

## Chapter

# AgNano, the Construction of Occupational Health Standards: A Status Update

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## Abstract

The regulation of chemical substances involves a negotiation between social actors to translate controversial scientific evidence about risks into legal norms. This chapter addresses the discussion elicited by a public consultation on a voluntary regulation guide on silver nanoparticles (AgNP) in workplaces. It examines the comments made from 2016 to 2018 by diverse social actors – business representatives, non-governmental organizations (NGO), and independent researchers – to two successive draft versions of a Recommended Exposure Limit (REL) in working environments with AgNP. The REL is a voluntary guideline on permissible exposure limits elaborated by the NIOSH in the U.S. The methodology used was a qualitative content analysis, structured upon a historical and sociotechnical contextualization of nanotechnologies carried out through literature review. The findings show how different social actors position themselves in the controversy, revealing a pattern of behavior consistent with their position in the research, production, and commercialization of this new nanomaterial. While a group of actors, aligned with the interests of AgNP producers, proposed the restriction of mandatory and AgNP-specific regulation, another group of more heterogeneous actors, identified with the interests of workers and consumers, demanded more scientific and technical information and stricter health protection measures.

**Keywords:** nanosilver, risks, recommended exposure limits, regulation, occupational health

## 1. Introduction

The regulation of chemical substances involves a difficult negotiation between social actors to translate often controversial scientific evidence about risks and safety into legal norms. When the regulation faces chemical substances with uncertain risk, as in many of the nanomaterials, the difficulties increase.

This article addresses the public discussion of a proposal for a voluntary guide to regulate the exposure limits to silver nanoparticles (AgNP) in workplaces in the United States. The draft guide, known as *Recommended Exposure Limits* (REL), was prepared by the *National Institute for Occupational Safety and Health* (NIOSH) on-demand from the *Centers for Disease Control and Prevention* (CDC), and went through two stages of discussion and rework during 2016–2018. We examine the public online discussion of both drafts by different social actors, basically academics, business organizations, and non-governmental organizations (NGOs).

Analyzing this discussion required placing nanotechnologies in their historical and socio-technical context. Nanotechnology is the intentional manipulation of matter to form new structures with a dimension smaller than 100 nanometers. Nanoparticles have particular physical–chemical properties (electrical, optical, magnetic, thermal, mechanical) and are different from the same material on a larger scale [1]. The interaction of nanoparticles with biological systems is highly unpredictable and their use may involve unknown risks [2].

From mid-2000s there was an explosion of nanotechnology products in the market. Although there are no detailed records, StatNano [3] registered 8 452 products until November 2018, present in almost all economic sectors.

The development of this emerging technology coincides with the wake-up call by the World Health Organization and the United Nations Environment Program on the global pandemic caused by toxic chemicals [4]. These organizations indicate that about five million people die annually from the exposure and handling of chemical substances and contact with consumer items that contain them [5, 6].

Silver is a metal known both for its toxicity and for its healing effects since ancient times [7]. Currently, its use in the form of nanoparticles is blossoming. The inventory of nanotechnology products of the *Woodrow Wilson International Center for Scholars* identified 442 using AgNP, and reports that silver is the most commonly used nanomaterial in the whole set of products [8, 9]. The antibacterial properties of AgNP justify its use in textiles, food packaging, paints, toys, environmental technologies, cosmetics, implants, and other medical devices; they are also used in the electronics industry (semiconductor printing, radio frequency identifiers, flexible circuits, solar panels) [10–12]. The United States produced 20 tons of AgNP in 2010; in 2014 between 450 and 542 tons were produced at a world level [13].

Toxic effects of AgNP on the human organism have been detected when certain exposure levels are exceeded [14]. In the workplace, the AgNP enter the body mainly through inhalation. The final destination within the organism is uncertain. Whereas there was a consensus to consider that were the lungs, more recent research has showed that they can move from the lungs to the liver, and eventually to the spleen and kidneys, accumulating [12], thus exposing workers to a variety of potential health threats. These characteristics of AgNP have raised the concern of CDC of the United States, which has recommended NIOSH to develop a voluntary guide (REL) of permissible exposure for AgNP [15].

The toxicity of silver in larger sizes, when certain exposure limits are exceeded, is already widely known, causing, for example, argyria, and there are safety regulations in this regard [16]. With the increasing use of AgNP, a debate arises about whether, in smaller sizes, such as nanoparticles, the toxicity of silver remains the same, as some of the actors who participated in the public consultation analyzed here argue, or if toxicity manifests itself differently, as other actors claim.

Regarding occupational safety, there are mandatory regulations and voluntary guides. In the United States, a chain of regulations can be identified. The first is the *Occupational Exposure Limits* (OEL), which are scientific studies about the maximum acceptable limit of particles in workplaces of hazardous substances of certain material or class of materials. The OELs are established considering functional categories (exposure period time according to the degree of concentration, maximum exposure, and an emergency category when danger is imminent).

Based on OEL, mandatory workplace standards called *Permissible Exposure Limit* (PEL) are developed. These are prepared by the *Occupational Safety and Health Administration* (OSHA). Voluntary standards, such as the Recommended Exposure Limit (REL) examined in this chapter can also be developed, often based on OELs. These are elaborated by NIOSH.

On December 18, 2015, the NIOSH put out a first REL draft, entitled *Current Intelligence Bulletin: Health Effects of Occupational Exposure to Silver Nanomaterials* [13] for public consultation. This received comments from different institutions, organizations and scientists, from which a second draft was prepared [13] and made public on August 24, 2018. The latter also underwent public consultation, which ended in November 2018. This article examines the two drafts with their corresponding comments available on the *website* of CDC (<https://www.regulations.gov/docket?D=CDC-2016-0001>). The analysis considers only the comments from the public, since the comments from peer reviewers asked by the agency are anonymous and not publicly available.

The antecedent of this draft REL is the existence of a PEL based, in turn, on a 1988 OEL, which controls the exposure to silver in the workplace. The OSHA imposes a PEL of  $10 \mu\text{m}/\text{m}^3$  for soluble and powdered silver. Both, the OEL study and the mandatory exposure limit established in the PEL, refer to silver in larger sizes; no standard exists, be it an OEL or a PEL, for nanosized silver. What is under construction, and is discussed here, is a voluntary guide, a REL. It is important to note that, at the beginning of this process, when NIOSH based the first draft of the REL for silver in nanosize on the existing OEL that referred to silver in larger sizes, implicitly proposed an equivalent regulatory treatment for silver and nanosilver. However, as the consultation process advanced, and critical comments were made on this point, NIOSH responded with a second draft that distinguishes nanoparticles in the air, establishing a much lower maximum exposure of  $0.9 \mu\text{m}/\text{m}^3$  and leaving the original exposure limit of  $10 \mu\text{m}/\text{m}^3$  for particles in dust, smoke, and soluble compounds. As will be seen, the public consultation evidenced that there are opposing positions regarding whether the OEL for silver is sufficient to elaborate a REL for nanosilver [11, 17].

The commentaries correspond to the following social actors: PISC, PBNS, NIA, CTA, SNWG, Faustman, Oberdörster, and Fox, briefly described in what follows.

- *PETA International Science Consortium Ltd* (PISC) is an international consortium aimed at promoting strategies to replace the use of animals in experiments [18].
- *Pennsylvania Bio Nano Systems* (PBNS) is a one-person company that advises nanotechnology companies regarding technical regulatory matters [16, 19].
- *Nanotechnology Industries Association* (NIA) is an association of companies and other entities related to the production and commercialization of nanotechnology products. It advises national and international institutions and organisms, such as the OECD and the ISO, and has the goal of promoting the use of nanotechnologies [20].
- *International Center for Technology Assessment* (CTA) is an NGO oriented to assess the social impacts of technologies [21].
- *Silver Nanotechnology Working Group* (SNWG) is an enterprise organization that promotes scientific knowledge production and public information regarding the beneficial use of silver nanoparticles in industrial products and final consumption [22].
- *Elaine Faustman* is an investigator for the Institute *Risk Analysis and Risk Communication*, and the *Department of Environmental and Occupational Health Sciences*, at the *University of Washington*, WA [23].

- *Guenter Oberdörster* is a recognized scientist specialized in the toxicology of nanomaterials at the *Department of Environmental Medicine*, of the *University of Rochester*, NY [17].
- *Mary A Fox* is an assistant professor at *Johns Hopkins Bloomberg School of Public Health*, and *Co-director of the Risk Sciences and Public Policy Institute* [24].

## 2. Methodology

This qualitative investigation was elaborated in four stages, that go from the general to the particular, placing the problem to analyze, which is the regulation of AgNP, within a broader historical and socio-technical perspective. The first three stages were built upon a revision of literature based on consultations to the Scopus, Web of Science, and PubMed databases, and the analysis of documents and databases of products that use nanotechnologies. The last stage was developed through content analysis of the interventions of the different actors in the public consultation of the REL document.

The first stage consisted of tracing the historical and socio-technical context in which nanotechnologies arose, which allowed us to underscore two aspects. First, the fast growth of nanotechnology products since the beginning of the century, most of them without regulation. Second, the entry of new chemical products such as silver nanoparticles into the market, without prior assessment of their risks, occurred in the context of the pandemic caused by toxic chemicals used in everyday consumer goods, as stated by the Organization World Health (WHO) and UNDP (United Nations Development Program).

The second stage was aimed at identifying the main characteristics of AgNP, both in technical terms and concerning their potential risks.

The third stage was to describe the object of study, that is, the voluntary guideline for AgNP regulation in preparation. This required explaining the main aspects and restrictions of the preparation of a voluntary guide such as a REL, which led to the identification of the contradictory nature of the process of transforming technical-scientific risk criteria into legal standards. Next, the actors (organizations or individuals) who commented on the drafts were identified.

The fourth stage consisted of the analysis of the NIOSH draft document and the comments made by the various actors in the public consultation. The content analysis was based on the information obtained in the previous stages. A voluntary guide such as the REL adapts scientific-technical information regarding the hazards/risks of a work environment with AgNP, to legal norms that involve different actors: The State, private companies, and workers. The first actor creates (and enforces when it is the case) the regulation; the second is the target group of the regulation, and the last group is the main subject of risk and beneficiary of the regulation. From the two fields in interaction, scientific-technical and legal, three dimensions of content analysis were derived, which were formulated as three specific questions to examine the positions defended by the different actors who participated in the discussion of the voluntary guide drafts.

First, based on the available methods, techniques and information, the standards, both mandatory (PEL) and voluntary (REL), conform to a given state of knowledge, feasible for further extension or revision, which, in turn, would lead to the updating of the rules. This raises the problem of how and when to regulate and limit (or expand) the production and marketing of new chemicals. In the case at hand, the question is stated as follows:

- At what point, regarding the progress in research and development (R&D), the production and commercialization of AgNP should a REL and/or a PEL be elaborated?  
Second, since the knowledge on hazard/risk is always incomplete and subject to controversies,
- How is the conflict between insufficient knowledge and administration of risks solved?  
Third, being the main involved actors, namely the State, the companies, and the workers,
- What are the actors' opinions regarding the level of responsibility on risk (the producer, the regulatory organism, or the worker), and what should be the degree of access to the relevant information (confidential or public)?

### 3. Results and discussion

When examining the social actors who commented on the document, clear differences in the relationship they maintain with the subject under discussion emerge. NIA and SNWG are industrial representatives and PBNS a business advisor. This group of three actors has a conflict of interest regarding the subject because their final goal is the production and incorporation of AgNP in consumer products and their commercialization. PISC is an animal rights defense organization; therefore, it has a conflict of interest regarding the *in vivo* methods of risk assessment. Oberdörster, Faustman, and Fox are researchers from research centers who have declared no conflict of interest in articles published on the subject. CTA is an NGO, based in the United States, aimed at assessing and advising society on the economic, ethical, social, environmental and political impacts that result from the application of technologies, without a declared conflict of interest, although manifestly biased towards workers and consumers. This different location of the actors regarding the subject necessarily determines their perspectives.

In the following subsections, we examine the arguments deployed by the actors in their commentaries to the document under consultation, organizing them around the three questions formulated in the methodology.

*I. At what point should REL and/or PEL be elaborated regarding the stage of R&D, production and commercialization of the AgNP?*

Despite the enormous variety of nanoparticles, and that each one can imply different health risks for workers, there is an element in common to all of them: the matter in nanoscale shows different biological and physicochemical properties compared to the same matter on a larger scale. Moreover, the same material behaves differently within the range of 1 to 100 nm, depending on its shape, crystallography, number of dimensions in the nanoscale and other characteristics. Nanoparticles' behavior also varies according to the route through which they enter the organism and the exposure time. Regarding silver, and without considering the nano size, several studies indicate different toxicity depending on the way it is presented (dust, soluble, etc.) [16], which already warns that size is associated with distinct toxic effects. In this context, it is relevant to ask: why do new chemicals enter the market without toxicity analysis, or assessed on the basis of methodologies developed for the matter in a larger size, as in the case of nanoparticles? Given the current pandemic caused by toxic chemicals, the uncertainty about the risks derived from the properties of the nano-sized matter, and the existence of sophisticated risk

assessment techniques, it is necessary to understand why there is such a temporary lag between entry of products with AgNP to the market and their regulation.

In the REL discussion, NIOSH presented a first draft of the document in 2016, then corrected it in 2018. In none of the versions, mention was made on the contradiction between the elaboration of a REL while AgNP continued to enter the market in various products without any specific regulation. In this way, the NIOSH is trying to “manage the existing situation”, adopting an *effective risk management* approach, without any mention to the possibility of modifying the path of production and consumption by controlling the market. There is also no mention of the fact that the regulation under discussion was already delayed, considering the increasing commercialization of products with AgNP since mid-2000s.

Within the commentators, only the CTA refers to this issue and advocates for a moratorium on the commercialization until there is enough data confirming the safety of AgNP:

*No data should mean no new production [...] companies should stop manufacturing unapproved nanosilver products [21].*

Except for this actor, the NIOSH proposals, and the commentators, take as a natural fact the marketing of products without sufficient data regarding their safety. In doing so, they promote an *ex-post* safety policy, instead of a preventive policy.

*II. How is the conflict between insufficient knowledge and administration of risk solved? The question of uncertainty.*

The discussion evidences three conflictive areas regarding knowledge and uncertainties on the dangers and risks of AgNP. The first one refers to the relationship between size and toxicological effects. The second relates to the way in which scientific data is interpreted and transformed into legal rules. The last conflictive point has to do with the validity of scientific methods and their limitations.

- i. The first area of controversy is the distinction between the effects of silver *vis a vis* nanosilver. The industrial actors and their advisors affirm that nanosilver has the same toxicological behavior as silver in a larger size and that there is already a PEL issued by OSHA on silver, which would make unnecessary the elaboration of a specific REL on AgNP. As already said, the first draft of the NIOSH proposal also considered the risks of AgNPs and silver in larger size equivalent. Later on, NIOSH changed this perspective and acknowledged the different risks of silver in nanoscale and larger sizes [15].<sup>1</sup> The industry working group commented:

*SNWG is extending support of the Agency's recommendation that effective risk management control practices be implemented so that worker exposures to all forms of silver, including silver nanomaterials, do not exceed the NIOSH REL of 10 µg/m<sup>3</sup> (8-hour time-weighted average) for silver metal dust, fume, and soluble compounds measured as a total airborne mass concentration. [...] workers will be more than adequately protected from any potential harmful exposures to all forms of silver, including nanosilver. [...] In light of some of the uncertainties concerning nanosilver, the SNWG believes that the toxicity of nanosilver is not significantly different from bulk or dissolved Ag (colloidal silver) [22].*

<sup>1</sup> Here is not the place to develop on this issue, but the reader must consider both the economic and political power of the chemical industry and the neoliberal phase of capitalism that has been replacing the control of the State over private enterprise by business self-responsibility, a transition from regulation to governance, from *hard to soft law* [25].

The industry working group begins supporting NIOSH's recommendation, but the support is limited to the first draft of the document, where 10 µg/m<sup>3</sup> was suggested as a limit, the same limit that OSHA uses for silver in larger size. In the following sentence, the commentator explicitly identifies silver and nanosilver as equal for risk analysis; and, in the last one, emphasizes that the uncertainties are the same for silver and nanosilver. In summary, SNWG argues that there is no need for a specific standard for nanosilver.

From the same opinion is the NIA,

*[...] the Association insists that silver nanomaterials do not present a different toxicological profile to other forms of silver, including colloidal silver. The antimicrobial action of silver, and therefore its toxicological profile, originates in silver ions (Ag<sup>+</sup>) and may not be attributed to the nanoparticles themselves [20].*

PBNS, an industry consultant entity, considers argyria as the final point in the organism of silver potential health risks, and argues that the maximum permissible contemplates all types of particles, so there would be no difference between nano and large-scale silver, and, since there is an OSHA PEL for the larger size, the NIOSH should not insist on the specificity of the nanosize. However, contradictorily, PBNS recognizes that nanomaterials can present "unexpected properties"; but, if the NIOSH understands that the endpoint of silver is argyria, there would not be, according to PBNS, a novel effect, and using the nano concept would be incorrect:

*In selecting argyria as the valid endpoint, there is then no novel use, nor first time exposure nor unexpected property. Yet, using the term nanomaterial implies that there should be a particle size dependence [19].*

The entire PBNS comment goes in the direction of invalidating the specificity of nano and suggesting to follow the OSHA's already approved criteria based on silver in a larger size [19].

It is worth noticing that the three industrial actors' arguments do not rebut the scientific articles published over the past two decades, which provide evidence about the different behavior of AgNP and silver in a larger size -- see, for example, the systematic review of Akter et al. [14]. In doing so, they are simply ignoring the available scientific information that does not fit their interests. Neither they refer to the current uncertainty involving the risks of the matter at the nanoscale, an aspect which is considered a crucial issue in the NIOSH first draft, which demands attention to the likely different risks associated with AgNP in the air, in the solid and liquid forms, due to the different routes of introduction into the organism.

The animal defense NGO (PISC), for its part, only emphasizes the need to replace analysis *in vivo* with *in vitro* and *in silicon*; and by not questioning the equalization of risks in nano and larger scales stated in the first draft of the document, reinforces the business position.

The remaining actors, the NGO and the independent researchers, recognize that nanosilver implies a different risk than silver in a larger size. Independent researchers, for example, explicitly call attention to the specific risks associated with nano size. Faustman argues that:

*While an OEL for micro-sized silver dust and silver fumes of 10 µg/m<sup>3</sup> is in place, we believe that the physicochemical properties of AgNPs allow for additional health risks not observed from exposure to micro-sized particles [23].*

Oberdörster also stresses the specificity of AgNP by emphasizing the different risks of inhaled nanoparticles, as well as indicating the liver as the final point of

destination in the organism of the nanosized silver [17]. CTA, meanwhile, shows that there is a much wider variety of AgNP on the market than the NIOSH draft recognizes; and that each of these varieties may have different risks, so a specific REL is necessary for each case [21]. Fox points out the need to specify when referring to pure AgNP, and, perhaps, it would be necessary to establish different RELs for soluble and insoluble nanoparticles [24].

- ii. The second area of controversy has to do with the degree of correspondence between the scientific references provided by the NIOSH document (bibliography) and its normative conclusions; that is, between the scientific-technical information and its legal adaptation.

NIA calls to reduce the scope of the regulation to a specific form of nanoparticles, spherical not covered; just because the bibliography of the NIOSH draft only includes this modality.

*[...] document scope should be revised to reflect the data presented in the Draft Bulletin. While NIOSH mentions the ISO definition of a nanomaterial, which includes particles, plates and wires, studies mentioned in the Draft Bulletin mostly address spherical silver nanoparticles. In addition, the studies in the document mostly focus on uncoated silver nanoparticles. As a result, the Draft Bulletin should explicitly focus on health effects of uncoated spherical silver nanoparticles [20].*

There is a huge variety of nanoparticles, and the regulation cannot deal with them one by one, but the industry takes refuge in this limitation of the cited literature to avoid or reduce the scope of the regulation. The industrial consultant PNBS takes a similar stand, asking for restricting the scope of the REL to strictly adjust it to the literature displayed in the document:

*Narrow the current REL (10 µg/m<sup>3</sup>) to substantively spherical primary particles, their aggregates and agglomerates, and caution that the REL does not extend to shapes with high aspect ratios [...] Narrow the current REL to uncoated silver-metal- particles [19].*

In the opposite direction, proposing to expand the scope of the REL, the CTA claims that the intended maximum of 100 nanometers established by the REL should be extended to 1,000 nm [21] and, to that end, introduces the argument that other governmental agencies, such as the FDA, have extended the analysis of AgNPs to 1000 nm, when it merits [26]:

*WHAT SIZE IS NANO? This review simply uses the narrow US government definition for “nano,” i.e. 1-100 nm. The NIOSH definition would be enhanced if it used the expanded standard used by the FDA, i.e. companies are asked to report as “nano” any change in size below 1000 nm that changes the properties of the chemical [21].*

The industry supports the 100 nm limit for nanosize and considers that existing analyses of silver in a larger size are appropriate to assess risks. SNWG, for example, supports the use by NIOSH of the categories of exposition of the existing PEL issued by OSHA. In doing so, it also agrees with equivalent toxicity assessments between nano-size and larger-size as stated in the NIOSH first draft [22].

Therefore, while independent scientists and the environmental NGO claim the necessity to expand the bibliographic references to better assess the risks of AgNP,



and raise questions on the ones used [24], in order to construct a broader regulation, companies prefer to keep the existing bibliographic references and seek to restrict the regulation scope.

- iii. Finally, the third area of controversy over risk uncertainties regards the validity of scientific methods and their limitations. Currently, most risk analyses include various techniques, *in vitro*, *in vivo*, *in silicon*. The analysis *in silicon* has expanded due to its speed, economy, and the possibility of standardizing the procedures, and also because of the ethical concerns regarding tests on animals. PISC, for example, suggests that NIOSH should replace analysis *in vivo* with *in vitro* and *in silicon* [27] and justifies this demand not only because of ethical but also methodological reasons, particularly regarding the uncertainties of extrapolating information from animals to humans:

*The dissolution of silver nanoparticles (AgNPs) in different physiological environments can be addressed using alternative methods (including in vitro and ex vivo), which are considered a vital tool in understanding AgNP behavior in vivo.*

*[...] Of note here is that there are many uncertainties in extrapolating toxicity outcomes from animals to humans, including variations in responses to chemicals in different species and strains of animals, gender differences within species of animals, as well as different toxic thresholds between species including humans [27].*

Some independent researchers have criticized NIOSH's preference for the application of the PBPK method to AgNP, rather than relying on research with *in vivo* methods. While the PBPK method is *in silicon*, the one used as the basis in independent studies extrapolates results from an analysis *in vivo* [11], which, among other things, suggests the liver instead of, or in addition to, the lungs, as the toxicological endpoint, as the first draft of the NIOSH suggests [23]. Moreover, the methods *in silicon* have been criticized by many epidemiologists because even when using several variables, they are always restricted compared to the number of variables present in a living organism [28]. Computerization also implies that the selection of the variables to be considered may be subject to manipulation [29, 30]. Oberdörster suggests that PBPK should not be used due to a lack of reliability:

*REL are not well justified, because of either questionable PBPK modeling using disputed data or of rather simplistic unscientific extrapolation [17].*

In the opposite position, SNWG applauds the use of the PBPK on which the NIOSH relies:

*In light of these standards based on argyria, the endpoint of concern, the SNWG applauds the use of the Bachler et al., 2013 PBPK model for silver nanoparticles to evaluate the potential adverse effects of working lifetime exposure to silver nanoparticles at the current NIOSH REL for silver (10 ug/m<sup>3</sup>, 8-hr TWA concentration of soluble or insoluble silver, total airborne particle mass sampling). This PBPK model was developed based on data in rats, extrapolated to humans, and validated with limited bioassay data in humans [22, 31].*

Many of the arguments deployed in the comments to the public consultation are not based on scientific information, but reveal how participants use the inconsistencies of the draft to limit, extend, or reject conclusions. This is evident, for instance, when the toxicological effects of silver in nano and larger scales are

considered equivalents in spite of mounting evidence indicating they are not; or when it is suggested to restrain the regulation to the form of nanoparticles mentioned by the bibliography of the first draft, instead to enlarging the references to include the as much scientific information on diverse nanoparticle forms as possible; or when the limitations of scientific techniques are not discussed in terms of their implications for the effective protection of the workers' health. Such examples reveal the intricacy of the process of regulation, in which scientific information is subjected to diverse interpretations from the perspectives and interests of different social actors.

*III. What are the perspectives of the actors regarding the hierarchy of responsibility on risk (producer, regulatory body, worker), and the degree of access to information (confidentiality or disclosure)?*

Risk analysis considers the potential hazard and the degree of exposure of the worker [32, 33]. Exposure can be reduced by an uncontaminated environment or using protective equipment. The legislation aims to avoid hazards, maintaining a pollution-free environment in the first instance, and when this is not possible, using personal protective equipment [34]. The REL draft reproduces this hierarchy of controls in its recommendations. Although this hierarchy of protection procedures is a widely established legal fact, the emphasis on one or another alternative is significant in the position of the different actors. Thus, for example, CTA is explicit in emphasizing hazard control: “*workplace controls, not respirators are needed*” [21], and at large:

*NIOSH, however, needs to stress even more strongly that in the absence of sufficient data on the inhaled toxicity of nanosilver products, that it is EXTREMELY important that workplaces implement a hierarchy of controls that keep workers from breathing any nanosilver. NIOSH needs to strengthen its risk management control practices to note that respirators will not be adequate to protect workers and that avoiding exposures is the best way to protect workers [21].*

The claim is valid because the REL is a voluntary guide, and, as long as there is no PEL from which the State can impose a firmer measure, the different approaches on how to avoid hazards lead to different responsibilities. Maintaining the work environment without risk is the responsibility of the employer, while the use of personal protective equipment places the responsibility on the worker. This criticism was assumed by NIOSH in the second draft:

*The revised document recommends using the hierarchy of controls, encouraging the elimination or substitution of silver nanomaterials before employment of engineering controls, with PPE, including respirators, being the final and least preferable control [35].*

Responsibility for risks is intricately linked to the availability of information. If workers do not have information about the materials they handle, their hazards, and the risk to which they are subjected, they can hardly adopt a preventive attitude towards illnesses and accidents. The publicity or confidentiality of the information that the companies handle is a point of contention. CTA asks NIOSH to use information about the effects of AgNP available at other government agencies, such as the EPA and the FDA, information that these agencies have because they have authorized the entry of products with AgNP into the market [21]. The given answer reveals that there are confidentiality clauses that frequently prevent this circulation of information:

*NIOSH collaborates with other Federal agencies when possible on chemical assessments to avoid a duplication of effort [35].*

SNWG insists on the confidentiality of potential requests for information by the NIOSH:

*In regard to the research needs discussed in Section 8 of the NIOSH document, one of the functions of the Silver Nanotechnology Working Group is to identify, gather and consolidate industry data in an anonymous manner to protect CBI (Confidential Business Information). If such a mechanism is needed by NIOSH to bring forth needed data as listed on p. 120–121 of the External Review Draft [3] in a manner consistent with CBI, the SNWG would be glad to serve in such a capacity [22].*

The analytical answer to the third question leads to a similar conclusion to the previous two. The three industrial actors agree to reduce the available scientific information, or raise doubts about its relevance, to ensure the confidentiality of data on the materials used in production. In the opposite position are the independent researchers, who insist on expanding the range of literature and methods related to the subject, and on sustaining the differences between silver and nanosilver. In addition to this, the environmental NGO demands to consolidate the employer's responsibility instead of the workers and asks for the dissemination of technical information.

#### 4. Conclusions

The analysis of the voluntary guide regarding workers' exposure to the risks of AgNP in occupational environments, as well as the comments made by several actors, allow us to draw some conclusions. The first and most general is that, except for one commentator, the issue under discussion is considered within a broader context in which the entrance of novel materials into the market, without assessment of their safety, is taken as a given fact. Therefore, the proposals are limited to administering the state of affairs, that is, the production and marketing of AgNPs and the commodities that incorporate them, notwithstanding the existence of scientific evidence of risks for the workers operating in its production or handling. Regulation faces an economic dynamic that overcomes it and aims just to lessen its side effects.

The second conclusion is that the commentators, despite responding individually to the draft, can be grouped analytically into two large groups, according to the coincidence of opinions. The first group responds to the interests of the producers and marketers of AgNP. Their views agree in restricting as much as possible the advent of mandatory regulatory measures. This is explicit in their arguments about the equivalent risks of AgNPs and silver in larger sizes. It is also evident when their spokesmen raise doubts about potential risks of AgNP; when they prioritize confidentiality over information on production processes, and when they derive the responsibility on risk control on workers. The second group, with less cohesion, demands to broaden the spectrum of scientific-technical information and to limit the production and marketing of commodities with AgNP until they are proved safe, in order to protect workers and consumers. The first group, more compact and convergent in their opinions, is clearly identified with business interests. The second, more dispersed, represent the interests of workers and consumers, as well as independent intellectuals who demand further investigation.

The third conclusion regards the role, largely transparent and responsible, of the government agency that conducted the process, the NIOSH. The transparency approach lies in opening the draft for public comments, as well as the flexibility demonstrated in the changes made in the second version of the document responding to the comments received. For example, a modification from the originally proposed exposure limit of  $10.0 \mu\text{g}/\text{m}^3$  for all particulate forms of AgNP to a  $0.9 \mu\text{g}/\text{m}^3$  in the specific case of AgNPs in the air. It is also relevant to highlight that the second draft included a specific mention of the hierarchy of risk control, placing the producer in the first position and secondarily the worker, specifying that the priority is to avoid hazards in the work environment, and only as a last resource, individual protection equipment must play its role.

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