PURDUE UNIVERSITY

Weldon School of Biomedical Engineering

The Convergence of Differences, The Future of Excellence

*BME 695*

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# Engineering Nanomedical Systems

***Lecture 16***

## FDA, EPA, and NIOSH regulatory issues


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# Relevance

While this lecture will examine the FDA regulations of the United States, these problems are very general and faced by any society that worries about bringing safe medicines and other products to its people.

# For example: There is an “FDA  in China too!

SFDA
www.sfda.gov.cn
State Food and Drug Administration,P.R.China

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What's New

SFDA Deputy Commissioner Bian Zhenjia meets Vice Minister of Health of Vietnam (2011-11-04)

SFDA Commissioner Shao Mingli

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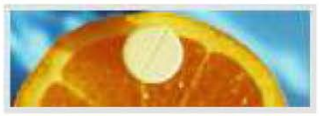

- Mission
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**REGULATORY GUIDE**

- Drug Registration
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- Health Food Registration
- Administrative Protection

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**LAWS & REGULATIONS**

- Drug Administration Law of the People's Republic of China
- Regulations for Implementation of the Drug Administration Law of the People's Republic of China
- Regulations for Supervision and Administration of Medical Devices
- Regulations on Administrative Protection for Pharmaceuticals

http://eng.sfda.gov.cn/WS03/CL0755/

# 16.1 Introduction and overview

How does the FDA think about nanomedical systems?

# How does the FDA think about nanomedical systems?

The FDA is listening to a large group of scientists from a variety of disciplines as well as established task forces, including the special task force report described in the following slides.

## A recent task force study making recommendation to the FDA regarding nanotechnology…

# Nanotechnology

A Report of the

U.S. Food and Drug Administration

Nanotechnology Task Force

July 25, 2007

http:www.fda.gov/nanotechnology/taskforce/report2007.pdf

# The Task Force meeting…

"As requested by the Commissioner, the Task Force opened a public docket and held a public meeting on October 10, 2006. The objectives of the meeting and the docket were to learn about:

New nanoscale material products under development in the areas of foods (including food additives and dietary supplements), color additives, animal feeds, cosmetics, drugs and biologics, and medical devices;

New or emerging scientific issues that should be brought to FDA's attention, including issues related to the safety of nanoscale materials; and

Any other issues concerning the use of nanoscale materials in FDA-regulated products regarding which regulated industry, academia and the interested public wished to inform FDA."

http:www.fda.gov/nanotechnology/taskforce/report2007.pdf

# The official response to this task force report…

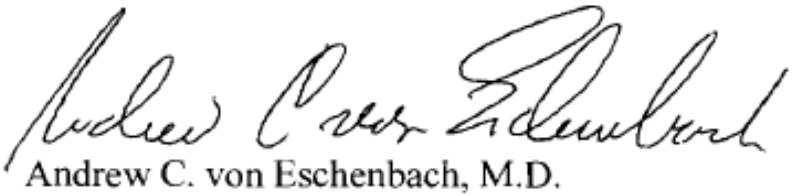
DATE: July 23,2007

TO: Deputy Commissioner for Policy
Associate Commissioner for Science

FROM: Commissioner of Food and Drugs

SUBJECT: Nanotechnology Task Force Report

Thank you for submitting to me the Nanotechnology Task Force Report. Nanotechnology holds great promise for the development of new treatments and diagnostics. However, as with other emerging technologies, it poses questions regarding the adequacy and application of our regulatory authorities. I commend you and the rest of the Nanotechnology Task Force on your efforts in developing this report and its recommendations to improve the FDA's scientific knowledge of nanotechnology and to address the regulatory challenges that may be presented by products that use nanotechnology. I appreciate the fact-finding efforts that the Task Force undertook, such as holding the October 2006 public meeting and soliciting public comment, to understand the issues and provide me with informed recommendations.
I endorse the report and its recommendations. This includes the recommendations to issue additional guidance to provide greater predictability of the pathways to market and for ensuring the protection of public health. Please move forward with these recommendations, pursuant to FDA's good guidance practice (GGP) process (21 CFR 0.1 15), as appropriate.



Andrew C. von Eschenbach, M.D.

http:www.fda.gov/nanotechnology/taskforce/report2007.pdf

# Task Force Mission…

"In August 2006, then Acting Commissioner of Food and Drugs, Andrew C. von Eschenbach, M.D., announced the formation of an internal FDA Nanotechnology Task Force. He charged the Task Force with determining regulatory approaches that would enable the continued development of innovative, safe, and effective FDA-regulated products that use nanoscale materials. The Task Force was asked to identify and recommend ways to address any knowledge or policy gaps that exist to better enable the agency to evaluate safety aspects of FDA-regulated products that contain nanoscale materials. Specifically, the Task Force was directed to:

- Chair a public meeting to help FDA further its understanding of developments in nanoscale materials that pertain to FDA-regulated products, including new and emerging scientific issues such as those pertaining to biological interactions that may lead to either beneficial or adverse health effects;
- Assess the current state of scientific knowledge pertaining to nanoscale materials for purposes of carrying out FDA's mission;
- Evaluate the effectiveness of the agency's regulatory approaches and authorities to meet any unique challenge that may be presented by the use of nanoscale materials in FDA-regulated products;
- Explore opportunities to enable innovation using nanoscale materials to develop safe and effective drugs, biologics and devices, and to develop safe foods, feeds, and cosmetics;
- Continue to strengthen FDA's collaborative relationships with other federal agencies, including the agencies participating in the NNI such as the National Institutes of Health (NIH), the Environmental Protection Agency (EPA), and the United States Department of Agriculture (USDA), as well as with foreign government regulatory bodies, international organizations, healthcare professionals, industry, consumers, and other stakeholders, to gather information regarding nanoscale materials used or that could be used in FDA-regulated products;
- Consider appropriate vehicles for communicating with the public about the use of nanoscale materials in FDA-regulated products; and
- Submit its initial findings and recommendations to the Commissioner within nine months of the public meeting."

http:www.fda.gov/nanotechnology/taskforce/report2007.pdf

# 16.2 Some details of the Nanotechnology Task Force Report

16.2.1 General findings of the report

16.2.2 Some initial recommendations of the Task Force

16.2.3 Where the FDA may need to meet EPA on nanoscale materials

16.2.4 Will FDA re-visit GRAS products containing nanomaterials?

# About the report…

"As other emerging technologies have in the past, nanotechnology poses questions regarding the adequacy and application of regulatory authorities. The then Acting Commissioner of the Food and Drug Administration (FDA) initiated the Nanotechnology Task Force (Task Force) in 2006 to help assess these questions with respect to FDA's regulatory authorities, in light of the current state of the science for nanotechnology. This report offers the Task Force's initial findings and recommendations to the Commissioner.

The report includes:

- A synopsis of the state of the science for biological interactions of nanoscale materials;
- Analysis and recommendations for science issues; and
- Analysis and recommendations for regulatory policy issues.

The report addresses scientific issues as distinct from regulatory policy issues in recognition of the important role of the science in developing regulatory policies in this area, rapid growth of the field of nanotechnology, and the evolving state of scientific knowledge relating to this field. Rapid developments in the field mean that attention to the emerging science is needed to enable the agency to predict and prepare for the types of products FDA may see in the near future."

http:www.fda.gov/nanotechnology/taskforce/report2007.pdf

# General findings of the report…

"A general finding of the report is that nanoscale materials present regulatory challenges similar to those posed by products using other emerging technologies. However, these challenges may be magnified both because nanotechnology can be used in, or to make, any FDA-regulated product, and because, at this scale, properties of a material relevant to the safety and (as applicable) effectiveness of FDA-regulated products might change repeatedly as size enters into or varies within the nanoscale range. In addition, the emerging and uncertain nature of the science and potential for rapid development of applications for FDA regulated products highlights the need for timely development of a transparent, consistent, and predictable regulatory pathway."

http:www.fda.gov/nanotechnology/taskforce/report2007.pdf

# Some initial recommendations of the Task Force…

"The Task Force's initial recommendations relating to scientific issues focus on improving scientific knowledge of nanotechnology to help ensure the agency's regulatory effectiveness, particularly with regard to products not subject to premarket authorization requirements.

The report also addresses the need to evaluate whether the tools available to describe and evaluate nanoscale materials are sufficient, and the development of additional tools where necessary."

http:www.fda.gov/nanotechnology/taskforce/report2007.pdf

# Where FDA may need to meet EPA on nanoscale materials…

"The Task Force also assessed the agency's regulatory authorities to meet any unique challenges that may be presented by FDA-regulated products containing nanoscale materials.

This assessment focused on such broad questions as whether FDA can identify products containing nanoscale materials, the scope of FDA's authorities to evaluate the safety and effectiveness of such products, whether FDA should require or permit products to be labeled as containing nanoscale materials, and whether the use of nanoscale materials in FDA regulated products raises any issues under the National Environmental Policy Act."

http:www.fda.gov/nanotechnology/taskforce/report2007.pdf

# Issue: Understanding Interactions of Nanoscale Materials with Biological Systems

"Some comments noted that although the nature and unique properties of many nanoscale materials are not well understood, some nanoscale materials have been observed to be toxic in certain assays and under some specified conditions, or, based on their behavior in biological systems, raise suspicions of potential toxicity. .
Some comments stated that nanoscale materials have a unique ability to interact with proteins and other essential biological functional elements. Some noted: that nanoscale materials can be more biologically active than non-nanoscale materials; that basic research is needed on such issues as interactions with subcellular structures and dose/concentration; and that such research should take an interdisciplinary approach, making use of experts in toxicology, materials science, medicine, molecular biology and bioinformatics. The comments pointed out that there are differences in dose-response curves depending on whether the curves are expressed by mass, number of particles, or surface area."

http:www.fda.gov/nanotechnology/taskforce/report2007.pdf

# Issue: Adequacy of Testing Approaches for Assessing Safety and Quality of Products Containing Nanoscale Materials

Several comments expressed the concern that existing toxicology screening methods will not adequately assess toxicologic properties of nanoscale materials, and that these methods cannot be used in their present form to assess engineered nanoscale materials. Some comments pointed out that pharmacokinetics and pharmacodynamics of nanoscale particles are different from those of larger particles and that existing toxicity screening studies do not take these differences into account.

Comments stated that most toxicology tests are short-term, and might leave long-term effects unevaluated, especially because the long-term toxicity and effects for most nanoscale materials remain unknown. These comments noted that appropriate endpoints for *in vitro* assays can be difficult to determine, as single cell types are often not sufficient for evaluation of the function or health of organs or tissues that are made up of multiple cell types, and given that various types of tissues are exposed in the body.



http:www.fda.gov/nanotechnology/taskforce/report2007.pdf

# Perhaps the FDA will need to re-visit the safety of GRAS products containing nanomaterials?

The Task Force concluded that the agency's authorities are generally comprehensive for products subject to premarket authorization requirements, such as drugs, biological products, devices, and food and color additives, and that these authorities give FDA the ability to obtain detailed scientific information needed to review the safety and, as appropriate, effectiveness of products. For products not subject to premarket authorization requirements, such as dietary supplements, cosmetics, and food ingredients that are **G**enerally **R**ecognized **A**s **S**afe (GRAS), manufacturers are generally not required to submit data to FDA prior to marketing, and the agency's oversight capacity is less comprehensive.



http:www.fda.gov/nanotechnology/taskforce/report2007.pdf

# Products Not Subject to Premarket Authorization

"… there may be general differences in properties relevant to evaluation of safety and effectiveness (as applicable) of products using nanoscale materials compared to products using other materials. For example, size, shape, and charge of a nanoscale material can affect disposition or toxicity in the body in ways that differ from molecular forms of materials and that may be generalizable across different particle or other material types. Knowledge of such generalized differences could, for example, help inform FDA's: assessments of whether to take regulatory actions against products not subject to premarket authorization; efforts to obtain and develop further information; and efforts to develop guidance on data needs for products not subject to premarket authorization."



http:www.fda.gov/nanotechnology/taskforce/report2007.pdf

# Recommendations for Consideration

To be marketed, FDA regulated products must be safe and, as applicable, effective. FDA-regulated products must also meet all applicable good manufacturing practice and quality requirements. Adequate testing methods are needed regardless of whether a product is subject to premarket authorization or not. Accordingly, the following recommendations are relevant to all categories of FDA-regulated products. The agency should:

- Evaluate the adequacy of current testing approaches to assess safety, effectiveness, and quality of products that use nanoscale materials;

- Promote and participate in the development of characterization methods and standards for nanoscale materials; and

- Promote and participate in the development of models for the behavior of nanoscale particles *in-vitro* and *in-vivo*.



http:www.fda.gov/nanotechnology/taskforce/report2007.pdf

# 16.3 How will the FDA consider nanomedical systems?

16.3.1 Nanomedical systems are integrated nanoscale drug and drug delivery devices

16.3.2 Either a drug or a device? How about a "Combination Product"?

16.3.3 Drug-Biologic combination products

# Nanomedical systems are integrated nanoscale drug and drug delivery devices that may present a new paradigm to the FDA

"Research and development relating to nanotechnology applications promises the development of products having multiple, highly integrated functions. FDA will need to anticipate this shift in the nature of products received for review and authorization. For example, disease diagnosis, drug targeting, and non-invasive imaging elements are being combined in individual nanotechnology products. A goal of this report is to assist in the development of a transparent, consistent, and predictable regulatory pathway for such products."

http:www.fda.gov/nanotechnology/taskforce/report2007.pdf

# Multilayered, Multifunctional Nanomedical Systems – A "Combination" Product?

U.S. Food and Drug Administration

U.S. Department of Health and Human Services



## Definition of a Combination Product

As defined in 21 CFR § 3.2(e), the term combination product includes:

(1) A product comprised of two or more regulated components, i.e., drug/device, biologic/device, drug/biologic, or drug/device/biologic, that are physically, chemically, or otherwise combined or mixed and produced as a single entity;

(2) Two or more separate products packaged together in a single package or as a unit and comprised of drug and device products, device and biological products, or biological and drug products;

(3) A drug, device, or biological product packaged separately that according to its investigational plan or proposed labeling is intended for use only with an approved individually specified drug, device, or biological product where both are required to achieve the intended use, indication, or effect and where upon approval of the proposed product the labeling of the approved product would need to be changed, e.g., to reflect a change in intended use, dosage form, strength, route of administration, or significant change in dose; or

(4) Any investigational drug, device, or biological product packaged separately that according to its proposed labeling is for use only with another individually specified investigational drug, device, or biological product where both are required to achieve the intended use, indication, or effect.

# CDER-FDA Jurisdiction of Nanomedical Systems?

U.S. Food and Drug Administration

U.S. Department of Health and Human Services

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## Jurisdictional Update: Drug-Biologic Combination Products

On June 30, 2003, FDA transferred some of the therapeutic biological products that had been reviewed and regulated by the Center for Biologics Evaluation and Research (CBER) to the Center for Drug Evaluation and Research (CDER). CDER now has regulatory responsibility, including premarket review and continuing oversight, over the transferred products. More information about the transfer is available at http://www.fda.gov/oc/combination/transfer.html.

Combination products are assigned to a Center for review and regulation in accordance with the products' primary mode of action. When a combination product's primary mode of action is attributable to a type of biological product assigned to CBER, the product will be assigned to CBER. Similarly, when a combination product's primary mode of action is attributable to a type of biological product assigned to CDER, the product will be assigned to CDER. For drug-biologic combination products where both the drug and biological product components are regulated by CDER, the combination product will be assigned to CDER.

FDA has received several inquiries regarding the most appropriate procedures to follow in determining the lead CDER reviewing division for drug-biologic combination products where both the drug and biological product components of the combination product are regulated by CDER. FDA recommends that questions about the assignment of a drug-biologic combination product to a reviewing division within CDER be initially directed to CDER's Ombudsman at 301-594-5480. Alternately, in accordance with 21 CFR Part 3, sponsors may submit a Request for Designation (RFD) for such products. More information on the RFD process is available at http://www.fda.gov/oc/combination/assignment.html.

Office of Combination Products Home Page

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FDA Website Management Staff

# 16.4 FDA and Types of Clinical Trials

16.4.1 IND

16.4.2 Phase 1

16.4.3 Phase 2

16.4.4 Phase 3

16.4.5 Phase 4

# 16.4.1 Investigational New Drug (IND) Application

There are three IND types:

1. An Investigator IND is submitted by a physician who both initiates and conducts an investigation, and under whose immediate direction the investigational drug is administered or dispensed. A physician might submit a research IND to propose studying an unapproved drug, or an approved product for a new indication or in a new patient population.

2. Emergency Use IND allows the FDA to authorize use of an experimental drug in an emergency situation that does not allow time for submission of an IND in accordance with 21CFR , Sec. 312.23 or Sec. 312.34. It is also used for patients who do not meet the criteria of an existing study protocol, or if an approved study protocol does not exist.

3. Treatment IND is submitted for experimental drugs showing promise in clinical testing for serious or immediately life-threatening conditions while the final clinical work is conducted and the FDA review takes place.

Source:
http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/default.htm

# Requirements for an IND Application

The IND application must contain information in three broad areas:

1. Animal Pharmacology and Toxicology Studies - Preclinical data to permit an assessment as to whether the product is reasonably safe for initial testing in humans. Also included are any previous experience with the drug in humans (often foreign use).

2. Manufacturing Information - Information pertaining to the composition, manufacturer, stability, and controls used for manufacturing the drug substance and the drug product. This information is assessed to ensure that the company can adequately produce and supply consistent batches of the drug.

3. Clinical Protocols and Investigator Information - Detailed protocols for proposed clinical studies to assess whether the initial-phase trials will expose subjects to unnecessary risks. Also, information on the qualifications of clinical investigators--professionals (generally physicians) who oversee the administration of the experimental compound--to assess whether they are qualified to fulfill their clinical trial duties. Finally, commitments to obtain informed consent from the research subjects, to obtain review of the study by an institutional review board (IRB), and to adhere to the investigational new drug regulations.

Source:
http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/default.htm

# 16. 4.2 Phase 0 (IND - microdosing)

Phase 0 is a recent designation for exploratory, first-in-human trials conducted in accordance with the United States Food and Drug Administration's (FDA) 2006 Guidance on Exploratory Investigational New Drug (IND) Studies.[16] Phase 0 trials are also known as human microdosing studies and are designed to speed up the development of promising drugs or imaging agents by establishing very early on whether the drug or agent behaves in human subjects as was expected from preclinical studies. Distinctive features of Phase 0 trials include the administration of single subtherapeutic doses of the study drug to a small number of subjects (10 to 15) to gather preliminary data on the agent's pharmacokinetics (how the body processes the drug) and pharmacodynamics (how the drug works in the body).[17]

**A Phase 0 study gives no data on safety or efficacy**, being by definition a dose too low to cause any therapeutic effect. Drug development companies carry out Phase 0 studies to rank drug candidates in order to decide which has the best pharmacokinetic parameters in humans to take forward into further development. They enable go/no-go decisions to be based on relevant human models instead of relying on sometimes inconsistent animal data.

Questions have been raised by experts about whether Phase 0 trials are useful, ethically acceptable, feasible, speed up the drug development process or save money, and whether there is room for improvement



Source: http://en.wikipedia.org/wiki/Clinical_trial

# Phase I Clinical Trial in Humans

Phase I trials are the first stage of testing in human subjects. Normally, a small (20-50) group of healthy volunteers will be selected. This phase includes trials designed to assess the safety (pharmacovigilance), tolerability, pharmacokinetics, and pharmacodynamics of a drug. These trials are often conducted in an inpatient clinic, where the subject can be observed by full-time staff. The subject who receives the drug is usually observed until several half-lives of the drug have passed. Phase I trials also normally include dose-ranging, also called dose escalation, studies so that the appropriate dose for therapeutic use can be found. The tested range of doses will usually be a fraction of the dose that causes harm in animal testing. Phase I trials most often include healthy volunteers. However, there are some circumstances when real patients are used, such as patients who have terminal cancer or HIV and lack other treatment options. Volunteers are paid an inconvenience fee for their time spent in the volunteer centre. Pay ranges from a small amount of money for a short period of residence, to a larger amount of up to approx $6000 depending on length of participation.

# 3 Types of Phase 1 Trials

1. **SAD** (Single Ascending Dose) studies are those in which small groups of subjects are given a single dose of the drug while they are observed and tested for a period of time. If they do not exhibit any adverse side effects, and the pharmacokinetic data is roughly in line with predicted safe values, the dose is escalated, and a new group of subjects is then given a higher dose. This is continued until pre-calculated pharmacokinetic safety levels are reached, or intolerable side effects start showing up (at which point the drug is said to have reached the Maximum tolerated dose (MTD).

2. **MAD** (Multiple Ascending Dose) studies are conducted to better understand the pharmacokinetics & pharmacodynamics of multiple doses of the drug. In these studies, a group of patients receives multiple low doses of the drug, while samples (of blood, and other fluids) are collected at various time points and analyzed to understand how the drug is processed within the body. The dose is subsequently escalated for further groups, up to a predetermined level.

3. **Food effects** - A short trial designed to investigate any differences in absorption of the drug by the body, caused by eating before the drug is given. These studies are usually run as a crossover study, with volunteers being given two identical doses of the drug on different occasions; one while fasted, and one after being fed.

# Phase II Clinical Trials

Once the initial safety of the study drug has been confirmed in Phase I trials, Phase II trials are performed on larger groups (20-300) and are designed to assess how well the drug works, as well as to continue Phase I safety assessments in a larger group of volunteers and patients. When the development process for a new drug fails, this usually occurs during Phase II trials when the drug is discovered not to work as planned, or to have toxic effects.

Phase II studies are sometimes divided into Phase IIA and Phase IIB.

Phase IIA is specifically designed to assess dosing requirements (how much drug should be given).

Phase IIB is specifically designed to study efficacy (how well the drug works at the prescribed dose(s)).
Some trials combine Phase I and Phase II, and test both efficacy and toxicity.

Trial design

Some Phase II trials are designed as case series, demonstrating a drug's safety and activity in a selected group of patients. Other Phase II trials are designed as randomized clinical trials, where some patients receive the drug/device and others receive placebo/standard treatment. Randomized Phase II trials have far fewer patients than randomized Phase III trials.

# Phase III Clinical Trials

Phase III studies are randomized controlled multicenter trials on large patient groups (300–3,000 or more depending upon the disease/medical condition studied) and are aimed at being the definitive assessment of how effective the drug is, in comparison with current 'gold standard' treatment. Because of their size and comparatively long duration, Phase III trials are the most expensive, time-consuming and difficult trials to design and run, especially in therapies for chronic medical conditions.

It is common practice that certain Phase III trials will continue while the regulatory submission is pending at the appropriate regulatory agency. This allows patients to continue to receive possibly lifesaving drugs until the drug can be obtained by purchase. Other reasons for performing trials at this stage include attempts by the sponsor at "label expansion" (to show the drug works for additional types of patients/diseases beyond the original use for which the drug was approved for marketing), to obtain additional safety data, or to support marketing claims for the drug. Studies in this phase are by some companies categorised as "Phase IIIB studies."[19][20]

# Phase III Clinical Trials (continued)

While not required in all cases, it is typically expected that there be at least two successful Phase III trials, demonstrating a drug's safety and efficacy, in order to obtain approval from the appropriate regulatory agencies such as FDA (USA), or the EMEA (European Union), for example.

Once a drug has proved satisfactory after Phase III trials, the trial results are usually combined into a large document containing a comprehensive description of the methods and results of human and animal studies, manufacturing procedures, formulation details, and shelf life. This collection of information makes up the "regulatory submission" that is provided for review to the appropriate regulatory authorities[3] in different countries. They will review the submission, and, it is hoped, give the sponsor approval to market the drug.

Most drugs undergoing Phase III clinical trials can be marketed under FDA norms with proper recommendations and guidelines, but in case of any adverse effects being reported anywhere, the drugs need to be recalled immediately from the market. While most pharmaceutical companies refrain from this practice, it is not abnormal to see many drugs undergoing Phase III clinical trials in the market.

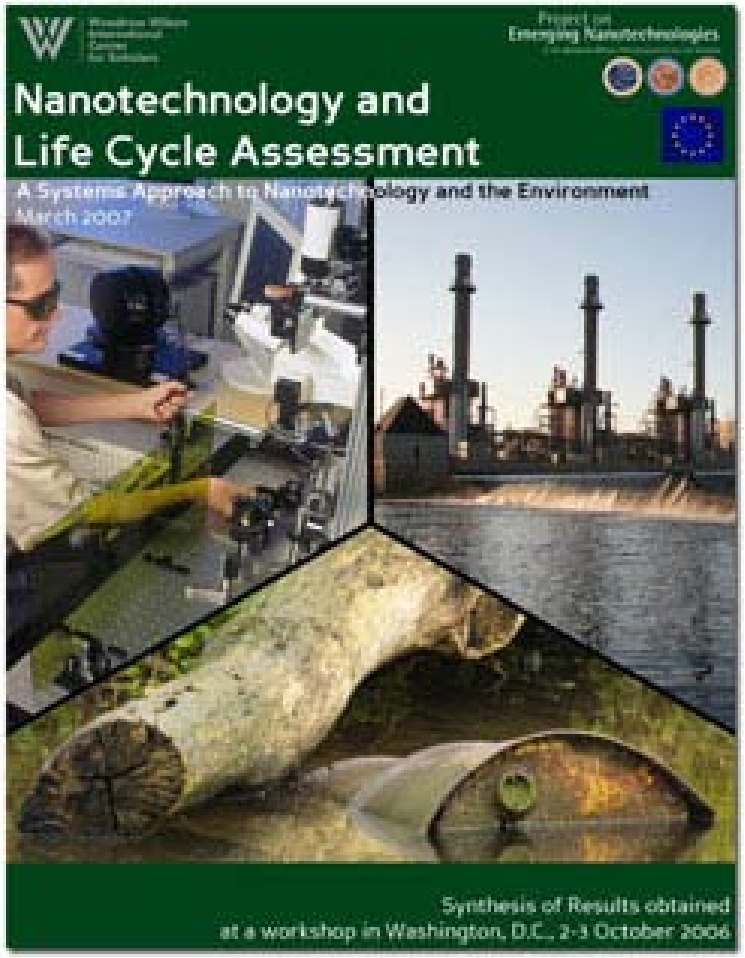
# Phase IV trials (also known as Post Marketing Surveillance Trial)

Phase IV trials involve the safety surveillance (pharmacovigilance) and ongoing technical support of a drug after it receives permission to be sold. Phase IV studies may be required by regulatory authorities or may be undertaken by the sponsoring company for competitive (finding a new market for the drug) or other reasons (for example, the drug may not have been tested for interactions with other drugs, or on certain population groups such as pregnant women, who are unlikely to subject themselves to trials). The safety surveillance is designed to detect any rare or long-term adverse effects over a much larger patient population and longer time period than was possible during the Phase I-III clinical trials. Harmful effects discovered by Phase IV trials may result in a drug being no longer sold, or restricted to certain uses: recent examples involve cerivastatin (brand names Baycol and Lipobay), troglitazone (Rezulin) and rofecoxib (Vioxx).

# 16.5 EPA and other regulatory agency issues

16.5.1 Assessing environmental impact of emerging nanotechnologies
16.5.2 Concept of life cycle assessment (LCA)
16.5.3 Toxicity of nanomaterials
16.5.4 Some recommendations of the 2006 International Conference on Nanotechnology and Life Cycle Assessment

# Assessing the environmental impact of emerging nanotechnologies




WASHINGTON, DC—Life cycle assessment (LCA)—a cradle-to-grave look at the health and environmental impact of a material, chemical, or product—is an essential tool for ensuring the safe, responsible, and sustainable commercialization of nanotechnology, U.S. and European experts conclude in a new report issued today.

With the number of nanotechnology-enabled products entering the market expected to grow dramatically—from $30 billion in 2005 to $2.6 trillion in global manufactured goods using nanotechnology by 2014—"numerous uncertainties exist regarding possible impacts on the environment and human health," the international authors observe in Nanotechnology and Life Cycle Assessment: A Systems Approach to Nanotechnology and the Environment

http://www.nanotechproject.org/111/32007-life-cycle-assessment-essential-to-nanotech-commercial-development

# Little is currently known about the toxicity of nanomaterials

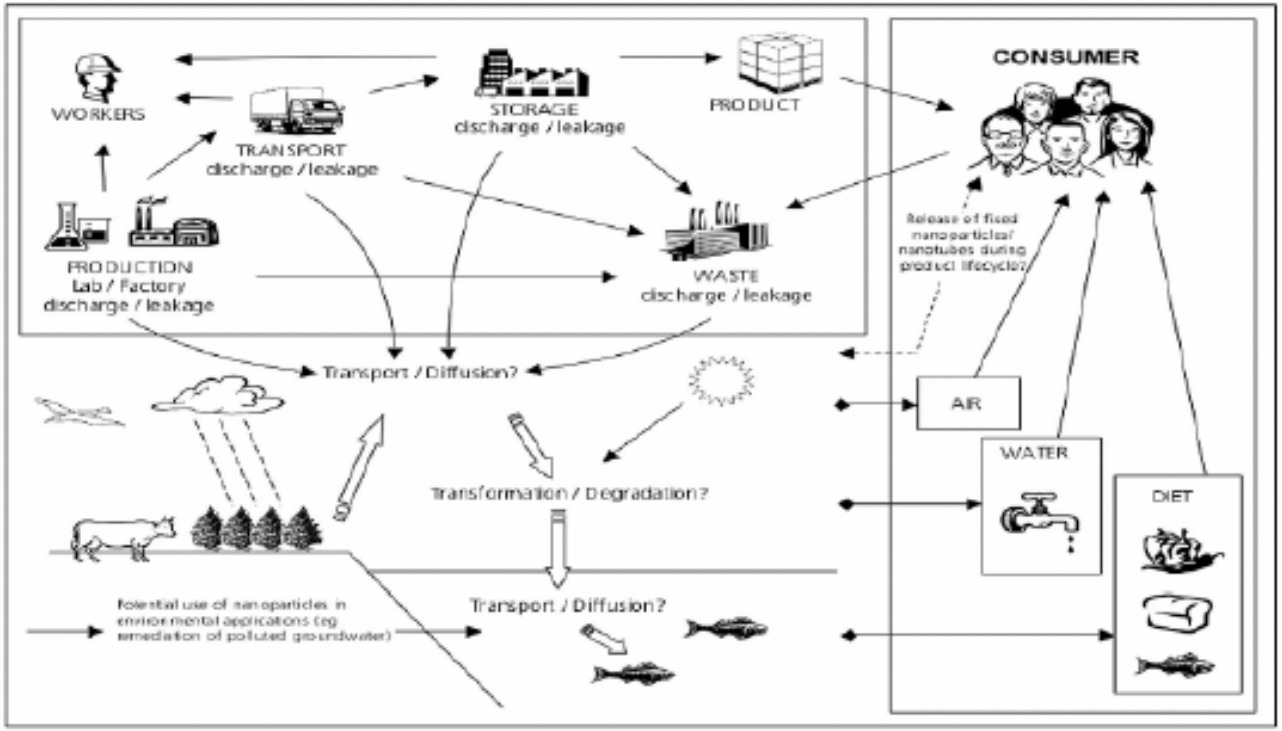



*Figure 1-1: Possible exposure routes for nanoparticles based on current and potential future applications (adopted from The Royal Society & Royal Academy of Engineering 2004)*

"The lack of toxicity data specific to nanomaterials is a repeating theme in this and in other studies related to nanotech environmental, health, and safety concerns," says Andrew Maynard, chief scientist for the Project on Emerging Nanotechnologies. "Nanotechnology is no longer a scientific curiosity. Its products are in the workplace, the environment, and home. But if people are to realize nanotechnology's benefits—in electronics, medicine, sustainable energy, and better materials for building, clothing and packaging—the federal government needs an effective risk research strategy and sufficient funding in agencies responsible for oversight to do the job."

http://www.nanotechproject.org/111/32007-life-cycle-assessment-essential-to-nanotech-commercial-development ( NanoLCA.pdf )

# Some Recommendations of the International Conference on Nano-technology and Life Cycle Assessment, Washington DC, 2-3 October 2006

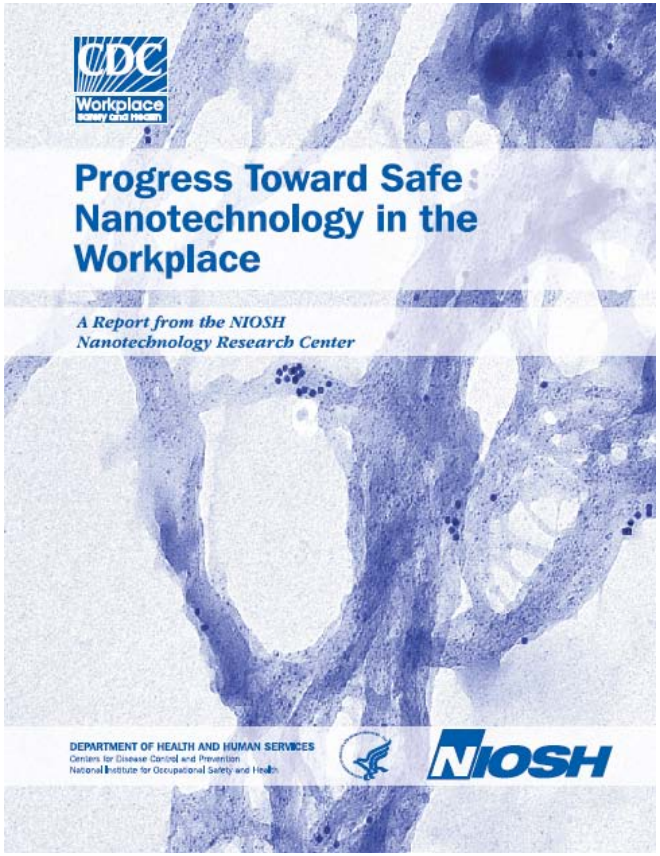
- **Do not wait to have near-perfect data;**
- **Be modest about uncertainties; clearly state relevant uncertainty aspects and assumptions;**
- **Draw conclusions in the case of major or significant improvements; otherwise, state that the nanoproduct and the conventional product are equivalent;**
- **At this early stage, target estimates in the direction of protecting humans and the environment;**
- **Separate the category indicators, grouping them by relevance/uncertainty;**
- **Take care about overselling the benefits of the new nanoproduct, since assessment methodologies will improve and might show "problems" in the future;**
- **Work with toxicologists and other scientists (geographical and socio-economic impacts) to review data and bound the issue;**
- **Make data available for future LCA comparisons at the highest disaggregation level that is acceptable from a confidentiality perspective; at a disaggregation level that is compatible with data availability (in terms of breakdown of processes); and as disaggregated as possible for further applications in assessment; and**
- **Include explanations of assumptions and approaches.**

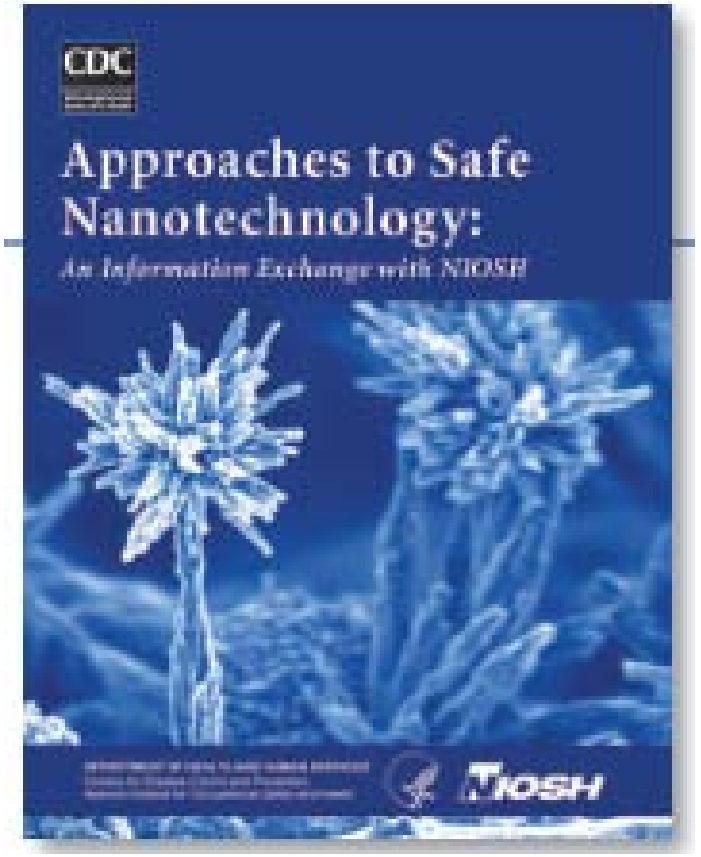
http://www.nanotechproject.org/111/32007-life-cycle-assessment-essential-to-nanotech-commercial-development ( NanoLCA.pdf )

# 16.6 Nanotechnologies and the workplace

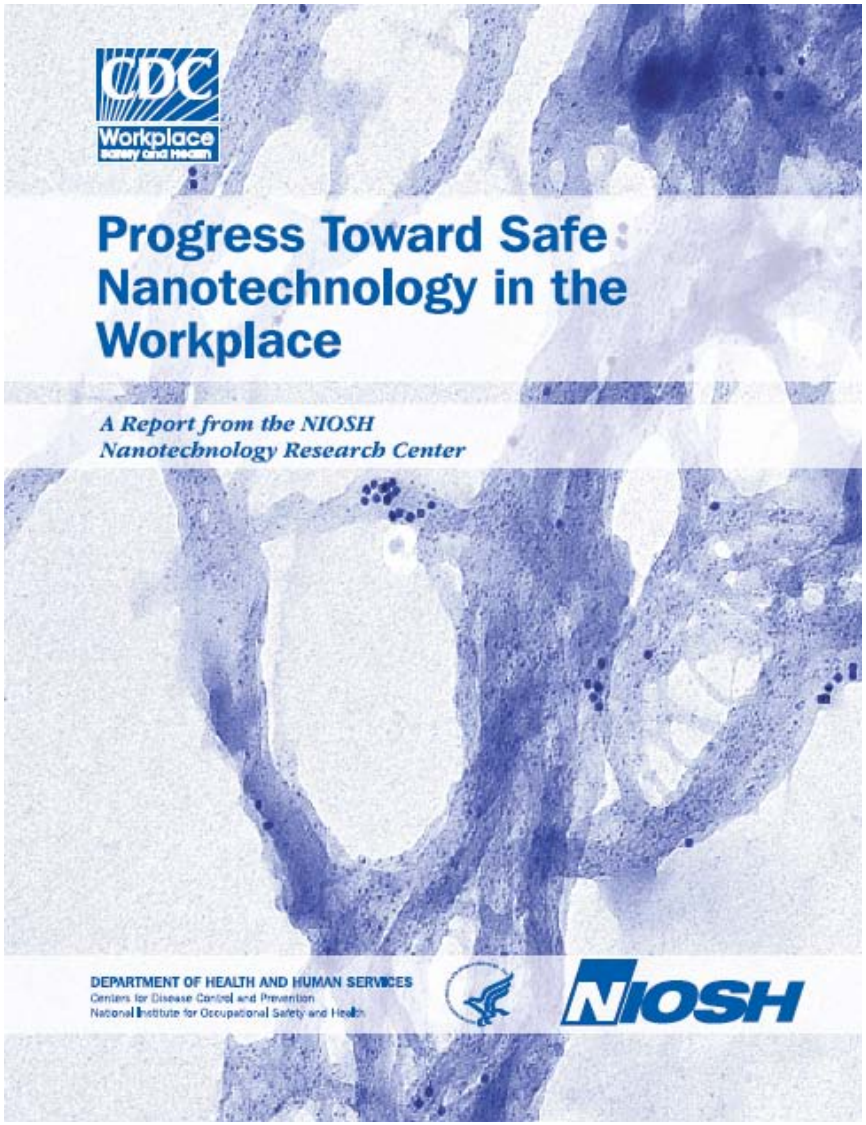
16.6.1 NIOSH – Formulating workplace safety standards for nanotechnology
16.6.2 Protecting workers in the workplace
16.6.3 Assessing hazards in the workplace
16.6.4 Establishing a Nanotechnology Safety System

# Nanotechnologies and the Workplace



# NIOSH (National Institute for Occupational Safety and Health) is attempting to formulate workplace safety standards




The goals for NIOSH's NTRC (Nanotechnology Research Center) are as follows:

1. Determine if nanoparticles and nanomaterials pose risks for work-related injuries and illnesses.

2. Conduct research on the application of nanotechnology for the prevention of work-related injuries and illnesses.

3. Promote healthy workplaces through interventions, recommendations, and capacity building.

4. Enhance global workplace safety and health through national and international collaborations on nanotechnology research and guidance.

http://www.cdc.gov/niosh/docs/2007-123/pdfs/2007-123.pdf

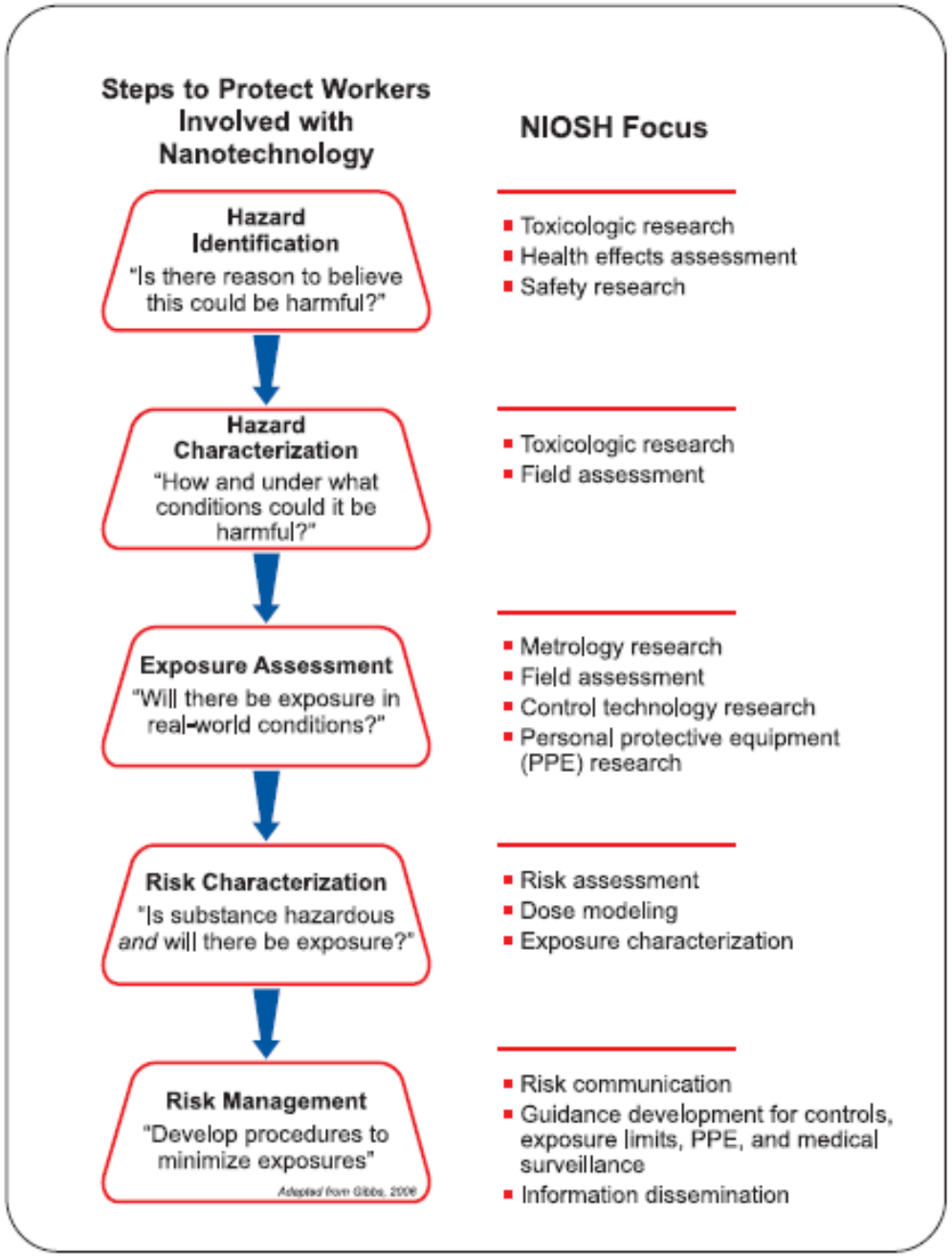


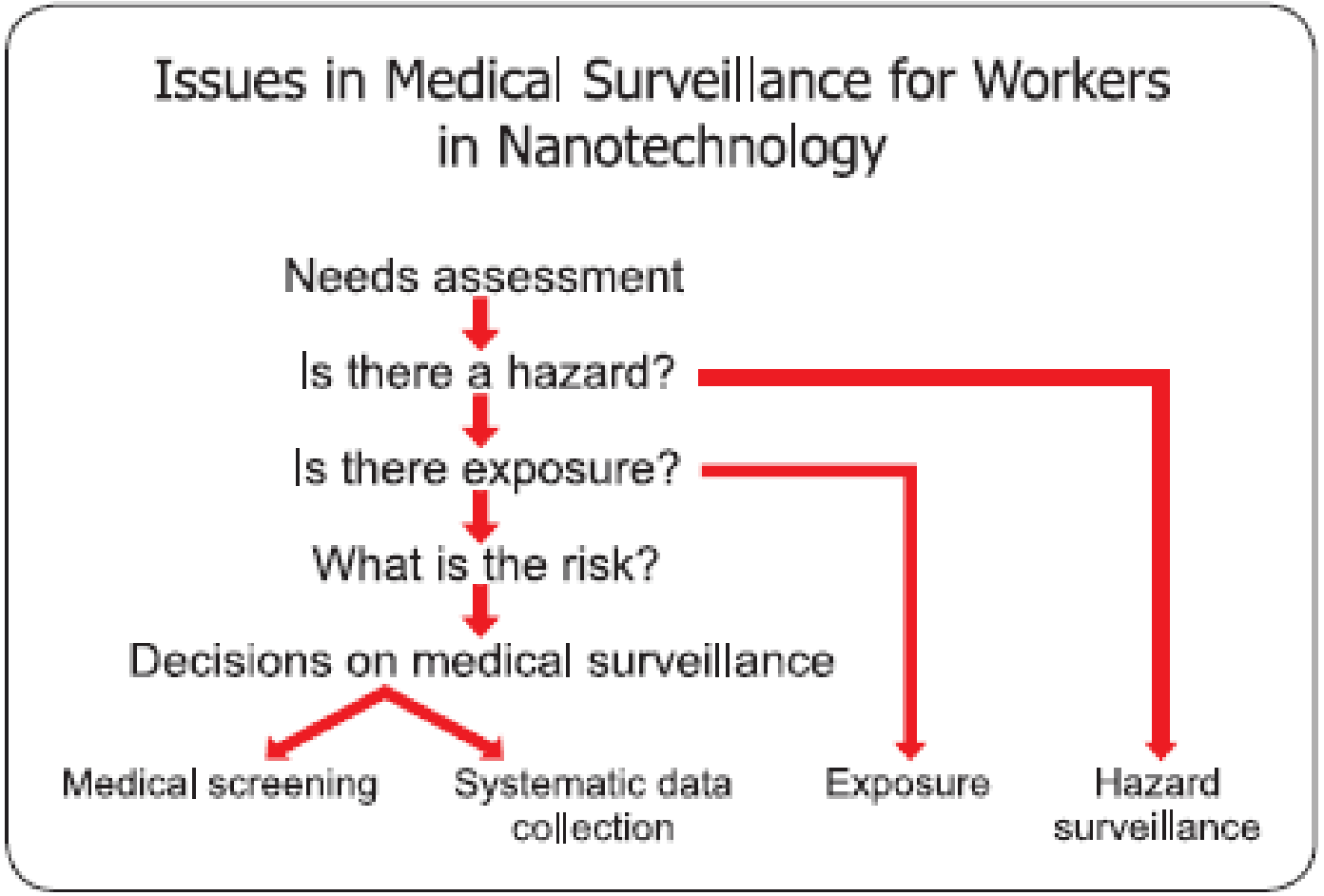

Figure 1. Steps to protect workers involved with nanotechnology

# Protecting Workers in the Workplace

Increasingly US workers will find themselves handling nanomaterials in the workplace. Appropriate protection standards must be put in place to insure their safety.

http://www.cdc.gov/niosh/docs/2007-123/pdfs/2007-123.pdf

# Assessing Hazards in the Workplace

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# Establishing a Nanotechnology Safety System


http://www.cdc.gov/niosh/docs/2007-123/pdfs/2007-123.pdf

# 16.7 The future of nano-healthcare products

# Nano Healthcare Products are Projected to Grow with Some Delays Due to Stringent Regulatory Barriers

| US NANOTECHNOLOGY HEALTH CARE PRODUCTS DEMAND (million dollars) | | | | | |
|---|---|---|---|---|---|
| | | | | % Annual Growth | |
| Item | 2004 | 2009 | 2014 | 09/04 | 20/04 |
| | | | | | |
| Nanotech Health Care Product Demand | 906 | 6500 | 27700 | 48 | 35 |
| Pharmaceuticals | 406 | 3000 | 16600 | 49 | 39 |
| Diagnostics | 465 | 1100 | 2200 | 19 | 14 |
| Medical Supplies & Devices | 35 | 2400 | 8900 | 133 | 50 |
| | | | | | |



http://www.freedoniagroup.com

## US Nanotechnology Health Care Product Demand to Reach $6.5 Billion in 2009

Cleveland, OH | May 10, 2005

Demand for nanotechnology health care products in the US is projected to increase nearly 50 percent per year to $6.5 billion in 2009. Gains will be led by the introduction of new, improved cancer and central nervous system therapies based on solubilization technologies. Diagnostic tests based on nanoarrays and quantum dots, and imaging agents based on superparamagnetic iron oxide nanoparticles will also see strong growth. In spite of progress in introducing new products, the vast potential of nanotechnology in the health care field will not be fully realized for at least a decade as stringent regulatory barriers and technical complexities delay the commercialization of targeted drug delivery systems, tissue regenerators and other breakthrough products. However, by 2020, demand for nanotechnology health care products is projected to exceed $100 billion. These and other trends are presented in ***Nanotechnology in Health Care***, a new study from The Freedonia Group, Inc., a Cleveland-based market research firm.

# References

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3. NIOSH workplace documents: http://www.cdc.gov/niosh/docs/2007-123/pdfs/2007-123.pdf

4. Nano Healthcare Products assessment: The Freedonia Group, Inc http://www.freedoniagroup.com

5. Chinese FDA http://eng.sfda.gov.cn/WS03/CL0755/