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Escola de Engenharia

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A qualitative approach to risk assessment and control in engineered nanoparticles occupational exposure

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in engineered nanoparticles occupational exposure

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A qualitative approach to risk assessment and control in engineered nanoparticles occupational exposure

Doctoral Dissertation for PhD degree in
Industrial and Systems Engineering

Done under supervision of
Professor Pedro Arezes (UMinho)
Professor Paul Swuste (TUDelft)

December 2015

STATEMENT OF INTEGRITY

I hereby declare having conducted my thesis with integrity. I confirm that I have not used plagiarism or any form of falsification of results in the process of the thesis elaboration.

I further declare that I have fully acknowledged the Code of Ethical Conduct of the University of Minho.

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ABSTRACT

The existing research effort and common use of nanomaterials, that are an opportunity for economic growth, pose health and safety problems. The research on the nanoparticles health effects performed during the last decade shows the possible harmfulness of several nanoparticles, including those already present in everyday use products, thus worker's health and safety are critical to the development of nanotechnology applications. Despite the increasing knowledge in the nanotoxicology field and occupational safety and hygiene, the uncertainties related to exposure to nanoparticles and related effects are important. Qualitative risk assessment methods and design based approaches are considered to be useful when dealing with those uncertainties and their improvement relevant research issues. This work included, among other things, three individualized, although related, studies. In the first one, the exposure to TiO_2 nanoparticles risk was assessed in a research laboratory using a quantitative exposure method and qualitative risk assessment methods. It was found that results from direct-reading Condensation Particle Counter (CPC) equipment and the CB Nanotool seem to be related and aligned, while the results obtained from the use of the Stofenmanager Nano seem to indicate a higher risk level. The main objective of the second study was to analyse and compare different qualitative risk assessment methods during the production of polymer mortars with nanomaterials. It was verified that the different methods applied also produce different final results. Accordingly, it is necessary to improve the use of qualitative methods by defining narrow criteria for the methods selection for each assessed situation, bearing in mind that the uncertainties are also a relevant factor when dealing with the risk related to nanotechnologies. The third study described the application of the Systematic Design Analysis Approach based on the hazard process model (bow-tie), as well as design analysis of the production process, during a development project to produce a new type of ceramic tile with photocatalytic properties. Applying Systematic Design Analysis Approach to the production process, made it possible to identify the emission and exposure scenarios and the related barriers based on the different technological options of the production process. The intervention model proposed will allow occupational safety and hygiene to be integrated into the new production processes development projects that will involve a multidisciplinary team. The current thesis aims to contribute to the improvement of occupational risk assessment and risk control in nanotechnologies, contributing to improve the use of qualitative risk assessment methods by drawing the attention for the importance of the information available on the nanomaterials and the differences obtained by using different methods for the same task and discussing possible ways to obtain more reliable results. The obtained results also shown that, when using a design-based approach, it is possible to reduce risks for workers in the workplace, by changing the production process, reducing or eliminating nanoparticles emission and consequently reducing workers' exposure.

Keywords: nanoparticles; exposure; control banding; emission scenarios; exposure scenarios; safety-by-design; bow-tie model; ceramics; polymers.

RESUMO

O esforço atual de investigação e o uso comum de nanomateriais, sendo uma oportunidade para o crescimento económico, colocam problemas para a segurança e saúde. A investigação sobre os efeitos das nanopartículas para a saúde realizada durante a última década mostra a possível nocividade de várias nanopartículas, incluindo aquelas incluídas em produtos utilizados no dia-a-dia. Assim, a segurança e saúde dos trabalhadores são críticas para o desenvolvimento de novas aplicações da nanotecnologia. Apesar do crescente conhecimento no campo da nanotoxicologia e na segurança e saúde ocupacional, são importantes as incertezas associadas com a exposição a nanopartículas e os efeitos relacionados O recurso a métodos de avaliação de risco qualitativos e abordagens baseadas no *design* é considerado útil para lidar com estas incertezas e a sua melhoria tema relevante de investigação. O presente trabalho incluiu, entre outras coisas, três estudos individualizados, no entanto interrelacionados. No primeiro estudo, é avaliado o risco de exposição a nanopartículas de TiO_2 num laboratório de investigação, utilizando um método quantitativo de avaliação da exposição e métodos qualitativos de avaliação do risco. Verificou-se que os resultados do equipamento de leitura direta *Condensation Particle Counter* e o CB Nanotool parecem estar relacionados e alinhados, enquanto os resultados obtidos com o método Stofenmanager Nano apontam para um nível de risco mais elevado. O objetivo principal do segundo estudo era analisar e comparar diferentes métodos qualitativos de avaliação do risco durante a produção de argamassas poliméricas contendo nanomateriais. Verificou-se que os diferentes métodos aplicados também produzem diferentes resultados. Assim, é necessário melhorar a utilização destes métodos definindo critérios mais apertados para a sua seleção em função do tipo de situação avaliada, tendo em conta que as incertezas são também um fator relevante quando se interage com o risco relacionado com as nanotecnologias. O terceiro estudo descreve a aplicação do *Systematic Design Analysis Design Approach*, baseado no modelo do processo de perigo (*bow-tie*) e na análise ao design do processo de produção durante um projeto de desenvolvimento para a produção de um novo tipo de ladrilho cerâmico com propriedades fotocatalíticas. Aplicando o *Systematic Design Analysis Design Approach* ao processo de produção foi possível identificar os cenários de emissão e exposição e as barreiras relacionadas, com base nas diferentes opções tecnológicas do processo de produção. O modelo de intervenção proposto vai permitir que a segurança e higiene ocupacionais sejam integradas nos projetos de desenvolvimento de novos processos de produção, os quais envolvem uma equipa multidisciplinar. A presente tese pretende contribuir para a melhoria da avaliação de riscos ocupacionais e o controlo do risco no sector da nanotecnologia, contribuindo para melhorar a utilização dos métodos qualitativos de avaliação de risco, chamando a atenção para a importância da informação disponível sobre os nanomateriais e as diferenças obtidas quando se utilizam diferentes métodos para a mesma tarefa e discutindo diferentes formas de obter resultados mais fidedignos. Os resultados obtidos demonstram, igualmente, que utilizando uma abordagem baseada no *design* é possível reduzir os riscos para os trabalhadores no posto de trabalho, alterando o processo de produção, reduzindo ou eliminando a emissão de nanopartículas e, assim, reduzindo a exposição dos trabalhadores.

Palavras-chave: nanopartículas; exposição; *control banding*; cenários de emissão; cenários de exposição; *safety-by-design*; modelo *bow-tie*; cerâmicos; polímeros.

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LIST OF ABBREVIATIONS AND ACRONYMS

ANSES – Agence nationale de sécurité sanitaire de l’alimentation, de l’environnement et du travail

BSI – British Standards Institution

CB – Control Banding

CPC – Condensation Particle Counter

ELPI – Electrical Low Pressure Impactor

ENM – Engineered NanoMaterialsEPFL – Ecole Polytechnique Fédérale de Lausanne

FR – Flame retardant

GWSNN – Guidance Working Safely with Nanomaterials and Nanoproducts

HAZOP – Hazard and Operability Study

HSE – Health and Safety Executive

IARC – International Agency for Research on Cancer

INRS – Institut National de Recherche et de Sécurité

IPA – Isopropanol

IPQ – Instituto Português da Qualidade

ISPESL – Istituto Superiore per la Prevenzione e la Sicurezza del Lavoro

LEV – Local exhaust ventilation

NIOSH – National Institute for Occupational Safety and Health

NP – NanoParticles

NVR – Nano Reference Values

OECD – Organisation for Economic Co-operation and Development

OEL – Occupational Exposure Limit

OH – Occupational Hygiene

OSH – Occupational Safety and Hygiene

PC – Polymer concrete

PEN – Project on Emerging Nanotechnologies

PM – Polymer Mortar

PMSN – Precautionary Matrix for Synthetic Nanomaterials

PtD – Prevention through Design

SDS – Safety Data Sheets

SMPS – Scanning Mobility Particle Sizer

SELFCLEAN – SELF-CLEANing ceramic surfaces

SEM – Scanning Electron Microscopy

SYDAPP – SYstematic Design Analysis APProach

TEM – Transmission Electron Microscopy

CHAPTER 1. INTRODUCTION AND THESIS OVERVIEW

1.1. Motivation

Nanotechnologies are a promising field of scientific and technological development. During the last years the increase in research and new applications has been astonishing (Cientifica, 2011; Palmberg, Dernis, & Miguet, 2009). The use of nanotechnology based products, like cosmetics, sunscreens or paints in everyday life is already common (Vance et al., 2015) and new features are expected (McDermott Will and Emery, 2014).Considering the new opportunities in important areas like fuel cells or hydrogen storage in energy and molecular electronic or quantum computer in electronics, or new solutions in the environmental (e.g. waste water treatment, soil remediation) or medicine (e.g. drug delivery, nanodevices) areas, nanotechnology assumes a major role in the future of humanity (Roco, Harthorn, Guston, & Shapira, 2011). One relevant question about nanotechnology is the foreseeable development of new types of nanomaterials (Renn & Roco, 2006) with unknown properties (Bleeker et al., 2015), representing a challenge to the scientific community.

Despite the differences found between the several nanotechnology market, recent estimates and previous projections (European Commission, 2012a; Market Spotlight, 2015; Palmberg et al., 2009), it is consensual that economic importance of the nanotechnologies is increasing. In Portugal there are a few research centers on nanotechnologies, and also some companies producing nanomaterials (Eugénio & Fatal, 2010) or using them in products, but updated data on the sector is not available. However, with the recent creation of the Technical Committee of Standardization CT 194 – Nanotecnologias, it was possible to identify several companies and research groups working with nanomaterials (IPQ, 2015). As the Portuguese production volume of nanomaterials is unknown, the worldwide figures are not well known (Hendren, Mesnard, & Wiesner, 2011; Piccinno, Gottschalk, Seeger, & Nowack, 2012). The existing estimates point to significant quantities of nano-TiO_2 and nano-SiO_2, ranging 10 000 t/year worldwide, while nano-Al_2O_3, nano-ZnO, other nano-metal oxides, nano-metals, fullerenes and carbon nanotubes are produced in lower amounts (Aitken, Chaudhry, Boxall, & Hull, 2006; Piccinno et al., 2012).

But, if nanotechnologies are considered relevant for the economic growth and to solve important problems that humanity is facing, troubles emerge related to the possible harmful effects of nanomaterials to human health and environment (Bleeker et al., 2015). Thus, the increasing use of products containing nano-objects will increase the release of these in the environment during all the lifecycle (Dowling et al., 2004), exposing workers and consumers. Having in consideration the existing concerns related to the hazardousness of nanomaterials, the increasing investment in new applications of nanomaterials is being followed by research in safety aspects related with nanomaterials, or also called nanosafety, which assumes a import role for the future (Savolainen et al., 2013).

If only one word was used to define the relation between nanomaterials and hazard that word would be "uncertainty". Uncertainty could be found in several fields of knowledge, such as nanotoxicology or occupational hygiene.

As uncertainty comprise risks, it is clear that risk management plays a key role when dealing with uncertainty. From an occupational safety and hygiene point of view, occupational risk management is the cornerstone of action in workplaces and with reduced information levels its importance grows.

The attention on the Occupational Safety and Hygiene issues related to nanotechnology has been highlighted by several international organizations (BSI - British Standards, 2007b; Environment Directorate OECD, 2010a; European Commission, 2012b; NIOSH, 2009; Technical Committee ISO/TC 229, 2008) considering the increasing number of workers exposed to nanoparticles. It was estimated that in 2008 around 400 000 workers worked in nanotechnology worldwide, including research activities (Roco, Mirkin, & Hersam, 2010).

Considering the uncertainties and the need to prevent harmful effects to the exposed workers several methods for exposure and risk assessment methods were proposed, both based on qualitative (Vervoort, 2012) and quantitative methodologies (Duarte, Justino, Freitas, Duarte, & Rocha-Santos, 2014). As a corollary, exposure assessment strategies were proposed (Brouwer et al., 2012; Ramachandran et al., 2011), with emphasis on the tiered approach (Environment Directorate OECD, 2015; IUTA et al., 2011). Although the existing differences between the proposed models, they are based on the increasing complexity from tier1 to tier 3. In tier 1 – Information Gathering, the use of Control Banding risk assessment tools (Brouwer, 2012) is considered, whilst in tier 2 – Basic Exposure Assessment, portable equipment, such as Condensation Particle Counter (CPC) is used to assess the workers exposure and tier 3 – Expert Exposure Assessment, complies the use of state-of-art measurement equipment (Environment Directorate OECD, 2015).

Considering the risk management process proposed on ISO/TS 12901-1: Nanotechnologies — Occupational risk management applied to engineered nanomaterials — Part 1: Principles and approaches (Technical Committee ISO/TC 229, 2012a), the importance of the risk control is highlighted. Several institutions have published recommendations for risk control during nanomaterials handling in research activities (R. Cornelissen, Samwel-Luijit, Vervoort, & Hoeneveld, 2014; Environment Directorate OECD, 2010a; NIOSH, 2012), and in general settings (BSI - British Standards, 2007b; I. R. Cornelissen, Jongeneelen, van Broekhuizen, & van Broekhuizen, 2011; NIOSH, 2009, 2013; Claude Ostiguy, Roberge, Ménard, & Endo, 2009; Technical Committee ISO/TC 229, 2008).

Another consensual question is the importance of the hierarchy of the controls referred by several authors as fundamental for risk management in nanotechnology (Amyotte, 2011; Defense, 2007; Fleury et al., 2013; Murashov, Schulte, Geraci, & Howard, 2011; NIOSH, 2009; Schulte et al., 2013; Technical Committee ISO/TC 229, 2012a; Tsai, 2010). In Figure 1.1 the hierarchy of controls in nanotechnology, as defined in ISO 12901-1:2012 (Technical Committee ISO/TC 229, 2012a) is presented.

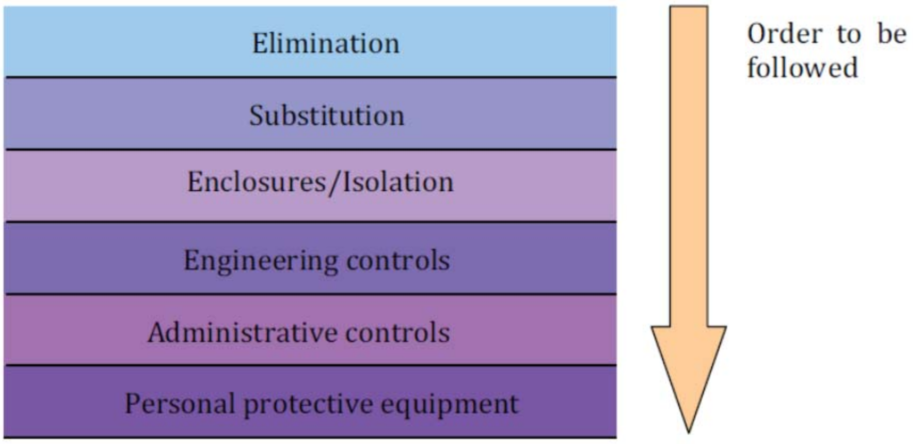

Figure 1.1 – Hierarchy of controls in nanotechnology indicating the order to be followed (Technical Committee ISO/TC 229, 2012a).

The models of exposure based in source/receptor (worker), which will be mentioned later in this thesis, call the attention for the succession emission → transmission → exposure leading that the hazard becomes an effective threat to the worker. It is possible to interrupt the sequence in any stage but it is consensual that acting in emission is more advantageous.

Considering the hierarchy of control measures, it is relevant the development of methods assisting definition of controls corresponding to the higher levels of that hierarchy, such as safety-by-design approaches.

The importance of safety concerns in an early stage of design of production processes and products is known for decades (Kletz, 1985). With the development of nanotechnology, several authors had pointed design of processes as an effective way to prevent risks (Amyotte, 2011; Morose, 2010; C Ostiguy, Roberge, Ménard, & Endo, 2009; Schulte, Rinehart, Okun, Geraci, & Heidel, 2008; Swuste & Zalk, 2013). Therefore, expressions as safe-by-design (Boulanger et al., 2013), safety-by-design (Donaldson, Murphy, Schinwald, Duffin, & Poland, 2011) or nanosafety-by-design (Bouillard & Vignes, 2014), among other similar expressions are used to define approaches leading to improve the safety of nanomaterials or to safer processes.

Another relevant concept is “safe innovation” that highlights the importance of risk management early in the design phase of nanomaterials (Bleeker et al., 2015). Safe innovation draws attention to hazard identification and risk assessment during the research & development process, aiming risk reduction or elimination.

“Nano-responsible development” aiming to emphasize the importance of considering and controlling the potential adverse impacts of nanotechnology in order to develop its capabilities and benefits (Schulte et al., 2014), gathers attention too and is considered one of the bases of the sustainable development (Helland & Kastenholz, 2008). Considering the current lack of regulation on the nanotechnologies (Bowman & Hodge, 2006), as nanomaterials are considered under the “traditional” materials regulations, such as REACH (Registration, Evaluation, Authorization and Restriction of Chemicals) and Chemical Agents Directive (Directive 98/24/EC) in Europe (European Commission, 2012b), corporate social responsibility is crucial as a driving force of environmental and occupational risk prevention (Kuzma & Kuzhabekova, 2011).

Despite the relevance of the design in safety, it is difficult to put it on practice. It seems that designers, project engineers, occupational safety and hygiene practitioners and other professionals do not know the potential power design represents to prevent risk exposure. Another possibility is that, knowing that potential, it is difficult to get people with different backgrounds, different interests and also different languages working together. Considering this scenario, it is important to improve risk management methods and tools leading to more reliable practices, both in exposure and risk assessment as well in risk control. As knowledge on nanomaterials' hazards is limited, and the existing qualitative risk assessment and quantitative exposure assessment methods are not fully applicable to all work situations, it is unavoidable to carry on research aiming improvement in the use of those methods. At the same time, it is relevant to contribute for the enhancement and dissemination of safety-by-design approaches, considering the potential of these approaches to lead to safer productions processes, through adoption of higher hierarchy control measures in early stages of development of those processes, or prior assembly of production facilities. The current thesis intends to contribute to the advancement of knowledge on these issues contributing to the validation of qualitative risk assessment methods and their rational application. In parallel, it intends also to improve the use of design as a prevention tool, leading to the elimination or reduction of the hazard.

1.2. Objectives

Based on the previous explanation of the current status about nanomaterials exposure among workers, the main objective of this thesis is to evaluate the suitability of qualitative risk assessment methods and design based approaches to improve occupational health risk prevention in engineered nanomaterials research and manufacturing, considering the existing uncertainties.

Therefore, the specific research objectives were defined:

- To Evaluate how quality of information on nanomaterials influence qualitative risk assessment results;
- To confirm the suitability of the qualitative risk assessment methods for assessing the risk on engineered nanomaterials activities and processes;
- To evaluate and improve the design-based approaches for risk control on engineered nanomaterials activities and processes
- To contribute to improve workplace operational control and risk management in the nanotechnologies field.

1.3. Thesis synopsis

Most of the chapters of this thesis particularly those from 2 to 5 (see Figure 1.2) are a compilation of scientific papers published in the sequence of the studies performed to accomplish the defined research objectives. Although all papers were already published (or submitted in its final format), some of them had been slightly changed in this thesis, as some minor errors were identified after its publication, namely some typographical or grammatical errors. The full reference and current status of each paper is indicated at the beginning of each chapter. Additionally, the thesis also has two additional chapters, one in the beginning and one at the end, as described in the following paragraphs.

The thesis starts with the current chapter where the subject of the thesis is introduced, by presenting the context and motivation of the current work, as well its objectives.

In Chapter 2, a review of literature on risk assessment and control is presented. This chapter aims to identify the current knowledge on nanoparticles characterization and qualitative occupational risk assessment and control in the nanomaterials field. In this first study, the most relevant results found in nanotoxicology are considered and the qualitative risk assessment methods specific for nanotechnology addressed. The Systematic Design Analysis Approach (SYDAPP) main principles and guidelines are presented and discussed.

In Chapter 3, the study "Risk assessment in a research laboratory during sol-gel synthesis of nano-TiO_2" is presented. The objectives of this study were to determine if qualitative and quantitative methods are suitable for risk assessment in research environments, to check if different methods retrieve similar results and to determine the influence from quality of information on nanomaterials risk assessment. In this study, different risk assessment methods, both qualitative and quantitative are used and their results compared. The influence of the information quality on nanomaterials' hazards is also discussed.

The following chapter, Chapter 4, consists in the research paper "Qualitative risk assessment during polymer mortar test *specimens* preparation – methods comparison". The study objective was to evaluate if different qualitative risk assessment methods retrieve similar risk levels for the same tasks. Three different work situations in a research laboratory were assessed with seven different qualitative risk assessment methods and the obtained risk levels and control measures recommended compared.

Chapter 5 includes the study "Systematic design analysis and risk management on nanoparticles occupational exposure" in which the SYDAPP is presented. The objectives of the study were to determine the suitability of SYDAPP to manage risks in a production line of photocatalytic ceramic tiles, to determine if a design approach of the production line of photocatalytic ceramic tiles generate relevant emission and exposure scenarios, to determine if a design approach of the production line of photocatalytic ceramic tiles generate alternative barriers to reduce exposure, including through emission reduction and to assess possibilities of the SYDAPP on reducing emission scenarios during photocatalytic ceramic tiles production. This paper also describes the photocatalytic ceramic tiles development project case-study, including the activities of the project team and presenting the results achieved in designing a safer production process. A model of intervention to implement SYDAPP is also suggested.

Finally, Chapter 6 summarizes the carried out work and suggests possible directions for future work.

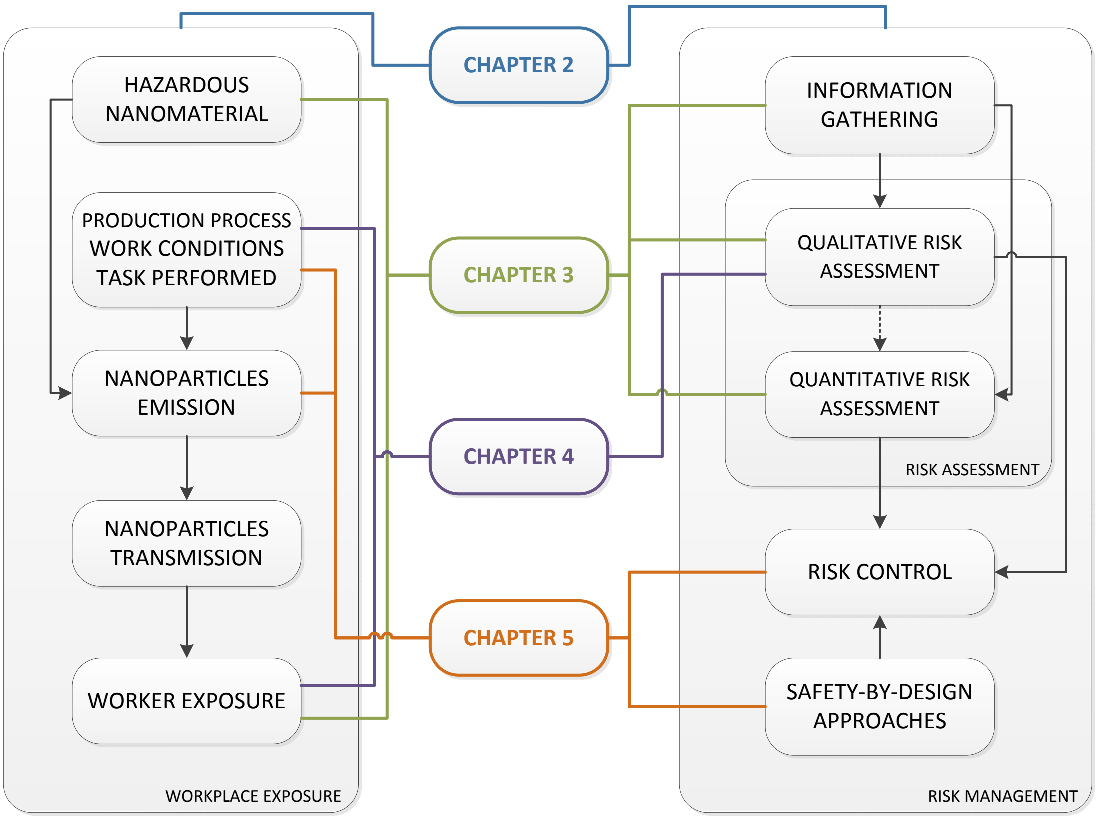

Figure 1.2 – Diagram of thesis chapters.

In Figure 1.2 the diagram of the thesis chapters is presented, showing in which chapter the main "workplace exposure" and "risk management" issues were considered during the current thesis and related research. Considering chapters 3, 4 and 5 together, it is possible to notice that a wide range of aspects were considered during this project. Moreover, subsidiary relations can be found contributing to the inter-relational characteristic of the different published papers.

Even if some of the developed work during this project was not included in the current thesis, the obtained results also served to develop additional publications, which are presented in this thesis as annexes. In Annex 1, the paper “Risk management of occupational exposure to nanoparticles during a development project. A case study” paper is presented. This paper was already accepted for publication in DYNA journal. Besides the description of the SYDAPP and its application during the development of photocatalytic ceramic tiles, which was also described in Chapter 5, it is focused on the production pilot-test carried out during the project. The results of risk assessment and exposure assessment performed on the pilot-test tasks and their contribution to improve the future production facilities OSH conditions are discussed.

Based on the compilation of the results obtained at the four published papers (Chapter 2 to 5) it is possible to achieve the initially proposed research objectives and contribute to improve qualitative risk assessment and control in work with engineered nanomaterials. Chapter 2 presents the general picture and introduces the basis for the subsequent research. In chapters 3 and 4 the qualitative risk assessment is studied based on the comparison between different methods (Chapter 3 and 4) and comparison with a quantitative risk assessment method (Chapter 3). In Chapter 5, the use of design is studied, as a support to identify risk control measures.

Considering the specific objectives, it is possible to relate them with the papers content, namely:

- To Evaluate how quality of information on nanomaterials influence qualitative risk assessment results – the influence in risk assessment results of the information gathered is discussed in Chapter 3;
- To confirm the suitability of the qualitative risk assessment methods for assessing the risk on engineered nanomaterials activities and processes – Chapters 3 and 4 are focused in this objective;
- To evaluate and improve the design-based approaches for risk control on engineered nanomaterials activities and processes – this objective is accomplished in Chapter 5.

- To contribute to improve workplace operational control and risk management in the nanotechnologies field – the contributions to the mentioned improvement can be found in Chapters 3, 4, and 5;

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CHAPTER 2. QUALITATIVE APPROACH TO RISK ASSESSMENT AND CONTROL IN ENGINEERED NANOPARTICLES OCCUPATIONAL EXPOSURE

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Abstract

The huge research effort and common use of nanomaterials, being an opportunity for economic growth, pose health and safety problems. The research on the nanoparticles health effects performed during the last decade shows the possible harmfulness of several nanoparticles, including those already present in everyday use products. Although the increasing knowledge in the nanotoxicology field, and also the occupational hygiene responses in order to develop quantitative methods to evaluate nanoparticles exposure risk, there is a uncertainty climate. The use of qualitative risk assessment methods appears as a suitable way to deal with the uncertainties and to support decisions leading to the risk control. Among these methods, those based in control banding, such as the CB Nanotool and the Stoffenmanager Nano, seems to become applied more frequently. Furthermore, the design approach to safety can be a valuable way to establish the strategy to protect the workers' health focusing in the production process in order to define the most effective measures to control the exposure risk.

2.1. Introduction

Nanotechnology is presented as part of a new industrial revolution, creating new opportunities in the areas of energy, materials, health, electronics, information technology and many other areas. Since Richard Feynman gave, in 1959, its conference "There's plenty of room at the bottom," which drew attention to the existing potential in the manipulation of matter at the atomic level (Feynman, 1960), that started the research (first), and then the development and use of hundreds of applications involving nanoscale materials.

According to the Project on Emerging Nanotechnologies (PEN) released information, the number of nanotechnology-based products available to consumers in March 2011 was about 1300 (WWICS, 2011). The main product categories were health and wellness (738), home and garden (209), automobile (126), and Food & Beverage (105) (WWICS, 2011). Massive investments are made worldwide in order to achieve new materials and products with innovative features.

However, this economic and social dawn is undoubtedly overshadowed by questions arising from possible adverse effects, either to human health or to the environment. From the previous experience, with particular emphasis on the issue of widespread use of asbestos and the nuclear technology, lead societies to think about if the scientific and technological development, and hence the economic development, can once again put a serious threat to people's health and well-being or environmental balance. On the other hand, the "precautionary principle" applied to the genetically modified organisms (GMOs), through a moratorium on its widespread use in agriculture, based on the lack of knowledge on harmful long-term effects, raises the doubt about the possible application the same principle to nanotechnology.

In this uncertainty climate, risk management is essential to sustain economic development without jeopardizing the environment and human health, especially in case of the industry and laboratories workers who are exposed to (possibly) dangerous nanomaterials.

In recent years, there has been a great effort in the development of knowledge in this area but the information available is still insufficient to establish whether the parameters for assessing the risk to the health of exposed workers or the exposure limit values that would refer to that same exposure. Both in the field of toxicology and in the industrial hygiene, improvements have been made to better characterize the risk during operations with nanomaterials but the results are still unsatisfactory.

This article goal is to identify the current knowledge on nanoparticles characterization and qualitative occupational risk assessment and control in the nanomaterials field.

2.2. State-of-the-art

In short, nanotechnology can be defined as the nanometer scale matter understanding and control, more specifically material smaller than 100 nm, resulting in size dependent new applications and purposes.

The European Commission published in the Official Journal of the European Union on 20 October 2011 the following definition for nanomaterial:

"«Nanomaterial» means 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."

In Occupational Hygiene the nanoparticle concept is more relevant for the personal exposure assessment. The nanoparticle definition, consistent with the previous concepts, is "particle with a nominal diameter (such as geometric, aerodynamic, mobility, projected-area or otherwise) smaller than about 100 nm" (Technical Committe ISO/TC 146, 2007).

At present, we are witnessing the transition from the first generation of passive nanostructures to the so called second generation nanotechnologies which include active nanostructures (M. C. Roco et al., 2011). In a longer term, it is anticipated the third generation nanotechnologies of "Systems of Nanosystems" development and trading and, later the fourth generation, "Molecular Nanosystems" dawn (Bowman & Hodge, 2006; Renn & Roco, 2006). Complexity is increasing as well as the related uncertainties so that, despite the achieved growing acknowledgment on nanomaterials, there are always new conditions that impose new challenges.

2.2.1. HUMAN HEALTH EFFECTS

When referring nanomaterials we must consider the variety of materials, both in its composition, shape, size and other characteristics, due to the different behaviors and toxicological effects identified in toxicological tests (Savolainen et al., 2010).

Over the last years, especially in the last decade, toxicological tests have been performed with different types of engineered nanoparticles (NP) (e.g., single-walled carbon nanotubes; ultrafine TiO_2; ultrafine carbon black; silver; etc.), on the attempt to understand their effects on the human body. These are mainly in vitro and in vivo tests performed according to techniques used for "traditional" materials. The NP tested present different behaviour in the human body when compared with larger particles of the same material. Furthermore, the showed effects in the lungs such as deposit in the alveoli, evade phagocytosis, produce interstitial inflammation, produce fibrosis, produce tumours or induce granulomas, some NP show the ability to pass the body barriers and enter in the circulatory system, penetrate in various organs, (Schulte, Geraci, et al., 2008)

With respect to carcinogenicity, the existing data are inconclusive, although some evidence of possible carcinogenic effect of nanoparticles that do not appear to result from its composition, namely in the carbon nanotubes (Becker, Herzberg, Schulte, & Kolossa-Gehring, 2011).

We are facing a scenario in which there is already a significant amount of information on the health effects of nanoparticles but where the uncertainty is yet large, while the scientific community tries to improve the information quality.

To establish a knowledge base necessary to assess the risk to human health associated with exposure to engineered nanomaterials, staged testing strategies proposals have been made (Savolainen et al., 2010).

A materials physiochemical and toxicity characterization base tests battery, presented in Table 2.1 was proposed by another author (Warheit et al., 2007).

Table 2.1 – Nanomaterials base set of hazard tests (Warheit et al., 2007)

Nanomaterial physiochemical characterization	**Mammalian hazard tests**	**Genotoxicity tests**	**Aquatic screening battery**
Size and size distribution Crystal structure Chemical composition Surface reactivity	Pulmonary bioassay Skin irritation Skin sensitization Acute oral toxicity Eye irritation	Bacterial reverse mutation Chromosomal aberration	Rainbow trout Daphnia Green algae

This tests set does not include all health affection relevant aspects, and can be regarded as a primary diagnosis to the concerned nanomaterial, and, subsequently, must be complemented by other tests to enable a more complete characterization.

The Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) sets a wider range of tests for the physicochemical characterization of NM, including the following: size and size distribution of free particles and fibers/rods/tubes, specific surface area, stability in relevant media (including the ability for aggregating and disaggregating), surface adsorption properties, water solubility, being also recommended the knowledge of chemical reactivity and, depending on the nature of the nanoparticles, photoactivation capabilities and the potential to generate active oxygen (SCENIHR, 2009).

In the same report the SCENIHR, although the information is yet scarce, refer the possibility to infer some effects through the data intercomparison when there are similarities in the characteristics of engineered nanomaterials with other particles already studied and characterized.

Another contribution to obtain reliable results in a more quick and economical way, is the proposed use of *in vitro* tests, specifically designed for nanomaterials and held in co-culture instead of only one type of tissue used for testing (Clift, Gehr, & Rothen-Rutishauser, 2011). In another study published in 2008 there has not been found correlation between the results of the *in vitro* and *in vivo* assays made to assess the effects of different types of nanoparticles on the lung tissue, leading to conclude that *in vitro* tests should be more sophisticated in order to better simulate the conditions of the lung (Sayes, Reed, Subramoney, Abrams, & Warheit, 2008).

Considering that the basic principles are established to frame the engineered nanomaterials characterization in relation to its harmfulness, it may be considered that the information resulting from it will contribute to workers' risk assessment, considering the necessary precaution whenever information is insufficient or less precise.

2.2.2. OCCUPATIONAL RISKS ASSESSMENT IN OPERATIONS WITH NANOMATERIALS

The methods used for risk assessment in Occupational Health and Safety can be divided into two groups: qualitative methods and quantitative methods. With respect to chemical contaminants exposure risk the quantitative methods are preferably used. In general, the methods include the measurement of the concentration of each chemical agent in the air of the worker's breathing zone, and taking into account the duration of the worker exposure, to compare the obtained value with the exposure limit value set for this agent to assess the risk to the exposed worker.

When the agent is a nanomaterial, even well-known and characterized, there are doubts about the best method for concentration measurement (Maynard, 2006) and the occupational exposure limits values are not yet defined, although there are some proposals for a few types of nanoparticles (Schulte, Murashov, Zumwalde, Kuempel, & Geraci, 2010).

In a paper on the nanoparticles exposure risk evaluation, an international group of researchers reported that the quantification of risk is full of uncertainties, such as the not yet fully understand contribution that the nanoparticle's physical structure has for its toxicological effects, the differences found among different nanoparticles concerning the behavior in the lung tissue or the absence of consensus on the particles most relevant characteristics to the exposure, i.e., if the specific surface area and/or the size distribution that seem more decisive than the mass (Zalk, Paik, & Swuste, 2009).

In this context, several authors refer the Control Banding as an appropriate method for assessing the exposure risk to nanoparticles (Beaudrie & Kandlikar, 2011; Maynard, 2007; Schulte, Murashov, et al., 2010). As examples of Control Banding methods developed for the nanoparticles exposure there are the CB Nanotool (Paik, Zalk, & Swuste, 2008) and the Stoffenmanager Nano (van Duuren-Stuurman et al., 2011).

Other qualitative methods are referred in bibliography, considered as an alternative to the lack of quantitative methodologies for assessing the risk from both occupational and environmental context, in particular, the experts judgment and a more structured variant, the expert elicitation (Kandlikar, Ramachandran, Maynard, Murdock, & Toscano, 2006; Murashov & Howard, 2009) and the multi-criteria decision analysis (Linkov, Satterstrom, Steevens, Ferguson, & Pleus, 2007).

At the current state of knowledge regarding the nanomaterials risks, in particular with respect to nanoparticles exposure, the choice to use qualitative risk assessment methodologies seems to be an acceptable option.

2.2.3. DESIGN ANALYSIS APPROACH

Some authors have been defending the need for methodologies that deal with the nanotechnologies risks based on the processes or products design (Amyotte, 2011; Fleury, Bomfim, Metz, Bouillard, & Brignon, 2011), referring, in particular, the "Design for Safer Nanotechnology" (Morose, 2010).

The importance of the occupational health and safety issues integration in the process design (systems, installations, production lines, machines, tools, etc.) is officially recognized (European Parliament & Council of the European Communities, 2006) but not always considered. Although the occupational safety and hygiene research pays more attention to risk analysis (Swuste, 1996), several authors in this domain have performed some investigation in the safety by design field, specially the Safety Science Group of Delft University of Technology (e.g., Stoop, 1990; Schupp et al., 2006; Hale, Kirwan and Kjellen, 2007). Swuste proposed a systematic approach towards solutions (Swuste, 1996) based on three complementary elements:

- Hazard process model;
- Design analysis;
- Problem-solving cicle.

A simple way to represent the hazard exposure in workplaces is using the model presented in Figure 2.1.

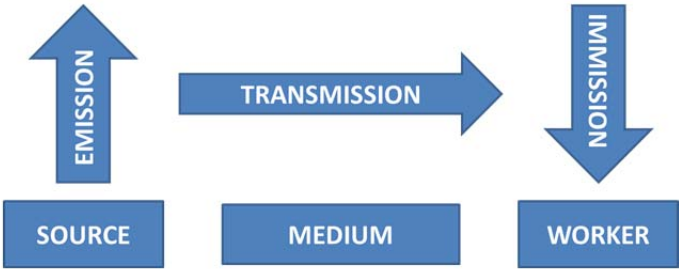

Figure 2.1 – Hazard process model (adapted from Swuste, 1996)

The term immission is not widely used in occupational hygiene. Instead, it is used the term exposure and the worker is referred as exposed worker. According to this model, it is possible to control de hazard acting on the three phases, eliminating or at least reducing the emission, the transmission and/or the immission. Both regulatory laws (Council of the European Communities, 1989) and occupational health and safety good practices and standards (IPQ, 2008) set priority on determining or considering the hazard control methods: first of all the hazard elimination or reduction (reducing emission), second acting on the transmission, and finally acting on the exposure. In other words, it is acting from the source to the exposed worker.

More complex models for nanoparticles exposure had been developed such as the conceptual model (Schneider et al., 2011; Tielemans et al., 2008). Although the more elaborated form, the essential aspects are common in both models.

The design analysis methodology allows to study and understanding the workplace conditions. In design analysis the production process is split into three levels of decision (Swuste, 1996), described below:

- Production function: is the highest level and divides the production process into his core activities;

- Production principle: identifies the general process, motive power and operational control methods by which the production function can be achieved;
- Production form: is the lowest level and specifies the detailed design by which the production principle will be accomplished.

If there is a large number of production processes, the type of functions (or unit operations in rigor), in which each process can be broke down, is relative small. The main unit operations categories are: material receipt, material storage, transport and feed, processing, packaging, waste disposal.

The processing operations can be subdivided in subcategories that vary from one industry sector to other, and once enumerated will permit to study the more effective and reasonable control measure or set of control measures to apply in each particular situation.

On the occupational safety & health point of view, the focus on the production function will allow to find the less hazardous way to achieve the same production result or to choose the best available technics to control the hazard.

The problem solving cycle has been proposed as a systematic approach to generate solutions in occupational risk management and provides a systematic tool to find solutions to control the existing risks (Hale, Heming, Catfhey, & Kirwan, 1997).

Applying it together with design analysis, it will permit to identify and develop the most suitable risk control measures in each engineered nanomaterial production process even in poor knowledge and high uncertainty situations. Combining different information sources will create synergies and conduct to the best available prevention and protection measures.

The design approach put the focus in the risk control, rather in risk assessment. It provides a tool to eliminate the risk, prevent exposure and/or protect the workers. Adapting the bow-tie model proposed by the safety science group (Ale et al., 2008) to the occupational hygiene field will help to establish the necessary barriers to control the risks arising from different workplace exposure scenarios.

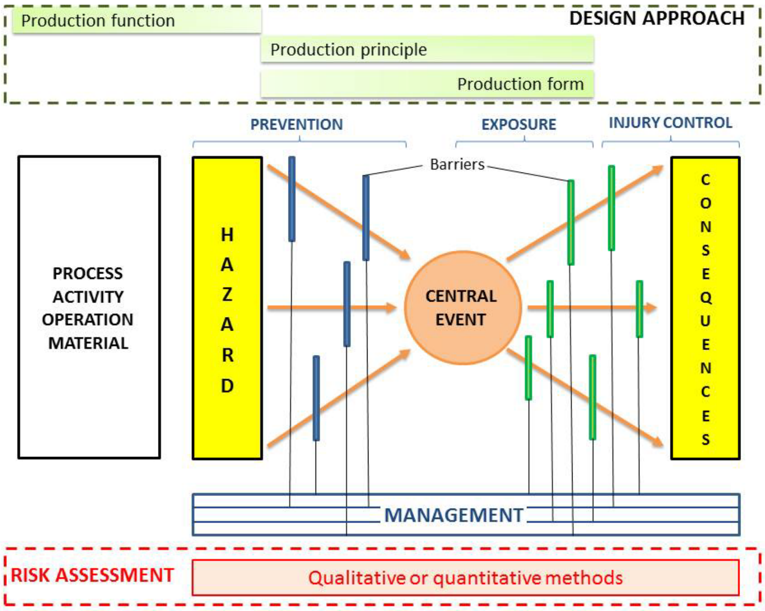

Figure 2.2 – Bow-tie model with arrows representing different exposure scenarios

The design analysis approach as described above can be a suitable method to deal with the nanotechnology occupational risks. The knowledge gap and the related uncertainties can be overcome with a methodology that focuses in solutions (risk control) rather than in the risk evaluation. Moreover, combining together the two focuses will allow to achieve the best practicable preventive actions.

2.3. Conclusions

The lack of information and the uncertainty related to NP occupational exposure are an actual problem. The current knowledge is evolving:

- Results from the in-vitro and in-vivo toxicological tests show harmful effects from the nanoparticles;
- Nanoparticles characterization battery tests are already available and will allow to obtain information to exposure risk assessment;
- Quantitative exposure assessment methods are not yet consensual and the same applies to the exposure limit values;
- Qualitative exposure risk assessment methods are in use and gather interest from the experts;

- The design approach to safety is presented as an alternative to develop safer product and processes in the nanotechnologies field.

Thus, there is an opportunity to develop additional research in this area in order to confirm the applicability of the qualitative risk assessment and the design analysis approach in the NP occupational hygiene field. The referred research should include qualitative risk assessment methods in the workplaces where NM are used. Applying the design approach, focusing on the risk control, it is possible to select the production processes that minimize workers' exposure.

CHAPTER 3. RISK ASSESSMENT IN A RESEARCH LABORATORY DURING SOL-GEL SYNTHESIS OF NANO-TIO$_2$

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Abstract

The occupational risks in the nanotechnology research laboratories are an important topic since a great number of researchers are involved in this area. The risk assessment performed by both qualitative and quantitative methods is a necessary step for the management of the occupational risks. Risk assessment could be performed by qualitative methods that gather consensus in the scientific community. It is also possible to use quantitative methods, based in different technics and metrics, as indicative exposure limits are been settled by several institutions. While performing the risk assessment, the information on the materials used is very important and, if it is not updated, it could create a bias in the assessment results. The exposure to TiO$_2$ nanoparticles risk was assessed in a research laboratory using a quantitative exposure method and qualitative risk assessment methods. It was found the results from direct-reading Condensation Particle Counter (CPC) equipment and the CB Nanotool seem to be related and aligned, while the results obtained from the use of the Stofenmanager Nano seem to indicate a higher risk level.

Keywords: nanoparticles; occupational hygiene; exposure; inhalation; control banding.

3.1. Introduction

There is a huge amount effort put into the research of new materials in the field of nanotechnology. Most industrialized countries promote the research programmes of their universities, research institutions and companies (Directorate for Science, 2009). Portugal is not an exception, and Portuguese universities have several research teams working in the area of nanotechnology. Since 2004, the number of papers on nanotechnology published by researchers from Portuguese universities has increased (Eugénio & Fatal, 2010), reflecting the work done in several fields, such as materials, electronics, chemistry and health care, among others.

The occupational safety and hygiene (OSH) issues in nanotechnology research laboratories are receiving special attention due to the increasing activity in the field. As researchers are dealing with materials with unknown or poorly known proprieties, a precautionary approach to the risks is very important (Groso, Petri-Fink, Magrez, Riediker, & Meyer, 2010). These concerns are also reflected in the number of publications from several Health & Safety-related institutions, which have established safety guidelines for nanotechnology research laboratories (NIOSH, 2012; The UK NanoSafety Partnership Group, 2012).

Considering that the quantitative methods often used in Occupational Hygiene (OH) are not fully suited to assessing the hazards of nanoparticle exposure, qualitative risk assessment tools have garnered interest among researchers and practitioners in the field of occupational safety and hygiene (Silva, Arezes, & Swuste, 2013). Several methods based on different approaches, aims and with different levels of complexity have been developed in recent years. Vervoort (2012), for an example, identified 32 different methods in a literature review carried out in 2012 (Vervoort, 2012). Qualitative risk assessment tools for nanoparticles based on the control banding (CB) approach have been discussed as useful tools for risk assessment related to worker's exposure to engineered nanoparticles, and several authors and institutions have found it helpful in nanotechnology occupational risk management (Beaudrie & Kandlikar, 2011; Environment Directorate OECD, 2010a; Kuempel, Geraci, & Schulte, 2012; Murashov & Howard, 2009; C Ostiguy et al., 2009; Schulte, Geraci, et al., 2010; Technical Committee ISO/TC 229, 2012b; The UK NanoSafety Partnership Group, 2012). The CB risk assessment approaches have been tested in research environments (Groso & Meyer, 2013; Paik et al., 2008) and their appropriateness has been discussed (Brouwer, 2012).

Quantitative methods to measure the concentration of airborne nanoparticles were also able to be used to assess the exposure in research laboratories (Fleury et al., 2013; Ramachandran et al., 2011), resulting in the advancement of OSH intervention in the field of nanotechnology.

The present study was conducted in the materials research laboratory of a Portuguese university, where several nanomaterials and nanostructured materials are studied. During the research process, various situations involving the possible emission of nanoparticles may occur due to the manipulation of nanomaterials. The purpose of this paper is to compare the risk assessment results obtained with different qualitative control banding tools, namely the CB Nanotool and the Stoffenmanager Nano, and the results from measurements of airborne particle concentration.

The underlying research questions in this study were the following: 1. does the quality of information on nanomaterials influence the results of risk assessment; 2. are the qualitative risk assessment methods suitable for assessing risk in a materials research work environment; and 3. do different methodologies, both qualitative and quantitative in nature, identify comparable risk levels for the same tasks?

3.2. Methodology

3.2.1. CONTROL BANDING – CB NANOTOOL

Based on the control banding risk assessment methodology, an international group of researchers developed a pilot method for the qualitative risk assessment of nanoparticles, known as CB Nanotool (Paik et al., 2008). The referred tool was tested and underwent some adjustments in subsequent research (Zalk et al., 2009).

The method consists of determining the severity of the hazard, based on the nanomaterial's characteristics, and determining the probability of exposure, based on the nature of the work (tasks, operations) to be performed.

3.2.1.1. Severity determination

The severity of the nanomaterial is determined by the factors presented in Table 3.1.

Table 3.1 – CB Nanotool severity band factors

Material form	Factor	Characteristics				
		Points assigned				
Parent material hazard (Maximum possible points: 30)	**OEL (µg/m3)**	< 10	10 - 100	101 - 1000	Unknown	> 1000
		10	5	2,5	7,5	0
	Carcinogen?	Yes	No	Unknown		
		4	0	3		
	Reproductive hazard?	Yes	No	Unknown		
		4	0	3		
	Mutagen?	Yes	No	Unknown		
		4	0	3		
	Dermal hazard?	Yes	No	Unknown		
		4	0	3		
	Asthmagen?	Yes	No	Unknown		
		4	0	3		
Nanoscale material hazard (Maximum possible points: 70)	**Surface reactivity**	High	Medium	Low	Unknown	
		10	5	0	7,5	
	Particle shape	Tubular or fibrous	Anisotropic	Compact or spherical	Unknown	
		10	5	0	7,5	
	Particle diameter (nm)	1-10 nm	11-40 nm	>40 nm	Unknown	
		10	5	0	7,5	
	Solubility	Insoluble	Soluble	Unknown		
		10	5	7,5		
	Carcinogen?	Yes	No	Unknown		
		6	0	4,5		
	Reproductive hazard?	Yes	No	Unknown		
		6	0	4,5		
	Mutagen?	Yes	No	Unknown		
		6	0	4,5		
	Dermal hazard?	Yes	No	Unknown		
		6	0	4,5		
	Asthmagen?	Yes	No	Unknown		
		6	0	4,5		

The severity band results from the sum of the points of all factors according to the following scale: 0-25: low severity; 26-50: medium severity; 51-75: high severity; 76-100: very high severity.

3.2.1.2. Probability determination

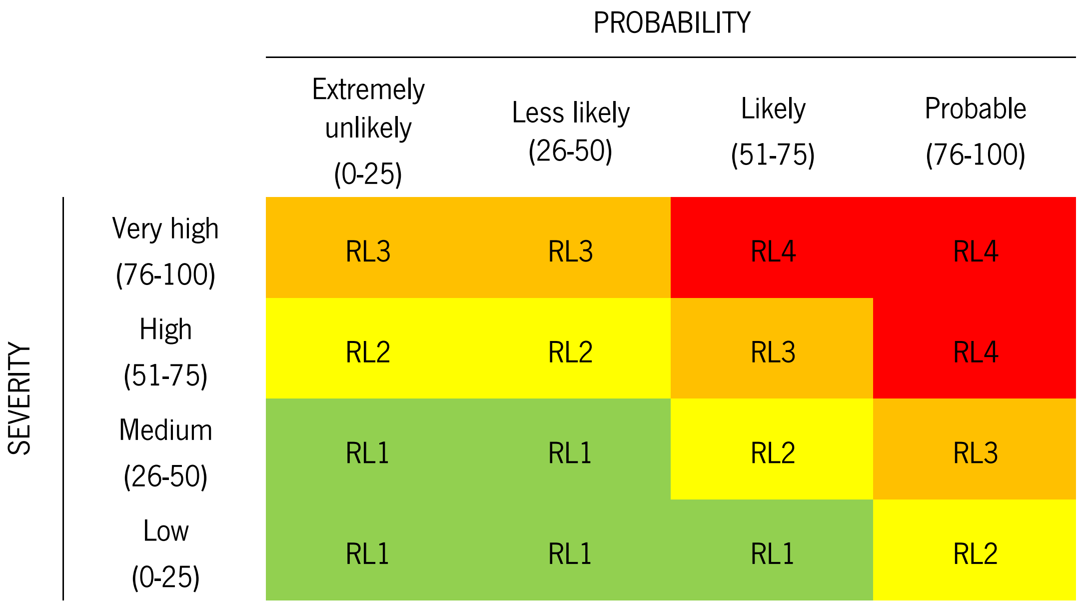
To determine the exposure probability, the factors present in Table 3.2 are considered.

Table 3.2 – CB Nanotool probability band factors

Exposure	**Factor**	**Characteristic**				
		Points assigned				
Exposure probability (Maximum possible points: 100)	**Estimated amount of chemical used in one day (mg)**	> 100	11-100	0-10	Unknown	
		25	12,5	6,25	18,75	
	Dustiness	High	Medium	Low	Unknown	
		30	15	7,5	22,5	
	Number of employees with similar exposure	> 15	11-15	6-10	1-5	Unknown
		15	10	5	0	11,25
	Frequency of operation (annual)	Daily	Weekly	Monthly	>Monthly	Unknown
		15	10	5	0	11,25
	Operation duration (hours per shift)	> 4	1-4	30-60 min	< 30 min	Unknown
		15	10	5	0	11,25

To obtain the probability band score, the points of all factors are summed and the probability is determined using the following scale: 0-25: extremely unlikely; 26-50: less likely; 51-75: likely; 76-100: probable.

The risk is assigned using a 4x4 matrix, resulting from a combination of the severity and probability determinants (Figure 3.1).



SEVERITY		PROBABILITY			
		Extremely unlikely (0-25)	Less likely (26-50)	Likely (51-75)	Probable (76-100)
	Very high (76-100)	RL3	RL3	RL4	RL4
	High (51-75)	RL2	RL2	RL3	RL4
	Medium (26-50)	RL1	RL1	RL2	RL3
	Low (0-25)	RL1	RL1	RL1	RL2

Figure 3.1 – CB Nanotool matrix

One of four risk levels (or control bands) is determined (Zalk et al., 2009):

- RL1 – General ventilation
- RL2 – Fume hoods or local exhaust ventilation
- RL3 – Containment
- RL4 – Seek specialist advice

To perform the risk assessment, one can use the CB Nanotool 2.0 available on the Internet at http://controlbanding.net/Services.html.

3.2.2. STOFFENMANAGER NANO

The Stoffenmanager Nano is a web-based qualitative risk assessment tool regarding operations with manufactured nano-objects. It was developed from the existing Stoffenmanager dangerous substances risk assessment tool created by a consortium (van Duuren-Stuurman et al., 2011) and consists of the combination of a hazard band and an exposure band.

For the hazard band classification, the following characteristics of the manufactured nano-objects are considered:

- Particle size
- Solubility in water

- Persistent fibres or other structure
- Toxicological classification (the parent material, if it is unknown for the manufactured nano-object)

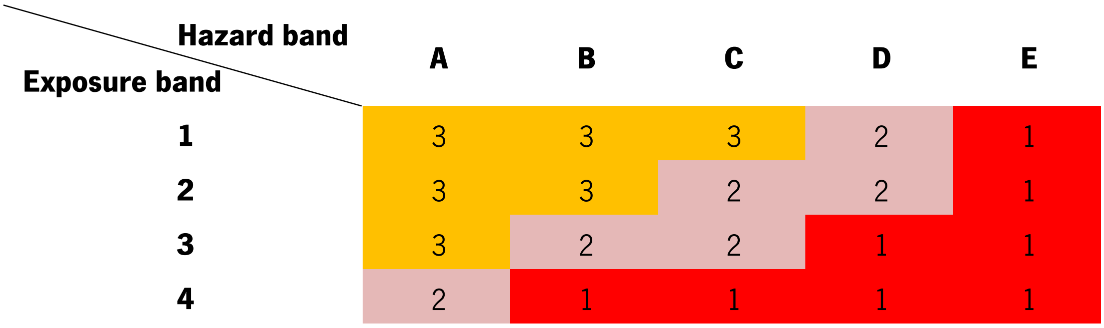
The combination of the assigned factors leads to a 5-band hazard classification from the lowest A to the highest E. In the case of several well-known nanomaterials, the hazard band may already be defined by the method, based on the available scientific information for each nanomaterial (van Duuren-Stuurman et al., 2011).

The exposure band is based on the conceptual model of exposure and takes into consideration the following items:

- Time and frequency of the task
- Emission potential from the source: activity emission potential, substance emission potential, near field/far field
- Transmission compartment: localized control, segregation, dilution/dispersion, separation, surface contamination
- Receptor (immission): personal protective equipment

The exposure band ranges from levels 1 (lowest) to 4 (highest) and are determined by the algorithm calculation, taking into consideration the previously mentioned factors related to exposure.

Combining the two, the hazard and exposure bands form a 5x4 matrix and a three-level risk or priority classification is obtained (see Figure 3.2). The method allows one to obtain a classification with or without considering the duration/frequency of the task (van Duuren-Stuurman et al., 2012).



Hazard band **Exposure band**	**A**	**B**	**C**	**D**	**E**
1	3	3	3	2	1
2	3	3	2	2	1
3	3	2	2	1	1
4	2	1	1	1	1

Figure 3.2 – Stoffenmanager Nano matrix

Risk assessment was performed with the online tool Stoffenmanager Nano 1.0, available at http://nano.stoffenmanager.nl/.

3.2.3. OTHER METHODS BASED ON CONTROL BANDING

In the literature, other control banding-based risk assessment tools can be found (Brouwer, 2012):

- Precautionary Matrix for Synthetic Nanomaterials (Höck et al., 2011);
- ANSES (Claude Ostiguy, Riediker, Triolet, Troisfontaines, & Vernez, 2010);
- Danish NanoSafer;
- Guidance on Working Safely with Nanomaterials and Nanoproducts (I. R. Cornelissen et al., 2011).

The Precautionary Matrix for Synthetic Nanomaterials is not intended to be a risk assessment tool. Rather, it helps to identify risk factors not only during the processing of nanomaterials but also during research and other life-cycle phases of the nanomaterial, focusing on the workers, users and environmental protection (Höck et al., 2011).

The ANSES control banding risk assessment tool was developed to be integrated in a risk management process, based on the PDCA (Plan, Do, Check, Act) improvement cycle. The COOSH Essentials for chemical risk assessment is the basis of the ANSES tool. In the chemical hazard of the parent material, the nano-form material or an analogous nanomaterial is considered together with some incremental factors to assign one of the 5 hazard bands. For the exposure band, the emission potential from the nanomaterial is considered, taking into account the physical form of the nanomaterial, and increases with volatility, dustiness, and processing factors, giving rise to a four-level band (Claude Ostiguy et al., 2010).

According to Brouwer (2012), Danish NanoSafer is applicable to the down-stream use of powdered nanomaterials. The four-level hazard band is based on the occupational exposure limit (OEL) of the bulk material recalculated for the size and density of the material, the biopersistence and shape, and the surface functionalization. The exposure band results from the amount of powder handled, the activity level, and the dustiness index of the powder in a simpler model, or the particle concentration in the near field and the far field may be estimated using the emission rate and ventilation factors. The assignment to one of the five levels of the exposure band is given by the ratio of the emission rate to the OEL of the bulk material, recalculated to account for surface area concentration (considering all particles 200 nm in diameter).

The Guidance on Working Safely with Nanomaterials and Nanoproducts (I. R. Cornelissen et al., 2011) presents hazard and exposure bands with three levels each. The hazard is defined in terms of the solubility, persistence and fibrous characteristics of the nanoparticles, while the exposure results from the possibility of nanoparticle emission during the work.

3.2.4. AIRBORNE PARTICLE MEASUREMENT AND OCCUPATIONAL EXPOSURE LIMITS

During work with manufactured nanomaterials, workers are potentially exposed to airborne nanoparticles. Unlike in the case of work with traditional materials, the occupational hygiene measurement methods are not fully suitable when the agent is a nanomaterial. Even in the case of well-known and characterized nanoparticles, such as TiO_2, silica or carbon black, doubts have been raised regarding the best method for measuring concentration (Maynard, 2006).

Nonetheless, it is possible to assess exposure using various direct-reading equipment and sampling media for subsequent analysis (Ramachandran et al., 2011).

The use of direct reading equipment is possible, but the availability of several different types and the doubts in the exposure metrics pose difficulties when choosing the most suitable method, leading to recommendation of a multi-metric approach (Ramachandran et al., 2011). This approach is not practical for occupational hygiene practitioners due to the inherent costs and entropy in the workplace. Currently, there are several available methods to measure the concentration of and to characterize airborne nanoparticles (C Ostiguy et al., 2009):

- Mass concentration: cascade impactors, piezoelectric microbalances, tapered element oscillating microbalance, electrical low pressure impactor (ELPI), scanning mobility particle sizer (SMPS)
- Surface area: diffusion charger, direct-reading instruments, SMPS, transmission electron microscopy (TEM)
- Number concentration: condensation particle counter, electrometers, SMPS, ELPI, scanning electron microscopy (SEM), TEM
- Granulometric distribution: SMPS, differential electrical mobility sizer, cascade impactors, ELPI, SEM, TEM

– Chemical composition: laboratory techniques, TEM, SEM

Moreover, doubts have been raised about the appropriate nanoparticle dose metric, as the OEL values have not yet been fully defined, although there are some proposals for a few types of nanoparticles (Schulte, Murashov, et al., 2010; van Broekhuizen, van Veelen, Streekstra, Schulte, & Reijnders, 2012).

The uncertainties related to this issue are still high. Because the health hazard and, consequently, both the hazard band rating and the OEL are assumed from toxicological information, the existing doubts in nanotoxicology (Clift et al., 2011; Gonzalez, Lison, & Kirsch-Volders, 2008; Hankin, Boraschi, Duschl, Lehr, & Lichtenbeld, 2011) are a contributing factor to the overall risk assessment uncertainty.

Another relevant aspect is possible dermal exposure, which is not as important during work with micro-sized particles but becomes more significant in nanoparticle exposure (NIOSH, 2012; Stern & McNeil, 2008).

3.2.4.1. Groups of materials

The British Standards Institute in the published document PD 6699-2 ''Guide to safe handling and disposal of manufactured nanomaterials'' (BSI - British Standards, 2007b) establishes indicative OEL referring to four categories of nanoparticles, presented in Table 3.3.

Table 3.3 – Indicative OEL for nanoparticle categories referred in PD 6699-2

Nanoparticle type	Benchmark value	Notes
Fibrous nanomaterials	0,01 fibres/ml	Assessed by scanning or transmission electron microscopy
Nanomaterials with the bulk form already classified as carcinogenetic, mutagenic, asthmagenic or a reproductive toxin	0,1 x WEL	WEL: Workplace Exposure Limit of the bulk material, usually expressed in mg/m^3
Insoluble nanomaterials	0,066 x WEL or 20 000 particles/ml	WEL: Workplace Exposure Limit of the bulk material, usually expressed in mg/m^3
Soluble nanomaterials	0,5 × WEL	

The Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung (IFA) of Germany defined benchmark values for certain types of nanomaterials, taking into account their properties. In addition to defining these reference values, several recommendations for the use of the benchmark values are stated (IFA, 2013).

Table 3.4 – Benchmark values for nanoparticles types defined by IFA

Nanoparticle type	Benchmark value	Notes
Metals, metal oxides and other biopersistent granular nanomaterials (density of > 6 000 kg/m^3)	20 000 particles/cm^3	Particle size between 1 and 100 nm
Biopersistent granular nanomaterials (density < 6 000 kg/m^3)	40 000 particles/cm^3	Particle size between 1 and 100 nm
Carbon nanotubes (CNTs) satisfying the WHO respirable fibre criterion with possible asbestos-like effects	0,01 fibres/cm^3	Recommended the use of CNT with statement from the producer
Ultrafine liquid particles (such as fats, hydrocarbons, siloxanes)	Maximum Workplace Limit (MAK) or workplace limit (AGW) applicable to the substance	

In the Netherlands, the values proposed by the IFA are being used, with minor changes, as Nano Reference Values (NVR) for provisional use until no occupational exposure values based on health evidence are determined (van Broekhuizen, van Broekhuizen, Cornelissen, & Reijnders, 2012).

Table 3.5 – Dutch Nano Reference Values

Nanomaterial description	**NRV**	**Nanomaterial type**
Rigid biopersistent, nanofibres for which asbestos like effects cannot be ruled out.	0,01 fibres/cm^3	Carbon nanotubes or fibre-like metal oxides for which asbestos like effects cannot be ruled out.
Biopersistent granular nanomaterials with a diameter of between 1 and 100 nm and density of > 6 000 kg/m^3	20 000 particles/cm^3	Gold, silver, cerium dioxide, cobalt oxide, iron and iron oxides, lead, antimonium dioxide, tin dioxide.
Biopersistent granular nanomaterials with a diameter of between 1 and 100 nm and density of < 6 000 kg/m^3	40 000 particles/cm^3	Al_2O_3, SiO_2, TiO_2, ZnO, nano clay, C_{60}, carbon black, dendrimers and polystyrene. Nanofibres for which asbestos like effects are explicitly excluded.
Non-biopersistent nanomaterials with a diameter of between 1 to 100 nm.	Common occupational exposure limits	Fats, siloxanes and common salt.

For nano-TiO_2, the IFA-proposed benchmark value is 40 000 particles/cm^3, which has also been assumed as the NRV in the Netherlands. According to the BSI proposal, the reference value that should be assumed is one tenth the OEL of bulk titanium dioxide.

3.2.4.2. Measurement strategy

It seems evident that the measurement strategy for assessing the exposure to nanoparticles could be the same as that used in the case of assessing the exposure to chemical agents. There is accumulated knowledge in “Field Hygiene” that could be used in nanotechnology workplaces. Among the different guides focused on chemical agent exposure, the Occupational Exposure Sampling Strategy Manual (Leidel, Bush, & Lynch, 1977) and the EN 689:1995 - Workplace atmospheres - Guidance for the assessment of exposure by inhalation to chemical agents for comparison with limit values and measurement strategy (CEN/TC 137, 1995) could be mentioned as giving relevant guidance for exposure assessment strategies.

However, several authors consider exposure to nanoparticles to be relevant during cleaning and maintenance tasks, or when malfunctions occur in the process (Brouwer, 2010; Swuste & Zalk, 2013; van Tongeren et al., 2010), leading to a special focus on those situations prior to considering normally functioning operations (Wang et al., 2012; Zimmermann et al., 2012).

3.2.5. INFORMATION GATHERING

One of the most important issues when performing risk assessment in occupational hygiene is information gathering, in regard to both contaminant characteristics and workplace factors. The importance of this knowledge and its use in achieving accurate results in risk assessments has been stressed in several publications, including the previously mentioned Occupational Exposure Sampling Strategy Manual (Leidel et al., 1977) and EN 689:1995 - Workplace atmospheres - Guidance for the assessment of exposure by inhalation to chemical agents for comparison with limit values and measurement strategy (CEN/TC 137, 1995).

Information collection is important for both qualitative and quantitative risk assessment methodologies. Qualitative methods provide users with a list of information needed to assess risk, while with quantitative assessments occupational, hygienists can follow the previously referred to or equivalent guidelines. In the ISO PDTS 12901-2, one can find a thorough list of information required for qualitative risk assessment (Technical Committee ISO/TC 229, 2012b), which may also be used as support for quantitative risk assessments.

Concerning workplace factors, it is necessary to gather information by interviewing workers and technical staff, by observing behaviours, and by inspecting the equipment and facilities.

Information on the properties of nanomaterials is available in safety data sheets (SDS) provided by the nanomaterials’ supplier and from scientific literature.

SDS are a helpful information source in the field of occupational safety and hygiene (OSH). In Europe, SDS are regulated by REACH (Registration, Evaluation, Authorization and Restriction of Chemicals) legislation, and their contents are defined according to The Globally Harmonized System of Classification and Labelling of Chemicals (GHS), established by the United Nations. With respect to nanomaterials, there is a guide on how to prepare SDS issued by the Swiss State Secretariat for Economic Affairs (State Secretariat for Economic Affairs (SECO), 2010), and more recently, the Technical Committee ISO/TC 229 has developed the Technical Report ISO/TR 13329 Nanomaterials — Preparation of Material Safety Data Sheet (MSDS) (Technical Committee ISO/TC 229, 2012c).

Typically, the scientific literature is not directly available to OSH practitioners and technical staff, but several national and international organizations provide freely available information resulting from nanotoxicology research through websites and publications. The US National Institute for

Occupational Safety and Health (NIOSH), the Health and Safety Executive (HSE) in the UK and the French Institut National de Recherche et de Sécurité (INRS) are national bodies that disseminate information on nanoparticle hazards, while at the international level, there is the Organisation for Economic Co-operation and Development (OECD).

3.2.6. SOL-GEL TIO_2 PREPARATION

3.2.6.1. Process description

The preparation of the sol-gel was divided into three phases, corresponding to three different groups of tasks, performed on different days:

- **Phase 1**: A mixture of isopropanol (IPA) with water (H_2O) and titanium isopropoxide $Ti\{OCH(CH_3)_2\}_4$ (400 ml) was stirred (600 rpm). A water and nitric acid (HNO_3) mixture was added drop by drop to induce TiO_2 precipitation as titanium hydroxide, suspended in the sol-gel solution; precipitation began after 40 min. After precipitation, the suspension was placed in a rotary evaporator and the IPA was removed (bath at 60°C). Finally, a dry powder remained in the container. This powder was mixed with water, and the evaporating process was repeated for 40 min. The process ended with the production of a crystalline gel structure. This gel was mixed with water to form the sol and was rotated in a closed-circuit to homogenize. The sol was dried again in a rotary evaporator in preparation for calcination (images 1 to 4 in Figure 3.3).
- **Phase 2**: The dried powder was weighed in ceramic crucibles (3 crucibles with 2 g of powder in each). The powder was calcinated at approximately 400 °C to become anatase TiO_2 or at higher temperatures to become rutile or a mixture of the two crystalline forms (image 5 in Figure 3.3).
- **Phase 3**: The calcinated powder was crushed by hand in an agate mortar. There were approximately 4 g of powder, crushed in 0.5 g batches (image 6 in Figure 3.3).

Figure 3.3 – Titanium dioxide preparation process – 1) Precipitation; 2) Rotary evaporation; 3) Sol in the rotary evaporator; 4) Dried gel; 5) Weighing of the gel in a balance; 6) Crushing in an agate mortar

The sol-gel method is a bottom-up process that can produce "pure" particles as well as doped particles or particles coated with Ag (Tobaldi, Pullar, Gualtieri, Seabra, & Labrincha, 2013).

During Phase 1, the produced gel can produce particles approximately 10-50 nm in size, connected by hydroxide bonds to form an agglomerate structure that still maintains nanoscale properties.

This is considered a "safe" nanomaterial production process with low emission potential, due to the hydroxide bonds that retain the individual nanoparticles. From a safety point of view, one major disadvantage is the use of dangerous substances such as titanium isopropoxide, IPA and nitric acid.

3.2.6.2. Work conditions

The work was performed in a closed room with an open door and an aspiration booth functioning at the side of the sol-gel reactor. No personal protective equipment was used by the research workers except during the crushing process, during which the operator was wearing a FFP2 respirator.

3.3. Results and discussion

3.3.1. COMPARING INFORMATION FROM SDS AND SCIENTIFIC SOURCES

The toxicology of titanium dioxide in both fine and ultrafine particle form has been heavily studied over the last decades. In spite of this, the information available has not made it possible to conclude the effects on human health. This scenario makes it difficult to establish a sound risk assessment; moreover, it impedes regulation of the use of titanium dioxide.

The health effects mentioned in scientific literature and in reports from international organizations are shown in Table 3.6.

Table 3.6 – Information on titanium dioxide health risks in literature (non-exhaustive)

Source	**Information**
International Agency for Research on Cancer (IARC) (IARC, 2010)	Carcinogenic Group 2B, this means "possibly carcinogenic to humans" (fine TiO_2)
National Institute for Occupational Safety and Health (NIOSH, 2011)	Exposure to ultrafine (or nano) TiO_2 should be considered a potential occupational carcinogen agent Recommends airborne exposure limits of 2,4 mg/m^3 for fine TiO_2 and 0,3 mg/m^3 for ultrafine (including engineered nanoscale) TiO_2
BAuA - Federal Institute for Occupational Safety and Health (Creutzenberg, 2013)	The toxicokinetic analysis in lungs (particulate and soluble TiO_2) and in remote organs (liver and brain) showed a small solubility effect under physiological conditions. Translocation to remote organs (liver and brain) was negligible. Lung tissue inflammation was found in the specimens exposed to higher doses. The NOAEL evaluation resulted in 3 mg/m^3. The results were similar for three different types of TiO_2 (with and without surface modification).
Long et al. (2006)	Stimulate immortalized brain microglia to produce reactive oxygen species
Jaeger, Weiss, Jonas and Kriehuber, (2012)	Cytotoxic and genotoxic potential in human keratinocytes in vitro
Shi, Magaye, Castranova and Zhao, (2013) – review article	Epidemiological studies thus far have not been able to detect an association between the occupational exposure to TiO_2 particles and an increased risk for cancer Pulmonary inflammatory responses and lung cancers are the most important adverse effect observed in experimental animals due to TiO_2 NP exposures Some evidence has shown that TiO_2 NPs cannot penetrate the intact skin into the human body

Table 3.7 presents a few examples of information on the health hazards mentioned in the SDS of different types of nano-sized titanium dioxide. The SDS were collected by performing a primary Internet search in July, 2013 and a secondary search in May, 2014.

Table 3.7 – Health hazard information in titanium dioxide SDS (examples)

Safety data sheet	**Information**
KRONOClean Version 2 Date: 22.03.2011	CAS: 13463-67-7 - Titanium dioxide (IV) Hazard information: Heavy formation of dust There are no indications of CMR effects in humans. IARC's overall evaluation was that "Titanium dioxide is possibly carcinogenic to humans (Group 2b)"
Version 3.18/REG_EU Date: 17.09.2012	CAS: 13463-67-7 - Titanium dioxide (IV) Hazard information: Not a hazardous substance or mixture according to Regulation (EC) No. 1272/2008 It is the opinion of many inhalation toxicologists that the tumour formation observed in rats results from a species-specific mechanism involving overloading of the rat lung (overload phenomenon). /.../ IARC evaluation scheme results in an overall assessment of titanium dioxide as "possibly carcinogenic to humans" (Group 2B)
Sigma-Aldrich Version 5.1 Date: 18.04.2013	CAS: 1317-70-0 - Anatase Not a hazardous substance or mixture according to Regulation (EC) No. 1272/2008 This product is or contains a component that is not classifiable as to its carcinogenicity based on its IARC, ACGIH, NTP, or EPA classification IARC: 2B - Group 2B: Possibly carcinogenic to humans [Anatase (TiO_2)]
Version 5.2 Date: 13.05.2014	
Nanomaterialstore.com Date: 5/10/2010	CAS: 1317-70-0 - Anatase Hazard description: Xn Harmful (R 20 Harmful by inhalation. R 40 Possible risks of irreversible effects) To the best of our knowledge the acute and chronic toxicity of this substance is not fully known. IARC-3: Not classifiable as to carcinogenicity to humans. ACGIH A4: Not classifiable as a human carcinogen: Inadequate data on which to classify the agent in terms of its carcinogenicity in humans and/or animals. The Registry of Toxic Effects of Chemical Substances (RTECS) contains tumorigenic and/or carcinogenic and/or neoplastic data for components in this product.

The information that could be used to establish the health hazard due to TiO_2 exposure is not consistent with different information sources. In particular, the information included in SDS from different suppliers differs. Even within the same SDS, it is possible to find contradictory information, which could be explained by the use of information related to micro-sized TiO_2 and nano-sized TiO_2 or, in this case, a lack of information. The IARC's carcinogenicity classification is based on results of studies of micro-TiO_2 that were extrapolated to nano-TiO_2 by NIOSH (NIOSH, 2011), which is not referred to in any of the consulted SDS, and only one SDS was not updated after the cited publication.

3.3.2. MEASUREMENTS RESULTS

During the laboratory tasks, measurements were performed with a condensation particle counter TSI CPC 3007, which detects particles from 10 nm to >1 μm.

Given the duration of the different tasks performed during the sol-gel process, it was decided that the concentration during the entire period should be measured. Air was collected in the vicinity of the worker's location but not from his breathing area and was thus not a personal sampling. Prior to the task, the background concentration of particles in the work room was measured.

During phase 3 (powder crushing), air sampling was not possible due to equipment failure.

3.3.2.1. Phase 1 measurements

Prior to beginning the sol-gel process, the airborne particle background concentration was measured. The results are presented in Table 3.8.

Table 3.8 – Noise (background concentration) measurement in phase 1 workplace

Mean concentration (particles/cm^3)	18 900
Minimum concentration (particles/cm^3)	17 600
Maximum concentration (particles/cm^3)	20 100
Standard Deviation (particles/cm^3)	955
Sample Time (s)	300

During the operations, the CPC equipment continuously collected data with a 1-min integration time. Given the duration of the different tasks performed, the total duration of this phase was approximately 2 h 40 min. The results are presented in Table 3.9.

Table 3.9 – Measurement results during phase 1 of the sol-gel process

Mean concentration (particles/cm^3)	25 400
Minimum concentration (particles/cm^3)	14 700
Maximum concentration (particles/cm^3)	132 000
Standard Deviation (particles/cm^3)	10 400
Sample Time (s)	13 260

Figure 3.4 presents the time variation of the airborne particle concentration during the entire process. It is possible to identify certain concentration peaks.

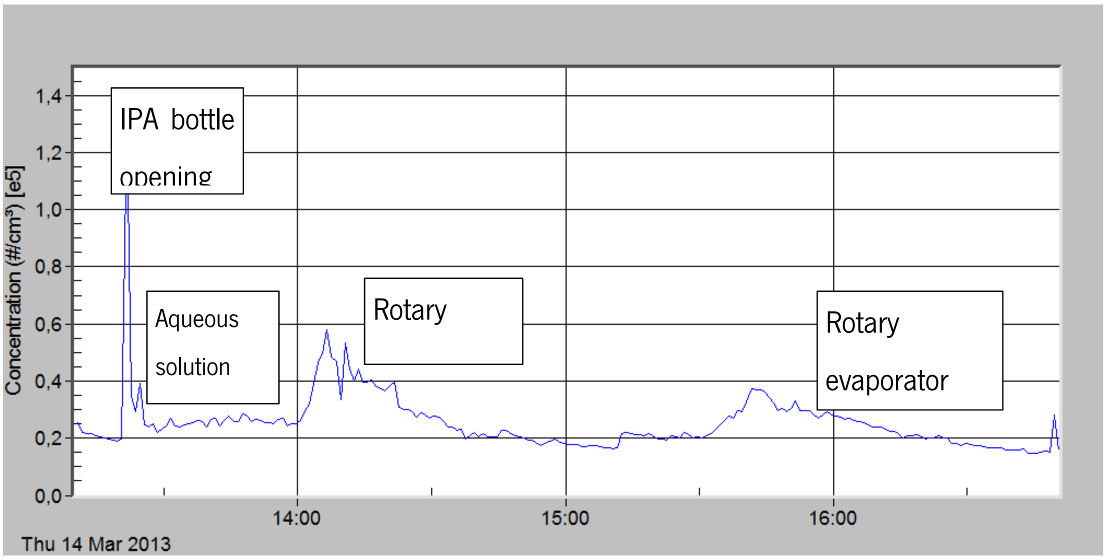


Figure 3.4 – Graphical representation of the airborne particle concentration during phase 1 of the sol-gel process

The mean concentration during phase 1 surpasses the background level by 6 500 particles/cm^3; if it is compared with the minimum value during sampling, a 10 700 particles/cm^3 increase is found. In Figure 3.4, there are three identifiable periods when the concentration of airborne particles increased. The first occurred when the IPA bottle was opened, although no explanation for that fact was identified. As it was not related to the process itself, no further investigation was conducted. The other two periods correspond to the rotary evaporator operation. Despite being a closed-circuit equipment, it is possible that leakage occurs during its operation, and particles carried by evaporation may escape to the workroom air.

As stated before, the sampling was not personal; however, as it was performed in the vicinity of the worker's location near the equipment, it could be considered to be a good indicator of personal exposure. Comparing with the reference values for titanium dioxide presented in Table 3.4 and Table 3.5, (40 000 particles/cm^3) the excess of 6 500 particles/cm^3 over the background concentration or the excess of 10 700 particles/cm^3 over the minimum are clearly below the reference value. Furthermore, the tasks took less than 3 hours to complete, much less than the 8-hour duration considered for the reference values.

3.3.2.2. Phase 2 measurements

Prior to the beginning of the phase 2, the airborne particle background concentration in the laboratory was measured. The results are presented in Table 3.10.

Table 3.10 - Noise (background concentration) measurement in phase 2 workplace

Mean concentration (particles/cm^3)	19 200
Minimum concentration (particles/cm^3)	19 100
Maximum concentration (particles/cm^3)	19 300
Standard Deviation (particles/cm^3)	123
Sample Time (s)	120

During the operations, the CPC equipment continuously collected data with a 1-s integration time. Given the duration of the tasks performed, the total duration of this phase was approximately 3 min. The results are presented in Table 3.11.

Table 3.11 – Measurement results during phase 2 of the sol-gel process

Mean concentration (particles/cm^3)	23 100
Minimum concentration (particles/cm^3)	15 500
Maximum concentration (particles/cm^3)	86 800
Standard Deviation (particles/cm^3)	10 900
Sample Time (s)	162

Figure 3.5 presents the time variation in the concentration airborne particles during phase 2. It is possible to identify certain concentration peaks in the short duration.

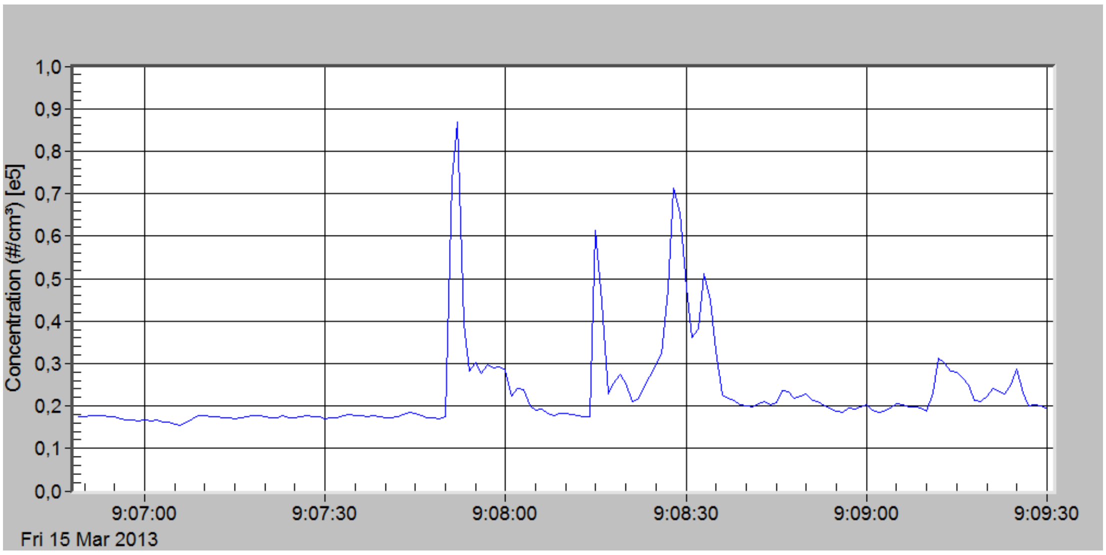


Figure 3.5 – Graphical representation of the airborne particle concentration during phase 2 of the sol-gel process

The weighing operation was of short duration, lasting less than 3 minutes. The mean concentration increment over the background concentration is approximately 4 000 particles/cm^3, related to the manipulation of the dried gel. With respect to the minimum value during the operation, the mean concentration exceeds this value by 7 600 particles/cm^3.

Similar to the results of phase 1, the particle concentration is below the reference value.

3.3.3. QUALITATIVE RISK ASSESSMENT

The qualitative risk assessment of the different tasks was performed using two tools: CB Nanotool 2.0, and Stoffenmanager Nano 1.0.

3.3.3.1. CB Nanotool

The information input for the qualitative risk assessment with CB Nanotool is presented in Table 3.12, together with the corresponding score.

Table 3.12 – Information input for risk assessment using CB Nanotool 2.0

CB NANOTOOL		Phase 1		Phase 2		Phase 3	
Severity band		***Answer***	***Score***	***Answer***	***Score***	***Answer***	***Score***
Parent material	Lowest OEL (mcg/m^3)	2 400	0	2 400	0	2 400	0
	Carcinogen?	Yes	4	Yes	4	Yes	4
	Reproductive hazard?	No	0	No	0	No	0
	Mutagen?	No	0	No	0	No	0
	Dermal hazard?	No	0	No	0	No	0
	Asthmagen?	No	0	No	0	No	0
Nanoscale material	Surface reactivity	Medium	5	Medium	5	Medium	5
	Particle shape	Compact or spherical	0	Compact or spherical	0	Compact or spherical	0
	Particle diameter (nm)	11-40 nm	5	11-40 nm	5	11-40 nm	5
	Solubility	Insoluble	10	Insoluble	10	Insoluble	10
	Carcinogen?	Yes	6	Yes	6	Yes	6
	Reproductive hazard?	Unknown	4,5	Unknown	4,5	Unknown	4,5
	Mutagen?	Unknown	4,5	Unknown	4,5	Unknown	4,5
	Dermal hazard?	Unknown	4,5	Unknown	4,5	Unknown	4,5
	Asthmagen?	Unknown	4,5	Unknown	4,5	Unknown	4,5
Severity band score			**48**		**48**		**48**
Severity band output		**Medium**		**Medium**		**Medium**	
Probability band		***Answer***	***Score***	***Answer***	***Score***	***Answer***	***Score***
Estimated maximum amount of chemical used in one day (mg)		15 000	25	6 000	25	6 000	25
Dustiness		None	0	Low	7,5	High	30
Number of Employees with Similar Exposure		1-5	0	1-5	0	1-5	0
Frequency of Operation (annual)		Monthly	5	Monthly	5	Monthly	5
Operation Duration (per shift)		1-4 hr	10	< 30 min	0	30-60 min	5
Probability band score			**40**		**37,5**		**65**
Probability band output		**Extremely Unlikely**		**Less Likely**		**Likely**	

For the severity band, it was necessary to consider the information related to both micro- and nano-TiO_2. The main source used in this assessment was the Current Intelligence Bulletin 63 - Occupational Exposure to Titanium Dioxide (NIOSH, 2011). Based on the increased suspicion of carcinogenicity, this health effect was also considered. Other health effects were not considered for micro-TiO_2, classified as having unknown health effects in its nanoscale form because the existing results are not conclusive, and doubts have emerged from the available research results (NIOSH, 2011; Shi et al., 2013). The particle shape and size were found in a technical article on the sol-gel preparation of TiO_2 (Tobaldi et al., 2013), and the surface reactivity was classified as medium, based on the cited NIOSH document that mentioned a low surface reactivity compared to crystalline silica particles.

The probability band factors were defined by the task characteristics, namely the quantity of materials used, the number of people involved (one operator) and the duration of the tasks. The dustiness was estimated by the materials characteristics of the liquid and wet materials in phase 1, the dried gel in phase 2, and the calcinated powder (during grinding) in phase 3, resulting in none, low and high classifications, respectively. The frequency of operation was assumed to be monthly, as the process is performed a few times per year.

In Table 3.13, the results of the risk assessment from the scores in Table 3.12 are presented.

Table 3.13 – Risk assessment results using CB Nanotool 2.0

Phase	Severity band	Probability band	Overall risk band	Control required
1- Sol-gel process	Medium	Extremely Unlikely	RL1	General ventilation
2- Weighing to calcination	Medium	Less Likely	RL1	General ventilation
3- Powder crushing	Medium	Likely	RL2	Fume hood or local exhaust ventilation

The severity band is "Medium" and is consistent with previous assessments, including those of nano-TiO_2 (Zalk et al., 2009). The probability band ranges from extremely unlikely for phase 1 to likely for phase 3, mainly resulting due to the dustiness factor.

It should be emphasized that the severity band score lies close to the borderline between “Medium” and “High”. Any change upwards in one factor could change the hazard band to “High” and would consequently move the overall risk to one level up.

3.3.3.2. Stoffenmanager Nano

Table 3.14 presents the information input for the Stoffenmanager Nano risk assessment.

Table 3.14 – Information input for risk assessment using Stoffenmanager Nano

STOFFENMANAGER NANO	**Phase 1**		**Phase 2**		**Phase 3**	
Hazard band	***Answer***		***Answer***		***Answer***	
Particle size	< 50 nm		< 50 nm		< 50 nm	
Solubility in water	No		No		No	
Persistent fibres or other structure	No		No		No	
Toxicological classification	Unknown		Unknown		Unknown	
Hazard band output	**D**		**D**		**D**	
Exposure band	***Answer***		***Answer***		***Answer***	
Duration of task	3 h 40 min		2 min 30 s		30 min	
Frequency of task	Monthly		Monthly		Monthly	
activity emission potential	low		low		low	
substance emission potential	low		low		medium	
near field/far field	near		near		near	
localized control	no		no		no	
segregation	no		no		no	
dilution/dispersion	yes		yes		yes	
separation	no		no		no	
surface contamination	no		no		no	
personal protective equipment	no		no		yes	
Exposure band output	**Time class**	**Task class**	**Time class**	**Task class**	**Time class**	**Task class**
	1	**2**	**1**	**2**	**1**	**2**

The hazard band factors were defined using the same standards as those for the CB Nanotool assessment. Regarding the toxicological classification, it was decided to consider it as “Unknown”, based on the classification from the nano-TiO_2 entry in the OECD list. Nevertheless, had the material been classified as “Carcinogenic”, the same hazard band “D” would have been obtained.

The exposure band factors were defined considering the task itself, the facilities and the adopted protective measures:

- Phase 1: wet chemistry (synthesis within solution), tasks in the breathing zone of the only worker, daily cleaning of the premises, no inspections or maintenance on a regular basis, working room with 100-1000 m^3 volume, natural ventilation, use of a product with low emissions, no work in a cabin, no personal protective equipment
- Phase 2: handling of products in small quantities, tasks in the breathing zone of the only worker, daily cleaning of the premises, no inspections or maintenance on a regular basis, working room with 100-1000 m^3 volume, natural ventilation, no control measures at source, no work in a cabin, no personal protective equipment
- Phase 3: handling of products in small quantities, tasks in the breathing zone of the only worker, daily cleaning of the premises, no inspections or maintenance on a regular basis, working room with 100-1000 m^3 volume, natural ventilation, no control measures at source, no work in a cabin, use of a FFP2 respirator

The Stoffenmanager Nano exposure band can be determined with or without considering the task duration and frequency. For the three phases of the process, the exposure band, accounting for the time factors, is the lowest at “1”, while the exposure band assigned to the task itself is at level “2”.

Table 3.15 presents the results of the risk assessment using Stoffenmanager Nano.

Table 3.15 – Risk assessment results using Stoffenmanager Nano 1.0

Phase	**Hazard band**	**Exposure band time**	**Risk time**	**Exposure band task**	**Risk task**
1- Sol-gel process	D	1	**2**	2	**2**
2- Weighing to calcination	D	1	**2**	2	**2**
3- Powder crushing	D	1	**2**	2	**2**

The risk level for each phase of the process is “2”, the intermediate level on the three-level scale, considering both the task itself and the duration and frequency. The hazard band “D” level is the determinant for this result, as it is the minimum risk level at this hazard band level.

3.3.4. DISCUSSION

One major aspect that has a strong influence on the risk assessment is the information on the nanomaterial characteristics. Depending on the information source used, the assessment may yield different results. TiO_2, in bulk form, may have different toxicological characteristics depending on the reference. The varying information included in the SDS also reflects the existing doubts in the scientific and technical community about the health effects of nano-sized TiO_2 and the most appropriate methods to assess the related risk (NIOSH, 2011; Warheit, 2013). TiO_2 is considered to be one example of a low-toxicity nanoparticles, and its micro-sized particles are used as a negative control in toxicological studies due to its low toxicity and low solubility (Donaldson & Poland, 2012). It is important to mention that in most in vitro and in vivo tests, it is necessary to have high doses of exposure to produce any effect. As an example, one can consider the inflammatory response of lung tissue; when low doses are used, the inflammation is very little, and the effects disappear after a recovery period (Creutzenberg, 2013; Ma-Hock et al., 2009).

Inconsistent information found among the analysed SDS is consistent with recent studies on the SDS of nanomaterials. In these studies, it was found that there was a lack of information necessary for the safe use of nanomaterials, including information on their toxicity and physicochemical properties (Eastlake, Hodson, Geraci, & Crawford, 2012; Lee et al., 2013).

When using the web-based Stoffenmanager Nano 1.0 tool, one of the mandatory fields is the OECD nanomaterials list, which includes a significant number of currently used nanoparticles (in fact, the list in Stoffenmanager Nano 1.0 does not exactly match the latest version of the OECD list (Environment Directorate OECD, 2010b)). As TiO_2 is one of the nanoparticles included in the list, the D hazard class is automatically assigned based on known hazard information collected by the method’s authors. This could be considered to be one advantage to the users, as they are not dependent on the SDS information; however, it is still recommended that other information sources be sought.

In the current case, it seems that the Stoffenmanager Nano 1.0 risk assessment is less sensitive to different work conditions. The result is mostly reliant on the classification of nano-TiO_2 as a D hazard class material, where the minimum level of risk is 2 for an exposure band of either 1 or 2. This is an example of a precautionary approach to maximize the risk evaluation. Nonetheless, as this method considers the protection measures in place, this contributes to levelling the assessment, particularly when individual or other protective measures are considered in higher risk operations. In contrast, CB Nanotool does not take into consideration any control measures; in fact, the CB Nanotool risk assessment output indicates the level of control recommended for the assessed task.

When CB Nanotool is used, uncertainties about the properties of nano-TiO_2 are present, increasing the uncertainty of the risk assessment, owing to the differences between different toxicology studies. This type of uncertainty is one of the challenges posed to OSH practitioners when performing risk assessments in the field of nanotechnology.

The results from comparing the airborne nanoparticle concentrations are in line with those from CB Nanotool, both assigning a low risk level for the phase 1 and phase 2 tasks. In contrast, Stoffenmanager Nano concludes a higher risk level. Taking into consideration different aspects of the exposure assessment, it seems reasonable to assume that the Stoffenmanager Nano assessment overestimates the risk in both cases. With respect to the phase 3 tasks, both qualitative methods suggest an intermediate risk level. Brouwer (2012) mentions that CB Nanotool is well adapted to research environments, whereas Stoffenmanager Nano is more appropriate to industry operations, and the obtained results seem to demonstrate this fact.

Apart from the obtained results, the field work was limited by a number of constraints, and these limitations should also be acknowledged. Although it was possible to carry out the measurements of the concentration of TiO_2 particles, this study was limited by the fact that it was only possible to perform the assessment once, mainly due to the availability of the research laboratory. Another limitation was the fact that the concentration measurements were performed by applying a generalized method, i.e., a method that is not specific to TiO_2 particles.

3.4. Conclusions

If the analysts performing the risk assessment, in particular when using a qualitative risk assessment tool, do not have access to updated information on the materials and only use the available hazard information in the material's SDS, they may produce inaccurate assessments and, most likely, underestimate the risk of worker exposure. The available information on the nanomaterials influences the risk assessment results. Therefore, extra care should be taken to obtain more reliable and updated information.

For the particular case study of a research work environment described in this paper, the qualitative risk assessment tools were suitable to assess the risks for workers, and a consistent correlation between the exposure measurements and the CB Nanotool results was found. Stoffenmanager Nano appeared to overestimate the risks, which would assure increased worker protection. With improving knowledge about and experience with the qualitative risk assessment methods, it is possible to choose the most appropriate one for different situations being analysed.

Using airborne particles concentration measurements and the qualitative assessment methods, it was found that the compared methods do not always yield similar results. Given the existing uncertainty related to nanoparticle exposure risk is significant, the different results can be accepted.

In general, it is already possible to perform risk assessments in the field of nanotechnology using both quantitative and qualitative methodologies. In considering any given case, it is recommended to use complementary approaches, which may reduce the overall uncertainty and help to maintain a precautionary attitude, even when the results appear to indicate low risk.

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CHAPTER 4. QUALITATIVE RISK ASSESSMENT DURING POLYMER MORTAR TEST SPECIMENS PREPARATION – METHODS COMPARISON

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Abstract

Polymer binder modification with inorganic nanomaterials (NM) could be a potential and efficient solution to control matrix flammability of polymer concrete (PC) materials without sacrificing other important properties. Occupational exposures can occur all along the life cycle of a NM and "nanoproducts" from research through scale-up, product development, manufacturing, and end of life. The main objective of the present study is to analyse and compare different qualitative risk assessment methods during the production of polymer mortars (PM) with NM. The laboratory scale production process was divided in 3 main phases (pre-production, production and post-production), which allow testing the assessment methods in different situations. The risk assessment involved in the manufacturing process of PM was made by using the qualitative analyses based on: French Agency for Food, Environmental and Occupational Health & Safety method (ANSES); Control Banding Nanotool (CB Nanotool); Ecole Polytechnique Fédérale de Lausanne method (EPFL); Guidance working safely with nanomaterials and nanoproducts (GWSNN); Istituto Superiore per la Prevenzione e la Sicurezza del Lavoro, Italy method (ISPESL); Precautionary Matrix for Synthetic Nanomaterials (PMSN); and Stoffenmanager Nano. It was verified that the different methods applied also produce different final results. In phases 1 and 3 the risk assessment tends to be classified as medium-high risk, while for phase 2 the more common result is medium level. It is necessary to improve the use of qualitative methods by defining narrow criteria for the methods selection for each assessed situation, bearing in mind that the uncertainties are also a relevant factor when dealing with the risk related to nanotechnologies field.

4.1. Introduction

The need for a building material with high strength and durability afforded the development of a relatively "new" composite material: polymer concrete (PC) (Maria Cristina Santos Ribeiro, 2006). Although the PC advantages, its usage is only competitive in applications in which durability, strength or other particular requirements render conventional materials unusable, where the initial higher price of PC is mitigated by their superior short and long-term performances. PC present, however, some drawbacks brought by resin matrix like high sensitivity to high temperatures and creep phenomena, and mainly, the deficient behavior under fire (Fowler, 1999; M.C.S. Ribeiro, Rodrigues, Ferreira, & Marques, 2008; Tavares, Ribeiro, Ferreira, & Guedes, 2002). Polymer binder modification with inorganic nanomaterials (NM), leading to nanocomposites (NC), could be a potential and efficient solution to control matrix flammability without sacrificing other important properties. Although the NM use as flame retardant (FR) is promising, this technique is still giving the first steps (Ribeiro, Pereira, & Martins, 2010; Ribeiro, Pereira, Sousa, Nóvoa, & Ferreira, 2013). The majority of research work on the subject of polymer flame retardancy by means of NM has been carried out on polymer-clay NC. Other emerging nanoparticles that have also shown likely effects on polymer thermal degradation are metal oxide nanoparticles such as aluminium oxides (Al_2O_3). The few studies focusing on this issue show promising results attesting that alumina nanoparticles incorporation can improve thermal stability and other relevant properties of final composite (Baskaran, Sarojadevi, & Vijayakumar, 2011; Laachachi, Ferriol, Cochez, Lopez Cuesta, & Ruch, 2009; Moreira, Sphaier, Reis, & Nunes, 2011; Ribeiro et al., 2010; Ribeiro et al., 2013).

There is a lack of knowledge on the effects of engineered nano-Al_2O_3 in the human body, as existing studies are divergent. In a comparative inhalation study, it was clearly showed that Al_2O_3 nanoparticles (20 nm) induced an inflammatory reaction in rat lungs; however, others similar studies showed that there were no or only slight acute effects on animals due to nanoalumina inhalation, even after high doses (Som, Wick, Krug, & Nowack, 2011). For a final assessment additional research will be needed (Som, Wick, Krug, & Nowack, 2011).

The global market for NC will be worth 3.000 billion dollars in 2015, since they have an increasingly decisive role in various industries (Kiliaris & Papaspyrides, 2010). However, this new technologies rise is related with new human and environmental risk factors (Beaulieu, 2009). Occupational exposures can occur all along the life cycle of NM and "nanoproducts" from research through scale-up, product development, manufacturing, and end of life. Quantitative toxicity studies on engineered NM are still relatively sparse and until now there are not known direct implications to the humans health (Soto, Garza, & Murr, 2007).

Risk assessment is an important part of the process to achieve safer workplaces in the nanotechnology field. Because of the limited amount of data on NM, many of the assumptions and estimations are based on the traditional chemical risk assessments. Recently, several exposure assessment approaches have been developed, since the traditional risk and exposure assessment methods seem to be not fully adequate to assess risk related to nanotechnologies, mainly due to existing doubts on the most adequate dose metrics and to the lack of data on the chronic health effects (Kuempel, Geraci, & Schulte, 2012). In this scenario, qualitative risk assessment helps on supporting decisions in the risk management process (Schulte, Murashov, Zumwalde, Kuempel, & Geraci, 2010). The validation of the different proposed qualitative risk assessment methods is an on-going work in the scientific community, and it is expected that modifications could occur (Brouwer, 2012).

Meanwhile, it is necessary to raise the awareness of the nanotechnology potential risks and one of the ways is through qualitative risk assessment. Under this framework, the present study is an effort to contribute to an enhanced performance and use of qualitative risk assessment methods during the production of polymer mortars (PM) materials with NM. The research question underlying this study is: Do different qualitative risk assessment methods identify comparable risk levels for the same tasks?

This research work was developed at INEGI laboratories, and the tasks were performed in typical work conditions.

4.2. Materials and Methods

4.2.1. TASKS UNDER EVALUATION

In the production process of PM, a commercially available unsaturated polyester resin (Aropol® FS3992, Quimidroga Portugal-Produtos Químicos Unipessoal Lda) was applied as polymer binder. Alumina NM (NanoDur®, Al_2O_3, 99.5% purity), for polymer binder modification, was purchased from Cymit Quimica S.L. (Spain), with 45 nm average size and 36.0 $m^2.g^{-1}$ specific surface. Siliceous foundry sand (SP55, Fundipor), with an average diameter of 245 μm, was applied as mineral aggregate. Manual stirring and ultrasound sonication techniques were used to disperse the

NM into the resin system (2.5% by weight of resin), and afterwards, the mixture was added to the sand aggregates (with a binder to sand ratio of 1:4) and thoroughly mixed in a mechanical mix device. The final mixture was casted into standard prismatic moulds.

The laboratory scale production process was divided in 3 main phases: 1 - Pre-production: handling, weighing, adding nanoalumina to the resin and cleaning; 2 - Production: stirring, pouring the mixture into the mould and cleaning; and 3 - Post-production: demoulding, cutting and cleaning. During the production process, the nanoalumina is present in powder (phase 1), suspension (phase 2), or inserted in a cured polymer matrix (phase 3), which allowed testing the assessment methods in three different situations.

The production process only involved a single operator who used collective protection measures existing in the lab (mechanical ventilation/general exhaust), and personal protective equipment (two pairs of nitrile gloves, three latex gloves, a mask with ABEK1 P3 filters, protection goggles, type 5 category III disposable coverall and disposable polypropylene shoe covers).

4.2.2. RISK ASSESSMENT METHODS

The risk assessment involved in the manufacturing process of PM was made by using the qualitative analyses based on: French Agency for Food, Environmental and Occupational Health & Safety method (ANSES), from France; Control Banding Nanotool (CB Nanotool), from United States of America; Ecole Polytechnique Fédérale de Lausanne method (EPFL), from Swiss; Guidance working safely with nanomaterials and nanoproducts (GWSNN), from. The Nederlands; Istituto Superiore per la Prevenzione e la Sicurezza del Lavoro (ISPESL), from Italy; Precautionary Matrix for Synthetic Nanomaterials (PMSN), from Swiss; and Stoffenmanager Nano, from The Nederlands.

4.2.2.1. French Agency for Food, Environmental and Occupational Health & Safety method (ANSES)

ANSES is a risk assessment method by control bands. The risk values are obtained by overlapping the hazard bands and emission potential bands. The hazard bands are defined according to the severity level of the hazard, resulting from the analysis of the available information of similar chemicals. The hazard levels may assume five classifications from HB1 - very low (no significant risk to health) to HB5 - very high (severe hazard requiring a full hazard assessment by an expert). The exposure bands are defined according to the nanomaterial emission potential, whether raw or included in a matrix. The exposure bands can assume four levels: EP1 – solid, EP2 – liquid, EP3 – powder, and EP4 – aerosol. From the resultant matrix it can be defined the control level that corresponds to technical solutions for collective prevention to be implemented at the workplace (CL1 - natural or mechanical general ventilation to CL5 - full containment and review by a specialist required) (Ostiguy, Riediker, Triolet, Troisfontaines, & Vernez, 2010).

4.2.2.2. Control Banding Nanotool (CB Nanotool)

CB Nanotool is a four by four factors matrix that relates severity parameters on one-axis and probability parameters on the other. The severity parameters consider that the physicochemical and general properties of NM are often unknown. Adding information about the parent material solves partially this problem. The overall severity score is determined based on the sum of all the points from the severity factors. The probability axis fits with traditional information. The probability scores are based on factors determining the extent to which employees may be potentially exposed to NM. The obtained control bands by risk level can be classified in RL1 – general ventilation to RL4 – seek specialist advice (Zalk, Paik, & Swuste, 2009).

4.2.2.3. Ecole Polytechnique Fédérale de Lausanne method (EPFL)

EPFL method consists in a decision tree for "nano-laboratories" with three risk classes, which correspond to similar approaches applied to other hazards types (biological, chemical or radiation). This decision tree analyses the established collective protection measures, NM form/state handling typology, NM quantity use, possibility to release dust or aerosol and NM agglomeration ability. The risk classification can be Nano1 (low) to Nano3 (high). With the risk classification it can be defined several safety measures (Groso, Petri-Fink, Magrez, Riediker, & Meyer, 2010).

4.2.2.4. Guidance working safely with nanomaterials and nanoproducts (Guidance)

GWSNN risk assessment method analyses different scenarios through a three by three decision matrix, informing the policy options and procedures to guarantee safe working conditions with NM. The hazard category can be classified as: 1 - soluble NP, 2 - synthetic, persistent NM, and 3 - fibrous, nonsoluble NM. The exposure classification is made based on the NM potential exposure in the different activities related with the polymeric NC production: I - no emission of free NP due to working in full containment, II - emission of NP embedded in a matrix is possible, and III - emission of free NP is possible. The recommended control measures range from level A (applying sufficient ventilation, if needed local exhaust ventilation and/or containment of the emission source and use appropriate personal protective equipment) to level C –(the hierarchic Occupational Hygienic Strategy will be strictly applied and all protective measures that are both technically and organizationally feasible will be implemented) (Cornelissen, Jongeneelen, van Broekhuizen, & van Broekhuizen, 2011).

4.2.2.5. Istituto Superiore per la Prevenzione e la Sicurezza del Lavoro, Italy method (ISPESL)

The ISPESL risk assessment method is based on ten different factors (A to J). The aforesaid factors are denominated "factors level risk" and each one of them may assume three increasing values, 1 (low) to 3 (high), referred to as "risk levels". Since the use of NM presents uncertainty about danger level, the risk assessment takes into consideration these aspects through the index denominated "corrective factor" (within the range 0.5 and 2.0) [15]. The risk is estimated through the "factor level risk" (flr) sum (from A to J) and then multiplied by the "corrective factor" (cf). The evaluation result consists in three risk levels (risk level "low" 5-15, "medium" 16-35, and "high" 36- 60) (Giacobbe, Monica, & Geraci, 2009).

4.2.2.6. Precautionary Matrix for Synthetic Nanomaterials (Precautionary Matrix)

The PMSN estimates the precautionary need that represents the relation between the parameters: "Nano-relevance according to the precautionary matrix" (N), "Potential effect" (W), "Potential exposure" (E), and "Specific framework conditions" (S). The precautionary matrices are logically completed and evaluated in two iterative steps: 1st - a rapid evaluation to demonstrate knowledge gaps and uncertainties, which leads to a preliminary precautionary matrix; 2nd- exact clarifications on the fundamentals of the results from 1st step and from the specific answers to knowledge gaps that afford a finished and definitive evaluation of precautionary matrix. The potential risk can be classified into class A (the nanospecific need for action can be rated as low, even without further clarification) or class B (nanospecific action is needed; existing measures should be reviewed, further clarification undertaken and, if necessary, measures to reduce the risk associated with development, manufacturing, use and disposal implemented in the interest of precaution) (Höck et al., 2011).

4.2.2.7. Stoffenmanager Nano

The Stoffenmanager Nano is a risk-banding tool to prioritize health risks occurring as a result of exposure to NP for a broad range of occupational scenarios and to assist implementation of control measures to reduce exposure levels. In order to prioritize the health risks, it is made the combination between the available hazard information of a substance with a qualitative estimate of potential for inhalation exposure. Input parameters for the hazard assessment of NP are selected based on the available information (e.g.: safety data sheets, product information sheets). The method was converted into an online tool that offers a practical approach for risk prioritization in exposure situations where quantitative risk assessment is currently not possible. The obtained priority bands by risk assessment can be classified in 1 (highest priority) to 3 (lowest priority) (van Duuren-Stuurman et al., 2012).

4.3. Results and discussion

4.3.1. RESULTS

4.3.1.1. Inputs for the assessment – risk determinants

From the previous sections it is possible to verify that the different methods consider different characteristics from the nano-objects (hazard band) and take in consideration different aspects from the tasks performed (exposure likelihood band). Are also relevant the scale considered to each parameter, and the weight that each parameter assumes in the final result of the assessment. These differences will influence the obtained results with each method.

In short it is possible to have a wide view of the considered hazard factors of each method in Table 4.1.The toxicity of the nanomaterial, or its bulk form, is directly considered by five of the methods. Solubility of the nanoparticles and fibrous form are also considered by the majority of the methods, although the toxicity itself could result from these factors, and also from reactivity and size, considered as relevant factors in three of the seven methods. The ISPESL method includes the fire and explosion hazard factor which is relevant for safety risk assessment, biasing the result when only the health effects are considered.

Table 4.1 – Hazard band factors

Hazard factor	ANSES	CB Nanotool	EPFL	Guidance	ISPESL	Precautionary Matrix	Stoffen-manager
Toxicity (nano and/or bulk material)	●	●		●	●		●
Solubility	●	●		●		●	●
Fibre form (particle shape)		●	●	●			●
Reactivity	●	●				●	
Size		●			●		●
Fire and explosion					●		

In Table 4.2 the factors that could determine the worker's exposure are presented.

Table 4.2 – Exposure (or likelihood) band

Exposure factor	ANSES	CB Nanotool	EPFL	Guidance	ISPESL	Precautionary Matrix	Stoffen-manager
Quantity		●	●			●	●
Duration/ frequency (time) factor		●			●	●	●
State of material (e.g. solid, liquid)	●		●				●
Release of nano-objects (e.g. dustiness)	●	●		●		●	●
Aggregation/ agglomeration			●		●		
Embedded in a matrix				●		●	●
Number of workers		●			●		
Risk control / organization					●		●
Containment			●	●			
Type of process/task	●		●				●

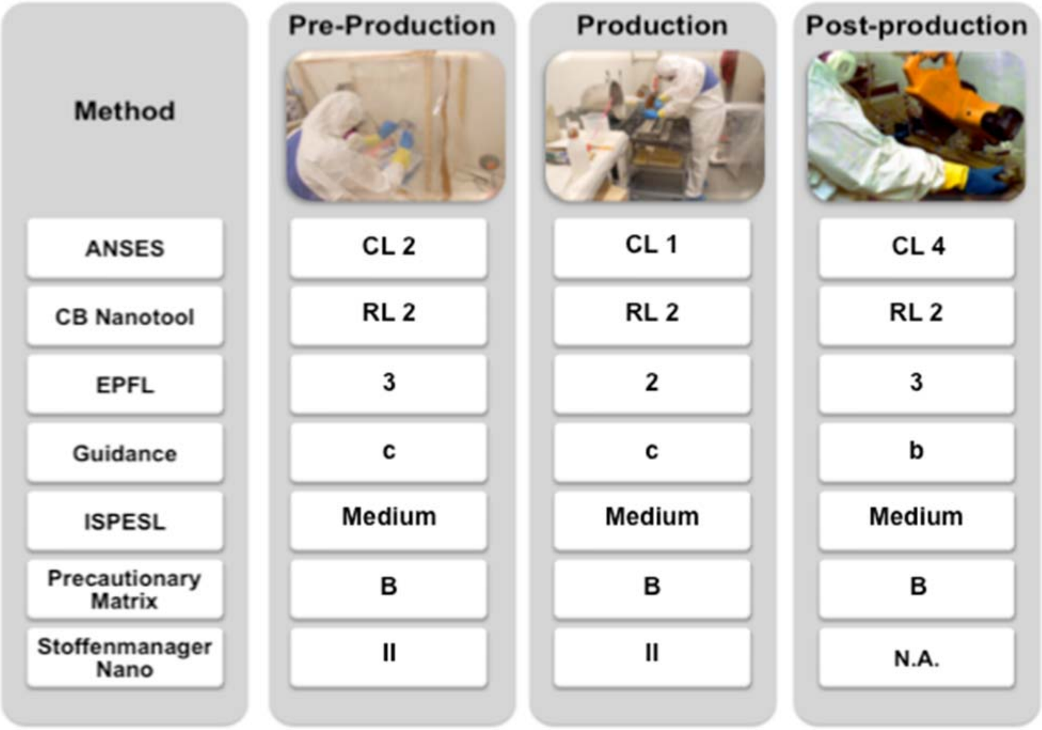
The ISPESL and Precautionary Matrix methods include also general factors that influence the final result of the assessment, taking in account the uncertainty on the information gathered. These factors are related to the knowledge on the materials and, in the Precautionary Matrix also on the size and state of aggregation/agglomeration of the nanomaterials present. CB Nanotool leads with the uncertainty, introducing a score for "unknown" in several parameters corresponding to 75% of the scale.

4.3.1.2. Inputs for the assessment – information gather

The information on nanoalumina and the tasks performed is of major importance for the risk assessment result. The aluminium oxide is a relatively inert material. For the risk assessment it was considered that nanoalumina is a non-soluble, non-fibrous material and its carcinogenicity, mutagenicity and toxicity for reproduction are unknown. In Phase 1, nanoalumina is a solid (powder), in Phase 2 it is in liquid suspension and finally, in Phase 3 it is embedded in a matrix. Based on the assumption that the materials in nano-form are more reactive than its bulk material, nano-Al_2O_3 is considered more reactive than the parent material. Some doubts arise due to information lacking about dustiness, styrene evaporation rate influence on NP release and agglomeration/aggregation of the airborne nanoparticles.

The total amount of nanoalumina used in each phase is 30 g and the tasks durations are around 50 min for Phase 1, 1h50 min for phase 2 and around 30 min for Phase 3. For the frequency factor it was considered that the tasks were performed on a monthly basis.

Figure 4.1 shows the obtained results of the application of the 7 different risk assessment methods for all the considered stages.



Method	Pre-Production	Production	Post-production
ANSES	CL 2	CL 1	CL 4
CB Nanotool	RL 2	RL 2	RL 2
EPFL	3	2	3
Guidance	c	c	b
ISPESL	Medium	Medium	Medium
Precautionary Matrix	B	B	B
Stoffenmanager Nano	II	II	N.A.

Figure 4.1 - Comparing the results of the different risk assessment methods (N.A. – Non Applicable)

4.3.2. DISCUSSION

Analysing the results, it was found that the most critical operation in the PM processing is the pre-production phase, because it deals with NMs in powder state and may lead to typical scenarios of exposure. However, it was verified that the used qualitative risk assessment methods had different final results (Figure 4.1).

In phases 1 and 3 the risk assessment tends to be classified as medium-high risk, while for phase 2 the more common result is medium level. The consideration of different assumptions as risk determinants could explain some of the found differences. It is also relevant to consider the sensibility of the methods regarding the different exposure scenarios, as some of them give the same risk level for the three different phases.

In respect to phase 3, divergent results are obtained: while ANSES and EPFL methods point to an increasing risk level, when comparing with the other phases, with the Guidance and Stoffenmanager Nano lower risk levels are obtained (CB Nanotool, ISPESL, and Precautionary Matrix present the same risk level, despite some variations on the exposure scores).This divergence arises from the consideration that NP embedded in a matrix are released together with other material in large particles, thus not resulting in exposure to free NP, assumed by the Guidance and Stoffenmanager Nano methods.

Bearing in mind that these assessment methods are risk management tools it is also relevant to compare their outputs considering the risk control measures. In Table 4.3 the control measures recommended or necessary to low the risk to an acceptable level, according to each different method.

Table 4.3 – Risk control measures

Method	Phase 1	Phase 2	Phase 3
ANSES	Local ventilation	Natural or mechanical general ventilation	Full containment
CB Nanotool	Fume hood or local exhaust ventilation	Fume hood or local exhaust ventilation	Fume hood or local exhaust ventilation
EPFL	High level technical, organizational and individual control measures	Medium level technical, organizational and individual control measures	High level technical, organizational and individual control measures
Guidance	Mandatory technical and organizational protective measures	Mandatory technical and organizational protective measures	Technical and organizational protective measures considering economical feasibility
ISPESL	Existing controls are sufficient	Existing controls are sufficient	Existing controls are sufficient
Precautionary Matrix	Review existing control measures and if necessary improved	Review existing control measures and if necessary improved	Review existing control measures and if necessary improved
Stoffenmanager Nano	Medium priority, enclosure necessary to reduce exposure level	Medium priority, enclosure necessary to reduce exposure level	N. A.

As observed on Table 4.3, the risk control measures recommended (when there are specific recommendations) by each method are different. Depending on the method considered, the user could be led to implement technical, organizational or individual control measures with different degrees of efficacy and/or complexity.

The use of various parameters and/or differences in their interpretation can lead to differences in risk level results. These methods should be reviewed in order to give more convergent results avoiding unequal final outcomes, and their selective and/or complementary application could also help to improve risk management in the workplaces.

4.4. Conclusions

The occupational risks are a key issue to be considered especially in the early stages of any new material production. By studying proactively emerging risks, one can prevent future problems. The risks are inherent to any technology and nanotechnology is no exception.

Within this scope, in this study the different qualitative risk assessment methods were used to evaluate the risk during the production stages of PM with nanoalumina. The experimental study was conducted in a laboratory environment but provides an overview of the measures that could be applied during the PM production at an industrial scale.

The results obtained with the qualitative methods were divergent; however, generally the methods consider that the pre-production stage is the one with the higher risk.

The results of this study highlight the need to improve the qualitative methods, together with the definition of narrow criteria for the methods selection for each assessed situation, bearing in mind that the uncertainties are also a relevant factor when dealing with the risk related to nanotechnologies field. Thus, more research work is needed to fill existing gaps.

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CHAPTER 5. SYSTEMATIC DESIGN ANALYSIS AND RISK MANAGEMENT ON NANOPARTICLES OCCUPATIONAL EXPOSURE

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Abstract

Worker's health and occupational safety are critical to the development of nanotechnology applications, since some nanomaterials present a risk of adverse effect on human beings. This paper describes the application of the Systematic Design Analysis Approach based on the hazard process model (bow-tie) as well as design analysis of the production process, during a development project to produce a new type of ceramic tile with photocatalytic properties. Applying the bow-tie model together with the design analysis to the production process, it is possible to identify the emission and exposure scenarios and the related barriers based on the unit operations and the different technological options to perform them. Alternatives to the production process were considered, falling back on solutions to reduce emissions, and consequently the exposure to nanoparticles. The intervention model proposed will allow occupational safety and hygiene to be integrated into the development process that will involve a multidisciplinary team. Systematic Design Analysis Approach is a suitable method for occupational safety and hygiene risk management. This approach proved to be effective in generating relevant emission and exposure scenarios, as well as identifying possible barriers to control such emission scenarios.

Keywords: emission scenarios; exposure scenarios; safety-by-design; bow-tie model; ceramics.

5.1. Introduction

Nanotechnology based products are becoming ubiquitous, as a result of their growing use in an increasing number of products (Palmberg et al., 2009; Yokel & Macphail, 2011). While materials such as carbon black and amorphous silica have been used for several decades (Dowling et al., 2004; European Commission, 2012b), other engineered nanomaterials (ENM) present a production increment over the last few years (Aschberger, Micheletti, Sokull-Klüttgen, & Christensen, 2011; Kaluza et al., 2009). According to the information available from the Project on Emerging Nanotechnologies (PEN) website, the number of nanotechnology based products available to consumers in October 2013 was approximately 1628 (WWICS, 2013), showing the widespread use of ENM in several industry sectors. Among other ENM, amorphous silica, carbon black, and titanium dioxide (TiO_2) are included amongst the more widely used nanomaterials considering both the quantity and number of applications (Aitken et al., 2006; Piccinno et al., 2012). In the balance report of the first year of the mandatory declaration of nanomaterials in France, those three substances together with calcium carbonate are in the top four materials regarding the quantities produced or imported (Eymery, Aurélie, Cadene, Merckel, & Thieret, 2013).

One of the common uses of nano-sized TiO_2 is currently in the production of photocatalytic construction materials, like ceramics, concrete or mortars (Chen & Poon, 2009; Shen et al., 2015). Ceramic tiles with photocatalytic characteristics can have several uses, such as providing a surface that degrades organic dirt, making them easier to clean and avoiding the use of detergents (Chen & Poon, 2009). These photocatalytic ceramic tiles and other construction materials are also able to transform some air pollutants including nitrogen oxides, contributing to cleaner ambient air, and exhibit anti-bacterial properties (Chen & Poon, 2009).

Together with the scientific and economic importance of nanotechnology products, questions arise concerning the possible adverse effects to human health (Ellenbecker & Tsai, 2011; Schulte, Geraci, et al., 2008). Thus, occupational risk management in nanotechnology industries is a key issue, with limitations arising from a lack of knowledge and uncertainty related to the occupational exposure to ENM (Silva et al., 2013).

Some authors have been defending the need for methodologies that address the risks related with nanotechnologies based on the processes or products design (Amyotte, 2011; Fleury et al., 2011; Köhler, Som, Helland, & Gottschalk, 2008; Schulte, Geraci, et al., 2010). An approach cited in the literature is the “Design for Safer Nanotechnology” proposed by Morose (2010) in which the author proposes an intervention during the design stage for nanoparticles and products that incorporate nanoparticles. Schulte et al. (2010) also mention the Prevention through Design (PtD) initiative as a valuable approach to manage the occupational risks. Swuste and Zalk (2013) also proposed the use of the design analysis to achieve safer production processes in the nanotechnology field. Additionally, (Reijnders, 2006) defends that acting on the source is important to reduce exposure during the production process.

Risk management (not only the occupational risk) is gaining relevance since issues such as sustainability (Helland & Kastenholz, 2008) and cleaner production (Wu, Olson, & Birge, 2013) are being considered.

The work presented in this paper was performed during the development project of photocatalytic ceramic tiles using TiO_2 (anatase form), and made by common ceramic production processes that was part of a funded research project.

The aim of this paper is to present the work carried out to establish a safer production process resulting from a development project. The research questions underlying this analysis are 1) Does a design approach of the production line of photocatalytic ceramic tiles generate relevant emission and exposure scenarios? 2) Does a design approach of the production line of photocatalytic ceramic tiles generate alternative barriers to reduce exposure, including through emission reduction? 3) What are the possibilities of the Systematic Design Analysis Approach (SYDAPP) on reducing emission scenarios during photocatalytic ceramic tiles production? 4) Is a design approach a suitable method for risk management purposes in the production line of photocatalytic ceramic tiles?

In this paper, first we present the design analysis and the bow-tie model as the basis for the SYDAPP and we describe the research activities. The results include the design analysis of the production process, the identification of emission and exposure scenarios and the definition of one possible process with lower exposure risk to the TiO_2 nanoparticles. Finally, we discuss the results and answer the research questions posed.

5.2. Materials and methods

A growing interest in nanomaterials will see their increased use in a large number of applications. Considering the possible hazardous health effects of some types of nanoparticles, it is relevant to take into account the safety issues in previous stages in the development process of products. It is relevant to know the hazards associated with nanomaterials and the potential exposure of workers to define the most effective ways to control the related occupational risks.

5.2.1. RESEARCH ACTIVITIES

The Selfclean project lasted for approximately two years from the first exploratory tests to the final product prototype. The occupational safety and hygiene (OSH) intervention, including the work described in this paper had a six-month duration in addition to a further two months for the OSH issues report.

The project team included four researchers from the materials department of one university, two ceramic engineers and an OSH practitioner from one technological institute, and one ceramic engineer from a ceramic tiles company. The university researchers are experts in materials science, the company engineer expertise is in ceramic processing technology. The technological institute engineers predominantly focused on the material performance tests, while the OSH practitioner had particular expertise in the OSH aspects in the ceramics industry.

Thus, the project meeting discussions on the health and safety aspects were held in an interdisciplinary environment. These discussions were complemented by observation and information collection during the laboratory and semi-industrial tests performed during the project.

OSH issues were included in the agenda of three plenary meetings throughout the project. During those meetings, the safety and health concerns related to the project were raised. For approximately 45 min in each of these meetings, the SYDAPP was presented and the team members had the opportunity to contribute to the process design analysis and related emission and exposure scenarios. The input from participants was collected based on the presentation of the process unit operations and participants were invited to present their own ideas.

The group discussions gathered contributions especially for the design analysis, the identification of emission and exposure scenarios and the possible barriers. The ceramic technology experts proposed alternative production principles and forms, including their feasibility evaluation, helping to identify their impact on the possible scenarios.

In parallel, several head-to-head informal meetings were held by the OSH practitioner and the other members of the group, including the ceramic company engineer and the university researchers, refining the knowledge on the different options available and to confirm the information collected during the meetings and project tests.

Finally, based on the information collected, the OSH practitioner elaborated a report for the project manager.

In Table 5.1, the main events during the project are presented in a chronological order.

Table 5.1 – Main events that occurred during the research project and their relation with OSH issues.

Month	Event	OSH issues
1	4th project meeting (1st including OSH issues)	General information on the project. Presentation of OSH objectives for the project.
1	Laboratory test	Observation and information on the production process. Possible scenarios.
2	5th project meeting	Presentation of toxicological data on TiO_2. Presentation of the SYDAPP to the project team. Discussion on possible process operations.
2	Laboratory test	Observation and information on the production process. Possible scenarios.
3	Pilot-test of the industrial conditions	Observation and information on the production process. Discussion on possible process alternatives. Possible emission and exposure scenarios identification.
6	6th project meeting	Discussion of the results. Possible processes and solutions to lower the risks associated with the production process.
8	Report on OSH aspects of the project	Process design analysis completed. Emission and exposure scenarios identified. Proposed solutions for risk control.

5.2.2. SYSTEMATIC DESIGN ANALYSIS APPROACH

Although the occupational safety and hygiene research pays more attention to risk analysis (Swuste, 1996), several authors in this domain have conducted research in the safety by design field, especially the Safety Science Group of Delft University of Technology (Hale et al., 2007; Schupp et al., 2006; Stoop, 1990). For example, Swuste (1996) proposed a systematic approach towards solutions based on three complementary elements:

- Hazard process model;
- Design analysis;
- Problem-solving cycle.

The two first elements are the basis for the SYDAPP. Combining the process design analysis with the emission and exposure scenarios identification together, it is possible to acquire a clear vision of how the different process operations will affect a worker’s exposure. Other risk management tools could be used to refine the results, as mentioned in section 5.3.3.

5.2.2.1. Design analysis

The design analysis method allows the workplace conditions to be studied and understood. In the design analysis, the production process is split into three decision levels as shown in Figure 5.1 and described below:

- **Production function**: the highest level dividing the production process into its core activities, similar to the unit operations;
- **Production principle**: identifies the general process, motive power and the operational control methods by which the production function can be achieved;
- **Production form**: the lowest level that specifies the detailed design by which the production principle will be accomplished.

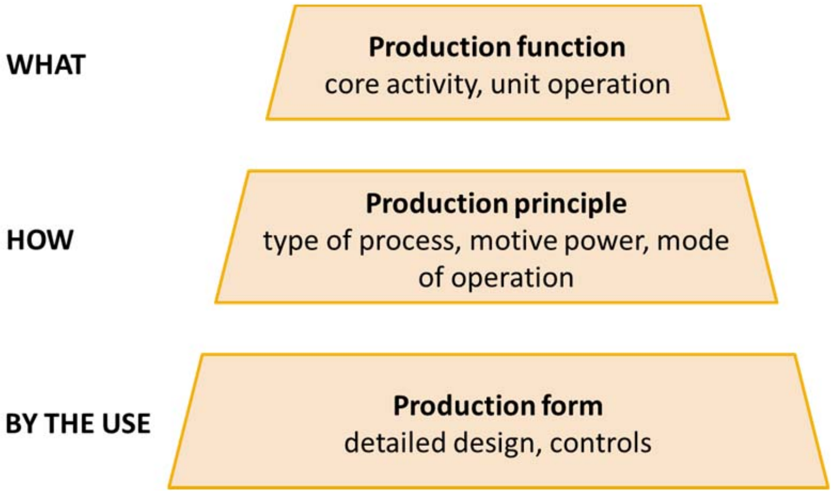

Figure 5.1 – Scheme representing the design analysis hierarchy.

If there is a large number of production processes, the type of functions (or the unit operations) in which each process can be broken down is relatively small. The main unit operation categories are: material reception, material storage, transport and feed, processing, packaging, waste disposal. The processing operations can be subdivided in subcategories that vary from one industry sector to another, and once enumerated will permit the study of more effective and reasonable control measures or set of control measures to apply in each particular situation. In the ceramic tiles industry, examples of processing production functions or unit operations include milling, conformation, drying, glazing, firing, and sorting, among others.

At the production principle level it is possible to choose the type of process to achieve a function (e.g., different shaping processes), the motive power (e.g., electricity or combustible fossil fuels), and the mode of operation (e.g., manual operation, mechanical or automatic). There are several hundred different production principles available to fulfil the unit operations. As examples of the different principles for ceramic tile conformation (shaping), pressing, extrusion or slip casting are possible techniques that are available.

At the production form level, the machine, the equipment or set of equipment that will actually be used in the process (e.g., the hydraulic press type if shaping by press is the principle defined to achieve the unit operation "conformation") is defined. It is also at this level that the exposure controls are defined (e.g., whether a local exhaust ventilation (LEV) or a closed cabin will be used).

From an occupational safety and health point of view, focusing on the production functions and principles will allow less hazardous processes to be discovered that achieve the same production result, or at least to choose the best available techniques to control a hazard.

In the present case, the departure point was the proposal of one production process at the production form level. Then, it was reduced to the production function level. From there, it was possible to propose alternative production principles and forms to the production process from our discussions, as described in Chapter 5.3.

5.2.2.2. Hazard process model - Bow-tie

The bow-tie model is used in the safety science field as a tool to prevent the occurrence of accidents (Visser, 1998). Its adaptation to the occupational hygiene field helps to establish the necessary barriers to control the risks arising from different workplace exposure scenarios (Silva et al., 2013). The use of the bow-tie model as a support tool to risk management is also referenced by Fleury et al. (2011), and an example of the use of this model, defining exposure scenarios and evaluating the risks during the production of carbon nanotube polymer composites is presented in another article (Fleury et al., 2013).

The central event occurs when a nanomaterial emission occurs, which leads to the exposure of a worker (if any worker is present). Considering the case of one hazardous nanomaterial, the way the hazard will cause damage (the consequence) will result from the completion of the sequence (see Figure 5.2): hazardous nanomaterial → hazardous nanoparticle emission scenario → central event → worker present → exposure to nanoparticle scenario → consequences to the worker (health effects). This sequence will be completed in several different scenarios (both in emission and exposure), unless barriers (risk control measures) are effectively implemented to reduce or eliminate these scenarios. These barriers are physical entities, such as engineering controls on the left-side of the central event, or personal protective equipment on the right-side of the central event, which can block the pathway to the previewed scenarios.

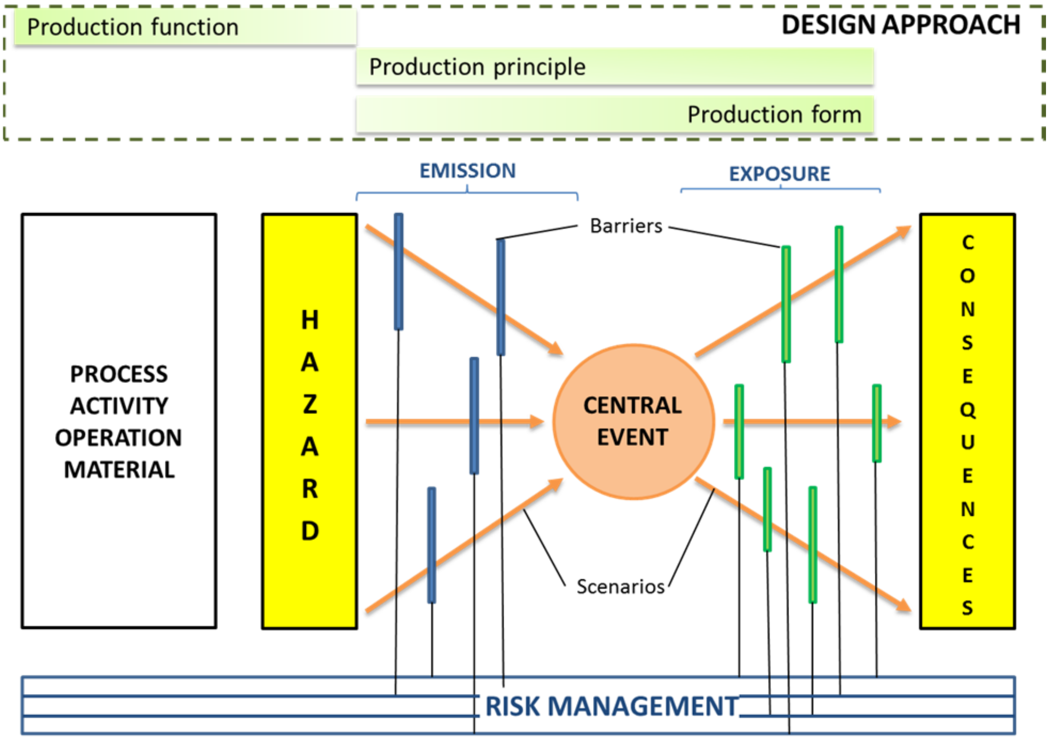

Figure 5.2 - The Bow-tie model includes arrows which represent different emission and exposure scenarios.

The emission scenarios result from the process operations, both under normal conditions or when disturbances occur. Furthermore, nanoparticle emission can result from support activities, such as maintenance or cleaning. Once emission occurs, the workers present could be exposed to the released nanoparticles by different routes and from different causes, the exposure scenarios.

The bow-tie model also stresses the importance of management as the entity responsible to implement the barriers (Guldenmund, Hale, Goossens, Betten, & Duijm, 2006), assessing the necessity (based on a risk assessment), buying, installing, monitoring and maintaining these barriers (administrative controls are not effective barriers on emission or exposure reduction, apart from their usefulness when acting on risks).

Considering the bow-tie model and the design analysis together, it is possible to relate the occupational setting with the production process in detail (see Figure 5.2).

The emission and, consequently, the exposure are identified at the production form level. Thus, the options to reduce emission and exposure are usually limited to LEV and personal protective equipment. As these controls could become ineffective due to a high level of exposure or their own characteristics, it turns out that it is useful to act at the production principle or production function level, which provides more operative controls.

In this research, the focus was on the inhalation hazard of nano-TiO_2. The identification of the emission and exposure scenarios related to possible production process operations based on the analogy with the ceramic tiles production process, and also in the testing observations. As the OSH practitioner had extensive experience in the ceramic field, he assumed a major role in this task. The collection of information is particularly important when the SYDAPP is used during a project where "real" production facilities are not available.

5.2.3. RISK ASSESSMENT

Using the SYDAPP, it is possible to define different production processes and to assess their risks, and consequently to identify the processes of lower risk. In effect, combining the production functions and principles (and forms) that could lead to reductions in both the emission and exposure, it is possible to project safer processes. Then, it is possible to use qualitative risk assessment methods for risk management in a design phase. Using qualitative risk assessment methods, taking particular attention of the exposure or probability bands, as the hazard band will be the same in all cases, it is possible to evaluate the relative risk of each production process operation by considering different production functions, principles and forms.

Several authors and institutions consider Control Banding risk assessment tools helpful in nanotechnology OSH (Beaudrie & Kandlikar, 2011; Environment Directorate OECD, 2010a; Kuempel et al., 2012; Murashov & Howard, 2009; C Ostiguy et al., 2009; Schulte, Geraci, et al., 2010; Technical Committee ISO/TC 229, 2012b; The UK NanoSafety Partnership Group, 2012). There are quite a few methods for qualitative risk assessment available, which were developed under different assumptions and purposes including the CB Nanotool (Zalk et al., 2009), the

Stoffenmanager Nano 1.0 (van Duuren-Stuurman et al., 2012), the Precautionary Matrix for Synthetic Nanomaterials (Höck et al., 2011), the ANSES (Claude Ostiguy et al., 2010), and Guidance on Working Safely with Nanomaterials and Nanoproducts (I. R. Cornelissen et al., 2011).

In this particular example, the CB Nanotool was used and the probability scores for the different work situations determined taking the corresponding exposure scenarios previously generated into consideration. The probability band of the CB Nanotool includes the estimated amount of chemical used, the dustiness, the number of employees with a similar exposure, the frequency of operation and the operation duration (hours per shift). For the severity band, some physicochemical characteristics of the nanomaterial and toxicological properties of both the nano-form and the "bulk" form of the material are considered (Zalk et al., 2009).

5.2.4. TITANIUM DIOXIDE HEALTH EFFECTS

Due to the widespread use of TiO_2, its potential effects to humans and the environment has received significant attention by academia and public health and environmental institutions over the last decades (Donaldson & Poland, 2012; IARC, 2010; NIOSH, 2011; Shi et al., 2013). Over the last few years, toxicological research has been extended to include nano-sized TiO_2 (NIOSH, 2011). In general, the in-vitro and in-vivo tests for micro- and nano-sized TiO_2 demonstrate potential harmful health effects in humans (NIOSH, 2011).

In 2006, the International Agency for Research on Cancer (IARC) classified TiO_2 as a carcinogenic Group 2B substance. This means that TiO_2 is "possibly carcinogenic to humans" based on sufficient evidence of the carcinogenicity in animals, but there is inadequate evidence of the carcinogenicity in humans (IARC, 2010).

Recently the US National Institute for Occupational Safety and Health (NIOSH) published a report reviewing the scientific knowledge on both micro- and nano-sized TiO_2 inhalation occupational exposure hazards (NIOSH, 2011). In this bulletin, the evidence on the health effects was evaluated, and the results of different research studies compared. The main findings and conclusions of the review are:

- TiO_2 carcinogenicity does not result from its direct action but results from a secondary genotoxicity mechanism that is not specific to TiO_2, but common to other insoluble or poorly soluble particles and it is related to particle size and surface area;

- exposure to ultrafine (or nano) TiO_2 should be considered a potential occupational carcinogen agent;
- for fine particles (>100 nm), the information to assess their carcinogenicity is limited;
- different crystal structures (rutile, anatase and mixtures) show different results in in-vitro studies unlike in in-vivo studies;
- the scientific evidence supports surface area as being the critical metric for occupational inhalation exposure to TiO_2;
- the exposure to TiO_2, both fine and ultrafine, should be kept as low as possible (NIOSH, 2011).

In the referred study, NIOSH recommends the exposure limits of 2.4 mg/m^3 for fine-TiO_2 and of 0.3 mg/m^3 for ultrafine (including engineered nanoscale) TiO_2, as time-weighted average (TWA) concentrations for up to 10 h/day during a 40-hour work week.

Toxicological studies point to other possible effects in human body cells, revealing potential cytotoxicity and genotoxicity in different human cells (Jaeger et al., 2012; Long et al., 2006). In a recent review article on the nano-TiO_2 toxicological data, it is shown that nano-TiO_2 exhibits a greater toxicity than TiO_2 micro-particles (Shi et al., 2013). However, many in-vitro and in-vivo studies reported use very high doses and present contradictory results (Shi et al., 2013).

5.3. Results and discussion

The results achieved, including design analysis and generation of emission scenarios, are presented and it is proposed a model for intervention using SYDAPP.

5.3.1. PRODUCTION PROCESS AND THE DESIGN ANALYSIS

After the preliminary tests, the planned photocatalytic ceramic tiles production process was defined and proposed the use of already existing equipment in the ceramic production plant. Then, the first step was to detail the production process, dividing it into its functions, principles and forms (see Table 5.2). This work was performed during the project meetings from contributions from all project team members.

Table 5.2 – Photocatalytic ceramic tiles production process divided in production functions, production principles and production forms.

Production Function	**Production Principle**	**Production Form**	**Description**
Reception of raw materials	Discontinuous transport, mechanically driven	Palletized bags, forklift	The nano-TiO_2 is received in paper bags, which are packed in wood pallets. The pallets are handled with a forklift and/or an electric pallet-truck.
Storage of raw materials	Discontinuous transport, mechanically driven	Palletized bags, forklift	
Transport of raw materials	Discontinuous transport, mechanically driven	Palletized bags, forklift	
Feeding raw materials (sack emptying)	Pouring, worker emptying the bags, manual operation	Emptying bags to a container	The TiO_2 powder is poured into water and is dispersed in the liquid with a column stirrer to obtain a homogenized slurry. When the suspension is homogeneous it is milled in a micro-balls mill to de-aggregate. Finally, the slurry is sieved.
Mixing raw materials	Mechanical stirring, mechanically driven	Column stirrer and micro-ball mill, container	
Surface coating	Spraying, automatic	Air-less spraying, booth Disk glazing, booth Spray-gun, booth	The slurry is applied in the already fired ceramic pieces by a spray technique.
Transport of materials	Continuous transport, mechanical, automatic	Parallel belt line, ceramic tiles loading and unloading machines, storage boxes	The coated tiles are transported over two parallel trapezoidal belts on the glazing line. At the end of the line the tiles are loaded on a “ceramic tiles box” for storage before firing. At the kiln, the tiles are unloaded from the box and transported to the kiln entrance over parallel trapezoidal belts and/or a roller conveyor.
Processing - firing	Continuous firing, thermal, automatic	Roll kiln	After the coating, the pieces are fired (2nd fire) at a temperature of approximately 950 °C in a continuous roll kiln.

Production Function	Production Principle	Production Form	Description
Sorting	Visual sorting, manual operation, and mechanical automatic transport	Ceramic tiles sorting line	The fired pieces are sorted (finding defects in the surface and body of the pieces) and packed in cardboard boxes.
Packaging	Packing in card boxes, mechanical, automatic	Ceramic tiles packaging line	

The production process presented in Table 5.2 is similar to the usual ceramic tiles production process. The more relevant unit operations for the nanoparticles emission and exposure are those related to the processing of raw materials and surface coating. In these unit operations, the potential to generate airborne particles is higher than in the other unit operations.

During the project meetings, from the contributions of the team members, it was possible to define alternative production principles and forms for the production process. The results are presented in Table 5.3, where it is possible to see that there are some alternative options to the initially proposed process, particularly in the surface coating with non-spraying techniques.

Beside the possible changes in the process itself, other possible actions with a positive impact on the emission and exposure scenarios generated during the design analysis group discussions include:

- **Acquisition of a pre-prepared slurry** – the raw materials reception, storing and transport unit operations will not be necessary, as the product will arrive to the facilities in the liquid form and the reception, storage and transport will be in the liquid form. Additionally, the pouring of raw materials (sack emptying) will be eliminated, which is one of the dusty operations in the process;
- **Replacement of nano-TiO_2 by fine-TiO_2** - allows the hazards to be reduced as the fine-TiO_2 is less hazardous than ultrafine TiO_2. It is also expected that the quantity of dust will be reduced. Thus, the occupational health risk for workers in the production line will also be reduced. In the bow-tie model, this type of intervention is considered prior to the emission itself.

Table 5.3 – Alternative production principles and forms proposed for the photocatalytic ceramic tiles production process.

Production Function	**Production Principle**	**Production Form**	**Comment**
Feeding raw materials (sack emptying)	Automatic process	Robot emptying the bags	It is possible to reduce the worker's exposure through automation of the operations, and one possibility is the use of a robot to manipulate the sacks.
Mixing raw materials	Ultrasound agitation	Ultrasound agitator, container	The ultrasound agitation could be more effective and will not create dust during the mixing phase and, possibly, the micro-ball milling may not be necessary, avoiding one processing operation.
Surface coating	Roll printing, automatic	Rotocolor© machine	These glazing processes do not have any dust emission. In contrast, they usually use solvents (especially ink-jet) or other organic mediums for suspension. Ultrafine particles could be dragged/drawn to the air during solvent evaporation faster than during water evaporation.
	Serigraphy, automatic	Ceramic tiles serigraphic machine	
	Ink-jet printing, automatic	Kerajet© machine	
	Dip coating		These glazing processes do not have any dust emission. However, they could be problematic in achieving the desired surface effects; especially the glaze layer, which is usually too thick.
	Curtain, automatic	Bell glazing	
	Waterfall, automatic	Vela© system	

5.3.2. GENERATION OF EMISSION SCENARIOS

Considering the bow-tie model together with the design analysis as presented on Figure 5.2, it is possible to identify the emission and exposure scenarios for each production function, and the related principles and forms. Once complete, it is possible to define the appropriate barriers, both on the emission and exposure side of the bow-tie. The scenarios and barriers are defined for the normal functioning situations, process disturbances, facilities cleaning and equipment maintenance.

In Table 5.4 possible emission scenarios leading to a central event and emission barriers related to different production principles are presented.

It is possible to see that when a pre-prepared slurry is acquired, the emission scenarios related to airborne dust are drastically reduced, with more relevance now on the emission occurring from workers emptying bags into the mixing vessel.

Other operations in which a change in the production principle can eliminate the normal functioning and process disturbances emission scenarios is surface coating. Comparing the spraying production principle with possible alternatives, the emission resulting from spraying and spray gun clog would disappear. Roll printing, serigraphy or ink-jet printing glazing processes do not have any dust (spraying) emission. In contrast, they usually use solvents (especially the ink-jet process) or other organic mediums for suspension. Other possible alternatives include dip coating, curtain or waterfall, as they also do not have any dust emission. However, such techniques may prove problematic in achieving the desired surface effects; especially the glaze layer, which is usually too thick.

The exposure scenarios and barriers (right-hand side of the bow-tie) were also generated, taking particular attention to the work situations in which it was not possible to eliminate the emission through changes in the production principle, in particular the scenarios related to cleaning and maintenance. In these cases, LEV and personal protection equipment are the most appropriate resources.

The automation of operations could also reduce the number of exposure scenarios, as the workers stay far from the dust source.

Table 5.4 – List of emission scenarios and related barriers associated to possible options for the production principle.

Production function	Production principle	Normally functioning		Process disturbances		Cleaning		Maintenance	
		Emission scenario	Emission barrier	Emission scenario	Emission barrier	Emission scenario	Emission barrier	Emission scenario	Emission barrier
Raw materials reception, storing and transport	Mechanical, discontinuous transport			Damaged bags, powder spills	Metal containers	Cleaning powder spills	Vacuum-cleaner		
Feeding raw materials	Manual operation	Dust release		Powder spills		Cleaning powder spills		Intervention on dirty equipment	
	Automatic process	Dust release	Closed cabinet	Powder spills	Closed cabinet	Cleaning powder spills	Vacuum-cleaner	Intervention on dirty equipment	
Pre-prepared slurry				Slurry spills	Closed containers	Cleaning dried slurry spills			
Mixing raw materials	Mechanical stirring			Slurry spills		Cleaning dried slurry spills		Intervention on dirty equipment	
	Ultrasound agitation			Slurry spills		Cleaning dried slurry spills		Intervention on dirty equipment	
Surface coating	Spraying, automatic	Spraying (aerosol release)	Closed cabin with LEV	Slurry spills, spray gun clog		Cleaning dried spills		Intervention on dirty equipment	
	All non-spraying technics, automatic			Slurry spills		Cleaning dried spills		Intervention on dirty equipment	
Material transport	Mechanical, automatic			Tiles jam in line or loading /unloading machines		Removing jammed material			

Along with the emission and exposure barriers, administrative control measures are possible, including housekeeping and maintenance procedures, which will contribute to the risk management. However, they should not be assumed as basic emission and exposure barriers, rather as contributors to risk reduction. For example, if slurry spills are cleaned right after their occurrence (work procedure), no dust will be generated.

The definition of the production functions, principles and forms, including the different alternatives that make it possible to achieve the desired final product and the identification of the emission and exposure scenarios and corresponding barriers are crucial to the approach success.

In Figure 5.3, an early phase production process that was proposed is presented, prior to the design analysis.

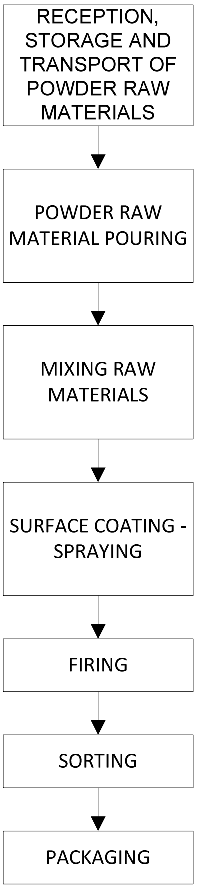

Figure 5.3 – Flow-chart representing Option 1 for the production process.

An alternative option for the production process resulting from the SYDAPP is presented in Figure 5.4.

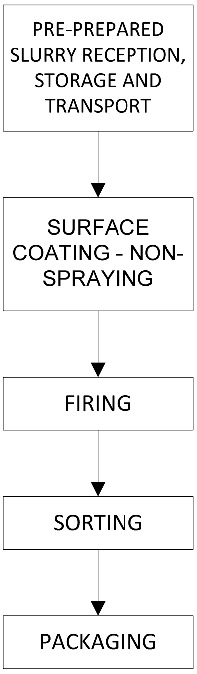

Figure 5.4 – Flow-chart representing Option 2 for the production process.

The main factors differing between the two options presented in Figure 5.3 and Figure 5.4 are:

- Option 1: the slurry preparation is in-house and the surface coating is by a spray technique;
- Option 2: the slurry preparation is outsourced and a non-spraying technique is employed to coat the tile surface.

5.3.3. PRODUCTION PROCESS RISK ASSESSMENT

Considering the process unit operations from the two optional production processes shown in Figure 5.3 and Figure 5.4, it is possible to obtain an estimative of the risk in each operation, using the CB Nanotool. It was assumed the same severity band, “Medium”, in each operation related to the nano-TiO_2.

Either by reducing the number of operations and replacing higher risk level operations by safer ones, the overall risk level is reduced. As shown in Table 5.5, some of the unit operations considered in the Option 1 process are assigned a probability level of Likely and a risk level RL2 – Fume hood or LEV, while in the Option 2 process, the probability ranges from Extremely Unlikely to Less Likely, and the risk level is RL1 – General Ventilation for all operations.

Table 5.5 – Comparing the risk assessment between two alternative processes.

Production function	**Production principle**	**Exposure scenario**	**Probability**		**Risk Level**	
			Process option 1	**Process option 2**	**Process option 1**	**Process option 2**
Raw materials reception, storing and transport	Mechanical, discontinuous transport	Cleaning powder spills	Likely	-	**RL2**	**-**
Feeding raw materials	Manual operation	Cleaning powder spills	Likely	-	**RL2**	**-**
		Maintenance on dirty equipment	Less Likely	-	**RL1**	**-**
Mixing raw materials	Mechanical stirring	Cleaning dried liquid spills	Less Likely		**RL1**	**-**
		Maintenance on dirty equipment	Less Likely		**RL1**	**-**
Acquisition of pre-prepared slurry		Cleaning dried liquid spills	-	Less Likely	**-**	**RL1**
Surface coating	Spraying, automatic	Operation control (aerosol release)	Likely	-	**RL2**	**-**
		Cleaning dried liquid spills	Less Likely	-	**RL1**	**-**
		Maintenance on dirty equipment	Less Likely	-	**RL2**	**-**
	Non-spraying, automatic	Operation control	-	Extremely Unlike	**-**	**RL1**
		Cleaning dried liquid spills	-	Less Likely	**-**	**RL1**
		Maintenance on dirty equipment	-	Less Likely	**-**	**RL1**
Material transport	Mechanical, automatic	Removing jammed material	Less Likely	Less Likely	**RL1**	**RL1**

It should be stressed that this risk reduction is obtained mainly based on the emission reduction and is not dependent on the use of personal protective equipment or by fulfilling work and safety procedures.

Acting at the production form level, it is possible to control the risks using LEV during the spraying operation. However, when using LEV it must be assured that the system is effective and that new tasks of increased risk for workers who need to clean and maintain the LEV system are created.

Repeating the process with different process options, it is possible to identify the different levels of risk for different solutions.

5.3.4. SYSTEMATIC DESIGN ANALYSIS APPROACH - INTERVENTION MODEL

The work conducted during this project has made it possible not only to test the design analysis as a tool to generate possible emission and exposure scenarios but also to propose a model of intervention in an existing or planned production process, using the SYDAPP. The main tasks of the proposed model are (see also Figure 5.5):

1. Applying the design analysis to a process, identifying the production functions, principles and forms;
2. Identifying the emission and exposure scenarios during normal functioning, process disturbances, cleaning and maintenance. In this phase, Hazard and Operability Study (HAZOP) or an equivalent method is used;
3. Identifying possible emission and exposure reduction barriers;
4. Performing a risk assessment for each operation;
5. Generating different production process alternatives based on the design analysis;
6. Repeating steps 2, 3 and 5 for alternative production processes, and eventually repeating step 1 also.

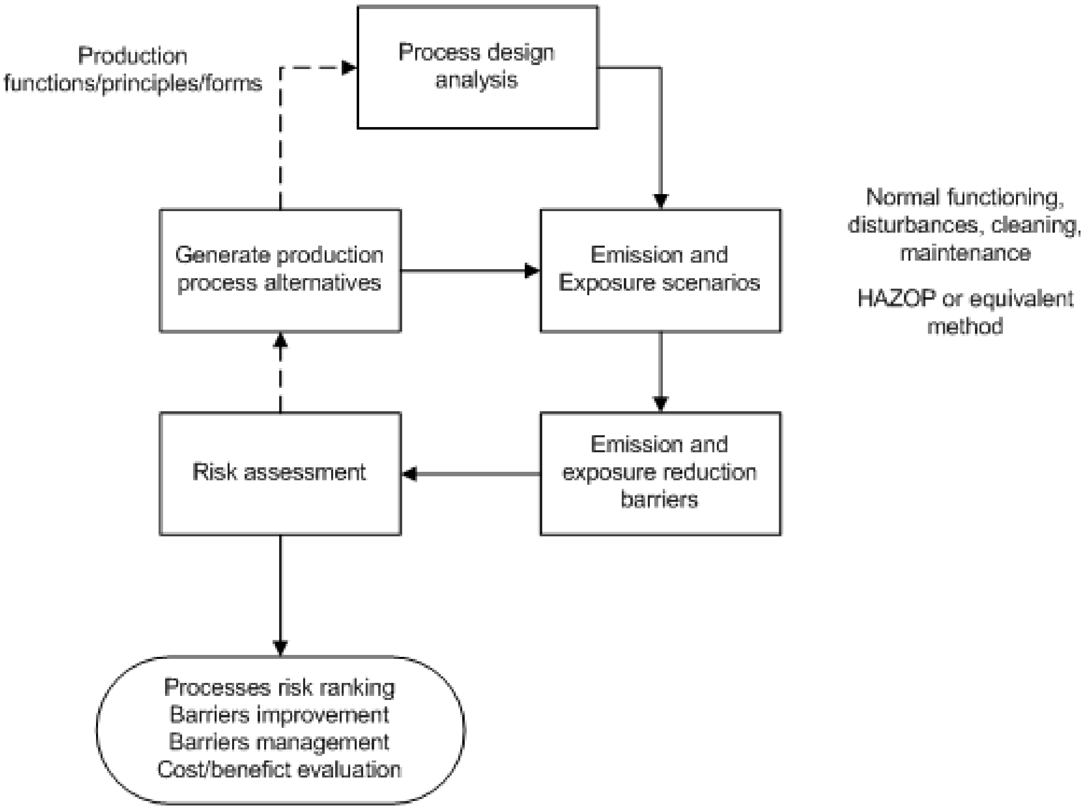

Figure 5.5 – Scheme representing the SYDAPP intervention model.

At the end of this procedure, several results can be obtained when considering the situation in study:

- Different options for the production process, risk ranked;
- Improvements in the emission and exposure barriers for the existing process (or projected one);
- Improvements in the barriers management (supervision, maintenance, etc.);
- Basic information for cost/benefit evaluation.

The SYDAPP approach can be used in different production processes with different levels of complexity and technological demands. The multidisciplinary team should include individuals with fair expertise in the concerned technology and OSH because the critical aspects of this tool are the definition of the production functions and production principles, and the identification of the emission and exposure scenarios.

5.3.5. DISCUSSION

The SYDAPP allows the project team to be involved in discussions, both to perform the design analysis of the production process and to identify the emission and exposure scenarios and related barriers. One of the major advantages of the SYDAPP is the creation of a cooperative environment between process engineers, safety practitioners and all other people involved in the development of the product, facilitating communication and understanding inside a multidisciplinary team. With this approach, it is possible to really involve the designers and engineers in the occupational risk management.

When using the bow-tie model, it is possible to identify different ways to reduce the risk to workers, both on the emission and exposure sides. It becomes, in some way, "natural" to accomplish the control measures hierarchy as defined in regulations, international standards and scientific literature (BSI - British Standards, 2007a; Council of the European Communities, 1989; Fleury et al., 2013).

The production functions and production principles are crucial to design solutions, as emission is directly related to the production functions applied. These functions will limit the number of possible principles, and consequently the number of forms. The actual emission, resulting in exposure always becomes visible at the production form. Conventional occupational hygiene control measures, such as LEV, enclosure, etc. will act upon the production-form. However, when the emission (and the related exposure) is too excessive, or the substances exposed to are too dangerous, (re)design approaches will be the only option left to reduce or eliminate emission (apart from cancelling production). (Re)design consists of changing the production principles under an unchanged production function, or changing or eliminating production functions. This last option is very effective because the corresponding principles and forms will also be eliminated. Using pre-mixed slurries instead of mixing powdered raw materials is an example where all functions related to raw material processing are eliminated. When a company introduces these changes, it is reducing the sources of emission and exposure substantially at the initial phase of the production process. Obviously, other companies will need to perform these production functions, but when volumes are large enough, these firms can also modify their production methods, for example, by changing their mode of operation from manual to automatic.

Accordingly, the use of a supply chain with OSH purposes is one question raised by the SYDAPP. The design analysis performed along the supply-chain helps to identify opportunities to transfer higher risk operations to facilities prepared to address these risks, allowing others to focus on the core process operations, which will ultimately result in safer workplaces by implementing cost-effective solutions.

One important characteristic of the SYDAPP is the focus on the hazard emission rather than on the exposure. The action on the hazard is related to the source and, consequently, it is more effective in eliminating or reducing hazards. This encompasses a preventive attitude regarding the hazard that contrasts with corrective actions after exposure.

This research was conducted during the project as part of the deliveries, and there were no opportunities to repeat any activities. As such, the researchers had to address any constraints in real-time, and it was not possible to explore all possibilities arising from the SYDAPP intervention model as proposed in section 5.3.4.

Further research will be needed on the use of the SYDAPP intervention model in more complex situations, including in the production stage of nanomaterials, as the current research was performed in a downstream use situation.

5.4. Conclusions

The use of the SYDAPP helps identify solutions to reduce the exposure of workers to ENM. As shown in the current case, it is advantageous to apply it in a development project, or in other words, during the project phase, before the final process design is set.

SYDAPP could be a useful method to help the nanotechnology community improve OSH, as the work performed allows the proposed research questions to be answered.

With this approach, it was possible to generate emission and exposure scenarios resulting from the photocatalytic ceramic tiles production process operations, and the bow-tie proved to be a helpful concept model to achieve this.

Following the emission scenarios identification, it was also possible to define emission reduction barriers. In the particular case of the production of photocatalytic ceramic tiles, it was possible to identify opportunities to reduce the emission of nanoparticles, resulting in the proposal of an intrinsically safer production process.

Through the SYDAPP, it was also possible to reduce the emission scenarios resulting from the photocatalytic ceramic tiles production process, identifying alternative production principles and opportunities for the elimination of hazardous unit operations as a result of outsourcing.

The case study presented in the current paper shows that by using the SYDAPP, it is possible to manage the OSH risks in the production line of photocatalytic ceramic tiles and to help defining possible controls, considering the desirable hierarchy for their definition.

The scientific relevance of this work is highlighted by the demonstration that SYDAPP is a particularly suitable method for the OSH risk management. It was demonstrated that this approach was proved to be effective in generating relevant emission and exposure scenarios, as well as related possible barriers to reduce particularly emission scenarios.

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CHAPTER 6. CONCLUSIONS AND FUTURE WORK

6.1. Conclusions

This thesis has analysed the topic of occupational risk management in nanotechnology, in particular the risk related with exposure to nanomaterials. Since this thesis results from a compilation of four papers, the specific and detailed conclusions of each paper were already presented at the corresponding chapters. Therefore, this last chapter is a summary of those conclusions and a description of how the main four thesis' objectives were achieved and to what extent.

The first specific objective of this thesis was to evaluate how the quality of information on nanomaterials influences qualitative risk assessment results. This objective was addressed in chapter 3 and the results obtained in the corresponding paper show that information included in the Safety Data Sheet is not sufficient to perform risk assessment in the most accurate possible way. Accordingly, the worker's exposure risk will be underestimated, since the quality of available information on the nanomaterials influences the risk assessment results. It is also concluded that additional care should be taken to obtain more reliable and updated information on the considered nanomaterial.

The second initially defined objective was to confirm the suitability of the qualitative risk assessment methods for assessing the risk on engineered nanomaterials activities and processes. By comparing different risk assessment methods in Chapters 3 and 4, it was possible to confirm that qualitative risk assessment methods are suitable and appropriate for assessing the risk on engineered nanomaterials activities and processes. Nevertheless, some improvement needs to these methods were also identified. Despite the mentioned suitability, when performing qualitative risk assessment, it is important to select those methods that are more proper to the situation under study and to compare the results obtained with different methods. Considering that qualitative risk assessment methods are considered basic risk management tools, the use of exposure measurement equipment, such as Condensation Particle Counter, or even more sophisticated and reliable equipment, will allow clarifying doubts in specific cases.

The third specific objective was to evaluate and improve design-based approaches for risk control on engineered nanomaterials activities and processes. Regarding this, it was concluded that SYDAPP is a useful approach for risk control on engineered nanomaterials activities and processes, since it allows identifying the emission and exposure scenarios in the workplace and helps defining the barriers to control those scenarios. Accordingly, SYDAPP helps to identify solutions, to reduce the exposure of workers to engineered nanomaterials and it is advantageous to apply during the project development, before the final process design being set.

Last but not least, the fourth objective was to contribute to improve workplace operational control and risk management in the nanotechnologies field. The carried out work, namely the work presented at chapter 3 to 5, as well as in Annex 1, allowed to conclude that the developed research has contributed to improve workplace operational control and risk management in the nanotechnologies field, considering that it is pointed the improvement of risk assessment and risk control as an overall result. Particularly, SYDAPP could help at identifying some opportunities to reduce the emission of nanoparticles, allowing the proposal of intrinsically safer production processes.

In general terms, it can be also concluded that nanotechnology is growing as a new sector of research, industry and commerce, therefore it becomes relevant that the corresponding OSH practices can be planned and implemented to cover and answer all workers' safety challenges.

SYDAPP proved to be a suitable approach to integrate OSH in product and production processes development projects, enabling an effective risk management at an early stage of the projects. Moreover, this approach allows the involvement of the technical and scientific staff in prevention activities. Thus, it helps to include occupational risk management in projects work plans and engage people with different backgrounds and concerns in the common target of designing safer production processes. Additionally, the use of the supply chain as a prevention factor was identified as a possible alternative, bearing in mind that specialized suppliers can be more effective and efficient on applying more reliable risk control measures.

Considering the existing uncertainties, the available methods for risk assessment proved to be useful tools for risk management providing information for decision taking. Hopefully, the nanotechnology industries managers will be able to realise that, by using a design-based approach, it is possible to reduce risks for workers in the workplace through an implementation of production process changes.

6.2. Future work

During the current study, researchers had to deal with some decisions and challenges, which in some cases resulted in a few limitations for the current thesis. Because nanotechnology is an emerging field in Portugal, it is still difficult to have access to workplaces involving exposure to engineered nanomaterials. Therefore, researchers had no opportunities to perform the research in such settings. Additionally, the field work had to be done "in one shot", as some operations were done only once, so data collection and measurements could only be at one time.

Based on the previous, further work could consist in the application of SYDAPP in new exposure situations or settings, either existing or planned production facilities, by using the proposed intervention model to validate the results obtained in the presented case study.

Additionally, qualitative risk assessment methods should be used and compared amongst them and with results from the exposure assessment using direct measurement equipment and/or filter collection. The consolidation of exposure and risk assessment methods is still an important field of research.

6.3. Thesis' additional outputs

During this PhD. project several other outputs resulted from the carried our work that were not included as chapters. Among the most relevant outputs, it is possible to list the following:

- Silva, Francisco, Arezes, Pedro, Swuste, Paul "A Qualitative Approach to Risk Assessment and Control in Engineered Nanoparticles Occupational Exposure", International Symposium on Occupational Safety and Hygiene, Guimarães, 14 de Fevereiro de 2013, 363-364 (short paper).
- Silva, Francisco, Arezes, Pedro, Swuste, Paul "A Qualitative Approach to Risk Assessment and Control in Engineered Nanoparticles Occupational Exposure", 2° Encontro Nacional de Nanotoxicologia, Lisboa, 3 de Abril de 2013 (conference communication).
- Silva, Francisco; Arezes, Pedro; Swuste, Paul; "Qualitative risk assessment and control in engineered nanoparticles occupational exposure"; 6th International Symposium on Nanotechnology, Occupational and Environmental Health (NanOEH), Nagoya, 30 de Outubro de 2013 (conference communication).

- Silva, Francisco; Arezes, Pedro; Swuste, Paul; “Nanotechnology: an overview on OSH aspects in Europe”; International Symposium on Occupational Safety and Hygiene, Guimarães, 13 de Fevereiro de 2014, 391-393 (short paper).
- Silva, Francisco; Arezes, Pedro; Swuste, Paul; “Risk assessment in a research laboratory during sol-gel synthesis of nano-TiO_2”; International Symposium on Occupational Safety and Hygiene, Guimarães, 14 de Fevereiro de 2014, 388-390 (short paper).
- Silva, Francisco; Arezes, Pedro; Swuste, Paul; “Nanomaterials in construction – occupational safety and health aspects”; CINCOS’14 Congresso de Inovação na Construção Sustentável, Porto, 13 de Novembro de 2014, 11-18 (conference paper).
- Silva, Francisco; Arezes, Pedro; Swuste, Paul; “Risk assessment in a research laboratory during sol-gel synthesis of nano-TiO_2”; Nanosafe2014, Grenoble, 20 de Novembro de 2014 (conference communication).
- F Silva, S P B Sousa, P Arezes, P Swuste, M C S Ribeiro, J S Baptista “Qualitative Risk assessment during polymer mortar test specimens preparation – methods comparison”; Nanosafe2014, Grenoble, 20 de Novembro de 2014 (conference communication).
- Silva, Francisco; Arezes, Pedro; Swuste, Paul; “Systematic design analysis and risk management on engineered nanoparticles occupational exposure”; International Symposium on Occupational Safety and Hygiene, Guimarães, 12 de Fevereiro de 2015, 350-352 (short paper).

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ANNEX 1 - RISK MANAGEMENT OF OCCUPATIONAL EXPOSURE TO NANOPARTICLES DURING A DEVELOPMENT PROJECT. A CASE STUDY

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Abstract

The production of nanotechnology based products is increasing, along with the conscience of the possible harmful effects of some nanomaterials. Along with technological advances, there is the need to improve safety and health knowledge and apply that knowledge to the workplaces. The "safety-by-design" approaches are getting attention as helpful tools to develop safer products and production processes. The Systematic Design Analysis Approach could help to identify the solutions to control the workplace risks defining the emission and exposure scenarios and the possible barriers to interrupt them. Managing risks during a photocatalytic ceramic tiles development project it was possible to identify relevant nanoparticles emission scenarios and related barriers and defining possible ways to reduce it, leading to an inherently safer production process.

Keywords: photocalytic ceramic tiles; risk assessment; systematic design analysis; inherently safer process.

1 Introduction

Photocatalytic ceramic tiles containing nano-sized titanium dioxide (TiO_2) have self-clean characteristics and are also able to transform some air pollutants like nitrogen oxides, contributing to a cleaner ambient air, and reveal anti-bacterial properties [1].

In general, the in-vitro and in-vivo tests done with both fine (particles with nominal diameter > 100 nm) and ultrafine TiO_2 particles (with nominal diameter <100 nm, also called nanoparticles or nano-sized particles), demonstrate potential for harmful health effects in humans. TiO_2

nanoparticles induce inflammatory responses in the lung tissue, particularly in high doses [2]. The International Agency for Research on Cancer (IARC) classified TiO_2 as “possibly carcinogenic to humans”, carcinogenic Group 2B substance [3]. National Institute for Safety and Health (NIOSH) in a review on the animal and human data relevant to assessing the carcinogenicity of TiO_2 published in 2011, concluded that exposure to ultrafine (or nano) TiO_2 should be considered a potential occupational carcinogen agent, and recommended an airborne exposure limit of 2.4 mg/m^3 for fine TiO_2 and 0.3 mg/m^3 for ultrafine (including engineered nanoscale) TiO_2 [4].

Some authors have been defending the need for methodologies that address the risks related to nanotechnologies based on the processes or product design [5]–[7]. One approach cited in the literature is the “Design for Safer Nanotechnology” proposed by Morose [8] in which the author proposes an intervention during the design stage for nano-objects and products that incorporate them. Schulte et al. [5] also mention the Prevention through Design (PtD) initiative as a valuable methodology to manage the occupational risks. Swuste and Zalk [9] also propose the use of design analysis to achieve safer production processes in the nanotechnology field.

The aim of this paper is to present the work carried out to establish a safer production process resulting from a development project. The research questions underlying this analysis are:

- Does a design approach of the production line of photocatalytic ceramic tiles generate relevant emission scenarios and related barriers?
- What are the possibilities of Systematic Design Analysis Approach (SYDAPP) on reducing emission scenarios during photocatalytic ceramic tiles production?
- Managing risks during the development phase of a new production process could help to define safer processes?

2 Methodology

2.1 FRAMEWORK

The work presented in this paper was performed during the development project of photocatalytic ceramic tiles, using TiO_2 (anatase) and made by common ceramics production processes that was part of the funded research project Selfclean.

The project lasted for approximately two years, from the first exploratory tests to the final product prototype. The OSH intervention, including the work described in this paper had six-month duration plus another two months to produce the OSH issues report.

The project team included several materials science researchers and engineers from one university, one technological institute and one ceramic tile company and one occupational safety and hygiene (OSH) practitioner.

The project's meeting discussions on the health and safety aspects were held with an interdisciplinary knowledge base. These discussions were complemented by observation and information collection during the laboratory and semi-industrial tests performed during the project.

OSH issues were included in the agenda of three plenary meetings of the project. For approximately 45 minutes in each of the meetings, the SYDAPP was presented and the team members had the opportunity to contribute their inputs to the process design analysis and related emission and exposure scenarios. The group discussions gathered contributions in particular from the design analysis, the identification of emission and exposure scenarios and the possible barriers. The experts proposed alternative production principles and forms, including their feasibility evaluation, helping to identify their impact on the possible scenarios. In parallel, several head-to-head informal meetings were held by the OSH practitioner with the other members of the group, including the ceramic company engineer and the university researchers, to refine the knowledge on the different options and confirm information collected during the meetings and project tests. Finally, the OSH practitioner, based on the collected information, produced a report for the project manager.

2.2 SYSTEMATIC DESIGN ANALYSIS APPROACH

Although the occupational safety and hygiene research pays more attention to risk analysis [10], several authors in this domain have done research in the safety by design field, especially the Safety Science Group of Delft University of Technology [11]–[13]. Swuste [10], for example, proposed a systematic approach towards solutions based on three complementary elements:

- Hazard process model;
- Design analysis;
- Problem-solving cycle.

The two first elements are the basis for the SYDAPP. Combining the process design analysis with the emission and exposure scenarios identification together, it is possible to acquire a clear vision of how the different process operations will affect a worker's exposure.

2.3 HAZARD PROCESS MODEL - BOW-TIE

The bow-tie model (see Figure 1) is used in the safety science field as a tool to prevent the occurrence of accidents [14]. Its adaptation to the occupational hygiene field helps to establish the necessary barriers to control the risks arising from different workplace exposure scenarios [15]. The use of the bow-tie model as a support tool to risk management is also referred by Fleury et al. [7], and an example of the use of this model, defining exposure scenarios and evaluating the risks during the production of carbon nanotubes polymer composites is presented in another article [16].

The bow-tie model also stresses the importance of the management as the entity responsible to implement the barriers [17].

Considering together the bow-tie model and the design analysis it is possible to relate the occupational setting with the production process with detail. The emission and, consequently, the exposure are identified at the production form level. Thus, the options to reduce emission and exposure are usually limited to LEV and personal protective equipment. As these controls could become ineffective due to the high level of exposure or their own characteristics, it turns out to be useful to act at production principles or production functions, providing more operative controls.

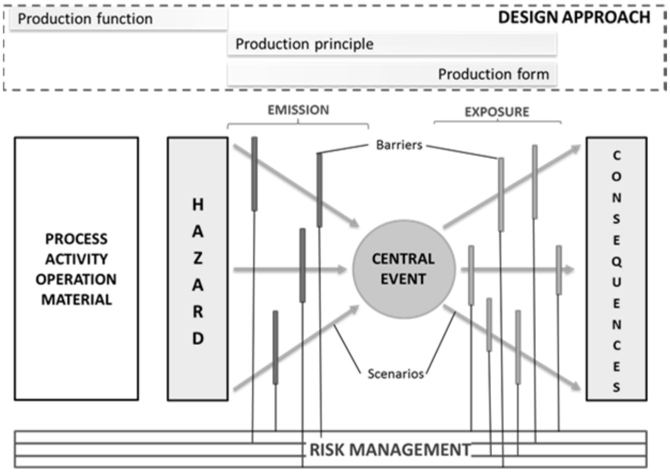

Figure 1 - Bow-tie model with arrows representing different exposure scenarios.

2.4 DESIGN ANALYSIS

The design analysis methodology allows studying and understanding the workplace conditions. In design analysis the production process is split into three levels of decision (see Figure 2), described below [10]:

- **Production function**: is the highest level and divides the production process into his core activities, similar to unit operations;
- **Production principle**: identifies the general process, motive power and operational control methods by which the production function can be achieved;
- **Production form**: is the lowest level and specifies the detailed design by which the production principle will be accomplished.

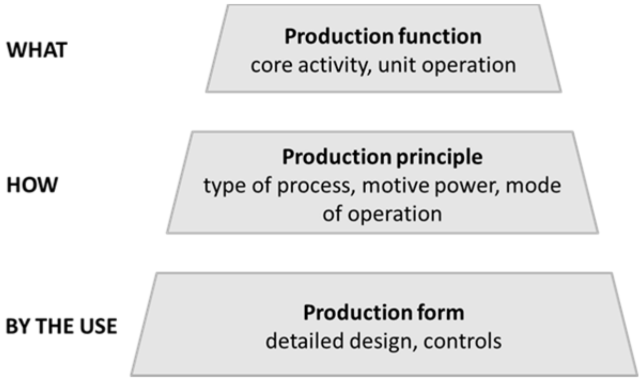

Figure 2 - Design analysis hierarchy.

If there is a large number of production processes, the type of functions (or unit operations in rigor) in which each process can be broke down is relative small. The main unit operations categories are: material reception, material storage, transport and feed, processing, packaging, waste disposal. The processing operations can be subdivided in subcategories that vary from one industry sector to other, and once enumerated will allow to study the more effective and reasonable control measure or set of control measures to apply in each particular situation. In the ceramic tiles industry some examples of processing production functions or unit operations are milling, conformation, drying, glazing, firing and sorting, among others.

At the production principle level it is possible to choose the type of process to achieve the function (ex. different shaping processes) and also the motive power (ex. electricity or fossil combustible) and the mode of operation (ex. manual operation, mechanical or automatic). There are a few hundreds of different production principles to fulfil the unit operations.

At the production form level it is defined the machine, the equipment or set of equipment that will be actually used in the process (ex. the hydraulic press type if shaping by press is the principle defined to achieve the unit operation “conformation”). It is also at this level that the exposure controls are defined (ex. a local exhaust ventilation (LEV) or a closed cabin).

On the occupational safety & health point of view, the focus on the production functions and principles will allow finding the less hazardous way to achieve the same production result or to choose the best available techniques to control the hazard.

2.5 RISK AND EXPOSURE ASSESSMENT

For risk assessment it was used a control banding based method, the CB Nanotool, which is a four by four matrix that relates severity parameters on one-axis and probability parameters on the other. The severity parameters consider physicochemical and toxicological properties of both nanomaterial and parent material, including, surface reactivity, particle shape and diameter, solubility, carcinogenicity and mutagenicity. The probability band scores are based on factors affecting the potential exposure to the nanomaterial, namely, the estimated amount of chemical used in one day, dustiness, number of employees with similar exposure, frequency of operation and operation duration. The obtained control bands by risk level can be classified in RL1 – general ventilation to RL4 – seek specialist advice [18].

For exposure assessment, the usual occupational hygiene method was used, namely the NIOSH 0500 for total dust [19], consisting in the collection of the airborne particles in one filter, through filtration of the workplace air. The samples were personal, thus the filter support was placed in the worker’s breathing area.

3 Results and discussion

3.1 PRODUCTION PROCESS AND THE DESIGN ANALYSIS

After the preliminary tests the planned photocatalytic ceramic tiles production process was defined and proposed the use of already existing equipment in the ceramic production plant. Then, the first step was to detail the production process, dividing in its functions, principles and forms (see Table 1). This work was performed during the project meetings, by getting contributions from all the project team members.

Table 1 – Production functions, production principles and production forms for the photocatalytic ceramic tiles production process

Production Function	Production Principle	Production Form	Description
Reception of raw materials	Mechanical, discontinuous transport	Palletized bags, forklift	The nano-TiO_2 is received in paper bags, which are packed in wood pallets. The pallets are handled with a forklift and/or an electric pallet-truck.
Storage of raw materials	Mechanical, discontinuous transport	Palletized bags, forklift	
Transport of raw materials	Mechanical, discontinuous transport	Palletized bags, forklift	
Pouring raw materials (sack emptying)	Manual operation	Emptying bags to a container	The TiO_2 powder is poured into water and is dispersed in the liquid with a column stirrer to get homogenized slurry. When the suspension is homogeneous it is milled in a micro-balls mill in order to de-aggregate. Finally, the slurry is sieved.
Mixing raw materials	Mechanical stirring	Column stirrer and micro-ball mill, container	
Surface coating	Spraying, automatic	Air-less spraying, booth disk glazing, booth spray-gun, booth	The slurry is applied in the already fired ceramic pieces by spray technic.
Transport of materials	Mechanical, automatic	Parallel belt line, ceramic tiles loading and unloading machines, storage boxes	The coated tiles are transported over two parallel trapezoidal belts on the glazing line. At the end of the line the tiles are loaded on a "ceramic tiles box" for storage before firing. At the kiln the tiles are unloaded from the box and transported to the kiln entrance over parallel trapezoidal belts and/or roller conveyor.
Processing - firing	Thermal, automatic	Roll kiln	After the coating, the pieces are fired (2nd fire) at a temperature around 950 °C in a continuous roll kiln.
Sorting	Manual, mechanical automatic transport	Ceramic tiles sorting line	The fired pieces are sorted (finding defects in surface and body of the pieces) and packed in cardboard boxes.
Packaging	Mechanical, automatic	Ceramic tiles packaging line	

The production process is similar to the usual ceramic tiles production process. The most relevant unit operations in the process are those related with the processing of raw materials and the surface coating.

During a project meeting, getting contributions from the team members, it was possible to define alternative production principles and forms for the production process. The possible options were the automation of the sack emptying operation, ultrasound agitation for raw materials mixing and a few non-spraying techniques to apply the TiO_2 aqueous suspension in the ceramic tiles (ex.: roll printing, serigraphy or ink-jet), as presented in Table 2.

Beside the possible changes in the process itself, other possible action with positive impact in the emission and exposure scenarios, generated during the design analysis group discussions, was the acquisition of pre-prepared slurry eliminating several unit operations, as the product will arrive to the facilities in the liquid form. In particular, pouring raw materials (sack emptying) will be eliminated, being this one dusty operation in the process.

Considering the bow-tie model together with the design analysis, it was possible to identify the emission scenarios and the barriers for each production function, and related principles and forms. The scenarios and barriers are defined for the normal functioning situations, process disturbances, facilities cleaning and equipment maintenance (Table 2). The identification of the possible emission scenarios and emission barriers was based on the knowledge of the processes and related engineering risk control measures.

It is possible to see that changing the production principle in the pouring raw materials function from the manual operation to the automatic operation will make it possible to introduce a barrier, a closed cabinet with LEV, in the emission scenario. Moreover, considering the acquisition of pre-prepared slurry, the emission scenario is eliminated.

Comparing the possible production principles for the surface coating, once again it is possible to eliminate the dust release emission scenario choosing a non-spraying technique instead the air-less spraying (or another spraying technique) to apply the TiO_2 on the ceramic tile surface.

Table 2 – Emission scenarios and related barriers related with possible options of production principle

Production function	**Production principle**	**Normally functioning**		**Process disturbances**		**Cleaning**		**Maintenance**	
		Emission scenario	**Emission barrier**	**Emission scenario**	**Emission barrier**	**Emission scenario**	**Emission barrier**	**Emission scenario**	**Emission barrier**
Raw materials reception, storing and transport	Mechanical, discontinuous transport			Damaged bags, powder spills	Metal containers	Cleaning powder spills	Vacuum-cleaner		
Pouring raw materials	Manual operation	Dust release		Powder spills		Cleaning powder spills		Intervention on dirty equipment	
	Automatic process	Dust release	Closed cabinet	Powder spills	Closed cabinet	Cleaning powder spills	Vacuum-cleaner	Intervention on dirty equipment	
Pre-prepared slurry				Slurry spills	Closed containers	Cleaning dried slurry spills			
Mixing raw materials	Mechanical stirring			Slurry spills		Cleaning dried slurry spills		Intervention on dirty equipment	
	Ultrasound agitation			Slurry spills		Cleaning dried slurry spills		Intervention on dirty equipment	
Surface coating	Spraying, automatic	Spraying (aerosol release)	Closed cabin with LEV	Slurry spills, spray gun clog		Cleaning dried spills		Intervention on dirty equipment	
	All non-spraying technics, automatic			Slurry spills		Cleaning dried spills		Intervention on dirty equipment	
Material transport	Mechanical, automatic			Tiles jam in line or loading /unloading machines		Removing jammed material			

3.2 PILOT-TEST

During the project, a pilot-test was performed, allowing simulating part of the production process operations and tasks. One additional operation was considered, weighing TiO_2, previous to pouring raw materials. For risk assessment 4 different tasks where considered: Task 1- Titanium dioxide weighing; Task 2- Pouring titanium dioxide; Task 3- Mixing slurry; Task 4- Surface coating.

Another relevant question was the use of fine TiO_2 instead of nano-sized form, resulting from the fact that the photocatalytic properties were optimized with that material.

The risk assessment of the unit operations was performed with the CB Nanotool, considering the possible use of nano-sized TiO_2. The severity factors are presented in Table 3.

Table 3 – CB Nanotool Severity band factors

Hazard Factor	**Answer**
Parent material hazard	
OEL (μg/m^3)	2400
carcinogen?	yes
reproductive hazard?	no
mutagen?	no
dermal hazard?	no
asthmagen?	no
Nanoscale material hazard	
Surface reactivity	unknown
Particle shape	spherical
Particle diameter (nm)	>40
Solubility	Insoluble
carcinogen?	yes
reproductive hazard?	unknown
mutagen?	unknown
dermal hazard?	unknown
asthmagen?	no

In Table 4 the exposure factors considered for the different tasks assessed are presented.

Table 4 – CB Nanotool probability band factors

Probability factor	Answer			
	Task 1	**Task 2**	**Task 3**	**Task 4**
Estimated amount of chemical used in one day (mg)	10^6	10^6	10^6	10^6
Dustiness	Medium	High	Low	High
Number of Employees with Similar Exposure	1 - 5	1 - 5	1 - 5	1 - 5
Frequency of Operation (annual)	Monthly	Monthly	Monthly	Monthly
Operation Duration (hours per shift)	< 30 min	< 30 min	< 30 min	1 - 4 h

The CB Nanotool assessment results are presented in Table 5.

Table 5 – Pilot-test risk assessment using CB Nanotool

Task	**Severity band**	**Probability band**	**Overall risk band**	**Control required**
1- Titanium dioxide weighing	Medium	Less Likely	RL1	General ventilation
2- Pouring titanium dioxide	Medium	Likely	RL2	Fume hood or local exhaust ventilation
3- Mixing slurry	Medium	Less Likely	RL1	General ventilation
4- Surface coating	Medium	Likely	RL2	Fume hood or local exhaust ventilation

During the pilot-test the airborne particles concentration was measured using the NIOSH 0500 method in order to have a perception of the worker's exposure to TiO_2 particles during the operations. Considering the tasks duration and the workers present in the workplace it was decided to sample during the TiO_2 aqueous suspension, including weighing raw materials, pouring raw materials and mixing, and performing two personal samplings on both the workers operating the glazing line (surface coating and transport of materials). The results of airborne sampling are presented in Table 6.

Table 6 – Airborne particles concentration during pilot-test tasks

Tasks	Sampling time (min)	Concentration (mg/m³)
Worker during raw material weighing and slurry preparation	33	1.1[1]
Surface coating in glazing line – Worker 1	160	0.9
Surface coating in glazing line – Worker 2	150	1.5

The sampling time corresponds to whole working time. Being the first attempt to produce the ceramic tiles, several disturbances occur during the process and the results should be considered just representing the conditions of the test and could not be considered as representing the future exposure during industrial production of this type of ceramic tiles, but could give a rough estimation.

3.3 DISCUSSION

The SYDAPP creates a cooperative environment between process engineers, safety practitioners and other people involved on the development of the process, facilitating the communication and understanding inside the multidisciplinary team. With this approach it is possible to really involve the designers and engineers in the occupational risk management.

The production functions and production principles are crucial to design solutions, since emission is directly related to production functions applied. These functions will limit the number of possible principles, and consequently the number of forms. The actual emission, resulting in exposure always becomes visible at the production form. Conventional occupational hygiene control measures, such as LEV, enclosure, etc. will act upon the production form.

However, when the emission (and the related exposure) is too excessive, or the contaminants are too dangerous, (re)design approaches will be the only option left to reduce or eliminate emission (apart from cancelling the whole production). (Re)design consist on changing production-principles under an unchanged production function, or changing or eliminating production functions. This last option is very effective, because the corresponding principles and forms will be also eliminated. Using pre-mixed slurries instead of mixing powdered raw materials is an example where all

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[1] Result below quantification limit. The uncertainty is higher compared with the other results.

functions related to raw materials processing are eliminated. When a company introduces these changes, it is reducing substantially the sources of emission and exposure at the initial phase of the production process. Obviously, other companies will need to perform these production-functions, but when volumes are big enough, also these firms can modify their production methods, for example, by changing their mode of operation from manual to automatic.

Accordingly, the use of the supply chain with OSH purposes is one question raised with SYDAPP. The design analysis performed along the supply-chain helps at identifying opportunities to transfer higher risk operations to facilities prepared to address it, allowing others to focus on the core process operations, which will ultimately result in safer workplaces by implementing cost-effective solutions. This approach is only acceptable if the risks are transferred to adequate facilities, not to less controlled subcontractors.

Both the CB Nanotool risk assessment and the airborne particles sampling are pointing to potential risk to workers during the pilot-test, considering the possible use of nano-sized TiO_2. It is clear that the pilot-test conditions do nor replicate exactly the future production conditions but could help to better understand the main emission and exposure scenarios. Replacing nano-TiO_2 by fine-TiO_2 it is possible to reduce the risk for workers. Based on the existing knowledge of the TiO_2 toxicological properties, it is clear that its nano form is more hazardous than the fine-TiO_2 [4]. Furthermore, the toxicological assays performed with nano-TiO_2 reveal potential effects to health resulting from the possible translocation of the nanoparticles in the human body and also from the capability to cells internalization. Considering the bow-tie model, acting on the hazard itself is an advantageous strategy to deal with the workplace risks as it is prior to the emission and, of course, the worker's exposure. The results obtained from the airborne particles sampling during the pilot-test shown that the exposure to TiO_2 airborne particles is below the proposed limit value of 2.4 mg/m^3, even considering that all the airborne particles were of TiO_2.

In the tests performed during the Selfclean Project, the medium size of the TiO_2 particles was in the range 150-200 nm, while the nano-sized TiO_2 particles have diameters below 100 nm. Accordingly to the International Commission on Radiological Protection (ICRP) respiratory tract deposition model for particles, referred by the International Organization for Standardization, it is evident that the probability of the particles with sizes in the 150 nm to 200 nm deposit in all respiratory tract is lower than particles smaller than 100 nm [20].

Considering the lack of knowledge on the potential for harm of the different types of nano-objects and the uncertainties related to risk and exposure assessment [21] the safety-by-design approaches gain relevance. Previous learning from the safety science field could help on defining ways to deal with potentially high risk production processes. The inherently safer process concept developed in the late 1970's, which focus on the avoidance or reduction of the hazard at source [22], [23] is adaptable to the nanotechnologies field. The SYDAPP allows the project team to identify the unit operations with lower emission potential.

4 Conclusions

The use of the SYDAPP helps on finding solutions to reduce the workers' exposure during the work with engineered nano-objects. As shown in the current case, it seems that there is advantage in applying it in a development project, or by other words, during the project phase, before the final process design being set.

With this approach it was possible to generate emission scenarios resulting from the photocatalytic ceramic tiles production process operations, being the bow-tie a helpful concept model to achieve this.

Following the emission scenarios identification, it was also possible to define emission reduction barriers. In the particular case of the production of photocatalytic ceramic tiles it was possible to identify opportunities to reduce emission of nanoparticles.

The risk management during the project phase allows developing safer production processes, changing materials, methods or equipment, resulting in the proposal of an inherently safer production process.

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