007:333), is FTA. This is a technique whereby studies are usually applied to only the potential failures which are considered serious enough to warrant detailed analysis.

van Leeuwen, Nauta, de Kaste, Odekerken-Rombouts, Oldenhof, Vredenbregt and Barends (2009:1085), argue that, as a quality tool FMEA has high improvement potential when applied to clinical laboratory processes. In addition these authors express the belief that FMEA is superior to other risk analysis tools, in that it is commonly used and well documented. These authors do, however, concede that there are certain drawbacks of this tool, namely, as a result of working with improvement indices as outlined by FMEA's priority categorisation, it may lead to the uptake of corrective action on only those failure modes with which the largest improvements could be realised. Thus, in the study conducted by these van Leeuwen *et al.* (2009:1087), they found that certain process steps that were thought to be uncritical were initially neglected but subsequently turned out to be of significant importance. Despite this finding, however, these authors conclude that although FMEA was not an 'absolute' method, they argue that FMEA is a useful addition to analytical validation when considering the risks of human failure (van Leeuwen *et al.* 2009:1087).

American Society for Quality (2011b:**Online**), states that Failure mode effect analysis is also known as 'potential failure modes and effects analysis' and 'failure modes, and effects criticality analysis (FMECA)'. An explanation is given that

"'Failure Modes' means the ways, or modes in which something might fail. Failures are any errors or defects, especially ones that affect the customer and can be potential or actual". An additional explanation is given that "'Effects Analysis' refers to the studying the consequences of those failures" (American Society for Quality, 2011b:**Online**).

Furthermore, it is stated that FMEA was initially used by the U.S. military in the 1940s, however this tool was later adopted and modified for use by the aerospace and automotive industries. The point of view is proffered that this adaptable tool is able to be developed for use by several differing industries, each maintaining their own individual FMEA standards. The American Society for Quality (2011b:**Online**), however, stated that before undertaking a FMEA process in practice, it is imperative to learn more about the standards and specific methods in the organisation or industry where it is being applied.

The American Society for Quality (2011b:**Online**), also highlights that during the exercise of conducting a FMEA procedure, there are certain basic quality tools that can be used, such as flowcharts, root cause analysis tool and even control charts, which are considered integral to some of steps which form the FMEA procedure. The overview expressed is that FMEA is considered valuable, as it documents current knowledge and actions about risks of failures for use in continuous improvement, but FMEA further adds value when used during design to prevent failures. FMEA can also later be used for control, before and during the ongoing operation of the process (American Society for Quality, 2011b:**Online**).

## 3.13 CONCLUSION

A thorough and extensive literature review into the current state of knowledge on the relevant subject matter is believed to be the only appropriate way in which research can be conducted. Through the identification of critical aspects pertaining to the research topic, in addition to consideration of the objectives of the research, areas for literature review were identified. A process of evaluation and comparison of the work of other researchers in the field of this author's research, yielded a concrete framework on which to conduct the required research.

Research continues in the direction of the illustration of the form of the research, by discussing the scientific method as a research method, as well as a data collection method. The following chapter will also outline a detailed description of the parameters associated with data collection, and provides an explanation on the guideline conventions pertaining to the validity and reliability of data for the manner that raw data is analysed.

# CHAPTER FOUR

# AN APPROACH TO THE IMPROVEMENT OF THE SELENIUM ANALYSIS PROCESS OF THE WESTERN CAPE PROVINCIAL VETERINARY LABORATORY

## 4.1 INTRODUCTION

This chapter explores and details the survey environment in which research for this dissertation is conducted. The undertaking is presented in this chapter to provide the reader with an understanding of the research environment, in the context of the specific approach adopted to address the research hypothesis. The chapter advances motivations for the scientific method approach to research, and extrapolates on the Six Sigma methodology which was utilized as a vehicle to conduct research and analyse data. The chapter then offers an explanation as to how the research design is constructed to ensure the reliability of data, and additionally provides insight on guidelines pertaining to the validity of data in an analytical chemistry survey environment.

## 4.2 THE SURVEY ENVIRONMENT

The survey environment in which research for this dissertation took place is primarily an analytical chemistry laboratory environment and was focussed specifically on one particular analytical process, namely, the selenium analysis test method. The primary concern of this research thus revolved around the 'investigation of current process steps of the test method' in an attempt to simultaneously mitigate constraints presented by the method, as well as improve the analytical test process. The chief objective of research is thus said to be resolution of the research hypothesis by conducting research on the analytical process steps, and thereby determine the extent of potential detrimental effects certain process steps may have on process results.

Weisberg, Needham and Hendry (2011:**Online**), define chemistry as the "study of the structure and transformation of matter", while Gryna, Chua and DeFeo (2007:195), define a process as "... a collection of activities that converts inputs into outputs or results. Thus, a process may simply be several steps in a manufacturing or service area". Furthermore, Process Management International, (2009:1) maintain that the ability to improve performance is crucial to the health of businesses, industries and the larger economy. A critical essential for 'business improvement' is, therefore, to maintain the focus of efforts on managing, improving and re-inventing business processes to continually optimise business systems.

With specific reference to processes performed in an analytical chemistry environment, Walker (1905:435), regards the practice of 'technical chemistry' as the performance of a chemical reaction, or series of chemical reactions, in the course of a method. According to this author, "Problems which are encountered by investigators in this field of endeavour may, therefore, be divided into classes according as they pertain to the chemical reaction involved, or to the process to be employed in carrying on this reaction" (Walker, 1905:435).

Elucidation on the statement is regarded to be, in the field of 'technical chemistry' the initial division or class of problems which the author makes reference to, is considered to be pure chemistry, even though the result of the solutions to this division of problems are, in fact, utilitarian in nature. The latter division of problems may be referred to as chemical engineering.

With regard to engineering disciplines at large, including mechanical, civil, electrical as well as chemical, the author cites the country Germany as an example, and voices a sentiment that in the area of engineering enterprises, that country excelled over counterpart countries such as America and England. Walker (1905:435) states his opinion that the reason why Germany excelled over counterparts, as well as the reason why this country successfully met problems confronting its chemistry industry, was due to the attention paid to the initial class of problems as divided above. The author believes that a successful approach was applied by Germany in recognising the value of chemical engineering when addressing problems encountered in the division of pure chemistry. By understanding that pure chemistry

is inseparably connected to her industries, Germany managed to secure her position as a front-runner in this discipline. The author further explains how success was secured by individuals in the field who were "trained in the spirit and methods of scientific research". Thus the most successful research in such a survey environment is only performed on the premise of the scientific method (Walker, 1905:436).

Blumberg Cooper and Schindler (2011:11), suggest that "...research is a systematic inquiry aimed at providing information to solve managerial problems", while Year of Science (2011:**Online**), stated that "Science and research are two words or concepts that are so closely related that they are almost interchangeable with one another" and that "Science can best be described as systematic gathering of knowledge of the world and its occurrences and phenomenon through observation and experimentation. Research can be defined as a systematic approach to gather information and data in order to arrive at an explanation".

Blumberg, Cooper and Schindler (2011:12) assert that "Good research follows the structure of the scientific method". The authors propose that there are several defining characteristics of the scientific method, as can be seen in Table 4.1.

**Table 4.1:** Actions which guarantee good research (**Source:** Blumberg, Cooper & Schindler, 2011:13)

| **Characteristics of Research** | **How can a researcher achieve it?** |
|---|---|
| Purpose clearly defined | In applied research, the researcher distinguishes between the defined symptom of the problem and the perception of the problem. In pure research, it is advisable to draw a distinction between the research dilemma addressed and the research problem being investigated. |
| Research process detailed | Research provides complete research proposal. |
| Research design thoroughly planned | Exploratory procedures are outlined with constructs defined. Sample unit is clearly described, along with sampling methodology. Data collection procedures are selected and designed. |
| High ethical standards applied | Safeguards are in place to protect study participants, organisations, clients and researchers. Recommendations do not exceed the scope of the study. The study's methodology and limitation sections reflect researcher restraint and concern for accuracy. |
| Limitations frankly revealed | Desired procedure is compared with actual procedure in report. Desired sample is compared with actual sample in report. Impact on findings and conclusions is detailed. |
| Adequate analysis for decision | Sufficiently detailed findings are tied to collection instruments. |

| | |
|---|---|
| maker's needs | |
| Findings presented unambiguously | Findings are clearly presented in words, tables and graphs. Findings are logically organised to facilitate reaching a decision about the problem. |
| Conclusions justified | Decision-based conclusions are matched with detailed findings. |
| Researcher's experience reflected | Researcher provides experience/credentials with report. |

An endeavour to investigate the disparity observed in analytical results of the selenium analysis process in the biochemistry survey environment, directed research to identify and understand all critical aspects which were indicated as those which play a role in the environment. Through adequate extrapolation of the highlighted research aspects (or variables), that have an influence on the unique selenium analysis process, the design of appropriate research steps was enabled. Shuttleworth (2008a:**Online**), avers that suitable research steps permits appropriate variables to be tested, and ultimately provide an answer to the research hypothesis according to the scientific method.

Appropriate research steps for this specific survey environment were thus developed from a scientific method platform. These steps maintained a primary focus on the variables of the research hypothesis, namely, 'variation in process, time and control', and the 'disparity in selenium testing results'. Influential aspects identified as role-players on the dependent and independent variables were deemed to include:

- Variable process aspects such as physical process steps, process time and process control measures, as the independent variable of the research hypothesis
- Disparity in results, as the dependent variable of the research hypothesis.

The scientific research design constructed for this survey environment was thus sufficiently capable to evaluate and isolate the effect the independent variable, namely, 'the effect of various process steps' on the dependent variable, namely, 'disparity observed in the results obtained from this process'. Potential variability in the process output, as a result of certain process steps, was identified as the critical subject of investigation. Research was therefore structured to test the variables accordingly. Research findings were ultimately secured with this structure, through the scientific research process or 'scientific methodology'.

Scientific research is commonly described as a seven phase process. Shuttleworth (2008a:**Online**), offers the phases to be:

- **Phase 1:** Formulate a general question defining the research process.
- **Phase 2:** Narrow and focus the research area to one fundamental hypothesis.
- **Phase 3:** Design steps that will test and evaluate the hypothesis.
- **Phase 4:** Observing and record the results of research.
- **Phase 5:** Analyses data.
- **Phase 6:** Conclusions and publishing.
- **Phase 7:** Cycles, scientific method generates data and ideas to recycle into the first stage."

Scientific foundations and scientific research design form the elementary basis of the PDCA cycle (Moen &Norman, 2011:2). Lean Six Sigma is a quality methodology which is PDCA based.

Blumberg, Cooper and Schindler (2011:11), were found to assert that "Control is a logical outcome of prediction". The authors explain that one of the aims of research conducted within a particular survey environment is to be able to understand, explain and predict a phenomenon which poses a problem, in order to secure a better position to control the specific phenomenon within that environment.

## 4.3 RESEARCH DESIGN AND METHODOLOGY

Blumberg, Cooper and Schindler (2011:57), proffer that 'research design' is the "...blueprint for fulfilling objectives and answering questions". The authors suggest that the construction of a research design incorporating diverse methodologies, allows researchers to achieve greater insight than if they followed the most frequently method encountered in literature, or suggested by a disciplinary bias.

In addition, citing Kerlinger (1986), the authors were also of the opinion that, although many definitions for research design exist, one such definition is "Research design is the plan and structured investigation so conceived as to obtain answers to research questions. The plan is the overall scheme or program of research. It

includes the outline of what investigator will do from writing hypothesis, and the operation implications to final analysis of data. A structure is the framework, organisation, or configuration of .... the relations among variables in a study".

### 4.3.1 Six Sigma as methodology for research design

Allen (2006:8), was found to regard Six Sigma as "... an organised and systematic problem-solving method for strategic system improvement and new product and service development that relies on statistical methods and the scientific method to make dramatic reductions in customers defined defect rates and/or improvements in key outputs variables". The author is further offers, "Six Sigma relates to combining statistical methods and the scientific method to improve systems".

Allen's (2006:8), contention is supported by Webb (2008:**Online**), who avers that "Six Sigma is essentially a method of quality improvement, which is also known as process improvement" Webb (2008:**Online**), was found to be of the opinion that Six Sigma is, in fact, currently the most sophisticated iteration of process improvement. The author elaborates by explaining that, in practice, Six Sigma is generally implemented after applying another method known as Lean. The complimentary two methodologies are able to secure a level of quality and improve process performance to a degree that cannot be accomplished in isolation of each other. Webb (2008:**Online**), also returned, that in essence, Lean Six Sigma is fact based, and Six Sigma is based on the scientific method as embodied in the five steps of a Six-Sigma project. The five steps are commonly known as DMAIC, which is an acronym for Define, Measure, Analyse, Improve and Control.

For scientific research, the use of Six Sigma methodology is believed to add value, based on research done by Zhang, Hill and Gilbreathe (2009:**Online**). These authors advance that their review of the methodology known as Six Sigma, found that four categorizations of the definition of Six Sigma exist, depending on its application by user. The authors state these categorisations to be:

- Six Sigma as a defect rate metric.
- Six Sigma as a set of tools and techniques, or improvement method.
- Six Sigma as an improvement approach or an improvement program.

- Six Sigma as an improvement philosophy.

In addition, the authors aver that the ultimate goal of scientific research is to advance human knowledge. Further, they state that "Since scientific research always follows a cumulative tradition, it is important to know what has already been studied before new knowledge is created". An interpretation of this from a Six Sigma perspective is seen to be: Six Sigma is a methodology which can be used to evaluate the current state of knowledge in order to improve upon it and enact practical change in the form of project implementation. As Six Sigma is firmly founded upon PDCA cycle which evolved from the scientific method, Six Sigma may therefore be regarded as a form of scientific methodology. Quality Intergrators Corporation (2011:**Online**), appear to be simpatico with this, by stating "Six Sigma is the application of the scientific method to business processes".

Blumberg, Cooper and Schindler (2011:57), were found to aver that research design expresses both the structure of the research problem, in addition to the plan of investigation used to obtain empirical evidence on relations of the problem.

These authors give the essentials of research design as being:

- The design is an activity and time based plan.
- It is always structured around the research question or research hypothesis.
- It guides the selection of sources and types of information.
- It is a framework for specifying the relationships among the study's variables.
- It outlines procedures for every research activity.

As Six Sigma's macro phases were found to be able to address all aspects required, as explained by Blumberg, Cooper and Schindler (2011:57), the research design outlined for the purpose of this dissertation therefore followed as:

- Define problem or 'selenium analysis improvement opportunity' phase.
- Measure process criteria phase.
- Analyse R-criteria phase.
- Improve and optimise 'selenium analysis process' phase.

- Control ‘selenium analysis process’.

### 4.3.2 Define problem or ‘Selenium Analysis Improvement’ opportunity phase

Process Management International (2009:3.5), maintain that effective process management begins and ends with process definition. The author states that “...planning changes without an initial process definition is merely shooting in the dark”. In addition, the author avers that it is impossible to maintain process improvements, unless the process is well defined and all the affected changes understood. This, therefore, necessitates an investigation to uncover different levels of details. The author argues that the objective of the ‘Define phase’ is to:

- Establish the purpose of the process.
- Determine how well it meets customer requirements.
- Define how the process is monitored.
- Determine what the process is saying about variation present in it.

Research design operation implications of this phase involved:

- The identification of process steps from a process map.
- Evaluation of a previously constructed Ishikawa diagram.
- Listed assignable causes of process problems.
- Pareto analysis to highlight the most critical problem.
- Detailed current state in order to streamline the process.
- Selection of the improvement opportunity to be addressed.

### 4.3.3 Measure ‘Process Criteria’ phase

Process Management International (2009:5.5), offer in the measure phase, process criteria (or measures) are collected and analysed to:

- Provide an assessment of the current performance of a process.
- Obtain information of changes to the process.
- Identify the signals of potential problems.

In order to resolve the research hypothesis as set out for this dissertation, it was determined that 'measures' required by research essentially bear direct relevance to the variables as indicated by the research hypothesis. Citing Imai (1986), Dahlgaard, Kristensen, and Gopal (2002:30), highlights that result measures known as R-criteria may be considered 'quality control points', while process measures known as P-criteria may be considered to be 'quality checkpoints'. These authors propose that a given 'process result' is measured by a quality control point, however the 'state of the process' may be measured by a 'quality checkpoint'. Therefore process characteristics which are expected to affect the results of a process are good potential quality checkpoints. The author, however, cautions that many states of a process exist, and therefore it is important to select the appropriate quality checkpoints. In the context of research required for this dissertation P-criteria or quality checkpoints which were measured, were practical process steps. The actual 'process results' obtained as a result of a process step, served as R-criteria or quality control points.

The author's elucidation of process measures highlights the importance of the construction of research design which enables both types of criteria to be measured. A specially selected set of quality tools therefore formed part of overall research design, taken from both the Lean and Six Sigma branches.

Guided by the research objective, during phase two, research was designed primarily on the Lean principles, as well as scientific method experimentation. Webb (2011:**Online**), was found to express the view that "The basic Lean principles are value, value stream, flow, pull, and perfection". The construction was designed to identify value in the analytical process, in order to obtain appropriate P-criteria for subsequently analysis in the next phase. Design also made provision for the collection of R-criteria through laboratory experimentation, as a means to construe the P-criteria. Operational implications entailed conducting a controlled study. The experiment was structured for specific data collection to determine variable effect of process steps on disparity observed in process results.

Therefore, experimental process runs were conducted in succession to each other, and in replica. The exercise is believed to be a demonstration of Carpi and Egger's (2003:**Online**), assertion that, "...according to the scientific research method known

as experimentation, the effect of the experimental manipulation can be observed on the dependent variable".

Due to the importance that all laboratory glassware and apparatus used during the course of a controlled study being chemically clean, the necessary arrangements were made to ensure that glassware used for sample processing was adequately acid washed prior to each trial run. All glassware and other laboratory utensils were also chemically cleaned with specialised Extran chemical laboratory detergent and rinsed with grade three, reverse osmosis deionised distilled water before being oven-dried.

From an archived population of all the previously processed biological samples, 10 non-probability purposively selected samples were identified to form the primary sample group. In addition to the 10 non-probability purposive samples, an in-house control sample was added to the sample group. All samples in that sample group were processed an amount of 13 times in replicate according to the existing analytical method process.

Furthermore, during 6 trial run repeats, an international 'certified reference material'(CRM) sample was included in order to determine the deviation from 'trueness' from the true accurate measurement. Analytical Reference Materials International (2011:**Online**), states "Certified Reference Materials (CRMs), with confidence intervals, should be used for establishing calibration curves. The quality of a CRM allows for estimating the accuracy of the analytical results obtained from the curve. The confidence intervals, of the CRM, and the quality of the curve fit will act as a guide for determining accuracy".

In addition to the in-house control sample and CRM, the experimental design included a blank sample, as well as a set of 5 standard calibration samples to establish a standard calibration curve for each analytical test process conducted. The blank and standard calibration samples were processed in precisely the same manner as the sample group with each analytical process run conducted. The experiment was designed so that data obtained from the use of calibration standards served the purpose of assessing precision of the process.

### 4.3.4 Analyse R-criteria phase

With an ultimate objective of 'process improvement', it is essential that the research design be structured to collect the appropriate R-criteria, in addition to the selection of the most fitting data analysis methods, to obtain accurate process performance information and identify causes of variation in the process. Foster (2007:454), offers that the Analyse phase of Six Sigma involves:

- Define your performance objectives.
- Identify independent variables.
- Analyse sources of variability.

In this phase research was designed to determine characteristics from process results, in order to define process performance, as a means to ultimately secure improvement. The design made process capability analysis possible. The importance of this is highlighted by the fact that without capability analysis, it would not be possible to determine the degree of variation in the process. Foster averred that capability analysis demonstrates whether certain quantitative parameters are meeting specification. The author explains that, should the quantitative parameters not meet specification, it may be assumed that too much variation exists within a process. As it is deemed that the study of variation is 'key' to answering the research hypothesis, research was adequately designed to collect and analyse the best data for this dissertation, in order to do so.

### 4.3.5 Improve and optimise 'Selenium Analysis Process' phase

Zhang, Hill and Gilbreathe (2009:**Online**), offer that in this phase, improvement solutions are developed to address root causes. Research design was constructed to analyse data and obtain further data for analysis in order to do this. Therefore, the research design was constructed to rely on both qualitative P-criteria, as well as quantitative R-criteria analysed by Six Sigma statistical tools, to direct the research to improvement solutions to address the root causes.

Gryna, Chua and DeFeo (2007:103), were found to share a view similar to that of Zhang, Hill and Gilbreathe (2009:**Online**), based on their assertion that during the

improvement phase, a remedy for root causes must be designed. The authors state, however, that it may require major re-planning of the process according to a structured approach. An argument was found, that "Lean Kaizen is a proven approach to continuously implement much-needed change and get rid of unnecessary waste" (American Society for Quality, 2011a:**Online**). Kaizen Analysis formed part of this research design, as it was used as a means to eliminate and reduce, process waste, by identifying different types of 'process wastes' known as 'muda', 'mura' and 'muri' in the current state process. After identification of wastes, the appropriate 'process standardisation' or 'heijunka' could be applied.

Gryna, Chua and DeFeo (2007:103), further contended that "Before a remedy is finally adopted, it must be proven effective". Therefore, research design needs to enable the collection and analysis of appropriate R-criteria, in order to prove that process improvement modifications are indeed effective. In this phase, research design entails further statistical analysis, based on the identified research parameters, as determined by the research hypothesis variables.

### 4.3.5 Control 'Selenium Analysis Process' phase

Research for the Six Sigma control phase was constructed around a quality tool known as 'failure modes effects analysis'. This well documented tool was believed to be the final step to 'an approach to the improvement of the selenium analysis process of the Western Cape Provincial Veterinary Laboratory'. The research design makes provision for activities to be designed and implemented in order to hold onto the gains accomplished by process improvement.

Zhang, Hill and Gilbreathe (2009:**Online**), state that "The DMAIC method emphasizes data analysis and fact-based decision making. The essence of the DMAIC method is to reduce variation in a process, to achieve high conformance to customer requirements". Thus, it is understood that the Six Sigma methodology provides an exceptional research structure and design, as used for the purpose of meeting the research objective for this dissertation.

## 4.4 DATA COLLECTION

Carpi and Egger (2003:**Online**), maintains that "Data (the plural form of the word datum) are scientific observations and measurements that, once analysed and interpreted, can be developed into evidence to address a question" Furthermore, the authors state that, as scientists build on the work of others and on their own work, it is important that their data collection methods are systematic and consistent. Detailed records must therefore be maintained so that others can see, and use, the data which is collected. Shuttleworth (2009:**Online**), is considered to support of Carpi and Egger (2003:**Online**), by the assertion that 'observation' and 'measurement' are the two fundamentals on which science is purely based. These fundamentals provide the basis for the data collection required by this dissertation.

Carpi and Egger (2003:**Online**), propose that the classical portrayal of the scientific method as a linear process, presents a number of challenges. Instead, the authors suggest that the successful utilisation of the scientific method is accomplished through the utilisation of multiple research methods in an empirical manner. In addition, Shuttleworth (2008b:**Online**), describes the scientific method as 'systematic and methodical', which ensures that researchers do not make mistakes or purposefully manipulate evidence. An explanation is offered by this author, that experiments done according to the scientific method are retested and repeated until a solid body of evidence is built up.

Two data collection research methods, namely, the experimentation model and comparison model, were identified as the most appropriate of the four possible data collection methods, as described by Carpi and Egger (2003:**Online**), for the research required for this dissertation. The following serves as an explanation as of how the two types of data required, namely P measures and R measures, were collected:

### 4.4.1 Experimentation data collection model

'Experimentation' is defined by Capri and Egger (2003:**Online**), as a "...research method in which one or more variables are consciously manipulated and the outcome of the effect of that manipulation on other variables is observed" Thus experimental

methods are commonly applied to quantify the magnitude of the response of a variable, or to determine causal relationships. In order to detect any sources of error in experimental designs, 'controls' are used. Controls provide a means of measuring the variability within a system.

Data collection for the scientific method is said to be the systematic recording of information, while data analysis is said to involve work to uncover trends and patterns in data sets. An explanation of those patterns and trends is provided through data interpretation. Different scientists can interpret the same data in different ways, as data interpretation is done based on the scientist's background knowledge and experience. By publishing their data and their techniques used to analyse and interpret data, scientists give the scientific community the opportunity to review the data and use in future research (Capri and Egger, 2003:**Online**).

Experimentation was used as a data collection method to obtain R-criteria during phase two (Measure process criteria phase). This was accomplished through following step by step experimental procedures, as outlined by standard operating procedures (SOPs) that were specifically drafted for the purpose of this research. The SOP attached as Annexure 2 was used to collect research data on the current state selenium process. Annexure 2 was specially designed for this research, based on an identical SOP currently being used in the Biochemistry laboratory at WCPVL, attached as Annexure 3. Quantitative result data is collected through experimentation.

Further data collection by the experimentation data collection method would be required by phase four (Improve and optimise selenium analysis process phase). Data collected for this phase would also be done according to a SOP. Annexure 4 is the SOP used to collect research data according from the modified process which is based on a European Standard (BSi 16159, 2010), which is attached as Annexure 5.

### 4.4.2 Comparison data collection model

Capri and Egger (2003:**Online**), state that the research method 'comparison' includes both prospective studies, that examine variables from the present forward,

as well as retrospective studies, that look at events that have already occurred. Data collected during the comparative component of research was collected through a combination of Lean Six Sigma tools, such as statistical tools to obtain quantitative result measures, as well as qualitative process measures obtained from a pareto analysis, ishikawa diagram, a process map, value stream maps, kaizen analysis and FMEA.

In the Define selenium analysis phase, 'process measure' data was collected for comparative evaluation through the use of pareto analysis, an ishikawa diagram and process map evaluation. In the Measure selenium analysis process phase which follows, data was collected through the use of the value stream mapping tool.

The Analyse R-criteria phase involved only the collection of 'result measures' through comparative analysis. Comparative data collection involved the analysis of raw process data collected through experimentation in the previous phase, to generate valuable statistical data by regression and correlation analysis. Additional statistical comparisons, in the form of hypothesis testing and process capability studies, generated further data for this dissertation.

The subsequent phase, known as Improve and optimise selenium analysis phase involved a shift of focus back to the collection of 'process measures', or P-criteria. Data was collected in this phase to direct research to improvement options through the use of Kaizen analysis. The final phase data collection involved collecting data through the use of FMEA quality tool. Data was obtained through the systematic evaluation of process modifications to ensure process improvement is maintained and adequately controlled.

Table 4.2 offers a graphic illustration of the types of data collected in each of the five Six Sigma phases.

**Table 4.2:** Data Collection Methods for P and R-criteria (**Source**: Own source)

| **Means of data collection:** | **Experimentation** | **Comparative** |
|---|---|---|
| Define Phase | | P-criteria. Pareto, Ishikawa, Process Map |
| Measure Phase | R-criteria: SOPs | P-criteria: Values Stream Maps |
| Analyse Phase | | R-criteria: Total Regression Analysis, Cochran's t-test hypothesis, ANOVA, Process Capability Studies |
| Improve Phase | R-criteria: SOPs | P-criteria: Kaizen Analysis |
| Control Phase | | P-criteria: FMEA |

### 4.4.3 Inductive and deductive approach

Research conducted according to the principles of the scientific method is considered to be inductive and deductive by nature. Dewey (2007:81), defines 'systematic inference' as "recognition of definite relations of interdependence between considerations previously unorganised and disconnected, this recognition being brought about by the discovery and insertion of new facts and properties". The author proposes that this type of systematic thinking entails 'double motion', including both scientific induction and scientific deduction. Furthermore, the author describes the motion towards the hypothesis as 'scientific induction', sequentially followed by a motion away from the hypothesis, returning to facts and a conclusion as 'scientific deduction'.

A definition for 'scientific induction' is provided by Dewey (2007:86), as "all the processes by which the observing and amassing of data are regulated with a view to facilitating the formation of explanatory concepts and theories". This author argues that these processes are all directed to selecting the precise, weighted and significant facts in order to support a hypothesis. According to Dewey (2007:86), important characteristics of these 'selective determination' processes are:

- The elimination of analysis processes which are likely to be irrelevant or misleading.
- Emphasis of the important components of research by collection or comparison.
- The deliberate construction of data by experimental variation.

Furthermore, this author provides a definition for 'scientific deduction' as "Deduction is the elaboration into fullness and completeness of meaning" and additionally states "Deduced results form the basis of comparison for observed results" (Dewey, 2007:95).

Shuttleworth (2009:**Online**), is of the opinion that inductive reasoning, or induction is the process of relating findings to the 'real world'. The author explains that the visionary part of sciences lies in relating findings back to the 'real world'. The statement is made that "The process of induction and generalization allows scientists to make predictions about how they think that something should behave, and design an experiment in order to test it. This experiment does not always mean setting up rows of test tubes in the lab or designing surveys. It can also mean taking measurements and observing the natural world".

Blumberg, Cooper and Schindler (2011:21), elaborate on the concept of induction by stating "To induce something is to draw a conclusion from one or more particular facts or pieces of evidence. The conclusion explains the facts, and the facts support the conclusion". This quotation illustrates the essential nature of inductive reasoning, as an inductive conclusion is said, by Blumberg, Cooper and Schindler (2011:21) to be "...an inferential jump beyond the evidence presented". In this text the concession is, however, found that, with inductive reasoning a situation may present itself where the conclusion found may be different to what is was originally inferred, or even possibly none of the original inferred conclusions may prove to be valid.

When describing deduction, the authors offer "Deduction is a form of inference that purports to be conclusive". They state "...the conclusion must necessarily follow from the reasons given" It may thus be considered that an inductive argument is

therefore radically different from the deductive type, as it does not have the same strength of relationship between reasons and conclusions. With deduction, 'reasons' are said to lead to the conclusion, and therefore represent proof. Blumberg, Cooper and Schindler (2011:21), conclude their depiction of deduction by adding "For deduction to be correct, it must be both true and valid:

- Premises (reasons) given for the conclusion must agree with the real world (true)
- The conclusion must necessarily follow from the premises (valid)".

Shuttleworth (2008b:**Online**) offers an opinion that experimental studies, also known as true experimental design is employed as principle method to extract process data. It is understood that this author regards 'true experimental design' as the most accurate form of experimental research, as it endeavours to mathematically prove or disprove a hypothesis with statistical analysis. Capri and Egger (2003:**Online**), were found to aver that "Experimental methods are used to investigate the relationship(s) between two or more variables, when at least one of those variables can be intentionally controlled or manipulated". 'Comparative research' as a scientific research method, is described as a means to "...determine and quantify relationships between two or more variables by observing differing groups that either by choice or circumstance, are exposed to different treatments." On the foundation of the views of these two authors it may consequently be considered that the two components, namely experimental component and comparative component follow differing approaches. Inductive reasoning approach appears to be associated to the experimental component and deductive reasoning approach associated to the comparative component of research.

The inductive and deductive approach, as applied in this research, may be summarised by the explanation provided by Blumberg, Cooper and Schindler (2011:22), who express the view that induction and deduction are used in research reasoning in a sequential manner. These authors state that induction occurs when a fact occurs and the question "Why is this?" is asked. In an attempt to answer the question, a tentative hypothesis is advanced. The hypothesis is found to be plausible if it explains the event or condition or fact that prompted the question. The research

process then follows by testing whether the hypothesis is capable of explaining the fact by the process of deduction.

## 4.5 VALIDATION OF ANALYTICAL DATA

### 4.5.1 Data uncertainty

"Uncertainty is the quantitative estimation of error present in data; all measurements contain some uncertainty generated through systematic error and/or random error" (Carpi & Egger, 2003:**Online**). These authors are of the opinion that acknowledging the uncertainty of data is an important component of reporting the results of a scientific investigation. Thus, to assure the validity of scientific data, it is critical for the researcher to calculate and report the uncertainty surrounding the data. Furthermore Carpi and Egger (2003:**Online**), argue that "...uncertainty is inherent in scientific research", and thus they proffer that once the concept of uncertainty is understood, as it applies to science, the purpose of scientific data analysis can be fully utilised to identify and quantify error and variability toward uncovering the relationships, patterns and behaviours that occur.

Bell (2001:**Online**), was of the opinion that a 'measurement result' is only complete if it is accompanied with a statement of uncertainty in the measurement. This author explains that there are two parameters associated to an uncertainty statement, namely the width of the margin, known as the 'interval' and the 'confidence level', which states how certain the researcher is that the 'true value' is within that margin.

UKAS (2011:**Online**), highlight the importance of taking data uncertainty into consideration to ensure the validation of laboratory result data, by the statement that "...uncertainty is a quantitative indication of the quality of a result". According to this author, estimating uncertainty is important to determine how well a measurement result represents the value of the quantity being measured. This allows users of the measurement result to assess its reliability of the data. This can be done for the purposes of comparison of results from different sources or with reference values.

Clause 5.4.6.2 of the SANS 17025 (2005:14), requirement states "Testing laboratories shall have and shall apply procedures for estimating uncertainty of measurement. In certain cases the nature of the test method may preclude rigorous, metrologically and statistically valid, calculation of uncertainty measurement. In these cases the laboratory shall at least attempt to identify all components of uncertainty and make a reasonable estimation, and shall ensure that the form of reporting does not give a wrong impression of the uncertainty. Reasonable estimation shall be based on knowledge of the performance of the method and on the measurement scope, and shall make use of, for example, previous experience and validation data".

To satisfy this requirement, research undertook to examine two international guides to the measurement of uncertainty, namely UKAS M3003 (2007), "Guide to the measurement of uncertainty and confidence" and Eurachem/CITAC Guide CG 4 (2000), "Quantifying uncertainty in analytical measurement". Both cite IS0 (1993), "Guide to the expression of uncertainty in measurement" as a foundation, and were seen to provide similar steps for the determination uncertainty associated with laboratory data. Annexure 6, 7 and 8 have been extracted from these documents. The approaches proposed by the two authors is considered to be summarised into the following steps being reported by them, to measure data uncertainty:

- **Step 1**: Specify measurand. Identify generic method of measurement and the specific detailed measurement procedure.
- **Step 2**: Specify uncertainty components. All influential sources (inputs) affecting the measurand are identified and categorised as either standard uncertainty or random uncertainty components.
- **Step 3**: Calculate uncertainty for standard components (system variability) using appropriate probability distributions.
- **Step 4**: Calculate uncertainty for random components from random sources using repeated measurements.
- **Step 5**: Convert each uncertainty to standard deviation.
- **Step 6**: Combine all uncertainties.
- **Step 7**: Calculate expanded uncertainty of combined uncertainties using the coverage factor.

- **Step 8**: Report the result in accordance to requirements.

An alternative approach was to account for uncertainty through 'total regression analysis' as proposed by Fraser (2011:72). The author maintained that the use statistical tests allow users to compare estimates and uncertainties, and make conclusions about such comparisons. This author states "In analytical work a frequently recurring operation is the verification of performance by comparison of data. Some examples of comparisons in practice are:

- Performance of two instruments.
- Performance of two methods.
- Performance of a procedure in different periods.
- Performance of two analysts or laboratories.
- Results obtained for a reference or control sample with the "true", "target" or "assigned" value of this sample".

The author offers that some of the most convenient and common statistical tools to quantify comparisons of the uncertainty associated to laboratory data, are the F-test, the t-test, regression analysis, Q-test and Grubbs test. In analytical work, correlation analysis can be used for comparing methods, whereas regression analysis can be used to construct calibration graphs of those methods. In practice, however, comparison of methods is usually however also done by regression analysis. The determination of "total regression uncertainty" is a powerful and effective tool to measure total uncertainty associated with result data obtained, and addresses all uncertainty aspects of an analytical method (Fraser, 2011:138).

Fraser (2011:Personal Email), however, highlights that effectiveness of "total regression uncertainty", as a measure of the total uncertainty of an analytical process, is dependent on specific requirements. The author cautions "...make sure that you take a large number of measurements of this parameter over time and then it will be more representative". This author's approach to uncertainty is believed to cover all aspects of uncertainty, and to address all the steps as explained by previous authors.

Ndlovu (2005:**Online**), was found to use regression analysis, and the determination of regression uncertainty in the research conducted by this author, in the field of

analytical chemistry. This author was found to statistically validate and determine uncertainty associated with research data. The work conducted by this author bears striking resemblance in terms of the determination of uncertainty, to the method proposed by Fraser (2011:6). Thus, uncertainty of data collected for this dissertation was statistically analysed and determined according to Fraser's (2011:6), 'total regression analysis'.

### 4.5.2 Data Error

Bell (2001:**Online**), offers the opinion that both data error and data uncertainty originate from the same sources, and thus it is important to distinguish between the two. The following definitions are provided by this author: "Error is the difference between the measured value and the true value of the thing being measured" and "Uncertainty is the quantification of doubt about the measurement result". The author additionally states that known sources of error are:

- **The measuring instrument:** instruments can suffer from errors including changes due to ageing, bias, wear, poor readability, noise (for electrical instruments) or other kinds of drift.
- **The item being measured:** stability of the item being measured may be influenced by external or environmental factors.
- **The measurement process:** due to factors associated to the actual measurement process obtaining measurements may prove challenging.
- **Imported uncertainties:** an example provided of this is calibration of instruments, which need to be incorporated into the uncertainty of measurements.
- **Operator skill:** the skill and judgement of an operator can also play a role in data error and data uncertainty.
- **Sampling issues:** as measurements made must be properly representative of the process being assessed, sample selection and condition can also be a source of data error and data uncertainty.
- **The environment:** temperature, humidity, air pressure and many other conditions can affect the measuring instrument or item being measured.

Eurochem (2000:**Online**), states "...error is regarded as having two components, namely, a random component, and a systematic component". The authors elaborate on concept of random error by explaining that it is derived from unpredictable variation, and although random error cannot be compensated for, it can usually be reduced by increasing the number of observations.

With regard to systematic error, Carpi and Egger (2003:**Online**), state that the use of control samples in scientific experiments assists a researcher to quantify error within an experiment and identify systematic error in order to either measure or eliminate it. The research design for this dissertation therefore made provision for control samples, included as essential and critical components of research design. Measurements taken of control samples served the purpose of providing the specification limits or the 'baseline' capable of detecting significant data error and invalid results. Carpi and Egger (2003:**Online**), however, highlighted that "Careful methodology can reduce uncertainty by correcting for systematic error and minimising random error. However, uncertainty can never be reduced to zero".

Fraser (2011:34), contended that random errors are "the errors that affect the precision of measurement. This type of error causes data to be scattered, more or less, symmetrically around the mean value" while systematic errors are, "the errors that affect the accuracy of a result". This type of errors causes the mean of a data set to differ from the accepted value". The author refers to random errors as 'indeterminate errors', and explains that the cause of this type of error is unknown and cannot be avoided. Systematic errors are referred to as 'determinate errors' and therefore can be determined, and should be avoided and corrected. Furthermore, the author explains that the determination of 'bias' in an analytical method as well 'standard error' provides a means to account for error in laboratory data when being statistically analysed. The data collected for this dissertation was therefore analysed, taking these two forms of data error into account when establishing confidence intervals for the data (Fraser, 2011:39).

### 4.5.3 Confidence in Data

Carpi and Egger (2003:**Online**), express the view as a result of error, scientific measurements are not reported as single values, but rather as ranges or averages with estimates of the error surrounding the value after repeated measurement of the value. The authors state that the standard deviation of a range of measurements can be used to compute a confidence interval around the value, and thereby provide an estimate of the probability that a similar result will be found if the study is repeated. These authors further aver that "Confidence statements do not, as some people believe, provide a measure of how "correct" a measurement is. Instead, a confidence statement describes the probability that a measurement range will overlap the mean value of a measurement when a study is repeated". These authors add that incorrectly reporting significant figures can introduce substantial error into a data set.

Gryna, Chua, and DeFeo (2007:582), define a confidence interval as "...a range of values that include (with a preassigned probability called a confidence level) the true value of a population parameter". Confidence limits are thus explained to be the upper boundary and the lower boundary of the confidence interval, and the confidence level is the probability that an assertion about the value of a population parameter is correct. These authors additionally state that confidence levels of 90, 95 or 99% are usually used in practice. They caution that confidence limits should not be confused with other limits, e.g., statistical tolerance limits, control limits or specification limits (Gryna, Chua, & DeFeo, 2007:582).

Siddharth (2009:**Online**), was found to assert that an inverse relationship exists between confidence interval width and certainty associated with a statistical inference made on a particular population. The author explains this by elaborating that the confidence interval relates to the reliability of the sample mean, as compared to the population mean, and provides the following example to illustrate this phenomenon: "Suppose the survey shows that 34% of the people vote for Candidate A. The confidence that these results are accurate for the whole group can never be 100%; for this, the survey would need to be taken for the entire group. Therefore if you are looking at say a 95% confidence interval in the results, it would mean that

the final result would be 30-38%. If you want a higher confidence interval, say 99%, then the uncertainty in the result would increase; say to 28-40%".

It appears that parallels may be drawn between the view of Siddharth (2009:**Online**), and that of Becker (1999:**Online**), who asserts that standard error becomes smaller as size of sample increases, by stating "As we increase our sample size, the standard error - and hence the confidence interval becomes smaller". Becker (1999:**Online**), maintains that statistics would be unnecessary if researchers were to gather information from an entire population However, error is involved whenever an experiment is run, or people are sampled for a survey. This author contended "Confidence intervals give us an estimate of the amount of error involved in our data. They tell us about the precision of statistical estimates (e.g., means, standard deviations, correlations) we have computed. Confidence intervals are related to the concept of power. The larger the confidence interval the less power a study has to detect differences between treatment conditions in experiments or between groups of respondents in survey research".

Fraser (2011:56) stated that "In most situations in analytical chemistry, the true value of the mean cannot be determined, because a huge number of measurements (approaching infinity) would be required. With statistics, we can establish an interval surrounding an experimentally determined mean within which the population mean is expressed to lie with a certain degree of probability. This interval is known as the confidence interval and the boundaries are called confidence limits". The method proposed by Fraser (2011:60), was used to determine the confidence interval and confidence limits for the data collected by this research dissertation.

## 4.6 CONCLUSION

Pragmatic and functional benefit is attained only from research that has been adequately constructed and designed, with the focus consistently maintained on the desired research objectives. For this research project, a suitable research design based on scientific methodology, and focussed at resolving the stated research hypothesis was constructed, following the extrapolation of critical factors pertaining

to the survey environment. The evaluation of the requirements of the specific survey environment, and the identification of Lean Six Sigma as a scientific research methodology, were simultaneously able to satisfy the requirements of research, as well as lead to the development of step by step standard operating procedures followed, in order to collect research data. As validation of data was identified in the survey environment as an essential and critical element of good research, this concern was addressed by the research design and data collection methods developed for this research.

Thus research design and methodology, as explained in this chapter, makes suitable provision for appropriate and adequate data collection for this research project, and further provides the framework by which the data will be interpreted and analysed in the next chapter.

# CHAPTER FIVE

# DATA ANALYSIS AND INTERPRETATION

## 5.1 INTRODUCTION

The chapter serves as presentation, and a record, of the exercise whereby raw data collected during the research study, was converted into utilitarian practical findings. Carpi and Egger (2003), define data collection "the systematic recording of information". These authors are of the opinion that 'data' is merely scientific observations and measurements, which, only once analysed and interpreted, can be developed into evidence to address a research question or hypothesis. Furthermore, it is only through the analysis of the data collected by a research study, that the "best course of action" to be taken, may be determined.

## 5.2 LEAN SIX SIGMA APPROACH TO DATA ANALYSIS

Data analysis was conducted in accordance to the structured approach proposed by Lean Six Sigma. Byrne, Lubowe and Blitz (2008:**Online**), offer that Lean Six Sigma builds on the knowledge, methods and tools derived from decades of operational improvement research and implementation, as seen in Figure 5.1.

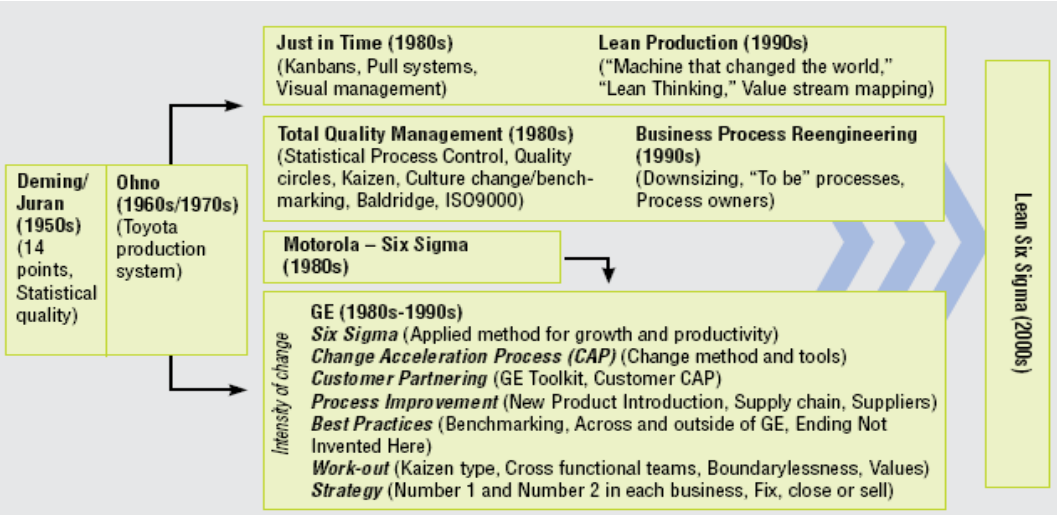


**Figure 5.1** : Evolution of Lean Six Sigma (**Source**: Byrne, Ludowe & Blitz, 2008:**Online**)

The improvement process known as Lean Six Sigma, encourages the consideration of the whole, including the inter-dependencies within it, to optimise any system over time. The methodology is, however, not specifically designed with the sole purpose of analysing data. It is rather considered to be a structured approach to learning about a specific process. This can however only be accomplished through the analysis data obtained from a process, in order to secure quality improvement on it.

Byrne, Lubowe and Blitz (2008:**Online**), argue that the core tenet of Lean Six Sigma is "...analysis based on fact". In addition, the authors proffer that the Lean Six Sigma approach to data analysis draws on the philosophies, principles and tools of both the Six Sigma and Lean methodologies as seen in Figure 5.2. The opinion is offered that the consequence of this amalgamation results in an approach to data analysis which is efficient, in addition to being effective, and promotes growth as opposed to simply cost cutting. The authors continue that this approach enables the user to refine existing processes, reduce costs, improve performance, provide better customer value and ultimately secure culture of quality innovation, and not only quality improvement.

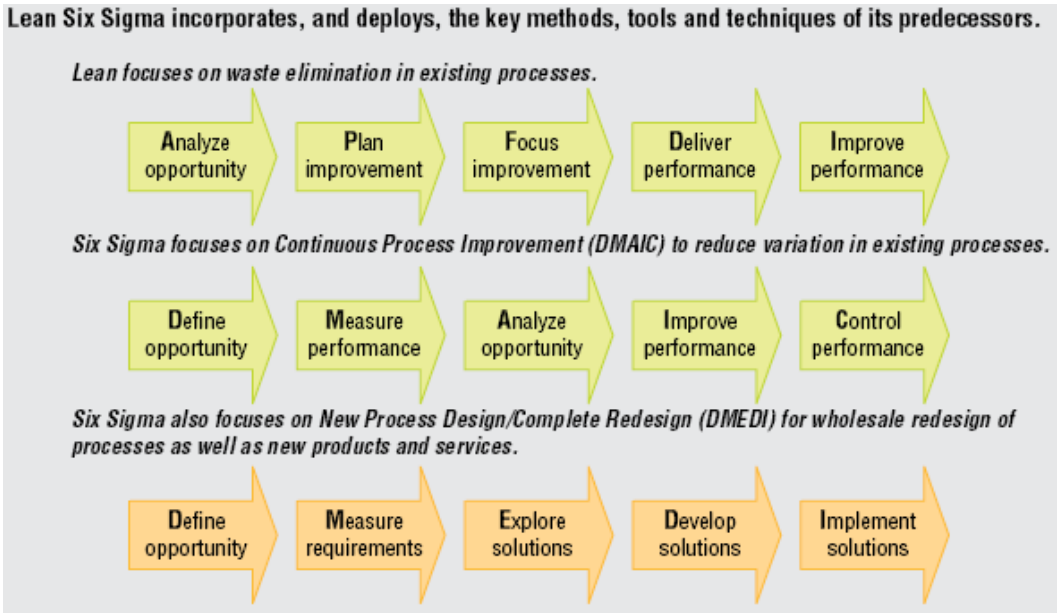


**Figure 5.2** Comparison of data requirements for Lean and Six Sigma (**Source**: Byrne, Lubowe &Blitz, 2008:**Online**)

Gryna, Chua and DeFeo (2007:67), provide a general definition for Six Sigma as "...a collection of managerial and statistical concepts and techniques that focus on

reducing variation in processes and preventing deficiencies". They state that the key focus is the relationship between input variables and the output of a process, expressed as $Y = f(X_1.....X_n)$. The definition for Lean provided by Gryna, Chua and DeFeo (2007:388), is: the process of defining systems to reduce costs by eliminating waste. It may therefore be construed that the analysis of data obtained from process for the objective of process improvement, may be successfully accomplished through Lean Six Sigma methodology. The Lean Six Sigma approach specifies the type of data required for analysis, promotes the focus on process optimization through streamline and analysis of variation, and ultimately advocates continuous cycles of process improvement.

Thus, in addition to process streamline, 'understanding variation' was therefore deemed one of the critical focal points of data analysis for improvement, according to the Lean Six Sigma approach. For this reason, it was necessary to chart a structured course towards learning about the variation in the process subject of this dissertation. Annexure 9A and Annexure 9B are provided as an illustration of the Lean Six Sigma process map used for the purpose of understanding variation in this dissertation. The importance of using data analysis to understand variation is emphasized by Process Management International (2009:1.4), who state the opinion that understanding variation allows decisions to be made, and "being on target with minimum variation" becomes the key driver for improvement.

Accordingly, the approach to data analysis is discussed in the sequence as commonly followed by the Lean Six Process Map. The macro-phases of this process map are:

- Define.
- Measure.
- Analyse.
- Improve/Optimise.
- Control.

## 5.3 DEFINE PROBLEM OR SELENIUM ANALYSIS IMPROVEMENT OPPORTUNITY PHASE

The Define phase of a Lean Six Sigma project requires that a clear definition of the problem, or 'improvement opportunity' be outlined. In alignment with the customer requirement of accurate, precise and reliable quality results, the selenium analysis process was selected as the subject for improvement. The investigation of recorded evidence of process failures, which had occurred over a period of twenty four months from March 2009 until March 2011, provided raw data (process measures), for root cause analysis. Causes of each process failure were listed, with the number of occurrences associated with each cause, as well as the calculated cumulative percentage, as seen in Table 5.1.

**Table 5.1** Table of assignable causes of quality problems in selenium analysis process (**Source:** Own source)

| Cause Number | Assignable Causes | Number of Occurrences | Cumulative Percentage Cut-off: 80% |
|---|---|---|---|
| 1 | Incomplete sample digestion | 23 | 43.4% |
| 2 | Equipment failure | 14 | 69.8% |
| 3 | Random power failure | 8 | 84.9% |
| 4 | Unforeseen time conflict | 4 | 92.5% |
| 5 | Operator error | 2 | 96.2% |
| 6 | Defective glassware | 1 | 98.1% |
| 7 | Software error | 1 | 100.0% |

The effects of the root causes of process failures can be seen in Table 5.2

**Table 5.2** Effects of problems in selenium analysis process (**Source:** Own source)

| Cause Number | Assignable Causes | Effect of process failure |
|---|---|---|
| 1 | Incomplete sample digestion | Process time varies from 15 to 18hrs |
| 2 | Equipment failure | Process delayed. Severity determines rework |
| 3 | Random power failure | Process delayed, rework |
| 4 | Unforeseen time conflict | Process delayed, rework |
| 5 | Operator error | Results invalidated. Rework |
| 6 | Defective glassware | Rework, only on samples affected |
| 7 | Software error | Rework |

The quality tool, known as a Pareto Chart, was used to highlight and prioritise problem areas in the current state selenium analysis process. This tool assigns a ranking and prioritisation of each cause of process failure. The tool drew attention to the most significant underlying source of the quality problems experienced in the process, as being associated with one specific process step.

Pareto, also known as the 80/20 rule, is a simple technique for prioritising possible changes. It is based on the Pareto principle which states that 20% of the causes, generate 80% of the results. Interpretation of the Pareto chart revealed that the three most critical sources of process failure were associated with the sample digestion process within the selenium analysis process.

A graphic depiction of findings is illustrated as shown in Figure 5.3.

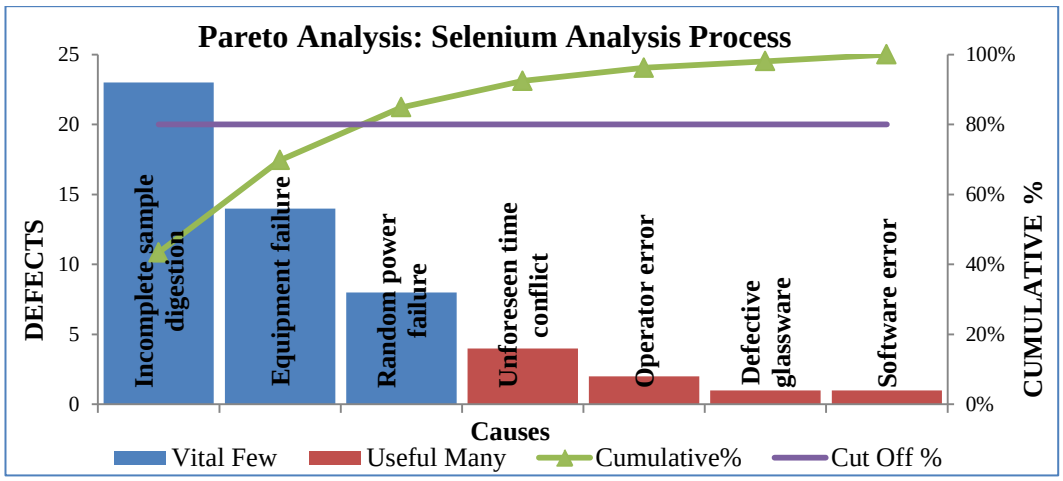


**Figure 5.3** Pareto Chart: Selenium Analysis Process (**Source**: Own source)

Gryna, Chua and DeFeo (2007:71), maintain that the Pareto principle is a data analysis tool, and may be considered an example of 'data mining'. These authors explain 'data mining' to be the process whereby data is analysed to extract information which is not offered by the raw data alone.

The results of the Pareto analysis, in addition to the results of Ishikawa analysis which was conducted, as discussed in Chapter Two, provided research with the information necessary for the Lean Six Sigma define phase. Further evaluation of

data resulted in the classification of the problem, according to decisive factors, as proposed by Gryna, Chua and DeFeo (2007:71), as being:

- **Chronic:** If the root cause is not addressed, quality problems would continuously impact on result quality of the selenium analysis process.
- **Feasible solution possible:** Plausible process modification was possible.
- **Significant impact:** Disparity in result quality had extended effects on service rendered by WC PVL. Both internal and external customers require good quality results from the Biochemistry section.
- **Measurable results:** Quantitative results process results are easily measurable and thus process data could be easily analysed.
- **Learning Experience:** Data collection and analysis serves as a learning process about the analytical process being studied.

## 5.4 MEASURE PROCESS CRITERIA PHASE

The Measure macro-phase specifies that the collected data must be analysed to measure performance and determine defect levels. The existing, or current state selenium analysis process was thus the subject for initial data collection. It was necessary to define and measure the variation found in it in order to improve on the process.

Lean Six Sigma draws a clear distinction between the two different types of measurements indices, namely process measures (P-criteria) and result measures (R-criteria). These distinctions were therefore made when analysing data collected for this dissertation. Data on both types of measure were collected for analysis.

### 5.4.1 Analysis of process measures (P-criteria)

Process Management International (2009:5.4), offer that process measures, are measures for data analysis that are considered an upstream point in the process, which influences the result measures, i.e. a change in the process measure will cause results to vary.

The tool used in the Define/Measure phase was 'Value Stream Mapping'. American Society for Quality (2011c:**Online**), state that a value stream map (VSM) is designed to provide an overview of an entire process. In addition, a VSM is used analyse the different processes within a process, which are required to deliver the service to the customer. The author explains that value stream mapping enables data analysis of key processes from graphical perspective, represented in one document, and states that it "Provides a road map for improvement by identifying waste and non-value added activities".

The process of mapping started with the identification of the 'value stream' for a specific process. This was followed with the draft of a current-state map, which provides the current conditions and states the activities involved during the current state process. The value map of the current state selenium process is seen in Figure 5.4

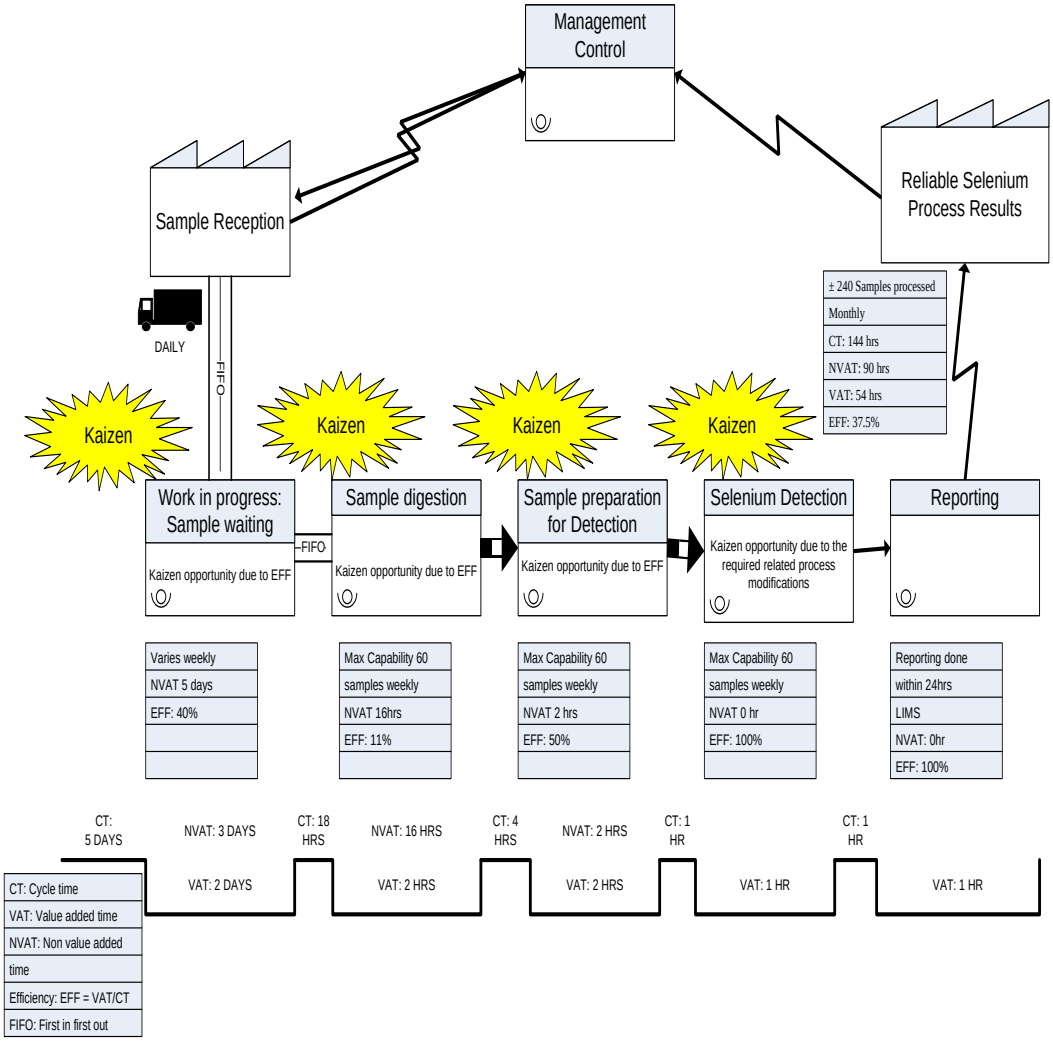


**Figure 5.4** Value Stream Map: Current State (**Source:** Own Source)

After the draft of the current state value map, a future state map is drafted, showing opportunities for improvement identified in the current-state map, to achieve a higher level of performance in future. The subsequent action to be taken once VSMs have been drafted, is the development of an implementation plan. American Society for Quality (2011c:**Online**), states that an implementation plan drives actions and tasks to move from the current state to the future state. Furthermore, the author asserts that the examination of the data, as illustrated in the VSMs, highlight and expose the sources of waste, and provides a blueprint for the lean implementation plan.

Analysis of process measures in the VSM provides research with relevant information about the process in order to improve upon it. The results of the analysis of P-criteria of the selenium analysis process are listed in Table 5.3:

**Table 5.3** Results of P-criteria analysis (**Source**: Own source)

| **Process Measure** | **Description** | **Finding** |
|---|---|---|
| Overall Process Efficiency (EFF) | EFF = VAT/CT | 37.5% |
| Total Value Added Time (VAT) | Total critical time required | 54 hrs |
| Overall Process Cycle Time (CT) | Average process cycle time | 144 hrs |
| Total Non-Value Added Time (NVAT) | NVAT = CT - VAT | 90 hrs |
| Kaizen Opportunities | Improvement opportunities | Sample waiting time, Sample digestion, Sample preparation and Selenium detection |

A future state VSM was drafted, whereby process modifications, earmarked as process improvement opportunities, were documented. The future state VSM is attached as Annexure 10. Comparative analysis revealed of both VSMs revealed that the process could be optimised from 37.5% efficiency to 90% efficiency.

### 5.4.2 Collection of result measures (R-criteria)

Process Management International (2009:5.4), argue that a result measure is data collected of overall process performance. R-criteria closely tracks how well customer requirements are being met. Specific ‘process result data’ was identified as

the R-criteria necessary for this dissertation, as these could be analysed to determine actual accuracy and precision of the process. A controlled study experiment was therefore designed and conducted, in order to obtain quantitative result measures or 'process results'. R-criteria are collected in this phase, for subsequent analysis in the proceeding phases. The objective of collecting R-criteria was to analyse the current state of the process and address the kaizen opportunities, as identified through the analysis of P-criteria. The raw data R-criteria collected for this dissertation may be seen in Annexure 11A to 11M.

## 5.5 ANALYSE PROCESS R CRITERIA PHASE

Primary tools used to analyse data in the Analyse phase of Lean Six Sigma process map are inherently Six Sigma tools; namely the statistical tools known as Statistical Process Control (SPC), including analysis of variation (ANOVA) and confidence intervals, and regression analysis. Process Management International (2009:7.1), were found to refer to this phase as "Listening to the voice of the process".

R-criteria data collected through controlled experiments, was statistically analysed according to the predetermined research design as described in Chapter Four. The order in which raw data was analysed and interpreted is provided is as follows:

- Total regression uncertainty analysis.
- CRM analysis.
- Precision, Analytical Bias and Horrat analysis.
- Analysis of individual standard curves of process runs.
- Systematic error analysis.
- Process capability analysis.

A comprehensive list of all the calculations done during data analysis is provided in Annexure 12. An explanation is offered of how the analysis was done, and which statistical tools were used to accomplish this, as follows:

### 5.5.1 Total regression uncertainty analysis

'Quantitative method characteristics' of the standard calibration curve of the current state fluorimetry selenium analysis process were identified through the analysis of raw data R- criteria. A description is provided for the reader, of each of the quantitative method characteristics used during the analysis of raw data, and may be seen in Annexure 13. This method of total regression uncertainty analysis is based on a combination of explanations which are provided by Levine, Ramsey and Smith (2000), Stone & Ellis (2011), and Fraser (2011).

The results of this analysis are as seen in Table 5.4:

**Table 5.4:** Method characteristics based on Total Regression Analysis (**Source**: Own source)

| **Calibration curve standard:** | |
|---|---|
| Number of standards | 5 |
| Number of replicates | 13 |
| Standard spread | 10ppb to 500ppb |
| Matrix of blank | Nitric Acid, Perchloric Acid |
| **Linearity of calibration curve:** | |
| **Linearity Correlation**: Correlation coefficient | 0.999978 |
| **Linearity Correlation**: Coefficient of determination | 0.999956 |
| **Significant Linearity:** $t_{stat}$ of slope | 260.5602 |
| **Significant Linearity:** $t_{crit}$ | 3.18 |
| **Significant Linearity:** $t_{stat} \rightarrow t_{crit}$ | Since $t_{stat} \rightarrow t_{crit,}$ Significant linearity exists. |
| **Significant Linearity:** $f_{calc}$ ANOVA | 67891.59 |
| **Significant Linearity:** $f_{crit}$ | 5.416 |
| **Significant Linearity:** $f_{stat} \rightarrow f_{crit}$ | Since $f_{calc} \rightarrow f_{crit,}$ Significant linearity exists. |
| **Significant Linearity:** Regression SS > Residual SS | Regression SS = 159473<br>Residual SS = 7.046805<br>Since Regression SS > Residual SS, significant |

| | |
|---|---|
| | linearity exists. |
| **Significant Linearity:** Regression MS > Residual MS | Regression MS = 159473<br>Residual MS = 2.348935<br>Since Regression MS > Residual MS, significant linearity exists. |
| **Significant Linearity:** Comment on significance of linearity | A strong linear positive relationship between x and y was found during regression and correlation analysis. |
| **Significant Linearity: %** Variation in detection of sample | 99.9956% |
| **Regression Parameters:** | |
| Slope | 5.6741 |
| Intercept | 0.362516 |
| Regression line equation | $\boldsymbol{Y = 5{,}6741\ X + 0.362516}$ |
| **Calibration uncertainties:** | |
| **Standard error of the regression:** Significance of standard error of regression | $S_{y/x}$ = 1.532624 |
| **Significance of standard error of the regression:** Comment on f-test result with CRM | f-test conducted to determine if systematic error = variance of CRM. (Calculation annexure)<br>$f_{calc} \rangle f_{crit}$ , thus rejected null hypothesis.<br>Therefore residuals were dispersed more widely than can be accounted for by random error. Systematic error is present in process. |
| **Uncertainty of slope** $S_b$ | 0.021777 |
| **Uncertainty of intercept** $S_a$ | 0.97762 |
| **Ratios of slope and intercept uncertainties:** $S_a$ and $S_b < S_{y/x}$ | $S_a$ and $S_b$ = 0.99939, thus $S_a$ and $S_b < S_{y/x.}$ This is evidence of good general precision |
| **Ratios of slope and intercept uncertainties:** $S_a/S_b$ | Ratio: 44.89<br>More standards are needed at the lower end of the standard calibration curve |
| **Ratios of slope and intercept uncertainties:** $S_b<S_a$ | $S_b<S_a$ thus working range is sufficient |
| **Confidence limits at 95%:** 95% CL of b: $b \pm tS_b$ | 5.6741 ± 0.0693 |
| **Confidence limits at 95%:** 95% CL of a: $a \pm tS_a$ | 0.3625 ± 3.1088 |
| **Limit of detection (LOD):** | |
| LOD from regression statistics | |

| | |
|---|---|
| | $Y_{lod}$ = 4.96 (lowest instrument response) |
| Concentration representing LOD from regression statistics | $X_{lod}$ = 0.81ppb (lowest concentration) |
| **Limit of quantitation (LOQ):** | |
| LOQ from regression statistics | $Y_{loq}$ = 15.69 (lowest response with reasonable reliability) |
| Concentration representing the LOQ | $X_{loq}$ = 2.70ppb (lowest concentration with reasonable reliability) |
| **Sensitivity:** | |
| Calibration sensitivity | $b = 5.6741 \neq 0$<br>The method can thus be said to be calibration sensitive to selenium |
| Analytical sensitivity | 5.6741 abs units/ppb |
| Inverse analytical sensitivity | 0.18ppb/abs units |

### 5.5.2 CRM analysis

The accuracy and precision of CRM measurements were also analysed in respect of average linearity and characteristics established for total regression analysis of the average process standard calibration curve.

The results of CRM analysis can be seen in Table 5.5

**Table 5.5:** Results of CRM Analysis (**Source:** Own source)

| | |
|---|---|
| **Mean measurement** | 0.5235ppm |
| Evidence from reputable CRM that method is selective / specific for selenium. | NCS ZC 71001: Beef liver Certified Reference Material. NCS ZC 71001 is certified at 0.56 ± 0.07 (ug/g) or ppm. Current state selenium method is selective and specific for selenium in CRM. |
| T test to determine significant difference between the mean and true value | $t_{calc}$ is less than $t_{crit}$, Thus null hypothesis is accepted which states that the results obtained from the analytical process is not significantly statistically different to the true CRM value. |
| 95% CL and CI | 0.52 ± 0.09 (True value: 0.56 ± 0.07) |

| | |
|---|---|
| Precision | 16.02% |
| Bias | -6.5% |
| Horwitz function | 1.82% |

### 5.5.3 Precision, Bias and Horrat analysis

Fraser (2011:19), regards precision to be "...the closeness with which results of replicate analyses of a sample agree". The author contends that precision is usually expressed in terms of 'standard deviation' as a measure of scattering or dispersion around the mean value. However, the author argues that standard deviation is actually a measure of 'imprecision' as the larger the standard deviation value is, the worse the precision is.

The following formula was used to determine precision in the current state selenium analysis process, as given by this author: %RSD (Relative Standard Deviation) = $\left[\frac{SD}{\bar{x}}\right]$.100. Precision of this analytical method was calculated to be 16.02%.

Bias is the consistent deviation of analytical results from the 'true' value and is caused by systematic error in an analytical process. The bias present in an analytical method may be determined using the following formula as proposed by Fraser (2011:43),: % Bias $= \left[\frac{\bar{x} - \mu}{\mu}\right]100$.

Bias of the analytical process was found to be -6.5%. Thus 'trueness' of the analytical method is 93.5%. An interpretation of this result is that, systematic error is found to be present in the analytical process.

Thompson (2004), was found to assert that the horwitz function is widely used as a benchmark for the performance of analytical methods. The horwitz function is used to calculate the horrat ratio of an analytical method, as a means to establish the method's performance with regard to precision. It is generally accepted practice that a horrat value of 2 or less, indicates that the method is of adequate precision. The formula used is: HORRAT = $RSD_{obs}$ / $RSD_{calc}$, where $RSD_{obs}$ refers to %RSD and $RSD_{calc}$ is represented by $\pm 2^{(1-0.5\log \mathbf{C})}$ and **C** is the mean of analyte in percentage.

The horrat ratio in respect to the CRM was found to be 1.82. Thus, the analytical method is considered to maintain adequate precision. It was found, however, that although a number of authors, including Fraser (2011:283), purport that a horrat value of less than 2 may be considered acceptable, Weaver and Trucksess (2010:188), assert that a horrat value of › 1.3 indicates that an analytical chemistry method exhibits unusually high variance. In addition, the Association of Analytical Chemists (2011:7), recommend that horrat value of an analytical method should lie between 0.3 and 1.3%.

Further analysis of process data was performed by calculating the overall process RSD, in respect to measurement observed from the samples processed by the selenium analysis process. This analysis may be seen in Annexure 14. The $RSD_{obs}$ used for this purpose was obtained from the average RSD observed across all samples and the $RSD_{calc}$ was obtained from CRM. The overall process horrat ratio was found to be 2.09%.

### 5.5.4 Examination of individual process run standard calibration curves

Data collected from each individual process run was analysed with statistical tools. Average readings from each calibration standard, in each process run calibration curve were calculated. Scatter plots and histograms were used to assess the existence of linearity. This graphic representation may be seen in Annexure 15. Examination of the data obtained from each process run calibration curve revealed disparity in the amount of selenium detected by the process. It appeared, from combined assessment of the scatter plots and histograms, that a variable amount of selenium was uniformly lost during each different process run, due an unknown experimental variable.

From the analysis of data during total regression analysis, research had established that, on average, the calibration curve of the current state selenium analysis process is linear. This finding is supported by the examination of individual calibration curve data when plotted on scatter plots. Disparity in observations was, however, observed when the same data was plotted into histograms using an identical x and y axis for each calibration curve. Interpretation of the histograms appears to reveal

that a uniform loss of selenium took place across the range of all five standards, in each of the thirteen calibration curves. This interpretation is made due to disparity observed in measurements, when the same concentration of standards was found to produce differing detection values, on different process runs. All standard calibration curves however remained linear.

This interpretation is supported by further analysis conducted in the form of single factor ANOVA hypothesis testing. For each concentration of standard in the calibration curve (10ppb, 50ppb, 100ppb, 250ppb and 500ppb), a null hypothesis was set stating that there was no significant statistical difference between the concentrations of selenium measured in a particular standard concentration, between the different process runs performed. The results of the ANOVA analysis rejected the null hypothesis and found that there was significant evidence to conclude that the mean concentration in each of the five different standard concentrations analysed varied among the thirteen different process runs of the selenium analysis method. The results of the ANOVA testing may also be seen in Annexure 15.

### 5.5.5 Systematic error analysis

As a means to determine the accuracy of an analytical process, a Cochran variant of the t-test was conducted. This independent, one sample hypothesis t-test test determines whether the systematic error present in the analytical process can be considered to be statistically significant. This is done by evaluating whether the measurements obtained from the process are different to the specified value provided by the internationally certified supplier. An average CRM measurement was obtained from replicate processing of the CRM sample. The null hypothesis was tested, which states that the population mean of CRM measurements ($\bar{x}$), obtained from the process is equal to the specified value ($\mu_0$). The following statistic is used: $t = \frac{\bar{x}-\mu_0}{s/\sqrt{n}}$, where s is the sample standard deviation and n is the sample size. The degrees of freedom used on this test is n-1.

Null hypothesis $H_0$: $\mu_{process} = \mu_{true}$

Where: Process CRM measurement = True CRM measurement

Alternate hypothesis $H_1$: $\mu_{process} \neq \mu_{true}$

Where: Process CRM measurement ≠ True CRM measurement

$t_{crit}$ 2.57

$t_{calc}$ 1.06

DF 5

Decision Rule:

Accept $H_0$ if $t_{calc} < t_{crit}$

Reject $H_0$ if $t_{calc} > t_{crit}$

Since $t_{calc}$ is less than $t_{crit}$, the null hypothesis is accepted, which states that the results obtained from the analytical process is not significantly statistically different to the true CRM value.

Although the mean of the test results obtained of CRM measurements by the process was found not to be equal to that of the true value of the CRM, the current state process was however found to produce results which are not significantly statistically different from the CRM true value.

### 5.5.6 Process capability analysis

Statistical analysis to determine if the analytical test process is capable of performing within the tolerance interval as specified by the internationally certified supplier of the CRM, was conducted using a process capability index. Process capability of an analytical chemistry process is determined by the following:

$C_p = \frac{(\Delta TE + USL) - (LSL - \Delta TE)}{6s}$ and $C_{pk} = \min[\frac{\Delta TE + \bar{x} - LSL}{3s}, \frac{\Delta TE + USL - \bar{x}}{3s}]$, where $C_p$ is a reflection of actual process capability and $C_{pk}$ reflects the process mean proximity to either LSL or USL. The LSL and USL are given as lower and upper reference values of normal healthy bovine liver. The important factor of total analytical uncertainty surrounding the analytical measurements obtained from the process is given by ΔTE.

LSL 0.25ppm

USL 0.50ppm

ΔTE 0.14

Thus: $C_p = \frac{(0.14+0.50)-(0.25-0.14)}{6\times0.084} = \frac{0.53}{0.52} = 1.02$

and

$$C_{pk} = \min\left[\frac{0.14+0.52-0.25}{(3\times0.08)}, \frac{0.14+0.50-0.52}{(3\times0.08)}\right]$$

$$C_{pk} = \min[1.63, 0.48]$$

$$C_{pk} = 0.48$$

As $C_p$ was found to be 1.02, the process is considered just capable of meeting the specification limits. Gryna, Chua and DeFeo (2007:691), argue that, although a process with a $C_p$ index of 1.0 is in statistical control, a $C_p$ index of between 1.0 to 1.33 indicates that the process requires heavy process control and inspection. The authors express the view that, $C_p$ of a process should ideally be at least 1.33. It is known that in reality, a process average will not remain at the midpoint of the specification range, and $C_p$ is considered to be only an estimate of potential process capability. The interpretation of $C_p$ is that under perfectly ideal circumstances, the selenium analysis process is capable of producing reliable 'process result measurements' with 0.3% outside of specification limits.

$C_{pk}$ was used to determine the performance capability of the selenium analysis process. A $C_{pk}$ value of 0.48, as calculated for this process indicates that the process mean is currently closer to the LSL. On the premise of Gryna, Chua and DeFeo's (2007:703), explanation of the relationship between capability indices and defect levels, it may be said that the selenium analysis process performance delivers 6,68% 'out of specification limits' process result measurements, on average. The interpretation made of this is, for the selenium analysis process to be considered acceptable with a $C_{pk}$ of 1.0, efforts should be focussed at centring the mean of this process, or reducing the standard deviation of result measurements obtained from the process.

Control charting is an additional means to determine process capability in terms of Lean Six Sigma. As the focus of Lean Six Sigma is on the elimination of variation, the use of control charts provides a mechanism to assess variability, in order to determine if the performance of a process is in a state of statistical control. Statit Quality Control (2011:**Online**), maintain that "...moving range charts are used when it is impossible or impractical to collect more than one single data point for each subgroup". Sample data obtained from the current state selenium analysis process was therefore analysed using moving range control charts. The charts of samples processed by the current state selenium analysis process may be seen in Annexure 16.

Analysis of moving range charts displays variability among measurements based on the difference observed between one successive fluorimetric detection measurement to the next, of the same sample. Evaluation of all the moving range charts found that, the current state selenium process is out of statistical control. In the case of each sample, analysed data points or measurements, were found to exceed one or both of the control limits set. Thus, in terms of process variation, the current selenium analysis process does not meet specifications due to systematic error present in the process.

## 5.6 IMPROVE AND OPTIMISE SELENIUM ANALYSIS PROCESS PHASE

The interpretation of statistical analysis conducted in the analysis phase of Lean Six Sigma highlights the direction for process improvement for research. Gryna, Chua and DeFeo (2007:98), state that this phase of Lean Six Sigma:

- Evaluates alternative remedies for quality improvement.
- If necessary, designs formal experiments to optimise process performance.
- Designs a remedy.
- Proves the effectiveness of the remedy.
- Deals with resistance to change.
- Transfers the remedy to operations.

Foster (2007:456), contends the Improve, or Kaizen phase involves off-line experimentation whereby the factors identified as those affecting laboratory performance are analysed. Define phase of Lean Six Sigma specified value in the process and identified the essential value stream. Analysis of the kaizen opportunities, using the kaizen analysis tool, identified forms of muda, mura and muri in the process. The identification of these provided the direction for heijunka, or process standardisation. Thus, the Improve phase led to the redesign of the selenium analysis process.

Table 5.6 provides a summary of the Kaizen approach followed.

**Table 5.6:** Kaizen approach to improvement to selenium analysis process (**Source**: Own source)

| **Problem Area** | **Lean Focus:** | **Problem** | **Description of problem** | **Lean Solution** |
|---|---|---|---|---|
| Sample waiting time<br>Sample digestion, Sample preparation | Mura | Volatile incoming work | Laboratory capacity to process inherently volatile incoming workload. Process cannot be streamlined | Microwave digestion |
| Sample waiting time<br>Sample digestion, Sample preparation | Muri | Too much work-in-progess (WIP) | WIP results in non-value added effort to control, track and prioritise samples and rework.<br>. | Microwave digestion |
| Sample waiting time | Muda | Long and unnecessary lead times | Individual samples queue until similar samples arrive to constitute an efficient test run | Microwave digestion |
| Sample digestion, Sample preparation | Muri | Variable lead time | Overnight digestion time was variable from week to week with open heat-block digestion | Microwave digestion |
| Sample detection | Heijunka | Accurate, precise and reliable results | Microwave digestion | Hydride generator detection |

The selenium analysis process was thus redesigned by substituting existing process with thoroughly researched modified steps. The modification from open-heat block digestion to microwave digestion, and fluorimetric detection to hydride generator detection, is regarded to be capable of addressing all the required improvement areas. The assumption is made that the consequence of modified selenium analysis process will be reliable process results obtained from an improved and controlled process, with reduced and standardised lead time, and use of fewer human and material resources.

Analysis of statistical data on the existing process also highlighted quality short-falls in the current state selenium analysis process. A further assumption is made that, the process capability and performance of the modified selenium analysis process will be a quality improvement over the current process, due to the elimination of the problem sources that were addressed by Lean Six Sigma Kaizen. The root cause of the systematic error which produces variable process results, is assumed to as a result of the sample digestion procedure. The open heat-block digestion procedure involves overnight digestion and is influenced by environmental factors such as room temperature and humidity, and thus the time of completion varies within a marginal interval of three hours. Microwave digestion is unaffected by those environmental condition, and thus allows stricter time and temperature control. This redesigned selenium analysis process is therefore more streamlined and standardised, than the current state selenium analysis process.

Following the design of the modified process, a formerly established experiment is to be conducted to test the improvement. R-criteria data obtained from the experiment is to be comparatively analysed against data which was obtained from the current selenium analysis process to measure the extent of the improvement.

### 5.6.1 Process variance analysis

Statistical analysis is to be conducted to determine if the variance observed in the two analytical processes are statistically different from each other. An independent two sample t-test is used to assess and compare the variance around the means of the

two laboratory methods. Data is obtained through replicate measurements of the CRM sample, which is processed by both analytical methods. An initial requirement for this is the determination of whether variances of the two analytical processes are equal or not. It is therefore necessary to conduct an f-test prior to the t-test. Thereafter, the appropriate t- test is conducted, based on whether the outcome of the f-test indicated either equal variance sample groups or unequal variance sample groups. The following statistics are used for this purpose: f-test = $\frac{{s_1}^2}{{s_2}^2}$. For equal variance, equal sample sizes the following t-test statistic to test whether the means are different is used, t = $\frac{\bar{x}_1 - \bar{x}_2}{s_{x_1 x_2} \cdot \sqrt{\frac{2}{n}}}$

where $s_{x_1 x_2} = \sqrt{\frac{{s_{x_1}}^2 + {s_{x_2}}^2}{2}}$

If the outcome of the f test statistic indicates that the two processes possess unequal variance then t-test statistic follows as t = $\frac{\bar{x}_1 - \bar{x}_2}{s_{\bar{x}_1 - \bar{x}_2}}$

where $s_{\bar{x}_1 - \bar{x}_2} = \sqrt{\frac{{s_1}^2}{n_1} + \frac{{s_2}^2}{n_2}}$.

In these formulae n is the number of replicates, the number 1 refers to the existing process while the number 2 refers to the modified process. For significance testing, the distribution of the test statistic is approximated as being ordinary student's t distribution with degrees of freedom being DF = $\frac{({s_1}^2/n_1 + {s_2}^2/n_2)^2}{({s_1}^2/n_1)^2/(n_1 - 1) + ({s_2}^2/n_2)^2/(n_2 - 1)}$.

Null hypothesis $H_0$: $\mu_{current} = \mu_{modified}$

Where: Variance in result measurements obtained from current state selenium analysis process = Variance in result measurements obtained from modified selenium analysis process

Alternate hypothesis $H_1$: $\mu_{current} \neq \mu_{modified}$

Where: Variance in result measurements obtained from current state selenium analysis process ≠ Variance in result measurements obtained from modified selenium analysis process

Decision Rule:

Accept $H_0$ if $t_{calc} < t_U$ and if $t_{calc} > t_L$

Reject $H_0$ if $t_{calc} > t_U$ and if $t_{calc} < t_L$

### 5.6.2 Nonparametric difference in process mean analysis

Further statistical analysis to determine the extent of the quality improvement due to Lean Six Sigma process modification may be performed on the means of the two analytical processes. This analysis establishes the extent of the difference between the means (obtained from repeated measurements), of two analytical processes for the same analyte. Data is obtained through replicate readings of a sample population which are processed by both analytical methods.

The variable of interest is the difference between the values of the observations, rather than the values of the observations themselves. The following statistic is used for the repeated measures paired t-test: $t = \frac{\overline{D} - \mu_D}{s_D/\sqrt{n}}$,

where $\overline{D} = \frac{\sum_{i=1}^{n} D_i}{n}$, and $s_D = \sqrt{\frac{\sum_{i=1}^{n}(D_i - \overline{D})^2}{n-1}}$. This test statistic follows a t distribution with n-1 degrees of freedom.

Null hypothesis $H_0$ : $\mu_D = 0$

Alternate hypothesis $H_1$: $\mu_D \neq 0$

Where: $\mu_{Difference} = \mu_{current} - \mu_{modified}$

Decision Rule:

Accept $H_0$ if $t_{calc} < t_U$ and if $t_{calc} > t_L$

Reject $H_0$ if $t_{calc} > t_U$ and if $t_{calc} < t_L$

### 5.6.3 Optimised design of modified process

Foster (2007:456), contends that the Taguchi method is a standardised approach for determining the best combination of inputs to produce a product or service. The

Taguchi approach advocates that the design may be approached from four perspectives namely:

- Robust design.
- Tolerance Design.
- Concept Design.
- Parameter Design.

Research conducted for this dissertation relied on the design from the parameter design approach. Parameter design refers to the selection of control factors and the determination optimal levels for each of the factors. Parameters within the current state process were investigated, and modifications were made to the design to bring the current state process into control. Analysis of process capability and process performance data obtained from the modified process provides evidence of design optimisation.

## 5.7 CONTROL SELENIUM ANALYSIS PROCESS PHASE

Measurement and analysis that takes place in the Control phase of the Lean Six Sigma Process Map is done through the use of a feedback loop. Gryna, Chua and DeFeo (2007:106), describe the feedback loop as "...measurement of actual performance, comparison with standard performance, and action on the difference". The authors state that activities are designed and implemented in this phase to maintain gains of improvements secured.

According to Gryna, Chua and DeFeo (2007:106), the steps in this phase are:

- Design controls and document the improved process.
- Validate the measurement system.
- Determine the final process capability.
- Implement and monitor the process controls.

### 5.7.1 Analysis of control measures (FMEA)

FMEA Information Centre (2011:**Online**), offers the view that FMEA is a systematic, highly structured assessment, which generates a comprehensive review

to safeguard against system performance problems. The authors explain that FMEA can be described as a qualitative reasoning approach relying on the evaluation of component failure modes. The following three key questions are answered by the quality tool, known as the FMEA process:

- What could fail in each component of my service design?
- To what extent might it fail and what are the potential hazards produced by this failure?
- What steps should be implemented to prevent failures?

Examination of the modified process steps identified potential failure points focused on of the their potential effect on the results of selenium analysis process as listed in Table 5.7

**Table 5.7** Quality risk assessment of modified selenium analysis process (**Source:** Own source)

| **Risk assessment possible** | **Process Step** |
|---|---|
| Yes, FMEA | Registration of Samples in Biochemistry |
| Competency Records | Sample preparation by technician |
| Yes, FMEA | Microwave sample digestion |
| Yes, FMEA | Sample reduction and dilution |
| Yes, FMEA | Sample detection |
| Yes, FMEA | Review and issue results |

FMEA was selected as the quality tool for risk analysis, due to the ease of interpretation of results. This well documented tool which is commonly used to prioritized risks and monitor the effectiveness of risk control activities. The FMEA technique generated the qualitative descriptions of potential performance problems and their associated quantitative consequence estimates. FMEA analysis of the process steps may be seen in Annexure 17.

The following failure modes action steps seen in Table 5.8 were documented and recommended for implementation, following analysis of FMEA evaluation:

**Table 5.8:** FMEA Recommendations (**Source:** own source)

| **Failure Mode** | **Action Step Recommended** |
|---|---|
| Sample Registration failure | Internal Lab: 'Selenium analysis sample' control worksheet |
| Digestion failure | Failure Type 1: Ensure maintenance schedule upheld |
| | Failure Type 2: Previous selenium method as backup |
| Reduction phase failure | Ensure back-up apparatus available: water bath and thermometer |
| Incorrect measurement parameters (detection instrument) | Ensure adequate training provided to technicians. Training records and competency certificates serve as evidence |
| AA failure | Failure Type 1: Ensure maintenance schedule upheld |
| | Failure Type 2: Ensure spare part selenium lamp in stock |
| HG failure | Failure Type 1: Ensure maintenance schedule upheld |
| | Failure Type 2: Ensure spare part piping in stock |
| Reporting: Electronic system | None: Wait until system online |

### 5.7.2 Final process capability, implementation and management of improved process

The final steps of the Lean Six Sigma process map for the improvement of the selenium analysis process involves the analysis of process data collected in final process capability studies, followed by the implementation and management of the improved process. This data serves as validation records of process improvement. Once the improved process is set into operation, data is regularly and periodically collected to monitor, and evaluate that process gains are maintained.

The analysis of data which led to the development and implementation of control steps by the Lean Six Sigma approach ensures improved process improvement. The Lean Six Sigma process map is, however, found to advocate continuous cycles of improvement. Therefore, the data on the implementation of control steps should also be continuously periodically collected and assessed to maintain a focus on continuous improvement of the selenium analysis process.

## 5.8 CONCLUSION

This chapter tenders a Lean Six Sigma presentation of the analysis of data for an analytical chemistry process. The interpretations obtained through data analysis, are converted into utilitarian practical findings to resolve the research hypothesis set by this dissertation. The use of the combination of Lean and Six Sigma methodologies during the analysis of research data, highlighted process areas considered to be wasteful and inefficient due to variability. This enabled the process being researched, to be streamlined and optimised, ultimately to provide better value to the customer. Simultaneously the Lean Six Sigma process map identified variability in the process. Data analysis, as proposed by the methodology, provided a tool to understand and reduce variability which has an effect in quality of results.

The following and final chapter of the research dissertation will draw key findings from the interpretations generated through data analysis. Based on the key findings obtained from the interpretations of data analysis, conclusions are drawn and practical recommendations are made.

# CHAPTER 6

# CONCLUSION

## 6.1 INTRODUCTION

Reliable results represent the pinnacle assessment of the quality of an analytical chemistry process. Disparate process results therefore, naturally, pose a tremendous challenge in any chemistry laboratory. By definition, reliable results are said to be both accurate and precise (Pratt, 1983:130). In a credible chemistry laboratory, seeking accreditation, evidence of disparity in result quality may be construed to be evidence of ineffectual quality practices, and therefore command quality improvement. This chapter presents conclusions and offers recommendations based on the research conducted on a diagnostic service rendered by WC PVL, known as the selenium analysis process. All conclusions are resolutely based on the findings of data analysis conducted from data obtained from the process, in addition to a comprehensive literature study.

## 6.2 THE RESEARCH THUS FAR

The development of the research process, with the purpose of advancing scientific knowledge, permits the presentation of the following synopsis of the status of the research to its present position. The synopsis is provided in relation to the overall research conducted, and presented in preceding chapters which were:

- **Chapter 1:** This chapter provided research with raison d'être to conduct research. The research hypothesis, investigative questions and the research objective were presented in this chapter. Furthermore, the chapter examined the scientific method, and scientific research was deemed the most suitable type of research to accomplish the research objectives.
- **Chapter 2:** This chapter outlined the important research background and explored the motives behind research. The chapter included an abbreviated literature review on the trace element selenium. Furthermore, the chapter discussed background research experimentation, which was conducted to test the feasibility of the research variables identified. The results of background

research as explained in the chapter, directed research in a practical direction, to be able to use quality tools during research, in order to make a meaningful difference in the research environment.

- **Chapter 3:** This chapter involved a very comprehensive, but specialised literature review in the areas pertaining to process quality in laboratories. The literature review provided research with the necessary understanding and knowledge to be able to construct an appropriate research design to accomplish the research objective. It enabled research to identify the data requirements, as well as the data collection methods required. Further, it provided research with understanding and knowledge to be able to be able to analyse, interpret and draw conclusions from data.
- **Chapter 4:** In this chapter the specific research design and methodology used to conduct research was delineated and discussed in detail, with motivations as to why the research design was identified as the most appropriate for the type of research conducted. Lean Six Sigma was presented as methodology with the dual advantages of both research and improvement in the particular research environment. Data collection methods were detailed, and the parameters used to assure the validity of research data were also discussed.
- **Chapter 5:** A presentation of the systematic and logical analysis of research data was offered in this chapter. Data was analysed and interpreted according to the structure proposed by the Lean Six Sigma approach. Detailed descriptions, explanations and calculations were provided for inspection, in form of annexures which are referred to in the ambit of the chapter. The logical order provided by the Lean Six Sigma approach, permitted data analysis and interpretations to flow into rational conclusions presented in the following chapter.
- **Chapter 6:** In this concluding chapter, final analogies will be drawn from literature review and data analysis, which enable key research findings to be stated. On the foundation of the key research findings, conclusions and recommendations are made. The conclusions are to serve the simultaneous purpose of both, ‘secure a practical improvement recommendation for the research environment’ in addition to ‘resolve the hypothesis’.

## 6.3 ANALOGIES DRAWN FROM THE LITERATURE REVIEW

The importance of accurate selenium detection is emphasised by Campbell (1984:645), and Janz *et al* (2010:143), who are found to argue that the margin between deficient and toxic levels of selenium in healthy organisms, is very narrow. Thus, it is critical for an analytical laboratory conducting diagnostic testing to ensure that the results, rendered by selenium analysis, are accurate. Selenium analysis methods in general however, have traditionally posed challenges to laboratories who provide this diagnostic service. This is because, suitable methods can only be developed around the complex chemistry associated to this trace metalloid element (Tarin, 2006:36), (Campbell, 1984:647), (Kurkova, Skrypnik & Zalieckiene, 2008:40) and (Galgan and Frank, s.a.).

Furthermore, literature review highlights that sample digestion in an open system, leads to the loss of selenium in samples as selenium volatilises from a sample at temperatures exceeding 70$^{o}$C (Kurkova, Skrypnik &Zalieckiene, 2008:40). Additionally, sample digestion in a closed system using fluorometric method for selenium detection is not possible, due to selenium oxidation state, as well as interference from nitrate ions and analyte pH (Kurkova, Skrypnik & Zalieckiene, 2008:41), (Tarin, 2006:36) and (Campbell, 1984:646). Laboratory trials conducted at WC PVL support the views of these authors. The analogy is thus drawn that microwave digestion as a means to overcome challenges associated with open heat-block digestion, is only possible with hydride generation detection.

Further literature review conducted on the use of perchloric acid, directed attention to the view that this acid which commonly used during open heat-block digestion, is regarded to be severely hazardous to the operator and environment (Desert Research Institute, 2004:**Online**) and (The University of Alberta, Department of Environmental Health and Safety,2011:7). The analogy is drawn that the elimination of the use of perchloric acid from the sample digestion procedure, can be regarded as an improvement to the process.

Walker (1905:435), was of the opinion that analytical problems faced in the field of chemistry may be effectively and decisively addressed, when approached from

technical perspective by individuals "...trained in the spirit and methods of scientific research", while Moen &Norman, (2011:2) argued that scientific foundations and scientific research design form the elementary basis of the PDCA cycle. Webb (2008:**Online**), maintains that, in essence Lean Six Sigma is fact based, and Six Sigma is based on the scientific method as embodied in the five steps of a Six-Sigma project. As the DMAIC steps of Six Sigma were developed on the frame provided by the PDCA, the analogy is drawn that process improvement and a resolution to the research hypothesis may be secured through this methodology.

Byrne, Lubowe and Blitz (2008:**Online**), offered that the amalgamation of Lean and Six Sigma produces a dominant and innovative tool, which is capable of process improvement through the reduction of process variation, with concurrent process streamlining. Khalil, Khan and Mahmood, (2006:2) are of the opinion that the consequential effect of this amalgamation is an improvement, observed in both process efficiency and effectivity. Process Management International (2009:5.5), offer that there are two types of data measure collected for process improvement, namely R-criteria (result measures) and P-criteria (process measures). While Six Sigma offers a systematic approach to process improvement and advocates the use of statistical tools to accomplish process improvement (Pyzdek, 2000:140), the Lean methodology relies on different tools to streamline the process, such as value stream mapping an kaizen analysis. (Anvari, Ismail and Hojjati, 2011:1586). The analogy is drawn that, the Six Sigma tools may primarily be used to analyse R-criteria in the context of this research, and Lean tools may be primarily used to analyse P-criteria.

American Society for Quality (2011:**Online**), states that an implementation plan through value stream mapping drives actions and tasks, to move from the current state to the future state. This is done by identifying a value stream in a process. Furthermore, VSM tool allows the user to determine the efficiency of both current and future state processes. Additionally, Hubbard (2010:**Online**), maintained that Kaizen analysis allows the user to identify waste in a process, in the form of muda, muri and mura. Muda has traditionally been given much more prominence when compared to mura and muri. The object of Kaizen analysis is, however, to determine heijunka. Examination of the laboratory process reveals that muda, muri and mura share equal importance the research service process. Analogies drawn from this is

process standardisation, is therefore regarded as process improvement A further analogy drawn from literature review is that it may be assumed that process efficiency may be improved from 37.5% to 90%, through heijunka identified in Kaizen analysis.

FMEA Information Centre (2011:**Online**), offers the view that FMEA is a systematic, highly structured assessment, which generates a comprehensive review to safeguard against system performance problems. An analogy drawn from literature review is FMEA is able to assure process and quality features, which are designed into the modified selenium analysis process.

## 6.4 ANALOGIES DRAWN FROM THE DATA ANALYSIS

Results of data analysis for this research study had to address the following objectives set for this research study:

- Identify critical root causes affecting the quality of results in the selenium analysis process.
- Identify a value stream within the process.
- Minimize the risks posed by the current state selenium process.
- Optimise the selenium yield of the current state process.

### 6.4.1 Analogies drawn from R-criteria

Analogies drawn from the analysis R-criteria highlighted the following:

- Current state selenium analysis process result quality was variable.
- Current state process accuracy, and process precision could be improved.
- Overall current state process performance was poor.
- Systematic error was present in current state selenium analysis process.
- The current state process was experiencing a disparate loss in selenium yield from process run to process run.

### 6.4.2 Analogies drawn from P-criteria

Analogies drawn from the analysis of P-criteria highlighted the root causes for problems in the process as the following:

- Sample digestion was the root cause of quality problems associated to the selenium analysis process
- A value stream was identifiable in the process.
- Muda, or non-value adding activities were identified as a form of process waste, should be removed through modification.
- Muri, or volatile work-in-progress was identified as a form of process waste, should be removed through modification.
- Mura, or unstandardised working practices during the process was identified as a form of process waste, should be removed through modification.
- Heijunka, or process improvement is possible in the form of process modification
- The design of process control features assures the quality output, in the modified process design.

## 6.5 KEY RESEARCH FINDINGS

Khalil, Khan and Mahmood (2006:2), assert that Lean Six Sigma is "...a combination of certain tools and techniques to provide Six Sigma practitioners another philosophy to reduce process and production times while minimising the variation and reducing waste at the same time". Examination of the current state selenium analysis process with this quality tool yielded the following facts, which are stated to be the research key result findings:

- The Selenium analysis process is source of problematic quality of results.
- Investigations revealed that the open-block sample digestion procedure was a root cause of quality problems associated to the process.
- Modification in digestion process cannot be successfully implemented without modification in selenium detection, from fluorimetric selenium detection to hydride generation selenium detection.

- A value stream, of value added activities is identifiable in the current state process.
- Current state selenium analysis process efficiency is 37.5%.
- Current state selenium analysis process can be modified to be 90% efficient.
- Process result quality was found to be reasonably accurate, that is, accurate within confidence levels.
- Process result quality was found to be reasonably precise, that is, precise within a wide margin, however the chemistry method exhibits unusually high variance.
- Systematic error is present in the analytical method, and is believed to be the source of poor analytical accuracy and precision.
- Un-standardised process steps result in systematic error.
- The current state selenium process has a process capability index of 1.02, and is potentially capable.
- Process performance is unacceptable. This process requires heavy process control and inspection.
- Variation within the process of out of statistical control.
- Definite process variation appears to provide evidence of a loss in the selenium yield within current state selenium process, which was found to quantitatively vary from week to week.
- Process redesign offers a remedy in the form of a modified selenium analysis process, which is assumed to produce superior process results, in terms of accuracy and precision.
- Control features may be built into the modified process design.

## 6.6 RESEARCH CONCLUSIONS FROM KEY RESEARCH FINDINGS

In this section the key research findings are discussed and a conclusion is made to answer each research questions in the order that they were posed by this dissertation. The research questions are:

- Can a modified process design, focussed on digestion procedure be established with better control features, in order to overcome variation within the process?

- Will a modified digestion process result in reduction of associated biohazard and other risks, associated with the selenium analysis process?
- Will a modified digestion process result in optimising selenium yield?
- Will a modified process design ultimately translate into an improvement in quality, in terms of the reliability of results?

### 6.6.1 Process Variation

Citing Taguchi (1986), Park and Anthony (2008:5), state "...variation is the main enemy of quality". The objective of research conducted for this dissertation, involved the study of process variation and the effect of this variation on the process output, namely process results. The use of the Lean Six Sigma quality tool, in addition to literature study, suggests that the current state selenium analysis process modification is unquestionably possible. Key research findings conclude that process modifications may be assumed capable of an improvement in process efficiency from 37.5% to 90%. Process modifications include, the modification of the sample digestion procedure from open heat-block digestion to microwave digestion, in addition to the simultaneous modification of selenium detection from fluorimetry to hydride generation detection technique. These modifications will eliminate all forms of 'process waste' and standardise process steps. The result will significantly reduce variability in process steps and enable stricter control measures, thereby improve process result quality.

Efficiency of the current state process was calculated to be 37.5%, yet a stream of value added activities was identifiable in the current state process. Current state process results were found to be reasonably accurate and precise, yet the overall process performance of the process is poor.

With a process modification from open heat-block digestion to microwave sample digestion, it is possible to perform all process steps during normal laboratory operating hours. This is regarded to be an extremely valuable control feature, as it allows a process operator to be present throughout the duration of the procedure.

A key research finding was that systematic error is present in the analytical process. Open heat-block sample digestion is more susceptible to environmental factors, such as room temperature and humidity. Thus, overnight process time is variable, within a three hour margin, and this is found to be one of the sources of systematic error in the process. Microwave sample digestion in a closed system provides stricter control, through the complete digestion of samples, within a very strictly controlled time.

The key research finding was made that, variation in process results is out of statistical control. The importance of temperature control is emphasised by the loss of volatile selenium at temperature above 70$^{o}$C, when heated in an open vessel system (Kurkova, Skrypnik & Zalieckiene, 2008:40). Microwave sample digestion allows very strict temperature control, and is seen as a control feature to overcome variation.

Background research conducted within the biochemistry survey environment, however, revealed that process modification from open heat-block method of sample digestion is impossible without modification of selenium detection procedure, from fluorimetry to hydride generation as well. This is due to specific selenium chemistry requirements of this trace mineral, in addition to practical laboratory constraints. A further control feature, which is secured by process modification to hydride generation detection, is the elimination of complex DAN preparation during sample preparation, before detection. Additional chemical manipulation is assumed to progressively add to the amplitude of variation that is being allowed in the process. Hydride generation detection allows samples to be analysed without any additional chemical manipulation after the required selenium reduction.

A further advantage, which is seen as a control feature with hydride generation detection is that, samples may be stored in a 4$^{o}$C refrigerator. This allows for degree of controlled operator flexibility, that does not affect the accuracy and precision of result quality, should an unexpected laboratory emergency be presented.

In conclusion it is therefore stated that process standardisation, in terms of time and stricter temperature control, in a closed digestion system is regarded to be capable of

overcoming process variation. A modified process design, focussed on both sample digestion and sample detection, may be established for the selenium analysis process. The modified design is assumed to be capable of overcoming unacceptable systematic error process variation present in the process, as well as provide the process with better control features.

### 6.6.2 Risk Analysis

An evaluation of key research findings was done to determine if that a modification in selenium analysis digestion procedure results in a reduction of the risks associated with the current state analysis process.

Key research findings state that the current state selenium analysis process is potentially capable, but process performance is poor, based on process capability studies. The process requires heavy process control and inspection. A further key research finding is that variation within the process is out of statistical control due to inherent systematic error in the current state process. Process result quality is therefore compromised by the current state selenium process. The key research finding that process redesign is assumed to produce superior results in terms of accuracy and precision, leads research to draw the conclusion that a modified selenium analysis will result in a reduction in risk of compromised result quality.

Additionally, perchloric acid, as used in the current state selenium analysis method was identified as a major biohazard and explosive risk associated to the process. Desert Research Institute (2004:**Online**), found that perchloric acid is highly corrosive, unstable and explosive at temperatures above $150^{o}C$, reacts violently with oxidisable material, and organic materials are especially susceptible to spontaneous combustion in the presence of perchloric acid. Furthermore, The University of Alberta, Department of Environmental Health and Safety (2011:7), states the use of perchloric acid is hazardous, both to the operator and to the environment. A modification of the selenium analysis method, without the use of perchloric acid may thus be undeniably regarded as a form of reducing risks associated with the process. Microwave digestion does not make use of perchloric acid in order to obtain complete organic decomposition of sample material.

While process modification addresses the important risks associated with the current state selenium analysis process, FMEA ensures controls are in place for potential risks associated with the modified selenium analysis process. FMEA pre-emptively addressed any additional risks, and ensured that the risks associated with the modified selenium analysis process, is minimal.

In conclusion therefore: A modified selenium analysis process, which includes a modified sample digestion process, will result in the reduction of biohazard and other risks associated to the selenium analysis process.

### 6.6.3 Selenium yield

A key research finding was that definite process variation, appears to provide evidence of a loss in the selenium yield within current state selenium process. Results of open heat-block digestion of the current state process were found to quantitatively vary from week to week.

The assumption is made the occurrence of a loss in selenium yield is as a result of the open system, on the basis of Kurkova Skrypnik &Zalieckiene's (2008:40), view. The authors state that the main difficulty with selenium analysis process is sample mineralization. As the organic forms of selenium (dimethylselenide and dimethyldiselenide) volatilize from a sample at a temperature exceeding $70^{o}$C, a loss in selenium yield can occur, and thus cede inaccurate analytical results.

In conclusion, the assumption is made that a modification in the selenium digestion process from open heat-block to closed system microwave digestion will optimise the selenium yield of the selenium analysis process.

### 6.6.4 Process Quality Improvement

Pratt (1983:130), argues that, with regard to analytical laboratory results obtained from an analytical method, accuracy can be defined as the extent to which measurements agree with the true value of the quantity being measured. Precision is considered to be the reproducibility of measurement, and reliability is the ability of a

method to be both accurate and precise. To accomplish process improvement of an analytical laboratory method, it may therefore be construed that modification made to secure improvement be done on the basis of improving the 'reliability' of the method.

A key research finding is that result quality of the selenium analysis process was found to be reasonably accurate, based on analysis of CRM. Although a Cochran variant t-test found the CRM values obtained from the process to not be statistically different from the true CRM value, an f-test revealed that definite systematic error was present in the analytical process. Fraser (2011:34), contends that systematic error reduces the accuracy of a process. Furthermore, the author argues that systematic error can, and should be eliminated from an analytical method.

A further key research finding of research is that the current state selenium analysis method produces results which are only precise within a wide margin. This is substantiated by %RSD, which was found to be 16.02%, analytical bias which was found to be -6.5% and the horwitz ratio of the current state selenium analysis process which was found to be 1.82. The analytical method exhibits a high degree of process variation.

The key research findings that, the current state analytical process is potentially capable, with a $C_p$ of 1.02, however, the performance of the analytical method is poor, based on a $C_{pk}$ index of 0.48, are regarded as persuasive mitigating factors in support of process improvement. It is assumed that process modifications to a future state selenium analysis process, which involves microwave sample digestion and hydride generation detection, is a means to eliminate inherent systematic error in the process, and improve both the accuracy and precision of the analytical method. On this foundation, the reliability of the analytical method will be improved and therefore ultimately, the result quality of the selenium analysis process will be improved.

Sited on the assumption that the reliability of the modified selenium analysis process is an improvement on the reliability of the current state selenium analysis process, it

may be stated that in conclusion, a modified process design will ultimately translate into an improvement in quality in terms of the reliability of process results.

## 6.7 RESEARCH HYPOTHESIS

Research hypothesis is stated as:

**$H_0$** : Variation in process, time and control procedures have a direct impact on the disparity in selenium testing results.

Based on the conclusions obtained from the key research findings of the research conducted in the ambit of this dissertation, it may be said that there is significant evidence to accept the null hypothesis. It was found that variability of the dependent variable of the research hypothesis, associated to the process, had a significant and detrimental impact on the independent variable of the research hypothesis, namely, the result quality of the selenium analysis process.

From this the analogy can be drawn that "Variation in steps of the process, time and control procedures, have a direct impact on the disparity in selenium testing results".

## 6.8 RECOMMENDATIONS

The following recommendations are made as a result of the research conducted:

- The current state selenium analysis process must be modified to ensure reliability of process results.
- Process modification must be made to address process variability, as a result of process steps, time and control procedures in the process, which are found to produce disparate results.
- Process modification from open heat-block to microwave digestion is recommended.
- Process modification from fluorimetric selenium detection to hydride generation is recommended.
- It is further recommended that the modified process be monitored, and continuous evaluation takes place according to the Lean Six Sigma cycle, in

order to maintain the focus on continuous improvement of the selenium analysis process.

## 6.9 CONCLUSION

The function of an analytical laboratory facility is to provide accurate and precise analytical data to its customers. The use of competent laboratory analysts with necessary skills, appropriate chemical reagents, and first-rate laboratory equipment is tantamount to the reliability of results. The research which has been conducted demonstrates however, that it is in fact, an adequate analytical process which is the cornerstone of good analytical practice and good result quality.

Analytical methods should therefore be continually assessed and validated for accuracy and precision. Lean Six Sigma may be regarded as a choice tool, and advanced approach to accomplish this. The Lean Six Sigma approach supports the ISO/IEC 17025 Standard, which states the general requirements for the competence of testing and calibration laboratories. The standard is used in laboratories to implement a quality system, aimed at improving their ability to consistently produce valid results. While the standard is the basis for accreditation, it may be said that the true essence of the ISO/IEC 17025 is about ‘competence’. Accreditation is simply formal recognition of a demonstration of that competence. This research has found that the ‘Lean Six Sigma approach to analytical process improvement’, to be, the demonstration of competence in practice.

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