The quality of selected food products containing nanosilica additive (E551) in South Africa.

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D.Tech: Quality

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JOURNAL PAPERS SUBMITTED ARISING FROM THIS STUDY (UNDER REVIEW)

Thakur, R.[1], Singh, S[2]. 2016. Title: Nanotechnology in the food industry: A contextual evaluation of opportunities, risks and regulation relevant to the South African landscape. Paper submitted to the *Trends in Food Science and Technology* on 17 February 2016 (Ms. No: TIFS-2016-69).

ABSTRACTS AT CONFERENCES ARISING FROM THIS STUDY

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Abstract

The proliferation of nanotechnology, whilst perceived to be positive for human advancement, introduces potential risks when applied to food. Silicon Dioxide (E551), a common food additive made up of particles in the nano-range, is found in spices, salt, sweets and some frozen foods and functions as an anti-caking agent to allow these food products to flow and mix evenly. According to Codex Alimentarius, E551 is generally regarded as safe (GRAS), provided that food manufacturers apply good manufacturing practice (GMP) principles and use the lowest possible amounts necessary. Smaller nanoparticles are more readily taken up by the human body than larger sized particles and could be injurious to human health. While the use of E551 is strictly regulated in some countries, there is growing debate regarding the health and safety implications for consumers and the quality of food. This study examined the quality of selected food products containing E551 (nanosilica) in South Africa (SA).

A mixed method paradigm (qualitative and quantitative) and an experimental research strategy were adopted. Respondents were purposefully selected, their participation in this study was voluntary and confidentiality was maintained. Pilot studies were conducted for the semi-structured interviews and the survey, with a sample size of one food expert and three food technologists, respectively. The main study consisted of interviews, a survey and experimental work. The interviews, conducted with five food experts, were recorded and transcribed to ensure credibility. The results were interpreted and analysed against existing literature using thematic content analysis. The findings suggest that it was critical for food manufacturers to demonstrate the safe use of products without posing any safety risks to the consumer and the environment; and for the South African government to address and regulate the application of nanomaterials in food either by legislation or guidelines. The survey was conducted with a sample population of thirty food technologists who reported that public awareness of nanotechnology was limited as many consumers were not familiar with this technology. Descriptive and inferential statistics were used to analyse the quantitative data. Content validity ensured that the survey focused on concepts and constructs that emerged from the review of literature on the application of nanotechnology in food products. Cronbach's alpha index was used to assess the

reliability of the surveys and found α = 0.862 and α = 0.809 for food additives awareness and nanosilica safety in food, respectively.

Different characterisation methods, such as Fourier Spectra Infrared Spectroscopy (FT-IR), Energy Dispersive X-ray Spectroscopy (EDX) and X-ray Diffraction (XRD), were used to determine the type and form of silica, and its levels in selected food brands available in SA. This was compared against similar products manufactured and packed in the European Union (EU) and Asia. This study benchmarked against the EU standard because of its more stringent guidelines in the field of nanotechnology and regulations. The results indicate that while the comparative EU food sample conformed to the European Food Safety Association (EFSA) permissible level of 1 %, the South African sample levels were higher. Even though the regulatory standards are different in both countries, the potential health effects remain the same. Significantly, the most prominent finding of this study is that the form of silica in some of the South African and Asian products were crystalline in nature, rather than synthetic amorphous silica (SAS), which is indicative of E551. Thus, it stands to reason that the generalised limit set by Codex Alimentarius was inadequate to regulate and control the quantity and type of E551 used as it varied from each of the selected samples.

The identification of traces of crystalline silica is of concern since studies in literature showed that exposure to and ingestion of crystalline silica that was not food grade, is likely to induce perilous health effects such as cancer and fibrosis in humans. In light of this finding on the crystalline nature of silica in the studied brands, it is therefore imperative that specific limits and regulations be put in place and enforceable in SA to ensure that products sold are in line with acceptable standards as found in some developed countries like the United States of America (US) and EU.

In view of the above, and to ensure proper monitoring and minimal risk exposure, a risk management framework, a ‘Hazard identification, Access the risks, Control the risks’ (HAC) model, was developed and recommended to ensure that the correct form and type, and limits of silica is used and the associated risk controls applied.

Keywords: Nano-additives, E551, Toxicity, Compliance, Risk Model

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Acronyms and Abbreviations

ADI	Acceptable Daily Intake
CAS	Chemical Abstracts Service
EC	European Commission
EDX	Energy Dispersive X-ray Spectroscopy
EFSA	European Food Safety Association
EHS	Environmental Health and Safety
ENMs	Engineered nanomaterials
EPA	Environmental Protection Agency
EU	European Union
FDA	Food and Drug Agency
FT-IR	Fourier Spectra Infrared Spectroscopy
GI	Gastrointestinal
GIT	Gastrointestinal Tract
GLP	Good Laboratory Practices
GM	Genetically Modified
GMP	Good Manufacturing Practice
GRAS	Generally Recognised as Safe
HAC	Hazard identification, Access the risks, Control the risks
IBD	Inflammatory Bowel Syndrome
ISO	International Organisation for Standardisation
ISO/TR	International Organisation for Standardisation/Technical Report
MNO	Manufactured Nano-objective
NAFDAC	National Agency for Food and Drug Administration and Control
NICNAS	National Industrial Chemicals Notification and Assessment Scheme
NMs	Nanomaterials
NNA	National Nanotechnology Agency
NNI	National Nanotechnology Initiative
NNS	National Nanotechnology Strategy

NPs	Nanoparticles
MNOs	Manufactured Nano-objects
OECD	Organization for Economic Cooperation and Development
OELs	Occupational Exposure Limits
OSHA	Occupational Helath and Safety Administration
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals
SA	South Africa
SAS	Synthetic Amorphous Silica
SCENIHR	Scientific Committee on Emerging and Newly Identified Health Risks
SEM	Scanning Electron Microscope
Si	Silica
SIO_2	Silicon Dioxide
UK	United Kingdom
US	United States of America
WHO	World Health Organization
XRD	X-Ray Diffraction

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Chapter One - Introduction

1.1 Overview of the study

The incorporation of Engineered Nanomaterials (ENMs), such as synthetic amorphous silica (SAS), into food products has generated widespread concern due to specific properties it has that which may potentially pose a risk to human health. A number of scientific articles and reviews (Wollstonecroft 2011; Edame, Ekpenyong and Fonta 2011; Boye and Arcand 2013, Athinarayanan, Periasamy, Alsaif, Al-Warthan and Alshatwi 2014; and Higashisaka, Yoshioka and Tsutsumi 2015), have highlighted the applications of nanomaterials (NMs), including SAS (also known as food-grade silicon dioxide (E551)) in selected food products. These studies established that due to its nanoscale size, which is between 1 nanometre (nm) to 100 nm, ENMs exhibit novel and improved physical, chemical and biological properties compared to their bulk counterparts. As a result, there have been safety concerns raised on potential risks when ENMs are applied to food, particularly the possibility that nanoparticles (NPs) could be toxic to humans when ingested or inhaled (Bieberstein, Roosen, Marette, Blanchemanche and Vandermoere 2013; Coles and Frewer 2013; Yang, Song, Cheng, Xiang, Chen, Liu and Wang 2014; van Kesteren, Cubadda, Bouwmeester, van Eijkeren, Dekkers, de Jong and Oomen 2015). Given these safety concerns, there is a need to develop a standardised risk management framework in order to protect the health and safety of the public, consumers, workers and the environment.

This chapter provides an insight into the background of the study as well as an explanation of the problem statement. The aim and objectives of the study are subsequently set out in an attempt to resolve key aspects of the research problem. This is followed by the rationale which outlines some of the issues associated with the incorporation of ENMs in selected food products. A synopsis of the structure and flow of the study is then presented to demonstrate the research methodology that was adopted and appropriately applied to the problem.

1.2. General background to the study

According to Passagne, Morille, Rousset, Pujalte and Lazou (2012), SAS is one of the most popular NMs. It has been used since the 1960s in a variety of industrial and consumer products, including cosmetic, pharmaceutical and food applications.

Fruijtier-Polloth (2012) describes SAS as a distinct, manufactured form of silicon dioxide, consisting of nano-sized primary particles of nano-sized aggregates and agglomerates. Literature reviewed from 1994 to 2009 (Lewinson, Mayr and Wagner 1994; OECD 2004; and Becker, Fernandes, Rothhardt, Bruckner, Schuster, Kobelke and Marques 2009) considered the application of SAS in consumer products as safe if occupational standards and recommended usage levels were adhered to. However, recent studies from 2010 to present (Dekkers, Krystek, Peters, Lankveld, Bokkers, van Hoeven-Arentzn and Oomen 2011; Asmatulu, Zhang and Asmatulu 2013; Dekkers, Bouwmeester, Bos, Peters, Tietveld and Oomen 2013; and Yang *et al.* 2014) raised concerns about the hazards and health risks of 'nanosilica'. These studies found that nanosilica particles have high toxicity that could be injurious to human health. Bouwmeester, Brandhoff, Marvin, Weigel and Peters (2014) observed that this was mainly size-related due to a much larger surface-to-mass-ratio when compared to the larger-sized bulk counterpart materials. Furthermore, Martirosyn and Schneider (2014) suggested that the possible accumulation of insoluble NPs in humans may be responsible for compromised gastrointestinal (GI) functioning.

Peters, Kramer, Oomen, Herrera-Rivera, Oegema, Tromp, Fokkink, Rietveld, Marvin and Weigel (2012) found that food additive, E551, consists of SAS and is present in food products, *inter alia* coffee, coffee creamer, soup and sauce powders, and seasoning mixes, as an anti-caking agent. E551 has also been used for years in beers and wines as a stabilising agent. As of 2016, E551 remains a permitted food additive under the "Codex General Standard for Food Additives" (CODEX STAN 192 1995). The Codex Alimentarius is an international food standards body set-up by the World Health Organisation (WHO 1987) and the United Nations' Food and Agriculture Organisation (FAO). It provides voluntary guidelines to enable developing and poor nations to improve food safety for their own population.

According to a WHO report (1987), the Codex specifies an acceptable daily intake (ADI) which is the amount of a food additive, expressed on a body weight basis, that can be ingested over a lifetime without appreciable health risk; and it further specifies the maximum use level of an additive, which is the highest concentration of the additive determined to be functionally effective in a food or food category and agreed to be safe. These levels are indicated in Table 1-1. Additives in food which do not contain maximum use levels are regarded as having good manufacturing practice (GMP)

principles. GMP means that the quantity added to the food must be limited to the lowest possible level necessary to accomplish its desired effect (CODEX Stan 192-1995).

Table 1-1: Prescribed levels of E551 concentrations in food (adapted from Commission 2013)

Food Category	Max Level
Dried whey and whey products	10 000 mg/kg
Powdered sugar, powdered dextrose	15 000 mg/kg
Salt	GMP
Salt substitutes	GMP
Complementary foods for infants and young children	2 000 mg/kg
Coffee, coffee substitutes, tea, herbal infusions, and other hot cereals and grains	GMP

Although maximum levels are stipulated for some products, it is noteworthy that common products, like salt and coffee, are regarded as having adopted GMP which calls on food manufacturers to apply appropriate E551 levels in some food products; that is, to use levels or amounts of additive at their own preference as long as the desired effect is achieved. This is cause for concern in light of studies conducted by Busk (2011); Asmatulu *et al*. (2013); and Dekkers *et al*. (2013) which showed harmful effects of NPs to humans. In the same light, it must be noted that when GMP was formulated for the application of SAS in food additives, little was known about particle size in general and nanotechnology in particular. As a result, it is conceivable that E551 was not regarded as an ENM.

Whilst most developing nations, including SA, follow the Codex Alimentarius standards, developed areas like the EU and the US, have implemented their own threshold level of E551 into food products. In the EU, the E551 permissible limit as an anti-caking agent for dried powdered products, is set at 10 000mg/kg; this also includes products such as coffee and coffee creamers. The E551 permissible limit as

an emulsifier and colourant is set at 50 000mg/kg (Regulation EC. No 1333/2008). In the US, E551 is permitted as a direct additive to food (at 20 000mg/kg) (Code of Federal Regulations, Title 21).

The safety of food products containing ENMs has attracted attention concomitant with their growing use. Rotaru, Sava, Borda and Stanciu (2005) described a number of issues they believed were affecting the development of food safety regulations globally. These issues include the standards employed for establishing regulations, how governments approach regulation, and the trade consequences of national food safety controls. Milicevic, Skrinjar and Baltic (2010) observed that food quality structures were becoming more stringent in response to real and perceived food safety problems, more so now with the advent of nanotechnology.

Most nations have at least one national standards body accountable for developing standards which have become essential to domestic and international trade. In the case of nanotechnology, the development of standards is taking place concurrently with research and commercialization activities, rather than at a later stage in product development as in the case in more established fields. Two principal players leading legislative efforts in the application of nanotechnology in foods are the EU and the US. Thus, many nanotechnology standards are being developed from the outset at the international level in harmony with other countries, rather than by individual countries solely on a national basis (Saner and Merchant 2015).

The International Organisation for Standardisation (ISO) uses standards to ensure that services and products are reliable, safe and of good quality. These global standards are aimed to achieve uniformity and to avert technical barriers to trade throughout the world. This study focuses on ISO technical reports, ISO/TR 13121:2011 standard '*Nanotechnologies – Nanomaterial risk evaluation'* and ISO/TR 12885:2008 standard '*Health and Safety Aspects in an Occupational Setting'*. As such, the theoretical framework for this study is based on regulations and compliance standards relating to nanotechnology in the food sector.

ISO/TR 13121:2011 standard '*Nanotechnologies – Nanomaterial risk evaluation*' is a technical report that describes the risk evaluation and risk management processes for NMs. It presents a comprehensive review of best practices towards evaluating the safe and ethical introduction of NMs in order to protect the health and safety of the public,

consumers, workers and the environment. This standard presents an adaptable framework towards risk analysis of NMs.

Another pertinent ISO standard related to this study involves the safe use and handling of ENMs by workers in the manufacturing chain. In particular ISO/TR 12885:2008 describes health and safety practices in occupational settings relevant to nanotechnologies. The use of ISO/TR 12885:2008 could help organisations, researchers, workers and other people to prevent adverse health and safety consequences during the production, handling, use and disposal of manufactured NMs.

Given the absence of formal regulations for ENMs' use and application in SA, this study seeks to examine the quality and levels of E551 in selected food products and to recommend appropriate risk assessment guidelines for its use as a nano-additive in food (with due consideration of the country's unique sociocultural milieu).

1.3 Statement of the problem

The rapid proliferation of nanotechnology into consumer products, especially food, has raised a number of concerns over their safety to the consumer and effect on the quality of the food. Studies by Chaudhry and Castle (2011); Aebi, Anklam, Baun, Donaldson, Fadeel, Fears, and Stamm (2011); Fleischer, Jahnel, and Seitz (2014) point out that concerns may arise mainly from the current lack of knowledge with regards to the potential effects and impact of ENMs on human health and the environment, and from the lack of appropriate regulatory contexts. However, as with many newly emerging technologies, there are still significant challenges to overcome in taking nanotechnology-enabled applications to the market. Currently, little is known regarding the health effects of human exposure to these materials (Shatkin 2012). No comparative study relating to compliance and quality assurance of nano-additives between SA (developing country) and the UK, EU and the US (developed countries) has been found.

This study will explore the quality of food products containing nanosilica additives in SA, with the aim of proffering recommendations on the appropriate applications of ENMs to safeguard the consumers' health; and also stimulating relevant government

agencies into formulating suitable legislation and regulation for the use and application of ENMs in food.

1.4 Aim

The aim of this study is to examine the quality of selected food products containing the nano-engineered form of silica.

1.5 Objectives

The objectives of the study are:

- To determine the current scope of application of nano-additives in food products in South Africa.
- To conduct a review of literature in chapter two which will serve as a means to determine the effects of nano-additives derived food and potential risks to consumers; this will also serve as preliminary data to be presented in chapter three.
- To establish the existence and compliance of the South African regulatory requirements on nano-additives in food.
- To determine levels of E551 found in selected food products available in South Africa by using analytical methods such as Fourier Spectra Infrared Spectroscopy (FT-IR), Energy Dispersive X-ray Spectroscopy (EDX), Scanning Electron Microscope (SEM), and X-ray Diffraction (XRD). The food products sampled in this study are coffee, coffee creamer, soup, and seasoning.
    - To proffer quality standards and guidelines for the appropriate application of E551 in South Africa.

1.6 Delimitations

Nanotechnology has applications in several fields of human endeavour. The focus of this study is specifically on the food additive E551. Given that a study of nanotechnology application in the food industry in SA will be Herculean and near impossible, this study is thus limited to food experts in Durban, KwaZulu-Natal. This is due to time constraint, confidentiality clauses from experts, and resources that limit the study to only one city.

1.7 Significance of the study

The study is important as the results will determine the impact of ENMs on human health and could thus serve as a roadmap for the appropriate use and application of the E551 food additive in the SA food industry.

The study will also be beneficial to relevant government agencies as it would provide information on ENMs regulation across the globe and the applicability to the South African context.

The study is also significant to academia as it will provide an understanding of the differences and doubts in existing literature regarding ENMs and food additives, vis-à-vis their impacts on human health.

1.8 Justification of the study

There is not much known on the impact of nanotechnology on human health. As a result of obvious negative consequences, some nations are realising that the use of ENMs can have potentially harmful effects. Based on this, nations like the US and EU are beginning to regulate the use of ENMs and their application in foods. However, in SA, there is nothing as yet in the pipeline regarding ENMs regulation in food, particularly food additives.

Although this study looks at aspects of food technology, the focus is on proffering a quality framework for the application of E551 in food, within the South African context. The research conducted in this study will help the general understanding of nanotechnology in consumer food products, thus encouraging further research towards the use of ENMs in food.

1.9 Ethics

Ethics clearance for this study was granted by the Durban University of Technology (Addendum 1). Participation in the study will be voluntary and all information about the respondents will be confidential. Raw and personal data will be stored securely for five years and thereafter will be destroyed.

1.10 Overview of Research Methodology and Research Design

This study has been stimulated by inductive reasoning. Through the use of scientific reports, research and development publications, scholarly articles, standard requirements and legislative guidelines, the study investigated the adequacy of current strategies.

The study further proposed a new risk assessment framework for the application of ENMs in food additives in SA.

The strategy that was adopted was both theoretical and empirical.

A qualitative and quantitative research approach was used for the study. In addition to the consultation of literature sources, semi-structured interviews and surveys were conducted with experts. Data collection involved purposeful sampling of literature, interviewing of researchers, and experimental work. The information gathered was analysed and utilised fully, in order to achieve the research aim and objectives. The validity of the study was based on credibility, dependability, trustworthiness and transferability (Lincoln and Guba 1985).

1.11 Structure of the study

The study comprises five chapters:

Chapter 1 - Introduction and Background

This chapter presented an overview of the study covering aspects such as background, aim and objectives, justification, and the structure of the study.

Chapter 2 – Review of Literature

This chapter reviews related literature from journals, periodical, books, and conference proceedings. It also highlights the application of ENMs in food products, and provides an overview of nanosilica and its potential toxicological effects on human health, standards and global regulations, and nanotechnology in SA.

Chapter 3 – Research Design and Methodology

Data collection in the form of experimental work, semi-structured interviews and desktop research is presented.

Chapter 4 – Results and Discussion

Results are presented in the form of tables and graphs. The results are further used to inform policy, compliance and standards on food products containing nanosilica.

Chapter 5 – Conclusions and Recommendations

The envisaged strengths, weaknesses and challenges associated with the integrated framework (above) will be presented. The chapter will discuss the conclusions that are drawn from this study. The main points and findings are summarised and recommendations are provided for future research.

Chapter Two - Literature Review

This chapter reviews literature related to ENMs that are intentionally incorporated into selected food products for an intended purpose. The review introduces E551, which is known to contain NPs, and explains its characteristics and its application as an anti-caking agent. The literature review is structured into five sections. Section one discusses some of the definitions related to the field of nanotechnology. It is anticipated this will provide clarity on terms of which are often used interchangeably in the field of nanotechnology. Section two provides an overview of the application of nanotechnology in the food sector, including the benefits and the risks associated with the application. Section three deals with the toxicity concerns linking ENMs to potential health effects on the human body. This is considered pertinent due to the lack of knowledge on the safe use of ENMs in foodstuff. Section four presents an overview and discussion of different regulatory measures for ENMs in food, including legislation and guidance for safety assessment in the geographic locations of the EU, the US, and SA. Section five discusses the compliance to standards applicable for nanotechnology in food, such as ISO technical reports 13121: 2011 and ISO 12885: 2008, as these are the underpinning standards with respect to assessing the quality of E551.

2.1 Nanotechnology and Definitions

The concept of nanotechnology, and the probability of influencing matter at the atomic level, was first mooted at a seminal lecture, "*There's Plenty of Room at the Bottom*", by physicist Richard Feynman (1960). Feynman may not have realised the magnitude of his postulations at the time, but more than half a century later his ideas are creating an impact in virtually all sectors of the global economy. However, along with its possibilities, every technology carries with it a concern regarding its potential to cause harmful effects on human life and the environment, and nanotechnology is no exception.

According to Sodano, Gorgiano, Quaglietta and Verneau (2016), there is no internationally harmonised definition for '*nanomaterial*'. Bleeker, de Jong, Geertsma, Groenewold, Heugens, Koers-Jacquemijns, van de Meent, Popma, Rietveld and Wijnhoven (2013) established that in some cases terms like '*nanoparticles',*

'nanomaterials' and '*nanotechnology*' are used interchangeably. Karim (2014) pointed out that different persons, organisations, and countries were defining the term '*nanotechnology'* from different perspectives in order to suit their own specific purposes. This was consistent with Boverhof, Bramante, Butala, Clancy, Lafranconi, West and Gordon (2015) who further noted that this was the reason there were variances in nano-specific definitions globally. Significantly, Justo-Hanani and Dayan (2014) asserted that the lack of a proper definition was the result of limited and inconclusive knowledge on the characterisation and toxicity of NMs. As such, it can be reasoned that a universally accepted definition of nanomaterial can only be reached when the gaps in knowledge relating to the safety aspect of nanotechnology are fulfilled. Hence, more comprehensive standards for the safety assessment of ENMs are strongly needed. This will enable products containing ENMs to be identified and regulated accordingly.

Due to the global differences in the description of terminologies in nanotechnology, it is imperative to describe some of the important terms in this study. These are discussed below.

2.1.1 *Nano*

Garia (2010) stated that the word '*nano*', in layman terminology, refers to something small, tiny, and atomic in nature. It is used to refer to a unit of measurement like millimetre, centimetre, metre, kilometre, feet, yard, bite, byte, among others. According to the International System of Units (Système International d'Unités, SI) a 'nanometre' (nm) is one billionth of a meter or one millionth of a millimetre. By comparison, and as observed by Sparks (2012), the diameter of an average human hair is approximately 100 000 nm and a red blood cell is about 7 000 nm in diameter. Along the same lines, Chau (2014) observed that a specimen measuring one nanometre is so miniscule that it cannot be seen under a regular microscope.

2.1.2 Nanotechnology

Chau (2014:03) defined nanotechnology as, '*the engineering and manipulation of materials at the molecular scales, far smaller than a cell*." Neethirajan and Jayas (2011) estimated the range of dimensions is roughly between 1 nm -100 nm. The comparison is illustrated in Figure 2-1.

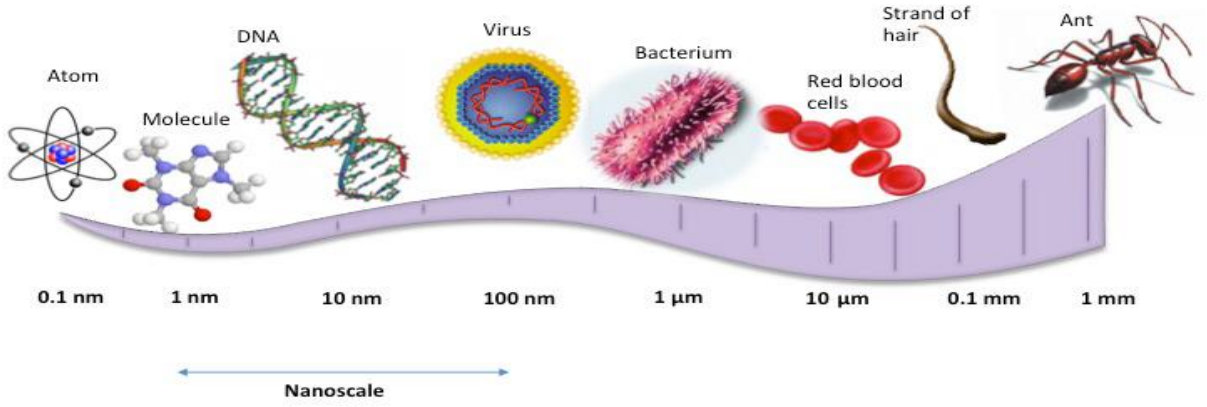

Figure 2-1: Visual examples of the size and scale of nanotechnology (adopted from Neethirajan and Jayas 2011)

Interestingly, Karim (2014) observed that most of the characteristics of nanotechnology can be found from the definition suggested by the American National Nanotechnology Initiative (NNA) program. These characteristics are as follows:

- Research and technology progress at the atomic, molecular, or macro-molecular ranks, in the length scale in the region of 1 nm to 100 nm range.
- Producing and using structures, devices and systems that have novel properties and purposes due to its miniscule and/or intermediate size.
- Capability to control or influence on the atomic scale.

2.1.3 Nanomaterial

The definition of a *nanomaterial,* as stated in a report by the European Union (2011:14) is: "*A natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50 % or more of the particles in the number size distribution, one or more external dimensions is in the size range 1 nm – 100 nm".*

According to Amenta, Aschberger, Arena, Bouwmeester, Moniz, Brandhoff, Gottardo, Marvin, Mech and Pesudo (2015), this definition is broadly applicable across different regulatory sectors within the EU and is aimed at promoting uniformity for policy

purposes. However, the definition came under review in November 2014 when the European Parliament voted to adopt a 10% threshold of particles in the nanorange to be applied in the description of ENMs in food. Consequently, Roebben, Rauscher, Amenta, Aschberger, Sanfeliu, Calzolai, Emons, Gaillard, Gibson, Holzwarth, Koeber, Linsinger, Rasmussen, Sokull-Kluttgen and Stamm (2014) argued that such a threshold could pose a challenge for detection and quantification for NPs and thus lead to more delays in effecting appropriate regulations.

Cushen, Kerry, Morris, Cruz-Romero and Cummins (2012:30), in their effort, noted that a nanomaterial was an *"insoluble or biopersistent and intentionally manufactured material with one or more external dimensions, or an internal structure, on the scale from 1 to 100 nanometres*". The term was further stretched by Zhang, Asiri, Liu, Du and Lin (2014) who propounded that these materials often exhibit chemical, physical, and biological structures which are different from their macroscale counterparts, even if the molecular or elemental composition is the same. This aligns with Ravichandrika, Kiranmayi and Ravikumar (2012) and Aschberger *et al*. (2014) who observed that although a material may not necessarily exhibit nanoscale features, it can still possess properties that are clearly different from those of the macroscale just because of its reduced size. This means that smaller particles have an increased surface-to-volume-ratio compared to their larger counterparts. This suggested that the specific surface area of ENMs can be extremely high which can render it more biologically and chemically active. The above studies concluded that NMs possess unique physio-chemical, optical and biological properties which can be manipulated suitably for desired applications.

2.1.4 Nanoparticle

Nogi, Naito and Yokoyama (2012) described a *nanoparticle* as a microscopic particle or powder with at least one dimension of less than 100 nm, as shown in Figure 2-2. This description resonated with Park, Jin, Yu, Ha, Jang, Bong, Woo, Sung and Piao (2014) who found that there were three types of NPs, namely '*engineered*' NPs (such as buckyballs and gold nanoshells), *'incidental'* NPs (such as those found in welding fumes, cooking and diesel exhaust), and *'naturally occurring'* NPs (such as salt spray from the ocean, or forest-fire combustion).

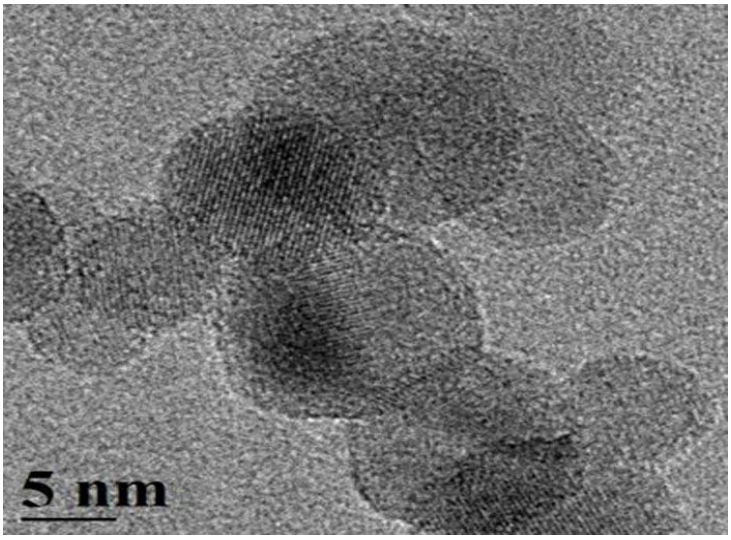

Figure 2-2: Transmission Electron Microscope (TEM) image of silicon nanoparticles
(sourced from www.materialsview.com 2013)

Nogi *et al.* (2012) suggested that NMs are materials developed using NPs which can either be natural or man-made. This study takes cognizance of this as it focused on one such material, namely synthetically amorphous silica (E551).

2.1.5 Nanofood

According to Joseph and Morrison (2006), the term '*nanofood'* is used to describe food that has been cultivated, produced, processed or packaged using nanotechnology techniques or tools, or to which manufactured NMs have been added. Although many nano-sized particles occur in nature, the focus here is on NPs that are purposely manipulated or engineered for use in commercial food products, such as E551. It can therefore be established that most of the definitions used in the field of nanotechnology are solely based on the size characteristic, which is 1 nm to 100 nm. Yet Gilbertson *et al*. (2015) found this problematic. Whilst accepting the pre-occupation with size, the aforementioned authors significantly pointed out that NMs were a diverse group of materials with varying chemical properties and, as such, a more encompassing definition was required. This resonated with Magnuson, Munro, Baldwin, Lopez-Garcia and Socolovsky (2013) and Coles and Frewer (2013) who highlighted that a lack of a clear definition of nanotechnology terminology can lead to misinterpretation and inconsistencies when communicating risks.

Pointedly, this suggests that a uniform and internationally agreed definition of nanotechnology is essential. This could perhaps help define the scope for the risk assessment of E551, which in turn, could affect the regulatory framework on its application in food. The next section will present the application and scope of ENMs in the food sector.

2.2 Overview of nanotechnology in the food sector

This section provides an overview of the incorporation of ENMs in the manufacturing and production of selected food products. Although literature (Alfadul and Elneshwy 2010; Chaudhry and Castle 2011; Basford and Harch 2014; and Pillai, Hunt and Duncan 2014) showed that there are many benefits associated with this technology in the areas of food packaging and improving food safety, taste, and texture; there are nonetheless considerable knowledge gaps concerning the potentially hazardous effects on human health and the environment.

2.2.1 Engineered nanomaterials (ENMs)

According to Cockburn, Bradford, Buck, Consable, Edwards, Haner, Hepburn, Howlett, Kampers and Klein (2012), food naturally contains many nanostructured materials. Three main classes of NMs have been identified in literature:

- Natural food structures include naturally occurring biopolymers (carbohydrates, proteins or lipids) that have at least one dimension in the nanometre range (Chaudhry and Groves 2010; Chaudhry and Castle 2011; Amenta *et al*. 2015).
- Engineered particulate NMs whose components are completely metabolised within the body or excreted, such as nanoemulsions or nanoencapsulations of nutrients (vitamins) (Morris 2011).
- Persistent or slowly soluble engineered particulate ÉNMs such as synthetic amorphous silica (E551), nanosilver (anti-microbial agent), and titanium dioxide (food additive) (Morris 2011).

Methner, Hodson and Geraci (2010) found that the production and use of ENMs was developing at a swift rate globally and new applications are expected to affect many manufactured goods. Presently, ENMs are found in many commercial materials, structures and devices.

Blasco and Pico (2011) reported that the US was the market leader in the use of nanoscale materials, followed by the EU with a global share of the sector of around 30 percent.

In 2007, the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) also expanded on the use of ENMs in other sectors. It observed ENMs were not only used in a variety of commercial products such as sunscreens, cosmetics, tyres and electronics, but its application also extended to techniques like drug delivery, medical diagnosis, biomedical imaging, ground water remediation and so forth. Whilst Martirosyan and Schneider (2014) maintained that this technology was projected to bring a range of benefits to the food sector, an increasing number of studies (Casabona, San-Epifanio and Cirion 2010; Chaudhry and Castle 2011; Cushen *et al.* 2012) cautioned that exposure to certain ENMs, due to their explicit physiochemical properties, can impact basic cellular processes, such as proliferation and metabolism in humans. In other words, due to their very minute size, ENMs can lessen the effectiveness of barriers in the human body which, in normal circumstances, will prevent the infiltration of foreign materials into the body and their agility within the body. The aforementioned authors suggested further studies in order to unravel the biological outcomes of nanofood ingestions.

This is consistent with Bergin and Witzman (2013) who reported that there were a limited number of studies addressing the route or trajectory of NPs once they are ingested or inhaled by humans. They submitted that this was a major point of concern which required further research which would perhaps enable the safe design and application of NPs for human consumption. This is important, as an earlier study by Singh, Singh, Prasad and Gamber (2008) drew attention to the backlash experienced when genetically modified (GM) foods were first introduced to the public. For instance, Costa-Font, Gil and Traill (2008) reported that GM foods were not well received by consumers because of a perceived risk that it was harmful to them. Consequently, Chen and Yada (2011) noted that the risk assessment of nanotechnologies in the food sector would establish a sound foundation on which commercial products can be launched with assurance, or withdrawn to safeguard consumers and the environment from potential hazards. Most important it would ensure the safety of food products and gain the trust and confidence of the public.

2.2.2 Nanotechnology in Food

According to Cushen *et al*. (2012), the food industry, like any other sector, is driven by innovation, competitiveness and profitability. As a result, Handford, Dean, Henchion, Spence, Elliott and Campbell (2014) noted that it was constantly seeking new products and processes with the focal intention of enhancing the overall characteristics of food products, such as flavour, textures, prolonging of shelf-life, better safety and quality, and traceability. Consequently, Bhattacharyya, Reddy, Hasan, Adeyemi and Marye (2015) asserted that nanotechnology was one such process, and could potentially transform the food industry by meeting the demands for the improvement of prevalent food products and the development of novel ones. Whilst, Athinarayanan *et al.* (2014) observed that the international market value for nano-based food and food products was valued at around US$ 4 million in 2006, the afore-mentioned authors noted that this amount was predicted to reach US$ 75.8 billion between the periods 2015 to 2020.

Kimbrell (2006) reported that ENMs can be found in various consumer products including food, feed, biocides and veterinary drugs. Bouwmeester *et al*. (2014) broadly divided the use of ENMs in the food industry into three categories: food, food additives and food packaging, citing that there are various products for each category already on the market. These categories were further classified by Mir and Manzoor (2014) who established that ENMs can be either organic, inorganic, or surface functionalized materials.

Although Potter and Hotchkiss (2012) concurred that '*molecular engineering'* could potentially revolutionise the food market, they expressed concern regarding its potential to cause harmful health effects on humans.

Other studies (Abbott and Maynard 2010; and Aschberger and Christensen 2011) reported that the surface area of NPs appears to be the chief activator for its toxic effect. This view is supported by Trybula and Newberry (2013), who reported that there was a lack of scientific information on nanoparticle exposure. Their study concluded that present protocols prescribed for bulk counterparts may not be adequate to determine the safe exposure levels for NMs. This in itself is a gap in research because there is ongoing exploration on acceptable levels of exposure and ingestion for ENMs.

Whilst noting that toxicity was likely to vary among specific NPs, Handford *et al.* (2014) proposed that risk evaluation of nanoparticle exposure must be performed on a case-by-case basis. Handford *et al.* (2014) has resonance to this study, which aims at developing a risk management framework for the safe production and use of ENMs in South African food products, specifically E551.

2.2.3 Current and Potential Applications

Calzolai, Gilliland and Rossi (2012) reported that although there was limited published evidence of the deliberate use and presence of NPs in commercially available food and food packaging, there are several food-grade nanoparticle products already on the market. Titanium dioxide (E171) and silicon dioxide (E551) are the most widely used food additives containing NPs.

According to Codex Alimentarius, food additive means: "*any substance not normally consumed as a food by itself and not normally used as a typical ingredient of the food, whether or not it has nutritive value, the intentional addition of which to food for a technological (including organoleptic) purpose in the manufacture, processing, preparation, treatment, packing, packaging, transport or holding of such food results, or may be reasonably expected to result, (directly or indirectly) in it or its by-products becoming a component of or otherwise affecting the characteristics of such foods"* (Furia 1980:2).

A number of studies (Morris 2008; Groves 2008; Buzby 2010; Brown and Kuzma 2013; Gmoshinski and Khotimchenko 2015) identified the current and short-term projected applications of nanotechnology in the food sector. They maintain that all aspects of the food industry from ingredients to packaging are now looking into nanotechnology applications. As a result, there are numerous potential benefits arising from the application of nanotechnology in food, which makes it relevant for developing countries, as well as for developed nations. According to Athinarayanan *et al*. (2014) these benefits include preservation, processing, packaging and monitoring, leading to better taste, improved texture and longer shelf-life of food.

Chaudhry and Groves (2010) listed the currently known applications of nanotechnology in food as follows:

- Where food ingredients have been processed or formulated to form nanostructures, for example to reduce the amount of salt, fat, colour or other additives to promote healthy option foods.
- Where nano-sized, nano-encapsulated, or engineered NP additives have been used in food, for example to improve the properties of food by altering flavour, colour, texture and consistency.
- Where NMs have been incorporated to develop improved, 'active', or 'intelligent' materials for food packaging, for example, to sense when a food product has passed its use-by-date.
- Where nanotechnology-based devices and materials have been used for nanofiltration, water treatment and nanosensors for food safety and traceability.

Table 2-2: Potential range of benefits arising from nanotechnology

Description	Benefits	Description
Nanostructures of food ingredients	Nanosized ingredients, additives	Improved texture, flavour, taste
Nanoencapsulations of supplements based on micelles and liposomes	Delivery system for supplements	Taste masking; protection from degradation during processing
Nanoparticle form of additives and supplements	Nano-engineered particulate additives	Antimicrobial; health benefits; enhanced bioavailability of nutrients
Improved and active nano-composites, intelligent and smart packaging	Food packaging	Improve flexibility, durability, temperature/moisture stability, barrier properties
Membrane filtration	Effective separation of target material from food	Higher quality food products and fluids
Surface disinfectant	Engineering NPs	Non-contaminated foods, protection from pathogens
Nanoparticle-based intelligent inks; reactive nanolayers	Nanolithography depositions	Traceability, authentication, prevention of adulteration

The potential range of benefits is limitless and is presented in Table 2-2. Several studies (Chaudhry and Castle 2011; Momin, Jayakumar and Prajapati 2013; Aschberger *et al*. 2014; and Amenta *et al.* 2015) have identified the prospective

applications of nanotechnology in the food sector. These include the development of nanosized food ingredients and additives to enhance flavour and food texture; nutrient supplements which would have higher stability; food packaging which would result in improved food quality, safety and nutritional value of food. Thus, it can be argued that the potential range of benefits can significantly improve the welfare of people living in developing and poor countries by increasing food security, reducing poverty and improving public health and nutrition.

In addition, and resonating with the aforementioned authors, Handford *et al.* (2014) expanded on the potential benefits in both developed and developing countries. These benefits included:

- Extended product shelf-life: aims to extend the product shelf life and maintain food safety by reducing the growth rate of microorganisms. Longer shelf-life of food products will contribute to reducing food waste, and a more dependable food supply (Kaale, Eikevik, Rustad and Kolsaker 2011).
- Novel flavours and textures: permits the introduction of new properties to materials; potentially leading to novel flavours (Pusztai and Bardocz 2006).
- Reductions in fat: can potentially aid in the development of healthier, low-fat food products as smaller particles improve food's spreadability and stability (Neethirajan and Jayas 2011).
- Anti-caking agent: presently serves as a food additive to prevent ingredients from binding together (Rahman and Padavettan 2012).
- Tracking, tracing, and brand protection: can aid food industries in providing authentication, and track and trace features of a food product for avoiding counterfeiting; preventing adulteration and diversion of products destined for a specific market (Neethirajan and Jayas 2011).
- Pesticides: can develop more efficient food production methods with less use of agrochemicals such as pesticides, antibiotics, and veterinary medicines. This will result in less carryover of harmful chemical residues in food (Kan and Meijer 2007).

Significantly, and as explained by Chaudhry and Castle (2011), the current application involving food additives, such as silicon dioxide, titanium dioxide, iron oxides, and metallic silver, is to improve flow properties, colour and stability during the processing

phase, and has been used for several decades without it being recognised as nanotechnology.

The above-mentioned food additives are currently approved by Codex Alimentarius. As illustrated in Table 2-3, these compounds are presented with their E-number classification, properties and possible use in the food sector. E-numbers are an indication of European safety approval for additives listed under Regulation (EC) 1333/2008.

Table 2-3: Metal and metal oxide compounds in food and food-contact materials

Material	Classification (E number)	Uses
Titanium dioxide	E171	Colouring Agent (white)
Iron Oxides	E172	Colouring Agent (various colours)
Metallic silver	E174	Labelling colour for food packaging
Metallic gold	E175	Colour
Silicon Dioxide	E551	Anti-caking agent

Significantly, while the incorporation of additives containing NMs has been used for many years and offers numerous benefits, Dekkers *et al.* (2013) warned that unless well-balanced risk-benefit analyses can be made, the potential for human health risks remains a threat. Whilst Table 2-3 depicts several food additives which contain NPs, this study focused only on E551.

2.2.4 Nanosilica (E551)

Several studies (Aureli, Basaran and Porfiri 2012; Bosch, Maier and Morfeld 2012; De Temmerman, van Doren, Verleysen, van der Stede, Francisco and Mast 2012; and Athinarayanan *et al*. 2014) described E551 as a nanostructured material, consisting of aggregates and agglomerates of primary particles in the nanorange. Dekkers *et al.* (2011) used the term '*nanosilica*' to describe silica particles and agglomerates/aggregates with an exterior size in the nanometre range (in principle between 1 and 100 nm, but due to analytical issues a range between 1 and 200 nm is considered). They further pointed out that this morphology and dimension of the silica

particles are not usually stated on food labels. In the food industry, E551 has been used for several decades as a stabilising agent to clear beers and wines, and as an anti-caking agent to maintain flow properties of powder products, and to thicken pastes. It is generally recognised as safe (GRAS) by Codex Alimentarius and has been approved for use as a food or animal feed ingredient.

2.2.4.1 Manufacture of silicon dioxide

Fruitjtier-Polloth (2012) described three main types of silica which are all found under CAS No. 7631-86-9. They are crystalline silica, amorphous silica (naturally occurring or as a by-product in the form of fused silica or silica fume), and synthetic amorphous silica (SAS) which includes silica gel, precipitated silica, pyrogenic (fumed) silica and colloidal silica, as illustrated in Figure 2-3. Crystalline silica occurs in multiple forms.

According to Napierska, Thomassen, Lison, Martens and Hoet (2010), quartz is a widespread and well-known material and upon heating, it is transformed into b-quartz, trydimite and cristobalite. Porosil is the family name for porous crystalline silica.

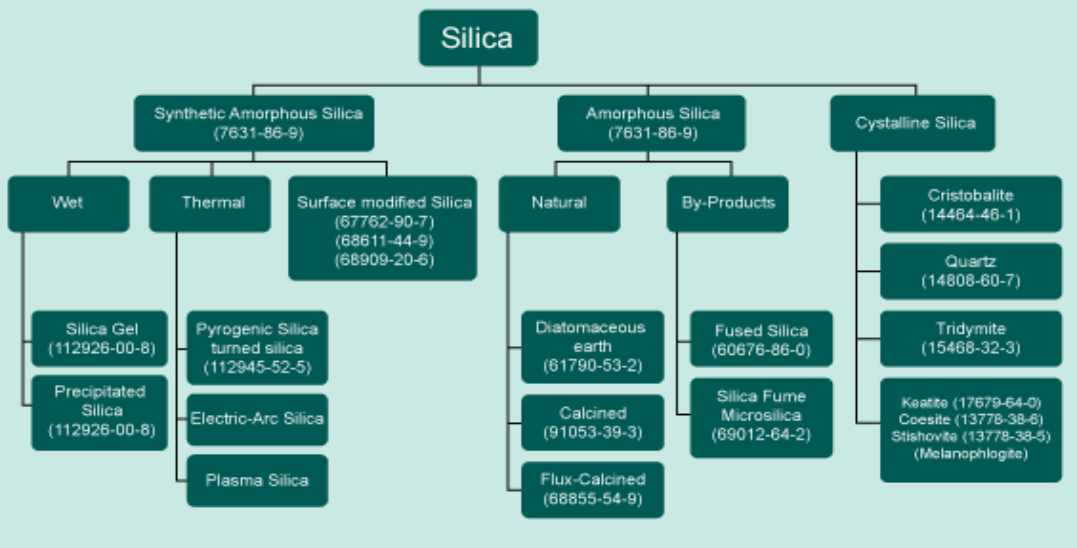

Figure 2-3: Different forms of silica
(adopted from IMA Europa 2014)

In this study only food grade silica, which is SAS, is discussed. SAS is manufactured either by a thermal route (described by CAS number 112945-52-5) yielding pyrogenic silica, or by a wet route (described by CAS 112926-00-8) yielding either precipitated

silica or silica gel (Dekkers *et al*. 2013). Generally, SAS contains no detectable amounts of crystalline silica.

2.2.4.2 Physical and Chemical Properties

Silicon Dioxide is described as a white fluffy powder or granules; hygroscopic and slightly soluble in water (Aguilar *et al.* 2009). It is distinguished from other forms of silica by its high chemical purity and its finely particulate nature (Fruitjtier-Polloth 2012). Typical physico-chemical properties for E551 are shown in Table 2-4 below.

Table 2-4: Physical and chemical properties of E551

Property	Result
Physical State	Solid
Form	Powder, granules
Colour	White
Melting point	>1700^{0}C
Flammability	Non-flammable
Vapour pressure	Not Applicable
Water solubility	Slightly soluble

2.2.4.3 Techniques to characterise E551 in food matrices

Contado (2015) reported that the characterisation to determine detection, measurement and quantification of NPs in food products was challenging. He recommended a combined use of different methods was more feasible to measure the set of physico-chemical parameters required.

Dekkers *et al*. (2013) analysed food products containing E551 and found that the particle sizes ranged from 30 nm – 200 nm. It has been previously stated and further asserted by Asmatulu, Khan, Nguyen and Yildirim (2010) that almost all properties of NMs are completely different from their bulk-size counterparts. Since the properties are completely different, their toxicity could be different as well. Several toxicological studies (Kumar 2006; Karakoti, Hench and Seal 2006; Brayner 2008; Asmatulu *et al*.

2010) have reported that particles less than 100 nm induce toxicity in many cell-cultured human and animal models. The next section will explore the toxicity concerns linking NPs to the potential health effects to consumers.

2.3 Potential toxicity of nanosilica

Despite the wide applications of nanosilica, there are still growing concerns about its effects on the human body. Hristozov and Malsch (2009) and Pillai *et al.* (2014) found that toxicity of NMs are dependent on their properties, including size and size distribution, surface area, shape, aggregation/agglomeration state, and chemical composition. Dekkers *et al*. (2011) reported that although E551 has been a permitted ingredient for application in food for decades, it now seems that more information is available on the behaviour and potential risks of NMs in general, suggesting that the health risk of exposure to SAS may be reassessed in view of the current information. According to Codex, E551 is scheduled to be re-assessed by December 2016 (EFSA 2011).

Bearing in mind that the intake of NPs may potentially pose a health risk, it is vital that consumers be provided with guidelines for preventing an intake in excess of the estimated accepted daily intake (ADI). Moreover, this ADI needs to be reduced until a conclusive evaluation is presented.

2.3.1 The fate of NPs in the body

According to Silva, Reis, Ferreira and Oiveira (2015), the potential routes of NP exposure may occur by means of: 1) inhalation via the respiratory tract; 2) dermal exposure via the skin; or 3) ingestion/oral exposure via the gastrointestinal tract (GIT), as illustrated in Figure 2-4. This is aligned to an earlier study (Chau, Wu and Yen 2007) which reported the same three potentially harmful possible routes for NPs to enter into the body.

Martirosyan and Schneider (2014) posited that in whatever form ENMs exist in food, whether a nanostructured food ingredient, nanocarrier, or NPs incorporated in food packaging; human exposure is likely to occur through ingestion. Furthermore, they suggested that due to the huge surface area of the gastrointestinal tract (GIT), ingestion was possibly the most common route of intentional exposure to various NPs.

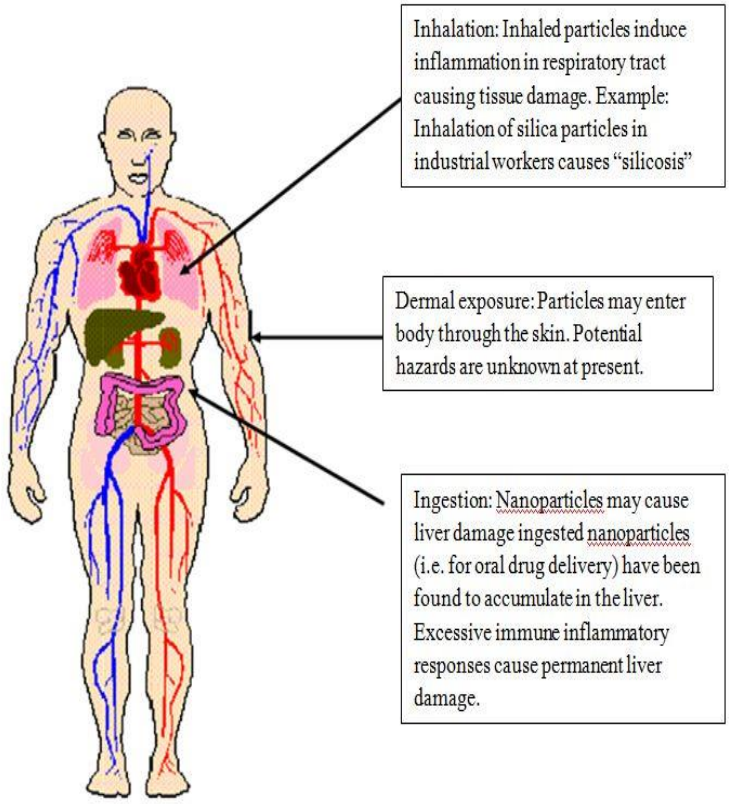

Figure 2-4: Entrance of nanoscale materials into the body through inhalation, dermal exposure, and ingestion, resulting in many potential hazards
(adopted from Colvin 2003)

Although there is currently a scarcity of literature regarding metabolism or biotransformation of ENMs upon oral administration in the human model, Martirosyan and Schneider (2014) reported on a possible association between high levels of dietary NPs uptake and Crohn's disease, which is an inflammatory bowel disease (IBD) that causes inflammation in the intestinal tract.

They further inferred that the possible accumulation of insoluble NPs in humans may be responsible for compromised GIT functioning. An earlier study by Buzea, Pacheco, and Robbie (2007) implied that contact exposure to some NPs can be linked with the occurrence of autoimmune diseases such as systemic lupus erythematous, scleroderma, and rheumatoid arthritis. This was supported by other studies (Bouwmeester, Dekkers, Noordam, Hagen, Bulder, De Heer, Ten Voorde, Wijnhoven, Marvin and Sips 2009; Busk 2011; Asmatulu *et al.* 2013; Dekkers *et al.* 2013) which

stated that nanosilica particles have high toxicity that could be injurious to human health.

In-vivo studies (So, Xu, Loening, Gambhir and Rao 2006; Yamashita, Yoshioka, Higashisaka, Mimura, Morishita, Nozaki, Yoshida, Ogura, Nabeshi and Nagano 2011) showed that high doses of nanosilica fed to mice caused a higher value of alanine aminotransferase activity and that the ingestion of 70-nm silica particles induced foetal reabsorption and restricted the growth of foetuses in pregnant mice. Related studies (Chang, Chang, Hwang and Kong 2007; Wu, Wang, Sun and Xue 2011) showed that high doses of silica particles induced oxidative stress-dependent cytotoxicity in multiple cultured mammalian cell lines.

Momin *et al.* (2013) reported that exposure to certain NPs (carbon black, silicates, titanium dioxide and iron oxide) may lead to oxidative damage and inflammatory reactions of the gastrointestinal tract in humans. In an earlier study, Silvestre *et al.* (2011) found that long-term exposure to some NPs has been associated with acute toxic response including lesions of the kidney and liver, as well as numerous forms of cancer.

Considering the increasing use of silica NPs in food products, Bouwmeester *et al.* (2014) noted that some foodstuffs which contain NPs may not have their safety claims tested before they are available on the global market and accessed through the internet. As a result, Cushen *et al.* (2012) agreed this created challenges in developing a standardised safety testing method for nano-food products.

Reviews investigating the toxicology and safety aspects of NPs (Bouwmeester, Dekkers, Noordam, Hagens, Bulder, De Heer, Ten Voorde, Wijnhoven, Marvin and Sips 2009; Chaudhry and Castle 2011; and Cockburn *et al.* 2012) suggested that there was limited knowledge on existing usage levels and exposure from applications of NPs in food and food-related products. In the same vein, Magnusson, Jonaitis and Card (2011) conducted an evaluation of literature to determine the current state of knowledge regarding the safety of naturally occurring and engineered NMs for food and food-related applications.

The Magnusson *et al.* (2011) study concluded that although the application of NMs potentially offers many benefits, the health risks of using nano-sized particles are relatively unknown.

Azoulay (2012) and Coles and Frewer (2013) independently concurred that despite several products having already made their way onto the marketplace, substantial gaps and questions continue with respect to physico-chemical characterisation, toxicity, and application of conventional risk assessment paradigms. Their review identified a lack of long-term studies to assess the toxicity of NMs following oral exposure. Short-term studies identified in this study revealed that once in the body, NMs may potentially dispense into tissues such as the liver and spleen as major organs of the mononuclear phagocyte system, and a smaller fraction of the nanomaterial may distribute to other tissues (Landsiedel, Fabian, Ma-Hock, Wohlleben, Wiench, Oesch and van Ravenzwaay 2012; and Lankveld, Oomen, Krystek, Neigh, Troost–de Jong, Noorlander, Van Eijkeren, Geertsma and De Jong 2010).

A related study by van Kesteren, Cubadda, Bouwmeester, van Eijkeren, Dekkers, de Jong and Oormen (2015) found that NMs may, in contrast to larger particles, be able to pass cellular barriers such as the gastrointestinal epithelium which can make them become systemically accessible and enter cells. This may be a result of NMs being potentially more reactive than the corresponding non-nanosized chemical substances, probably due to their large surface area. The above findings are significant because in the case of daily exposure, this behaviour of NMs in the human body may result in accumulation over time. It is therefore important that such possible accumulation be considered in risk assessment. It is pertinent to state that the risks associated with NM usage can be reduced if food production and processing industries adhere strictly to laid down regulations and standards put forward by ISO.

It can be argued that regulating the processes involved in food production, processing and conservation is not as thorough as it should be in most developing countries, particularly those based in Africa. The reason for this is that most African countries grapple with the problem of providing food security for their teeming population. Thus, the focus is often not on food quality, but on food provision. Furthermore, Kessler (2011) noted that nano-derived food ingredients such as food additives have been

reported in relation to potential implications for consumer safety and regulatory controls.

A 2008 survey by the German Federal Institute of Risk Assessment showed that current consumer opinion in the EU, whilst conducive to many nanotechnology applications, is not entirely favourable in regard to its use in food (Siegrist, Stampfli, Kastenholz and Keller 2008). This reverberates with the point raised by Chaudhry and Castle (2011) regarding food irradiation and GM crops when it first appeared in the public domain. They found that there was a lack of clear communication from food manufacturers to consumers in respect of consumer safety and benefits of GM. This created a negative public response in many countries, including under-developed nations. The public outcry that greeted GM foods could provide a learning curve and spur regulators to take action to safeguard the consumer against unrestrained use of nanotechnology in the food industry.

Bernstein, Foley and Bennet (2014) called on all nanotechnology stakeholders to ponder both short-term and long-term benefits, limitations, and risks of nanotechnology as it impacted on all areas of life. In a related study, Khan (2015) focused on the ethical and social implications of nanotechnology. He believed that the lack of proper regulatory frameworks is of great concern, and suggested that nanoproducts were presently being developed in a regulatory vacuum as uncertainty relating to toxicity and human health still remain unanswered.

The section above summarised existing data on the potential food safety implications and health hazards connected with the consumption of food containing NPs. The next section provides an overview of how ENMs are regulated in the UK, US, EU and other industrialised countries and how this can benefit a developing country like SA where presently minimal information on the impact of ENMs in food is known.

2.4 Global regulations on the use of ENMs in food

This section provides some prerequisites for SA to adopt in order to develop safety assessment guidelines for the safe use of foods containing ENMs.

2.4.1 Regulatory aspects in European Union, United States, and South Africa

Aung and Chang (2014) emphasised that the goal of food regulations was to guarantee the safe production of products in order to avoid possible risks that may occur.

Although Scott-Fordsmand, Pozzi-Mucelli, Tran, Aschberger, Sabella, Vogel, Poland, Balharry, Fernandes and Gottardo (2014) concurred, they highlighted that the appropriate regulations to govern the safe application of nano-derived food was still lacking. Subsequently, Gnach, Lipinski, Bednarkiewicz, Rybka and Capobianco (2015) found there was growing public concern on the subject of toxicity and adverse effects of NPs on human health and the environment. This was consistent with Berekaa (2015) who stated that the establishment of regulatory systems will enable the capable management of potential risks associated with the use of ENMs in food.

Chaudhry, Gergely and Bowman (2007) found that whilst some developed countries like the US, Australia, and New Zealand have used their existing laws to offer some protection to consumers, the EU and Switzerland are the only regions to include nano-specific provisions in their existing legislation for food. However, whilst Chaudhry and Castle (2011) maintained that the existing laws in the above nations were adequate enough to embrace nanotechnology,

Momin *et al*. (2013) disagreed and maintained that existing legislation fell short of addressing risks posed by nanofoods due to the uncertainties arising out of detecting and measuring NMs in complex matrices such as food. The work by the aforementioned authors thus suggested that that quality standard varied between developed nations like the EU, US, and Switzerland and developing countries like SA, China, and Cuba, amongst others. Nanotechnology regulations and guidelines in selected countries are discussed below.

2.4.1.1 European Union

Iles, Martinovic and Kozak (2011) found that the EU was the international front-runner in the development and execution of laws for nanofood applications. Cushen *et al*. (2012) noted that the regulations of nanotechnology in the EU countries were contained within the scope of horizontal and vertical legislations. The former encompasses attributes of nanotechnology even though it does not specifically aim to

do so, and the latter legislation (which is more recent) is aimed at specifically regulating nanotechnology and industries likely to use this technology.

In terms of a list of EU regulations currently covering nano-specific provisions within its framework, the most relevant horizontal measures in the EU are general food laws.

According to Amenta *et al*. (2015), these general EU food laws include the General Product Safety Directive 2001/95/EC; Registration EACH Regulation (EC) No: 1907/2006; and the Classification, Labelling and Packaging Regulation (EC) No: 1272/2008. General Product Safety Directive 2001/95/EC covers all food goods on the EU market, and food products must conform to safety provisions as set out in EU law. Responsibility is placed on the manufacturer to inform consumers of potential risks associated with the product. In regards to the application of ENMs in food products, Cushen *et al*. (2012) commented that this regulation provides the appropriate measures to prevent the potential risks associated with NMs.

The regulation of chemicals is covered under Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) Regulation (EC) No 1907/2006 which is the directive for the registration, evaluation, authorisation and restriction of chemicals. Although there are no provisions specifically for NMs in REACH, they are however, covered by the 'substance definition' addressing chemicals of any size, shape or physical state. NMs have to be registered and a safety data sheet compiled indicating that it is safe to be placed on the market. Hence, the onus is on manufacturers and importers to ensure that the substances they manufacture do not have any adverse effects to users and consumers. Hullman (2007) asserted that this regulation provided a practical, comprehensive and transparent framework for the hazard identification and risk assessment of ENMs.

The Classification, Labelling and Packaging Regulation (EC) No 1272/2008 is complimentary to REACH and provides a general framework for hazard classification and labelling of substances. The Regulation requires that hazardous properties of NMs be communicated through the supply chain, which includes users and consumers. These properties have to be indicated on the product label.

Klaschka (2012) emphasised that the system of classification and labelling of hazardous substances and hazardous consumer products has proven to be a very

efficient tool for risk communication. Even though SAS falls within the scope of the existing REACH regulation, Amenta *et al*. (2015) expounded that the implementation of nano-specific regulations was yet to be realised in the EU due to the present lack of scientific knowledge around NMs. Similarly, Bleeker *et al*. (2013) felt that the lack of scientific knowledge has resulted in the dearth of appropriate risk assessment for the characterisation criteria of NMs.

Vertical legislation applicable to nanotechnology in the EU includes the Food Additives Regulation (EC) No: 1333/2008; the Novel Food Regulation (EC) No: 258/97; and Regulation (EC) No: 1169/20119 on Provision of Food Information to Consumers. Substances added to food for a technological purpose, such as synthetic amorphous silica (E551) and TiO_2 (E171); or to improve solubility, flavour or bioavailability; are covered by the Regulation (EC) No: 1332/2008.

As reported by Hristozov (2013), food additives have to undergo pre-assessment testing before entering the market. Amenta (2015) noted that this authorisation procedure was based on scientific risk assessment principles to ensure that only safe ingredients are contained in food and feed. Whilst it was observed that the changes in the starting material used in the production method of an additive, such as change of particle size, was not covered by existing authorisation principles, Amenta (2015) stated that food additives permitted before 2009, including E551, was expected to undergo a new safety evaluation by EFSA.

The use of nanotechnology in food processing is covered by Regulation No. 258/97 concerning "*Novel Foods*" in a report by the European Parliament and Council (European Union 1997). "Novel Food" is described as, 'food developed using new technologies'; however it does not include food consumed prior to 1997. Novel food has to undergo safety assessment protocols by EFSA before being placed on the market. Regulation No: 1169/20119 on the provision of food information to consumers (known as the Food Labelling Regulation) contains new food labelling requirements with nano-specific provisions. It establishes a new labelling requirement aimed at *"informing consumers of the presence of engineered nanomaterials in food."* It further sets down requirements that food which contains ENMs is to be listed clearly on the label. The listed ingredient must be stated followed by the word "nano" in brackets.

It is clear from the above that most applications of nanotechnology in food in the EU is subjected to some practice of an approval and pre-assessment process before being allowed for use. It can therefore be inferred that these measures are set in place to manage potential risks associated with ENMs.

2.4.1.2 United States of America

According to Pillai *et al*. (2014), the Food and Drug Administration (FDA) has the legal responsibility in the US, to maintain the safety of food, additives, food contact materials, and feed additives that are positioned on the market, under the authority of the Federal Food, Drug, and Cosmetic Act. Although the Act does not contain any specification for nano-based products and the FDA has not yet adopted a regulatory definition of NMs, it has however, issued specific guide-lines for food-related application of ENMs. Chau *et al.* (2007) reported that the FDA has recommended preliminary safety assessments of "*food ingredients and food contact substances produced at a nanoscale.*"

In addition, the US has sought to create a coordinated nanotechnology strategy through the National Nanotechnology Initiative (NNI) launched in 2000 and situated within the White House. The NNI seeks to coordinate the nanotechnology-related research, development and policy activities of 25 different federal agencies. It has grown into the central program through which federal funding of nanotechnology is channelled (Falkner and Jaspers 2012).

Debate continues as to whether the US regulatory framework affords regulatory agencies sufficient authority and instruments to deal with the application of nanotechnology in consumer products (Davis, Parra-Vasquez, Green, Rai, Behabtu, Prieto, Booker, Schmidt, Kesselman and Zhou 2009; Gao Jin, Shen, Sinko, Xie, Zhang and Jia 2015). Breggin, Falkner, Jaspers, Pendergrass and Porter (2009) found that regulatory authority for NMs and nano-based products is divided between several federal agencies. The Environmental Protection Agency (EPA) regulates any chemical substances or pesticides that are, or contain, NMs.

The Occupational Health and Safety Administration (OSHA) deals with workplace safety dimensions (Reese 2013), while the Consumer Product Safety Commission is concerned with protection against risks from consumer products. Finally, the

Department of Agriculture deals with food and feed safety dimensions. One finding that is consistent here is the uncertainty regarding what the future oversight of nanotechnology in the US should be. For example, right now the FDA does not have specific regulations for nanotechnology because it claims it regulates products, not technologies (Blasco and Pico 2011).

Nevertheless, Blasco and Pico (2011) believed that many nanotechnology products in the future, including food, cosmetics and medicines, will come under the jurisdiction of the FDA. As the US remains the leading country in nanotechnology research and development, it is important for policy makers to prioritise issues relating to standard setting and risk assessment of NM.

2.4.1.3 Other Industrialised Countries

Some industrialised countries, including Australia and Canada, have also investigated the potential risks of ENMs. According to Falkner and Jasper (2012), countries like Korea, New Zealand, Australia and Canada have developed guidelines on the safe handling of ENMs. Nanotechnology-based food products in Canada are regulated under existing legislative and regulatory frameworks (Chau *et al*. 2007). In Australia and New Zealand food authorities adopted a range of strategies to manage the potential health risks associated with the use of nanotechnology in food (Amenta *et al*. 2014). One of the strategies was to post an electronic copy of its Handbook for Notifiers (NICNAS 2013) which provides guidance for importers and manufacturers of nano-based chemicals in the region.

However, none have adopted nanotechnology-specific rules and regulations beyond safety frameworks (Gruere 2012). Michelson (2008) reported that some countries such as China, India, Russia, Brazil and SA are investing large sums of public funding in basic and applied research in nanoscience. China has initiated research programs into potential Environmental, Health and Safety (EHS) hazards and developing regulatory frameworks, while others like India have barely begun to identify regulatory challenges (Falkner and Jasper 2012).

2.4.1.4 South Africa

Takeuchi, Kojima and Luetzow (2014) reported that SA does not have any specific legislation or guidelines for the use of ENMs in the food sector during or after

production. Currently, food additives like E551 are regulated under the Foodstuffs, Cosmetics and Disinfectant Act 54 of 1972 (Regulation 25 of 2004). The Act follows the Codex Alimentarius guiding principle which states that food manufacturers should employ GMP principles to ensure their products are safe, untainted, and suitable for their intended use (Kempen, Bosman, Bouwer, Klein and van der Merwe 2011).

In 2005, the Department of Science and Technology launched the National Nanotechnology Strategy (NNS), which aimed to co-ordinate nano research and development at a national level around six focus areas: water, energy, health, chemical and bio-processing, mining and minerals, and advanced materials and manufacturing. The South African government articulated that the technology will provide solutions to some of the country's key development challenges, such as the provision of safe water and the innovative delivery of health services (SA Department of Science and Technology 2006). Consequently, Musee, Brent and Ashton (2010) asserted that the adoption of nanotechnology is therefore being encouraged in SA, and NMs are being manufactured on a small scale for research and development purposes only. However, according to Musee *et al.* (2010), SA has yet to develop a national research strategy to investigate the environmental, health and safety (EHS) risks of nanotechnology.

In light of the above, the afore-mentioned authors proposed the following intervention mechanisms and strategies that can help to establish a nationally coordinated research programme to investigate the potentially adverse effects of nanotechnology:

- The development of sustainable funding mechanisms to sustain educational platforms at tertiary institutions.
- The development of stakeholder-specific educational programmes to offer general information and generate the levels of awareness that are essential for encouraging familiarisation with issues and risks related to the EHS aspects of nanotechnology.
- The development of training and research programmes to boost and attract an existing labour force in diverse disciplines, to pursue career opportunities in EHS nanotechnology-related areas.

Although laudable, these developments have not yet impacted on the food vertical which, if not addressed, can potentially have a huge impact on the rest of the continent.

Poorer countries on the continent arguably depend on SA to proactively develop adequate standards and compliance laws for the use of nanotechnology in this area.

As critical as the issue of food intake is, it is rather disheartening to note that the government, in its NNI, did not take into cognisance the impact nanotechnology applications might have on the food industry. The focus, it seems, is solely on the economic benefits rather than on the health of the populace. It is noted that regulation of the process involved in food production, processing and conservation is not as efficient (with respect to thoroughness and speed) in most developing countries in Africa. Furthermore, as noted earlier, food provision and food security tends to be prioritised above food quality in most African countries.

2.4.2 Labelling regulations

Due to health and safety concerns, compliance regulations are necessary to manage probable adverse effects, mitigate risks, and protect consumers. Currently there are no internationally recognised and accepted regulatory bodies regulating the use and applications of nanotechnologies or nanoproducts (Coles and Frewer 2013; and Momin *et al.* 2013).

As of 2010, the only regulation overtly requiring the labelling of nano-enabled product was EC Regulation 1123/2009 of the European Council and Parliament in the case of cosmetics (European Parliament and the Council 2009). No country had presented a mandatory labelling requirement for food, or any other product. In July 2010, a draft regulation voted in by the European Parliament did call for the labelling of nanomaterial in food products, and extended the legislation on novel food (including Genetically Modified foods), but it still faced opposition from the European Council (Gruere 2011). In 2000, Taiwan introduced the ‘‘Nano Mark’’ program to ensure the validity and truthfulness of nano-related voluntary claims (Asmatulu *et al.* 2013).

Industries in certain countries have also developed codes of conduct that sometimes include labelling; such as the case of retailers in Switzerland (Asmatulu 2013). Furthermore, organic food labelling standards in several countries (the United Kingdom, Australia, Austria, Canada and the United States) have excluded the use of nanomaterial without providing a specific definition. According to Gruère (2011), some

countries have also used both approaches in conjunction, but there was no evidence of any other formal voluntary labelling policy at the national level as of 2010.

Abe (2011) asserted that at the international level, the ISO has been working towards an international labelling standard for nanotechnology. The draft technical specification (ISO/TS13830:2011) is entitled ‘‘*Labelling of Manufactured Nano-Objects and Products Containing Manufactured Nano-Objects”*. The International Organisation for Standardisation (2010) provides guidance on the format and content of claims related to ‘‘manufactured nano-objects (MNOs) and products, preparations and mixtures containing MNOs’’. For example, Magic Nano was a bath cleaning aerosol that was released in Germany and recalled in 2006 due to the hospitalization of several customers after use. This resulted in large negative press coverage for nanotechnologies. An official report by the German Federal Institute for Risk Assessment later revealed that the product did not contain NPs in its aerosol version (Aschberger *et al*. 2014). The Magic Nano incident highlights the need for a strong, affect-based reaction against nanotechnology (Kahan, Slovic, Braman, Gastil and Cohen 2007; Kahan, Braman, Slovic, Gastil and Cohen 2009; Sylvester, Abbot and Marchant 2009). This can create a persuasive argument for some form of regulatory oversight to minimise the actual risks of a harmful occurrence, and also build public confidence and trust that the technology is being adequately overseen (Sylvester *et al*. 2009; and Marchant, Sylvestter and Abbot 2009).

According to Coles and Frewer (2013), the success of the advancements of nanotechnology in the food industry will be dependent on the consideration of regulatory issues. Legislation is essential to manage potential adverse effects, mitigate risks, and protect consumers. Various government agencies worldwide are becoming increasingly interested in the use of nanotechnology in the food sector. Problems arising from nano-food applications are related to the practically non-existent laws to regulate their use (Coles and Frewer 2013).

The above section summarised existing literature on the existence and compliance of global regulatory aspects relating to the use of ENMs in food products. Overall, it was found that there are substantial differences in world regulations between SA and developed nations in respect to nanotechnology in food. As a result, the approach towards safety evaluation on NMs varies between countries. It can therefore be

deduced that not all food products incorporating ENMs qualify to the same safety and quality standards.

Significantly, Kohler and Som (2014) reported that it was against this background that manufacturers and organisations found themselves confronted with the risk of product liability; that is, the question of who has to bear the risks resulting from the lack of scientific data in the field of nanotechology. The next section introduces the risk management process and the factors needed for its successful implementation.

2.5. Quality Management and Risk Assessment of E551

This section describes the steps to identify the risks, assess the risks, and identify the control mechanisms that are required to manage the risks of ENMs in food products.

Current food safety standards do not specifically address the data requirements and measurement approaches to assess potential risks at nanoscale level. Typically, risk assessment relies on the provision of sufficient reliable data to inform an assessment in each case to determine the effects of NMs (Foods Standards Agency 2008). Sekhon (2010) found that the regulation of nano-based products is unclear and one of the factors is related to the lack of safety testing in which regulatory bodies are required to formulate regulations. It is this lack of scientific data that has triggered growing concern among all stakeholders, including government, manufacturers, and consumers.

2.5.1 Risk assessment

As previously highlighted, ENMs have novel properties which are ascribed to their small size, physico-chemical properties, chemical composition and surface-to-mass-ratio.

Nel, Xia, Madler and Li (2006) reported that it was these characteristics that made ENMs different from their conventional counterparts, and as a result, may lead to unexpected toxicological effects that need to be addressed by risk assessors. This aligns with Maynard and Aitken (2007) and Cushen *et al. (*2012) who argue that risk assessments are crucial for the application of nanotechnologies in the food industry as these materials may pose potential risks owing to their novel properties. The work by the aforementioned authors therefore suggests that all applications of this new technology must be assessed for safety of use.

The CODEX Alimentarius Commission (1999) defines risk assessment as: "*a process intended to calculate or estimate the risk to a given target organism, system or population, including the identification of attendant uncertainties, following exposure to a particular agent, taking into account the inherent characteristics of the agent of concern as well as the characteristics of the specific target system".* This process involves a method of identifying, analysing and characterising risk. In line with the Codex framework (Codex Alimentarius Commission 1999), risk assessment is made up of four steps, namely, hazard identification, hazard characterisation, exposure assessment, and risk characterisation.

CODEX Alimentarius provides the following definition for the steps applied in risk assessment. The steps are further elaborated with terms of reference.

- Hazard identification – *"the identification of the type and nature of adverse effects that an agent has an inherent capacity to cause in an organism, system or population".* Here, perhaps, a general description of ENMs and its intended use is required (ISO 13121: 2011).
- Hazard characterisation – *"the qualitative and, wherever possible, quantitative description of the inherent property of an agent or situation having the potential to cause adverse effects".* This infers the presentation of numerical data and analysis of the extent of the adverse health effects associated with the identified ENMs. The impact of varying amounts of the hazardous material on human health can also be considered quantitatively, that is, in a dose-response relationship (WHO 2005).
- Exposure assessment – *"evaluation of the exposure of an organism, system, or population to an agent (and its derivatives)."* In regards to ENMs, this means that validated analytical methods for characterisation is required for their detection and measurement in the workplace where risk to occupational exposure may be the highest due to ENMs being handled in large quantities (ISO 12885: 2008 and Aschberger, Johnstone, Stone, Aitken, Hankin, Peters, Tran and Christensen 2010).
- Risk characterisation – "*the qualitative and, wherever possible, quantitative determination, including attendant uncertainties, of the probability of*

occurrence of known and potential adverse effects of an agent in a given organism, system, or population".

In the risk characterisation step, all data from the previous three steps is pooled in order to attain a risk estimate that offers an educated guess of the likelihood and severity of the adverse health effects that could occur (WHO 2005).

In the EU, the Directorate General of Health and Consumer Protection set up the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR), to provide opinions on questions concerning emerging or newly identified health and environmental risks, related to issues which require a comprehensive assessment of risks to consumer safety or public health (SCENIHR 2010). Nanotechnologies fit this profile.

SCENIHR focuses on nanotechnologies' risk assessment, with specific attention on establishing recognised terminology in the field so that research can be integrated to a certain extent. Rocco and Bainbridge (2005) observed that potential benefits of nanotechnologies were being published at an increasing rate. This suggested that risk analysis was urgently required. Maynard (2011) was of the view that an integrated system of research was necessary to completely understand the repercussions of nanotechnologies on human health, and to anticipate adverse health effects and proactively reduce them. In Maynard's ideal research team, risk assessors would work together with toxicologists and food technologists among others.

The work by the aforementioned authors also suggests that in order for nanotechnologies to be recognised for its full potential, it must be accepted by consumers. In addition, Pidgeon, Harthorn, Bryant and Rogers-Hayden (2009) noted that to be accepted, it must be clear to the public that not only do the benefits outweigh the risks, but that the risks are mediated. This implies that risks have been identified, characterised and evaluated with appropriate counter measures. This is a further gap of research. This study contributes to closing this gap by proposing a risk assessment model for the identification, characterisation, and evaluation of ENMs in food.

A number of general approaches to the risk assessment of NMs have been identified in literature. The most notable are the ISO technical reports relating to

nanotechnology. ISO/TR 13121:2011 provides a comprehensive review of best practices towards evaluating the safe and ethical introduction of NM.

A further notable report is ISO/TR 12885 (2008) which describes health and safety practices in occupational settings relevant to nanotechnologies.

2.5.1.1. ISO/TR 13121:2011

ISO/TR 13121:2011 describes a process for identifying, evaluating, addressing, making decisions about, and communicating the potential risks of developing and using manufactured NMs, in order to protect the health and safety of the public, consumers, workers and the environment (ISO 2011). This standard presents an adaptable framework towards risk analysis of ENMs with a particle range below 100-nm. Hence, it is suitable for the safe application of E551.

Geyer, Kittel, Vollebregt, Westra and Wriedt (1999) posited that manufacturers involved in the production, supply or application of any material should understand and recognise the risks that any material may pose, not only to the health of their workforce but also to their customers and to the environment. In order to manage such risks, Kleindorfer and Saad (2005) stated that certain measures needed to be set in place. Frater, Stokes, Lee and Oriola (2006) elaborated that this required manufacturers to address the gaps in knowledge to gain a better understanding of the risks associated with these materials, whether it be to comply with regulation, pre-empt possible regulation, or show responsibility. Thus, a report such as ISO/TR 13121:2011 will be useful to food manufacturers in identifying best practices for the safe use of NMs in food.

A life cycle system for nanomaterial risk assessment profiling methodologies for physical and chemical properties, and hazards associated with exposure to NMs is presented in Figure 2-5. Using these profiles, a risk evaluation is described. Risks may then be managed and reviewed using methods recommended in the standard.

Even with the ISO technical reports in place to assist food manufacturers with risk analysis of ENMs most food companies did not have processes in place to identify if there are nanomaterials in their products, or to confirm the safety of those products. Significantly, Soliman and Heusen (2013) pointed out that since the long-term impact of nanomaterials on the natural environment and human health was still unknown, it

was difficult to comprehensively regulate this technology in a single piece of legislation that would capture its risks.

Rather, according to the aforementioned author, nanotechnology should be regulated by a series of laws that govern the exposure to humans in specific areas such as food, environment, medicine and agriculture. As such, Reichow (2015) suggested that in the meantime risk management could provide a suitable framework for the responsible handling of NMs in the face of lack of knowledge and absence of nano-specific regulations.

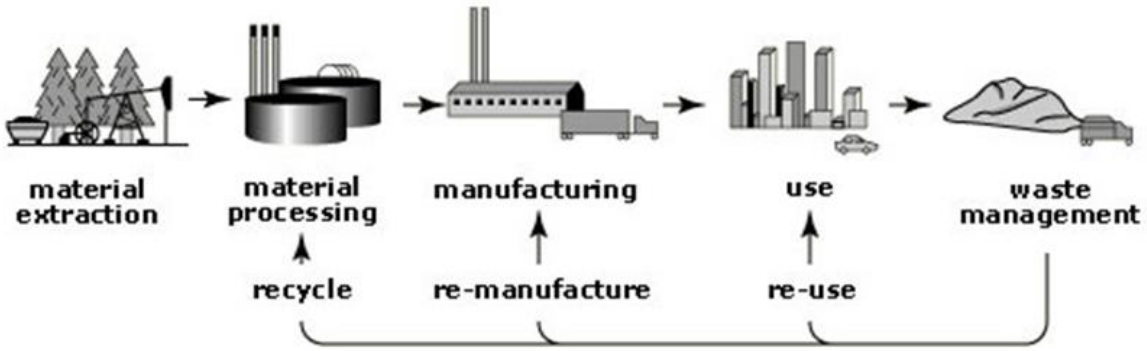

Figure 2-5: Life cycle system for nanomaterial risk assessment (adopted from Tarr 2014).

2.5.1.2 ISO/TR 12885:2008

Equally important is worker exposure to NM. Since the occupational health and safety effects of ENMs are generally unknown, it has become challenging to predict the effect of some ENMs exposures on worker health (ISO 2008).

In addition, the ability of the human body to recognise and appropriately react to most NPs is essentially unknown at the moment. ISO/TR 12885:2008 thus provides guidelines to prevent exposure during the production, handling, use and disposal of ENMs. Some of the aspects the report addresses include:

- Assessing the workers' personal exposure, to check that it complies with regulation.
- Assessing the workers' personal exposure association with possible health effects related to inhalation and dermal exposure.

- Assessment of effective control measure deployment.

Boutou-Kempf, Marchand, Radauceanu, Witschger and Imbernon (2011) reported that there was limited published information on nanoparticle exposures in the workplace, even though workers involved in the manufacturing and handling of NPs and NMs are likely to be exposed via inhalation. Maynard and Aitken (2007) found that the main reason for this sparseness of information was that measuring exposure to NPs was not an easy task. Given the limited amount of information about risks to health that may be associated with NMs, taking measures to minimize worker exposures is prudent.

In light of the above, Schulte, Geraci, Hodson, Zumwalde, Kuempel, Murashov, Martinez and Heidel (2013) called for a precautionary risk management approach to protect the nanomaterial workforce against the risk of adverse health effects. This precautionary approach entailed reducing exposures by means of engineering controls and personal protective equipment (PPE). The work by the aforementioned authors therefore suggests that although ISO/TR 12885:2008 provided guidance for assessing nanoparticle exposure, there was still insufficient scientific evidence to decide on which particle size range and health-relevant exposure parameters should be measured. Nevertheless, as current food standards and food laws may not be adequate to identify, assess and control any potential risks arising from the use of ENMs food, compliance reports like ISO/TR 13121:2011 and ISO/TR 12885:2008 can offer relief in safely managing NMs and worker exposure in the food sector by providing safety assurance guidelines.

Similarly, Heinz (2013) reported that whilst the main purpose of food standards was to provide consumers with safe food, ISO/TR 13121:2011 and ISO/TR 12885:2008 provided a method of preventing problems and crisis that may arise. It is conceivable that such preventative approaches will ensure consumer confidence in the safety and quality of food manufactured and processed with nanotechnology.

2.5.2. Quality

Trienekens and Zuurbier (2008) stated that it was the responsibility of the food industry to provide customers and consumers with food that meets all the established quality and safety requirements. ISO: 9001 defined quality as: *"The totality of features and*

characteristics of a product or service that bear on its ability to satisfy stated or implied needs". Quality management therefore incorporates 'fitness for purpose' as it ensures higher quality products and service delivery. Foster (2012) defined quality of a product as conforming to the design specifications thereby making it a product of good quality.

Quality guru David Garvin articulated both the definitions and dimensions of quality. He observed that most definitions of quality were transcendent, product-based, user-based, manufacturing-based, or valued-based. Garvin used these definitions of quality to develop a list of eight quality dimensions, as illustrated in Figure 2-6. These include performance; features; reliability; conformance; durability; aesthetics; and perceived quality. Garvin believed that developing a good understanding of quality principles will lead to customer satisfaction. Only when this is achieved should the product be considered to be of a good quality (Birch 2014). The quality consideration is pertinent to this study in terms of developing a risk assessment framework for food-grade silica. Gavin's eight quality dimensions are discussed below (Garvin 1988) and adapted for nano-additives.

- **Performance:** This is the efficiency with which a product achieves its intended purpose. It can therefore be inferred that an effective risk assessment framework for the application of E551 will have to provide the necessary structure for rationalising decisions on the risks that the consumer is prepared to accept. Such acceptance will take into account consumer willingness to tolerate risks in return for benefits.
- **Features:** These are the attributes of a product that supplement the product's basic performance. Given the lack of characterisation and toxicity methods for ENMs, it can be further inferred that tested analytical techniques can be applied to determine characterisation and toxicity features.

- **Reliability:** This is the propensity of a product to perform consistently over its useful design life. In regards to the risk assessment framework, the analytical techniques could perhaps apply to all food-grade NPs.

- **Conformance:** When a product is designed certain numeric dimensions for the products' performance need to be established. It is therefore feasible that the conformance of ENMs will be in line with standards and documents

containing technical specifications and criteria that will be used as a guide in order to ensure that products, processes and services are designed with quality.

- **Durability:** This is the degree to which a product tolerates stress or trauma without failing. Perhaps here, the risk assessment framework must be flexible enough to adapt to new analytical techniques, potential risks and benefits of ENMs in food which may arise in the future.
- **Serviceability**: This is generally determined by the ease of repair of a product. It can be inferred here that food manufacturers should be able to easily apply the framework to ensure compliance.
- **Aesthetics:** The design of the framework may relate to the design, colour and layout.
- **Perceived quality**: This is based on the customer's opinion on the quality of a product.

Figure 2-6 illustrates that each dimension of quality imposes different demands on the organisation, and the implication is that food companies must define the dimensions of quality on which they hope to compete, and should then focus their human and capital resources on these elements (Opara and Mazaud 2001).

Significantly, Opara and Mazaud (2001) advised that an organisation was likely to be more successful in pursuing a strategy of high product quality if it selected a small number of dimensions on which to compete, and then tailored them closely to the needs of its chosen market.

Similarly, Basu (2004) believed that the orientation of quality adopted will undoubtedly influence the quality standards, that is, the product specifications and the techniques and tools used to assess them.

Figure 2-6: Garvin's eight dimensions of quality (adopted from Garvin 1986)

2.6 Summary

This chapter identified a number of potential applications and benefits of nanotechnology in the global food industry. It also provided evidence that there are existing scientific gaps in knowledge which limits the ability of the food industry to make an informed choice on NM use.

These gaps are mainly in relation to knowledge of the applications, consumer and environment safety, and the lack of risk assessment data and guidance on risk assessment methodologies. In addition, there are uncertainties over the adequacy of current global regulations of nanotechnology applications for food-related products.

Chapter Three- Research Design and Methodology

This chapter details the research design and the methodological rationale adopted in this study. The preliminary and pilot study conducted is reviewed and the main study is introduced. The collection of data is discussed and the sampling used to generate data is described. Finally, the study discusses the analysis of data. The survey of the main study examines the current scope and awareness of E551 in food products from the perspective of food technologists. The semi-structured interviews examine the existence and compliance of the SA regulatory requirement of nano-additives in food products. This assessment provides a broader scope surrounding the debate on ENMs in food. The experimental aspect of this study focuses on the characterisation and identification of E551 in selected food products in SA.

3.1 Introduction and Background to the Research Methodology

Studies assessing the toxicity of E551 in food indicated that due to its nanoparticle properties, it may pose a health risk and research findings showed harmful implications of the use of these ENMs in the food industry. Studies (Chang *et al*. 2007; Wu *et al*. 2011) showed that high doses of nano-sized silica particles induced oxidative stress-dependent cytotoxicity in multiple cultured mammalian cell lines. A study by Momin *et al.* (2013) observed that exposure to NPs like silicates, may lead to oxidative injury and inflammatory reactions of the gastrointestinal tract in humans. Similarly, Athinarayanan *et al.* (2014) found that high concentration of E551 caused significant cytotoxic effects on lung fibroblast cell viability in humans. This indicates that high doses of E551 are harmful to both humans and animals.

Similar studies on other NPs used in food products have also set-off warning bells on potentially adverse effects to humans. Sanders, Degn, Mundy, Zucker, Dreher, Zhao, Roberts and Boyes (2012) reported that Titanium Dioxide (E171) used as a colourant in food was capable of inducing “tumour-like” changes in exposed human cells. Schrand, Rahman, Hussain, Schlager, Smith and Syed (2010) conducted toxicity assessments of certain metal-based NPs and found that as the particle size decreases, the toxicity level increases. It can therefore be inferred that as long as NPs remain in food, the risks to human health is very high.

Despite the growing concern of the aforementioned scholars, research illustrates that there are substantial uncertainties regarding food companies' level of awareness and attitudes towards the use of nanotechnology in food applications. Additionally, existing scientific gaps in knowledge in relation to potential health risks and environmental safety are impeding the implementation of effective legislation. The theoretical and interpretivist strategy for this study relied on the accumulated knowledge gained from all literature sources. The empirical strategy adopted was based on observation and experimental work.

Due to the nature of this study, a methodological triangulation of both qualitative and quantitative methods was adopted (Babbie and Mouton 2006; Creswell and Plano-Clark 2011). The intention of a triangulated mixed methods design was to attain a better understanding of the research problem. This is, as pointed out by Creswell (2008), achieved through merging, analysis and interpretation of qualitative and quantitative data collected simultaneously. Furthermore, there is a danger in qualitative research of a selective perception, where the researcher observes only that which supports the theoretical conclusions. This, argues Babbie (1998), may be partially avoided by augmenting the qualitative observations with quantitative ones.

Advocates of mixed methodology (Babbie and Mouton 2006; Creswell 2008; Sarantakos 1993) argue that triangulation methodologies enhance the accuracy or credibility of the study. On the other end of the spectrum, some authors (Lincoln and Cuba 1985; Smith and Hesbusius 1996; De Vos 2002) expressed the view that a combination of both methodologies is highly problematic. They argued that both approaches can be time consuming and very costly, thus extending studies beyond the designated time limits. The aforementioned authors advocated that researchers should identify a single research design for the overall research.

Five methods are frequently combined to enrich research. Studies (Creswell 2009; Creswell and Plano-Clark 2011; Johnson and Christensen 2012) noted that the mixed methods approach allowed the researcher to build knowledge on pragmatic grounds, and in doing so permitted him/her to draw from both quantitative and qualitative assumptions.

Both qualitative and quantitative methods were employed in this study because different methods are warranted at different stages of the research to gain a more holistic view of the phenomenon.

Welman, Kruger, and Mitchell (2005) state that when one conducts research to investigate a research question, one collects data from the objects of one's enquiry in order to solve the problem concerned. Yin (2003) argues that the research approach is the logical sequence that connects the empirical data to a study's initial research questions and, ultimately, to its conclusions. Furthermore, Babbie and Mouton (2005) indicate that research design addresses the planning of scientific inquiry in designing a strategy for finding out something.

The research approach adopted for this study therefore uses both deductive processes (testing ideas against observations) and inductive processes (developing ideas from observations). Deductive processes are generally associated with quantitative research, and inductive processes with qualitative research (Creswell and Plano-Clark 2011; Schutt and Check 2012). It has been pointed out by Creswell and Plano-Clark (2011) that by combining both deductive and inductive processes, the researcher tends to base knowledge claims on pragmatic grounds.

Significantly, literature has documented that the strengths of using a mixed methods research design lies in its straightforwardness and the opportunities it provides for the exploration of the quantitative results in more detail (Creswell and Plano-Clark 2011; Johnson and Christensen 2012). An earlier study (Ivankova, Creswell and Stick 2006) listed several methodological challenges in using a mixed methods design. This includes decisions related to prioritising the quantitative or qualitative approach; implementing the data collection and analysis sequentially or concurrently; connecting the quantitative and qualitative phases during the research process; and integrating or mixing the results of the two phases of the study.

The inseparability of qualitative and quantitative methods was captured aptly by De Vos (2005) who contended that the quantitative method cannot exist without the qualitative knowledge of research conventions, and further argued that it was impossible to express qualitative perspectives without communications being partially amenable to quantitative representations. Significantly, Ary, Jacobs, Sorensen and Walker (2010) postulated that the compatible fusion of qualitative and quantitative

methods in a single research study converges with the assertion of pragmatism, thereby increasing the concrete and practical methodological options available to researchers. Pragmatism means judging the worth of the study by its purpose, resources available, and procedures followed and by the end results within the given context for a specific audience (McKeown 2013; Denscombe 2014).

Table 3-1: Types of mixed method research designs
(adopted from Creswell and Plano-Clark 2011)

The convergent parallel design	Uses simultaneous timing to implement the quantitative and qualitative elements during the same phase of the research process.
The explanatory sequential design	Occurs in two distinct phases. This design starts with the collection and analysis of the quantitative data, followed by the subsequent collection and analysis of the qualitative data. Of significance, the qualitative results build on the initial quantitative results.
The exploratory sequential design	Starts with the collection and analysis of the qualitative data, followed by the subsequent collection and analysis of the quantitative data. In contrast to the explanatory sequential design, the quantitative results build on the initial qualitative results.
The embedded design	Collects and analyses the quantitative and qualitative data within a traditional quantitative or qualitative design. For example, a qualitative strand may be added within a quantitative design, such as an experiment.
The transformative Design	Uses a theoretical perspective as an overarching framework to quantitatively and qualitatively analyse the data.
The multiphase design	Combines both sequential and concurrent strands over a period of time to address a programme objective. This design is generally used in programme evaluation where quantitative and qualitative approaches are used over a period to support. the development, adaptation, and evaluation of specific programmes.

Creswell and Plano-Clark (2011) identified six mixed methods research designs, which are briefly described in Table 3-1.

As this study sought to examine the quality of selected food products containing nanosilica, with the intention to proffer a road-map towards regulating the aforementioned additive in South Africa, a mixed exploratory sequential design was used, consisting two distinctive phases (Creswell and Plano-Clark 2011). A broad overview on the mixed method design of this study is outlined in the next section.

3.2 Methodological Paradigm of this study

The central premise of this study is that there are still significant challenges to overcome in managing, controlling and taking nanotechnology-enabled applications to the market (Chaudhry and Castle 2011). As this study aimed to look at the level of application of nanotechnology additives in food products in South Africa, the benefits and health risks to consumers, and the legislative framework regulating nano-additives in the country as well as globally, a mixed methods exploratory sequential design consisting of two distinct phases, was used (Tashakkori and Teddlie 2010; Creswell 2013; Venkatesh, Brown and Bala 2013). In line with Welman and Kruger (2002), the qualitative aspect of the study was based on literature and interviews with selected experts on food safety and nutrition. Furthermore, the qualitative phase was used to compare compliance of regulatory req99uirements in the EU, US and the UK to that of SA.

The quantitative aspect (Welman and Kruger 2002) of the study was used to determine the awareness of the application of E551 in SA. This information was sought from food technologists, food security academics and experts from Durban. In addition, characterisation techniques were used to confirm the amounts of nanosilica that were present in selected food products, and this was benchmarked using the European food standard. This standard is used in this study as the EU, together with Switzerland, are the only world regions where nano-specific provisions have been incorporated into existing legislation for food (Aschberger Gottardo, Amenta, Arena, Moniz, Bouwmeester*et* and Peters 2015).

In the first phase of the mixed methods exploratory sequential design, the qualitative data was collected through individual semi-structured interviews. Semi-structured

interviews were used in this research because the process allowed for prepared questions from which more questions could be asked during the interviews. Cohen, Manion and Morrisson (2000) suggested that during qualitative interviews new insights and changes may arise in the respondents; therefore semi-structured interviews will enable the researcher to probe more. The semi-structured interviews were conducted in English and recorded on a digital Smartphone with the informed consent of the respondents. The results were interpreted and analysed against existing literature using thematic content analysis. Thematic analysis looks at identifiable themes and patterns of experience (Aronson 1994). This enabled the researcher to meet the third and fourth objective of this study, namely:

- To establish the existence and compliance of the South African regulatory requirements on nano-additives in food.
- To proffer a road map for the appropriate application of nanotechnology (E551) in South Africa.

The second, quantitative, phase of this study builds on the qualitative results obtained in the first phase. As Johnson and Christensen (2008) explain, a quantitative approach tests hypotheses with empirical data to see if these were supported. The quantitative (numerical data) was collected using surveys. In order to ascertain the current scope and awareness of nano-additives in consumer food products in South Africa, descriptive and inferential statistics was used to analyse the quantitative data. In addition, the selected food products were further characterised to determine the level of silica content in the product.

This enabled the researcher to meet the first and second research objectives namely:

- To determine the current scope of application of nano-additives in food products in SA.
- To investigate from literature the effects of nano-additives derived food and the potential toxicity risk to consumers.

3.3 Preliminary Work

Typically a review of literature contains the systematic identification, location, and analysis of documents containing data related to the research problem. It not only surveys what research has been done in the past on the topic, but it also appraises,

encapsulates, compares and contrasts, and correlates various scholarly books, research articles, and other relevant sources that are directly related to the current research (Fink 2014).

The term *Literature Review* is also used to describe the written component of a research plan or information which discusses the reviewed documents. Aveyard (2014) stated that these documents can include articles, abstracts, reviews, monographs, dissertations, other research reports, and electronic media. Furthermore, the literature review has several important purposes that make it important. Gay, Mills and Airasian (2006) found that the major purpose of reviewing literature was to determine what has already been done that relates to your topic. This knowledge prevents any unintentional duplicating of another person's work. Hence, it can be advocated that the overall function of the literature review was to provide a justification of the proposed research project, indicating how it will be different to that which is already published.

Thus the review of literature undertaken in chapter two was used to identify a gap of knowledge in the research focus area of nanotechnology, specifically risk assessment and the potential health implications that may arise from nanotechnology application in food. In doing so, it provided a rationale for this study. However, due to the novelty of this research focus area, preliminary work was deemed necessary to establish current practices and thinking in nanotechnology.

Higashisaka *et al.* (2015:43) stated that: "*Although the safety and potential toxicity of silica NPs need to be yet clarified toward a conclusive evaluation at present, ADI of it should be specified and the guideline for preventing its excess intake over the estimated ADI needs to be considered."* More notably, Bradley, Castle and Chaudhry (2011) observed that food safety and regulatory bodies such as EFSA and the FDA reported that very little progress was made in terms of safety assessments of NMs in the food sector world-wide. According to EFSA (2011:36): *"Available information about safety after oral intake of ENMs is minimal, and absorption, distribution, metabolism, and excretion information that is essential for risk analysis is yet poorly understood".* Smolkova, Yamani, Collins, Gutleb and Dusinska (2015:70) further indicated that the *"absence of standardised assays and analytical approaches to test epigenic effect of nanoparticles is a reason for concern".*

In light of the above, technical reports relating to nanotechnology such as ISO 13121: 2011 and ISO 21185: 2008 formed the preliminary data which provided the framework for risk evaluation, and worker exposure was used as a point of departure to inform the study on risk assessment.

3.4 **Pilot Work**

Yin (2013) suggested that the researcher embark on a small scale enquiry, referred to as a pilot study, in order to identify possible problems and risks and gain practical knowledge of and insight into the research area. Furthermore, it is argued that the reliability of the questionnaires can be boosted by careful piloting (Brown 2015). Likewise, Arain *et al.* (2010) agreed that the execution of a pilot study ensured that observational categories are appropriate, exhaustive and effectively operationalised for the purpose of the study.

Pilot studies were conducted for the interviews and the survey. Purposive sampling, which falls under the non-probability category, was used in this study. A sample size of one food expert and three food technologists was used for the interviews and survey, respectively. During the pilot phase, the researcher exposed the research framework to these respondents to establish validity in terms of the study's aims, target population, the "general level of response to be expected" and procedures for data collection (Cohen *et al.* 2000).

The pilot study not only helped to determine the competence in individuals within the sample to participate in this study, but more importantly, it helped to identify mistakes or ambiguous questions phrased by the researcher that respondents could not answer (Yin 2015; Denscombe 2014). For the pilot study of the interview, a list of eight open-ended questions (Addendum 2) was conducted with one respondent (who was not part of the final study). The following was suggested by the respondent:

- The respondent recommended that the issue of food security versus food quality be included in the list of questions to get a better understanding on the psyche of average SA consumer.
- A question addressing strategies that can be implemented by government to minimise the potential health risks that nanotechnology posed to human.

In light of the above, two more questions were added in order to engage respondents on the importance of regulations in monitoring food additives containing NPs in SA, as well as the current debate surrounding the safety of nanotechnology application in food.

The pilot study for the survey used 18 open-ended questions (see Addendum 3). The pilot work was conducted on three respondents (who were not part of the final study) and the purpose was to validate the instrument and test its reliability. The pilot study significantly identified the following drawback of the questionnaires that were used:

- All respondents found that the open-ended questions were ambiguous. Hence it was recommended that the questionnaire be re-designed or re-structured using a combination of both open and close-ended structured questions for ease of reading and clear understanding.

In light of the aforementioned feedback the questionnaire was modified to include a combination of open-ended and close-ended questions in order to achieve a robust analysis of the current scope and awareness of nano-additives in consumer food products.

3.5 Research Methods: Main Study

A characteristic of mixed methodology is that there is a relationship between theory and practice (Greene, Kreider and Mayer 2011). In order to maintain this relationship, the following sections detail the ethical issues, sampling, data collection and analysis procedure for both the quantitative and qualitative phases.

3.5.1 Ethical Issues

Research has an ethical-moral dimension (Brown and Mitchell 2010). This requires the researcher to maintain a moral and professional obligation and to be guided by ethics, even when the respondents involved are unaware of ethics (Canfield-Davis and Jain 2010). This study was approved by the Faculty Research Ethics Committee of the Mangement Science Faculty, Durban University of Technology (Addendum 1). Ethical issues were addressed in this study by means of a letter handed to respondents. In both the qualitative and quantitative phases, each participant signed

a consent form and was informed that participation in this study was voluntary and that the anonymity and confidentiality of information would be maintained (Addendum 4).

The consent form described all the features of the study in terms of its purpose, procedures, and benefits, as well as the respondents' rights to engage voluntarily and withdraw at any time. Furthermore, respondents were assured that the transcription was undertaken by the researcher only and was made available to the supervisor when requested. Areas that were unclear to the Respondents were also clarified. Respondents to the semi-structured interview also consented to the interview being recorded electronically by the researcher.

3.5.2 Sampling

Sampling is the process of selecting a representative portion of a population with some common defining characteristic for study (Babbie 1998; Creswell 2009). Purposeful sampling technique allows the researcher to determine and/or control the likelihood of specific individuals being included or excluded in the study. The most basic consideration in sampling is "size and representativeness" (De Vos 2005). A sample is considered representative if the aggregate characteristics of the sample closely approximate the same characteristics as the population relevant to the research question (Maxwell 2012).

The target population for this study was food experts. Because of time and financial resource constraints, this research was restricted to purposive sampling.

The criteria for selecting the respondents for the semi-structured interview for the main study included expertise in either food-related issues and/or consumer affairs. Although 10 candidates were identified for the interview of the main study, only five agreed to participate. The five who courteously declined cited that a lack of knowledge in the area of nanotechnology prevented them from adding value to the study. It is worth noting, and as pointed out by Cohen *et al*. (2000), that the key issue in determining sample size is the type of data being collected and the extent to which generalised claims will be made.

The criteria for selecting the respondents in the survey included being a graduate of either food technology or nutritional studies. Overall, 30 respondents responded to the survey for the main study.

3.5.3 Data Collection

Data collection is an important aspect of any type of research study. Inaccurate data collection can impact the results of a study and ultimately lead to invalid results (Creswell 2013). Furthemore, Palinkas, Horwitz, Green, Wisdom, Duan and Hoagwood (2015), stated that qualitative data collection methods play an important role in impact evaluation by providing information which is useful and easy to understand. The afore-mentioned authors found that qualitative data can be used to improve the quality of survey-based quantitative evaluations by helping to generate evaluation hypotheses, strengthening the design of survey questions, and expanding or clarifying quantitative evaluation findings.

3.5.3.1 Data Collection Instruments

Data collection instruments are the tools used for data collection. Schensul, Schensul and LeCompte (1999) stated that these tools can include questionnaire, interview, observation and reading. In addition, Mackey and Gass (2015) emphasised that it was the researcher's responsibility to ensure that the instrument chosen was valid and reliable. The aforementioned author further maintained that the validity and reliability of any research project depended to a large extent on the appropriateness of the instruments. This meant that whatever procedure the researcher used to collect data, it must be critically examined to check the extent to which it is likely to give the expected results. In this study, the researcher undertook to conduct semi-structured interviews and administer questionnaires to a selected group of respondents.

Data from the questionnaires were coded and captured on SPSS software using bar and pie charts. Interviews were categorised into themes and then coded using frequency distribution tables. Using univariate analysis, data was analysed and thereafter interpreted to draw conclusions.

3.5.3.1.1 Qualitative Phase: Semi-structured Interviews

Blanche, Durrheim and Painter (2006) believe that an interview is a natural process that facilitates interaction with the respondents. Semi-structured interviews give the researcher an opportunity to know the respondents intimately in order to understand how they think and feel. The focus of the semi-structured interviews in this study was

to establish the existence and compliance of the South African regulatory requirements on nano-additives in food respondents.

The semi-structured interviews were also used to elicit information on experts' views on the appropriate application of nanotechnology (E551) in SA. The interviews provided a platform for the experts to show how they perceived the current debate surrounding the use of ENMs in consumer food products and also express their own point of views on the subject matter. Seliger and Shohamy (1989) believed that by allowing for the maximum freedom of expression of the participant, ample and often unexpected information emerges. De Vos (2005) suggested that in order to minimise the amount of irrelevant information that interviews generate, several specific and defined questions, in the form of a semi-structured interview schedule, should be prepared before the interview process. Based on the pilot study, two more questions were added to the list of questions (Addendum 5). The interviews lasted between 25 – 35 minutes.

3.5.3.1.2 Quantitative Phase:

a) Survey: Questionnaire

Based on the pilot study of the survey, the following improvements were made to the questionnaires of the main study:

- The language structure in terms of ambiguity was dealt with and irrelevant items were removed from the survey. Clearer and more concise questions were introduced. For example, questions 1 – 7 in Addendum 3 was revised into structured Likert Scale questions, as shown in Addendum 6. The re-structured questions of the survey also avoided items with low reliability.
- To provide more choices, the survey used a 5-point Likert Scale (Strongly Agree; Agree; Neutral; Disagree; and Strongly Disagree), and Yes/No responses.
- A combination of three open-ended questions was included which required respondents to provide their own opinions on the subject-matter.

b) Characterisation techniques and basic procedures

As this study aimed to determine the concentration and form of silica present in common food products imported and sold in SA, the following characterisation techniques were applied: EDX, XRD and FT-IR. Branded South African, EU and Asian

produced or packed coffee samples were purchased at a local food market in Durban, KwaZulu-Natal and used as received.

Table 3-2: Selected food samples and their country of origin

Food Sample	Country of Manufacture
Coffee	United Kingdom
	Poland
	Malaysia
	South Korea
	South Africa
Seasoning	South Africa
Instant Soup	South Africa
Coffee creamer	South Africa

In addition, and as illustrated in Table 3-2, three common household South African manufactured products, namely seasoning, instant soup and coffee creamer were also purchased from the same food market. Each sample product's list of ingredients was carefully read. The labels stated it contained E551 and did not contain any other silica-containing ingredients. In addition, commercially available food-grade silica, with a size range of 70 nm, was purchased from Sigma Aldrich and used as a control and point of reference for the identification of the presence of E551 in the the different food samples.

As illustrated in Table 3-2, the selected samples that were analysed to characterize the amount of nanosilica content were manufactured in the UK, Poland, Malaysia, South Korea and SA.

3.5.3.1.2.1 Fourier Spectra Infrared Spectroscopy (FT-IR) Analysis

Functional groups of the samples were determined by the use of a Varian 800 FT-IR, Scimitar Series instrument with Attenuated Total Reflectance (ATR) in the range of 400-4000 cm^{-1}, and a resolution of 2 cm^{-1} (Department of Chemistry, Durban

University of Technology). This was to confirm the presence of the chemical compound SiO_2 in the selected food samples. The sample (0.1 g) was ground in an agate mortar and thoroughly mixed with KBr (FT-IR grade. 0.001 g).

Transparent pellets were prepared in a stainless steel die by applying a uniaxial load of 10 MPa pressure (Carver press).

3.5.3.1.2.2 Energy Dispersive X-Ray Spectroscopy (EDX) and Scanning Electron Microscope (SEM) analysis

Energy Dispersive X-Ray Spectroscopy was used in conjunction with scanning electron microscope (S-3000N-Carl Zeiss, Mechanical Engineering Department, Durban University of Technology) operating at controlled atmosphere conditions at 20 kV to characterise the surface morphology and the elemental composition of the selected food products. Prior to SEM observation, the surface was coated with a thin, electric conductive gold film to prevent a build-up of electrostatic charge.

3.5.3.1.2.3 X-ray diffraction (XRD)

The X-ray diffraction analysis was performed to observe the type and form of silica used in the food product samples.

The XRD patterns were recorded using a diffractometer Empyrean (PANalytical Instrument, Co-radiation 1.54056 $A^{0,}$ Department of Geology, University of KwaZulu-Natal) and analysed between 10 – 60^0 (2 theta). The voltage, current and pass time used were 40 kV, 40 mA and 1s, respectively. According to Dutrow and Clark (2008), XRD is a widely used method for the identification of amorphous and crystalline nature of materials.

3.5.3.2 Data Analysis

The data collected for analysis in this research consisted of the digital recordings of the semi-structured interviews, questionnaire responses and characterisation procedures. As mentioned earlier, a mixed method approach was used in this study. This approach assumed that data gathered would generate a better understanding of the research problem.

3.5.3.2.1 Qualitative Phase: Semi-structured interviews

The semi-structured interviews were transcribed and analysed using thematic content analysis. Thematic analysis looks at identifiable themes and patterns of experiences (Aronson 1994). The individual interviews were transcribed by the researcher who is able to type up data from interviews. .

The data was then coded according to themes that arose. Coding is described as a process of segmenting and labelling text to form broad themes (Babbie and Mouton 2006). Knowledge on the use of E551 in food products, understanding of food standards and regulations both globally and locally, potential health impact of NPs, the South African food nano landscape, and recommended guidelines for implementation of nano legislation in SA, were drawn as themes and analysed. A careful reading of literature on the effects of nano-derived food also underpinned the construction of key themes from the data.

3.5.3.2.2 Quantitative Phase

Two broad categories exist in statistics, namely descriptive and inferential. The purpose of descriptive statistics is to describe, organise and summarise a particular set of quantitative data (Lind, Mason and Marchal 2002). Whilst such statistics make no predictions, they are useful in summarising results for an experiment. Univariate descriptive statistical procedures were used to analyse the survey data in this study. The data was analysed using SPSS software. Bar graphs and pie charts are used to present the data in Chapter Four.

With reference to the inferential statistical analysis, Johnson and Christensen (2012) explained that inferential statistics uses the laws of probability to make inferences and draw conclusions about the sample data. Essentially, inferential statistical tests are used to examine the research question in a study (Creswell 2009). Field (2008) indicated that correlation is most appropriate to determine the relationship between variables.

3.5.3.3 Data Triangulation

Data triangulation implies the collection of accounts from different respondents in a prescribed setting, from different stages in the activities of the setting and, if

appropriate, from different sites of the setting (Banister, Burman, Parker, Taylor and Tindal 1994).

Data triangulation also entails the cross-checking of the consistency of specific and factual data items from various sources via multiple methods at different times (Guba and Lincoln 1989; Patton 1990). In this study data triangulation entailed the comparison of qualitative data received from semi-structured interviews with food and consumer affairs experts, with quantitative data from the questionnaires of food technologists and nutritionists. Using this dual approach does not result in a single, clear-cut, consistent picture, but rather presents a challenge to improve comprehension of the various reasons for the existence of inconsistencies between the two sets of data (Patton 1990).

The surveys and the semi-structured interviews satisfy the conditions for data triangulation (Goddard and Melville 2006).

3.5.3.4 Reliability and Validity

The two most important aspects of precision are reliability and validity. Reliability refers to the reproducibility of consistent results of a measurement under circumstances where characteristics being measured have not changed (Leedy and Ormrod 2010).

Reliability is quantified simply by taking several measurements on the same subjects and by comparing one's measurements with values that are as close to the true values as possible. Poor reliability degrades the precision of a single measurement and reduces the ability to track changes in measurements in experimental studies (Hopkins 2000).

Cronbach's alpha is a measure of reliability for quantitative research. More specifically, alpha is a lower bound for the true reliability of the survey (Leontitsis and Pagge 2007). Mathematically, reliability is defined as the proportion of the variability in the responses to the survey that is the result of differences in the respondents. This means, according to Krosnik (1999) that answers to a reliable survey will differ because respondents have different opinions, not because the survey is confusing or has multiple interpretations.

In qualitative research, reliability can be thought of as the trustworthiness of the procedures and data generated (Stiles 1993).

This means that qualitative research is concerned with the extent to which the results of a study or a measure are repeatable in different circumstances (Bryman 2001). According to Roberts, Priest and Traynor (2006), qualitative analysis was a particularly reliable approach to data handling. Here, specific codes are created to describe the data, such as statements from interview transcripts, and these may be revisited to confirm previously coded data to check for stability over time (Roberts 1999). Using computerised data software packages, such as NVivo (QSR), can enhance reliability.

In this study, Cronbach's alpha index was used to assess reliability for the survey. Internal consistency of items such as individual questions in a questionnaire can be measured using statistical procedures such as Cronbach's alpha coefficient (Cronbach 1981). Qualitative content analysis was applied as a measure of reliability for the interviews. The data was recorded and transcribed. The results were interpreted and analysed against existing literature using thematic content analysis.

Validity refers to the agreement between the value of a measurement and its true value. Objectivity is defined as the relationship between the researcher and the researched and the ability of the researcher to report subjects' responses without bias (Denzin and Lincoln 1994). In quantitative research, validity describes the extent to which a measure accurately represents the concept it claims to measure (Punch 1998). Roberts, Priest and Traynor (2006) described two broad measures of validity in quantitative research, that is, external and internal. External validity addresses the ability to apply with confidence the findings of the study to other people and other situations, and ensures that the conditions under which the study is carried out are representative of the situations and time to which the result applies. Internal validity addresses the reasons for the outcomes of the study and helps to reduce other, often unanticipated, reasons for these outcomes.

The three approaches to assess internal validity are content validity, criterion-related validity, and construct validity (Eby 1993). Content validity is supported by literature reviews and is intended to measure the relevance and representativeness of items, such as individual questions in a questionnaire. Criterion-related validity can be used

to establish if a tool such as a questionnaire can be compared to other similar validated measures of the same concept or phenomenon.

Construct validity involves the relationship between the concepts under study and the construct of theory that is relevant to them.

In qualitative research, Krefting (1991) noted that validity was assessed in terms of how well the research tools measure the phenomenon under investigation. Johnson (1997) found that a potential difficulty in achieving validity here, may arise out of selective collection and recording of data, or from interpretation based on personal perspectives. However, reduction in bias can be achieved by the practice of researchers sharing interpretations and theorising with the research respondents. In this way, respondents can check, amend and provide feedback as to whether they are recognisable accounts. Halcomb and Andrew (2005) reported that triangulation was another way of enhancing the validity of qualitative research. This included cross-case analysis and comparisons across data from different groups of respondents, and cross checking with published literature.

In this study, content validity ensured that the questionnaire focused on concepts and constructs that emerged from the review of literature on the application of nanotechnology in food products. For the qualitative part of this study, triangulation was used to heighten the consistency, comprehensiveness and validity of the research.

3.6 Summary

This chapter presented the mixed method paradigm (qualitative and quantitative) and experimental research strategy adopted for this study. It outlined the purposeful sampling of respondents, data collection instruments and data analysis tools. In addition, both the preliminary work and the pilot studies are described. The design of the main study indicated a sample population of five and thirty for the interviews and survey, respectively. The experimental work undertaken in the main study involved the characterisation of selected food samples, such as coffees, seasoning, instant soup and coffee creamer. Techniques such as EDX, XRD and FT-IR were presented in order to determine the level, type and form of silica present in the selected food samples. Cronbach's alpha index and qualitative content analysis was used to

establish the reliability of the survey and interviews respectively. Content validity, thematic analysis and triangulation were presented to establish the validity of this study.

Chapter Four – Results and Discussion

This chapter presents the outcome of the data gathering process, reports the results, and discusses the findings obtained from the three data collection instruments; namely, the semi-structured interviews, the surveys and the experimental analysis of selected commercially available food products containing E551. The data collected was analysed in relation to the four objectives outlined in chapter one, that is: (1) to determine the current scope of application of nano-additives in food products in SA, (2) to establish the existence and compliance of the South African regulatory requirements on nano additives in food, (3) to determine the level and form of silicon dioxide present in selected food samples available in South Africa; and (4) to suggest appropriate application of a quality framework for ENMs in South Africa. Excluding the data obtained from the interviews, all the data in the sections below were statistically analysed in an attempt to examine the quality of selected food products containing the Nano-engineered material Silica (E551).

4.1 Qualitative phase – Interviews

In the study, semi-structured interviews were conducted with five food experts based in Durban, SA. This section outlines the findings from these interviews, more specifically the key themes that emerged.

4.1.1 Existence and Compliance of the South African Regulatory requirement of nano-additives in Food

In this phase, analysis of the data gathered from the interviews resulted in the identification of the following five broad themes, namely:

- Safety of nano-additives for human consumption.
- Global standards for nano-additives approval.
- Mechanism for safety of food containing nano-engineered materials in South Africa and globally.
- Importance of regulations in monitoring food additives in South Africa.
- Directives in place to ensure safety of South African consumers from influx of imported foods containing nano-engineered materials.

Themes were identified in line with achieving the second research objective that is: To establish the existence and compliance of the South African regulatory requirements on nano-additives in food. In addition, and in supporting the discussion on themes, relevant quotes from the data generated from the interviews were used. Data from semi-structured interviews was transcribed verbatim and used as such during discussion.

4.1.1.1 Theme 1: Safety of additives for human consumption

All the food experts are of the opinion that food additives, particularly nano-engineered materials, are not safe for human consumption. It is worth mentioning that the concerns raised include: lack of scientific data to support the benefits of ENMs in food; and potential long-term health impact on consumers, such as liver and organ damage. Arising out of the health concerns of food additives, particularly in the use of silicon dioxide, all the interviewees felt it posed a health risk to humans. In their own words:

> *"Yes, I have read a lot of articles on silicon dioxide that it could be detrimental to the human liver and other organs based on research done on rats".*

With this considered and coupled with a lack of adequate research on potential effects on the human model, one of the food experts felt that there is a need for more research and testing.

Respondents also suggested that there should be more control and regulations regarding the use of safe levels. In their own words:

> *"There is a need for more research and testing. We cannot condemn it entirely because additives have its own level. It is important to be informed about amounts and levels that need to be added. Therefore, it is imperative to have permissible level".*

The most noteworthy attribute resulting from this theme is that the amount of additives added into food is a critical factor in assessing its safety. This was further corroborated by one of the food experts who stated:

> *"Scientists usually want to put up values that are recommended within permissible limits.*

"The reason being is that they do not want to say this value is dangerous, as it were. They want to give you a value that is within a stipulated time of consuming that food that is to an extent safe. So the important thing is as long as nanosilica is added to food as an anti-caking agent most of those industries, especially those who do pastry, they probably use this. As you know, they do not want your flour to cake – that would affect the quality and consumers may not want to buy.

"In South Africa, I am not sure of laws regulating nanoparticles in food. My concern, is however, the amount- whether it is high or low. What is the amount that can pose a risk? But generally, food additives are expected to be very low. Very, very low so as not to impair the taste of the food and not interfere the complex of the food matrix, which would not affect the consumers in the long run".

From the foregoing theme, it appears that the safety of food additives, particularly the use of ENMs such as E551, must depend on some specific standards and guidelines to ensure food manufacturers are in compliance with the acceptable permissible limits.

4.1.1.2 Theme 2: Global standards for additives approval

As stated in the literature review, global standards such as ISO/TR 13121 (2011) presents a comprehensive review of best practices towards evaluating the safe and ethical introduction of NMs. It describes a process for identifying, evaluating, addressing, making decisions about, and communicating the potential risks of developing and using manufactured NMs, in order to protect the health and safety of the public, consumers, workers and the environment. With reference to health safety of the food additives, the food experts felt that:

"Globally, we need laws for additives, especially nanosilica which in recent times is generating some controversy in terms of safety".

It can also be gathered that food regulatory bodies like CODEX Alimentarius, WHO, and several other bodies in developed countries must come together and promulgate laws to food manufacturers, particularly with respect to the permissible levels. It was noted that:

"I think if we have a uniformed standard, it will help other food industries in developing countries to follow suit on what is recommended".

For example, in SA, although the application of E551 in food industries is in compliance with CODEX Alimentarius, some of the food experts believed that SA should adopt the European Union (EU) standard in terms of nanomaterial applications in the food industry. One respondent said:

"We must use the EU regulations as a template. If they are already regulating this, that should form the basis for a South African regulation. Let's take it from there. Let's see what they have done. We should be looking at the developed nations for guidelines. We do not have to re-invent the wheel but rather take from the developed countries and adapt to the South African context".

More importantly, one food expert cautioned that SA must tailor the aforementioned EU standards to suit the South African landscape by researching more into the use of ENMs for food applications. Presently, the EU is the only global region where nano-specific provisions have been incorporated in legislation for food. These provisions include nano-specific information requirements for ENMs risk assessment and a legally binding definition of the term 'nanomaterial', as well as the obligation on food suppliers to label or report the presence of ENMs in food products (Coles and Frewer 2013). As such, all interviewees agreed that international standards such as ISO 9001: 2015; ISO 13121: 2011; and ISO 12885: 2008, played an important role in the governance of nanofood by providing methods and safety guidelines of managing and monitoring products entering the food market. Accordingly, this will prevent problems and crisis relating to food safety standards and guarantee that producers provide safe food to consumers.

This is consistent with Lamerding and Fazil (2000), who highlighted that the main purpose of a risk assessment framework was to provide consumers with safe food. Another respondent noted:

"EU is developed. South Africa is coming up gradually. They have a permissible level of 0.05. But we need to do our own research to find out if it is toxic. If it's not, we can follow suit. So we might deploy whatever is done in EU, we can do same in South Africa. However, we also need to know how these compounds

interact with other compounds in the food matrices. At least we know in EU this is their practice".

In summary, it can be gleaned that there is uncertainty regarding the safety of E551. Hence, there is a need for a unified standard, particularly in providing a method for regulating the safe application of ENMs in food. More particularly, SA would benefit from such a standard as it would to prevent potentially long-term detrimental health effects associated with ingestion of NPs.

4.1.1.3 Theme 3: Mechanism for safety of food containing nano-engineered materials in South Africa and globally

With regard to providing a framework on regulating food containing nano-engineered materials, some of the interviewees felt that a framework for regulating nano-additives used in food must have a holistic approach. They pointed out that government as well as stakeholders must become more conscious of what goes into their food. It was noted that:

"I think government should provide the framework, but also stakeholders from manufacturers to consumers have a role to play. Firstly, the government must bring about regulations. Regulatory bodies must look at the content of the food and examine this against at regulating standards. Furthermore, food manufacturers have a social responsibility to the consumers. They have to start looking at the risk factors associated with nano-engineered materials rather than profit".

"Manufacturers must not be profit-orientated but quality-orientated. It is therefore vital that consumers get into the habit of reading food labels".

Considering the growing number of food products containing ENMs entering the market, there is a need for food manufacturers to inform consumers of its use. Consumer trust and confidence in nano-food can only be achieved through transparent regulation. Therefore, food manufacturers, as a point of responsibility and duty, owe it to consumers to label their products accordingly. This must be done in simple language and in a form which enables the man on the street to comprehend what is contained in his food product.

Although public information regarding knowledge of the use of nano-engineered material as food additives is lacking, one food expert believed that:

> *"Even at this moment, the level of information is not out, there is therefore need to be conscious of the use of nano-engineered materials in food. South Africa urgently need regulatory mechanisms. Information has to flow from production level to consumer".*

Handford *et al.* (2014) indicated that consumer awareness and acceptance of nanotechnology was a significant marketing fear. It therefore stands to reason that such concerns should be clearly addressed in the development of regulatory approaches. Likewise, Mampuys and Brom (2015) found that ethical concerns should be a priority in policy development, given the debate over the issue of GM foods in Europe.

Poor consumer information was identified as originating through a lack of research into the benefits and risks associated with using nano-engineered materials in food.

> *"The first step, there should be more research if these compounds are dangerous and at what level they pose a risk to humans. And when this has been established, then the next level is formulating a law to food industries to say that whatever food you are manufacturing in South Africa, this is the amount that is permissible. As this would prevent indiscriminate use of nanosilica".*

A discussion on the importance of regulating and monitoring the use of nano-engineered materials (E551) as an additive by food manufacturers is presented next.

4.1.1.4 Theme 4: Importance of regulations in monitoring food additives in South Africa.

All the food experts felt that regulating and monitoring food is vital in terms of product quality and consumer safety. One respondent said:

> *"It is very much important. Food regulatory bodies in any country have to guarantee safety first. That's the main reason why you have regulatory bodies – main reason to guarantee consumer safety".*

Generally, E551 is deemed a "generally regarded as safe" (GRAS) food additive by the CODEX General Standard for Food Additives (CODEX Alimentarius Commission

1994). It requires food manufacturers to apply Good Manufacturing Practice (GMP) principles by using the lowest possible level necessary to accomplish the desired effect.

South African food manufacturers comply with the CODEX Alimentarius, which gives them the discretion to use nano-additives to meet their own particular requirements. Of concern, one of the interviewees believed that the practice of GMP in the application of E551 means that no threshold limit is used. As such, this could lead to large amounts of E551 being consumed and result in potential health effects.

> *"Research into food additives must have common grounds in terms of uniformed standards. All companies must use same amounts in terms of additives. It is not wise to give manufactures GMPs to use amounts. It will be detrimental to consumers".*

Similarly, some of the food experts were concerned that manufacturers are being driven by profits and tend to compromise consumers' safety. One noted:

> *"We need food regulations. A large number of food manufacturers are motivated by money and profits. You need to have regulations. Every country has to protect its citizens, one of the human rights. One of the ways, is to make sure manufacturers follow guidelines and standards. Safety of consumers depends on it".*

Food quality and safety are important facets of the right to food. As such, standards like the Codex Alimentarius, have become the global reference point for consumers, producers, food agencies and the international food trade.

However, with the incorporation of ENMs in food and studies pointing to its potential health effects, it would seem that the Codex Alimentarius may not be adequate to suitably protect the rights of consumers to safe and fairly marketed foods. In addition, one of the food experts further depicted the importance of regulatory and monitoring food additives as follows:

> *"In Nigeria, for example the use of bromate in bread. It was a common ingredient for bread bakers to increase bread volume. It gives a bigger appearance. It was discovered this was not safe for human consumption. In*

Nigeria, we have a regulatory body called National Agency for Food and Drug Administration and Control (NAFDAC). They are in charge of food regulations and cosmetics. One case in study is the issue of using bromate in bread-making. NAFDAC informed bread makers that they were no longer permitted to use bromate in bread again because of possible health effects. And because alternatives were more expensive, some of the bread makers did not stick to the regulation. NAFDAC went around inspecting those particular outlets still using bromate. They impounded the manufacturers and the bread".

Considering that many nano-food products may enter the market in the near future, manufacturers applying for market approval have to demonstrate the safe use of such new products without posing undue safety risks to the consumers. Hence, it is crucial for SA to develop a suitable framework to monitor the application of ENMs in food as the benefits of applying safe approaches can only be realised by compliance to standards and regulations.

Conclusively, the aforementioned theme underscores the importance of regulating, as well as the importance of monitoring the use of E551 in consumer food products.

4.1.1. 5 Theme 5: Directives in place to ensure safety of South African consumers from influx of imported foods containing nano-engineered materials

Principal international trading partners of SA include countries within the EU and Asian countries like China and Malaysia. Whilst the EU was the chief importer of goods between 1990 to 2005,

Asian countries have now emerged as leaders of imported goods (Edwards and Jenkins 2014). It is thus necessary to consider the quality of goods entering the country. One of the food experts is of the view that government should play a proactive role by means of regulating not only nano-food within SA but also nano-food coming into the country, to ensure uniformity and prevent technical barriers to trade.

"First line of approach must be from government. They have to put in place regulations, the government needs to be proactive. Some of these imported foods are not regulated, even from production phase. It is then difficult to regulate from the point of consumption. South Africa must regulate what comes

into the country. You regulate to make sure the health standards are met right from the point of entry, that is, the border".

For example, and to further buttress the aforementioned statement, one of the food experts cited that:

"China would not export certain foodstuff into Europe because of the stringent food laws there. Some countries manufacture food exclusively for export, whilst some of this is not the food they would feed their own population because of its poor quality".

With the majority of its population living under the poverty line, it stands to reason that many South African citizens are more concerned with the availability of food than with the quality of food. This resonated with similar sentiments expressed by Adenle, Morris and Parayil (2013) following the introduction of GM technology as a means of tackling food security problems and poverty reduction in Africa. Whilst GM technology offers great potential for increased food production, its development continues to be threatened because of lack of scientific expertise and public concern.

In terms of food quality and its relationship to the ordinary South African, one interviewee stated:

"Food quality to a common man is not a high priority. Level of education of what they are consuming is very low. Often people consume food without any knowledge of what exactly they are eating. We are not conscious. If we are more conscious we may be more wary of the quality of the food we eat".

Significantly, since the fall of the apartheid government, very little has changed in terms of economic distribution of wealth amongst the different races in SA. While SA is food secure at a national level (de Cock *et al*. 2013), the interviewees further suggested that this may not be the case for all households in the country. Given the high inequality of income and asset ownership, the link between poverty, income and food security remains unclear. Hence, targeting policy to reduce poverty remains a challenge.

Ultimately, and from the above-mentioned, it can be deduced that poverty and lack of knowledge of the use of ENMs are, in all likelihood, the major concerns for the ordinary

South African consumer. Equally essential, the interviewees acknowledge that in ensuring the safety of the South African consumers:

> *"There should be a link between research body, regulatory body, and the scientific communities in raising new concerns so as to examine the use of nano-engineered materials critically in order to make regulations."*

Whilst there exist good intentions towards nanotechnology in SA, such as the Nano Advisory Board recently launched by the Department of Science and Technology (DST) and the NNS aimed at research and development (R&D) applications in an effort to tackle some of the country's key development challenges, there has yet to be any meaningful impact on the food vertical. It is therefore incumbent on SA to develop adequate standards and compliance laws for the use of nanotechnology in this area. This could, in effect, potentially also have a huge impact on the rest of the continent. In line with these concerns, the next (quantitative) phase of this study therefore explores the current scope, awareness, and application of nano-engineered materials in South African food products.

4.2 Quantitative phase - Survey

Before discussing the findings of the survey, this section will deliberate on the issue of reliability. The internal consistency of the survey was assessed through Cronbach's alpha reliability coefficient.

As stated by George and Mallery (2003), Cronbach's alpha reliability coefficient normally ranges in value from 0 to 1 and may be used to describe the reliability of factors extracted from dichotomous and/or multi-point formatted questionnaires or scales. The closer Cronbach's alpha coefficient is to 1.0, the greater the internal consistency of the items in the scale.

Table 4-1 Presents the Cronbach's alpha guideline proposed by George and Mallery (2003), which is used to determine reliability of the survey in this study.

Table 4-1: Cronbach's alpha reliabilty coefficient
(adapted from Statistics: How to 2016)

Cronbach's alpha	Internal consistency
α ≥ .9	Excellent
α ≥ .8	Good
α ≥ .7	Acceptable
α ≥ .6	Questionable
α ≥ .5	Poor
α ≤ .5	Unacceptable

Table 4-2 illustrates that the Cronbach's alpha coefficient score for each statement on food additives awareness (α 0.862) in the survey were good. Similarly, the reliability of the statement for nanosilica safety in food (α 0.862), which mainly addressed the awareness of additives approval and safety in food (Table 4.2), was also good. This indicates that there was a level of consistent scoring by the respondents.

Table 4-2: Survey scale in Quantitative Analysis

Survey scales/factors	Cronbach's alpha α	Survey items (Table 1 and 2)
Food additives awareness	0.862	Statement 1-4
Nanosilica safety in food	0.809	Statement 1-3

4.2.1 Current scope and awareness of nano-additives (E551) application in food products in South Africa.

This section presents a reflection of the findings from the questionnaires administered amongst food technologists within Durban, SA, in order to gauge their perception of the current scope and awareness of nano-additives in consumer food products available in SA.

4.2.1.1 Awareness of food additives

As illustrated in Table 4-3, respondents were asked to provide their awareness of food additives and their functions in general. A majority (66.7%) of the respondents strongly affirmed that food additives enhance food flavour, its appearances, and preservation. These findings are in line with European legislation (Regulation 1333/2008/EC) which states that food additives are added to improve flavour, appearance and preservation of food.

More than two thirds (36.7%) of the respondents agreed on the statement of additives adding nutritional value to food. This finding supports the views of Weaver *et al.* (2014) that processed food contributes to nutritional security, which ensures that food quality meets human needs. Interestingly, some of the respondents (23.3 %) remained neutral on this issue. A likely reason the respondents were unable to make a conclusive decision could arise from the current debate on whether additives play an "enrichment" role, that is, in replacing nutrients lost during processing, or a "fortification" role, whereby adding nutrients at higher amounts than that which is naturally occurring in food (Weaver *et al.* 2014).

The majority (33.3%) of respondents agreed that they were familiar with the function and purpose of anti-caking agents used in food products. Moreover, a large number (40%) of respondents agreed anti-caking agents improved the flow characteristics of certain foods. This finding is consistent with Rahman and Padvettan (2012) who found that anti-caking agents in food prevent ingredients from binding. Hence it can be inferred that most people are aware of anti-caking agents used for certain intended purposes in food.

Table 4-3: Awareness of food additives

Statement on food additives awareness	Number of survey respond-ents	Awareness ratings				
		Strongly Agree (%)	Agree (%)	Neutral (%)	Dis-agree (%)	Strongly Disagree (%)
Food additives enhance flavour, appearance, and preservation	30	30.0	66.7	0	3.3	0
Food additives add nutritional value to food	30	6.7	36.7	23.3	20.0	13.3
Familiarisation with anti-caking agents in food product	30	16.7	33.3	30.0	20.0	0
Anti-caking agents improve flow characteristics	30	20.0	40.0	33.3	6.7	0

4.2.1.2 Awareness and safety of nanosilica application in food

On the issue of anti-caking agents containing *nanosilica* particles, Table 4-4 shows that the majority (43.3%) of respondents remained neutral. A likely reason for the respondents' neutrality is the lack of understanding of the terms used in the study of nanotechnology. This finding is in line with studies (Garcia 2010; Bleeker *et al.* 2013; and Karim *et al.* 2014) which found that the lack of proper definitions and descriptions of the terms presently used in nanotechnology has generated confusion. These studies established that in some cases, terms like 'NPs', 'NMs' and 'nanotechnology' were used interchangeably.

Approximately a third (36.7%) of respondents indicated they were aware of how food additives were approved for use in food. Furthermore, more than two thirds (70%) of respondents remained neutral on the safety of nano-additives for human consumption.

This finding is consistent with Bilbao, Avena-Bustillos, Wood, Williams and McHugh (2010) who asserted that the main concern about nanotechnology applied in the food sector is directly linked to the lack of scientific knowledge of processes and objects at the nano level which could potentially lead to harmful health effects to consumers. Hence, it can be deduced from the findings that conclusive evidence on the safety of several food additives now known to contain NPs is lacking.

Interestingly, few respondents (13%) disagreed that food additives were safe for human consumption. It is likely that this points towards doubt in food manufacturers regarding how to ensure the safe application of nanofood additives for consumption and may be attributed to the dearth of information on the application of nanotechnology in consumer products. This is consistent with assertions by Vandermoere, Blanchemanche, Bieberstein, Marette and Roosen (2011) that consumer perception and awareness of the technology will increase as awareness of the science itself increases.

Similarly, communication flow aimed at enabling consumers to make educated choices related to nanofood should be carefully considered from a risk-related perspective, as well as from a consumer perspective.

Table 4-4: Awareness and safety of nanosilica application in food

Statement on nanosilica safety in food	Number of survey respond-ents	Awareness of additives approval and safety in food				
		Strongly Agree (%)	Agree (%)	Neutral (%)	Dis-agree (%)	Strongly Disagree (%)
Familiarisation with nanosilica particles in food additives	30	6.7	23.3	43.3	26.7	0
Awareness of additives approval in food product	30	10.0	26.7	36.7	23.3	3.3
Food additives safe for human consumption	30	6.7	6.7	70.0	13.3	3.3

4.2.1.3 Familiarisation of E-numbers

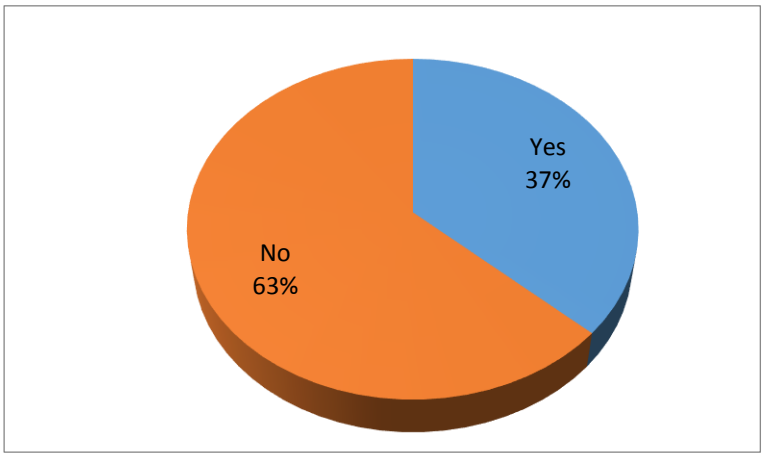

Figure 4-1: Knowledge of E-Numbers on food labels

The majority of the respondents (63%) agreed they are unable to readily identify what most of the E-numbers on food labels represented. Only some respondents (37%) were knowledgeable as to what E-number codes represented on food labels. The most frequently remembered E-number codes of anti-caking agents amongst respondents were: sodium bicarbonate (E500); potassium aluminium silicate (E555); and silicon dioxide (E551). These findings are in line with Grunert, Wills and Fernandez-Celemin (2010) that only a minority of shoppers are able to identify what E-numbers represent on food labels, even though E-numbers were perceived as a way to enlighten consumers about what food additives are present in their products. Therefore, it can be concluded that most people are not familiar or knowledgeable on the meanings of the E-numbers on food labels.

4.2.1.4 Suitable compliance standards in SA to determine the safety of food products containing NPs

As shown in Figure 4-2, the findings reveal that most (70%) of the respondents felt that there were no suitable compliance standards available in SA to assess the safety of food products containing NPs. These findings are in line with Takeuchi *et al.* (2014) that there is no specific legislation or guidelines for the use of ENMs in the food sector in SA.

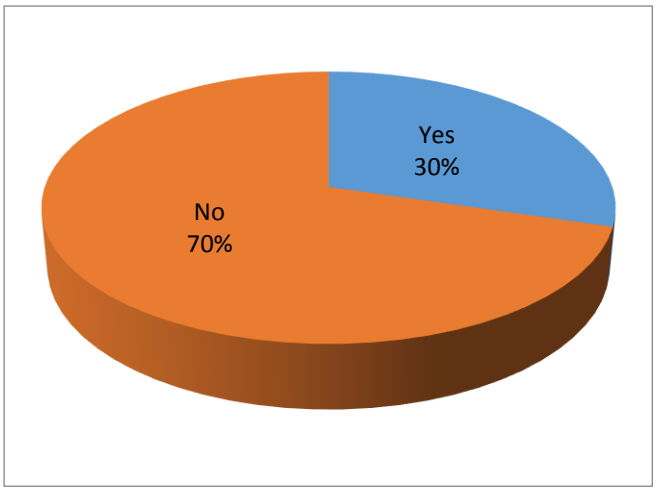

Figure 4-2: Adequate testing standards in SA for food products containing nanonanoparticles

Currently, food additives like E551 are regulated under the Foodstuffs, Cosmetics and Disinfectant Act 54 of 1972 (Regulation 25 of 2004). The Act follows the Codex Alimentarius guiding principle of GMP. This means there are no regulatory levels when E551 is applied to food. This is very concerning in light of public debate on the possible harmful effects of NPs to humans. More concerning is the fact that E551 is permitted in certain foods for infants and young children such as processed cereal-based foods (CODEX Alimentarius Commission 2011).

Given the infancy of this technology in food and the lack of long-term independent data to evaluate its efficacy and safety, this is cause for grave concern.

4.2.1.5 Safety of nanotechnology in food application

In terms of the safety of nanotechnology in food applications, and as demonstrated in Figure 4-3, a majority (55%) of the respondents perceived that nanotechnology application in food is not safe. On the contrary, other respondents (45%) felt that the application of nanotechnology in food applications can be deemed safe. These findings support Azoulay (2012); Coles and Frewer (2013); and Dekkers *et al.* (2013) who independently identified knowledge gaps in risk assessment of NPs in food which may lead to health risks.

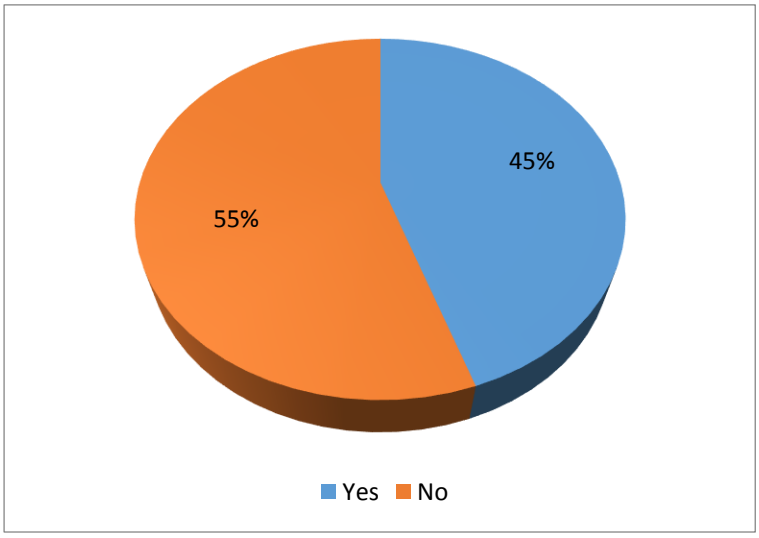

Figure 4-3: Safety of nanotechnology in food application

It can therefore be established that much of the debate generated around the safe use of nanotechnology in food applications has focussed on the uncertainties and unknowns, and the lack of toxicological data. Thus, in order to justify the benefit from the advantages of this technology, the potential health risks need to be understood.

4.2.1.6 Awareness of health implications resulting from the ingestion of nano-derived particles

Findings in Figure 4-4 revealed that 93% of the respondents have no knowledge of impairment to health associated with the ingestion of NMs. This is consistent with Handford *et al.* (2014) in that the possible effects of NPs through ingestion are mostly unknown due to lack of long-term toxicology research.

The remaining respondents (7%) affirmed they were aware of incidents of damage cause by NMs to human health. Their response of the health effect associated from NMs is described as: "*breathing of ultra-fine particles causes lung inflammation and damage from its use in sun screen*", as well as "*any food preserved using silica is dangerous to health*". These findings support the views of Martirosyan and Schneider (2014) that exposure to NPs may potentially lead to an immunomodulatory effect that may cause an inflammatory response leading to inflammation-associated diseases such as Crohn's disease. It can therefore be deduced that, at the moment, there is no sound evidence and no general conclusion on whether food derived from nanotechnology, is safer or more dangerous.

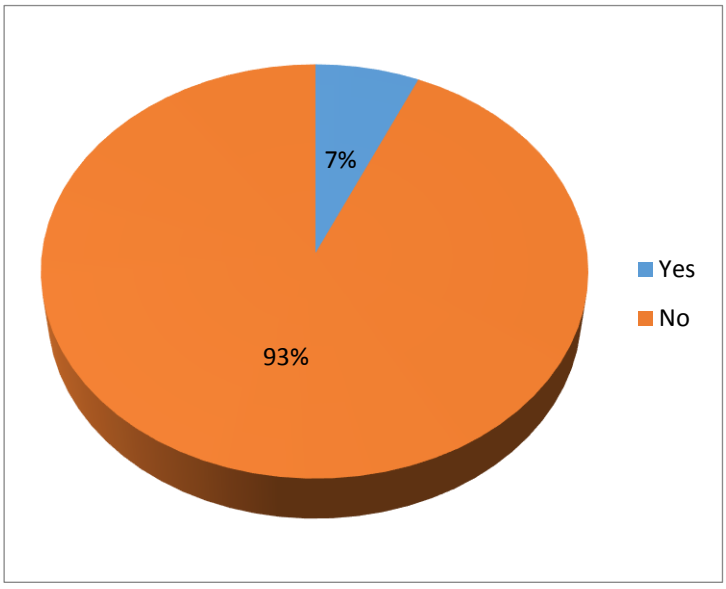

Figure 4-4: Awareness of cases of health implications caused by ingestion of nanoparticles

4.2.1.7 Consumer Awareness in South Africa on the inclusion of NPs in food products

As shown in Figure 4-5, a large majority (89%) of respondents felt that public awareness of the application of nanoparticles in food is very limited.

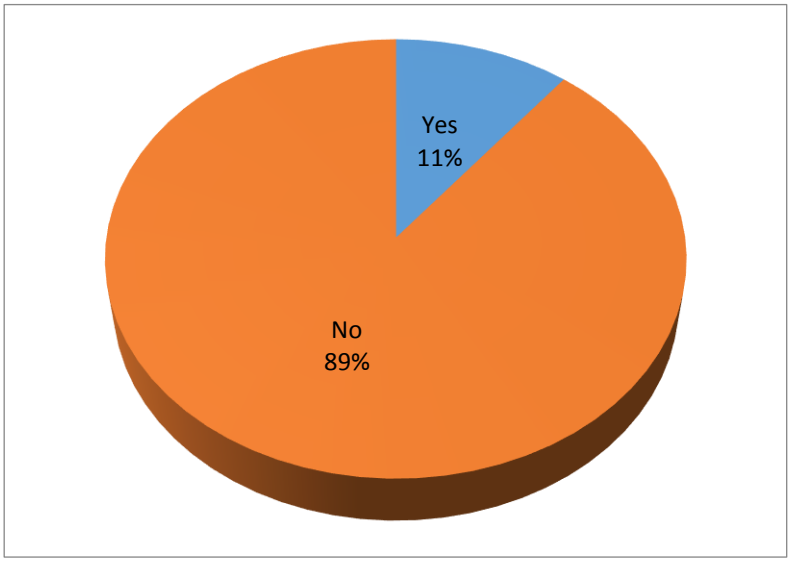

Figure 4-5: Awareness of consumer in SA of the inclusion of nano-particles in food products

These findings are in keeping with assertions by Yawson and Kuzma (2010); Frewer *et al.* (2011); and Rollin, Kennedy and Wills (2011) that a large portion of the public is not familiar with nanotechnology and people who have heard about it possess limited knowledge of the technology. As a result, ordinary consumers may not directly judge the benefits and risks derived from nano-food.

Due to this lack of awareness it is therefore important for the scientific community to learn from previous introductions of new technologies and to be particularly sensitive in the area of food. For example, GM foods were not well-received by consumers because there was a perceived risk associated with them. It is therefore incumbent on SA to proactively develop adequate standards and compliance laws targeted to help meet critical human health, nutritional and societal needs.

4.3 Quantitative phase - Analytical techniques for the identification and quantification of E551 in the selected food samples

Commercially available food-grade silica (nanosized range of 70 nm), CAS No 112945-52-5 was used as a point of reference for the identification of the presence of E551 in the selected food matrices. The analytical techniques used are discussed in the next sections.

4.3.1. Fourier transform infrared spectroscopic (FT-IR)

The FT-IR was used to identify the structure constituents of the food products. This was to confirm the presence of the chemical compound, silicon dioxide (SiO_2). As illustrated in Figure 4-6, the FT-IR spectra for commercially available food silica measured with several bands from 500 cm^{-1} to 450 cm^{-1}.

Prominent absorption peaks of silicon dioxide were observed at 1094 cm^{-1} and 480 cm^{-1}, which is associated with silica. Silicon dioxide is detected by the broad stretching frequency of the Si-O-Si in silica ions around 1094 cm^{-1}, 798 cm^{-1} and 470 cm^{-1} (Gui-Long, Changyun, Pi-hui, Jian and Zhuoru 2011; Athinarayanan *et al.* 2014).

From Figure 4-7, the FT-IR spectra of the instant soup, seasoning, and coffee creamer shows the presence of silica at absorption peaks of 1094 cm^{-1}. The Broad bands appearing at wave number values of 1094 cm^{-1} are indicative of the presence of SiO_2 in the aforementioned South African food products.

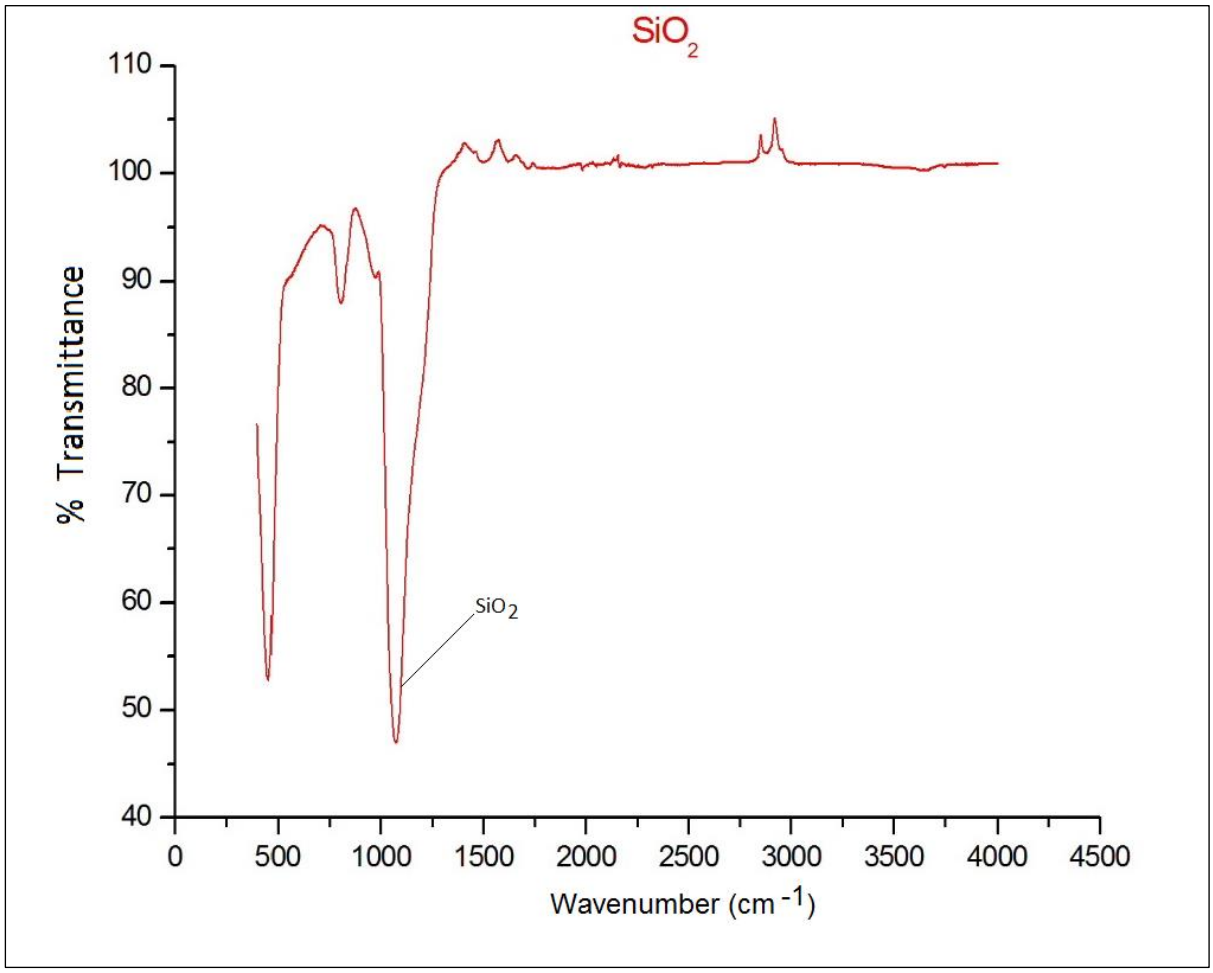

Figure 4-6: FTIR spectra of commercially available food grade silica

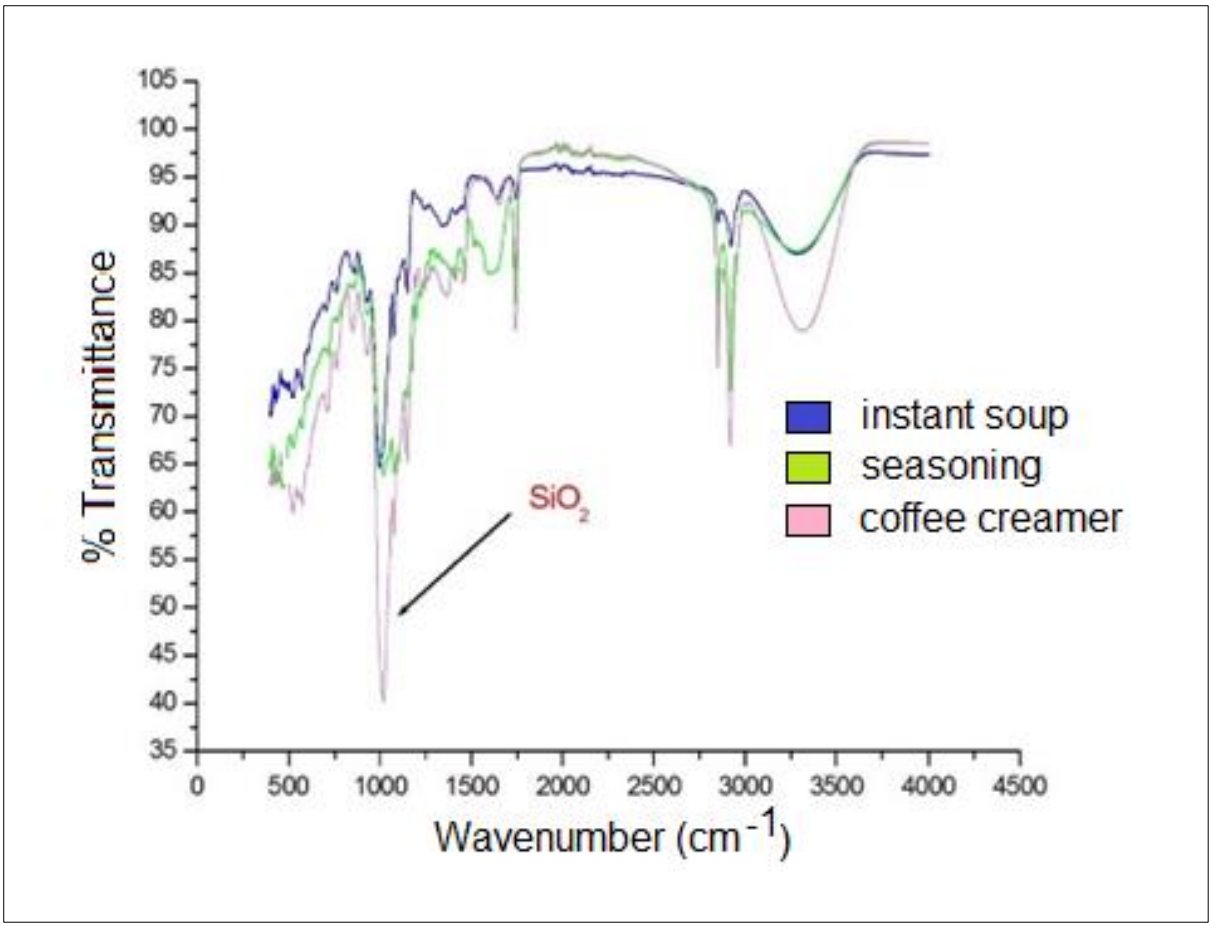

Figure 4-7: FT-IR spectra showing the presence of silica in (blue) soup; (green) seasoning; (pink) coffee creamer

Similarly, and as illustrated in Figure 4-8, depicts the functional groups present in coffee processed and packed in SA, South Korea, Poland, Malaysia and UK, respectively. The finger print, that is, the peak value elucidates the presence of SiO_2 and OH groups (present of surface of nanosilica) and the intensity of peak quantifies the amount of silica in processed coffee. From the above figure it was observed that peak values are constant at 1096 cm^{-1} for SiO_2 and 3000 cm^{-1} for OH. Increases in intensity for both peaks are directly proportional to each other, which confirms presence and increase in silica in processed cofffee. It was further observed that the South Korean processed coffee had the highest amount of silica and the least being in UK processed coffee. The amount of silica in processed coffee decreases in following order South Korea >> SA >> Malaysia >> Poland >> UK.

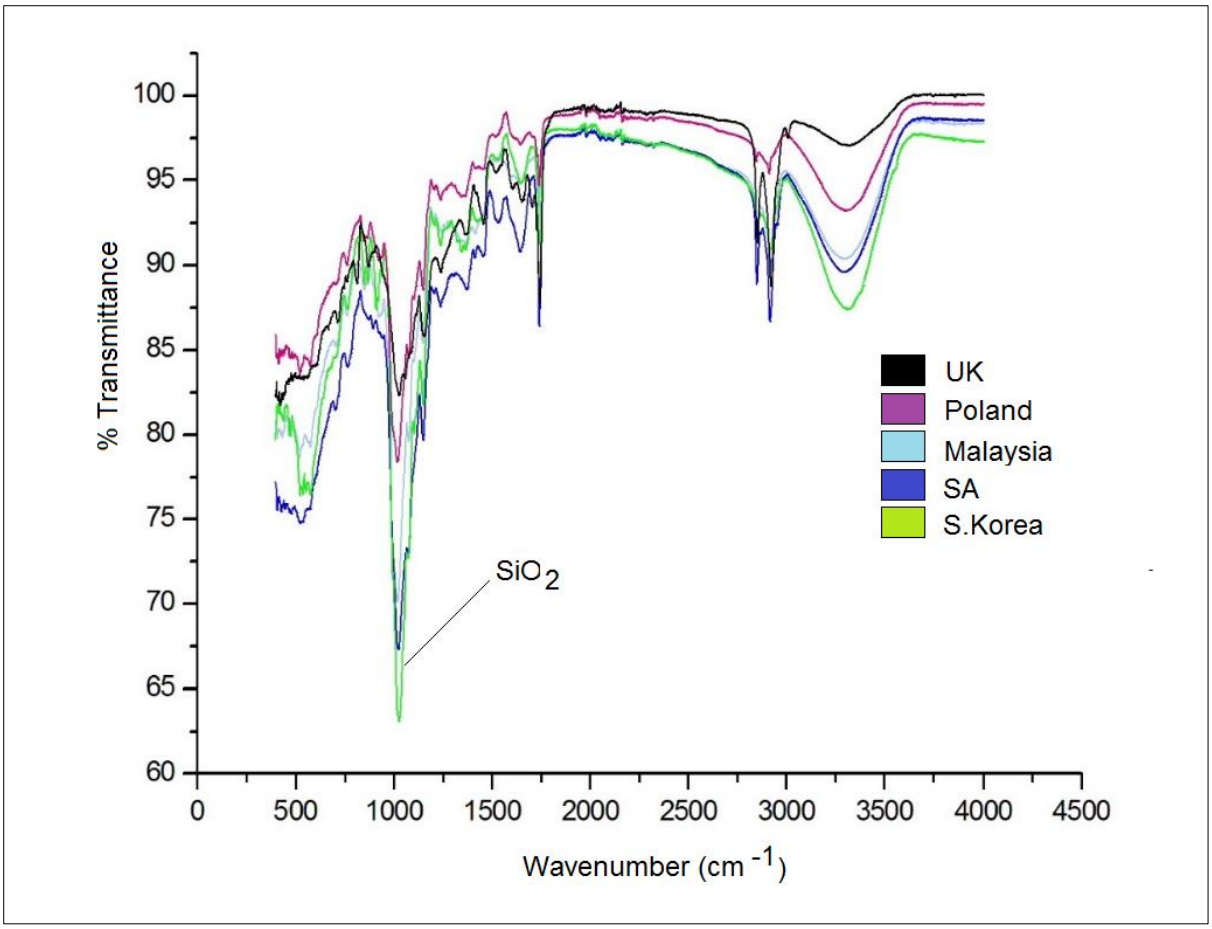

Figure 4-8: FT-IR spectra showing the presence of silica in coffee: (cyan) South Africa processed coffee; (blue) South Korea processed coffee; (green) Poland processed coffee; (pink) Malaysia processed coffee; (black) United Kingdom processed coffee.

4.3.2 X-ray diffraction (XRD)

In addition, and as illustrated in Figures 4-9 to 4-11, the XRD pattern was used to identify the form of silicon dioxide that is present in the selected food samples. It was imperative to determine the form of silica in the samples because E551 is prescribed to be amorphous in nature (Athinarayanan 2014). The selected samples were compared to a peak with a 2Ø value of 22º which is indicative of SAS (Addendum 7).

Figure 4-9 (a) – (d) which examined the SA samples of instant soup, coffee, seasoning and coffee creamer, showed that seasoning and coffee samples were crystalline in nature whicle the instant soup and coffee creamer were amorphous in nature.

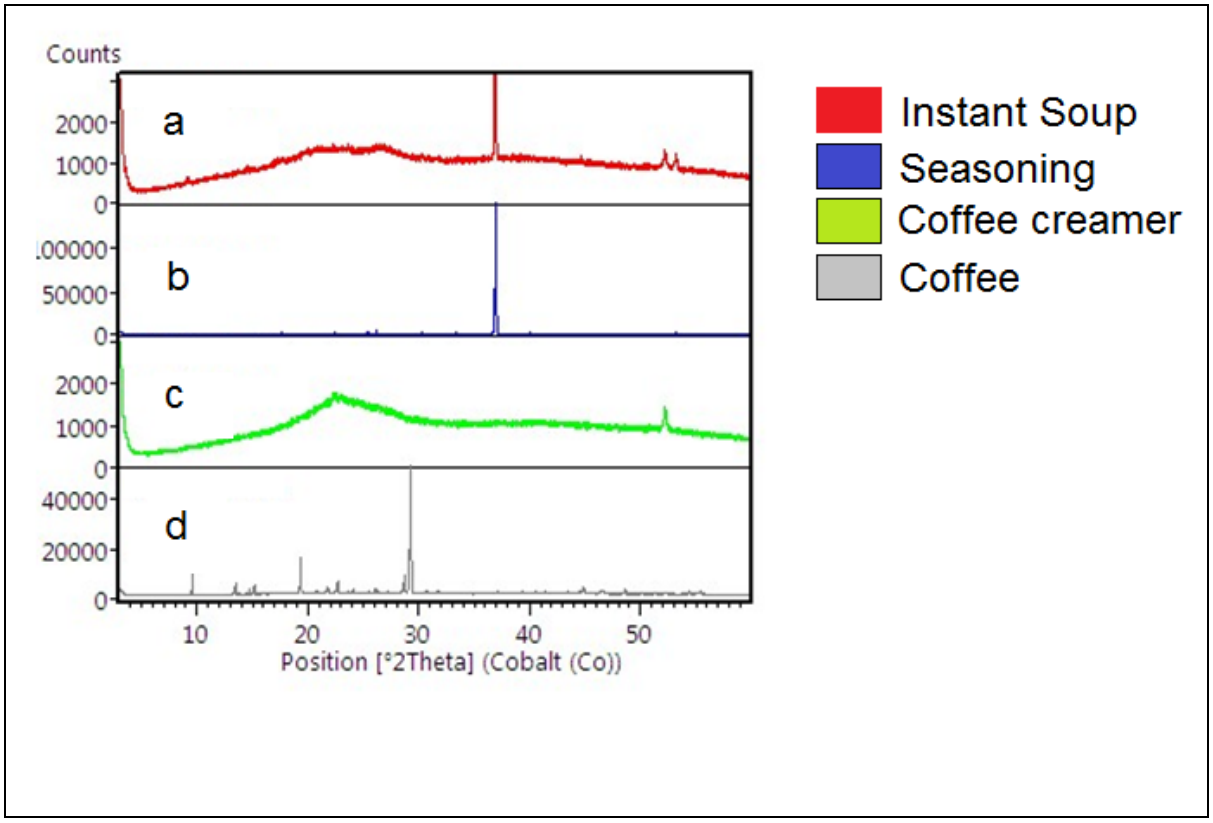

Figure 4-9: XRD pattern of selected South African food product (a) Instant Soup; (b) Seasoning; (c) Coffee creamer; (d) Coffee

Figure 4-10 (a) and (b) which examined the Asean countries' coffee samples revealed that the South Korean sample was amorphous in nature whilst the Malaysian sample showed traces of crystalline.

Figure 4-11 (a) and (b) illustrates the Poland and UK coffee samples where both samples were amorphous in form which was indicative of E551.

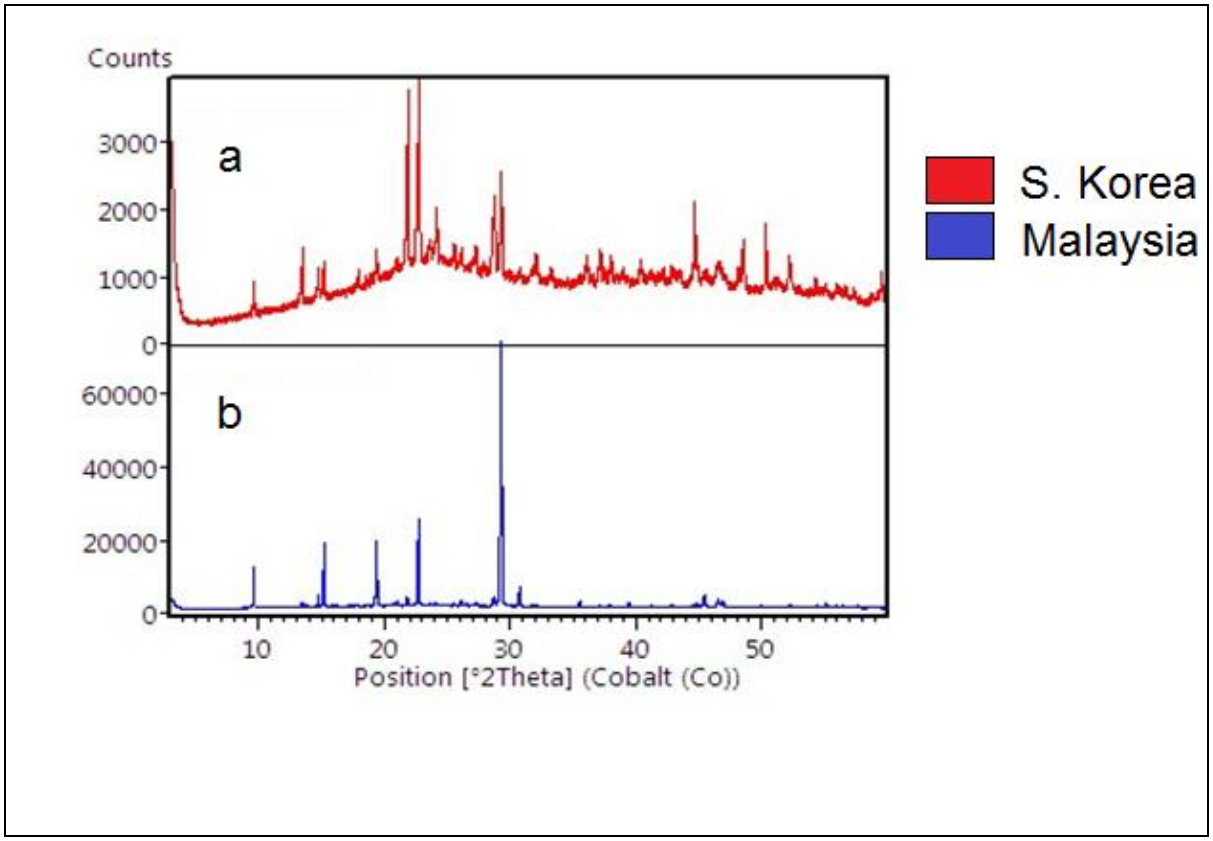

Figure 4-10: XRD pattern of selected Asian food product (a) South Korea coffee; (b) Malaysia coffee.

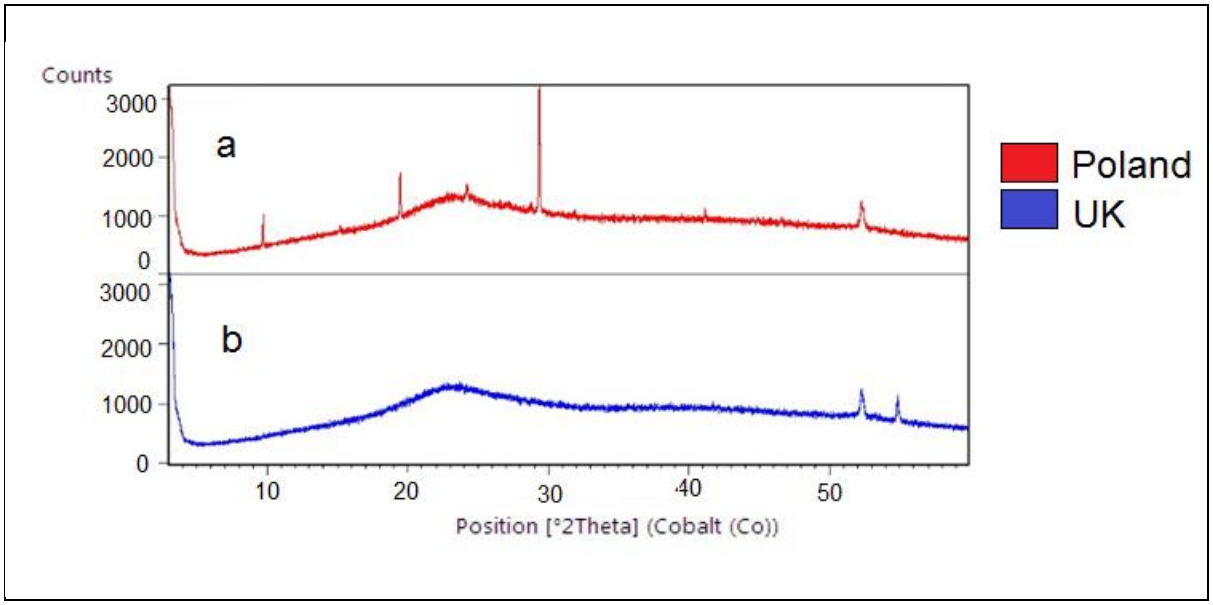

Figure 4-11: XRD pattern of selected EU food product (a) Poland coffee; (b) UK coffee.

4.3.2.1 Type of silica found in the selected food samples

The type of silica found in the selected food samples is illustrated in Table 4-5.

Table 4-5: Forms of Silicon dioxide found in the selected food samples

Type of product	Country processed and packed	Form of Silicon dioxide present
Coffee	South Africa	Crystalline
Soup	South Africa	Amorphous
Coffee	United Kingdom	Amorphous
Coffee	Poland	Amorphous
Creamer	South Africa	Amorphous
Coffee	Malaysia	Crystalline
Coffee	South Korea	Amorphous
Seasoning	South Africa	Crystalline

Although labelling on the sample products indicated the incorporation of E551, XRD results, illustrated in Table 4-5, revealed that some of the products, namely the Asean sample manufactured in Malaysia, and some of the South African samples (seasoning and coffee), showed the presence of crystalline silicon dioxide. In other words, these products were incorrectly labeled.

The identification of crystalline silica is of concern, since literature (Peters *et al.* 2012; Dekkers *et al* 2013; Athinanaryan 2014) established that E551 is amorphous silica. According to Cocco *et al.* (2001) and Cocco (2010) exposure to crystalline silica is likely to induce perilous health effects such as cancer and fibrosis. These results are commensurate with Aung and Chang (2014) in that the current disclosure on food labels does not necessarily imply that food is authentic, good quality and safe.

This finding resonates with calls by experts interviewed in this study, for a need to regulate and monitor the influx of imported food, particularly from developing nations in Asia (*Theme 4 and 5*).

In summary, the most noteworthy contribution in the foregoing section demonstrated the benefit of regulating and monitoring the quality of additives such as E551, used in commercially-available food products in SA. This can be achieved by adopting an appropriate risk management system to ensure that the correct form of ENMs are incorporated in food. Such an approach will ensure product safety and quality for food that incorporates ENMs.

4.3.3 Energy dispersive x-ray spectroscopy (EDX)

With reference to the levels of silicon dioxide that are present in the sample products, SEM with an EDX set-up was used to analyse the *Si* content in the food product. According to Contada, Ravani and Passarella (2013), the *Si* content in commercially available food products is indicative of the E551 (silicon dioxide) count in the product.

The EDX spectrum revealed the intensity of the elemental mineral present in the selected South African food products. As shown by the EDX spectrum in Figure 4-12, the highest peak of silica was detected in seasoning (Sample b), whereas the lowest peak of silica was observed in the coffee (Sample d).

Table 4-6 shows that the *Si* levels in wt% in all selected South African commercially available food products revealed different Silicon dioxide (E551) counts. Based on the Si level in the selected food samples, it can be gathered that the amount of E551 added into the food matrices are subject to the discretion of the manufacturers. This is further supported by the EDX spectrum shown in Table 4-7.

Table 4-6: Silicon dioxide levels in selected South African food samples

Products	Si content Wt%
Coffee	0.05
Creamer	0.09
Seasoning	0.64
Instant soup	0.13

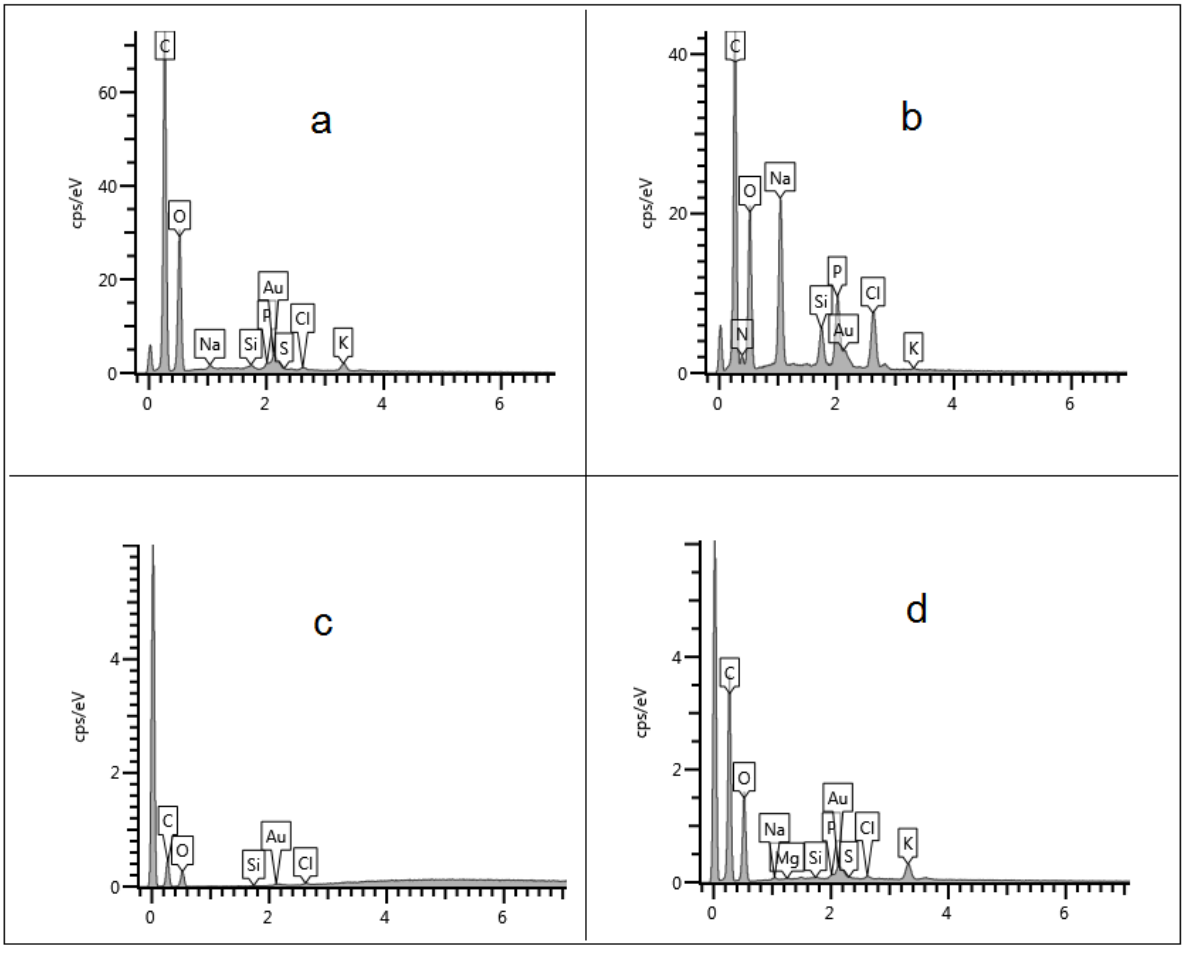

Figure 4-12: EDX spectrum of selected South African food product (a) creamer; (b) seasoning; (c) instant soup; (d) coffee

More so, and as demonstrated in Table 4-7, a powdered coffee mixture processed and packed in SA was compared against other coffee products processed and packed

in South Korea, Poland, Malaysia, and UK, respectively. Elevated *Si* levels are evident in the coffee products processed and packed in SA, South Korea, and Malaysia. In contrast, the *Si* level in coffees processed and packed in Poland and UK, respectively, were not detectable with the EDX analytical techniques, indicating that the *Si* level was lower than the detection limit of the EDX instrument and the EU legislation of maximum 0.01wt.%. Granting that both the FT-IR (Figure 4-8) and the XRD (Figures 4-9 and 4-11) confirmed the presence of silica in both coffee samples, it is indicative of the low levels present in the Poland and UK samples.

Table 4-7: Silicon dioxide levels in selected coffee samples

Type of product	Country process and packed	Si content *Wt%*
Coffee	South Africa	0.05
Coffee	South Korea	0.30
Coffee	Poland	Not detectable
Coffee	Malaysia	0.07
Coffee	UK	Not detectable

Even though no prescribed threshhold limit for the toxicity of *Si* has yet been determined, this finding is concerning in light of studies as shown in chapter two, section 2.3.1 that high concentration of isolated E551 triggered cellular damage, mitochondrial membrane potential depletion, and ROS generation when they exposed normal human lung fibroblast cells to different levels of E551.

As already noted in Table 4-7, high Si level is evident in the coffee product processed and packed in SA, South Korea, and Malaysia. In contrast, the Silicon dioxide level in coffees processed and packed in Poland and UK, respectively, were not detectable with the EDX analytical techniques.

Consistent with Electron Microscope Unit (2013), the absence of *Si* counts in the Poland and UK coffee indicates the low content of E551 additives added to both coffee products. These findings are further supported by both FT-IR (Figure 4-8), and XRD (Figures 4-9 and 4-11) that confirmed the presence of amorphous silicon dioxide (E551) in both coffee products.

Overall, and as deducted from the aforegoing phase, the salient feature is that South African food products (seasoning 0.64 wt%, instant soup 0.13 wt%, creamer 0.09 wt%, and coffee 0.05 wt%) had an elevated silica weight concentration as compared against the EU countries (Poland and UK).

As mentioned in chapter one, section 1.2, the Codex Alimentarius permits the addition of E551at its lowest possibe limit. It can be infered that this permit is being very loosely applied because, from the samples investigated above, there is no uniform quantity of Si that is applied to similar products.

Overall, and as deduced from the foregoing phase, the salient feature of this section indicates that due to the elevated Si levels in the South African food sample, the Codex Alimentarius may not be suitable to food products containing ENMs. The above findings deserve action because, in the case of daily exposure, the accumulation of NMs in the human body derived from multiple food products containing nanoparticles, may be in excess of its daily recommended concentration and thus bioaccumulate over time (Michel, Scheel, Karsten, Stelte and Wind 2013). This is especially concerning considering the amorphous nature of the SA samples and the ongoing debate regarding the application of nanotechnology to food.

In summary, the findings of the experimental work in this study demonstrated the need for more stringent regulations and monitoring of the quality and quantity of nanosilica used in commercially-available food products in SA. In light of recent concerns raised around the health and safety of consumers from the ingestion of nanoparticles, it has become imperative to identify and understand food materials and food processing at the nanoscale (Cushen *et al.* 2012). Furthermore, it can be argued that regulating the processes involved in food production, processing and conservation is not as thorough as it should be in most developing countries particularly those based in Africa.

In light of the above findings, this study proposes a quality management framework, referred to as the HAC model (Figure 4-13) for the application of E551 in food products in SA. (HAC is an acronym for '*Hazard identification, Access the risks, Control the risks*').

4.4 Proposed model for risk assessment, communication and management tools for food grade nanosilica

As reported in this study, ENMs compared to their bulk-scale counterparts, have novel or distinct properties due to their nanoscale size. For this reason, unexpected toxicological effects might occur if not properly handled or used (Arts *et al*. 2014). Significantly, considering the increasing use of silica NPs in consumer products, their fate and effects on human health are of growing concern. As such, McAlea (2015) reported that organisations involved in the manufacture and supply of this material carry the responsibility to understand the risks that this material may pose not only to customers, but also to the health and safety of their workforce. Therefore, they need to put in place measures that are necessary to manage and minimise these risks.

As described in section 2.4.1., studies showed that the exposure to certain NPs (carbon black, silicates, titanium dioxide and iron oxide) may lead to oxidative damage and inflammatory reactions of the gastrointestinal tract in humans. More concerning, a study by Silvestre *et al.* (2011) found that long-term exposure to some NPs were associated with acute toxic response including lesions of the kidney and liver, as well as numerous forms of cancer. As such, Bouwmeester *et al.* (2014) noted that there were calls by food agencies to have the safety of silica NPs in foods tested before they are available on the global market.

Furthermore, and as highlighted in section 2.5.1., there is a dearth of frameworks in SA to effectively regulate and monitor the application of nano-food additives like E551. As ENMs are already on the market, it would seem that in some cases the risks are poorly understood and inadequately controlled. This has resulted in minimal regulation or lack of regulation.

According to Hansen *et al*. (2008), several government agencies, academic scholars, as well as industry stakeholders, have contended that the basic principles of risk assessment can be applied effectively to NPs as long as some adjustments are implemented since present safety and risk assessment requirements are based on

knowledge gathered for bulk counterpart materials which may not necessarily be adequate for NMs. This implies that conventional study approaches need to be redesigned for the application of NMs in food products.

From the literature review of this study, several challenges have been identified that have contributed towards a number of strategies for the managing and monitoring of nanotechnology within the food sector. Fautz *et al*. (2014) highlighted that some global regulatory agencies have been receptive and have embarked on approaches for more effective risk assessment methods which would result in the adoption of more laws to safeguard consumers.

The following challenges have been identified in this study:

- Lack of a harmonised global definition for nanotechnology in order to expedite regulatory discussions and exchange of information on risk assessments.
- Knowledge gaps on the oral bioavailability and toxicity of the different types of ENMs, with special attention to those parts of the body that are normally protected by barriers like the blood–brain barrier and placenta.
- Lack of information and awareness on products containing NPs that are on the market or being developed. This includes the type of ENMs used and the estimated consumption of these products.
- Deficiency of regulatory approaches for the disclosure of information on ENMs being produced including the products in which they are incorporated.

It has also been established, and as indicated in section 2.6.1, that the present state of knowledge on ENMs is limited and consequently inhibits risk assessors from addressing the safety aspects of food products in a coherent and comprehensive manner.

Whilst granting that this effectively increases uncertainties, Puzynet *et al.* (2011) advocated for the development of quality-controlled databases to obtain information on the occurrence of ENMs in food. Such a database would be a valuable resource to identify certain patterns of behaviour and/or toxicity of NPs, such as toxicological size-thresholds. Significantly, this could be applied in the risk assessments in food and, as such, reduce the risks associated with nanomaterial usage. Additionally, this study

found that the scientific community and policy makers are keen to avoid the situation that developed when GM foods were introduced into the market, in which a public backlash and lack of confidence was displayed by the majority of consumers.

This backlash was blamed on lack of public engagement, thus consumers were not provided with a platform to engage with the scientific community on the issue of engineered food (Rothstein 2013).

In the light of the above concerns, the researcher proposes a quality management system, known as the HAC, or '*Hazard identification, Access the risks, Control the risks' model*. The HAC model can be adopted by a food manufacturing organisation incorporating E551 into its product.

4.4.1 Benefits of the HAC model

As highlighted in section 2.1.1, risk assessment of nanotechnologies in the food sector would establish a sound foundation on which commercial products can be launched with assurance, or withdrawn to safeguard consumers and the environment from potential hazards. As there are no efforts in place to regulate NMs in food in SA as yet, according to Musee *et al.* (2010), adherence to a risk management framework would establish parameters for the safe and controlled application of E551. Hence, the three step HAC model that is proposed would pre-empt potential regulation or demonstrate responsibility in the production of food products incorporating NMs.

This study established that certain food samples contained traces of crystalline silica. This is of concern as a study by Dekkers *et al*. (2011) demonstrated that E551 is amorphous in nature and does not contain crystalline silica. This means that the product listed in the ingredients list is not indicative of E551.

The findings in this study have direct implication on compliance to labelling regulations in SA and elsewhere in the world.

Hazard identification (step 1 in Figure 4-13) is one the most crucial features of the model. The characterisation techniques suggested in the model would enable good science-based decision-making for the application of E551 in food products.

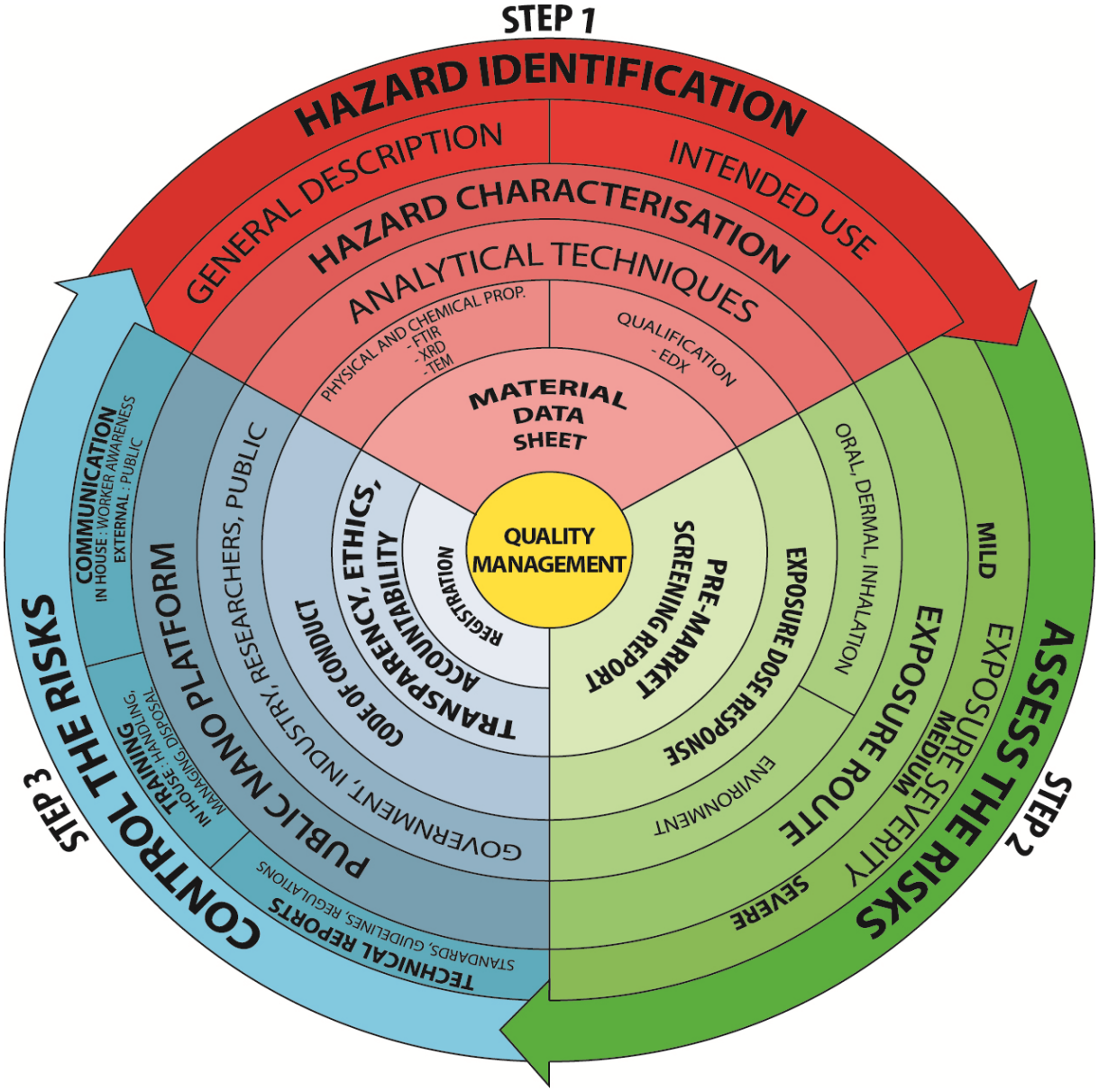

Figure 4-13: Proposed HAC model for the incorporation of E551 in food products in SA (developed by Researcher).

Another advantage of the model is the risk control measures proposed. Results from the semi-structured interviews and questionnaires revealed that the majority of consumers were unfamiliar with the use of nanotechnology in food products due to lack of information and awareness. As reported in sections 4.1.3 and 4.2.1.2. lack of awareness can subsequently result in distrust toward food manufacturers if products are found to be unsafe.

Thus, a feature like a public nano platform between all relevant stakeholders, including government, industry, scientific community and consumers, will provide greater transparency and comprehensive information regarding NMs and their application in food. Grieger et al. (2016) agreed that engaging consumers on matters relating to NMs in food on a public platform could avoid potential backlashes and suspicion as occurred with GM foods.

In addition, Grieger *et al.* (2016) observed that these benefits will result in a number of positive developments towards overcoming existing challenges such as labelling of nano products and public acceptance of the technology. As such, the aim of the model was to develop a list of activities that should be undertaken to demonstrate the best risk management methods to use to ensure that food safety, worker safety and effective risk control measures are considered when working with E551.

The features of the HAC model were consolidated from a variety of sources that included technical reports such as ISO standards; regulations and guidelines; research papers; as well as interviews, surveys and experimental work using analytical techniques conducted by the researcher. This served as a point of departure in developing the proposed model. The basis of the proposed model takes its root from the relevant EU regulations relating to NMs.

The researcher was guided by the literature review which established that the relevant EU regulations were the ideal choice to base the model upon. The EU is, firstly, the only region globally to have established nano-specific provisions in its existing regulations for the management and use of nanotechnology, and secondly, the applicable laws and EU directives are simple to understand.

4.4.2. The HAC model – description and usage

The HAC model as shown in Figure 4-13 illustrates a proposed risk management model for the incorporation of food grade silica into selected food products. The steps proposed cover the activities of hazard identification, hazard characterisation, followed by exposure route, a risk assessment and exposure severity. Since this process centres on the manufacturing of E551, the proposed model provides an organisation with a platform for the handling and managing of NMs and the various likely associated exposures during its life-cycle.

In addition, the HAC model will provide management with the minimal control measures and safeguards that are critical when working with this particular ENM. As previously stated in this study, very little is known about the risks and hazards of NMs to human health and the environment. It can therefore be argued that these steps will ultimately deliver the necessary quality and safety controls needed to ensure that food products containing E551 enter the market with consideration given to minimise the health risks to consumers and the environment.

The steps of the proposed model are discussed in detail below:

Step 1: Hazard Identification

As discussed in section 2.6.1, hazard identification is the first sub-step in a risk assessment process. Assessment of the steps under hazard identification will offer the organisation a better understanding of food-grade silica, its characteristics, its intended use, and the potential hazards associated with it. This data is crucial to ensure the correct handling of E551 and anticipate its behaviour when interacting with its environment. According to Keikotlhaile and Spanoghe (2011), there are two sub-steps of hazard identification:

Sub-Step 1.1: General description and intended use

This sub-step establishes a general description of the nanomaterial being evaluated and its intended function. As illustrated in figure 2-2., there are various forms of SiO_2 available on the market and as such specific identification of SiO_2, which in this case is SAS, must be established at this juncture. One of the ways of confirming E551 is its CAS number (Dekkers *et al*. 2013). The function of E551 and its permissible levels in food products can be sourced from international food standards like Codex Alimentarius (Commission 2013), as shown in section 1.2. The next step characterises the nanomaterial's physical and chemical properties.

Sub-Step 1.2: Hazard Characterisation

This sub-step is to determine the material profile of E551, such as its physical and chemical properties; its inherent environmental, health and safety hazards; and finally the associated potential health risks throughout the NM life-cycle (ISO 13121: 2011).

A material profile is important from a toxicological and health perspective. As indicated in this study, as the size of the particle decreases, its surface area increases, this allows for a greater proportion of its atoms to be displayed on its surface area. These atoms on its surface area may potentially be chemically and biologically reactive which could contribute to the development of adverse health effects.

A report (WHO 2010) informed that the objective of hazard characterisation was to obtain a qualitative or quantitative description of the inherent properties of the agent having the potential to cause adverse health effects as a result of exposure. So, once the ENM is identified and described in *sub-step 1,* its physical and chemical properties must be evaluated. This information can be derived from scientific data guideline documents such as EFSA (2009) *Risk evaluation of silicon dioxide* as well as from the scientific community in the form of published academic literature (Aureli *et al*. 2015; Bosch *et a*l. 2012; De Temmerman *et al.* 2012; and Athinarayanan *et al*. 2014) as stated in section 2.3.3.3. Some of the available characterisation methods such as FT-IR, XRD, EDX and TEM techniques were used in this study and reported in section 4.3.

Whilst these analytical techniques are recommended here, it must be noted that there is currently ongoing research addressing other techniques. These techniques include inductively coupled plasma optimal emulsion spectrometry (ICP-OES) and Raman Spectroscopy for characterising ENMs in complex matrices such as food (Blasco and Pico 2011). As such, characterisation techniques for E551 must be updated when necessary in light of future and emerging information. The process of developing these profiles is important as it will contribute to the knowledge base by building on the data gaps identified in this study.

After chemical composition and physico-chemical properties are identified, the risk of E551 can now be determined for its potential exposure levels. The next step will assess the risks associated with the levels of exposure during the handling of E551.

Step 2: Assess the risks

This part of the model concerns the assessment of the exposure to workers as a result of the manufacture, handling and use of E551.

As described in section 2.6.1.2., exposure assessment is used to determine the levels of exposure and the relevant routes and pathways by which people who are in contact with hazardous materials are exposed. Here, information from the characterisation of E551 in the previous step is evaluated to identify the magnitude of risks associated with exposure. The steps for exposure assessment is discussed with considerations for the severity of the exposure and the routes of exposure.

Sub-Step 2.1 Exposure Route

As discussed in section 2.4.1, there are three possible routes by which workers can be exposed to ENMs, namely, ingestion, inhalation and penetration. However, as with most particles in the workplace, inhalation is considered to be the primary route by which NM can enter the body (ISO 12885: 2008). This step identifies the three exposure routes.

- ***Inhalation:*** In the workplace, this is considered the primary route in which NPs can enter the human body. As reported by Martirosyan and Schneider (2014), once in the body, NPs can deposit in all regions of the respiratory tract.
- ***Ingestion****:* In the workplace NMs can be ingested via contaminated food or water or contaminated surfaces or skin contact (ISO 12885: 2008).
- ***Penetration:*** This contact can occur through lack of unprotected clothing or contaminated surfaces in the workplace (ISO 12885: 2008).

It is pertinent for the organisation to adequately assess the levels of exposure as studies reported in section 2 further highlighted that, in the case of daily exposure, the behaviour of NMs in the human body may result in accumulation over time. As such, possible accumulation must be considered in risk assessment (Cockburn *et al*. 2012).

Adherence to this part of the model will ensure that workers who are exposed to NMs in their workplace receive sufficient instructions, information and training to understand the risks to their safety and health caused by potential exposure to NMs, and the precautions that should be taken to avoid or minimise such exposure. If there are uncertainties about the health and safety impact of these NMs, workers must be informed about this, and adequate precautionary measures implemented by employers such as personal protective equipment (PPE) must be implemented as stipulated in EU Directive 89/391/EEC (Marendaz, Suard and Meyer 2013).

Sub-Step 2.2: Exposure severity

In this sub-step, users must determine how often the person is exposed to the risk (frequency) and for how long (duration). If possible, the likely dose to which the person is exposed should be determined. Users must consult safety data sheets and academic literature as shown in section 2.4., which reports on levels of exposure that can potentially have adverse health effects. Exposure severity must be measured as mild, medium or severe (Savolainen *et al*. 2010).

Step 3: Control the risks

In the final part of the proposed model, users will evaluate the information from step 1 and step 2 to implement the appropriate standards, policies and guidelines in order to control the identified or perceived risks.

This study identified the risk controls that are appropriate for the proposed model. These included technical reports such as relevant ISO standards and pertinent regulations relating to NMs, training in the handling of NMs, and communication risk management to build trust along the life-cycle of NMs.

Sub-Step 3.1: Technical reports, regulations, training, and risk communication

Technical reports such as ISO/TR 13121: 2011 and ISO/TR 12885: 2008 provide users with specific guidelines on critical information needed for risk assessment of NMs. The approaches offered in these two reports are appropriate for the food sector and the workplace respectively.

Relevant regulations: Here, users can review appropriate measures that are in place globally towards the safe handling and application of NMs. As reported in section 2.5, Takeuchi *et al.* (2014) noted that SA has yet to develop a national research strategy to investigate the environmental, health and safety risks of nanotechnology. In the meantime, SA can adopt safety assessment guidelines from EU regulatory frameworks as mentioned in chapter two section 2.4.1.1. The relevant regulatory frameworks relating to food safety and NMs include REACH (Regulation EC No. 1907/2006); Classification, Labelling and Packaging Regulation (Regulation EC No 1272/2008); Framework Directive 89/391/EEC; and General Product Safety (Directive 2001/95/EC). The above regulatory frameworks are adapted for the proposed model.

Regulations such as REACH and CPL can provide a direction towards an appropriate implementation of nanotechnology application in SA.

***In-house training*:** Here the organisation will ensure that those involved in the handling, managing and disposal of E551 are properly trained and supervised. As reported in section 2.6.1.2, ISO/TR 13121:2011 and ISO/TR 12885:2008 can offer relief in safely managing NMs and worker exposure in the food sector by providing safety assurance guidelines.

***Risk communication*:** In this step, the organisation will ensure that the potential risks identified in step 1 and 2 are communicated to workers (internal) to create awareness of effects and side-effects of exposure scenarios and the safety precaution measures available to them. Similarly, this step also allows users to communicate with the public (external) on the risks and benefits of E551. As highlighted in section 4.1. by respondents in this study, the intention of participation initiatives by the food sector to the general public cannot be to convince them to accept that the risks are acceptable. Rather, the intention here is to include all stakeholders in the communication process by making it easier for them to obtain the necessary information, as well as providing options for dialogue and participation to converge at an inclusive solution.

Sub-Step 3.2 Nano-platform

This sub-step allows the organisation to engage relevant stakeholders such as government representatives, industry partners, the scientific committee and the general public, on the potential risks of NM.

Sub-step 3.2 also ensures the availability of objective information on the status of on-going scientific research in this field.

Food experts interviewed in this study believed that consumer trust and confidence in nano-derived food could only be realised if objective information is provided by food manufacturers. Furthermore, and as reported in section 4.1.3, considering that many nano-food products may enter the market in the near future, Dalton-Brown (2015) suggested that manufacturers who apply for market approval should have to demonstrate that the safe use of such new products will not pose undue safety risks to consumers. Hence a platform, such as the one proposed in this model, will provide

options for dialogue and participation of all stakeholders in order to obtain the necessary information.

Sub-Step 3.3: Code of Conduct

This step will enable the organisation, as well as other stakeholder dealing with NMs, to act responsibly and ethically during the manufacturing and production of NMs by employing the best scientific standards, including good laboratory practices (GLP) and GMP. A code of conduct, according to FDA (2009), exists to ensure that the common goal of operators and regulators of food establishments is to produce safe, quality food for consumers.

As shown in section 4.3.2.1., some of the selected products characterised in this study revealed a different form of silica, other than SAS, which is indicative of E551. Significantly, this study found that the current food labelling system cannot guarantee that food is authentic, good quality and safe (Aung and Chang 2014). Adherence to the risk controls mentioned above will ensure that the organisation makes sound decisions on risk identification and assessments for E551 in step 1 and 2 and more importantly, evaluates how the organisation will manage the risks which are presented in step 3.

Outputs of the proposed model will include a safety data sheet (SDS) which will provide critical information relating to the material profile of E551 and its health and safety issues; as well as a pre-market screening report affirming that E551 meets all the necessary requirements for market approval.

Asmatulu (2013) observed that even though there is continuous research, the field of nanotechnology is evolving more rapidly than the generation of data on the health and safety aspects of NMs. This remains an area to be researched further. As such, when undertaking a nanomaterial risk assessment in the workplace, employers may encounter difficulties related to: (1) not enough information on the hazardous properties of NMs; (2) no unanimity on the standardised techniques and devices to be used for quantifying exposure levels and for identifying NMs; and (3) limited information on the effectiveness of risk reduction measures (such as filters and gloves, amongst others).

Also, following traditional risk management models which were designed for conventional/macro materials presents some challenges as the principles followed in these models may not be applicable for the same particles at nanoscale (Jahnel 2015). Moreover, particles of the same ENM may behave differently under different conditions. Thus, there may still remain uncertainties around the nature of hazards, issues in exposure assessment, questions about appropriate control methods, and lack of occupational exposure limits (OELs) or nano-specific regulations. Hence, ENMs should be assessed on a case-by-case approach, as suggested by Cockburn *et al.* (2012).

The next chapter will provide the conclusions drawn from this study. This will include the identification of limitations which will steer this study for future research.

Chapter Five – Conclusion and Recommendations

This study examined the quality of selected food products containing nanosilica in SA. A mixed method strategy was adopted. Data collection was done using experimental work, semi-structured interviews, and questionnaires. Purposeful sampling was used to seek relevant information and advice from experts. This chapter concludes the study and draws on the discussion of the aforementioned techniques to provide recommendations and propose directions for future research.

5.1 Conclusions

This study found that a growing number of products containing NPs and NMs were entering the market. As a result, increased attention has been focused on nanotechnology, particularly its application in selected food additives incorporated into particular food products. But many questions remained unanswered, perhaps due to the lack of communication between the food industry and the public about the possible applications of NMs and current and future developments.

The semi-structured interviews conducted with experts revealed that the application of nanotechnology in the food sector was yet to impact on SA as there were no adequate standards or compliance laws to ensure the safe application of ENMs, such as E551, in food products. Overall, the experts who participated in this study, called for more transparency and dialogue between all stakeholders to discuss potential benefits and risks of nanotechnology in food products. More importantly, this study found that such a flow of information would benefit SA in minimising the potential health risks associated with nanosilica that were identified. This is in line with achieving the study's objective, which is "*to determine the existence and compliance of the South African regulatory requirements of nano-additives in food*".

Significantly, the survey conducted in this study, reinforced the need for compliance and standards for nanotechnology in the food sector in SA. This is in line with the objective to "*determine the current scope and application of nano-additives in food products in SA*". To support this conclusion, the findings also showed that general

public awareness of nanotechnology in food was limited and many consumers were not familiar with this technology.

This study further revealed that the current SA Foodstuffs, Cosmetics and Disinfectant Act 54 of 1972 (Regulation 25 of 2004) which regulated E551 and followed the Codex Alimentarius guiding principle of GMP, may not be sufficient to deal with nanotechnology. This is cause for grave concern in light of public debate on the possible harmful effects of NPs to humans. More concerning is the fact that E551 is permitted in certain foods for infants and young children

In particular, and in terms of achieving the objective to "*determine the potential health risks associated with ENMs*", preliminary data, derived from the literature review, was presented in chapter three and served as a means to determine the effects of nano-derived food. This study found that there was growing debate regarding health and safety concerns related to the use of E551 in food products. Short-term studies showed that NPs may, in contrast to larger particles, cross cellular carriers such as the gastrointestinal epithelium and become systematically accessible and enter cells. The prominent aspect of this study showed that there were inadequate safety nets and food management systems to clearly define the risks associated with ENMs and, as such, consumers were not able to make informed choices for safe and quality-assured food.

One of the most prominent aspects of this study is that it explicitly underlined the different characterisation methods (FTIR, EDX, and XRD) used to "*determine levels of nanosilica found in selected food products available in SA*". This study found that the South African manufactured and packed products contained higher levels of nanosilica compared to products from the EU and Asia. It further revealed that the type of silica used in two of the four SA products was not indicative of E551, even though the label claimed this.

The identification of crystalline silica in the food products is of concern since studies showed that exposure to crystalline silica was likely to induce perilous health effects such as cancer and fibrosis in humans. This finding further demonstrated that the current food labelling system cannot guarantee that food is authentic, of good quality, and safe.

Significantly, the afore-mentioned finding demonstrated the benefit of regulating and monitoring the quality of nanosilica used in commercially-available food products in SA.

In line with achieving the objective, "*to proffer guidelines for the appropriate application of E551 in SA*", this study developed a risk management system, called the HAC ('*Hazard identification, Access the risks, Control the risks'*) model, that not only identifies the type of silica used, but also controls the health risks to workers who are exposed to it in the workplace.

It can therefore be argued that the study has achieved all of its objectives as set out in chapter one section 1.5, namely:

- To determine the current scope of application of nano-additives in food products in SA.
- Due to the novelty of this research focus area, to conduct a review of literature in chapter two which will serve as a means to determine the effects of nano-additive derived food and potential risks to consumers and will also serve as preliminary data to be presented in chapter three.
- To establish the existence and compliance of the South African regulatory requirements on nano-additives in food.
- To determine levels of E551 found in selected food products available in SA by using analytical methods such as Fourier Spectra Infrared Spectroscopy (FT-IR), Energy Dispersive X-ray Spectroscopy (EDX), Scanning Electron Microscope (SEM), and X-ray Diffraction (XRD).
- To proffer quality standards and guidelines for appropriate application of E551 in SA.

5.2 Recommendations

SA does not have any framework in place for the regulation, monitoring and safe use of nanotechnology in the food sector. The HAC model proposed in this study addresses this limitation and can be adopted for any food-grade NPs. Furthermore, the HAC model could potentially establish a sound foundation on which commercial products incorporating this food additive, can be launched with assurance, or

withdrawn to safeguard consumers and the environment from potential hazards. Finally, future research could also explore other food additives containing NPs.

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Addendum 1: Ethics Clearance Letter

MANAGEMENT SCIENCES: FACULTY RESEARCH ETHICS COMMITTEE (FREC)

26 May 2015
Student No: 19251504
FREC No: 22/13FREC

Dear Mrs R Thakur

MASTERS OF TECHNOLOGY: QUALITY

TITLE: THE QUALITY OF SELECTED FOOD PRODUCTS CONTAINING NANOSILICA ADDITIVE (E551) IN SOUTH AFRICA

Please be advised that the FREC Committee has reviewed your proposal and the following decision was made: Ethical Level 1 -Full Approval

Approval has been granted for a period of two year, after which you are required to apply for safety monitoring and annual recertification. Please use the form located at the Faculty. This form must be submitted to the FREC at least 3 months before the ethics approval for the study expires.

Any adverse events [serious or minor] which occur in connection with this study and/or which may alter its ethical consideration must be reported to the FREC according to the FREC SOP's.
Please note that ANY amendments in the approved proposal require the approval of the FREC as outlined in the FREC SOP's.

Yours Sincerely

[redacted]

Prof N Dorasamy
FREC: Chairperson

Addendum 2: Pilot Study – Semi-structured Interviews

The questions are designed to explore the usage of anti-caking agents in food products, namely E551 food additive which contain nano-sized silica. The semi-structured interview is conducted with food experts to ascertain their opinions on the justification and health implications of nano-sized particles in food additives.

1. Why are additives added to food? What are the benefits?

2. How is it approved for use in food? Is there a global standard?

3. What is nanosilica?

4. In your opinion is it safe for human consumption?

5. Are there other potential applications for nanosilica in food?

6. What are the benefits and risks of ENMs in food?

7. How important is regulations to monitor the safety of food in SA?

8. With the influx of imported food products from Asian and European markets, what directives are in place to ensure South African consumers are aware of what's in their food?

Thank for you very much your participation in this study. Your time and opinions are greatly appreciated.

Addendum 3: Pilot Study – Questionnaire

Dear Respondent,

I am conducting research as part of my Masters' studies entitled: ***The quality of selected food products containing nanosilica in South Africa.***

I will be very grateful if you can take a few minutes to answer the questions below. Confidentiality of the information will be respected.

Section A: Demography of the respondent

Please place an (X) in the appropriate block.

1. **Gender of respondent**

Male	Female

2. **Place of work**

Food Industry	Academia	Government Agency

3. **Level of experience**

1 – 5 years	6 – 10 years	Above 10 years

The questions are designed to explore the usage of additives in food products and the opinions on the justification and health implications of the E500 range of additives which contain nanosilica. The survey is conducted with food technologists based in Durban, South Africa.

1. Why are additives added to food?
2. How does the E-labelling system work?
3. How is food additives approved for use in food? Are there different standards in the United Kingdom, European Union and United States?
4. From the above how does this compare to the South African framework regarding additives in food?
5. What is the prevalence of Nano materials in: **a) food additives** **b)colourants**

6. <u>Description of Silica</u>

1. Briefly describe the source of this material?
2. In South African food products, is it manufactured or purchased?
3. If purchased, who produces it?
4. How is Silica manufactured?
5. What other NEM exists in food additives that are similar to this one?
6. How long has Silica been in the E500 range of additives?
7. What is the volume of Silica permitted in food products according to South African legislation? How does this compare with the UK, US and EU legislations?
8. What are the other potential applications of Silica in food products?

7. There are very strict regulations in most countries on this specific range of additives. Why?
9. Do they have any nutritional value?

10. In your opinion what are the benefits and risks of: **a) natural-produced additive** **b) nanoparticle additive**
11. What are the risks to human on the ingestion of nano-particles such as Silica? Can you discuss some reported cases?
12. From the question above, what is the stipulated amount of silica acceptable for human consumption according to the SA Food, Drugs and Cosmetics Act?
13. D**o you agree with these stipulations? If not what would you like to see changed in the E500 range of additives?**
14. With the influx of imported food products from Asian and European markets, what directives are in place to ensure South African consumers are aware of what's in their food?
15. Do you believe the average South African consumer is aware of nanoparticles in food products?
16. Should consumers be educated on this?
17. Would nanotechnology have any impact on modern food production such as Genetically Modified (GM) food?
18. Are there any applications that are intentionally not being used at this stage?

General Comments

Please articulate any other comment you may feel is relevant to this study.

Thank for you very much your participation in this study. Your time and opinions are greatly appreciated.

Addendum 4: Letter of Consent and Confidentiality

INSTITUTIONAL RESEARCH ETHICS COMMITTEE (IREC)
LETTER OF INFORMATION

Title of the Research Study:	**The quality of selected food products containing nanosilica additive (E551) in South Africa**
Principal Investigator/s/researcher:	Rookmoney Thakur
	(BTech: Journalism)
Co-Investigator/s/supervisor/s:	Dr Shalini Singh
	DTech: Quality

Brief Introduction and Purpose of the Study

Little is known about food additives which contain Nano Engineered Materials (NEM) which is added to preserve flavour or improve taste and appearance. It has been used for centuries; for example, preserving food by pickling (with vinegar), salting, as with bacon and dried tomatoes, or using sulphur dioxide as in some wines. With the advent of processed foods in the second half of the 20th century, many more additives have been introduced, of both natural and artificial origin. Some of these latter additives are open to debates and disagreements whether they should be allowed at all.

This study will focus on E500 additives which contain the Nano-materials Silicone Dioxide; Calcium Silicate; Magnesium Silicate; Potassium Aluminium Silicate; and Aluminium Calcium Silicate. These are found in spices, salt, sweets and some frozen foods for their anti-caking benefits. It has been known that inhaled silica can increase the risk of lung cancer. Research has shown that ingested nanoparticles which are commonly used in foods and supplements can travel to the liver, the kidneys and the brain, disrupting DNA and potentially leading to the development of cancer. The use of these additives are strictly regulated in some countries and periodically re-assessed. Despite this, available literature suggests that many uncertainties remain about nanomaterial contained in food. Lack of knowledge in regard to any new technology, or a lack of communication of the risks and benefits, can raise concerns amongst the public. For example, genetically modified foods were not well received by consumers because there was a perceived risk associated with them. This study will look at the level of application of nanotechnology additives in food products in South Africa; the benefits and health risks to consumers and will compare legislative framework to that in countries such as the United Kingdom (UK), European Union (EU) and the United States (US).

A mixed method strategy will be adopted. Data collection will be in the form of literature reviews, interviews and questionnaires. Purposeful sampling will be used to gather pertinent data. Expert advice from professionals like dieticians and food technologists will also be sought.

Outline of the Procedures:

Responsibilities of the participant: Participants will be asked to answer the supplied questionnaire and provide semi-structured follow-up responses. Consultation times will be done at the convenience of participants at venues of mutual suitability.

Inclusion/exclusion criteria: Purposive sample will be used to target potential respondents from accredited professional bodies. These interviewees will be selected from medical directories. At this stage approximately three to five health professionals such as food technologists and dieticians.

Explanation of tools and measurement outcomes: An interview survey method with no medical involvement of participants. Purposeful sampling will be used to gather pertinent data. Should follow-ups be necessary, this will be done at the convenience of participants.

Risks or Discomforts to the Participant: (Description of foreseeable risks or discomforts to for participants if applicable e.g. Transient muscle pain, VBAI, post-needle soreness, other adverse reactions, etc.)

None

Benefits: (To the participant and to the researcher/s e.g. publications) Increase body of knowledge on the subject of Nano additives in food products in South Africa

Reason/s why the Participant May Be Withdrawn from the Study: Non-availability of disinterest**. T**here will be no adverse consequences for the participant should they choose to withdraw.

Remuneration: (Will the participant receive any monetary or other types of remuneration?) No

Costs of the Study: (Will the participant be expected to cover any costs towards the study?) No

Confidentiality: (Description of the extent to which confidentiality will be maintained and how will this be maintained?) There is no confidentiality as participants are experts in their fields.

Research-related Injury: (What will happen should there be a research-related injury or adverse reaction? Will there be any compensation?) No

Persons to Contact in the Event of Any Problems or Queries:

Supervisor, Dr Shalini Singh (031-3735159) (0829757772) Please contact the researcher (031-4646991) (0785442461) or the Institutional Research Ethics administrator on 031 373 2900. Complaints can be reported to the DVC: TIP, Prof F. Otieno on 031 373 2382 or dvctip@dut.ac.za.

General:

Potential participants must be assured that participation is voluntary and the approximate number of participants to be included should be disclosed. A copy of the information letter should be issued to participants. The information letter and consent form must be translated and provided in the primary spoken language of the research population e.g. isiZulu.

INSTITUTIONAL RESEARCH ETHICS COMMITTEE (IREC)
CONSENT

Statement of Agreement to Participate in the Research Study:

- I hereby confirm that I have been informed by the researcher, __Rookmoney Thakur_____ (name of researcher), about the nature, conduct, benefits and risks of this study - Research Ethics Clearance Number: _____,
- I have also received, read and understood the above written information (Participant Letter of Information) regarding the study.
- I am aware that the results of the study, including personal details regarding my sex, age, date of birth, initials and diagnosis will be anonymously processed into a study report.
- In view of the requirements of research, I agree that the data collected during this study can be processed in a computerised system by the researcher.
- I may, at any stage, without prejudice, withdraw my consent and participation in the study.
- I have had sufficient opportunity to ask questions and (of my own free will) declare myself prepared to participate in the study.
- I understand that significant new findings developed during the course of this research which may relate to my participation will be made available to me.

_____	_____	_____	_____
Full Name of Participant	**Date**	**Time**	**Signature / Right Thumbprint**

I, _Rookmoney Thakur (name of researcher) herewith confirm that the above participant has been fully informed about the nature, conduct and risks of the above study.

_Rookmoney Thakur	_____	_____
Full Name of Researcher	**Date**	**Signature**

_____	_____	_____
Full Name of Witness (If applicable)	**Date**	**Signature**

_____	_____	_____
Full Name of Legal Guardian (If applicable)	**Date**	**Signature**

Please note the following:

Research details must be provided in a clear, simple and culturally appropriate manner and prospective participants should be helped to arrive at an informed decision by use of appropriate language (grade 10 level - use Flesch Reading Ease Scores on Microsoft Word), selecting of a non-threatening environment for interaction and the availability of peer counseling (Department of Health, 2004)

If the potential participant is unable to read/illiterate, then a right thumb print is required and an impartial witness, who is literate and knows the participant e.g. parent, sibling, friend, pastor, etc. should verify in writing, duly signed that informed verbal consent was obtained (Department of Health, 2004).

If anyone makes a mistake completing this document e.g. wrong date or spelling mistake a new document has to be completed. The incomplete original document has to be kept in the participant file and not thrown away and copies thereof must be issued to the participant.

References:

Department of Health: 2004. *Ethics in Health Research: Principles, Structures and Processes* http://www.doh.gov.za/docs/factsheets/guidelines/ethnics/

Department of Health. 2006. *South African Good Clinical Practice Guidelines*. 2nd Ed. Available at: http://www.nhrec.org.za/?page_id=14

Addendum 5: Main Study – Semi-structured Interviews

The questions are designed to explore the usage of anti-caking agents in food products, namely E551 food additive which contain nano-sized silica. The semi-structured interview is conducted with food experts to ascertain their opinions on the justification and health implications of nano-sized particles in food additives.

1. Why are additives added to food? What are the benefits?

2. How is it approved for use in food? Is there a global standard?

3. What is nanosilica?

4. In your opinion is it safe for human consumption?

5. Are there other potential applications for nanosilica in food?

6. What are the benefits and risks of ENMs in food?

7. How important is regulations to monitor the safety of food in SA?

8. With the influx of imported food products from Asian and European markets, what directives are in place to ensure South African consumers are aware of what's in their food?

9. In SA, do you think there is more concern on availability of food rather than quality?

10. Do you think there is adequate mechanisms in place to ensure safety of food containing nano-particles, in SA and globally?

Thank for you very much your participation in this study. Your time and opinions are greatly appreciated.

Addendum 6: Main Study – Questionnaire

The questions are designed to explore the usage of anti-caking agents in food products, namely E551 food additive which contain nano-sized synthetic silica. The results will be used to determine the general awareness and scope of application of nano-engineered materials in food additives. The questionnaire is directed at food technologists.

Please read each question carefully, and where necessary place an (X) in the appropriate box.

Statement	Strongly Agree	Agree	Neutral	Disagree	Strong Disagree
1. Food additives are substances added to food to enhance its flavour or appearance or to preserve it.					
2 Food additives add nutritional value to food.					
3. Food additives are safe for human consumption					
4. I am familiar with anti-caking agents in food products					
5. I am aware some of these anti-caking agents contain nanoparticles commonly referred to a nanosilica					
6. Anti-caking agents reduce the tendency of individual food					

particles to adhere and improve flow characteristics.					
7. I am aware how food additives are approved for use in food products					

8. Name Common Anti-caking Agents that you are aware of?

9. Do you know what E-numbers are? (e.g. E302, E401)

Yes No

10. Name some products that you are aware of in South Africa that contain E551 (nanosilica) food additives?

11. Do you believe there are adequate testing standards in SA to determine the safety of food products containing nano particles?

Yes No

12. Do you believe nanotechnology for any food application is safe?

Yes No

13. Has there ever been a product that you are aware of in which the nanomaterial caused damage to health?

Yes	No

If yes, please explain

……
……
……

14. Do you believe the average SA consumer is aware of the inclusion of nanoparticles in food products?

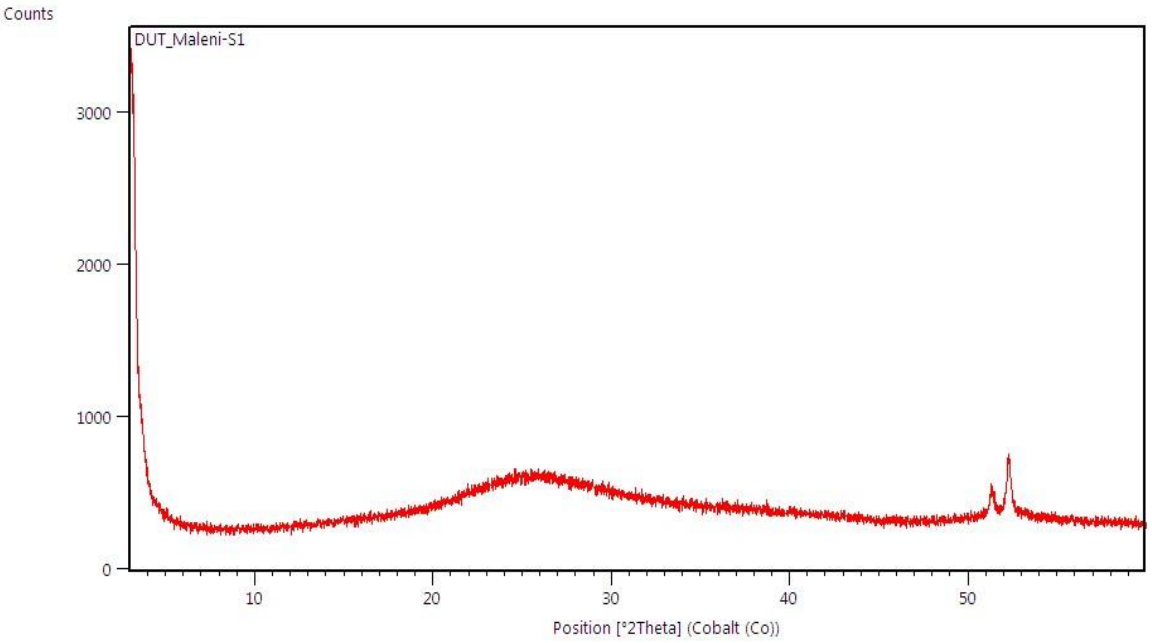
Yes	No

General Comments

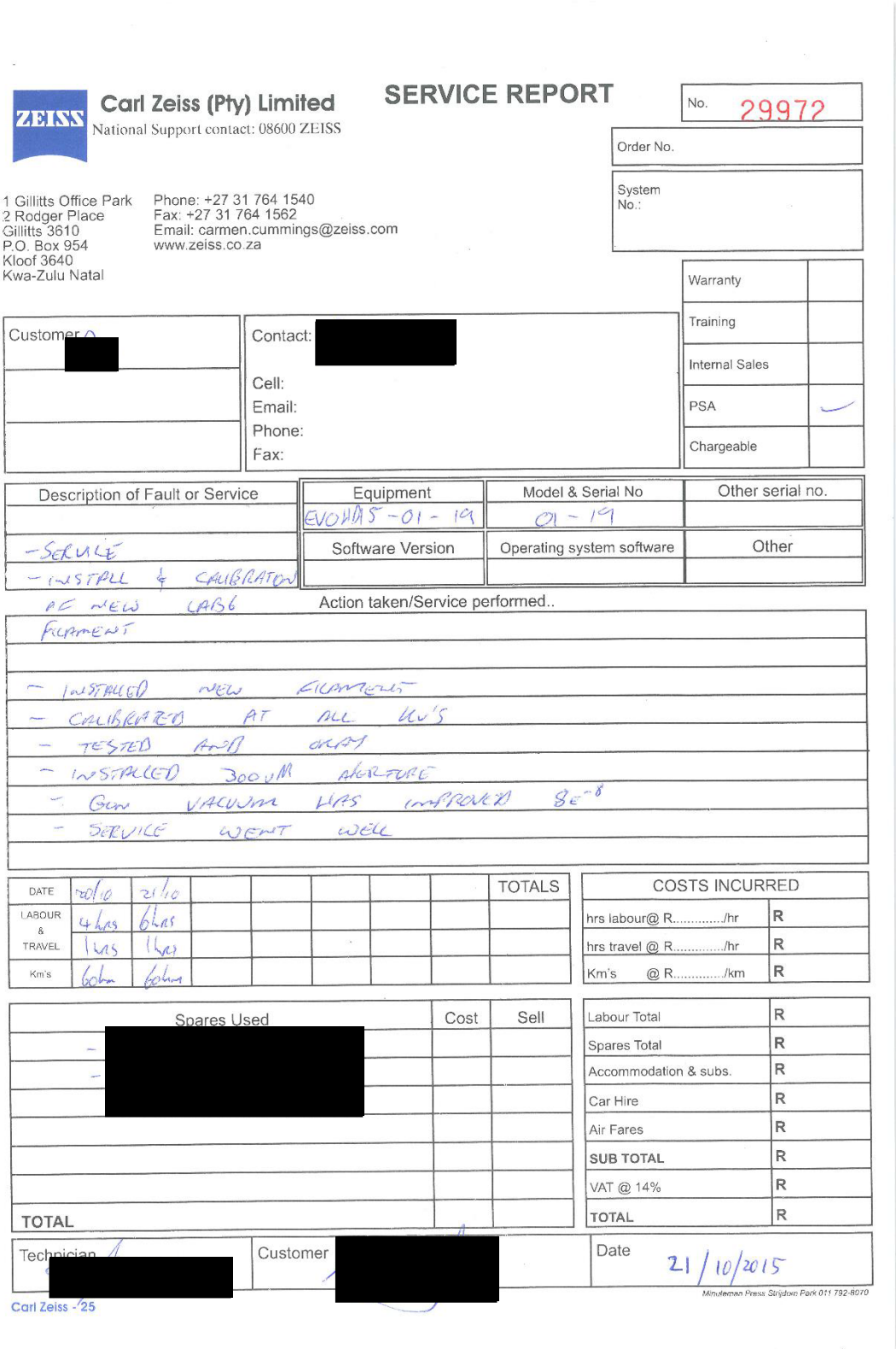
Please articulate any other comment you may feel is relevant to this study.

Thank for you very much your participation in this study. Your time and opinions are greatly appreciated.

Addendum 7: XRD diffraction peak 2Ø value of 22º which is indicative of SAS



Addendum 8: Validity and reliability of the instrument



Carl Zeiss (Pty) Limited
National Support contact: 08600 ZEISS

SERVICE REPORT

No. 29972

Order No.

System No.:

1 Gillitts Office Park
2 Rodger Place
Gillitts 3610
P.O. Box 954
Kloof 3640
Kwa-Zulu Natal

Phone: +27 31 764 1540
Fax: +27 31 764 1562
Email: carmen.cummings@zeiss.com
www.zeiss.co.za

Warranty	
Training	
Internal Sales	
PSA	✓
Chargeable	

Customer [redacted]

Contact: [redacted]
Cell:
Email:
Phone:
Fax:

Description of Fault or Service	Equipment	Model & Serial No	Other serial no.
– SERVICE	EVOHAS-01-19	01-19	
– INSTALL & CALIBRATION OF NEW LABS EQUIPMENT	Software Version	Operating system software	Other

Action taken/Service performed..

– INSTALLED NEW EQUIPMENT
– CALIBRATED AT ALL KV'S
– TESTED AND OKAY
– INSTALLED 300µM APERTURE
– GUN VACUUM HAS IMPROVED 8E-8
– SERVICE WENT WELL

DATE	20/10	21/10						TOTALS
LABOUR & TRAVEL	4 hrs	6 hrs						
	1 hrs	1 hrs						
Km's	60km	60km						

COSTS INCURRED	
hrs labour@ R...../hr	R
hrs travel @ R...../hr	R
Km's @ R...../km	R

Spares Used	Cost	Sell
– [redacted]		
TOTAL		

Labour Total	R
Spares Total	R
Accommodation & subs.	R
Car Hire	R
Air Fares	R
SUB TOTAL	R
VAT @ 14%	R
TOTAL	R

Technician [redacted]

Customer [redacted]

Date 21/10/2015

Minuteman Press Strijdom Park 011 792-8070

Carl Zeiss - 25