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Innovating Nanoparticle Safety: Storage, Handling, and Disposal Processes

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Innovating Nanoparticle Safety: Storage, Handling, and Disposal Processes

An Interactive Qualifying Project

Final Report

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Abstract

Uncertainty concerning nanoparticle safety measures stem from a scarcity of readily accessible, practical, and application-specific information. This constitutes a hazard for the workplace and the environment. We investigated nano-safety questions and interviewed researchers across Switzerland. We created a set of printable, customizable posters with clear guidelines and a 3-D model of a nanoparticle-ready laboratory space, which we both made available online. Through these solutions, we aim to improve the implementation of safe nanoparticle practices and save researchers time and frustration.

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Executive Summary

Switzerland has long been a frontrunner in the development of nanotechnology. Nanoparticles, whose applications broaden with ever-increasing use of nanotechnology, can hazardous to the health of people who come in contact with them. Current nanoparticle safety regulations are vague and leave the responsibility of determining the necessary safety procedures up to each facility. This means that laboratories must have to use their best judgment when creating guidelines but they have no accurate gauge as to how effective these processes are.

We began our project by conducting a literature review to familiarize ourselves with nanoparticles and the current safety guidelines. The results of this review constitute a significant portion of our report, and provide necessary background information for understanding our project. The next step we took to gather information was to conduct interviews across Switzerland with participants who work with nanoparticles in different ways. Over the course of our project, we conducted thirteen interviews with industry, research, and university labs. These interviews became an invaluable part of our project. Before embarking on these interviews we carefully crafted questions that would give us detailed information about how different laboratories have different safety procedures for the handling, storing and disposing of nanoparticles. The interviews are all summarized in our report, and provide insight into a variety of interpretations of the current governmental guidelines.

We used the results of these interviews to help innovate and implement solutions to safety problems that we discovered during our interviewing process. The solution implementations that we chose to develop further were a series of safety poster graphics and an interactive website. We created five posters that are available for any nanoparticle laboratory print and display for their own use. We include informational posters the general public, who may not know much about nanoparticles or the general safety measures to handle them. There are also warning and

danger signs, similar to existing ones used for lasers and other research activities that require special precautions. The nanoparticle label we created is an effective standard for the information is necessary for the documentation of stored nanoparticles.

The website that we developed has 3D models that show what handling and storage tools. The website has pages that are dedicated to describing each tool, and what attribute each one needs in order to be effective for nanoparticles. The website also presents our posters and report for anyone to use and read. This will make the information that we gathered readily available for anyone to access. Further, the website also provides a baseline implementation that can be easily updated as new information concerning nanoparticles is discovered.

While these two solutions address some of the glaring issues in the nanoparticle industry, there are many more problems that can be addressed. These issues include creating a standardized way to ship nanoparticles, an investigation into the safety of how nanoparticles are managed in waste disposal facilities, and innovating the safety practices in facilities that mass-produce nanoparticles. All of these problems can be addressed in subsequent projects, and the solutions to them can be readily added to the website we developed.

Chapter 1 Introduction

1.1 Need for Project

Nanoparticle science is an emerging field with the potential for advancements in an expansive range of sciences. Currently, laboratories throughout Switzerland use different safety procedures for the storage, handling, and disposal of nanoparticles. This presents an issue as small-scale nanoparticles can directly penetrate cell membranes and interfere with biological functions.[1] For people both inside and outside the workplace, these new hazards make it necessary to improve nanoparticle safety procedures.

With our project, we developed informational posters and an interactive website to guide safe interactions with common nanoparticles. Our goals included the development of a product innovation to enhance safe practices, and an intuitive safety resource for scientists of all backgrounds that can be implemented and expanded. With increased awareness for safety, we can push the scientific boundaries for future nanoparticle studies — without pushing the boundaries for human risk.

1.2 Approach

Current processes were inspected to develop a more methodical approach to nano-safety. We focused on learning and understanding NTB Buchs' specific safety practices as an example for what is acceptable and can be improved. Swiss regulations concerning nanoparticle handling,

[1] M. Geiser, B. Rothen-Rutishauser, N. Kapp, S. Schurch, W. Kreyling, H. Schulz*, et al.*, "Ultrafine particles cross cellular membranes by nonphagocytic mechanisms in lungs and in cultured cells," *Environmental Health Perspectives,* vol. 113, pp. 1555-1560, Nov 2005.

storage, and disposal are broad and leave most of the safety procedures up to the individual laboratories.[2]

Starting with NTB Buchs, we gathered information from various facilities on how nanoparticles are currently being handled with a focus on safety procedures. We then consolidated the practices of multiple academic and industry facilities and compiled our findings into quantitative data for analysis. This allowed us to determine the overall best practices for the health and safety of the manufacturer, consumer, and environment. Using an action-oriented interview style we gathered invaluable safety information from various facilities.[3]

Nanoparticles vary from one another in composition, state, and geometry. An optimal solution would be specific to each nanoparticle type. Due to time constraints, the scope of this project was limited to be implemented for the majority of nanoparticles. Our aim was to be applicable to as many laboratory facilities as possible by presenting our best practices in a user-friendly format.

After our initial literature review and conversations at NTB Buchs, we identified three areas with the most potential for improvement:

- Clear and consistent definition of safety procedures
- Time and effort reduction in the correct handling of nanoparticles
- Easy and quick access to the available information on correct handling of nanoparticles

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[2] E. Furrer, C. Studer, K. Knauer, L. Strotz, C. Bosshard and C. Manigley, "Sicherheitsdatenblatt (SDB): Leitfaden für synthetische Nanomaterialien", Staatssekretariat für Wirtschaft SECO, Zürich, 2010.

[3] K. Westhoff, "The Decision-Oriented Interview (DOI) as an in-depth selection interview," *Psychological Test and Assessment Modeling*, vol. 56, pp. 137-153, 2014.

1.3 Goals

The goals of this project are outlined using Figure 1.3.1: The 4 I's to Success. They start off broad and become more focused as the project progresses. The first "I" is Investigation, which was a literature review of current nanoparticle safety and handling procedures in different laboratories. We then conducted interviews with different facilities across Switzerland to learn about individual laboratory procedures. The subsequent step was to create and implement guidelines for the storage, handling, and disposal of nanoparticles, based on the best practices discovered in our interviews. Our final goal was to innovate a system for nanoparticle use that can be applied at NTB Buchs and in laboratories across Switzerland.

Figure 1.3.1: The 4 I's to Success

1.4 Project Timeline

As shown in Figure 1.4.1, we created a detailed timeline to keep us on track for the due date for the project. The timeline is a mixture of general times and definitive dates to give us the room for change. Over the course of our project, this timeline was used as a guide to make sure that we were achieving all the goals we set out in the beginning.

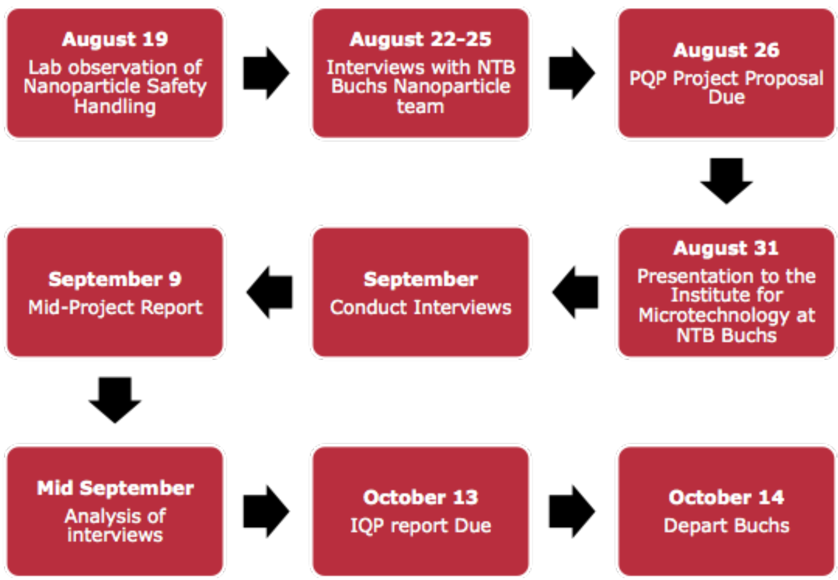

Figure 1.4.1: Timeline

This report is structured similarly to how we conducted our project. The next chapter, *Chapter 2 Literature Review*, showcases the findings of our literature review, then *Chapter 3 Methodology* explains our process for completing our project. *Chapter 4 Conclusions from Research* presents our findings from our interviews, the problems we discovered, and the solutions we considered. The final solutions are found in *Chapter 5 Solutions,* followed by an outline of the problems that could be turned into future projects in *Chapter 6 Recommendations for Future Work.* Our interview questions and the responses to them can be found in the appendices along with translations to our final posters and our final presentation.

Chapter 2 Literature Review

In order to develop a better understanding for the background of our project, we researched important questions about nanoparticles and their usage. We utilized a variety of resources while conducting this literature review, including the Web of Knowledge, government agencies, and academic websites.

2.1 Definition of a Nanoparticle

The basic definition for a nanoparticle is any particle within the range of 1 to 100 nanometers. Experts from the International Organization for Standardization (ISO) and American Society of the International Association for Testing and Materials (ASTM), provide additional details for the definition. They state that because particles are three dimensional, at least two dimensions must be below 100 nanometers. Nanotubes longer than 100 nanometers, but with diameters below that, are still classified as nanoparticles.[4] ISO excludes particles below a lower limit of 1 nm, to avoid single and small groups of atoms from being designated as nano-objects.[5] For the sake of this project we use the ISO and ASTM definition.

Many people have trouble visualizing the nanoscale, as it is inconceivably small. At one-billionth the size of a meter, nanoscale objects are 100 to 1000 times smaller than anything that can be seen with an optical microscope.[6] To help visualize it, we have provided a visual scale that compares objects to their relative place in size. As shown in Figure 2.1.1, nanoparticles are smaller than cells and are on a similar scale to proteins. This relative size is one reason that nanoparticles have a potential to be dangerous, as it is the main characteristic that determines their biological permeability.

[4] “Standard Terminology Relating to Nanotechnology.” ASTM E2456-06(2012), 2012

[5] “Nanotechnologies -- Vocabulary -- Part 2: Nano-objects.” ISO/TS 80004-2:2015, June 1, 2015

[6] "Metal Nanoparticles", *Max-Planck-Institut für Kolloid und Grenzflächenforschung*. Internet: http://www.mpikg.mpg.de/886767/MetalNanoparticles.pdf. [Accessed: 03- Oct- 2016].

Table 2.1.1: Definitions of nanoparticles from various organizations, such as ISO, ASTM, National Institute of Occupational Safety and Health (NIOSH), Scientific Committee on Consumer Products (SCCP), British Standards Institution (BSI), and Bundesanstalt für Arbeitsschutz und Arbeitsmedizin (BAuA)[7]

	Nanoparticle	Nanomaterial
ISO	A particle spanning 1-100nm (diameter).	-
ASTM	An ultrafine particle whose length in 2 or 3 places is 1-100nm.	-
NIOSH	A particle with diameter between 1 and 100 nm, or a fiber spanning the range 1-100nm.	-
SCCP	At least one side is in the nanoscale range.	Material for which at least side or internal structure is in the nanoscale range.
BSI	All the fields or diameters are in the nanoscale range.	Material for which at least side or internal structure is in the nanoscale range.
BAuA	All the fields or diameters are in the nanoscale range.	Material consisting of a nanostructure or nanosubstance.

[7] S. Horikoshi and N. Serpone, *Introduction to Nanoparticles*, Wiley. Internet: https://application.wiley-vch.de/books/sample/3527331972_c01.pdf [Accessed: 03- Oct- 2016].

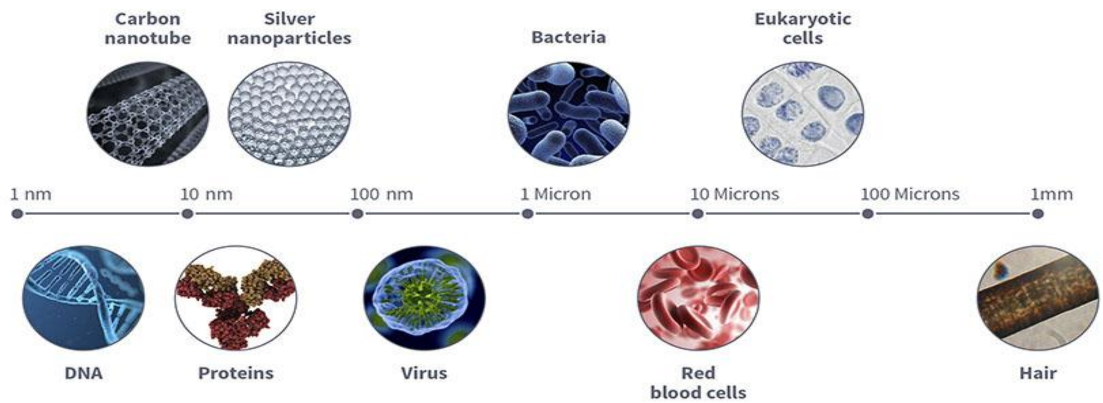

Figure 2.1.1: Differences among the nano (nm), micro (µm), and macro (mm) scales[8]

There are many different types of nanoparticles, which can be divided into four main groups: Carbon-based, metal based, dendrimers, and composites.[9] Carbon-based nanomaterials are often in the form of hollow spheres or ellipsoids, which are called fullerenes, the most common of which are carbon nanotubes. Metal-based nanomaterials include quantum dots, nanogold, nanosilver, and metal oxides. Metal nanoparticles have attractive optical properties and are used in a wide range of innovative scientific applications.[10] Dendrimers are polymers made of branched units; they can be used for drug delivery and as catalysts for chemical reactions. A nanocomposite is a matrix to which nanoparticles have been added, that can be used in many medical and electronic products.

[8] M. Davoren, "What is Nanotechnology?", *Pacific Environment Limited*, 2015. Intertnet: https://www.pacific-environment.com/news/nanotechnology-small-particles-big-risks/. [Accessed: 03- Oct- 2016].
[9] "Classification of Nanomaterials, The Four Main Types of Intentionally Produced Nanomaterials", *AZoNano.com*, 2007. Internet: http://www.azonano.com/article.aspx?ArticleID=1872. [Accessed: 30- Sep- 2016].
[10] "Types of Prevalent Nanoparticles", *Aranca.com*, 2015. Internet: http://www.aranca.com/knowledge-library/infographics/types-of-prevalent-nanoparticles. [Accessed: 30- Sep- 2016].

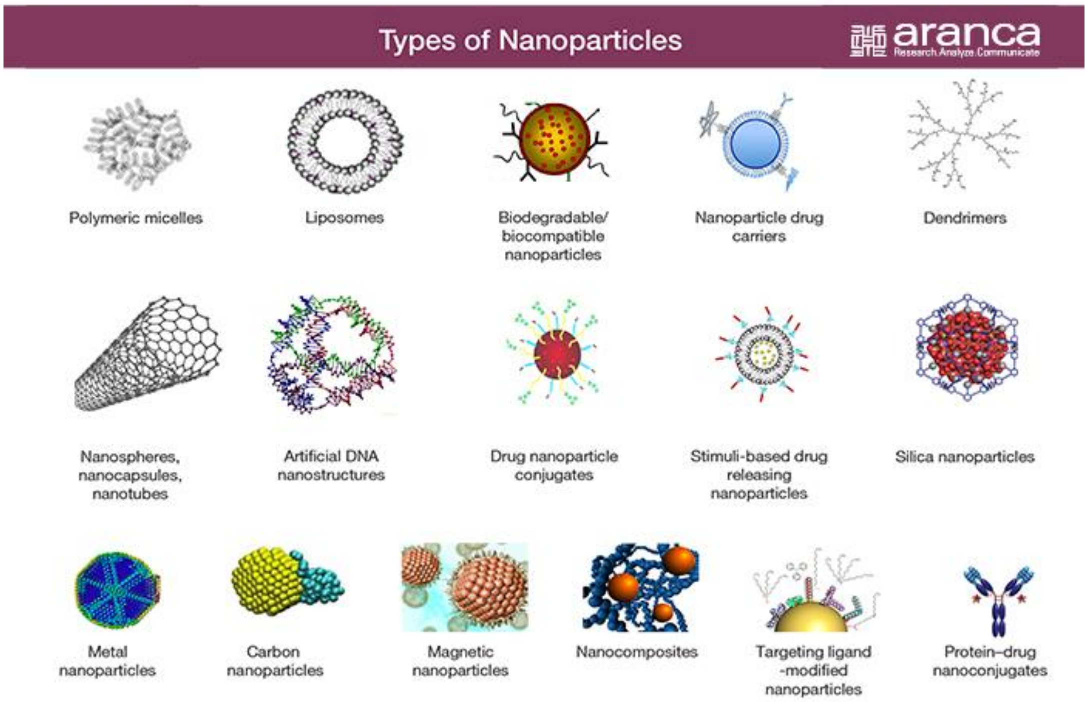

Figure 2.1.2: Overview of a few of the numerous types of nanoparticles[11]

Nanoparticles get many of their unique properties from their expanded surface area. When there is an increase in the ratio between surface area and the volume, the amount of material that can come into contact with surrounding materials increases, making the particle more reactive. The differences between various surface areas to volume ratios can be observed in Figure 2.1.3. This figure shows that the change in surface area from the 1cm^3 cube is increased by a factor of 60 million when the cm cube is made up of all 1nm^3 cubes. This geometry leads to increased reactivity, making nanoparticles effective catalysts and ideal candidates for water treatment and distillation.

[11] Ibid.

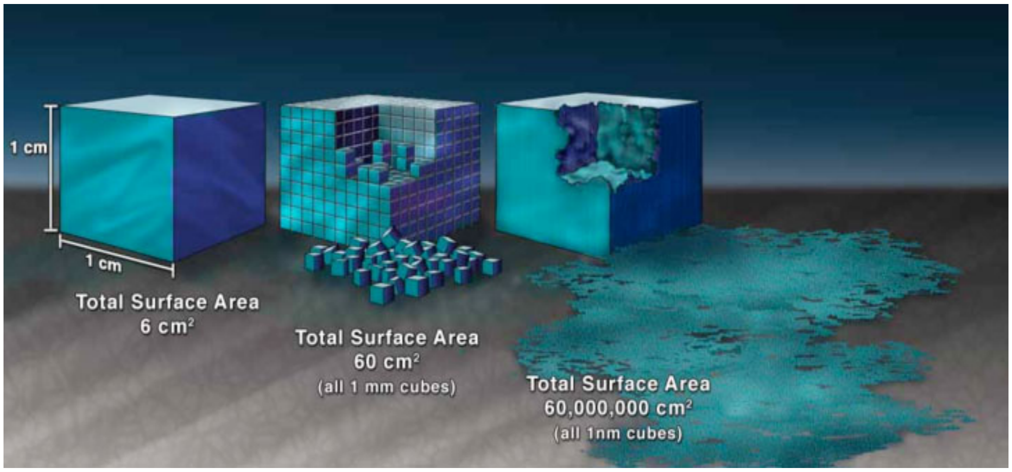

Figure 2.1.3: Differences in surface area for same mass blocks[12]

2.2 Nanoparticle Applications and Products

Nanoparticles are used in many fields such as, medicine manufacturing, material science, energy, electronics, environmental management, and more specialized fields. Figure 2.2.1 shows the wide variety of applications that nanoparticles can be used for. Medical examples of nanoparticle involvement include using polymeric micelle nanoparticles to deliver drugs to tumors, polymer coated iron oxide nanoparticles to break up clusters of bacteria, and protein-filled nanoparticles to stimulate immune responses. Manufacturing and material science use silver nanoparticles that can kill bacteria and make clothing odor-resistant, while zinc oxide can be used in industrial coatings to protect materials from UV rays.[13]

[12] "What's So Special about the Nanoscale? | Nano", *Nano.gov*. Internet: http://www.nano.gov/nanotech-101/special. [Accessed: 03- Oct- 2016].
[13] E. Boysen, "Nanoparticles Applications and Uses", *Understandingnano.com*. Internet: http://www.understandingnano.com/nanoparticles.html. [Accessed: 30- Sep- 2016].

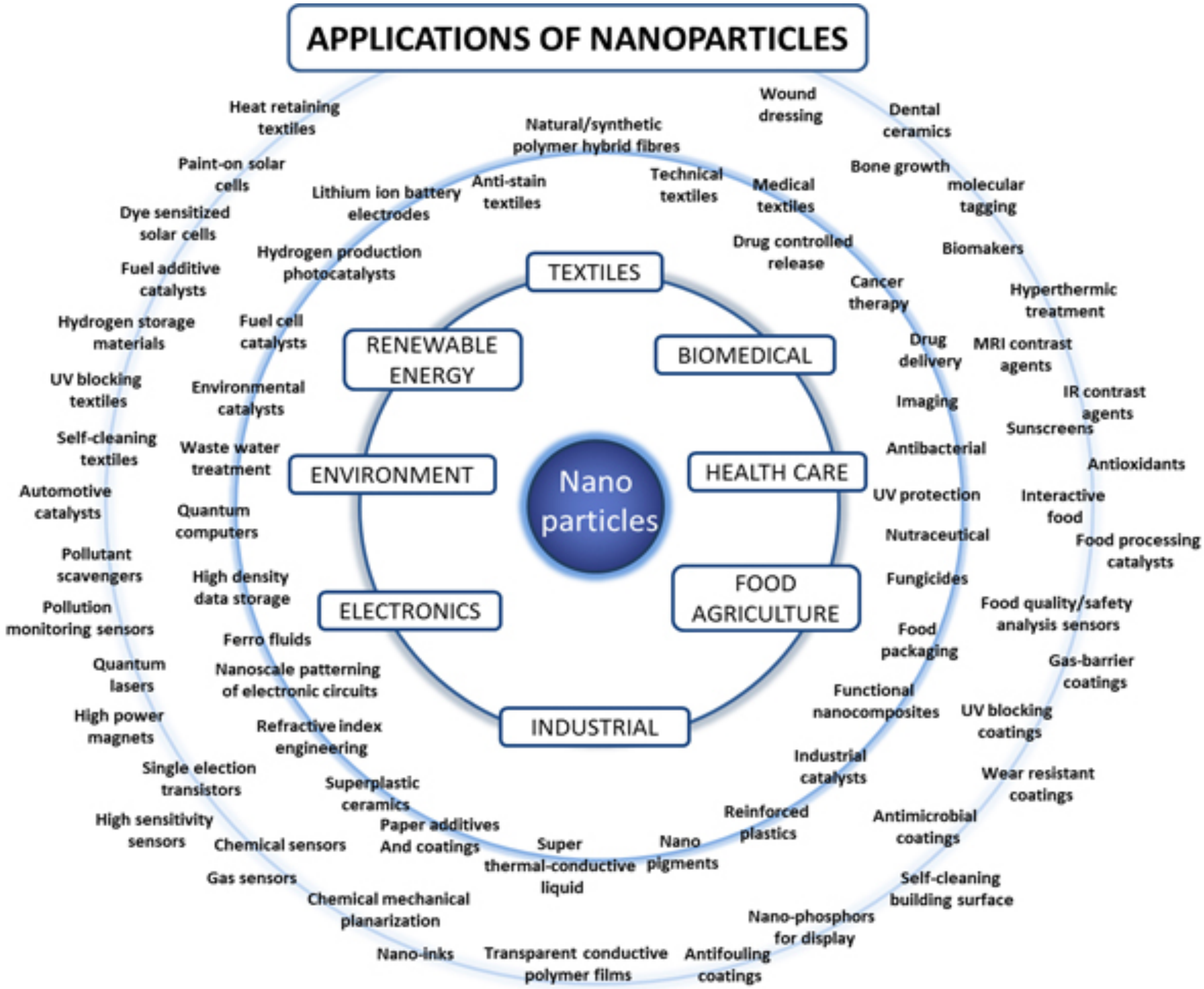

Figure 2.2.1: Common Applications of Nanoparticles[14]

[14] J. Simonsen, "Research Areas | John Simonsen", *People.forestry.oregonstate.edu*. Internet: http://people.forestry.oregonstate.edu/john-simonsen/research-areas. [Accessed: 04- Oct- 2016].

Products like scratchproof sunglasses, stain-repellent clothing fabrics and clear sunscreens have all been developed with the use of engineered nanoparticles. Titanium dioxide, an ingredient found in many every-day consumer products from edible snacks to glue, has been created in laboratories and are now embedded in our day-to-day lives. Used as an anti-caking agent, TiO_2 prevents products from agglomerating and clumping up. These components on a nanoscale have the same chemical composition as their macro-scale counterparts but provide new and unique qualities when used as nanomaterials.[15] This is only scratching the surface of potential nanoparticle technologies.

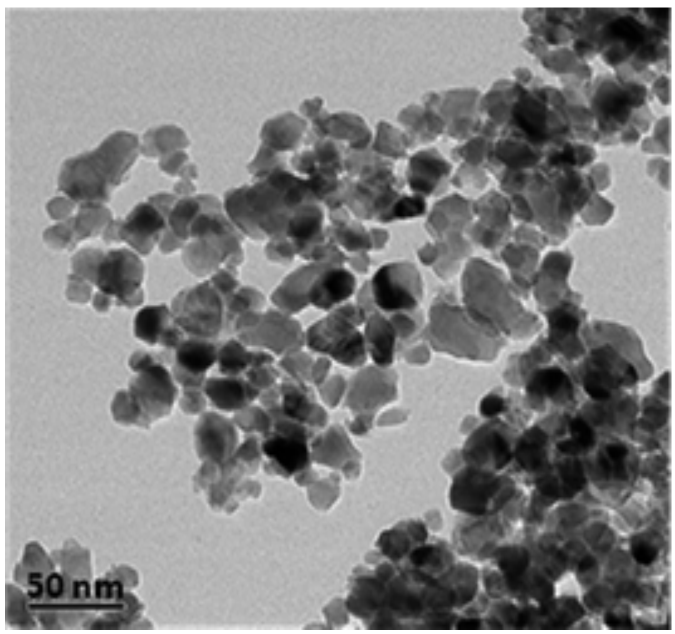

Figure 2.2.2: TEM image of titanium dioxide nanoparticles[16]

[15] Scientific Committee on Emerging and Newly Identified Health Risks, "The appropriateness of existing methodologies to assess the potential risks associated with engineered and adventitious products of nanotechnologies.", SCENIHR, Mar 10, 2006.

[16] A. Sotto, A. Boromand, S. Balta, J. Kim and B. Van der Bruggen, "Doping of polyethersulfone nanofiltration membranes: antifouling effect observed at ultralow concentrations of TiO2 nanoparticles", *Journal of Materials Chemistry*, vol. 21, no. 28, p. 10311, 2011.

From our interviews we were able to gain specific data about common applications used in laboratories across Switzerland. Shown in Table 2.2.1, we have broken down five different facilities into their nanoparticle applications, properties, and modes of operation. Each facility is one that we interviewed for this project, and are to remain anonymous. This data gives more insight into applications beyond the literature, and it is possible to understand what is used in theory and practice. Nanoparticles are used in research, for toxicity assessments, and to create products ranging from processing food to electronics. With scientific development constantly evolving, it is important to design safety guidelines that can encompass these wide varieties of applications.

Table 2.2.1: Interviewee application data

	Application	**Property**	**Mode of Operation**
Facility 1	In-vitro diagnostics	Fluorescent	Handling of powder
	Industrial energy harvesting	Magnetic	Synthesis
	Epoxy (customized)	Electro-conductive	Handling of powder
	Surface modification	Mechanically abrasive	Handling of powder
Facility 2	Road healing	Magnetically Inductive	Dispersed in solutions
	Ceramics	Electro-conductive	Synthesis and powder
Facility 3	Produce devices on substrates	Catalysts	Handling in liquid
	Liquid interfaces and systems (drug delivery)	Bioactivity	Powders and solutions
Facility 4	Integrated circuits	Electrical transport	On substrate
Facility 5	Toxicity studies of nanomaterials	Various	Powders and solutions

2.3 Protection Measures for Handling Nanoparticles

Since there is a lot still unknown about the long-term effects of nanoparticle exposure on users, it is widely expected to take as strict as possible precautions.[17] This means eliminating as many chances for exposure as is feasible. The most general cause of exposure is not using the proper safety gear.[18] Standard tests have showed that non-woven fabrics, such as high-density polyethylene textiles are more effective at blocking nanoparticles than their cotton-based counterparts. It is advised to take this into consideration whenever working with nanoparticles.[19] Tests looking at the diffusion properties of nanoparticles have shown that they may penetrate through commercially available gloves. Thus, it is advised to always use at least two pairs of gloves.[20] Typically, the protective equipment required for wet-chemistry would be appropriate for dealing with nanoparticles: non-permeable closed-toed shoes, long pants, shirts, gauntlet type gloves, goggles, and lab coats.[21] The British Standards Institution goes further into specific handling techniques for certain scenarios to lower exposure. For each scenario, nanoparticles are split into two groups: fibrous or toxic chemical, and insoluble or soluble; Table 2.3.1 summarizes these recommendations.[22] This table provides a starting point, upon which new guidelines can be built and updated as necessary.

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[17] G. Amoabediny, A. Naderi, J. Malakootikhah, M. Koohi, S. Mortazavi, M. Naderi and H. Rashedi, "Guidelines for safe handling, use and disposal of nanoparticles", *Journal of Physics: Conference Series*, vol. 170, p. 012037, 2009.

[18] "Nanotechnology and Nanoparticles- Safe Working Practices Information," Virginia Commonwealth University, Office of Environmental Health and safety, Jun 17, 2009. Internet: http://oehs.vcu.edu/chemical/nanotech.pdf. [Accessed: 3-Oct- 2016]

[19] C. Ostiguy, G. Lapointe, L. Menard, Y. Cloutier, M. Trottier, M. Boutin, M. Antoun, and C. Normand, "Nanoparticles – Actual Knowledge about Occupational Health and Safety Risks and Prevention Measures" IRSST, Montreal, Quebec, Canada, R-470, Sep 2006.

[20] Golanski Luana, Guiot Arnaud and Tardif Francois "Efficiency of Fibrous Filters and Personal Protective Equipments against Nanoaerosols" Nanosafe, Dissemination report, January 2008.

[21] Department of Energy (DOE), Nanoscale Science Research Centers, "Approach to Nanomaterial ES&H," USA, Rev. 2 – June 2007.

[22] British Standards Institution (BSI), "Nanotechnologies - Part 2: Guide to Safe Handling and Disposal of Manufactured Nanoparticles", 2007.

Table 2.3.1: Nanoparticle exposure controls in various scenarios[23]

Handling Scenario	Fibrous or Toxic Chemical	Insoluble or Soluble
Aerosolization	The work should be enclosed or otherwise separated from personnel	The work should preferably be enclosed or separated from personnel, though ventilated engineering controls such as extraction booths or hoods might be sufficient
Transferring, mixing, scooping of dry material	The work should be enclosed or otherwise separated from personnel.	The work should preferably be enclosed or otherwise separated from personnel, although ventilated engineering controls such as extraction booths or hoods might be sufficient.
Transferring, mixing, filling of suspensions	The process should preferably be enclosed or otherwise separated from personnel. However, in most cases, ventilated engineering controls should be sufficient.	Ventilated engineering controls such as extraction booths or hoods should be sufficient.
Maintenance and cleaning	The extent to which this process can be enclosed should be maximized. In practice, however, use of appropriate skin protective equipment should be effective. Cleaning cannot involve any deliberate aerosolization.	In most cases use of appropriate skin protective equipment should be effective. Cleaning cannot involve any deliberate aerosolization.

2.4 Detection and Characterization Methods for Nanoparticle Hazards

The techniques for detecting and characterizing nanoparticles are as diverse as the nanoparticles themselves. As of yet there is not a best way to measure nanoparticles, as each method measures only a specific attribute of the nanoparticle, such as their number, size, surface area, etc. They also vary depending on the state of the nanoparticles, be it an aerosol, in a liquid or solid matrix, or on a surface. For instance, the tests that look at the characteristics of nanoparticles cannot necessarily determine the number of nanoparticles present.[24]

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[23] Ibid.

[24] "Measurement Techniques For Nanoparticles," University of Essex for Nanocap, 2007

While researchers are studying and characterizing the properties of nanoparticles, there is also a need for measuring and identifying the presence of nanoparticles in the workspace. If the quantity of nanoparticle leakage is unknown, then there is no way to gage the safety of the experiment or device. The most difficult problem is the absence of detection methods that run in real time; it takes time to analyze samples and to differentiate nanoparticles from everyday nano-dust. It has been shown that air in a room can contain 10,000-20,000 nanoparticles/cm^3 and can reach up to 100,000 nanoparticles/cm^3 on an urban street.[25] There are particle counters in cleanrooms, but they normally cannot detect nanoscale particulates.

The current most effective strategy to determine the exposure of airborne nanoparticles is with a personal sampling device. The exact methods vary, but the idea remains the same: the device collects nanoparticles over the course of a predetermined period of time, and assesses the sample later for the particle count. There are multiple ways to do this, but there is a problem with differentiating between everyday nanoparticles and the ones that concern the observer. Normally pollutants are quantified by their mass, but that measurement is not sufficient for nanoparticles as their size is just as important as their quantity.[26]

Multiple techniques for measuring nanoparticles are outlined in Table 2.4.1 from the University of Essex for Nanocap.[27] They go more in-depth on some of the techniques in their report.

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[25] Scientific Committee on Emerging and Newly Identified Health Risks, "The appropriateness of existing methodologies to assess the potential risks associated with engineered and adventitious products of nanotechnologies.", SCENIHR, Mar 10, 2006.
[26] Ibid.
[27] “Measurement Techniques For Nanoparticles,” University of Essex for Nanocap, 2007

Table 2.4.1: Various techniques to measure nanoparticles and their uses[28]

Technique	Measures	Sample	Sensitivity	Notes
Transmission Electron Microscopy (TEM)	Particle size and characterization	< 1µg has to be prepared as a thin film and be stable under an electron beam and a high vacuum	Down to 1nm	Additions to TEM can provide more information e.g. Scanning Transmission Electron Microscopy (STEM), High-Resolution TEM (HRTEM) or in-situ measurements as Environmental TEM
Scanning Electron Microscopy (SEM)	Particle size and characterization	Sample must be conductive or sputter coated, easier to prepare than TEM sample	Down to 1 nm	Can be used in-situ as Environmental SEM
Atomic Force Microscopy (AFM)	Particle size and characterization	Samples must adhere to a substrate and be rigid and dispersed on the substrate. The appropriate substrate must be chosen. Air or liquid samples.	1nm - 8µm	A form of Scanning Probe Microscopy (SPM). Requires less time and cost than SEM and TEM.
Photon Correlation Spectroscopy (PCS)	Average particle size and size distribution	Sample must be a very dilute suspension	1nm - 10µm	Based on Dynamic Light Scattering, an extension of the technique is Photon Cross Correlation Spectroscopy (PCCS) for high concentration opaque suspensions giving particle size and stability of nanoparticles
Nanoparticle Surface Area Monitor (NSAM)	Human lung-deposited surface area of nanoparticles	Aerosol, concentrations 0 to 10000$\mu m^2/cm^3$, temp 10 - 35ºC	Down to 10nm	Similar to an Electrical Aerosol Detector (EAD).
Condensation Particle Counter (CPC)	Number concentrations of particles	Aerosol, concentrations 0 to 100,000 particles/cm^3, can be in a flow, higher temps to 200ºC possible	2.5 to 3,000nm	Can be used for a clow, hand held models available
Differential Mobility Analyzer	Particle size distribution	aerosol	Down to 3nm	Can be combined with other techniques to create Tandem DMA or DMPS
Scanning Mobility Particle Sizer (SMPS)	Particle size distribution	Aerosol, can be a concentrated sample of 1,000,000 - 2,400,000 particles/cm^3	3 - 1,000nm	Uses an electrostatic classifier and a CPC, can also add DMA

[28] Ibid.

Nanoparticle Tracking Analysis (NTA)	Particle size and size distribution	500µl suspension, temps 5 - 50ºC, wide range of solvents can be used	10 - 1,000nm	Use with DLS or PCS
X-Ray Diffraction (XRD)	Average particle size for a bulk sample	Larger crystalline samples (>1mg) required	Down to 1nm	Can identify individual crystals
Aerosol Time of Flight Spectroscopy	Particle size and composition	aerosol	100 - 3,000nm	The efficiency of this method is less for smaller particles
Aerosol Particle Mass Analyzer (APM)	Particle mass	Aerosol sample with particle density approx $1 g/cm^3$	Equivalent to 30 - 580nm	Gives only mass information and is not dependent on particle size or shape

2.5 Techniques for Nanoparticle Synthesis

Nanoparticle synthesis includes many different strategies, which can be simplified down to two general methods: top-down or bottom-up approach. As the names suggest, top-down begins with larger materials and breaks them into nanoscale particulates. Bottom-up refers to processes in which nanoparticles are formed atom-by-atom.[29] These are mainly chemical reactions from which ideal molecules are combined under specified conditions. A comprehensive overview of commonly used top-down and bottom-up approaches can be seen in Figure 2.5.1.

It is apparent that the top-down methods cover a smaller range of variation as opposed to bottom-up methods. This is because fragmentation of material through high-stress processes yields a broad size distribution (10-1000 nm), produces impurities, and leads to varied particle shapes or geometries.[30] When synthesizing from bottom-up methods, the user can better control the physical and chemical properties of the resulting nanoparticles. As such, many of the research advancements made in nanoparticle synthesis are based on bottom-up approaches.

[29] C. Murphy, "Two Ways to Make Nanoparticles", *Sustainable Nano*, Jun 10, 2014. Internet: http://sustainable-nano.com/2014/06/10/two-ways-to-make-nanoparticles/. [Accessed: 03- Oct- 2016].
[30] P. Gao, S. Horikoshi and N. Serpone, "Microwaves in Nanoparticle Synthesis. Fundamentals and Applications.", *Angewandte Chemie International Edition*, vol. 53, no. 31, pp. 7986-7986, 2014.

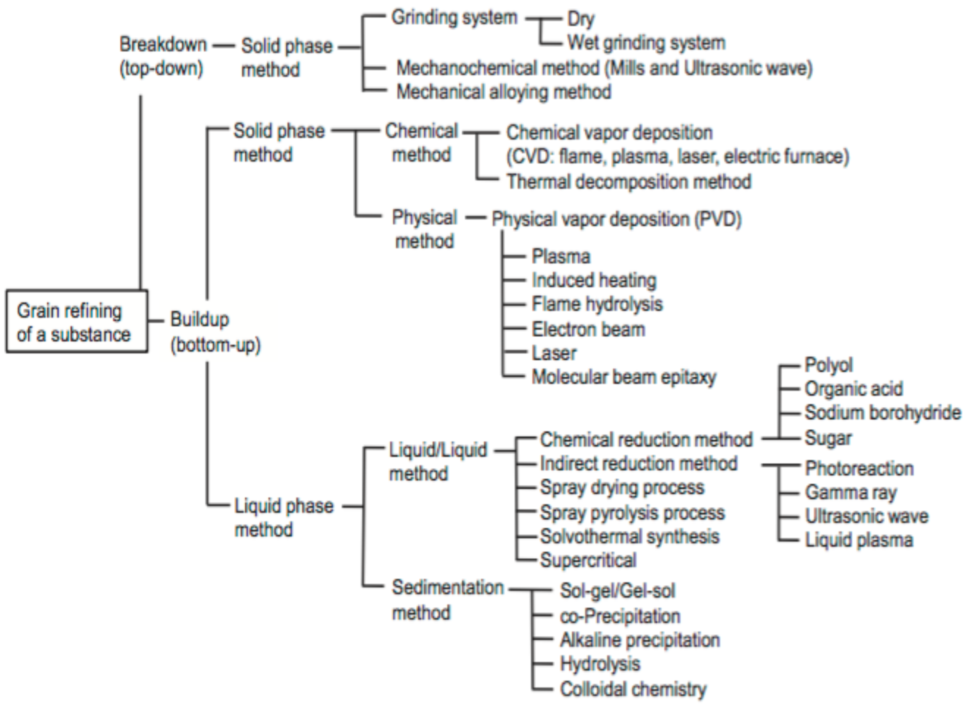

Figure 2.5.1: Types of nanoparticle synthesis methods[31]

One of the most frequently used top-down systems for generating nanoparticles is mechanical alloying with a planetary ball mill (See Figure 2.5.2). Since only a small amount of powder is required for the process, it is useful for laboratory research purposes. The mechanism consists of closed containers that rotate about a disk, while spinning around their own axis. Each contains milling balls, as well as the powder mixture. The centrifugal forces become synchronized when the turning disc rotates in one direction while the containers rotate in the opposite direction. This creates a high-energy impact at values up to 40 times gravitational acceleration to fracture and cold-weld the powder mixture.[32] As particles are made smaller, it is important to note that

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[31] Ibid.

[32] W. Cao, "High energy ball milling process for nanomaterial synthesis", *Understandingnano.com*. Internet: http://www.understandingnano.com/nanomaterial-synthesis-ball-milling.html. [Accessed: 03- Oct- 2016].

electrostatic and molecular interactions increase, which result in particle agglomerations that cannot be reduced further in size. So in certain situations, it is necessary to grind the material in a liquid medium to provide maximum dispersion and isolation of the particles. Typically, alcohol, water, and other solvents can be used depending on the application.[33]

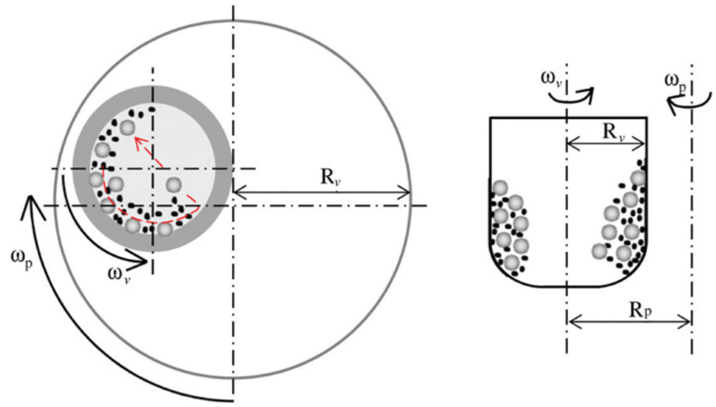

Figure 2.5.2: Mechanical alloying with a planetary ball mill[34]

A different top-down method utilizes ultrasonic cavitation (See Figure 2.5.3). This is a phenomenon that occurs when high-intensity sound waves propagate into a liquid media resulting in alternating high-pressure (compression) and low-pressure (rarefaction) cycles. Between the low-pressure cycles, small vacuum bubbles are created in the liquid, which collapse violently once the high-pressure cycle occurs. High-speed liquid jets of up to 1000 km/hr erupt from this collapse, which can be used to apply mechanical stress or accelerate collisions between particles suspended in the liquid. This makes ultrasound an effective means for dispersing and milling nanoparticles.[35]

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[33] "Nanoparticle Grinding and Dispersing", *Ceramicindustry.com*, 2006. Internet: http://www.ceramicindustry.com/articles/88104-nanoparticle-grinding-and-dispersing. [Accessed: 03- Oct- 2016].
[34] M. Abdellahi, M. Bahmanpour, "A novel technology for minimizing the synthesis time of nanostructured powders in planetary mills," *Mat. Res. Materials Research*, vol. 17, no. 3, pp. 781–791, 2014.
[35] "Ultrasonic Cavitation in Liquids", *Hielscher.com*. Internet: https://www.hielscher.com/cavitat.htm. [Accessed: 03- Oct- 2016].

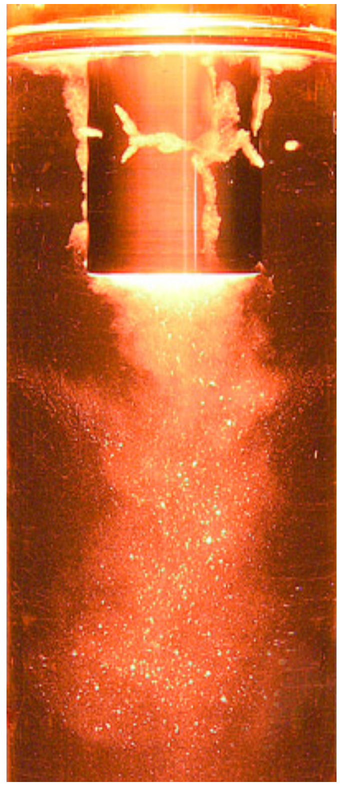

Figure 2.5.3: Ultrasonic cavitation for nanoparticle dispersion[36]

When producing nanoparticles from bottom-up methods, the simplest method of gas phase fabrication is inert gas condensation. This involves heating a material inside a furnace, sometimes up to 2000 ºC, while an inert gas is used to carry away the produced nanoparticles (Figure 2.5.4). This is useful for creating metallic nanoparticles, as many metals can be practically evaporated at these temperatures. For further variation, reactive gasses can be added to the furnace to facilitate reactions. Additional attributes, such as shape, size, and distribution can be controlled by the rate of evaporation, rate of condensation and the gas flow.[37]

[36] Ibid.
[37] "Gas phase synthesis", *Ninithi.com*. Internet: https://ninithi.com/gas-phase-synthesis/. [Accessed: 03- Oct- 2016].

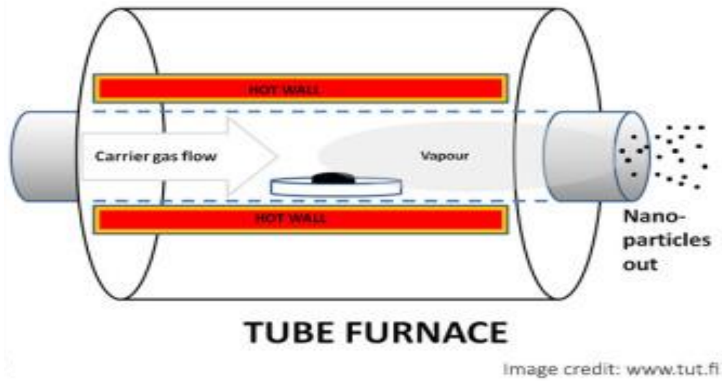

Figure 2.5.4: Inert gas condensation in a tube furnace[38]

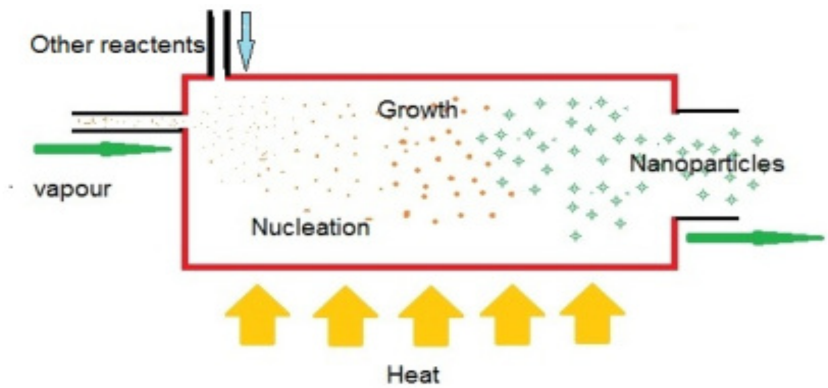

Figure 2.5.5: Chemical vapor synthesis[39]

Chemical vapor synthesis (CVS), shown in Figure 2.5.5, is a gas-phase synthesis method that is similar to inert gas condensation. However, it offers more possible variations with regards to particle properties. In CVS, chemical vapors of precursor materials are carried into a heated reaction chamber and managed in an environment that encourages nucleation and suppresses film formation. Usually, the time spent in the reaction chamber is the most vital parameter for controlling the resulting particles. Various precursors in solid, liquid and gas phase can be used, but they must all be vaporized before entering the reaction chamber. Supplying multiple precursors simultaneously, or flowing them into the reactor at different states can attain various

[38] Ibid.
[39] Ibid.

different outputs. The resulting nanoparticles can be produced in mixtures, coated or core-shelled. Since production is continuous, CVS is also considered a high throughput process. This allows for large volumes of nanoparticle production compared to other manufacturing techniques.[40]

2.6 Differences Between Natural and Artificial Nanoparticles

Naturally occurring nanoparticles have been present since the beginning of the Earth's history. They can be found in volcanic ash, fires, ocean spray, fine sand, dust, ice cores, biological matter and more.[41] Most of these occur from processes such as weathering, neoformation, and volcanic eruptions.[42] A study from the Center for the Environmental Implications of Nanotechnology (CEINT) estimates that soils are the most prolific generators of Earth's nanomaterials, while oceans provide the largest collective reservoir of these materials.[43]

In addition to their many origins, naturally occurring nanoparticles undergo complex transformations through chemical interactions and other factors. These include UV light, redox reactions, biotransformation, interactions with organic/inorganic ligands, and aggregation. This makes it difficult to gauge the potential hazards involved because their physical properties are constantly changing. Synthetic nanoparticles are equally, if not more diverse, than their naturally occurring counterparts, and fall into two general categories: incidental and engineered nanoparticles (Figure 2.6.1)

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[40] Ibid

[41] R. D. Handy, R. Owen, and E. Valsami-Jones, "The ecotoxicology of nanoparticles and nanomaterials: current status, knowledge gaps, challenges, and future needs," *Ecotoxicology,* vol. 17, pp. 315-325, Jul 2008.

[42] S. Lohse, "Nanoparticles Are All Around Us", *Sustainable Nano*, Mar 25, 2013. Internet: http://sustainable-nano.com/2013/03/25/nanoparticles-are-all-around-us. [Accessed: 03- Oct- 2016].

[43] M. Hochella, D. Aruguete, B. Kim, and A. Madden, "Naturally occurring inorganic nanoparticles: General assessment and a global budget for one of Earth's last unexplored geochemical components," in *Nature's Nanostructures,* 1st ed. Victoria, Australia, 2012, ch 1, pp. 1–42

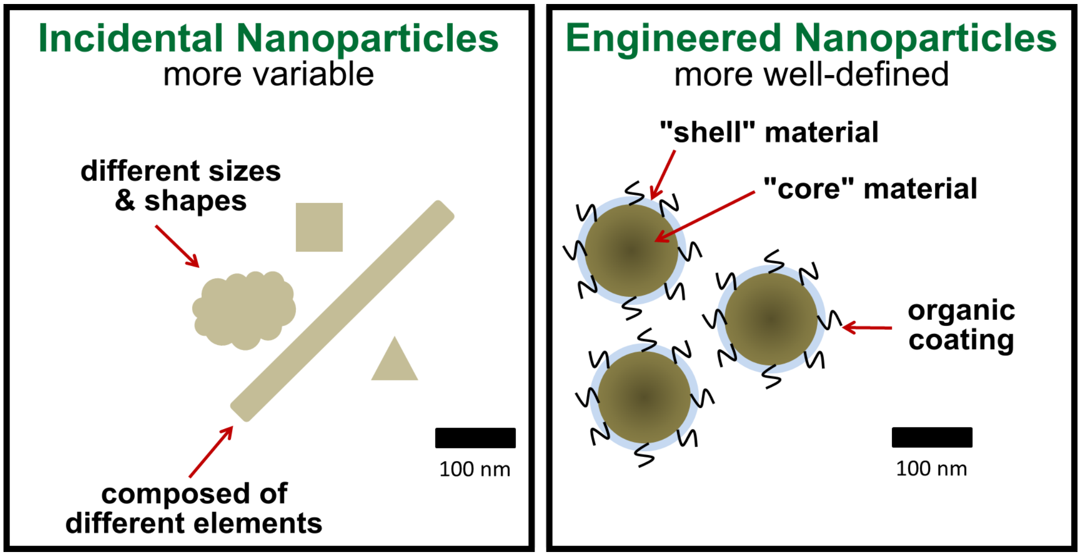

Figure 2.6.1: Incidental vs. Engineered Nanoparticles[44]

Engineered nanoparticles are designed to have certain individual properties for specific applications or products. They are synthesized to have precise sizes, shapes and compositions, and can contain different "cores" and "layers" of materials.[45] This is especially relevant to biomedical applications, in which the nanoparticle might act as a vessel for delivery of medication. For example, a nanoparticle might act as a core substance for which a small-molecule drug is attached, as well as a targeting molecule. By packaging these larger protein-based drugs into nanoparticles, the patient's immune responses can be minimized. This way the drug is not destroyed before it reaches the cancer cells, which can sicken the patient.[46]

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[44] S. Lohse, "Nanoparticles Are All Around Us", *Sustainable Nano*, Mar 25, 2013. Internet: http://sustainable-nano.com/2013/03/25/nanoparticles-are-all-around-us. [Accessed: 03- Oct- 2016].
[45] Ibid.
[46] "Breakthrough in Nano-Medicine Chemotherapy Drug Delivery in Phase II Trials-Prostate Cancer Foundation (PCF)", *Pcf.org*,2013.Internet:http://www.pcf.org/site/c.leJRIROrEpH/b.8730947/k.4E58/Breakthrough_in_NanoMedicine_Chemotherapy_Drug_Delivery_in_Phase_II_Trials.htm. [Accessed: 03- Oct- 2016].

Incidental nanoparticles, in contrast are created unintentionally as the byproducts of manufacturing or other human activities. The shapes and sizes, as well as chemical composition of these particulates are uncontrolled and differ widely. Processes that generate incidental nanoparticles include large-scale mining, product manufacturing, or more common occurrences, such as diesel engine emissions and starting a fire. Research from the University of Oregon also shows that common silver and copper items can discharge nanoparticles over time (Figure 2.6.2).[47] This demonstrates that there are various possible sources, even at home, where humans regularly come into contact with nanoparticles.

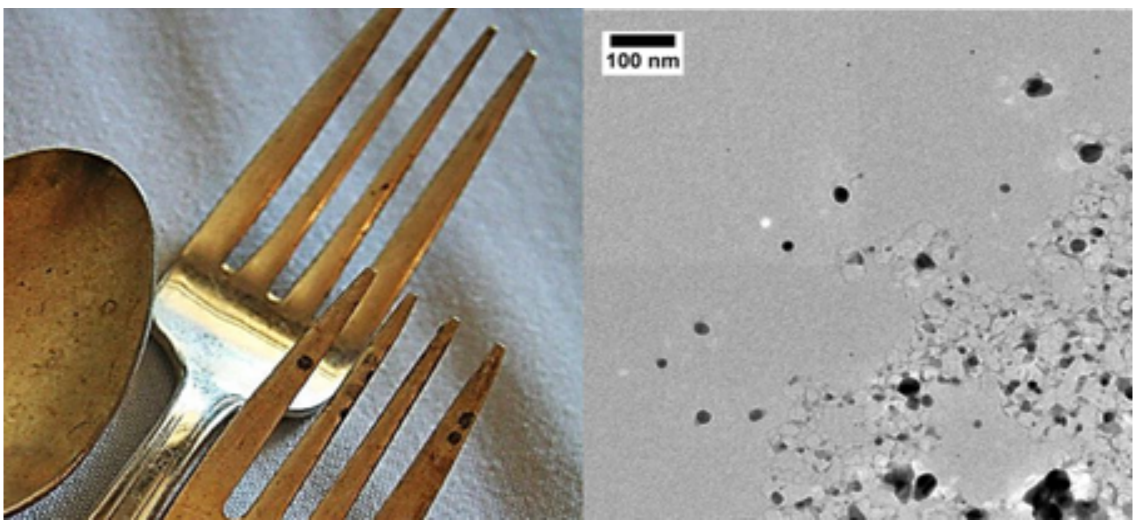

Figure 2.6.2: Silver fork nanoparticle residue under electron microscope[48]

[47] R. D. Glover, J. M. Miller, and J. E. Hutchison, "Generation of Metal Nanoparticles from Silver and Copper Objects: Nanoparticle Dynamics on Surfaces and Potential Sources of Nanoparticles in the Environment," *Acs Nano,* vol. 5, pp. 8950-8957, Nov 2011.

[48] S. Lohse, "Nanoparticles Are All Around Us", *Sustainable Nano*, Mar 25, 2013. Internet: http://sustainable-nano.com/2013/03/25/nanoparticles-are-all-around-us. [Accessed: 03- Oct- 2016].

2.7 Disposal of Nanoparticle Waste

The existing guidelines for the disposal of nanoparticles are vague. In many cases, the laboratories are left to determine if a special disposal method is required, unless they fall under the jurisdiction of regulations for macro-sized chemicals.[49] Therefore, laboratories use the same methods for disposing of nanoparticles as they do for any other chemicals. Usually, this means they send them off to a specific company or group to deal with the disposal.[50] Very little is specialized specifically for nanoparticles and much is left to the chemical disposal team to decide. Many institutions, including Massachusetts Institute of Technology, Virginia Tech, the University of California at Berkeley, the University of Pennsylvania, and the California Institute of Technology classify nanowaste as particularly hazardous and state that it must be specially collected for disposal.[51]

Although the major source of nanoparticles in normal waste treatment centers is from commercial products, research laboratories sometimes contribute as well. Even if they do not throw away the physical sample of nanoparticles or pour it down the drain, nanoparticles can contaminate normal rubbish such as gloves and paper towels. Whatever the outlet of disposal, the nanoparticles would ultimately arrive at one of four places: a recycling facility, incineration plant, landfill, or a wastewater treatment facility. Each place has the potential for the release of nanoparticles, with some more preventable than others. In recycling facilities there are plastics with nanoparticles in them that can be released as dust, but the dust is usually controlled as to not expose any humans or the environment. Nanoparticles can be released during the combustion in an incineration plant as ash or dust. Most plants have filters to collect pollutants, but many are

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[49] E. Furrer, C. Studer, K. Knauer, L. Strotz, C. Bosshard and C. Manigley, "Sicherheitsdatenblatt (SDB): Leitfaden für synthetische Nanomaterialien", Staatssekretariat für Wirtschaft SECO, Zürich, 2010.

[50] G. Amoabediny, A. Naderi, J. Malakootikhah, M. Koohi, S. Mortazavi, M. Naderi and H. Rashedi, "Guidelines for safe handling, use and disposal of nanoparticles", *Journal of Physics: Conference Series*, vol. 170, p. 012037, 2009.

[51] A. L. Holder, E. P. Vejerano, X. Z. Zhou, and L. C. Marr, "Nanomaterial disposal by incineration," *Environmental Science-Processes & Impacts,* vol. 15, pp. 1652-1664, 2013.

not rated for nanoparticles or can be damaged by them. Landfills have the most potential for nanoparticle release, be it by emission into air, water, or soil. Wastewater is turned into sludge that is then burned, or sometimes into fertilizer for agriculture. Little is known about the environmental impacts from nanoparticles in fertilizer,[52] though 100 percent of wastewater sludge is incinerated in Switzerland.[53]

Table 2.7.1: Possible leakage routes in waste treatment[54]

Waste treatment processes	Possible leakage routes
Recycling	-Imbedded in secondary materials
Incineration	-Flue gas emissions to the environment -Fly ash and bottom ash to landfills -Fly ash and bottom ash to storage facilities -Bottom ash to industrial applications (e.g. roads)
Landfilling	-Landfill gas emissions to the environment -Landfill surface emissions to the environment -Leachate to leachate treatment facilities -Leachate to wastewater treatment facilities
Wastewater treatment	-Emissions to surface water -Wastewater sludge to incinerators -Wastewater sludge to landfills -Wastewater sludge to agriculture applications

About half of the waste in Switzerland is incinerated, while the other half is recycled.[55] There are multiple possible pathways that nanoparticles can follow in an incinerator. As shown in Figure 2.7.1, nanoparticles arrive at the incinerator as a powder, or suspended in a liquid or a solid.

[52] OECD, *Nanomaterials in Waste Streams: Current Knowledge on Risks and Impacts*, OECD Publishing, Paris, 2016.
[53] F. Gottschalk, T. Sonderer, R. W. Scholz, and B. Nowack, "Modeled Environmental Concentrations of Engineered Nanomaterials (TiO2, ZnO, Ag, CNT, Fullerenes) for Different Regions," *Environmental Science & Technology,* vol. 43, pp. 9216-9222, Dec 2009.
[54] OECD, *Nanomaterials in Waste Streams: Current Knowledge on Risks and Impacts*, OECD Publishing, Paris, 2016.
[55] OECD, “Municipal waste”, OECD Environment Statistics, http://dx.doi.org/10.1787/data-00601-en

There are multiple possibilities for the particles to become airborne before incineration, such as evaporation or abrasion. During the actual incineration, the particles can either be destroyed, released as particulate, oxidized, or become trapped in the ash.[56] Many carbon-based nanoparticles, such as carbon nanotubes, can be destroyed in the incineration process, though only at sufficiently high temperatures. Carbon nanotubes are eliminated only at incineration above 850ºC, so only modern waste incinerators operating properly can destroy them.[57] Airborne particulates in the facility flow through a filter designed to remove pollutants from the air. In the EU, it is required for all incineration plants to have a flue gas treatment system that scrubs away dust and pollutants. The few studies that exist on the flow of nanoparticles through these systems predict that they remove most of the nanoparticles in the air. However, these studies only cover a few specific nanoparticles and are calculated using a non-empirical model.[58] There is also concern from nanoparticles left in the bottom ash, as it is often recycled and can lead to health hazards from working with it, or environmental hazards when it is used in road construction.[59]

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56 A. L. Holder, E. P. Vejerano, X. Z. Zhou, and L. C. Marr, "Nanomaterial disposal by incineration," *Environmental Science-Processes & Impacts,* vol. 15, pp. 1652-1664, 2013.

57 European Commission DG Environment (2009), How Nanotubes Could be Released Into the Environment, Original source: Köhler et. al. (2008), "Studying the Potential Release of Carbon Nanotubes Throughout the Application Life Cycle", Special Issue 12, Newsletter.

58 OECD, *Nanomaterials in Waste Streams: Current Knowledge on Risks and Impacts*, OECD Publishing, Paris, 2016.

59 Danish Ministry of the Environment, "Nanomaterials in waste: Issues and new knowledge", Environmental Project No. 1608, 2014, 2014.

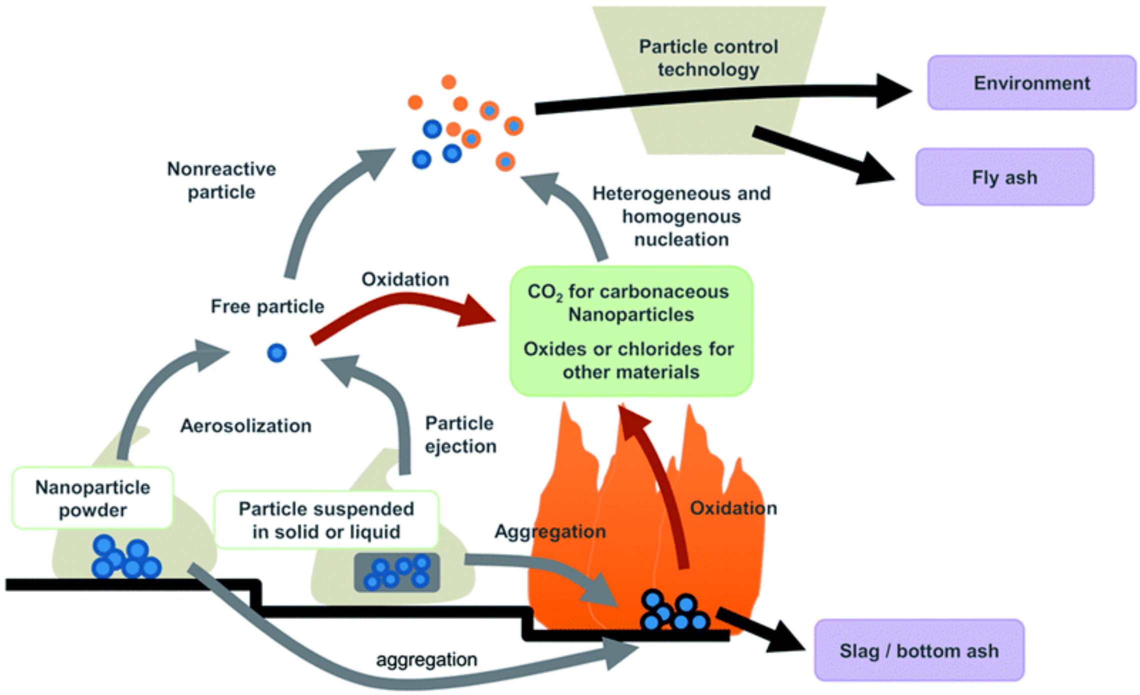

Figure 2.7.1: Possible pathways to the fate of nanomaterials within waste incinerators[60]

When recycling materials containing nanoparticles, there are three main concerns: the health of facility workers; the environmental impacts from residue that ends up in incineration, landfills, or sewage treatments; the contamination of products made from recycled materials.[61] There is a possibility of the nanoparticles leaching from the products and affecting their surroundings. These effects are barely studied and are poorly understood.[62]

[60] A. L. Holder, E. P. Vejerano, X. Z. Zhou, and L. C. Marr, "Nanomaterial disposal by incineration," *Environmental Science-Processes & Impacts,* vol. 15, pp. 1652-1664, 2013.
[61] Danish Ministry of the Environment, "Nanomaterials in waste: Issues and new knowledge", Environmental Project No. 1608, 2014, 2014.
[62] OECD, *Nanomaterials in Waste Streams: Current Knowledge on Risks and Impacts*, OECD Publishing, Paris, 2016.

2.8 Biological Interactions and Hazards of Nanoparticles

An important property of nanoparticles is the ability to interact with biological cells. With a high surface area to volume ratio, a large amount of the material can come into contact with surrounding materials, making nanoparticles highly reactive.[63] Nanoparticles can interact with cells in mainly in four ways: endocytosis, semi-endocytosis, adhesion (Figure 2.8.1), and penetration (Figure 2.8.2). Endocytosis is when the particle wraps around the cell membrane and fully enters the cell. Semi-endocytosis is when the particle is wrapped up, but remains suspended in the cell membrane. Penetration occurs when small-enough cells slip through the cell membrane and adhesion is when the particles stick to the cell membrane.[64]

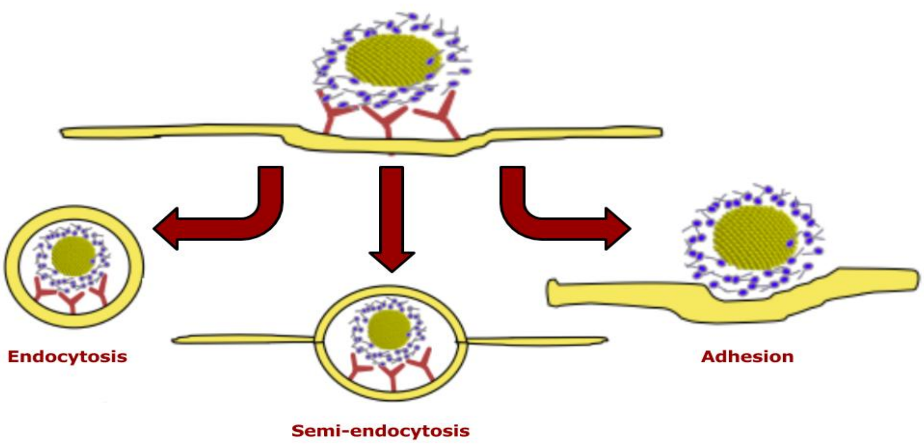

Figure 2.8.1: Nanoparticle interactions with cell membrane[65]

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[63] "What's So Special about the Nanoscale? | Nano"http://www.nano.gov/nanotech-101/special

[64] X. M. Chen, F. L. Tian, X. R. Zhang, and W. C. Wang, "Internalization pathways of nanoparticles and their interaction with a vesicle," *Soft Matter,* vol. 9, pp. 7592-7600, 2013.

[65] J. Ortiz, "How do Nanoparticles Enter Cells?", *Sustainable Nano*, 2014. Internet: http://sustainable-nano.com/2014/08/19/how-do-nanoparticles-enter-cells/. [Accessed: 03- Oct- 2016].

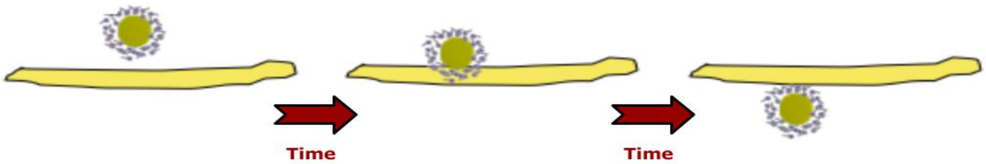

Figure 2.8.2: Nanoparticle penetration of cell[66]

The most prominent danger from nanoparticles comes from inhalation, as nanoparticles can easily become airborne. It is much easier for nanoparticles to enter the bloodstream and cells from the lungs than through the dermis, and have been shown to accumulate in other organs. Long fibrous nanoparticles, such as carbon nanotubes, have similar properties as asbestos and can have similar hazards.[67] For example, many studies have shown that the main effect to the lungs is inflammation.

2.9 Risk Assessment for Natural and Artificial Nanoparticles

According to the "Risk Assessment Characterization" given by the US Environmental Protection Agency (EPA), risk is dependent on three factors. These factors include the amount of a chemical present (hazard), the amount of contact with the chemical (exposure), and the effect of the chemical on the individual (vulnerability).[68] According to this definition, it is important to take into consideration all three factors when assessing the risk of a certain scenario. Risks are usually split into two categories "known risks" and "predictable risks". The EPA has set out a definition for known risks with a clear cause and effect of their impact. Predictable risks pose an unknown and it is unclear how much of the hazard, exposure, and vulnerability is present.

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66 Ibid.

67 C. L. Klein, K. Wiench, M. Wiemann, L. Ma-Hock, B. van Ravenzwaay, and R. Landsiedel, "Hazard identification of inhaled nanomaterials: making use of short-term inhalation studies," *Archives of Toxicology,* vol. 86, pp. 1137-1151, Jul 2012.

68 "About Risk Assessment | Risk Assessment | US EPA", Epa.gov, 2016. Internet: https://www.epa.gov/risk/about-risk-assessment#whatisrisk. [Accessed: 26- Sep- 2016].

Engineered nanoparticles fall under this predictable risk category, making them hard to define. However, with the failure of exposure comes a threshold of safety that is identifiable.[69]

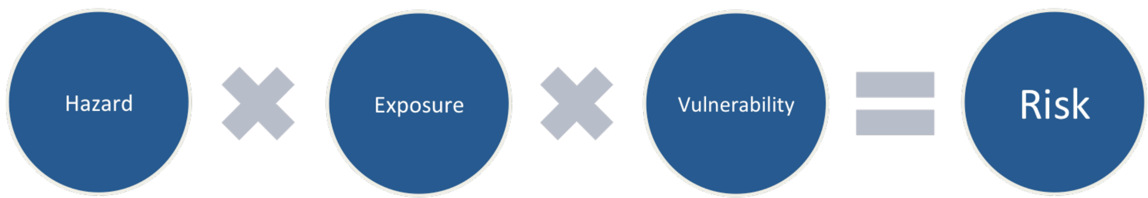

Figure 2.9.1: The relationship between hazard, exposure, vulnerability and risk

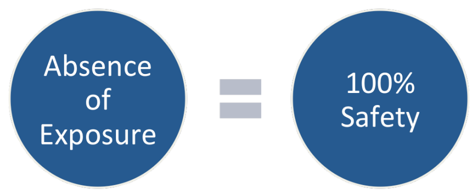

Figure 2.9.2: Absolute safety derived from risk assessment

While nanoparticle environmental risk factors are starting to be identified, it is important to recognize that manufactured nanomaterials created today are tied to consumer-based products with the consumer, and not the environment, in mind. This leaves grey areas in studies when it comes to how these nanoparticles affect the human body and interacts with other pollutants. A study from the international journal, *Ecotoxicology,*[70] brings up issues of whether manufactured nanoparticles pose added risks to the environment, as well as reflecting on already known information on natural nanoparticles.

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[69] D. Warheit and E. Donner, "How meaningful are risk determinations in the absence of a complete dataset? Making the case for publishing standardized test guideline and 'no effect' studies for evaluating the safety of nanoparticulates versus spurious 'high effect' results from single investigative studies", *Science and Technology of Advanced Materials*, vol. 16, no. 3, p. 034603, 2015.
[70] R. D. Glover, J. M. Miller, and J. E. Hutchison, "Generation of Metal Nanoparticles from Silver and Copper Objects: Nanoparticle Dynamics on Surfaces and Potential Sources of Nanoparticles in the Environment," *Acs Nano,* vol. 5, pp. 8950-8957, Nov 2011.

Exposure to natural nanoparticles heavily outweighs that of manufactured particles. It is known that prolonged exposure to natural nanoparticles can affect the lungs and the rest of the body, but small amounts are generally fine. *Ecotoxicology* ponders whether or not we should focus on the effects of manufactured nanoparticles at all, as humans have evolved and adapted in a nanoparticle saturated world.

The chemical reactivity of a nanoparticle is just as important as the structural form and shape. Manufactured nanoparticles can be created in a laboratory for specific purpose, but we also have accidental exposure in the form of air pollution and car emissions.

Ecotoxicology identified these five steps that should be taken to regulate ecotoxicity testing with manufactured nanoparticles:

- *The chemical characterization of the test material.*
- *Reference nanomaterials for regulatory ecotoxicology.*
- *Modifications to test methods or solution preparation that enable existing regulatory ecotoxicity tests to work with nanomaterials.*
- *Triggers for conducting the tests, and whether or not we need new tests, or additional measurements within existing tests, to quantify novel or unusual toxicological properties.*

One of the biggest issues in assessing the risks associated with materials on the nanoscale is their wide array of properties. The physical makeup of a nanoparticle encompasses structures of different sizes, forms, and molecular states. Because of this it becomes very hard to access the biological and environmental effects they have. A nanoparticle's mechanical, chemical, and electrical properties are different from a non-nano-sized particle of the same shape and material. While this makes them highly viable in the consumer-based world for adaptation into products, it hinders research on how to assess their susceptibility to health risks.[71] The following will be a breakdown of toxicity assessments based on some common classes of nanomaterials.

2.9.1 Metal Oxides

Metal-oxide nanoparticles are widely used in many commercial applications. Many of the nanoparticles, such as zinc oxide and titanium dioxide, are considered nontoxic because their bulk materials lack any signs of toxicity.[72] However, researchers have concerns about the safety of these nanoparticles, as they are known to exhibit antibacterial properties and genotoxicity to bacteria.[73] Studies have been conducted to determine the effects of metal oxide nanoparticles on multicellular organisms. They have shown that inhalation is the most hazardous form of exposure, as the nanoparticles have direct access to the body and can be transported to many vital organs, including the liver, kidneys, and spleen.[74] A study of the metal-oxide nanoparticles in sunscreens has found that the nanoparticles are unable to penetrate through intact skin.[75] However, the effects of these nanoparticles at longer exposures are largely unknown.

2.9.2 Metal Nanomaterials

Similar to metal-oxide nanoparticles, the bulk materials for metal nanoparticles are generally nontoxic, but this might not be the case for the nanoparticles themselves. For instance, silver

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[71] E. S. Bernhardt, B. P. Colman, M. F. Hochella, B. J. Cardinale, R. M. Nisbet, C. J. Richardson, *et al.*, "An Ecological Perspective on Nanomaterial Impacts in the Environment," *Journal of Environmental Quality,* vol. 39, pp. 1954-1965, Nov-Dec 2010.

[72] A. Djurišić, Y. Leung, A. Ng, X. Xu, P. Lee, N. Degger and R. Wu, "Toxicity of Metal Oxide Nanoparticles: Mechanisms, Characterization, and Avoiding Experimental Artefacts", *Small*, vol. 11, no. 1, pp. 26-44, 2014.

[73] S. Jomini, J. Labille, P. Bauda and C. Pagnout, "Modifications of the bacterial reverse mutation test reveals mutagenicity of TiO2 nanoparticles and byproducts from a sunscreen TiO2-based nanocomposite", *Toxicology Letters*, vol. 215, no. 1, pp. 54-61, 2012.

[74] J. Wang, G. Zhou, C. Chen, H. Yu, T. Wang, Y. Ma, G. Jia, Y. Gao, B. Li and J. Sun, "Acute toxicity and biodistribution of different sized titanium dioxide particles in mice after oral administration", *Toxicology Letters*, vol. 168, no. 2, pp. 176-185, 2007.

[75] R. Landsiedel, L. Ma-Hock, A. Kroll, D. Hahn, J. Schnekenburger, K. Wiench and W. Wohlleben, "Testing Metal-Oxide Nanomaterials for Human Safety", *Adv. Mater.*, vol. 22, no. 24, pp. 2601-2627, 2010.

nanoparticles have been shown to produce a strong toxic response from cells and animals, which is surprising as silver is not toxic when it is in bulk.[76] Other metal nanoparticles have been shown to interact with proteins and enzymes within mammalian cells. This can lead to interference with the antioxidant defense mechanism in cells, and cause reactive oxygen species to generate. Other effects include inflammation and perturbation, and the destruction of mitochondria causing apoptosis or necrosis.[77]

2.9.3 Carbon Nanomaterials

Carbon nanotubes have been wildly studied in recent years, but they are not the only carbon-based nanomaterials. There are also carbon nanospheres and carbon nanofibers. Through direct studying of the effects of these nanomaterials on cells, researchers have shown that they are toxic, but the hazardous effects are largely dependent on size and production method.[78] The nanomaterials generally caused proliferation inhibition and cell death. They also found in the same study that carbon nanotubes are generally less toxic than carbon nanofibers or nanospheres. Though, because carbon nanotubes' morphology is strikingly similar to asbestos, there is concern about its long-term effects and possible carcinogenicity. Thus, the effects of carbon nanotubes have been heavily investigated. Many of their underlying toxicity comes from oxidative stress, inflammatory responses, malignant transformation, DNA damage and mutation, and interstitial fibrosis.[79]

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[76] A. Lansdown, "Silver in Health Care: Antimicrobial Effects and Safety in Use", *Biofunctional Textiles and the Skin*, vol. 33, pp. 17-34, 2006.

[77] A. Schrand, M. Rahman, S. Hussain, J. Schlager, D. Smith and A. Syed, "Metal-based nanoparticles and their toxicity assessment", *WIREs Nanomed Nanobiotechnol*, vol. 2, no. 5, pp. 544-568, 2010.

[78] A. Magrez, S. Kasas, V. Salicio, N. Pasquier, J. Seo, M. Celio, S. Catsicas, B. Schwaller and L. Forró, "Cellular Toxicity of Carbon-Based Nanomaterials", *Nano Letters*, vol. 6, no. 6, pp. 1121-1125, 2006.

[79] Y. Liu, Y. Zhao, B. Sun and C. Chen, "Understanding the Toxicity of Carbon Nanotubes", *Accounts of Chemical Research*, vol. 46, no. 3, pp. 702-713, 2013.

2.10 Regulation of Nanoparticle Safety

Current guidelines for nanoparticle safety are vague and differ between organizations. Both the US Occupational Safety and Health Administration (OSHA) and the Swiss Federal Office of Public Health (FOPH) only give recommendations about how individual facilities should create their own safety guidelines, not enforced regulations.[80] An important note is that scarcely any of the publicly found safety regulations include nanoparticle-specific tools or preventative measures. For example, the "Nanoparticle Safety and Health Guidelines" provided by Purdue University include only standard laboratory attire, such as latex or nitrile gloves, goggles, laboratory coats, closed-toed shoes, and possibly respiratory protection.[81] The Swiss government notes in their outlines for a nanoparticle safety datasheet that there are no workplace exposure limits for synthetic nano-objects, and that since the effect of nano-objects on human health is still unclear, the exposure is to be kept to a minimum.[82] Proper safety guidelines should be regulated, so that updates to effective nano-specific protection can be quickly spread and implemented.

Similar to the state of its handling procedures, nanoparticle storage, transport, and disposal all seem to follow a similarly low level of regulation. In effect, nanoparticles are dealt with in the same way as other chemicals. They are stored in bottles, flasks, jars, bags, and other containers based solely on their chemical state. When used they are prepared for disposal by being dissolved in solution or congealed within a matrix. This makes dispersion and contamination less likely. Afterwards, they must be labeled as nanoparticle hazards, and collected by a chemical waste management facility.

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[80] "Federal Office of Public Health - Occupational health protection", *Bag.admin.ch*, 2016. Internet: http://www.bag.admin.ch/nanotechnologie/12171/12452/index.html?lang=en. [Accessed: 03- Oct- 2016].

[81] Occupational Safety and Health Administration. "Working Safely With Nanoparticles," OSHA, 2013.https://www.purdue.edu/ehps/rem/home/booklets/nanopolicy.pdf

[82] E. Furrer, C. Studer, K. Knauer, L. Strotz, C. Bosshard and C. Manigley, "Sicherheitsdatenblatt (SDB): Leitfaden für synthetische Nanomaterialien", Staatssekretariat für Wirtschaft SECO, Zürich, 2010.

The Swiss government also mentions that the specific properties of Nano-objects may also have risks to human health and the environment. From animal and cell experiments with Nano-objects, there is evidence of a possible health hazard. However, no general conclusions can be drawn about the risk potential of Nano-objects, so they suggest the "TOP" precautionary approach for dealing with nanoparticles. The TOP approach is based around reducing any possible exposure to a minimum.

1. T = Technical protective measures
   - Use of closed equipment
   - Avoid generation of dusts or aerosols
   - Suction of dusts or aerosols directly at the source
   - Exhaust air purification for exhaust air ("filter")
   - Separation of the working space and adaptation of the room ventilation (slight vacuum)
   - Cleaning only by suction or by damp wiping, no blowing off

2. O = Organizational protective measures
   - Minimization of the exposure time
   - Minimize the number of exposed persons
   - Restrict access
   - Instruction of personnel on dangers and protective measures (operating instructions)

3. P = Personal protective measures
   - The appropriate personal protective equipment (PPE) is needed if the above mentioned technical and organizational measures ensure insufficient protection.[83]

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[83] Ibid.

This literature review allowed us to be able to have a better understanding of nanoparticles and their usage. From this baseline, we were able to make informed decisions about the problems we discovered. The next section outlines our methodology and how we conducted the steps of this project.

Chapter 3 Methodology

3.1 Overview

The first step of our project was to develop an understanding of nanoparticle safety. This was done by conducting a literature review among all members of our team. Collectively, we determined which categories of nanoparticle knowledge would be necessary and relevant with regards to safety procedures. Then we set goals with regards to our research and our prospective audience. The literature review was tailored to provide a variety of readers the foundation for our conclusions, and to prepare us for our project. This increases awareness of the subject, raises the validity of our argument, and creates a willingness to learn more.

After researching secondary and tertiary sources, our next step was to gather primary accounts of nanoparticle safety procedures. Through the connections from NTB Buchs and our project advisor from WPI, we scheduled and conducted thirteen interviews across Switzerland. These interviews were with various industry and academic researchers who work with nanoparticles, and focused on their safety practices.

We determined that focusing on obtaining comprehensive qualitative accounts would prove more useful than straight statistical data. This is due to the vagueness and lack of regulation with regards to procedures and protective practices. Due to our relatively small sample size, trends may not be made apparent and statistical anomalies would be more difficult to discern. However, we did decide to take a basic quantitative account of common facility protection, individual protection, and environmental safety measures (Tables A.1, A.2, A.3). These were collected and organized in the same manner as a *Swiss Nano-Inventory* study conducted in 2008.[84] This

[84] K. Schmid and M. Riediker, "Use of Nanoparticles in Swiss Industry: A Targeted Survey," *Environmental Science & Technology,* vol. 42, pp. 2253-2260, 2008/04/01 2008.

enabled us to take quantitative data from our project and create a better conclusion through direct comparison of a statistical study with a larger sample size.

Once we collected all our interview information, we formatted and analyzed each member's individual notes to create a more concrete response and fill in missing information. From this condensed account of each interview, we combined our efforts to deduce important findings and create a conclusion. This provided us a basis to create recommendations for new rules on nanoparticle safety, and inform our audience on ideas or knowledge that may benefit them.

As a final goal, we created practical implementations supporting the ideas presented in our conclusion. These products would help to provide momentum for our recommended improvements in nanoparticle safety, as well as expand awareness in ways that a documented report might not be able to.

3.2 Interviewing Process

An important aspect of information gathering is to encompass a wide variation of sources while remaining relevant to the researched topic. Following this ideology, we created a list of interviews that we would be interested in. This included nanoparticle experts, non-experts, safety managers, scientists, corporate industries, and developers of guidelines. Due to limitations in contacts and connections, as well as some declined invitations, we were not able to interview every place of interest. However, we managed to fully encompass our different categories of interest within our sampling pool.

We researched various interviewing types including unstructured, semi-structured and structured interviews. Unstructured interviews have no preset questions and are very open-ended. Semi-structured interviews have set questions to guide the interview, but allow the interviewee to delve into more detail. A structured interview allows for the interviewee to answer just the posed questions, which creates less variability in responses.[85] Our decision was to interview in the semi-structured style. While we found it important to have focused and specific questions, we wanted each interviewee to openly express their way of thinking. This would give us a better understanding of how different individuals might feel about their safety practices. In support of this, we also designed our questions to be action-oriented. A full list of these questions can be found in *Appendix A Interview Questions*.

Before putting our questions directly into practice, we took preparatory measures to ensure that the interviews would be conducted smoothly. We tested our initial set of questions with scientists at our sponsor site, NTB Buchs, so that mistakes would be more forgiving. This helped us to remove irrelevancies and clarify questions that were vague. It also benefitted by highlighting questions that might be taken as culturally or socially insensitive. Following this, we also decided that interviewing in pairs might be less intimidating for the interviewee than groups of four, especially for smaller-scale laboratories. Businesses and research facilities operate differently in Switzerland than they do in the United States, so adaptation was important for the successful gathering of information.

3.3 Organization and Analysis of Data

In order to analyze our interviews, we created a spreadsheet that would be shared among all four team members. Each page contained the interview questions we asked on the left-most column, and then the individually recorded responses of each interviewer in successive columns to the right. Finally, once all the information was inputted, one person was designated to compile each interview question. This process is done in order to correct mistaken or misheard information and combine interview data in a consolidated way. For each of the thirteen interviews, we were

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[85] "Nanoparticle Safety and Health Guidelines", Purdue University, Jan 6, 2010

left with pages of raw data and by displaying our work side-by-side we were able to grasp the best possible answer from each interviewee.

During our interviews we filled out three Tables (A.1, A.2, A.3) that allowed for us to gain quantitative data that was used to evaluate the level of safety of each lab. These tables assessed the protective measures laboratories were taking in regards to the environmental protection, personal protective equipment, and general protection methods. Once we completed all our interviews, one person was responsible for compiling the tables from each interview into a graph that shows trends and correlated data. The purpose of which is to give our quantitative conclusions validation through measurable statistical data.

Once we compiled and gathered all of our information from the interviews, we differentiated between the good practices, and those that need improvement from each lab. We then noted the commonalities and outliers between the interview results. From these results we discovered problems that facilities were dealing with and potential solutions to these problems.

3.4 Implementation of Solutions

After formulating conclusions from our interviews and literature review, we identified four key problems that persisted in many of the laboratories we visited. We created a brainstorming document where we listed all of these problems and came up with a list of possible solutions that could be implemented. From the list of solutions, we identified two that would be possible to innovate in the remaining time of the project. The other solutions, while still feasible, could be potentially developed and implemented during future work and were added to *Chapter 6, Recommendations for Future Work*. Our team collaborated to plan the general outline of our newly proposed solutions, but split in groups of two for the actual designing and drafting of them. That way everyone was able to contribute in a meaningful way without overcrowding the workload and still resulting in quality work. The next chapter reviews and analyzes the responses that we received from conducting our interviews. It presents the common responses and highlights the outliers.

Chapter 4 Conclusions from Research

4.1 Overview of Interviews

Over the course of a month we conducted thirteen interviews with various government, research, and industry laboratories. The responses we received were varied and gave insight into how these laboratories have different nanoparticle processes. The majority of people we interviewed were interested in safety and verified the need for this project. These laboratories are interested in what other facilities are doing, so they can learn from them and improve their own guidelines; laboratories do not always talk with other institutions when creating safety guidelines. These responses will give some insight into how other laboratories handle, store, and dispose nanoparticles.

4.2 Responses

4.2.1 Safety Guidelines

We asked interviewees about their own lab's safety guidelines and how they compared to the government's guidelines. There were a few people who we interviewed who did not know what the Swiss governmental guidelines were (Appendix B, Interview 4, Question 22)(Appendix B, Interview 6, Question 21). Those who did know what the government guidelines were, all said that they had stricter guidelines than the governmental ones. This is because the Swiss government guidelines put all the responsibility on the company to keep the users and the environment safe. One of our interviewees is very involved in the Swiss guidelines and helped to create the precautionary matrix, which helps laboratories to create guidelines and find out where the holes in research are. This tool is free and available online at the official website for the Federal Office of Public Health (FOPH) in Switzerland. There have been several governmental projects to help make handling nanomaterials safer. It is an issue that is currently in predevelopment, and will continue to be a focus in the future (Appendix B, Interview 6). There are more guides that should be available in the next year that will be even more specific.

Individual facilities have to create their own safety guidelines because currently the Swiss law states that the institution is responsible for safety. Through our interviews we found that facilities had concerns with their own guidelines for two main reasons: it is hard to measure the exposure that the handler experiences, and nanoparticle safety should be considered on a case-by-case basis (Appendix B, Interview 6). There are no widely available particle counters that can effectively detect nanoparticles (Appendix B, Interview 1, Question 12). This means that no one knows with certainty how effective their processes are because they have no concrete way to determine how many particles they are coming in contact with. The dangers of nanoparticles differ enough from particle to particle that safety measures may not be effective for each particle. This means that receiving new nanoparticles can be a lot of work. The guidelines need to be flexible and broad enough to encompass all nanoparticles that they work with, but also be specific enough to be useful. These are some of the difficulties that many interviewees mentioned that they had when developing guidelines.

4.2.2 Storage

We inquired about nanoparticle storage in laboratories and facilities, and found that many facilities use double containers to store their nanoparticles. Some laboratories also had systems implemented where the nanoparticles were under restricted access (Appendix B, Interview 7, Question 21). There were a few laboratories that keep the nanoparticles in temperature-controlled, ventilated environments. The nanoparticle containers are often labeled on the outside with the quantity of the material, potential hazards, and the person associated with the project (Appendix B, Interview 3, Question 17). Overall, the standard storage procedure seemed to be a labeled and appropriate double container.

We asked about the documentation of nanoparticle storage, and found three main responses: the facility did lab-wide documentation; there was documentation on the individual samples, and laboratories that did not document nanoparticle storage. The facilities that documented all nanoparticles usually had a system that allowed them to see who was in charge of what nanoparticle and the quantity of the nanoparticle in the laboratory (Appendix B, Interview 2). The less-documented laboratories often had a labeling system that had the amount of the material, the person responsible for the nanoparticle, and potential dangers. There were also laboratories that did not document their nanoparticles, some of whom mentioned that this would be a good improvement (Appendix B, Interview 9, Question 21). Some interviewees were less interested in documentation of nanoparticles (Appendix, Interview 4, Question 21). Overall, there were many different ways to deal with documenting stored nanoparticles.

4.2.3 Handling

In the interviewing process we discovered that the handling processes of the laboratories were rather different. It is generally accepted that powders are more dangerous and most laboratories that we talked to treated it as a hazardous material. Many mentioned that when dealing with powders the first priority, before even ordering the material, was doing research on how it should be handled. One university laboratory mentioned that getting the powders into matrixes as quickly as possible was a big priority (Appendix B, Interview 1, Question 1). The equipment used for laboratories that handle powders varied depending on the facility interviewed. The aforementioned university laboratory also uses a glove box (Appendix B, Interview 1, Question 8). A different university laboratory uses only a fume hood (Appendix B, Interview 4, Question 8). Some laboratories will not work with nanoparticles in the powder form because they feel the risk is too high (Appendix B, Interview 2, Question 13).

The handling of non-powders is widely accepted as less dangerous than handling powders. One university laboratory that handles the powders in a glove box handles non-powders in a fume hood. One interviewee walked us through their process. They prepare all materials before getting the nanoparticles, then they make sure to inform the people around them that nanoparticles are going to be used, and they make sure that the disposal equipment is readily available. Then they handle the nanoparticles, trying to finish in one day if possible (Appendix B, Interview 1, Question 11). A different research laboratory noted that after they use the nanoparticles they always ensure to clean the workspace with a water wash and they never clean by scraping (Appendix B, Interview 2, Question 25).

Some of the most interesting answers came from the question "During your work with nanoparticles, where is the greatest threat?" The responses for this were largely lumped into two categories: dealing with powders, and under-informed people in the lab. There was an interviewee who said that the biggest threat was working with powders. This interviewee also handles the powders under a fume hood without a mask, and mentioned that sometimes the nanoparticles irritate their nose (Appendix B, Interview 4, Question 25). There are other laboratories that see the powders as the biggest risk, and will not let powders into the laboratory (Appendix B, Interview 2, Question 13). For dealing with the possibility of uninformed workers, some laboratories have specific, segregated places for dealing with nanoparticles. Though large majorities have nanoparticle handling in the same location as other laboratory experiments. Many interviewees mentioned that they were afraid that other people who are not working with the nanoparticles would be put at risk, since they are not informed about potential dangers (Appendix B, Interview 1 Question 23)(Appendix B, Interview 7, Question 24). There is also a fear of accidental exposure, as they are unable to measure exposure levels (Appendix B, Interview 3, Question 21).

4.2.4 Disposal

The interviewees were asked about their disposal methods. Just like the other steps, disposal methods should be determined on a case-by-case basis (Appendix B, Interview 6, Question 9). One laboratory mentions that they separate nanoparticle waste between sharp and non-sharp objects, each placed into a solid, enclosed receptacle that is sent to the chemical waste disposal department (Appendix B, Interview 2, Question 14). That same laboratory also labels all nano-waste with a carcinogenic Globally Harmonized System (GHS) sticker, as there is no other standardized hazard label for nanoparticles. A different university laboratory labels the waste and then gives it to a special waste facility that is outside the company. This laboratory sometimes pre-treats the waste before giving it away, by sealing the nanoparticles in a polymer or epoxy (Appendix B, Interview 1, Question 14).

Laboratories are also concerned about nanoparticle-contaminated waste, such as gloves, or paper towels. Most laboratories contain these items in a plastic bag (Appendix B, Interview 1, Question 14). However, while some laboratories throw these bags away in the normal trash, others send them to a chemical waste treatment company (Appendix B, Interview 2, Question 16). There was also one laboratory that did not know how to dispose of their nanoparticles, as they only recently started working with them. For now, they store the discarded nanoparticles in an enclosed container in their lab. (Appendix B, Interview 8, Question 15).

4.2.5 General Safety

There are a lot of precautions that laboratories go through to ensure the safety of their nanoparticle users. One question asked interviewees if they felt hindered by their safety procedures. One interviewee mentioned that they did not feel held back, but they wished they could judge the effectiveness of their procedures (Appendix B, Interview 1, Question 22). Another mentioned the processes for working with new nanoparticles in their facility can take a lot of time. There was also concern about difficulties when cleaning nanoparticles from the workspace. (Appendix B, Interview 5, Question 23). In general, most of the facilities were happy to have safety procedures and add to them as necessary (Appendix B, Interview 2, Question 24).

We also asked about what people would like to see in potentially new nanoparticle guidelines. A proposed expansion for new guidelines included better preparatory measures for new nanoparticles. This interviewee also wanted easier access to reliable sources (Appendix B, Interview 1, Question 24). A different interviewee wanted more feedback from doctors and biologists about specific biological implications of nanoparticles (Appendix B, Interview 3, Question 23). There was an interviewee who stated that they would prefer more specific disposal and filtration guidelines for comparison between their own working guidelines (Appendix B, Interview 5, Question 26). One interviewee noted how they wanted to improve the comfort and working conditions of the user, as it consequently makes the risk of mistakes lower (Appendix B, Interview 9, Question 26).

4.2.6 Synthesis and Acquisition

When asked about synthesis and the acquisition of nanoparticles, laboratories have tailored systems that are specific to their own applications. Not all of the laboratories synthesize their own nanoparticles. One laboratory uses flame synthesis, which includes running solid nitrates suspended in a water solution through a flame, producing nanoparticles. They then collect the nanoparticles through a filter using a vacuum. The whole process is under constant vacuum suction, so very few nanoparticles are released into the room or environment (Appendix B, Interview 11, Question 10). A different facility puts catalysts into a vacuum oven that is heated and exposed to methane to proliferate nanoparticle growth (Appendix B, Interview 3, Question 9). Another facility synthesizes iron oxide through wet chemistry, and then isolates the particles from the solution through evaporation in an oven. These agglomerated macro particles are then ground into a nanoparticle state. This process is done in a glove box with a vial and plunger, while a magnet is used to keep the substance in place (Appendix B, Interview 13, Question 5).

4.3 Correlations Between Statistics

A study conducted in 2008, referred to as the *Swiss Nano-Inventory,* surveyed facilities that handled nanoparticles with a series of quantitative questions.[86] This interview had a different focus as compared to interviews conducted for our project, however the *Swiss Nano-Inventory* did ask some questions that were relevant. We asked our interviewees a few of the same questions so we could compare some of the results over time. The other study had a much bigger sample size and they completed structured interviews over the phone versus the semi-structured in-person interviews that we conducted. These questions were only applicable to nine out of our thirteen interviews.

4.3.1 Identified Protection Measures

The first set of questions that was asked to the interviewees had to do with identified protection measures. Figure 4.3.1.1 shows the answers to these questions. The bars show the number of instances that the protection type was used in each category, liquid, powder, or solid. The protection types were particle counters/detection, personal protective equipment, filters, airflow, and separation. Particle counters/detection referred to laboratories that had a particle counting device or some sort of detection method. Personal protective equipment refers to the use of gloves, masks, glasses, and any other equipment that protects the user. Filter refers to some sort of air filtration device, and airflow refers to use of a fume cupboard or some sort of suction device. Separation refers to the application of closed environments such as closed or separate rooms.

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[86] K. Schmid, B. Danuser and M. Riediker, "Swiss Nano-Inventory: An assessment of the usage of nanoparticles in Swiss industry", Institut universitaire romand de Santé au Travail, Lausanne, 2008.

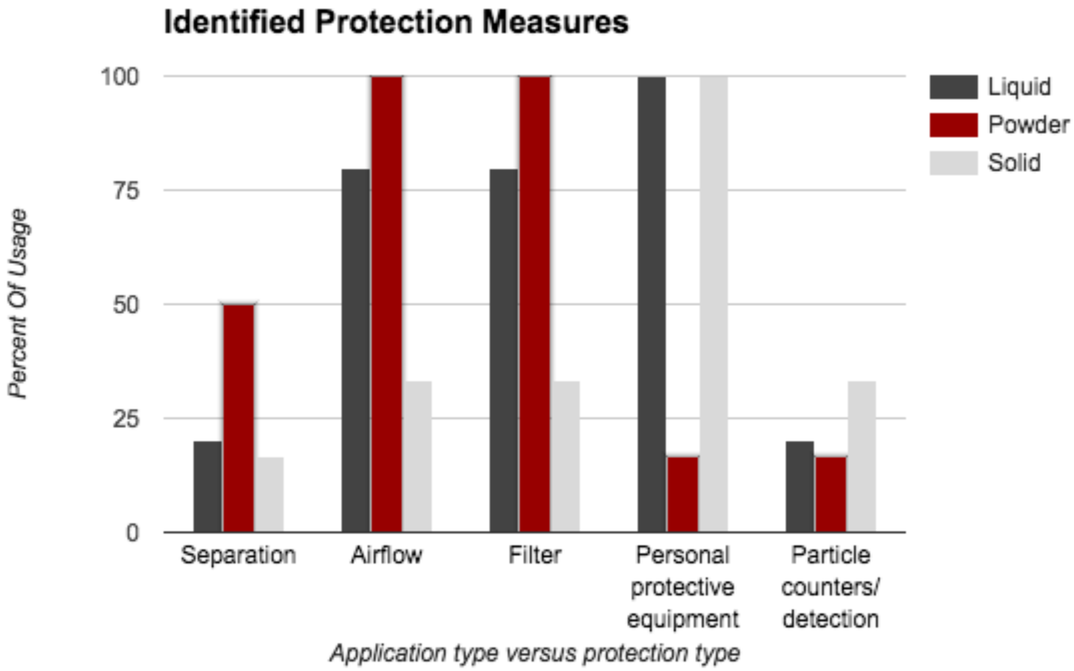

Figure 4.3.1.1: Identified protection measures

Figure 4.3.1.1 shows the percent of usage for each nanoparticle type, and shows the responses that we received when asking these questions. Between laboratories that use powders, 100 percent use airflow and filters, and only 50 percent use separation as a tactic. This figure also shows that overall, the most protection is used for powders and the fewest for solids. It should be noted that out of the responses, four laboratories used liquids, one used powder and liquid, five used powder, and six used solids. Airflow and filters are the most used methods among all three nanoparticle form factions. Separation and particles counters/detection are the least used methods among laboratories.

4.3.2 Individual Worker Protection

The second set of questions asked about the individual worker protections used when handling nanoparticles. This question was divided into three different categories: liquid, powder, and solid. The bars that are in different color categories show the instances of usage: gloves, glasses, fully closed clothing, half-open aspirations, breathing protection, and closed process. In this particular question set, there were five laboratories that dealt with liquid, six with powder, and six with solids.

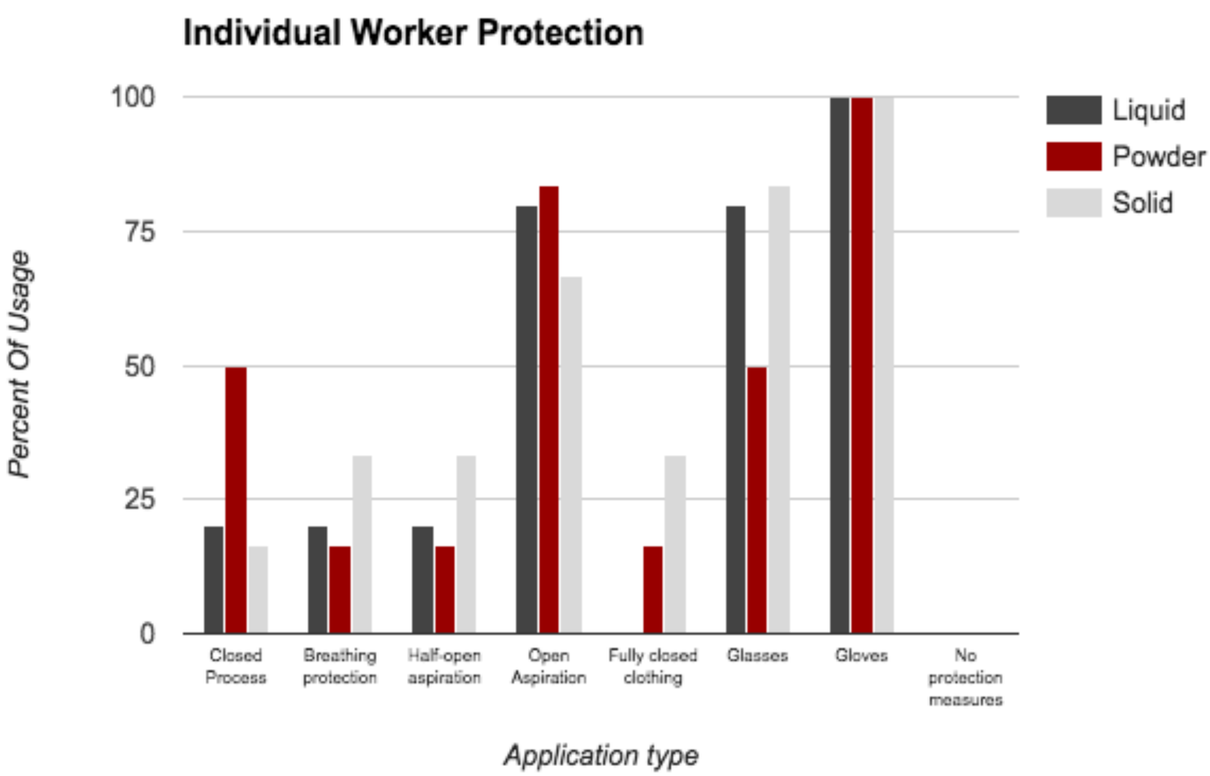

Figure 4.3.2.1: Individual Worker Protection

Figure 4.3.2.1 shows that 100 percent of the applications used gloves. The second most popular worker protection was open aspiration and glasses. The least used protection types were breathing protection, half-open aspiration, and fully closed clothing. Overall the protection for the user was used most for the powder.

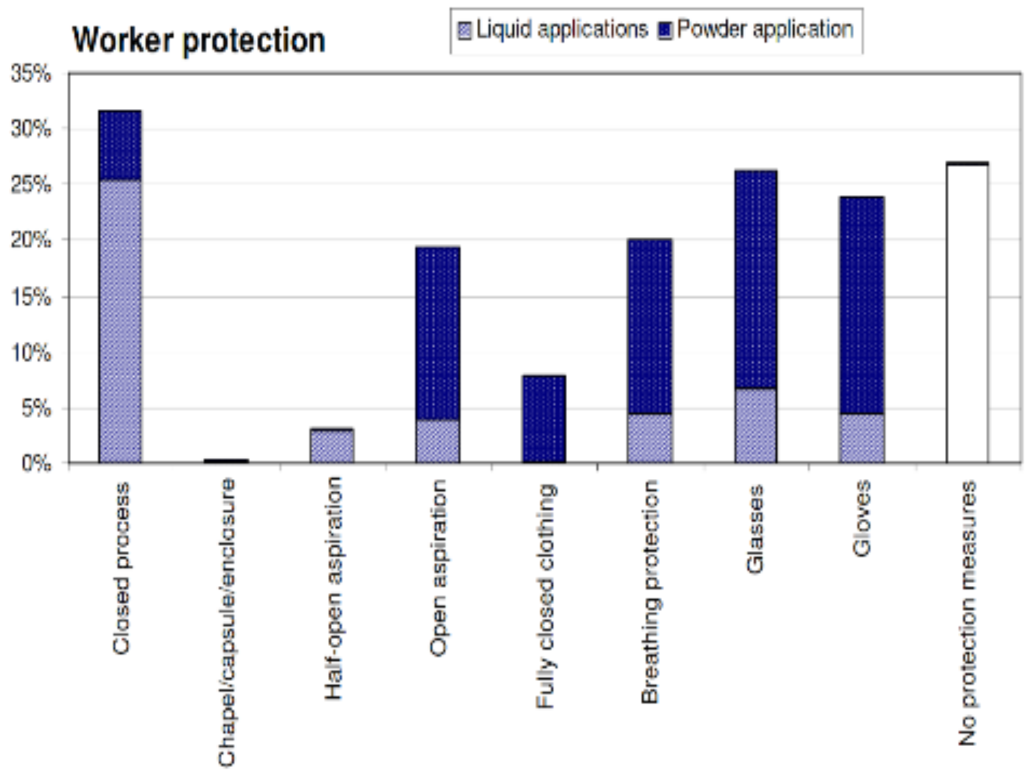

Figure 4.3.2.2: Worker Protection 2008 Study[87]

Figure 4.3.2.2 shows the results from the original study that took place in 2008. This has the same questions that we asked our interviewees. There are some changes in the percentages of the liquid vs. powder application. The sample size in the 2008 study was much larger than our sample size.

[87] Ibid.

4.3.3 Environmental Protection

The next set of questions asked about environmental protection. In this question a protection measure was considered to be any type of special waste treatment, pretreatment of the affluent, recycling for the process, general air recirculation, air filtration, and filtration of the exhaust air.

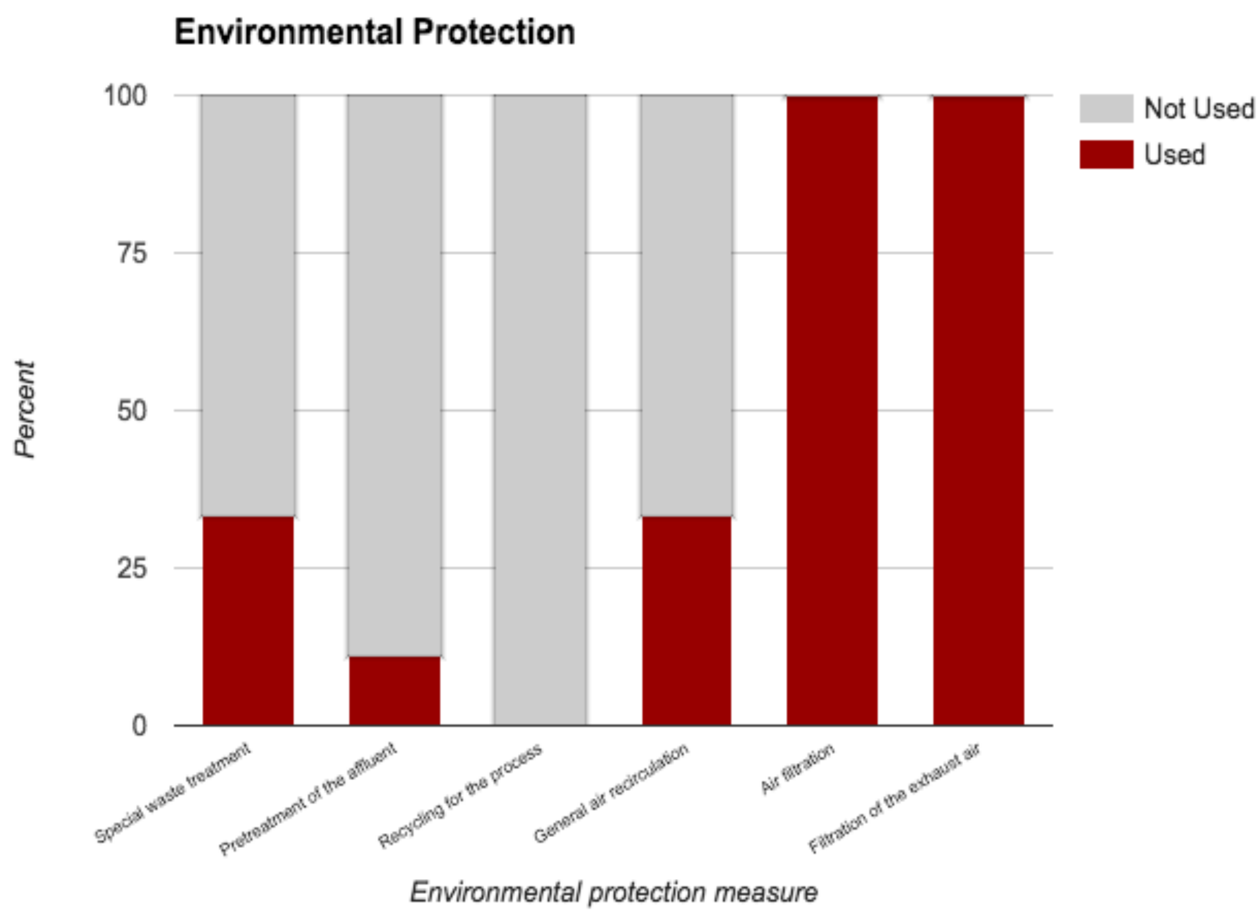

Figure 4.3.3.1: Environmental Protection

Figure 4.3.3.1 shows the environmental protection that was used by the laboratories. All of the laboratories used air filtration and filtration of the exhaust air, while zero used recycling for the process. One third of the participants used special waste treatment and general air recirculation.

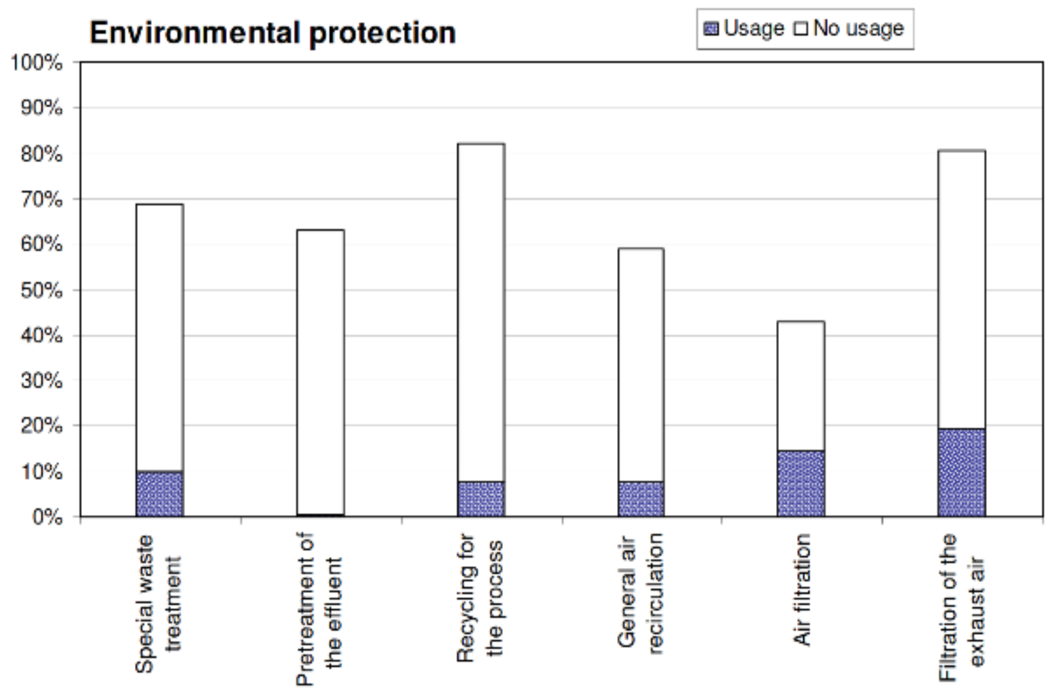

Figure 4.3.3.2: Environmental Protection 2008 Study[88]

Figure 4.3.3.2 shows the answers to the study that was conducted in 2008. This shows the percentage of usage of the same categories that our interview asked about.

[88] Ibid.

4.4 Discovered Problems

Each of the facilities that we visited has vastly different combinations of standard and non-standard safety equipment. For example, the same operation of suspending nanoparticle powder in a colloid might be done within a glove box, under a laminar fume hood, in a full-suit cleanroom, in a biological cabinet, or simply mixed out on a table without any safety enclosure. This points to a lack of knowledge on which equipment is efficient for nano-safety. In result, some facilities might be exposing themselves to unnecessary hazards, or overlooking potential improvements that might be readily implemented.

One common issue among facilities was the fear of unawareness. Although there was no worry for the researchers dealing with their own nanoparticles, it would become a problem if the people around them, who are untrained or unaware of the nanoparticle hazards, do not protect themselves properly, or improperly handle the nanoparticles. This is especially important at facilities that are not yet able to afford a separate nanoparticle room or building. Additionally, they might store, ship, and receive nanoparticles in the same process as other chemicals. From our interviews, we have heard stories in which this resulted in hazardous situations, so it is a real issue that requires addressing.

The training for dealing with nanoparticles ranged from very extensive to nearly nothing. Some laboratories used their regular training for both nanoparticles and everything else. For laboratories like this, a nano-specific training would be beneficial. It was also noted in more than one interview that users wanted to understand the specific health risks better. They felt as though they would benefit from having access to more information about nanoparticle risks.

4.5 Discovered Solutions

One of the problems we addressed was to increase the communication between facilities. By presenting ideal characteristics for nanoparticle equipment in a web-based format, researchers can make better selections for an ideal nanoparticle workplace. Secondly, we created safety posters to better inform people in the laboratory that are in close proximity to the workplace. The prospective audiences for our solutions are outlined in Figure 4.5.1.

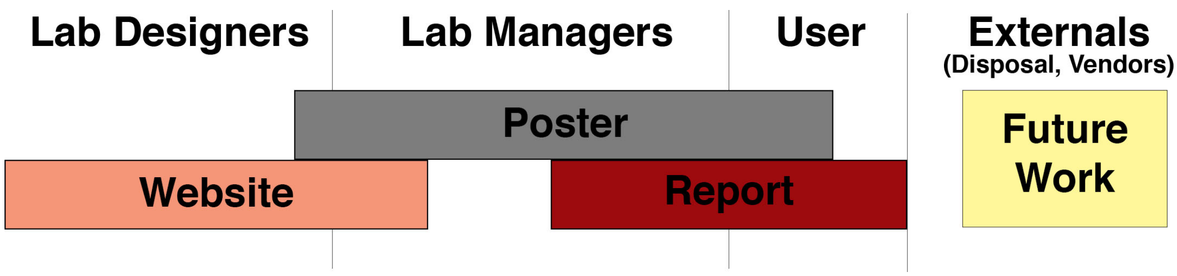

Figure 4.5.1: The beneficiaries of our solutions

Through our examinations of different facilities, it has become apparent which methods are more effective than others. As such, we designed a website that compiles the various effective implementations of nanoparticle safety equipment, as determined through our research. Each type of equipment is labeled depending on its usage for nanoparticle powder, liquid suspensions, and solid substrate applications. Through web-embedded 3D models, we present important characteristics that are necessary to make the product effective for nanoparticle processes. Additionally, we promoted existing company product models that fit these constraints. This way, researchers working with nanoparticles can make more informed decisions when purchasing or upgrading equipment.

A published document can be a useful resource for providing researched information to those who seek it. However, for users that are indirectly involved with nanoparticles, or simply unaware of the report, a more integrated solution is needed. Addressing this, we designed posters and graphics that can be placed in a laboratory. This effectively spreads vital information to lab participants, including that which provides awareness for hazard exposure and provides direction in preventing it. One of our initial creations was a hazard triangle for nanoparticles, that is derived from standard radiation and laser symbols. This additionally provides a basis for an official standardized nanoparticle warning triangle. We also designed a more informative danger sign, similar to standardized graphics used for other dangerous lab areas, such as lasers. To address the lack of knowledge of nanoparticles, we have created a poster that outlines what a nanoparticle is, and what hazards they can create. Another poster was created that showcased general guidelines for nanoparticle storage, handling, and disposal. To supplement this, we have provided a standard nanoparticle storage label that has space for all the important information about the nanoparticle. Both the posters and the website are discussed in the next section: *Chapter 5 Solutions*.

Chapter 5 Solutions

Through the course of our interviews and literature search we found multiple problems that needed addressing and focused on two of them. The first problem is the possible low awareness to the hazards of nanoparticles. Our solution to this was creating safety posters that can be used by any nanoparticle lab, and are available for free download online on a website that we developed. This website shows what ideal tools are recommended for work with nanoparticles along with a link to this report. These solutions are outlined more below.

5.1 Safety Posters

We have created posters for laboratory users to guide them into creating a safe work environment and information-based posters for laboratory visitors, students and the general public. These four posters are targeted at spreading awareness of nanoparticles, their benefits, and potential risks.

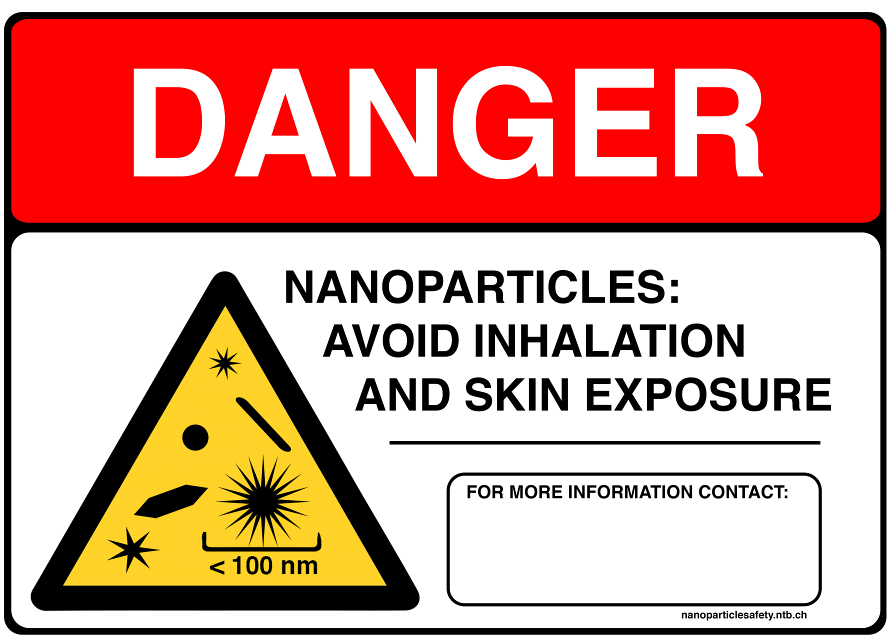

Figure 5.1.1: Nanoparticle Danger Sign

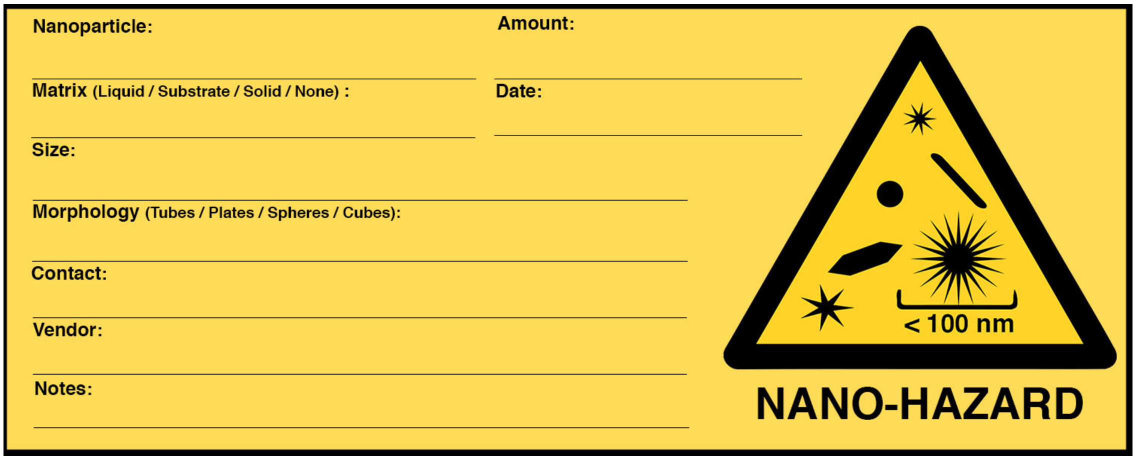

Figure 5.1.2: Nanoparticle Storage Label

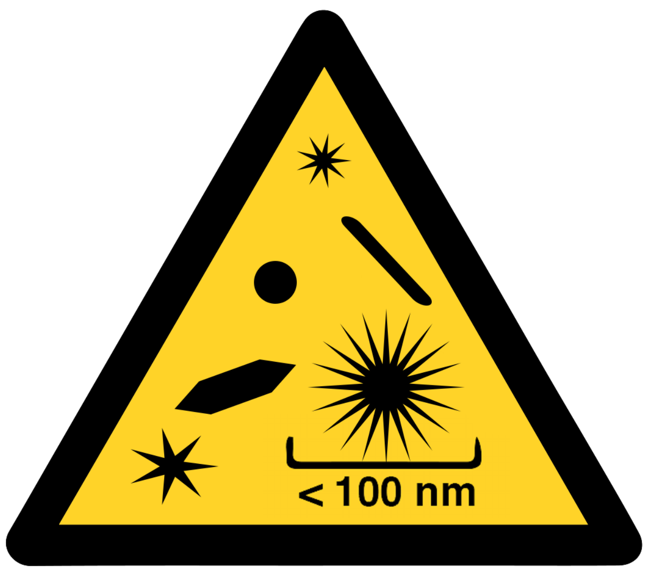

Figure 5.1.3: Nanoparticle hazard triangle

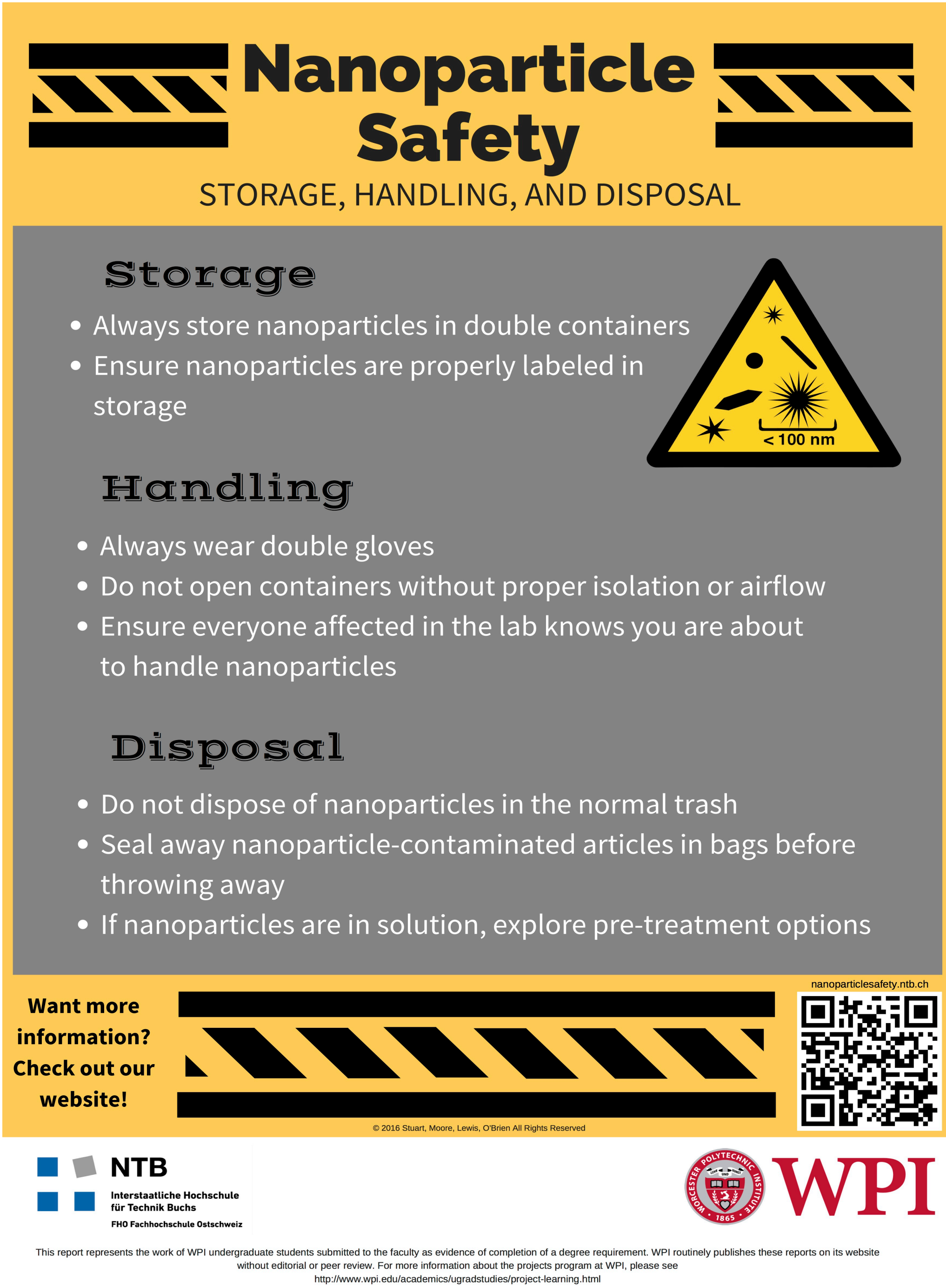

Figure 5.1.4: Nanoparticle Safety Poster

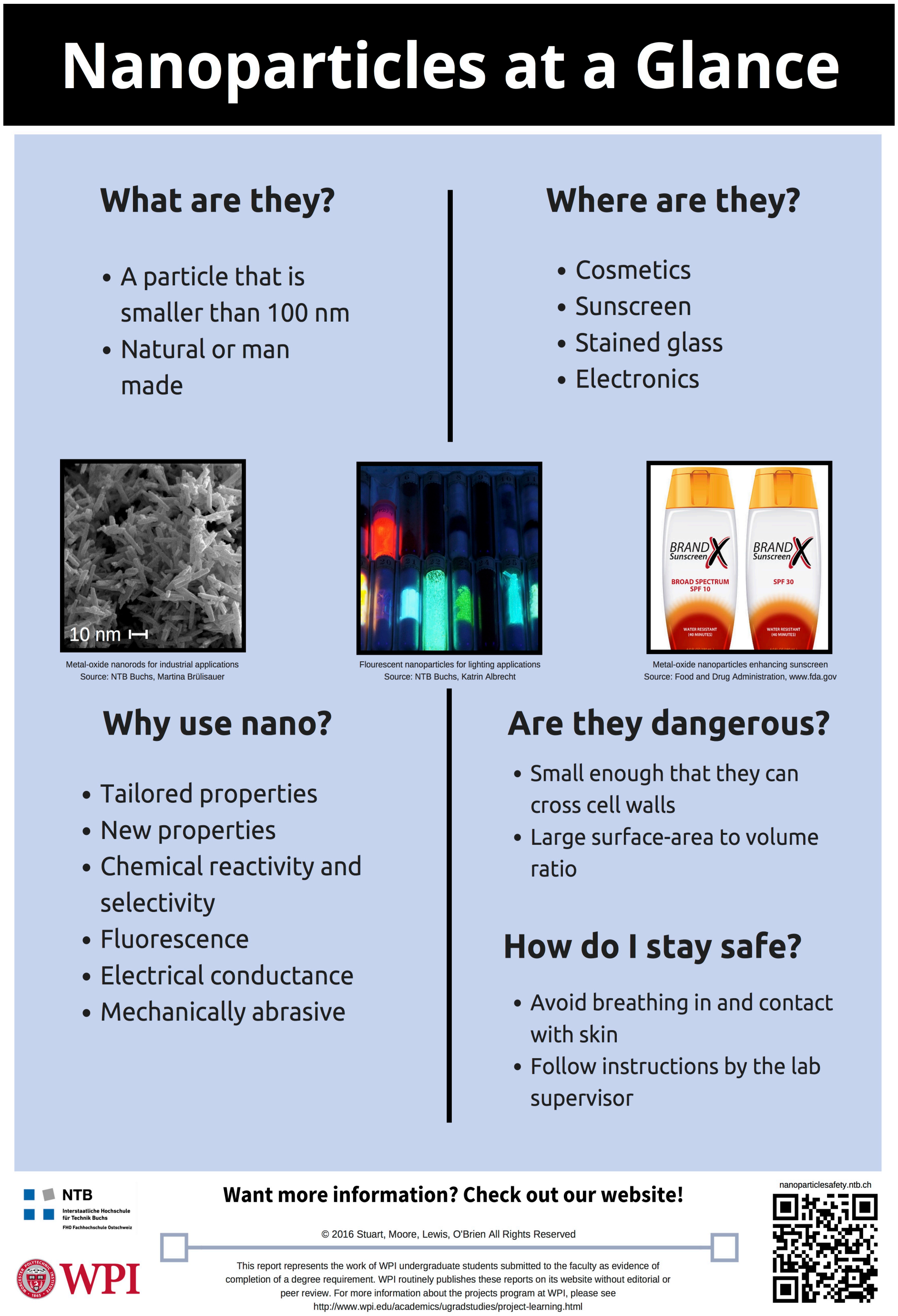

Figure 5.1.5: Nanoparticle at a Glance Poster

5.2 Online Nanoparticle Safety Tool

In order to provide practical information for direct improvements in nanoparticle safety, we created a website to showcase effective laboratory equipment. On the main equipment page, each item is listed with a picture and short description about its relevance to nanoparticle processes. Each includes a general price rating from one to five, and is labeled with its relevant nanoparticle applications: powders, liquid suspensions, or solid substrate. When one of these listed items is clicked on, a more detailed web page appears which provides a full description of safety research, and a 3-D model. This web-embedded model can me moved and rotated to show annotations associated with parts of the object. With this, product attributes necessary for safe nanoparticle handling is made apparent to the viewer. Fitting these criteria, we also present various company product examples by linking to their official online catalogs.

With solutions created in three formats, a secondary usage of the website was to provide a base network that would more effectively link our solutions together. Online we included download links for our posters, and directions to the database containing a copy of our report. Likewise, our posters and report referenced back to the website. This way, if one of our resources is used, the other two are also made available. Below are a few screenshots from our website. They showcase the formatting and layout of various pages, all of which can be viewed in detail on the website.[89]

[89] "Innovating Nanoparticle Safety," hosted by NTB, nanoparticlesafety.ntb.ch, Oct. 12, 2016

Figure 5.2.1: Front page of the website

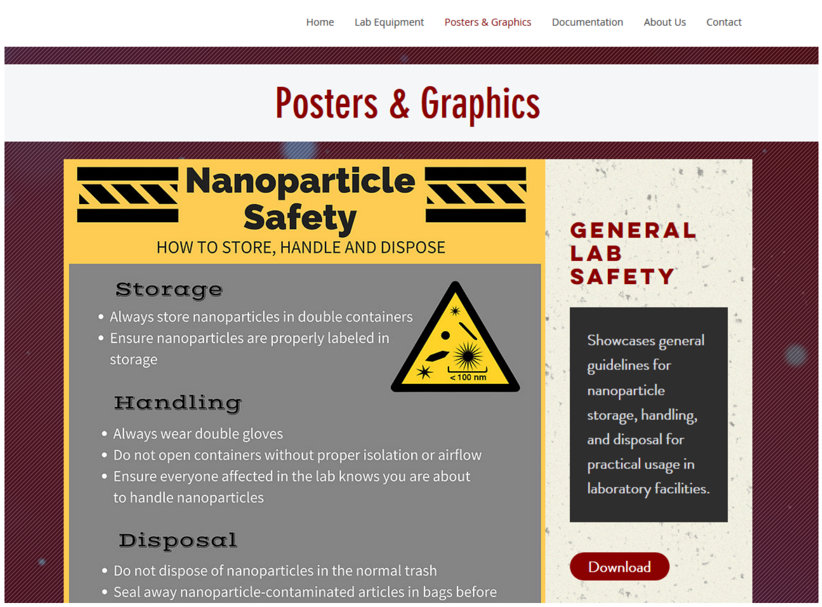

Figure 5.2.2: Posters & Graphics page

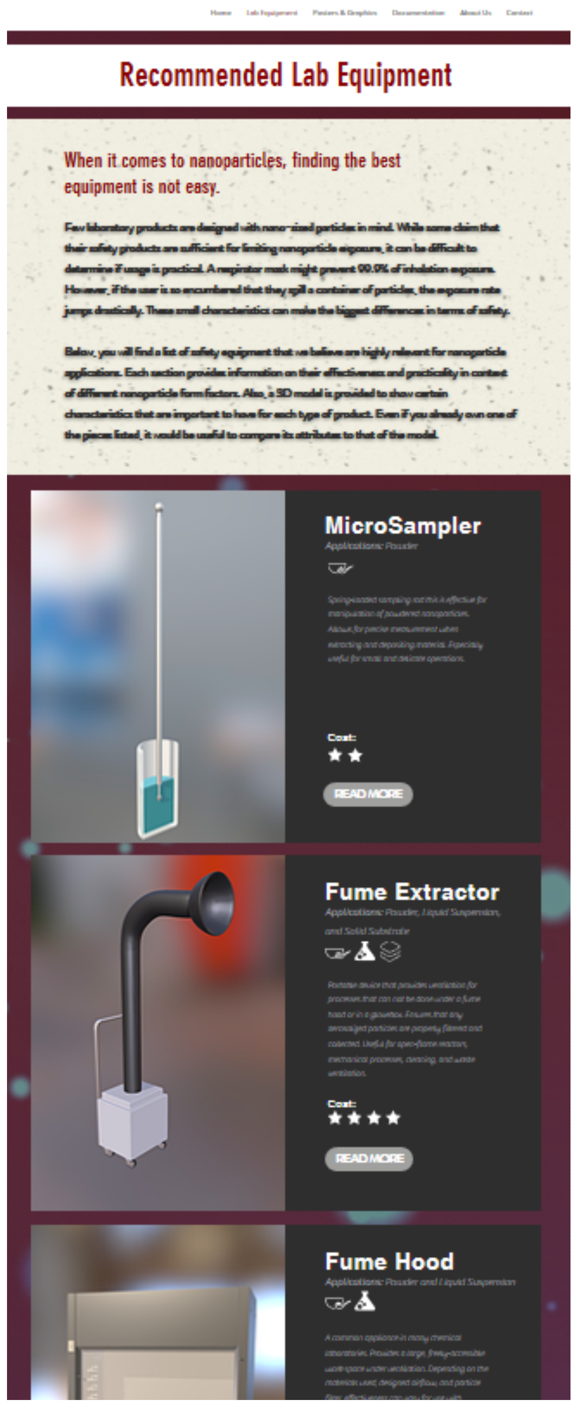

Figure 5.2.3: Recommended Lab Equipment page

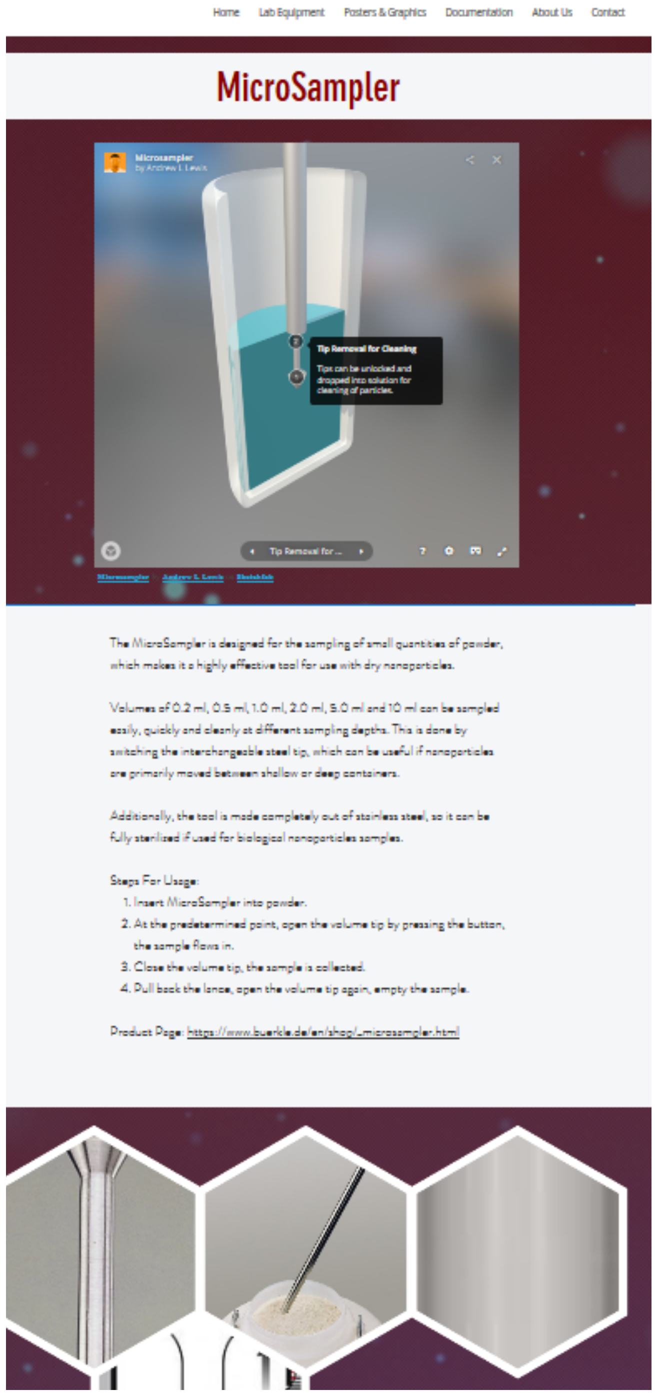

Figure 5.2.4: More information is provided for each item on its own page

Chapter 6 Recommendations for Future Work

During our project, we identified multiple problems in the nanoparticle industry that we could not address. They are presented here as possible focuses for future IQPs by WPI and nanoparticle research in general.

6.1 Interviewing of Toxic Waste Disposal Companies

Many facilities that we visited worked with nanoparticles to create products, learn about their future developments, and create tools to better detect them during the synthesizing process. However, all these facilities had little to no knowledge of what happened when the nanoparticles they been working on are taken to chemical waste facilities as toxic waste. Due to time constraints and no prior connections with these facilities we were not able to gain personal feedback from any disposal companies. While certain laboratories may be handling nanoparticles as safely as they can, most of our information on disposal comes from articles and journals rather than interviews. For future Interactive Qualifying Projects (IQPs, the junior-year degree project at WPI) this should be a topic to be looked at further.

6.2 Guidelines for Filtration Systems

Filtration systems are essential for nanoparticle safety as the largest concern is inhalation. They are used on glove boxes, fume hoods, clean rooms, and in incineration plants. The problem is that there is little known about how well filtration systems filter out nanoparticles, leading to a dearth in their regulation. Many filtration systems are simply unable to capture nano-sized particles, while others can only effectively capture certain nanoparticles, depending on their chemical properties. There is also concern that nanoparticles might harm filtration systems, even the ones that cannot filter out the tiny particles. Researchers would feel much safer if there were actual guidelines for the filtration systems for nanoparticles and with proof that those systems are good enough. An IQP could be conducted to look into such guidelines and consolidate the existing research.

6.3 Packaging/ Shipping Practices and Regulations

Current packing and shipping regulations for nanoparticles seem to be lacking. Many research laboratories are receiving packages of carbon nanotubes and silver nanoparticles in small zip lock bags. The particles are floating around in their packaging with no real sealant to prevent leakage. This makes us wonder about the lack of regulation in shipping and packaging practices for these particles. Most of the interviewees had either shipped or received nanoparticles in some way, but there was no obvious standard in each shipper's methods. The unanimous consensus left us wishing we had more time to look into package procedures for toxic materials and we think this could be a good area to cover in the future.

6.4 Safety in the Mass Production of Nanoparticles

Everyone we interviewed during our project worked with a tiny amount of nanoparticles at one time, usually on the order of milligrams. This makes dealing with safety easier, as the exposure to nanoparticles would be low. However, this is not always the case; there are companies that mass-produce nanoparticles, such as silver nanoparticles or carbon nanotubes, for various industry applications. It is concerning to consider what might happen if one of the factories overlooks the hazards of the nanoparticles and does not take the adequate safety precautions. This IQP has shown us that much of the safety guidelines for nanoparticles are left up to the implementer. Some people do not care about safety unless they are forced to, leading to a wide range of interpretations of the guidelines. Future IQPs should investigate these shortcomings and ways to improve safety guidelines for industry.

6.5 Nanoparticle Safety Training

Safety training for nanoparticles is often lumped together with the normal laboratory safety training. A future project could create a safety-training tool that could be used at various facilities or focus on one facility. Potential ideas for this project could include a series of slides that would teach standard nanoparticle handling procedures. Information could be added to the general safety procedures targeted to people who are not directly working with nanoparticles but are working in their proximity. This tool could also include a checklist to make sure all the important topics are covered during training to make sure all the important topics are covered during training. Additionally, the tool could include a quiz that could be taken upon completion of the training to prove proficiency.

6.6 Collection of Reliable Nanoparticles Safety Sources

One of the problems many interviewees ran into when working with a brand-new nanoparticle was the difficulty of finding reliable information about how to handle it. Sometimes the nanoparticle has never been worked with or studied before, but there are plenty that have. However, there is no concise database presenting the safety concerns and practices for each individual nanoparticle. Future projects could potentially work on this. However, this could become an onerous amount of work, as there are many different nanoparticles. The database would also need to be constantly updated, as it would become outdated within a year of its completion.

Many of these proposed project problems come from what we did not have the time to investigate, or from concerns voiced by multiple interviewees. While all of these problems can be addressed by their own projects, the solutions to them could easily be added to the website that was developed. Keeping the findings of these projects consolidated would continue to make the task of instituting safety guidelines for nanoparticles simpler.

Authorship Page

As a team, we collaborated in writing, editing, and formatting the entirety of this report. Our method for creating this report utilized each team member for each section. We also edited our final content in a group. This method for crafting our project allowed all members of the group be actively involved in the writing. This also allowed us to write the report in one cohesive voice, as opposed to conventionally breaking up each portion and potentially making a report that reads as though it was stitched together rather than crafted by a group. All group members were content with the distribution of work and the method by which we created this project.

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Appendix A Interview Questions

Note: We asked only the questions that pertain to each interviewee.

Opening

- Can we record this for future study? May we take photos? Video?
- What do you do at (insert company here)?
- What specific nanoparticles do you use?
- What applications do you use them for?
- How interested are you in learning about the safety procedures of other laboratories?
- What do you know about nanoparticle safety?

Quantitative Information

- What is the size of your institution?
- How many people work directly with nanoparticles?
- What protection types do you use for specific application types? (see Fig A.1)
- What protection types do you use for individuals? (see Fig A.2)
- What environmental measures do you implement for nanoparticle hazards? (see Fig A.3)

Synthesizing

- Could you walk us through your procedure for synthesizing?
- What do you do with the nanoparticles once you are done making them?

Working With

- Could you describe what you do with the nanoparticles?
- What tools or improvements to the workspace would you like to see?

- There is a new nanoparticle you want to work with/create, how do you go about creating safety guidelines for the handling, storage, and disposal of it?

Disposing of

- How do you dispose of nanoparticles? Why that way?
- How do you dispose of items that come in contact with the nanoparticles, such as gloves or containers?
- What happens to the nanoparticles when they leave your care?

Selling/Shipping

- To whom do you sell/ship your nanoparticles?
- What types of nanoparticles do you sell/ship?
- Could you run us through your packing procedures?
- Do you include safety information in the package? Why/why not?

Storage

- When you are not working with the nanoparticles, where/how do you store them?
- What do you consider when storing a new nanoparticle?
- How do you document storage of your nanoparticles?

General Safety

- How are your guidelines different from your governments? Why?
- Are there any parts of your guidelines that you feel could be improved?
- Do you feel held back by your safety procedures?
- Do you believe that nanoparticles can be dangerous?
- During your work with nanoparticles, where do you have to take the most caution?

Future of Safety

- What would you like to see from new guidelines?
- What would your ideal form of implementation be?

Comments about this Interview

- Are there any topics or areas that you would like to talk about that we didn't already discuss?
- Are there any questions that you have for us?

Table A.1: Identified Protection Measures

Application type versus protection type	*Number of companies identified*	*Separation*	*Airflow*	*Filter*	*Personal protective equipment*	*Particle counters*	*Other protection*	*No protection*
Liquid								
Liquid & powder								
Powder								
Solid								
Type not declared								
Type not known								
Total								

The protection types were:

- Separation (the application of closed environments like closed machines or separated rooms);
- Airflow (the use of a fume cupboard or a suction device);
- Filter (the use of some air filtering system);
- Personal protective equipment (the use of masks, gloves, glasses etc.).

Table A.2: Individual Worker Protection

Application type	Closed Process	Breathing protection	Half-open aspiration	Open Aspiration	Fully closed clothing	Glasses	Gloves	No protection measures
Liquid Powder								
% /w Application for Liquid * % with Application for Powder **								

*Out of total number of companies using liquid applications _____

**Out of total number of companies using powder applications _____

Table A.3: Environmental Protection

Environmental protection measure	***Used***	***Not Used***
Special waste treatment Pretreatment of the affluent Recycling for the process General air recirculation Air filtration Filtration of the exhaust air		
Total		

The protection measures include:

- Special waste treatment (own specialized treatment to dispose of waste)
- Pretreatment of the affluent (treating particulate matter to inoculate them before sending them to a waste management facility)
- Recycling for the process (recycling of the particulate matter)
- General air recirculation (circulation of air within a containment)
- Air filtration (filters capable of accumulating particulate matter)
- Filtration of the exhaust air (filters to collect particulate matter before releasing the air to the environment)

Appendix B Interview Responses

Disclaimer: These responses are not quotes, and have been paraphrased to single out important information. Some questions are tailored to the interviewee, and non-applicable questions are omitted.

Interview 1

1. How do you work with nanoparticles?
Works with nanoparticles while they are in a bound state (liquid, solid, polymer). If received as powder they are put into a matrix as soon as possible. Focuses on studying the effects the particles have on the material properties of substances.

2. If you synthesize, could you walk us through your procedure for synthesizing?
Rarely synthesizes nanoparticles, and there is no fixed process as most are different.

3. You just synthesized a brand new nanoparticle, what do you consider before working with it?
The first step when receiving a nanoparticle is to get information from the supplier and other reliable sources about how to work with it. Once he has come up with what safety measures he must take, he has to get approval from a secondary source (another chemist) to make sure they are good enough.

4. What is the size of your institution?
Approximately 30.

5. How many people work directly with nanoparticles?
5-6 people

6. What specific nanoparticles do you work with?
Metals, ionic, salt-like, ceramics, carbon nanotubes, and polymers. Large variety.

7. For what are they being applied?
Studying the physical properties: mechanics, electronics, and optical effects.

8. What protection types do you use for specific application types?
Glove box for powders, flume hood for most others.

9. What protection types do you use for individuals?
Respiratory mask, gloves, glasses and full suit

10. What environmental measures do you implement for nanoparticle hazards?
Air filtration

11. Could you describe what you do with the nanoparticles?
He does not work with powders himself, but for liquids he first prepares everything he needs for the task, as well as review any specifics on how to deal with the particles. Decides on how much to inform other people, does he need supervision, or should he be isolated? Prepares waste containers. Tries to finish in one day if possible, but if not, he stores it away with control and information systems and safety labeled in such a way that other people would not mess with it.

12. What tools or improvements to the workspace would you like to see?
An effective particle counter

13. When you are dealing with nanoparticles, when do you have to take the most precautions?
In the powder state, but otherwise, when working with volatile substances or when there is high probability of a spill.

14. How do you dispose of nanoparticles?
When he has specific information, he uses it, but otherwise he stores them in a labeled flask until they are sent to a chemical disposal company. Tools he works with are cleaned, usually rinsed really well before the standard cleaning procedure. If particularly contaminated, it is sealed into a polymer or epoxy and then thrown away. Gloves and stuff are put into plastic bags, then into a special container, but has no idea what happens to them.

15. What happens to the nanoparticles when they leave your care?
No idea

16. What are the hazards of improper nanoparticle disposal?
Not a lot of observable risks, so he compares it to asbestos as it can have similar long-term effects.

17. Do you think there is any chance of contamination with your current disposal methods?
Hopes not, but is always mindful of the risk. There is always a potential, as there is little to no way to know how effective their procedures are.

18. When you are not working with the nanoparticles, where/how do you store them?
Liquid or solids are labeled in a container inside another container. They are stored in a chemical storage closet that only certain people have access, such as chemists.

19. What do you consider when storing a new nanoparticle?
Separate by type and reactivity, similar to not putting acid with base. There is a green folder nearby with all relevant info.

20. How are your guidelines different from your governments?
Difficult to say. They regularly browse the legislation, but there is little in the way of concrete governmental guidelines for nanoparticles.

21. Are there any possible shortcomings in your guidelines?
Worried about the other people who might come into contact with the nanoparticles or work in the same room as them, as there is no formal training or instruction to them about nanoparticles.

22. Do you feel hindered by your procedures? What could make them better and safe?
No, but would feel safe with a better way to know that their guidelines are effective.

23. During your work with nanoparticles, where is the greatest threat?
That other people might be uniformed and are working in the same lab.

24. What would you like to see from new guidelines?
A solid procedure on how to prepare for a new nanoparticle. What things does he have to consider? Which sources are reliable? Maybe a consolidated resource of a bunch of nanoparticles.

Interview 2

1. What do you do at your facility?
Organizes and runs the clean room. Oversees safety procedures and training.

2. What specific nanoparticles do you use?
Carbon nanotubes, boron nitride, graphene, iron, nickel, gold, ferrozine.

3. What applications do you use them for?
Electronic applications. They look at electrical transport properties in solids. Integrated circuits. CNTs can have both mechanical and electrical properties for research.

4. How interested are you in learning about the safety procedures of other laboratories?
Interested in seeing what other laboratories and facilities are doing.

5. What is the size of your institution?
350 people

6. How many people work with the nanoparticles?
30 people

7. What protection types do you use for specific application types?
Cleanroom, airflow recirculation, personal protections

8. What protection types do you use for individuals?
Masks, goggles, full closed suit, 2 pairs of gloves, P3 breathing filter

9. What environmental measures do you implement for nanoparticle hazards?
Separation of waste that is taken by a special group/ company. Any chemical waste has a cancerous GHS sticker and is double contained.

10. Could you walk us through your procedure for synthesizing?
Chemical vapor deposition. Gas chamber with high pressure and heat are used to create CNTs and grow a forest of them on a substrate. Metal or quartz in a run vacuum chamber with a mass

flow controller that is pressure controlled and run by a software system. Uses a carbon - methane - hexane gas.

11. What do you do with the nanoparticles once you are done making them?
They send them to other facilities interested in material properties. They can be used in product development and have a high elasticity.

12. What do you do when working with a new nanoparticle?
The hazard department has a database. Material is tracked via barcode, with quantities and the items location. Everything is regulated by safety datasheets. No material is allowed with all of this information, registration and safety training. The department must also know if the material is classified as hazardous through breathing, indigestion or through the skin.

13. Could you describe what you do with the nanoparticles?
No powders are allowed. Always in a matrix or stuck onto a substrate. Wafers are carefully handled so that nanoparticles are unable to detach and become a hazard.

14. What tools or improvements to the workspace would you like to see?
Particles counters that can detect below 100 nanometers.

15. When do you have to take the most precautions in this process?
Most precaution comes when they open the tool because the atmospheric pressure causes turbulence and a potential discharge of nanoparticles.

16. How do you dispose of nanoparticles?
Two different bins. One for samples and sharp objects and the other for everything else. Both bins are double contained, go to chemical waste and have GHS labels on them.

17. How do you dispose of items that come in contact with the nanoparticles, such as gloves or containers?
In the rubbish bin

18. What happens to the nanoparticles when they leave your care?
Not sure.

19. What types of nanoparticles do you sell/ship?
Varies

20. Could you run us through your packing procedures?
Double contained in boxes. Shipped by normal Fedex /postal service.

21. When you are not working with the nanoparticles, where/how do you store them?
Nothing is stored in the cleanroom. Double contained in plastic boxes.

22. How do you document storage of your nanoparticles?
Raw material has a bar-code and is tracked. Samples are tracked by the individual researchers.

23. How are your guidelines different from your governments? Why?
Aware of standards. Holds a yearly workshop.

24. Do you feel hindered by your safety procedures?
Not at all. Aware of the risks, but happy to protect.

25. During your work with nanoparticles, where is the greatest threat?
When cleaning, never clean by scraping, always with liquid.

26. How are the people who work with nanoparticles trained?
Anyone working with nanoparticles gets specific training. Other are made aware of the dangers and know when to/ not enter the nanoparticle laboratory space. Training consists of to online presentations, written documentation, and a training test. Only then are they allowed to go into the laboratory and see the safety procedures.

Interview 3

1. What do you do at this facility?
This is a technical university. When it comes to nanoparticles they product devices and turn properties of materials into devices. They also create new devices and transistors.

2. What specific nanoparticles do you use?
Carbon nanotubes, catalysts, bio-based proteins, epoxies.

3. What applications do you use them for?
They produce devices on substrates. Electric transistors, sensors that measure gas, strength, temperature and pressure.

4. What is the size of your institution?
25,000 people

5. How many people work with the nanoparticles?
5 people

6. What protection types do you use for specific application types?
They do no work with free particles. The nanoparticles the do use are used in a separate laboratory with a fume hood.

7. What protection types do you use for individuals?
Gloves, goggles, coats and masks.

8. What environmental measures do you implement for nanoparticle hazards?
Any potential environmental risk would be implemented at other facilities they use.

9. Could you walk us through your procedure for synthesizing?
Catalysts are places in a special oven, heated to 150 ºC, exposed to CH_4, grown, contacted with electrodes, then the electrical properties are measured.

10. What do you do with the nanoparticles once you are done making them?
They are used for testing. We make contact with their electrical properties.

11. What tools or improvements to the workspace would you like to see?
Particle counters directly next to the oven.

12. There is a new nanoparticle you want to work with/create, how do you go about creating safety guidelines for the handling, storage, and disposal of it?
They rarely work with new particles. But no matter the particle they are always handled as dangerous material. There are studies on the safety and functionality of the substance and they handle it with care.

13. How do you dispose of nanoparticles?
They don't personally dispose of particles. They are brought to a group that disposes for them. Most particles are fixed on substrates or in devices.

14. How do you dispose of items that come in contact with the nanoparticles, such as gloves or containers?
They are locked in containers, and then placed in plastic boxes. The department sets the guidelines.

15. To whom do you sell/ship your nanoparticles?
They don't sell or ship nanoparticles.

16. When you are not working with the nanoparticles, where/how do you store them?
Liquids are placed in fridge in a chemical lab. Chips are stored in the clean room and placed in special boxes designed to keep dust out.

17. How do you document storage of your nanoparticles?
Nanoparticles are diluted and labeled. The labels contain information like the date, the owner, the contents and concentration of material. All students take care of their own personal samples.

18. Do you have specific guidelines that you follow?
Guidelines are set by the cleanrooms they use. They receive a general introduction training as well as host a yearly safety meeting.

19. Are there any possible shortcomings in your guidelines?
Not that they know of but it is always possible.

20. Do you feel hindered by your safety procedures?
Not by physical restrictions, but time restrictions. The team-operated processes are mandated by the clean room. So, they have to have the go ahead to work on certain processes. Sometimes this takes months to approve.

21. During your work with nanoparticles, where is the greatest threat?
Doesn't feel working with nanoparticles are dangerous because they follow the rules and regulations that are set. The only risk of exposed is by accidental.

22. How are the people who work with nanoparticles trained?
When you join the clean room you are showed safety slides, given reading material to read and have to take a quiz. A certain score must be obtained to gain access into the laboratories. People that are doing specialized work receive more training based on their needed skills.

23. What would you like to see from new guidelines?
Doctors and biologists giving more research on specific dangers from nanoparticles. Also, realistic conditions on what to do if their is an accident in the lab. Overall, more data and feedback on what are the potential causes for harm working with nanoparticles.

Interview 4

1. What do you do at your institute?
PhD Student working with dynamex of nanoparticles. Liquid interfaces and collaborates synthesis.

2. What specific nanoparticles do you use?
Silicon, silica, PMA, silicon PEC shells, gold particles

3. What applications do you use them for?
Self-assembly of liquid interfaces and systems with spaces greater than nanopillars. They also deal with the motion of particles and particle concentrations.

4. How interested are you in learning about the safety procedures of other laboratories?
Personally, yes. If not too dangerous.

5. What is the size of your institution?
25,000 people

6. How many people work with the nanoparticles?
2 people

7. What protection types do you use for specific application types?
For the poly uses laboratory gloves and fume hood. For liquids uses normal bench and fume hood. For small metals uses mask.

8. What environmental measures do you implement for nanoparticle hazards?
Don't wear the contaminated gloves and use the doorknob.

9. Could you walk us through your procedure for synthesizing?
They don't synthesize

10. Could you describe how you work with the nanoparticles?
Put on laboratory coat, gloves. Uses the particles under the fume hood, if density is too low, transfers into the fume hood, measure the nanoparticles and completes the work.

11.What tools or improvements to the workspace would you like to see?
I do not need improvements.

12. There is a new nanoparticle you want to work with/create, how do you go about creating safety guidelines for the handling, storage, and disposal of it?
I do not follow any particular protocol when dealing with new nanoparticles.

13. How do you dispose of nanoparticles?
They give the liquids to the laboratory manager and they give it to a disposal center.

14. How do you dispose of items that come in contact with the nanoparticles, such as gloves or containers?
If it is very volatile than they use glass containers. If it is aqueous than use plastic containers.

15. What happens to the nanoparticles when they leave your care?
I don't know what happens when nanoparticles leave our care.

16. To whom do you sell/ship your nanoparticles?
A university in Germany

17. What types of nanoparticles do you sell/ship?
All of the ones that we work with

18. Could you run us through your packing procedures?
Label the nanoparticles, fill out a form for the mail that informs them it is a hazardous material and then the company he works at does the rest.

19. Do you include safety information in the package? Why/why not?
It says do not eat/ inhale.

20. When you are not working with the nanoparticles, where/how do you store them?
They are stored in a sealed plastic container in a cupboard

21. How do you document storage of your nanoparticles?
We don't document nanoparticles.

22. How are your guidelines different from your governments?
I don't know what the governmental guidelines are

23. Are there any possible shortcomings in your guidelines?
I do not think so.

24. Do you feel hindered by your safety procedures?
No

25. During your work with nanoparticles, where is the greatest threat?
We receive them in a dry form; sometimes you do not know how sticky or agglomerated the dry particles are. Sometimes they blow off when getting transferred, they give irritation to my nose when this happens.

26. How are the people who work with nanoparticles trained?
We have no special training. We use the general safety training.

27. What would you like to see from new guidelines?
I will come back to this question (when we followed up they had nothing to add here).

28. Bonus: "We will give you a copy of our interview"
To be honest, he will not read your report. He's just too busy and the company he works for wouldn't put me in contact with anything harmful anyway. This all isn't relevant to me.

Interview 5

1. What do you do at here?
Ph.D. Student trying to disperse nanoparticles into bitumen for asphalt.

2. What specific nanoparticles do you use?
Iron Oxide 20-300 nm

3. What applications do you use them for?
Once dispersed in the asphalt, the iron oxide can be heated through induction, melting and refusing the bitumen, fixing micro cracks in the road.

4. How interested are you in learning about the safety procedures of other laboratories?
A lot, he wants to make sure it is perfectly safe, not just 'probably safe'.

5. What is the size of your institution?
25 people in his group.

6. How many people work with the nanoparticles?
Only him at this institution.

7. What protection types do you use for specific application types?
Small volumes: Laminar flow hood. Large volumes: glove box with HEPA nanofilter.

8. What protection types do you use for individuals?
Two pairs of gloves, laboratory coat, goggles.

9. What environmental measures do you implement for nanoparticle hazards?
Filter it out of the air, then the air goes to a separate division at the institution, who deals with it. Unsure what happens next.

10. Could you walk us through your procedure for synthesizing?
Used to do co-precipitation, but now mainly buys it in bulk.

11. Could you describe what you do with the nanoparticles?
Iron Oxide is hydrophilic, but it must be hydrophobic to be dispersed in bitumen. He coats the Iron Oxide to do this, working with them in flasks and handles with spatulas. Traps nanoparticles with magnet to keep them from escaping during solvent transfers.

12. What tools or improvements to the workspace would you like to see?
The institution needs actual equipment to deal with nanoparticles, as well as a particle counter. The table is tough to clean as it is rough.

13. How do you dispose of nanoparticles?
Special canister for nanowaste that goes to chemical disposal

14. How do you dispose of items that come in contact with the nanoparticles, such as gloves or containers?
Gloves are surrounded with dampened tissue, put in a plastic bag, then sent to chemical disposal.

15. What happens to the nanoparticles when they leave your care?
No clue.

16. To whom do you sell/ship your nanoparticles?
Receives nanoparticles in various ways: plastic container, inside a box, in a bag. Sometimes just loose in the bag, and visibly a powder.

17. What types of nanoparticles do you sell/ship?
Receives iron oxide

18. Do you include safety information in the package? Why/why not?
Inconsistent whenever he receives it. Sometimes it is below the particles, or no hazard labels on the box.

19. When you are not working with the nanoparticles, where/how do you store them?
At the institution there is a random box with a key only three people have access to, but they don't use it anymore as they don't store nanoparticles there anymore. At a partner institution they are kept in ventilated drawers specifically for nanoparticles.

20. How do you document storage of your nanoparticles?
There is a database with the location of the nanoparticles, organized by box# and letter distinguishing a shelf.

21. How are your guidelines different from your governments? Why?
No Clue

22. Are there any possible shortcomings in your guidelines?
Want is a better way to judge how effective the safety measures are.

23. Do you feel hindered by your safety procedures?
It is very difficult to safely clean up sometimes.

24. During your work with nanoparticles, where is the greatest threat?
Opening the bottle and moving the nanoparticles with the spatula

25. How are the people who work with nanoparticles trained?
"Nano-Guy" at partner institution personally teaches people in his group about nanoparticles and the safety procedures. He has a checklist to make sure he covers everything. Other people around him have are not trained and have no clue, especially the ones at the primary institution.

26. What would you like to see from new guidelines?
Disposal and filtration guidelines, so he can gauge how effective his are.

27. What would your ideal form of implementation be?
A sheet or checklist for proper safety training. A poster put up in the laboratoryfor people not familiar with nanoparticles, something clear and simple.

Interview 6

1. What do you do here?
Consulting mainly, is the bridge between research and market. New materials and technologies come to this company. There are two ways to do things "Bottom Up" come to our company when you have a new idea and then we research to see if the market is there. The second case is "Top Down" this is when we know there is a need in the market for something and then we look for a product to fill the need. All of these projects are based on new materials or hybrids, nano or not nano.

2. What specific nanoparticles do you use?
Doesn't use but consults for companies that work with: Metal oxide particles, ceramic nanoparticles used for reinforcing, polymeric nanoparticles for containers.

3. How interested are you in learning about the safety procedures of other laboratories?
Very much, one of the big problems is there are not good SOPs (Standard Operating Procedures) for nano laboratories and each laboratory does different things. Because of this we end up having a lot of "Round-robin testing" which makes comparing results very difficult. This makes inter laboratory exchange of information very important.

4. What is the size of your work place?
5 people

5. How many of your projects have worked with nanoparticles?
Worked on more than 12 years of projects. 4 to 5 are nano-related each year so the math would make it about 50.

6. What tools or improvements to the workspace would you like to see?
1st point: Improved Characterization. What is or isn't a nanomaterial, characterization methods are very difficult to apply. Sharing would be great but it is very difficult to know what other laboratories are doing. Info sharing would be great but many people are afraid of losing their ideas. 2nd point: Teaching. Establishing training for safety handling Europe has a problem with defining nanoparticles even using the ISO definition is difficult, better methods of measuring the surface would be nice. Many companies are now considered nano that weren't before and they many not know how to make it safe.

7. There is a new nanoparticle you want to work with/create, how do you go about creating safety guidelines for the handling, storage, and disposal of it?
When working on a new project he likes to use the "safe-by-design" method that means that you design a product with safety in mind. If we know how we need to be safe than it will be easier to design safely. We break it down to early development; you are precautionary in the beginning and teach them what questions to ask in the early stages. Most of the problems lie in products that are currently on the market because they may or may not be considered nano-companies by the wide definition.

8. How are nanoparticles defined?
Wording is important because the ISO definition is complex (ISO definition encompasses nano-structured materials, nano-pores, nano-objects which is not widely accepted). Past definition of a nanoparticle: fibers, plates, spheres. Present definition of a nanoparticle: spheres only. From a safety point of view this change is important. Most of the current rules implemented are through SUVA (an insurance company).

9. How do you dispose of nanoparticles?
Disposal of nanoparticles should be handled on a case-by-case basis, it depends so highly on the particle, and what the particle is in. hazard is intrinsic, you cannot change the amount of hazard a material has. You can measure the level of hazard but not change it. Hazard times exposure equals risk and absence of risk would create a 100% safe environment. Protective equipment makes the exposure less but the hazard remains the same. The issue in nanoparticles is we do not know what the level of hazard is so it is hard to determine the level of exposure that should be allowed. There are questions you should ask when disposing things, who is dealing with things and everything is case by case. Data and risks for many nanomaterials are very well available.

10. What is the ideal way you should dispose?
There are two ways to accomplish this. First, find material properties and create a database. Second, research laboratories and give raw data. Experts can tell you about exposure. Many disposal companies do not know what nanotechnology is. We need to have an open communication and create safety data sheets.

11. What types of nanoparticles do you sell/ship?
Experts look into info about things before they ship. You need to look at all possible scenarios; for example, sometimes there are nanoparticles in concrete and when you break the concrete the nanoparticles can be released into the environment. It is hard to know how well than nanoparticles are contained.

12. Could you run us through your packing procedures?
Disposal companies don’t know don't know things about nanoparticles and their current safety procedures only give so many options. Packing- everything is case by case as mentioned before.

13. Do you include safety information in the package? Why/why not?
Nanoparticles are handled like dust with specific precautions. While the mean size of the particle is taken into account on the label saying it contains nanomaterial, says nothing. When packing you ensure that the nanoparticles are not destroyed, and there is no release of particles.

14. How are your guidelines different from your governments? Why?
They are very connected to governmental guidelines; they want to help the industry. The action plan for synthetic nanomaterials was made in 2008. A website was created (public-nano). The law says that it is your responsibility to be safe but they don't tell you how to do it. Swiss government relies on "self control" and it is the companies’ obligation to make sure that they are safe. The government is currently making a guideline that it more concrete and it will come out in the next year or so.

15. Are there any parts of your guidelines that you feel could be improved?
The government is currently testing the guidelines. They have already found a few issues, for example the solubility of solutions depend on particle size. It is hard to know what is applicable and what is not. You can always assume the most dangerous situation, but that causes some issues; it is too expensive and it is too cumbersome for the user. Some companies are not using nano-technologies just for the reason that they simply don't know enough about risks.

16. Do you feel held back by your safety procedures?
When you are not sure - you are obligated to use maximum safety. This creates uncertainty among workers - not optimal. Maximum amount of safety has 3 issues - too expensive, nasty for

workers, doesn't work for companies (Entrepreneurial aspect). We do not know how to evaluate the effectiveness of safety.

17. During your work with nanoparticles, where do you have to take the most caution?
The biggest risk is getting nanoparticles in your lungs. This is widely accepted as the biggest risk.

18. How are the people who work with nanoparticles trained?
Nano-specific training is a high priority in my eyes. If a place needs nano training there is no specific nano training on how to handle it available to them. Cannot give overall nano training safety because it is not fully explored, and is very case by case, also there are too many different types. Concepts to think about: grouping, particulate matter different when they are the same?

19. What must be considered for new guidelines?
This is an up and coming field so it needs flexibility, people are trying to find scientific principles on nanoparticles all of the time. Small variances in a nanoparticle can cause a big change and we don't know if you can apply all of the properties of the normal chemical.

20. What would you like to see from new guidelines?
He would like to use the safe by design as a guideline; this would be case by case. You would have to look to the future and have to think about society and potential economic issues. People need to think to the future.

21. What would your ideal form of implementation be?
The ideal would be an exchange of information. Testing and improvement on the way companies are working with nanoparticles.

22. Are there any topics or areas that you would like to talk about that we didn't already discuss?
Info-nano website is very exciting. There is a precautionary matrix online to see where the knowledge gaps are, it is the best tool for thinking about how to handle the nanomaterials. Over 30 companies have used it and it could be a great jumping point for this project.

23. What do you think about the future of the nano-industry?

Nano-material are not implemented as much as people think that they are. There was a big "Nano hype" in the 2000. Not all of functionality of nanoparticles can be implemented.

Interview 7

1. What do you do here?
Head of the Nanoparticle-Biological interactions department that studies the effects of various nanoparticles on cell tissues and biological systems.

2. What specific nanoparticles do you use?
Very broad range. Iron Oxide for blood purification (takes out bacteria and toxins). Graphene (various shapes and morphologies). Carbon Nanotubes.

3. What applications do you use them for?
Research for biological applications. How nanoparticles interact with cells. How that can be dangerous or helpful.

4. What do you know about nanoparticle safety?
Studying biological effects of various nanoparticles for over 15 years.

5. What is the size of your institution?
Approx. 200

6. How many people work with the nanoparticles?
Approx. 10 in lab. Approx 50 total (including sister laboratories)

7. What protection types do you use for specific application types?
Bio-nano laboratory is separate. Avoids powders. Works with nanoparticles in small amounts (milligrams or less). Uses fume hoods and glove boxes.

8. What protection types do you use for individuals?
Double gloves. Apron. Goggles. Anything requiring a mask is done in a glove box. Uses different protection for different hazards as necessary.

9. What environmental measures do you implement for nanoparticle hazards?
Disposes of certain nanoparticles through waste management department. Facilities use air filtration and recirculation.

10. Could you walk us through your procedure for synthesizing?
Wet chemistry

11. What do you do with the nanoparticles once you are done making them?
Uses them with cell colonies and studies their effects.

12. Could you describe what you do with the nanoparticles?
Receives small amount of nanoparticles. Studies their properties themselves (since labels and descriptions are not always correct). Creates their own characterization based on purity, contaminants, size, surface charge, agglomeration, release of ions, and stability in a cell culture. Then tries to get a understanding of interactions with tissues and explores that in various ways.

13. What tools or improvements to the workspace would you like to see?
Few methods of depicting interactions with tissues, so would like a new tool to see the entire process. Something possibly based on X-ray.

14. There is a new nanoparticle you want to work with/create, how do you go about creating safety guidelines for the handling, storage, and disposal of it?
Performs own studies and documentation. Publish that or keep information between collaborators. Try to share as much as possible.

15. How do you dispose of nanoparticles?
Determines hazard and disposes accordingly. Carbon based particles can be thrown in normal trash for incineration. Waste management department disposes of heavy metals and higher volumes.

16. How do you dispose of items that come in contact with the nanoparticles, such as gloves or containers?
Does not manly have disposable objects that come in contact with nanoparticles. Can be thrown out normally.

17. To whom do you sell/ship your nanoparticles?
Ships to other laboratories, corporations or partners.

18. What types of nanoparticles do you sell/ship?
Large variation. However does not send powders.

19. Could you run us through your packing procedures?
Puts in two unbreakable containers (one within the other). Basic regulations for chemicals. Sometimes temperature controlled (for international flights).

20. Do you include safety information in the package? Why/why not?
Safety information is relayed to the person the material is shipped to. Usually by mail or email. Particularly for newly synthesized materials.

21. When you are not working with the nanoparticles, where/how do you store them?
Storage location with restricted access. Some kept stable at 4 degrees Celsius. Others at room temperature. Always in few milligrams. The rest are in key-restricted storage.

22. How do you document storage of your nanoparticles?
List that includes source, project, and person associated with the project, and the key person using the nanoparticles. Documents over 300 types of nanoparticles.

23. How are your guidelines different from your governments? Why?
More restricted. Formulates own assessment of hazards. Utilizes precautionary principle for unknowns.

24. Are there any parts of your guidelines that you feel could be improved?
Spirit of the people needs improvement. Make them aware of dangers and willing to act accordingly.

25. During your work with nanoparticles, where do you have to take the most caution?
Skin is a good barrier. Oral exposure is not serious, since gastro-intestinal tract can deal with foreign particulates. Most critical is inhalation, since biological defenses cannot remove the nanoparticles. It will cause inflammation that results in chronic effects.

26. How are the people who work with nanoparticles trained?
Everyone in the laboratory is made aware of each other's experiments, nanoparticles, and their hazards. Everyone is trained from young students to follow processes and recognize hazards.

27. What would you like to see from new guidelines?
Better material safety datasheets. Currently too vague. Needs more chemical information.

28. What would your ideal form of implementation be?
Provide information, but also design a culture interested in nanoparticle safety. More nanoparticle education in university.

Interview 8

1. What do you do here?
Health and Safety Officer for startup company.

2. What specific nanoparticles do you use?
Carbon nanotubes (all different shapes and morphologies), Carbon Black (semi amorphous). All of them are in small amounts (1 gram or less), and even then only 1% of that 1 gram aerosolized.

3. What applications do you use them for?
Develops their CNT detection products.

4. How interested are you in learning about the safety procedures of other laboratories?
Very interested in how others handle. Others may be potential customers.

5. What do you know about nanoparticle safety?
Knows about properties of various CNTs and hazards of inhalation.

6. What is the size of your institution?
5

7. How many people work with the nanoparticles?
3

8. What protection types do you use for specific application types?
Biological safety cabinet with HEPA filters on top. Particle detection that alerts leak of hazards.

9. What protection types do you use for individuals?
Gloves. Laboratorycoat. No mask (since the particles are mainly enclosed).

10. What environmental measures do you implement for nanoparticle hazards?
HEPA filter to be changed every 5-7 years

11. Could you walk us through your procedure for synthesizing?
Does not synthesize.

12. Could you describe what you do with the nanoparticles?
Order around 1 gram to 10 grams of CNT powder. Send it to a collaborating facility to reduce it to around 1mg in a special flask. Connect the flask to a series of flow tubes. Flow about a liter per minute of air through the system to aerosolize the nanoparticles. Sends them through detection devices for testing.

13. What tools or improvements to the workspace would you like to see?
A small part of the aerosol (sub micrograms, 100x under exposure limit) makes it through their system. Not a huge hazard issue, but would like to see better filters in the future.

14. To whom do you sell/ship your nanoparticles?
Ships to other collaborators.

15. What types of nanoparticles do you sell/ship?
CNTs

16. Could you run us through your packing procedures?
Leaves the particles in a flask. Seals the flask with para film. Pads the interior of the box. Ships them by normal Swiss Post. Only ships within Switzerland.

17. Do you include safety information in the package? Why/why not?
When receiving nanoparticles, safety information is not included inside or on the package. When shipping nanoparticles, collaborators already know what they are receiving and know the dangers of the material they are expecting.

18. When you are not working with the nanoparticles, where/how do you store them?
Store them in a glass flask with para film sealing the bottle.

19. How do you document storage of your nanoparticles?
Labels containers. However have few particles to document. No formal documentation.

20. How are your guidelines different from your governments? Why?
Use common sense and their own knowledge for safety. Have MSDS data.

21. During your work with nanoparticles, where do you have to take the most caution?
Loading powders into flasks has the highest risk for exposure. Particles are handled openly with gloves under the biological safety cabinet. Window is down and airflow filter is on.

22. How are the people who work with nanoparticles trained?
No formal training. Everyone informs one another of safety practices. Mentions that they have few people, so it is very critical to them that no one makes mistakes.

23. What would you like to see from new guidelines?
MSDS should be better, clearer and more up-to-date for toxicology findings.

24. What would your ideal form of implementation be?
Link by email when ordering nanoparticles that informs of safety practices.

Interview 9

1. What do you do at here?
Expert in Nanotechnology. Manages chemistry laboratories that handle nanoparticles.

2. What specific nanoparticles do you use?
Uses many different types of nanoparticles: metal oxides, polymers gold, nickel, silver, and cobalt.

3. What applications do you use them for?
Nano-divided materials, nano-fabrications, and nano toxicity projects. Evaluate the toxicity of nanoparticles.

4. How interested are you in learning about the safety procedures of other laboratories?
Yes, of course. Always willing to make conditions safer.

5. What is the size of your institution?
15 people

6. How many people work with the nanoparticles?
6 or 7 people work with nanoparticles directly

7. What protection types do you use for specific application types?
Two safety systems: fume hood and glove box. The glove box is generally not used for handling nanoparticles.

8. What protection types do you use for individuals?
Goggles, mask, gloves, laboratory coat. Mainly no contact with nanoparticles.

9. What environmental measures do you implement for nanoparticle hazards?
Based on the concentration, perform different procedures to inoculate the particles. Used wearable nanoparticle samplers and nanoparticle counters for the air to detect potential local hazards. Use special vacuum cleaner for opening solid nanoparticles to suck in nanoparticles that may aerosolize and escape from the top of the flask. The vacuum does not have filters, but instead deposits particles into water.

10. Could you walk us through your procedure for synthesizing?
We do not synthesize, we purchase.

11. Could you describe what you do with the nanoparticles?
Start by entering the laboratory with all of the proper equipment, then gather the materials that are needed. Put the vacuum over the opening of the nanoparticles (this is a special vacuum that goes into water rather than through a filter). Measure the weight of the nanoparticles, and close the nanoparticles container quickly. Disperse the liquid into the solid substrate. Use water to wash the walls of the container to be cleaned or thrown away

12. What tools or improvements to the workspace would you like to see?
The last nanotoxicity assessment was in 2012. Having permanent sensors in the hood where we work that would be able to tell if there was an issue with the nanotoxicity levels.

13. There is a new nanoparticle you want to work with/create, how do you go about creating safety guidelines for the handling, storage, and disposal of it?
Check the safety data sheet, this is a process that is not only used for nanomaterials. If there is a risk than the a recommendation will be made to the manipulator. An example of this is when PhD students were using metallic nanoparticles.

14. How do you dispose of nanoparticles?
Disposal depends on the toxicity and concentration of the nanoparticle. Throw them in the sink if it is safe. If it is a high concentration that aggregates them by evaporating the solvent to make particles larger and less volatile. If neither of those processes apply than give the waste to the safety officer in the company for chemical waste disposal.

15. How do you dispose of items that come in contact with the nanoparticles, such as gloves or containers?
Gloves and containers are collected into waste bags and given to a waste company.

16. What happens to the nanoparticles when they leave your care?
Does not know how nanoparticles are handled once they leave their care, but they give them all the information that they need to deal with waste.

17. To whom do you sell/ship your nanoparticles?
Do not often ship nanoparticles, but when they do they are dispersed or in a coating, they never get sent as a powder.

18. Could you run us through your packing procedures?
Close the boxes encapsulate the containers with various absorbing papers, or bubble wrap. They only get sent dispersed in water. They are shipped in the regular post.

19. Do you include safety information in the package? Why/why not?
Yes, information about the chemical is included in the packaging.

20. When you are not working with the nanoparticles, where/how do you store them?
The nanoparticles are stored in ventilated closed shelves that are connected to the ventilation of the building. Bags of powders are in solid containers. Containers with dispersed nanoparticles are stored in the fridge or on ventilated shelves.

21. How do you document storage of your nanoparticles?
We have no procedure for documenting the storage of our nanoparticles. This would be a potential improvement.

22. How are your guidelines different from your governments? Why?
Many of the systems are based on the Swiss guidelines. They have studied the Swiss guidelines in detail, including the responsibilities and roles of their collaborators and safety officers and employees.

23. Are there any parts of your guidelines that you feel could be improved?
There is always room for improvement, however nothing detailed comes to mind. Activities are always changing so the guidelines should be adapted as such. An example of this is when new equipment is installed there should be new guidelines that should be implemented.

24. During your work with nanoparticles, where do you have to take the most caution?
There are three hazards. Breathing, contact with skin and ingesting. The most difficult to control is breathing, that is the most hazardous part of the process.

25. How are the people who work with nanoparticles trained?
There is no specific training for nanoparticles. But they have general info sessions for yearly laboratory practices. Nanoparticle users have been given special training.

26. What would you like to see from new guidelines?
Improved working conditions and comfort of the user. The risk of mistakes is higher if the comfort is an issue.

Interview 10

1. What do you do here?
The company is a global non-profit research organization. The goal of this company is to serve industries, and foster innovation. The company is the applied research link between applied research and development. Specifically works with micro engineering, MEMs and microfluidics.

2. What specific nanoparticles do you use?
This is dependent on the customer, but has previously worked with carbon nanotubes and silicon dioxide.

3. What applications do you use them for?
Uses nanoparticles to create products, like sunscreen or carbon nanotube counters

4. **What is the size of your institution?**
21 people full time, 27 part time people

5. How many people work on projects related to nanoparticles?
6 people

6. Could you describe what you do with the nanoparticles?
Follows good laboratory practices (GLP). Required to read coursework, have a laboratory tour with the laboratory head, sign agreements, and learn procedures. They do not have nano-specific training.

7. What tools or improvements to the workspace would you like to see?
A nanoparticle counter that could count a more broad range of particles

8. There is a new nanoparticle you want to work with/create, how do you go about creating safety guidelines for the handling, storage, and disposal of it?
You get in touch with the chief safety officer.

9. How do you dispose of nanoparticles?
There is a company that handles all of the waste.

10. When you are not working with the nanoparticles, where/how do you store them?
The nanoparticles are labeled saying who was working with them, what they are, when they were working with it, and the expiration date.

11. How do you document storage of your nanoparticles?
There is an electronic list where all the in house products are documented. They also use GHS stickers that are added to the containers.

12. Are there any parts of your guidelines that you feel could be improved?
No. The guidelines are adapted when needed and safety is the number one priority

13. How are the people who work with nanoparticles trained?
You talk with the safety officer and do the EPFL training "Nanoparticles".

Interview 11

1. What do you do here?
Works with and produces nanopowders for ceramics, nanocomposites or coatings.

2. What specific nanoparticles do you use?
Inorganic nanoparticles, mainly oxides.

3. What applications do you use them for?
Fuel cells, catalysts and coatings for filtration.

4. How interested are you in learning about the safety procedures of other laboratories?
Learning about safety is never ending.

5. What is the size of your institution?
700 people

6. How many people work with the nanoparticles?
5 in this lab, 10-20 at location

7. What protection types do you use for specific application types?
Vacuums and various types of airflow/ ventilation.

8. What protection types do you use for individuals?
Goggles, FFF mask, gloves, laboratory coat. A full suit is used when cleaning the vents for the machine that synthesises nanoparticles.

9. What environmental measures do you implement for nanoparticle hazards?
Air that is released is constantly filtered out. The filter is also changed every 6-12 months.

10. Could you walk us through your procedure for synthesizing?
In-flame synthesis, where they run solid nitrates in a water solution through the fire, which produces very tiny nanoparticles. They suck it all up with a big vacuum, and catch some of the nanoparticles with a filter. The rest of the air is then filtered completely.

11. What do you do with the nanoparticles once you are done making them?
Characterizes them, figures out the morphology and size. Then, compresses them into pellets and looks at the electrical properties.

12. Could you describe what you do with the nanoparticles?
Observes the powders under a microscope. Looks at particle size and distribution.

13. What tools or improvements to the workspace would you like to see?
Take more precautions. They always need to be exposed to powder in their process so more accommodates for using nanoparticles in this state.

14. How do you dispose of nanoparticles?
Most of the nanoparticles are turned into pellets. So they only throw away contaminated wipes and gloves. Those are put into bags and stored in a special, ventilated trashcan. It is then thrown away normally, where it is incinerated with the rest of garbage.

15. How do you dispose of items that come in contact with the nanoparticles, such as gloves or containers?
Nanoparticle contaminated objects are put in a plastic bag and tied up, then put in a trash container that has vacuum constantly sucking air from its proximity. When this trash bag is full, it is thrown away as normal to be incinerated.

16. What happens to the nanoparticles when they leave your care?
Goes to incineration plant to be incinerated.

17. To whom do you sell/ship your nanoparticles?
They ship to collaborators.

18. Could you run us through your packing procedures?
Powders in small containers are placed in more than one bag. Shipping is done through normal mail.

19. Do you include safety information in the package? Why/why not?
No, collaborates are aware of the risks and hazards involved with working with nanoparticles.

20. When you are not working with the nanoparticles, where/how do you store them?
Stored in closed containers within the lab.

21. How are your guidelines different from your governments? Why?
They are very close.

22. Are there any parts of your guidelines that you feel could be improved?
Would want more information regarding the hazards of different nanoparticles.

23. Do you feel held back by your safety procedures?
No, they are generally okay.

24. During your work with nanoparticles, where do you have to take the most caution?
When opening the bottle. Collecting the powder from the filters in the synthesizing machine. Synthesizing the powders from the flame itself. Making sure the students are working properly and know the risks.

25. How are the people who work with nanoparticles trained?
Students are walked through processes and sufficient enough to work alone. People are advised to wash their clothes and show immediately after arriving home.

26. What would you like to see from new guidelines?
Clear guidelines about what to do with various particles and the danger between spherical and tube structures. Currently, everything is on the people working with the particles. More active control by the government is needed to check safety equipment and health risks for employees.

Interview 12

1. How do you handle nanoparticles?
All nanoparticles in powdered form are handled in a glove box. Outside of the glove box they are either in a sealed jar or in a matrix, never exposed.

2. What is the size of your institution?
Approximately 30.

3. How many people work directly with nanoparticles?
5-6 people

4. How do you receive the nanoparticles?
In various containers it all depends on the company. Some companies are better than others varying from packaging in bottles to small plastic bags.

5. What are some problems with your safety systems?
The filtration system is not made for nanoparticles, and can be damaged even if it does filter out all of them (which it probably doesn't).

6. Could you walk us through your procedure for synthesizing?
We flush out the glove box with nitrogen gas for an hour before opening it. Then, make sure the other vents are closed (multiple set ups lead to the same filter, only the glove box's vent should be open). Contaminated materials are stored in zip lock bags and we wear gloves and a mask when placing things in the glove box. We just use tweezers to open zip lock bags and put all waste in one large zip lock for containment.

7. What do you do with the nanoparticles once you are done making them?
We purge the glove box with nitrogen for 1 hour before removing everything. Then, particles in a solution are worked with under a special fume hood.

8. During your work with nanoparticles, where is the greatest threat?
They are most dangerous in particle form, as they are more mobile. Especially because some people don't consider them to be a threat. Solvents can evaporate with the particles while solids can release them under abrasion.

9. How do you dispose of nanoparticles?
Samples are put into a plastic matrix and thrown away. They are destroyed by the local trash incinerator and solvents are given to waste management.

10. What would you like to see from new guidelines?
More regulations because currently they are non-existent. They are vague suggestions and a lot of companies don't know the risks. Also, a way to measure nanoparticles in the environment and a way to make the work easier with regards to safety.

11. What would your ideal form of implementation be?
The best solution would be a chemical filter, but that is not ideal because would need different filters to detect different nanoparticles.

Interview 13

1. What do you do here?

Graduate student working on synthesis, functionalization and surface treatment of micro- and nanoparticles.

2. What specific nanoparticles do you use?

Only iron oxide of 30nm - 100nm. They aren't as dangerous as other nanoparticles.

3. What is the size of your institution?

Approximately 30.

4. How many people work directly with nanoparticles?

5-6 people

5. Could you walk us through your procedure for synthesizing?

In a solution, then you have to dry it out to isolate the iron oxide in a vacuum oven. Grind the particles down into a powder while in the glove box and use a magnet to keep them in place.

6. When you are not working with the nanoparticles, where/how do you store them?

Safest way to store them is in a matrix, usually in a solution

7. What could be done to make working with them safer?

A full on clean room, but that would be way too expensive. Also, an indicator to see how much you yourself have been contaminated while working.

8. How do you dispose of nanoparticles?

By pouring the solution into a large vessel after trying to dissolve them with another solution. But doesn't know what happens when the vessel is filled up. Any contaminated materials thrown in the rubbish to be incinerated as per usual

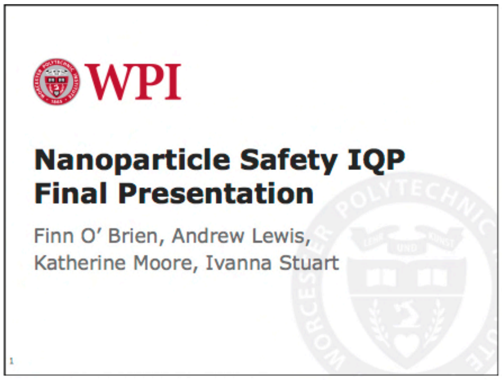
9. Are there any parts of your guidelines or procedures that you feel could be improved?

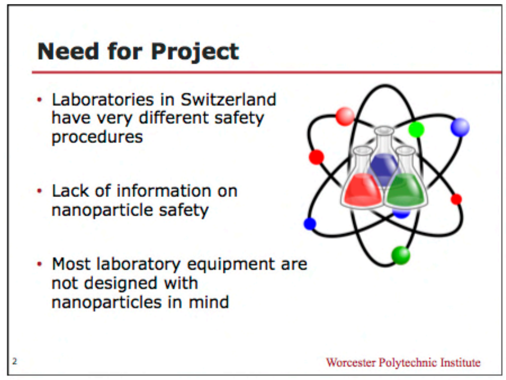
The glove box should have an airlock feature to minimize nanoparticles escaping. The whole thing is very inconvenient mainly because of the gloves and the size (too small).

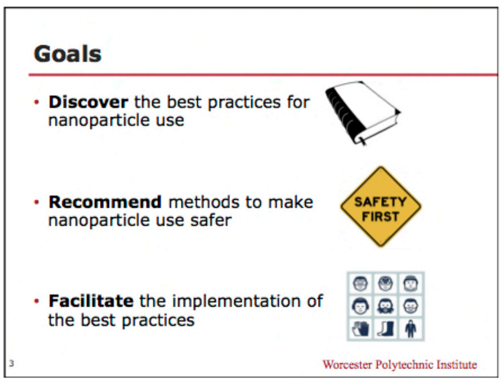
Appendix C Poster Translations

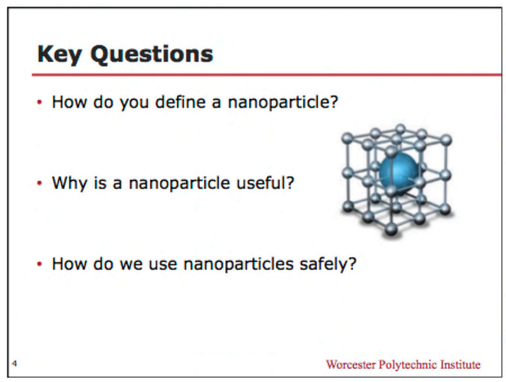
Figure C.1: Nanoparticle Danger Sign (German)

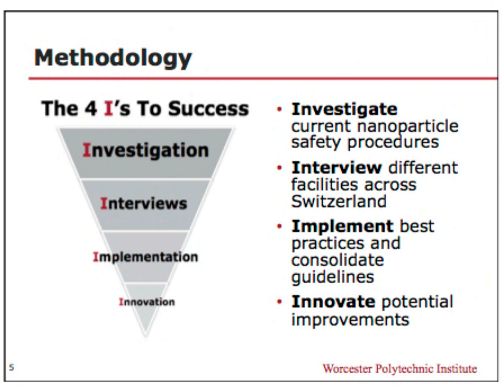
Appendix D Final Presentation

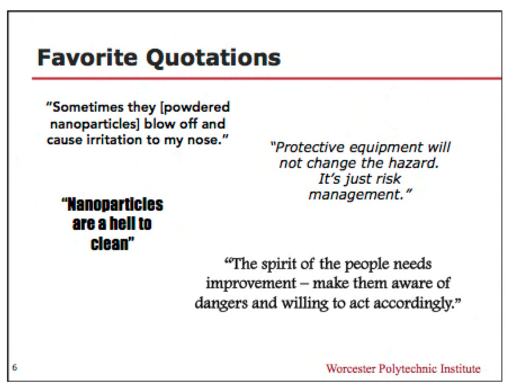




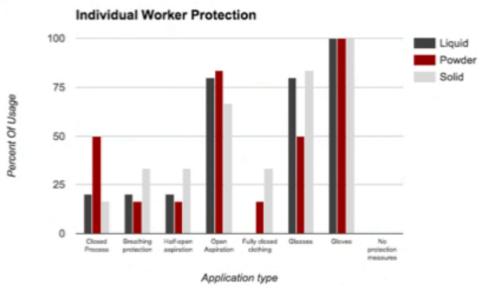








Quantitative Interview Results



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Solutions

Two solutions:

– Posters:
  - for laboratory users to guide them to a safe work environment and information-based
  - for laboratory visitors, students and the general public

– Website consolidates information online

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Posters and Graphics

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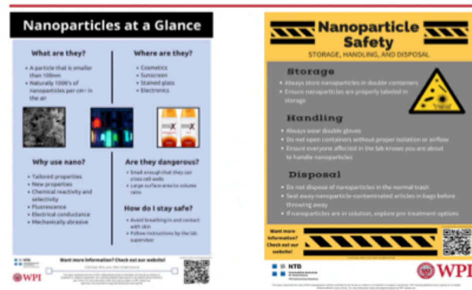
Posters and Graphics



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Website

http://www.nanoparticlesafety.ntb.ch/

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Recommendations for Future Work

- Interviewing of toxic waste disposal companies
- Packaging/shipping practices and regulations
- Nanoparticle safety training

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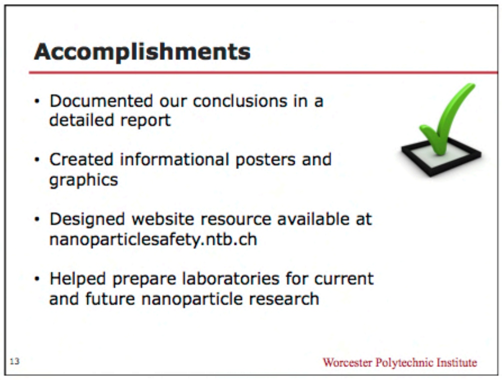
Accomplishments
• Documented our conclusions in a detailed report
• Created informational posters and graphics
• Designed website resource available at nanoparticlesafety.ntb.ch
• Helped prepare laboratories for current and future nanoparticle research
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