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Polymer nano and submicro composites risk assessment

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Abstract: Nanotechnology has been exponentially developed in the last years bringing promises to create new and better materials. However, these new technologies can expose workers to unknown risk factors while they are producing, processing and handling nanomaterials (NM). With the rapid growth of nanotechnology based products, researchers, manufacturers, regulators and consumers are increasingly concerned about potential impacts that these products could have. In order to prevent potential risks associated to NM, the related legal framework should be firstly known. Considering these features, this work is aimed at identifying applicable legislation to NM and its adequacy, as well as at analysing the risk assessment of polymer nano and submicro composites during their production in a laboratory context. In order to determine how to prevent/control the risks associated with the NM, the existent legal framework was analysed. No specific legislation for NM was found, but some related standard were identified. The risk assessment was based on qualitative ISPESL and EPFL methods. These methods had convergent on medium risk results, so some precautionary/prevention measures should be implemented. The outputs of this work highlight that the current knowledge about the NM is insufficient; thus, more research work will be need to fill the existing gaps.

Keywords: risk assessment, nanocomposite, legislation, prevention.

Avaliação de riscos de nano e submicro compósitos poliméricos

Resumo: A nanotecnologia tem-se desenvolvido de forma exponencial nos últimos anos, trazendo promessas de criação de novos materiais de elevado desempenho. No entanto, o surgimento destas novas tecnologias pode expor os trabalhadores a fatores de risco atualmente desconhecidos durante a produção, processamento e manuseio dos nanomateriais (NM). Com o rápido crescimento dos produtos baseados na nanotecnologia, investigadores, produtores, reguladores e consumidores preocupam-se cada vez mais com os potenciais impactos que estes poderão ter. Tendo em conta estes aspetos, o presente trabalho procurou identificar a legislação aplicável aos NM e a sua adequação, assim como avaliar os riscos relativos à produção em laboratório de compósitos poliméricos com nano e submicro partículas. Para determinar como prevenir/controlar os riscos associados com aos NM, foram primeiramente analisados os referenciais legais. A avaliação de riscos foi realizada com base nos métodos qualitativos ISPESL e EPFL. Não foi identificada legislação específica para os NM, contudo existem algumas normas aplicáveis. Os métodos qualitativos utilizados obtiveram resultados convergentes, risco médio. Com estes resultados, devem ser aplicadas medidas de prevenção/precaução. O conhecimento atual sobre os NM é insuficiente, portanto, são necessários mais trabalhos de investigação para preencher as lacunas existentes.

Palavras-chave: avaliação de riscos, nanocompósitos, legislação, prevenção..

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1. Introduction

Nanotechnology is one of the most promising technologies of this century, and it has been widely applied, in the last years, to create materials with new and better properties (Gupta, 2011; Ivask, Bondarenko, Jepihhina, & Kahru, 2010). Engineered nanomaterials (NM) typically possess nanostructure-dependent properties (e.g., chemical, mechanical, electrical, optical, magnetic, biological). These new modified-properties allow improving the performance of the traditional materials, leading to the development of unique new products. However, these same properties can potentially raise the nano biological activity; hence, NM are theoretically more toxic than the homologous materials at micro scale (Oberdorster et al., 2005).

Available data indicate that in 2011, the nanotechnology sector involved about 10 million employees worldwide, more than 1,300 products and a growth of over 500% between 2006 and 2011 (Nanotechnologies, 2011). Further, by 2020, it is predicted that the products related with nanotechnology will correspond to 20% of all products on the market (Nanotechnologies, 2011).

The terminology "polymer nanocomposite" describes a compound in which one or more constituent materials at nanoscale size are completely dispersed in the polymer (Aitken, Chaudhry, Boxall, & Hull, 2006). The used nanoparticles are, in general, inorganic such as clays, carbon nanotubes or chemical additives. Almost all types and classes of nanocomposite (NC) materials lead to new and improved properties when compared with their equivalents, macro and micro composites (Šupová, Martynková, & Barabaszová, 2011; Zou, Wu, & Shen, 2008). NC global market is worth $50-250 billion per year, but it is estimated that it would be worth $3000 billion by 2015, since NM are increasingly playing a decisive role in diverse market sectors (Kiliaris & Papaspyrides, 2010). However, the new technologies are usually related with new human and environmental risk factors (Beaulieu, 2009). The production, processing and handling of nanoparticles can expose workers by inhalation, ingestion and absorption through the skin. Exposure can also occur for final consumers that use these products sold in the market, often without taking great precautions (Crosera et al., 2009; Gupta, 2011). Nowadays there are more than one thousand consumption products associated to nanotechnologies, presenting a dilemma to researchers, manufacturers, regulators and consumers concerning human and environmental safety (ISO, 2011).

1.1. State-of-the-art review on potential harmful effects of nanoparticles on environment and human health

There is limited published information on the potential adverse effects on humans to nanomaterials exposure. German officials have described what it was, possibly, the first reported effect of the exposure to a nanomaterial based product: at least 77 people complained of severe respiratory problems over a one-week period, and some of them were hospitalised for fluid in the lungs, after using the “Magic Nano” bathroom cleaning product (Miles, 2006).

Another reported case concerns seven Chinese young females that worked in the same department in a print plant. After nano exposure, they suffered from the same symptoms: shortness of breath and clinical signs of pleural and pericardial effusions. Two of them eventually died, and all were previously in good health, and denied any history of smoking or prior occupational exposure to hazardous materials. The factory where the patients worked had one door, no windows and only one gas exhauster (a ventilation fan unit), which had broken 5 months prior to the occurrence of symptoms. The only personal protective equipment used by the workers, on an occasional basis, was cotton gauze masks. The paste material handled in the factory, a coating mixture of polyacrylic ester, was analysed and it was verified that contained oxide based nanoparticles (NP) with 30 ηm in diameter. This case arouses concern regarding the long-term exposure to some NP without adequate protective measures (Song, Li, & Du, 2009).

Laboratory-based studies, using different animal models as well as cell-culture-based in vitro experiments, have shown an increase in pulmonary inflammation, oxidative stress, inflammatory cytokine production, apoptosis and other effects or biologic responses to exposure to ultrafine particles (Oberdorster et al., 2005). Several investigations also already confirmed that nanoscale oxide particles have harmful effects to the aquatic ecosystems when they are released in these environments (Aruoja, Dubourguier, Kasemets, & Kahru, 2009; Blaise, Gagné, Férard, & Eullaffroy, 2008; Zhu et al., 2008).

Specific in vitro studies, which main results are summarized in Table 1, have also demonstrated the cytotoxic effects of several manufactured nano oxide materials, such as SiO_2, Al_2O_3, TiO_2 and MgO nanoparticles. SiO_2 is abundantly present in our natural environment in many forms (amorphous or crystalline) and although some published studies have proved that the use of amorphous SiO_2 is quite safe, chronic inflammatory responses were observed after inhalation of crystalline nano-SiO_2 and some cytotoxic effects were reported due to the absorption of high doses of amorphous nano-SIO_2 (Napierska, Thomassen, Lison, Martens, & Hoet, 2010; Som, Wick, Krug, & Nowack, 2011). Regarding the effects of nano-Al_2O_3 on the environment and human health, the scarce studies indicate that they could have similar impacts like nano-TiO_2 (e.g., geno and cytotoxicity, and DNA damage) (Som et al., 2011; Sun et al., 2011). Until now there are no studies concerning the human health effects of nano-$Mg(OH)_2$, and very few regarding nano-MgO. Further, these last ones present divergent conclusions, which point out the eventual importance of other characteristics of the nanoparticles, than the chemical nature, that might influence the final results (Maynard, 2012; Sun et al., 2011).

Table 1 - Nano oxides potential negative impacts to health and safety

Nanomaterial	Specific surface area (m^2/g)	Average diameter (ηm)	Impact
Al_2O_3	35-43	40-47	Moderately toxic (Jeng & Swanson, 2006)
	-	20	Inflammatory reaction (Som et al., 2011)
	64.7	39.7	Low cytotoxicity (Sun et al., 2011)
MgO	37.9	39.2	Cytotoxicity (Sun et al., 2011)
	-	<100	No obvious toxicity (Maynard, 2012)
SiO_2	-	20 -50	Cytotoxicity (F. Wang et al., 2009)
	268.01	15 ± 5	Higher cytotoxicity (Lin, Huang, Zhou, & Ma, 2006)
	52.48	46 ± 12	
TiO_2	-	6,57	Genotoxicity and cytotoxicity (J. J. Wang, Sanderson, & Wang, 2007).
	50	30	DNA damage (Kang, Kim, Lee, & Chung, 2008).
	24	63	Cytotoxic or DNA damage (Karlsson, Cronholm, Gustafsson, & Möller, 2008).
	20-40	<40	Slight toxicity (Jeng & Swanson, 2006).
	-	25-85	No obvious acute toxicity (J. Wang et al., 2007).

The aforementioned studies provide a preliminary understanding of the potential harmful effects of NP suspended in the air on human health, highlighting the urgent need to develop appropriate and effective protective measures on handling, production and final consumption of NP based products.

In particular, the protection of the human respiratory system from NP exposure is an emerging problem in occupational hygiene. Potential adverse health effects associated with inhalation of NP are probably more expressive than those that would result from exposure to microparticles. Studies indicate that respiratory protection masks, such as N95 type, do not always provide the expected respiratory protection because they demonstrate excessive NM (from 30-70 ηm) penetration (> 5%) (Bałazy et al., 2006; Rengasamy & Eimer, 2011).

Although the respiratory track, as the main route of entry of contaminants, is considered the main focus of concern in terms of safety, contamination via dermal absorption must also be taken into account given that the skin is the largest organ of the human body. The few existing studies on NM's skin penetration are not consensual. The discrepancies in results are probably related to the different techniques and methods applied, different laboratory conditions and the lack of standardized assessment protocols (Crosera et al., 2009). There are already evidences that NM can penetrate through the skin. Studies have shown that the fluorescent CdSe NM (5-8 ηm) are not only able to penetrate the stratum corneum of the pig skin, but also can migrate into the hair follicles, from where can migrate to the whole body. Furthermore, the chemical constituents of NM can penetrate the skin by dissolution and their effects on damaged skin are still unknown. Given this context, it would be advisable to wear disposable clothing, made of "non-woven" waterproof materials (Fleury, Bomfim, Metz, Bouillard, & Brignon, 2011; Groso, Petri-Fink, Magrez, Riediker, & Meyer, 2010; Rouse, Yang, Ryman-Rasmussen, Barron, & Monteiro-Riviere, 2006). Diffusion assays performed with NM showed that these particles can penetrate through most of the available gloves. It has been shown that most of the gloves' materials (e.g., nitrile rubber, butyl rubber, neoprene and latex) are significantly affected by exposure to NM, either in liquid colloidal solutions or at powder state (when the gloves are under some sort of mechanical stress). It was also found that protective gloves made of "non-woven" textiles such as high density polyethylene (Tyvek type) are quite more effective against NM penetration. Tests also revealed that the preparation process and the gloves thicknesses are also important parameters to take into consideration to avoid NM dermal exposure (Amoabediny et al., 2009). Preliminary data obtained during the assays, using NM at powder state, seem to indicate that there is NM penetration through the gloves when they are subjected to some kind of mechanical deformation over a long period of time (> 1 hour); thereby, the use of two or more pairs of gloves is recommended (Dolez, Vinches, Wilkinson, Plamondon, & Vu-Khanh, 2011). Finally, exposure by ingestion can also be associated with dermal exposure, due to the contact hand/mouth (Fleury et al., 2011; Groso et al., 2010; Kelly, 2008).

Quantitative toxicity studies on engineered NM are still relatively sparse, and the published data on nanoscale oxides support the need to carefully consider how NM are characterized when evaluating potential biological activity. But until now there are no direct implications of the health effects in humans except to caution against ingestion of large concentrations of NP. Even if the NP are toxic for humans beings, this does not mean they are not useful (Jeng & Swanson, 2006; Oberdorster et al., 2005; Soto, Garza, & Murr, 2007).

1.2. Research significance

NM based products, such as polymeric NC, are unlikely to present a direct exposure; hence, their potential risk is low to negligible, at least, for the final consumers. The NM that are most likely to present a health risk are nanoparticles, agglomerates of nanoparticles, and particles of nanostructured material. In each of these cases, potential exposure exists for NM in air and in liquid suspensions or slurries (Oberdorster et al., 2005), and this risk can occur during polymeric NC production. Further, in this process, the workers are also exposed to other chemicals like thermoset resins, catalytic systems and fillers, which cannot be forgotten. Also, it should be taken into account that some of the raw materials used in the NC production are flammable, toxic, irritant and volatile (ECHA, 2012).

The burden of work-related ill health is still high. The European Agency for Safety and Health at Work (EU-OSHA) estimates that annually there have been 74.000 work diseases in EU-27 (European Union) related to the use of hazardous substances at work (EU-OSHA, 2013b).

Under this framework, it is necessary to develop a safety special research concerning the production of polymeric NC in order to ensure that there is no, or limited impact, on human/environmental safety. The present research work aims to study the Portuguese legal framework relative to nanoparticles, in particular to nano oxides, and its suitability to analyse polymer nano and submicro composites risk assessment during their production in a laboratory environment. This project has been developed at the Institute of Mechanical Engineering and Industrial Management (INEGI).

2. Methodological approach

2.1. Materials an NC production

The risk assessment relative to polymer nano and sub-micro composites production was made with basis on an experimental work developed in a laboratory environment. The nano and sub-micro composites were produced by mixing an unsaturated polyester polymer matrix with different types of nano (Al_2O_3 and $Mg(OH)_2$) and sub-micro particles (SiO_2). The silica sub-micro particles (SiO_2, 98%) were provided by Innovnano (Portugal), and the alumina (NanoDur® 99.5% purity, Alfa Aesar®) and magnesium hydroxide ($Mg(OH)_2$, 99%) nanoparticles were acquired from Cymit Quimica S.L. (Spain) and Nanostructured & Amorphous Materials Inc. (USA), respectively. All particles have a spherical shape and their physical properties are specified in Table 2.

Table 2 - Nano and sub-micro particles characteristics

Particle	Specific Surface Area (m^2/g)	Specific gravity (g/cm^3)	Average particle size (ηm)	Crystalline phase
Al_2O_3	36	3,60	45	70:30 δ:γ
$Mg(OH)_2$	80	2,36	15	-
SiO_2	64	2,69	437	Amorphous

Both manual stirring and ultrasound sonication techniques were used in the mixing process. The main steps in the production process of polymeric NC are illustrated in Figure 1.

The production only involved one or two researchers who used personal protective equipment (a pair of nitrile gloves, three latex gloves, a mask with A_2P_3 filters, protection glasses and tyvek protective cloth) and collective protection (fume hood and ventilation/general exhaust).

Figure 1 - Main phases in the laboratory production process of polymeric NC

2.2. Legal texts

To determine how to prevent and/or control the risks associated with the NM, the existing legal framework should be firstly analysed. The polymeric materials, including NC, are considered chemicals and, hence, some of the legislation related to chemical agents and REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) should be applied.

The review was performed based on legal texts databases, like Electronic Republic Diary, EUR-Lex, European Agency for Safety and Health at Work (EU-OSHA) and other databases. The search was conducted by the combination of the keywords and sub-keywords; selection of the relevant legal texts by reading the text aim; and full text reading of the selected legal texts.

2.3. Risk assessment methods

The risk assessment usually involves hazard/exposure assessment, risk evaluation/characterization and risk reducing measures. The risk assessment involved in the manufacturing process was done using simple qualitative analyses based on tools developed by the *Istituto Superiore per la Prevenzione e la Sicurezza del Lavoro*, Italy (ISPESL) and the *Ecole Polytechnique Fédérale de Lausanne* (EPFL) (Giacobbe, Monica, & Geraci, 2009; Groso et al., 2010).

2.3.1. ISPESL method

The ISPESL method was structured and developed for analysing the NM occupational safety taking into account the strategy defined by the European Commission of a responsible approach. This risk assessment method (Table 3) is based on 10 factors (from A to J). The aforesaid factors are denominated “*factors level risk*” and each one of them may assume three increasing values: 1 (low), 2 (medium) and 3 (high), referred to as “*risk levels*” (Giacobbe et al., 2009).

Since the use of NM presents uncertainness about danger level, the risk assessment takes into consideration this feature through the index denominated “*corrective factor*”. This index assumes a value within the range 0.5 to 2.0 in accordance to the established level of scientific knowledge. This assumes the following values: 0.5 - good scientific knowledge; 1.0 - enough scientific knowledge; 2.0 - insufficient scientific knowledge (Giacobbe et al., 2009).

The evaluation risk (Equation 1) is calculated through the factor level risk (flr) sum (from A to J) multiplied by the corrective factor (cf). The evaluation result consists in several risk levels subdivided in an increasing way (risk level: "low" 5-15, "medium" 16-35 and "high" 36-60) (Giacobbe et al., 2009).

$$\text{Evaluation Risk} = \sum_{i=A}^{J} (\text{flr})_i \times \text{cf} \qquad (1)$$

Table 3 - ISPESL method resume table (Giacobbe et al., 2009)

Factors	**Risk level** **Low - 1**	**Medium - 2**	**High - 3**
A - Numerousness of the exposed workers	1 – 2	3 – 5	> 5
B - Frequency of exposure	< 2 h/day	> 2 h/day and < 6 h/day	> 6 h/day
C - Dimensions of the nanoparticles	> 70 η	> 10 ηm and < 70 ηm	< 10 ηm
D - Nanoparticles behaviour	High tendency agglomeration	Middle tendency agglomeration	High tendency dispersion
E- Frequency of direct manipulation	< 2 h/day	> 2 h/day and < 4 h/day	> 4 h/day
F - Effectiveness of PPD used	PPD used	Partial PPD used	No PPD used
G - Work organization/procedures	Good work practices	Simple and limited procedures	Any procedure or free access to the workspaces
H - Toxicological characteristics of the substances	P-Phrases: P302+352, P285	P-Phrases: P260, P305+351+338, P315, P280	H-Phrases: H319, H335, H351
I - Risk of fire and explosion	No considered	Improbable	Probable
J - Suitability of workspaces and installations	≤ class 100 clean room; use of chemical fume hood; use of dry box	1000 ≤ class clean room ≤ 10000	≥ class 100000 clean room
	Σ(A to J)		
Corrective Factor	0.5 - good scientific knowledge	1.0 - sufficient scientific knowledge	2.0 - insufficient scientific knowledge
Risk Assessment	Σ(A to J) x Corrective Factor		
Total Risk Level	Low [5 – 15]	Medium [16 – 35]	High [36 – 60]

2.3.2. EPFL method

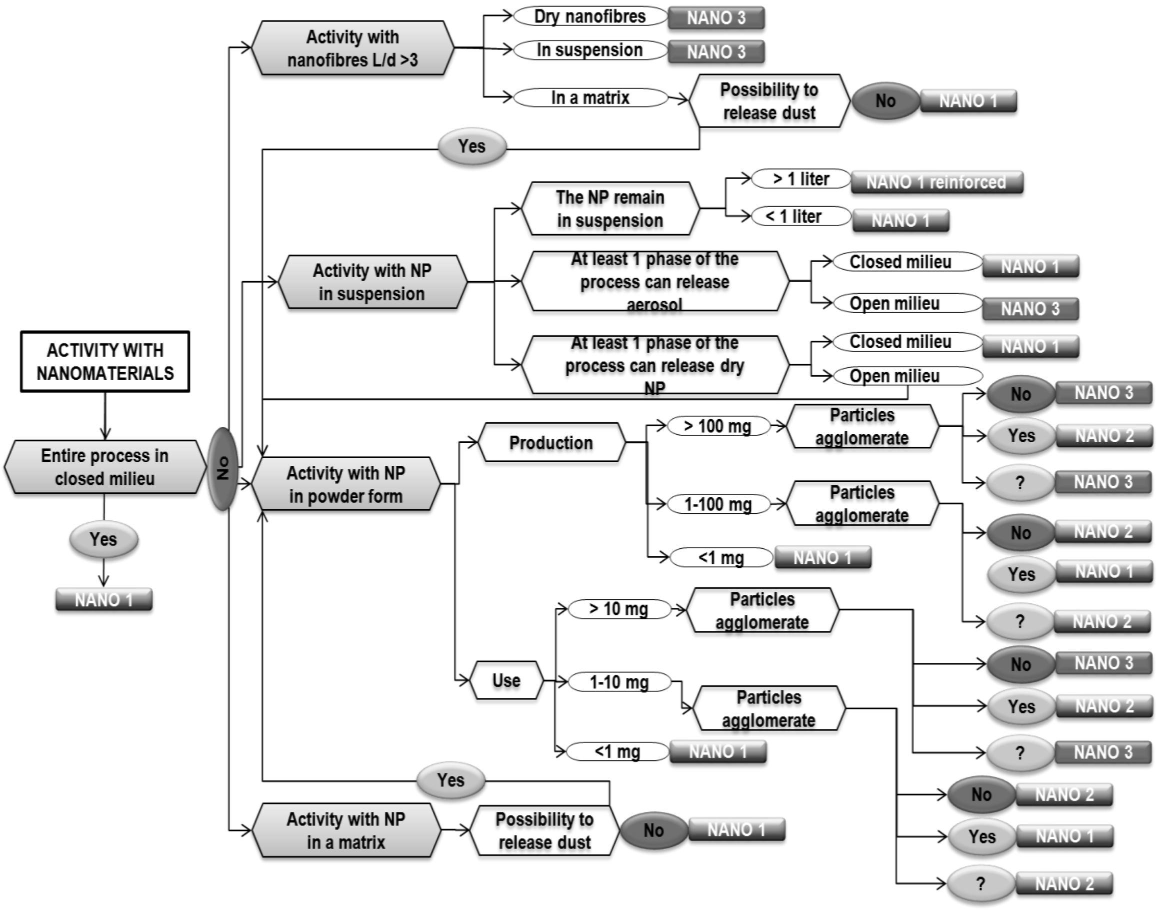
The EPFL method was developed based on an investigation "Online", aiming at identifying whether the researchers in the laboratories were following safety practices. It was obtained a surprising result: nearly three-quarters of the two hundred and forty surveyed researchers reported that they had no internal rules to follow in regarding the handling NM (approximately half of them do not have rules and over a quarter were not aware of any internal regulations) (Groso et al., 2010).

This method consists in a decision tree (Figure 2) for "nano-laboratories" with three risk classes, which correspond to similar approaches applied to other hazards types (biological, chemical or radiation) (Groso et al., 2010).

This decision tree analyses established collective protection measures (closed milieu – e.g., glove box or completely sealed environment), NM form/state (fibre, powder, suspension, and matrix), handling typology (production or use), NM quantity used, possibility to release dust or aerosol and NMs agglomeration ability. The risk classification can be $Nano_1$ (low), $Nano_2$ (medium) or $Nano_3$ (high) (Groso et al., 2010).

The risk classification allows to define several safety measures: technical (e.g., ventilation, flooring - tiling or linoleum, manipulation under fume hood and access restriction), organizational (e.g., restricted access – authorized persons only, training, conditioning of contaminated material – double bag for toxic waste and elimination – double packaging), personal (e.g., eyes protection – laboratory mask, respiratory protection – FFP_3 mask, body protection – non-woven lab coat and overshoes and hands protection – more than 1 pair of adapted gloves) and cleaning management (e.g., trained personnel, wet cleaning only and protective equipment) (Groso et al., 2010).

Figure 2 - EPFL decision tree (Groso et al., 2010)



The ISPESL and EPFL methods use different parameters to make the risk assessment. The ISPESL appears to be a more complete risk assessment method because it is based in the control of hazardous substances according to health regulations (COSHH) and physical properties. The EPFL method focuses mainly in the NP physical properties like shape (fibres and others), used form (powder, suspension or NP in a matrix) and particles ability to agglomerate.

The main differences between ISPESL and EPFL methods are summarized in Table 4.

Table 4 - ISPESL and EPFL main differences

		Physical			Chemical		Health		Exposure					Protection measures		Use
Characteristics		Shape	Size	Aggregation/ agglomeration	Flammability	Explosiveness	Carcinogenicity	Irritating	Amount of material	Nr. of exposed employees	Dustiness	Frequency	Duration of the task	Personal	Collective	Research/academic
Risk assessment methods	**ISPESL**	x		x					x		x				x	x
	EPFL		x	x	x	x	x	x		x		x	x	x	x	x

3. Results and discussion

3.1. Legal texts review

Recently, the Organisation for Economic Co-operation and Development (OECD) has recommended to its Member Countries the application of existing international and national chemical regulatory frameworks to manage the risks associated with manufactured NM. Most of these related regulations approved by the European Community can be interpreted as applying to NM the same procedures that have been applied to chemicals (based on existing laws and regulations for these products) (OECD, 2013).

In workplace, employers have the general duty to ensure the health and safety of workers in every aspect related to their work by conducting regular risk assessments - as specified in the “Framework” Directive 89/391/EEC - and these should also include possible risks from NM. In addition, Directive 98/24/EC on chemical agents at work imposes stricter rules for work risk management regarding these substances (in particular, the hierarchy of prevention measures that strengthens elimination or substitution as priority measures), which is also applied to NM as this fall within the definition of “substances”. If the NM, or the macro-scale material of the same composition, is carcinogenic or mutagenic, Directive 2004/37/EC on carcinogens and mutagens at work must also be fulfilled. In any case, national legislation may have stricter provisions and should be consulted. As NM are also considered substances, REACH regulation and the CLP (Classification, Labelling and Packaging of Substances and Mixtures) regulations are equally relevant (EU-OSHA, 2013a).

Until now there is still no specific legislation applicable to NP, however, some ISO (International Organization for Standardization), ASTM International (American Society for Testing and Materials) and BSI Group (British Standards Institution) standards appropriate to these materials have begun to emerge. In the traditional risk assessment, the exposure doses are compared with the occupational exposure limit values (OELs). There are no specific OELs for NP, however these standards propose, as a pragmatic orientation, the following limit values showed in Table 5 (Amoabediny et al., 2009; INRS, 2011; Kaluza et al., 2009; Lövestam et al., 2010; MESD, 2006).

Table 5 - OELs for NM

Description	Benchmark exposure levels
Fibrous; a high aspect ratio insoluble NM	0,01 fibres/ml
Any NM which is already classified in its molecular or in its larger particle form as carcinogenic, mutagenic, reproductive toxin or as sensitizing (CMRS)	0,1 x OEL
Insoluble or poorly soluble NM not in the fibrous or CMRS category.	0,066 x OEL
Soluble NM not in the fibrous or CMRS category	0,5 x OEL

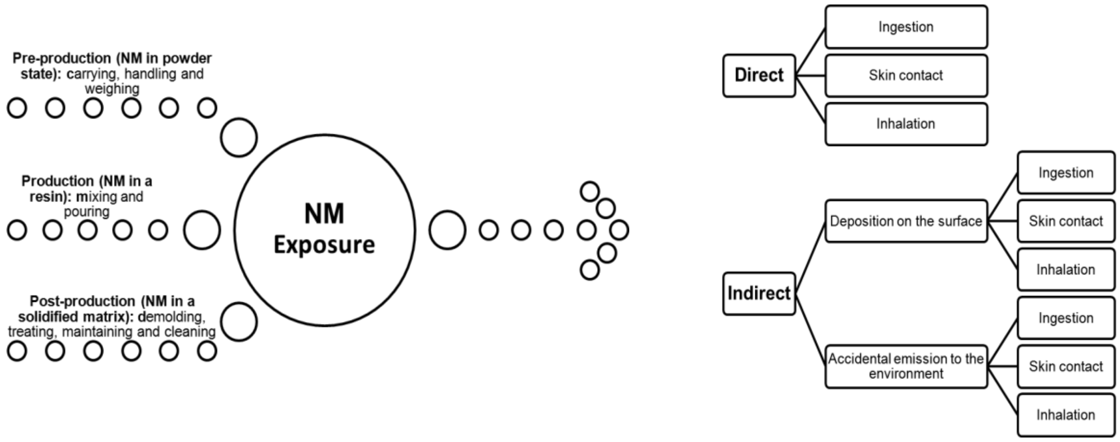
Regarding the safety analysis in the polymeric NC processing, all workers are protected by the Framework Directive, in which the basic principle is the risks prevention. This Directive demands that the employer carries out risk assessments and imposes a general obligation to ensure workers safety and health at their workplace. In addition to this legislation, there are others that make protection more complete and efficient.

Despite the legal framework potentially applicable to NM, there is nothing specific for these materials. Thus, the suitability of the legal framework is uncertain or even speculative. As chemicals, NM may be under the chemicals regulations. However, it is essential to create proper legal texts or review the existing ones in order to regulate NM use, and hence, to ensure confidence to consumers, workers and investors (Lövestam et al., 2010). Besides ensuring the consistency and avoiding market distortions, harmonized regulation would play a key role in minimizing risk and ensuring workers' health and environmental protection. The existing regulation is often based on parameters that may prove unsuitable for certain applications of nanotechnology. For instance, thresholds are often defined in terms of production volumes or mass, below which a substance may be exempt from regulation. The relevance of these thresholds should be reviewed and, when appropriate, amended. In the meantime, while specific NP regulations are not established, proactive approaches should be adopted.

3.2. Risk assessment: experimental results

The safety analysis in the laboratory NC production allowed the identification of different exposure scenarios. The main hazardous events and associated sequences that may lead to exposure in the workplace are shown schematically in Figure 3.

Figure 3 - Main events and NM exposure associated with the NC production



On composites production the particles go through different "states": in the pre-production phase, particles are at powder state; throughout production, particles are dispersed in a resin/solution; and finally, in the post-production phase, the particles are embedded in the solidified resin matrix. During all the steps involved in the production process, the handling of a variety of chemicals is required which can also expose the workers to potentially dangerous substances. The lesions may result from a single severe incident, but in most cases, they are the result of cumulative exposures.

The results obtained applying the qualitative methods are presented in Tables 6 and 7 for ISPESL and EPFL methodologies, respectively.

Table 6 - ISPESL method results

Particles	**Factors**										**Σ factors**	**Corrective Factor**	**Risk Assessment**	**Total Risk Level**
	A	**B**	**C**	**D**	**E**	**F**	**G**	**H**	**I**	**J**				
Al_2O_3	1	1	2	1	1	1	1	2	1	1	12	2	24	Medium
$Mg(OH)_2$	1	1	2	1	1	1	1	2	1	1	12	2	24	Medium
SiO_2	1	1	1	1	1	1	1	2	1	1	11	2	22	Medium

Table 7 - EPFL method results

Particle	**Stage**	**Process**	**State**	**Description**						**Risk level**
Al_2O_3, $Mg(OH)_2$ and SiO_2	1	Not fully isolated	Powder	Use	>10 mg	Tend to cluster				2
	2	Not fully isolated	"Liquid"	Can release dry particles	Process not fully isolated	Powder	Use	>10 mg	Tend to cluster	2
	3	Not fully isolated	"Solid"	Can release dust	Powder	Use	>10 mg	Tend to cluster		2

The selected qualitative methods had convergent results. A medium risk was obtained for both applied methodologies (Medium Risk Level for ISPESL method and Risk Level 2 for EPFL method). With these results, some precautionary and prevention measures should be made and enforced. It is considered that the most critical operation in the whole composite production process is the particles manipulation in powder state, in which lack of safety procedures (e.g., inappropriate containers), organizational aspects (e.g., information and training absence), or preventive maintenance (e.g., cracks in the containers) may lead to typical exposure scenarios. The cleaning is another critical task. Workplaces regular cleaning must occur at the end of each assay. This procedure prevents the increasing deposition amount of particles (which would lead to an increase of likelihood of exposure). Dry cleaning processes should be avoided and it should be choose the wet cleaning to prevent the NM release. The use of similar personal equipment in the pre-production and production stages is recommended.

3.3. Inferences for large scale production of NC

The release of NP, even when embedded in a matrix, can potentially occur during all stages, including during the use and disposal of the final product. The probability of exposure should be assessed throughout the entire life cycle of the NM, and the risks should be evaluated with a risk management tool that can be similar to the model applied for natural disasters. This is justified because until now there are few and limited detailed risk or life-cycle analyses on the specific implications/impacts of using NM. Additionally, procedures must be taken to ensure that the waste is removed from the system; thus, once the cleaning operation is completed, all waste should be placed in appropriate containers and stored for subsequent controlled disposal (Roes, Patel, Worrell, & Ludwig, 2012; Sweet & Strohm, 2006; Wardak, Gorman, Swami, & Deshpande, 2008).

An obvious step to mitigate possible risks related to NP is to take preventive measures. Eliminating the risk at source, by replacing the NP with more safety materials is one solution at first sight. However, this may be difficult to be implemented given the unique and singular characteristics of NP. The more effective solution is to prevent the risks in the design phase, at upstream, downstream and during manufacturing process. Organizational procedures should also be taken, such as employee training and good working practices, being strengthened and updated regularly, according to existing knowledge about "*nano safety*". In spite of the existing exposure limits for micro and macro particles with similar chemical composition, currently, there are no specific exposure limits and requirements for NP due to the lack of specific toxicological data. Therefore, the potential presence of NP in the workplaces should require that workers always use collective and individual safety equipment. In addition to the mentioned measures, the general measures for regulated hazardous chemicals should also be considered (Groso et al., 2010; P. Schulte et al., 2013; P. A. Schulte et al., 2013).

In today's global market, economic growth requires innovation that, in turn, is dependent upon research. Nanotechnologies present new challenges also with regard to risk assessment and management. Therefore, in parallel with technological development, appropriate R&D should be carried out to provide quantitative data on toxicology and ecotoxicology, enabling as this way the risk assessment and, when necessary, adjustments of the assessment methods (Sweet & Strohm, 2006). Paying attention to future intellectual, scientific and technical challenges in nanosciences and nanotechnologies, as well as excellence in R&D, is essential to ensure the competitiveness of enterprises.

4. Conclusions

The risks are a key issue to consider, especially in the early stages of any new technology. Tardily identified risks can have great social, health and environmental impacts, as has already happened with chlorofluorocarbons (CFC) and asbestos. By studying proactively the potential risks of emerging technologies, one can prevent future problems. The risks are inherent to any technology and nanotechnology is not exempt.

Within this scope, in this study the inherent risks associated to the main production stages of three different nano and submicro composites were assessed. The particles exposure scenarios during the different manufacturing processes were also identified and characterized. The experimental study was conducted in laboratory environment (small scale) but provided an overview of measures that could be implemented to improve the safety levels during polymer NC production on an industrial scale. The final NC are unlikely to present a direct risk because the NM are trapped into the solid resin; however, during the production phases in which NM are at powder and "liquid" state, special care is required as they could lead to NP exposure. The results obtained with the ISPESL and EPFL risk assessment methods were globally convergent: a medium risk level was attained in both qualitative methods. The applied risk assessment methods are normally used in research/academic field. The ISPESL is a more complete method because it analyses more parameters than EPFL method. These risk assessment methods use different parameters and this could lead, in other risk assessments situation and combined with the results interpretation, to non-convergent risk level results.

The main outputs of this work highlight the need for new risk assessment guidelines and standardized methodologies that allow obtaining more consistent and reliable data on risk levels and the most adequate measures that should be taken at workplace. Until then it is recommended using more than one risk assessment method, in order to have a multifaceted approach to analyse or assess the risks of NM. This way, the potential strengths of the different methods can be combined in order to thoroughly address a potential NM risk context, keeping in mind the different characteristics and parameters of each method. Though, further work will be required in order to identify the best combination of these different risk assessment methods, able to be applied, according to the specific risk context and NM potential exposure. However, it must be pointed out that in most of the cases qualitative analyses are not enough for a proper risk assessment. A qualitative analysis must be complemented with suitable quantitative methods. So there is the need for a standardized sampling instrument with a particle analysis gauge wide range, in order to allow obtaining more reliable data about the nanoparticles dimensions and chemical composition. There is a clear need to gather more information about exposure to NM in the production, handling and use.

With the currently legislation applicable to nanoparticles it is possible to implement prevention and protection generic measures. These measures should be adopted as soon as possible to ensure responsible development of nanoparticles manipulation and use. The Occupational Safety and Hygiene in workplace can never be regarded as “sealed” because it is a process in constant mutation, in which the different sectors should be prepared for new and emergent risk factors. Therefore, it is necessary to establish guidelines, standardized measurement methods and typical concentration values of NM, and set a specific legislative context. Recommendation 2011/696/EU (definition of NM) and the Commission Communication "Regulatory Aspects of Nanomaterials", indicate that the legal basis already exists; however, there is still a long way to go through in terms of safety regarding NM handling.

Current knowledge about nanoparticles toxicity is insufficient and the scientific preliminary assessments show that there are enough suspicions that nanoparticles can have harmful effects on human health. Thus, more research work is needed to fill existing gaps. Until further information, NM should be considered as risky materials.

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