

THE ROLE OF EPIDEMIOLOGY IN THE PREVENTION OF ADVERSE HUMAN HEALTH EFFECTS OF NANOTECHNOLOGY

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**National Nanotechnology Initiative: Human and
Environmental Exposure Assessment Workshop**

February 24- 25, 2009

Charge

- **Plenary**
 - Characterize health of exposed populations and environments (biota)
- **Breakout discussions**
 - Identify emerging needs
 - Build a dialogue toward consensus
 - Identify ongoing projects

Outline

1. Cascade of prevention
2. Role of Surveillance
3. Meta-analysis of literature
4. Meta-analysis of research in progress
5. Meta-analysis of grant opportunities
6. Identification of holes
7. Future directions

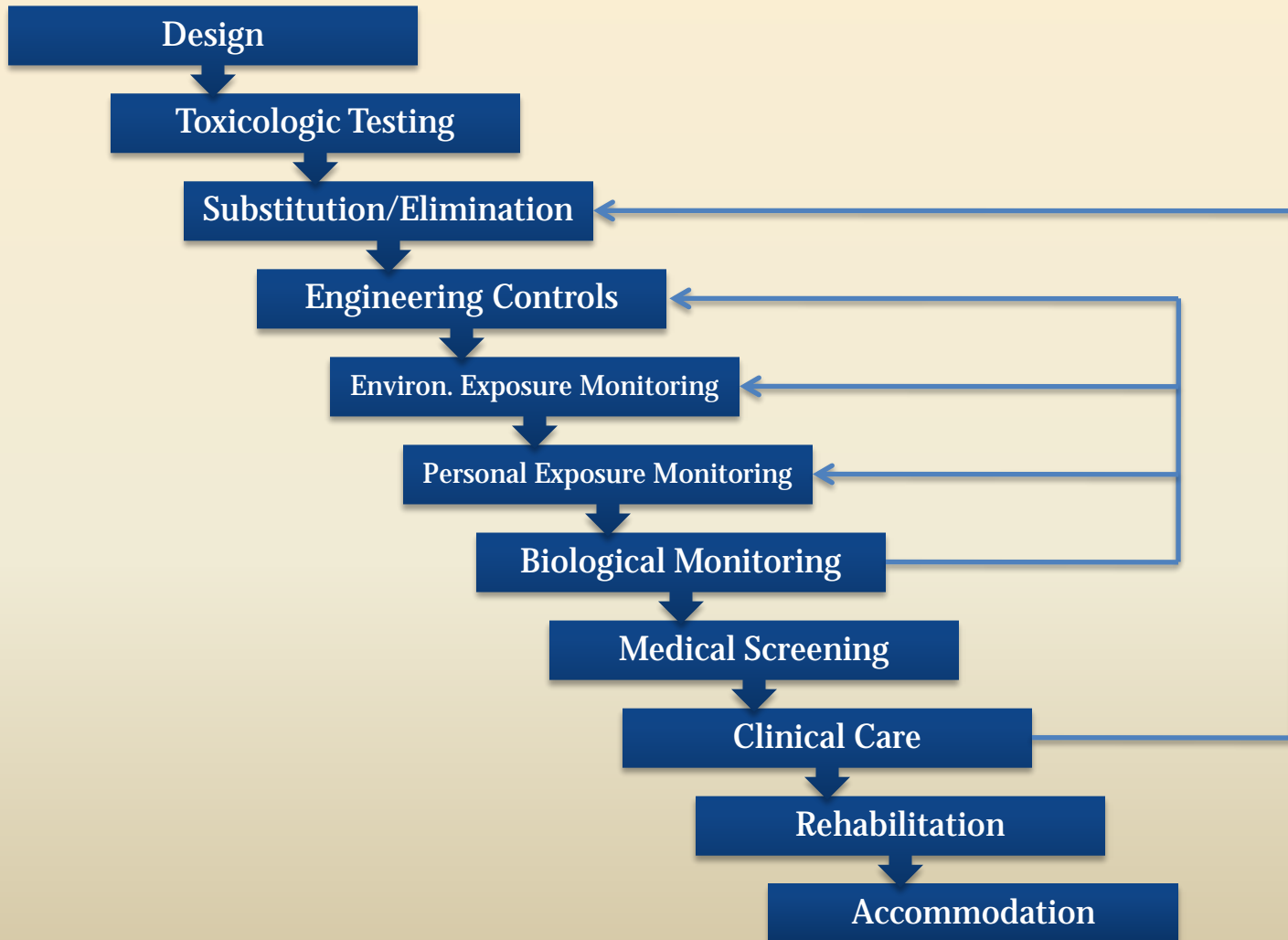
Basics of Prevention: The Cascade of Prevention



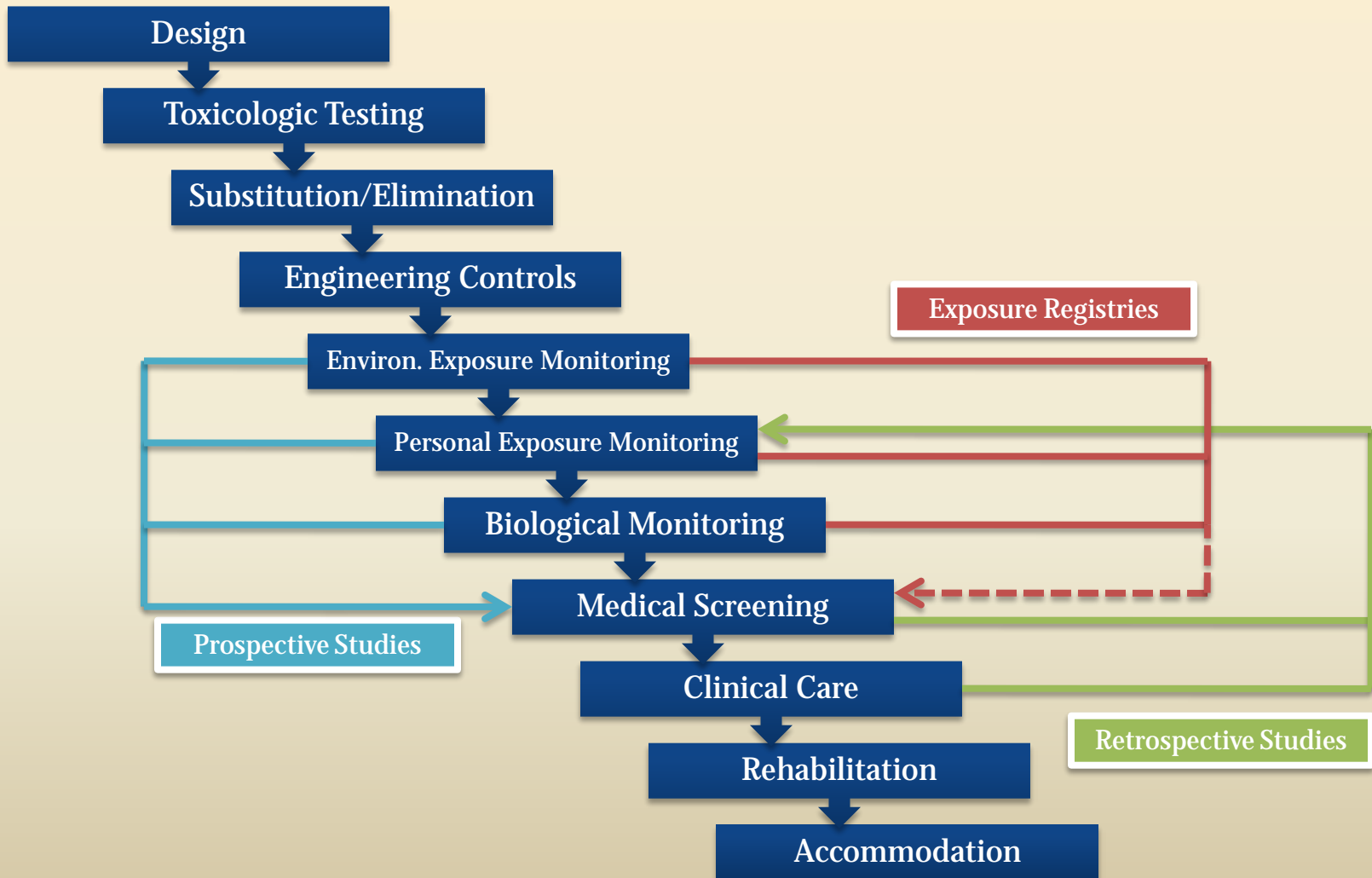
What is Surveillance and Where is it in the Cascade?

- “Ongoing systemic collection, analysis, and dissemination of exposure and health data on groups of workers for the purpose of early detection of disease and injury as well as patterns of occurrence presumably leading to prevention of subsequent disease.”

Where is Surveillance?



Major Types of Studies: Registries, Retrospective, Prospective



Meta-Analyses

1. Published literature?
2. Research activity in pipeline?
3. Research funding opportunities (pre-pipeline)?

Categorization of Literature

- Review articles
- Basic science studies for adverse outcomes / Toxicology
- Basic science studies for beneficial applications
- Clinical trials for beneficial applications
- Clinical trials on adverse health outcomes
- Methods for exposure assessment
- Exposure registries
- Epi: Morbidity studies
- Epi: Mortality studies
- Non-relevant articles

Results of a Systematic Review of Literature

PubMed (1890? – Present)

- nanotechnology & surveillance... 39
- nanotechnology & occupational... 46
- nanoparticles & surveillance... 38
- nanoparticles & occupational... 63

Medline (1950 – Present)

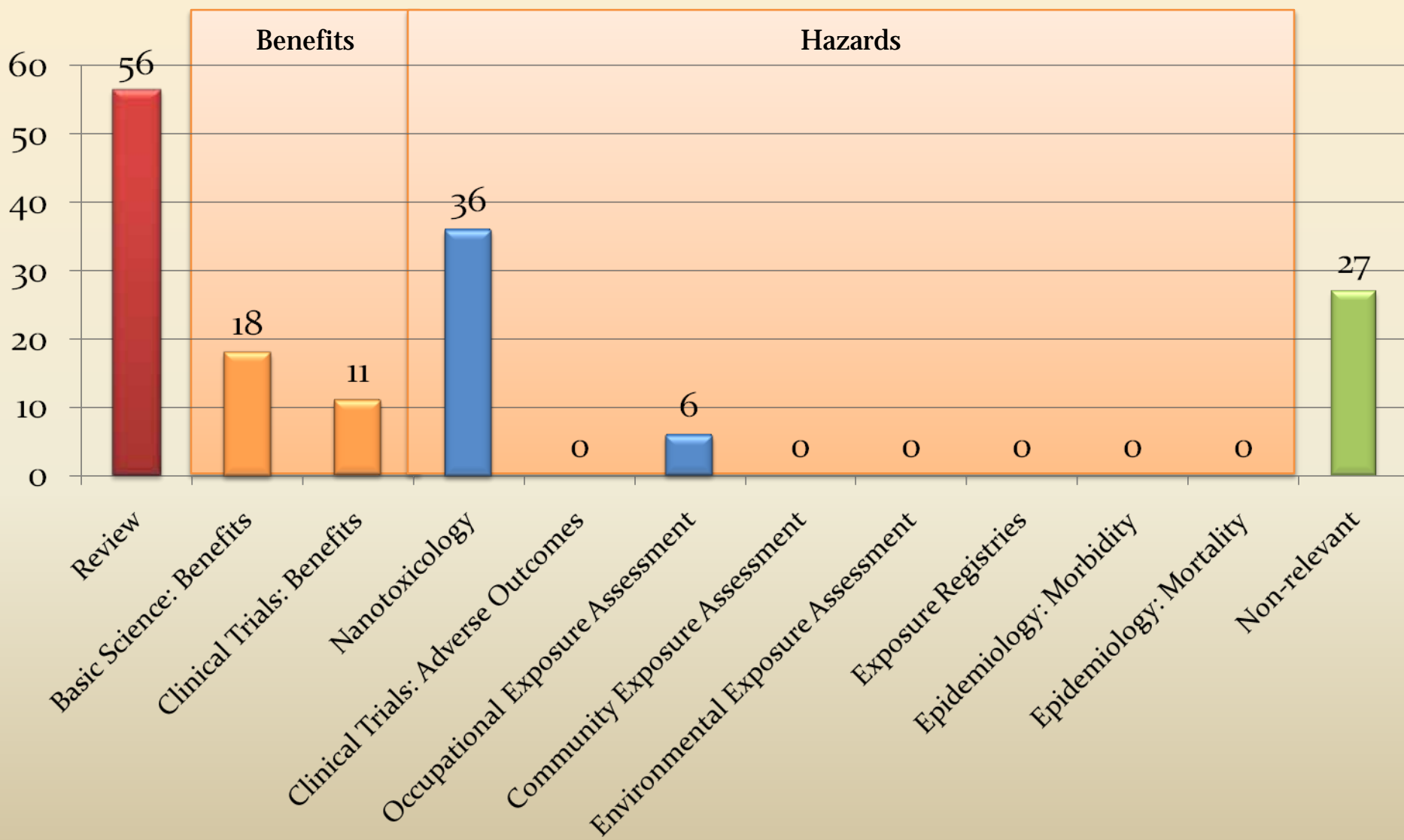
- nanotechnology & surveillance... 12
- nanotechnology & occupational... 32
- nanoparticles & surveillance... 8
- nanoparticles & occupational... 39

Cochrane Library (1998? – Present)

- nanotechnology... 11 (Clinical trials)
4 (Tech assessments)

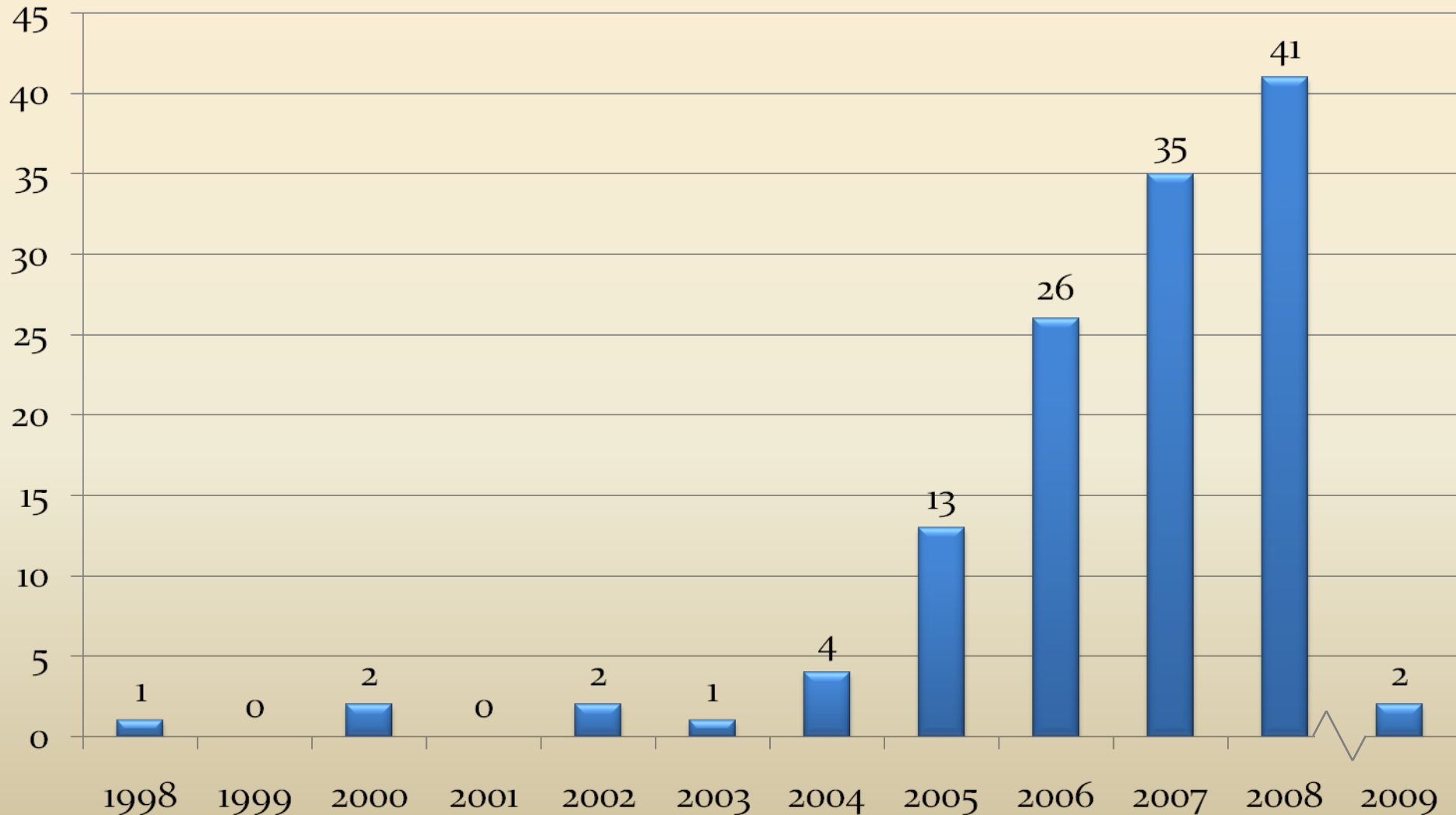
154 unique articles
292 total references

References by Primary Category (n=154)

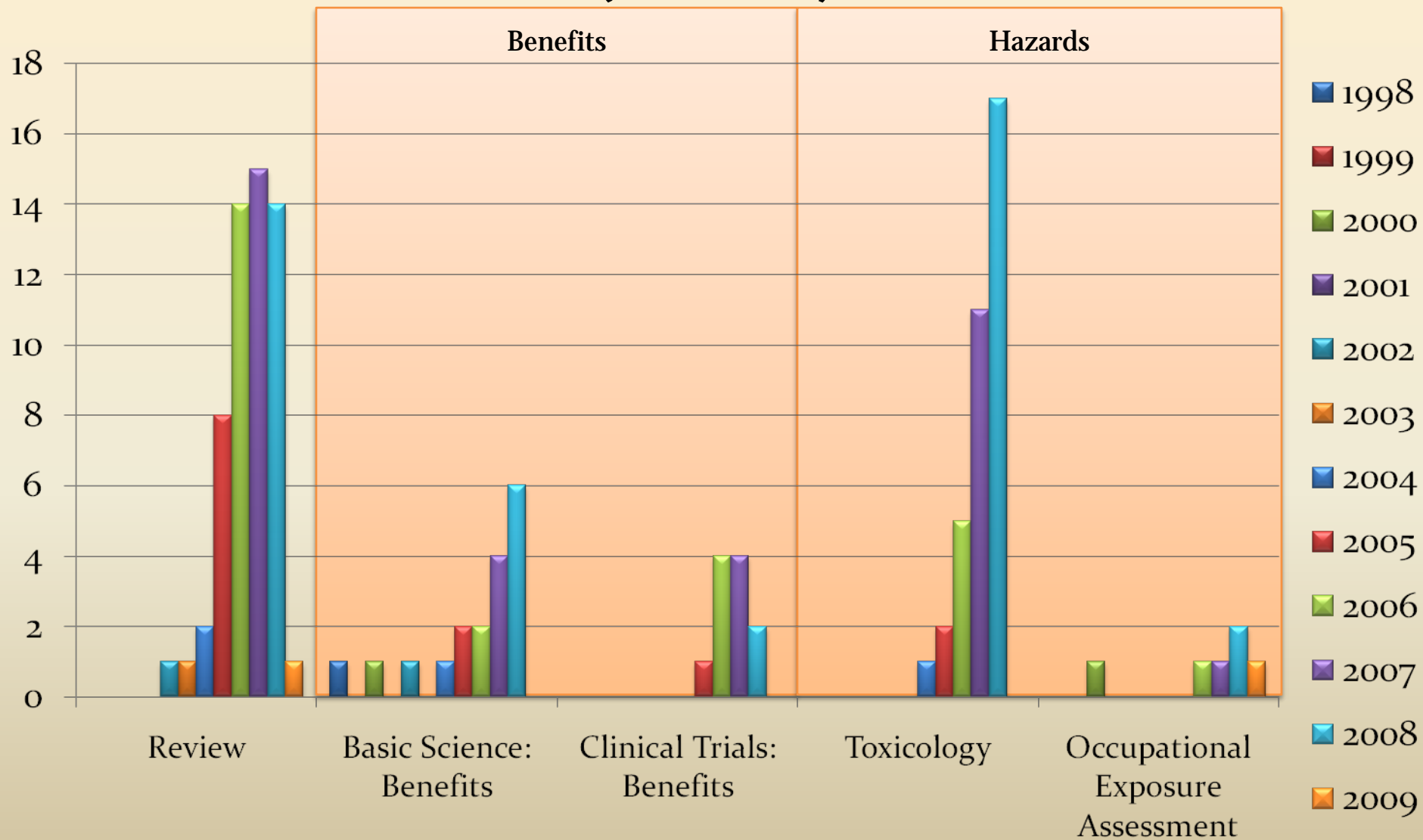


References by Year

(n=127)



References by Category by Year (n=127)

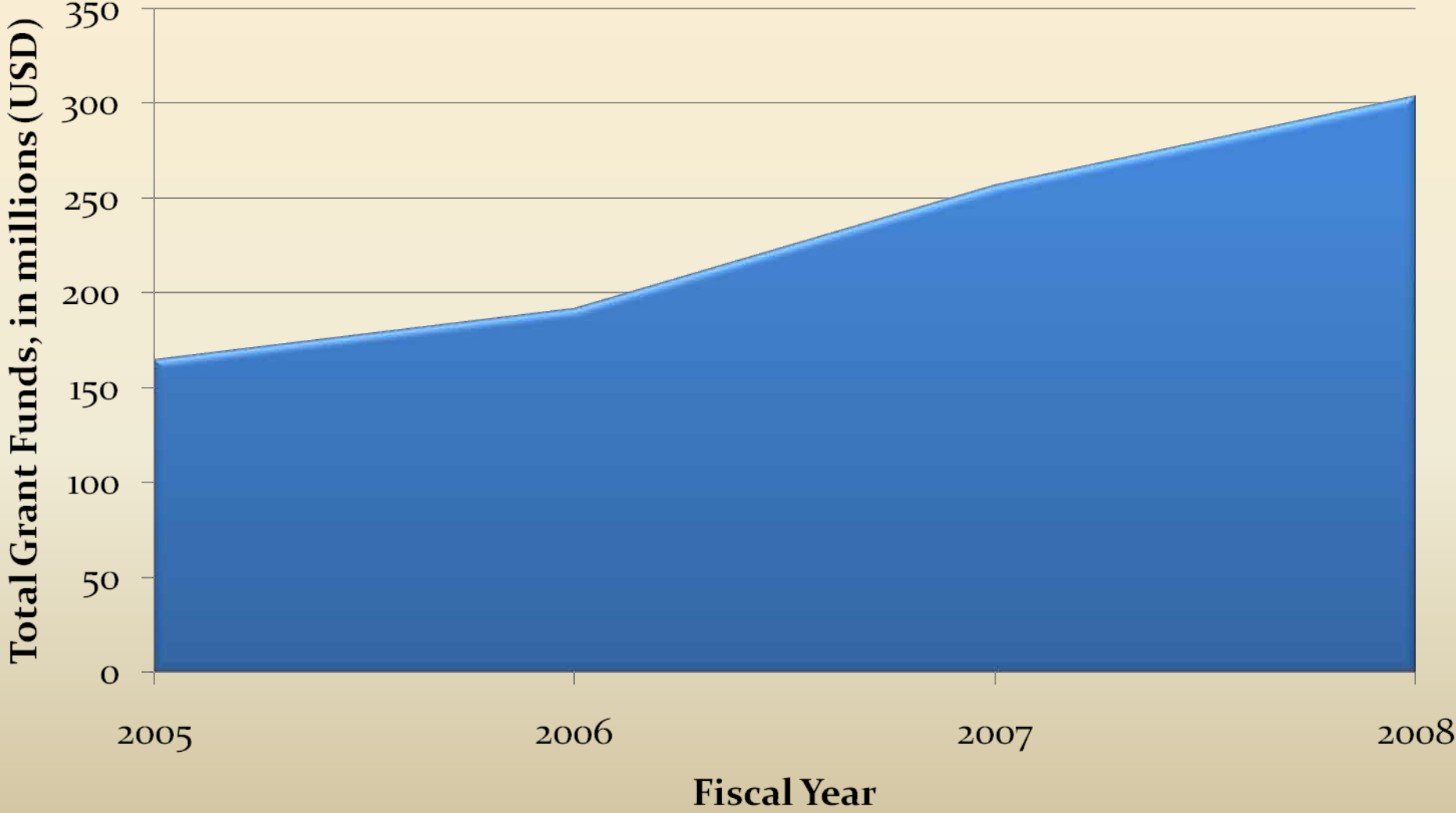


RESEARCH IN THE PIPELINE?

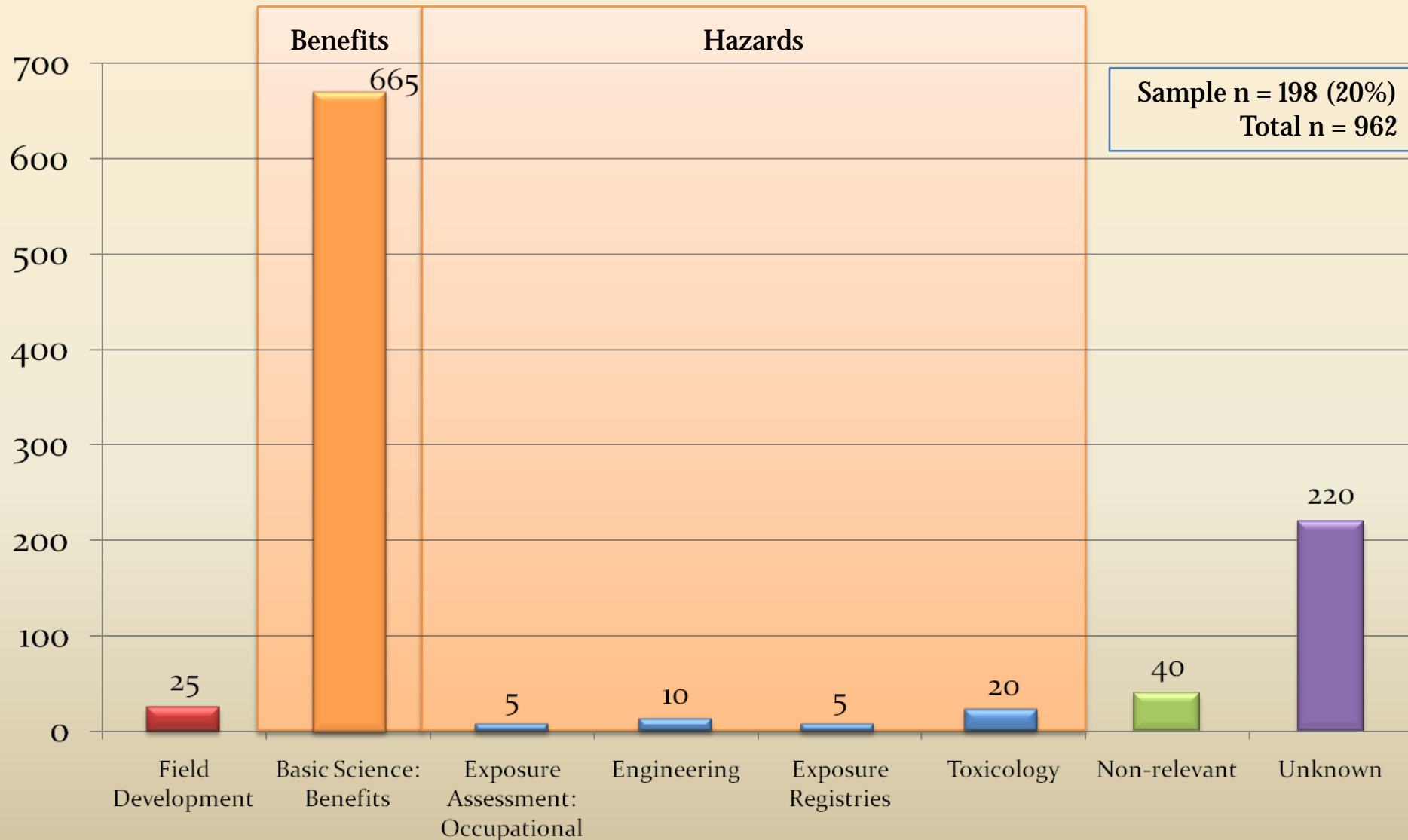
Analysis of Grant Awards

- **Source**
 - National Institutes of Health website
- **Limitations**
 - Grant titles; not abstracts

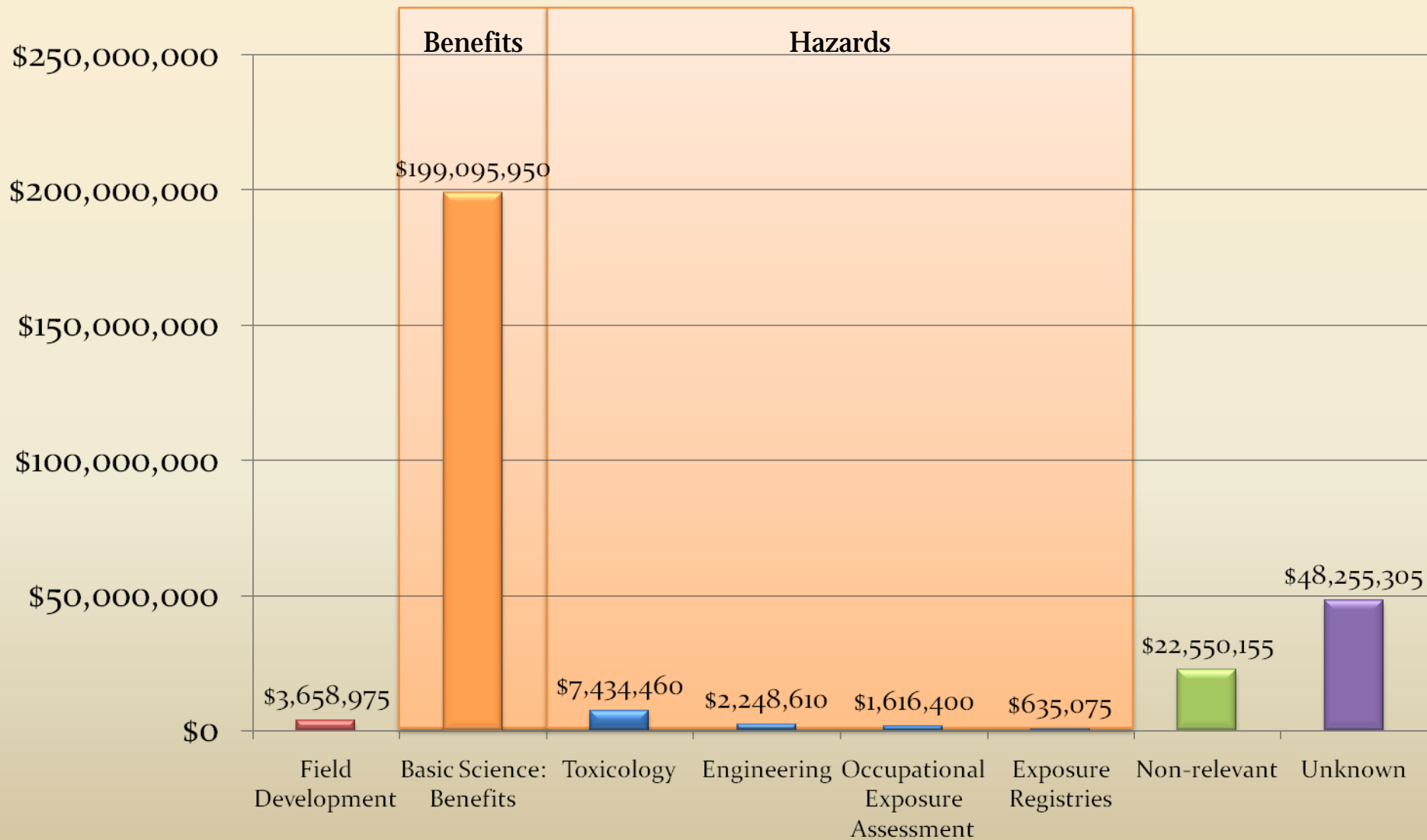
NIH Grant Awards for Research in Nanotechnology, FY 2005 - 2008



An Analysis of NIH FY2008 Grant Awards by Category within a Random Sample



Total NIH FY2008 Grant Awards by Category within Random Sample



**WAITING TO GO INTO THE
PIPELINE?**

Analysis of Federal Grant Opportunities

- **Sources**
 - Grants.gov (includes military, non-NIH / NSF)
 - National Institutes of Health
 - National Science Foundation
- **Method**
 - Automated search for “nanotechnology” or “nanoparticle(s)”; manual filtering for health issues
 - Review of RFA titles and abstracts

Grant Funding Opportunities for Research on Adverse Health Outcomes

Grants.gov (Federal)

- nanotechnology... 42
- nanoparticle(s)... 7

National Institutes of Health

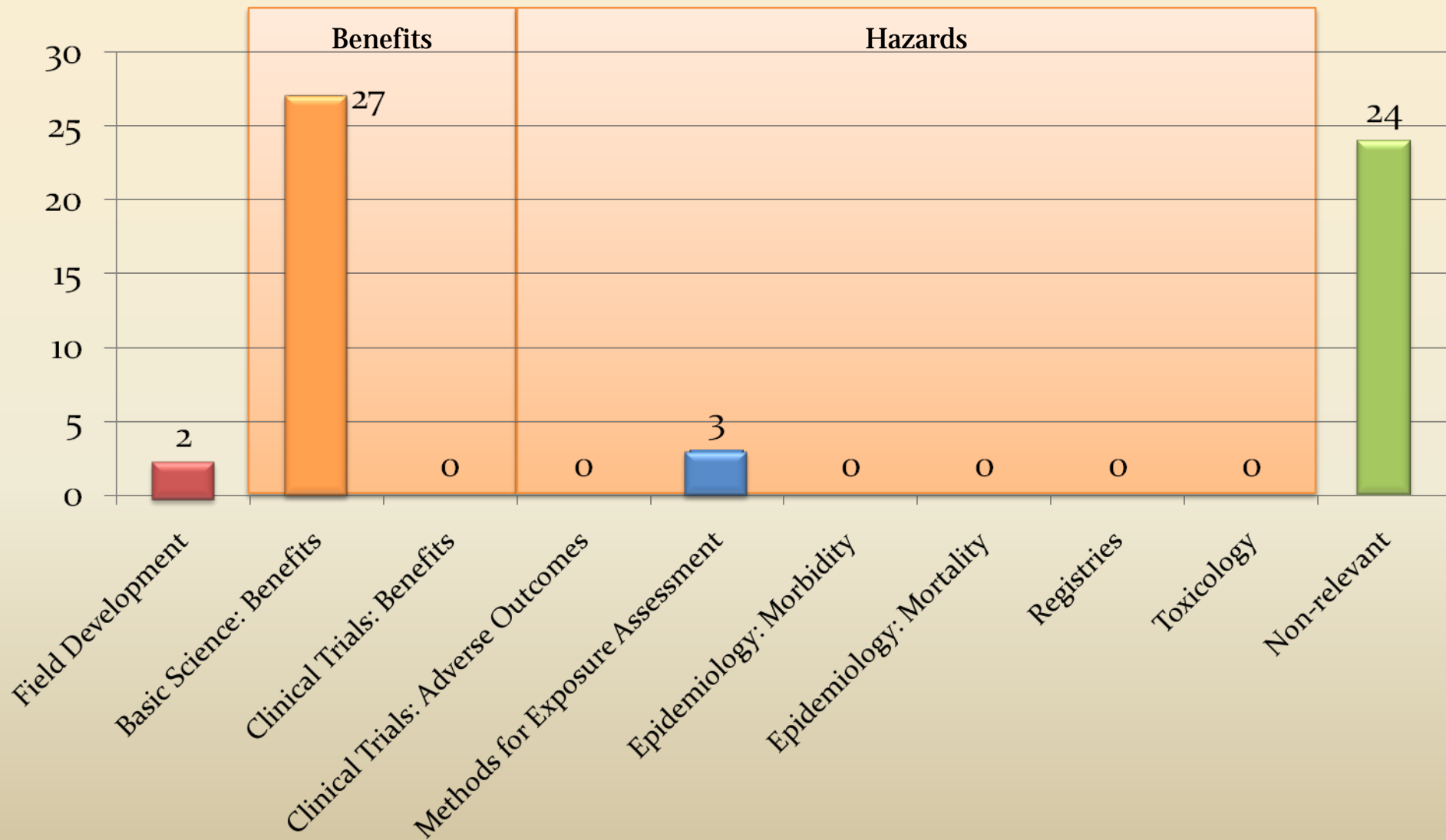
- nanotechnology... 21
- nanoparticles... 5

National Science Foundation

- nanotechnology... 23
- nanoparticles... 6

56 unique grants
103 total references

Grant Funding Opportunities for Research by Category (n=56)



Holes

- Non-published research
- Non-governmental research funding
- Non-funded registries
- Best practices survey for bio-monitoring; medical monitoring
- Development of epidemiologic methods
- Biomonitoring
- Medical monitoring
- Morbidity
- Mortality
- Workers, residents, and biota

WHAT NEEDS TO BE DONE?

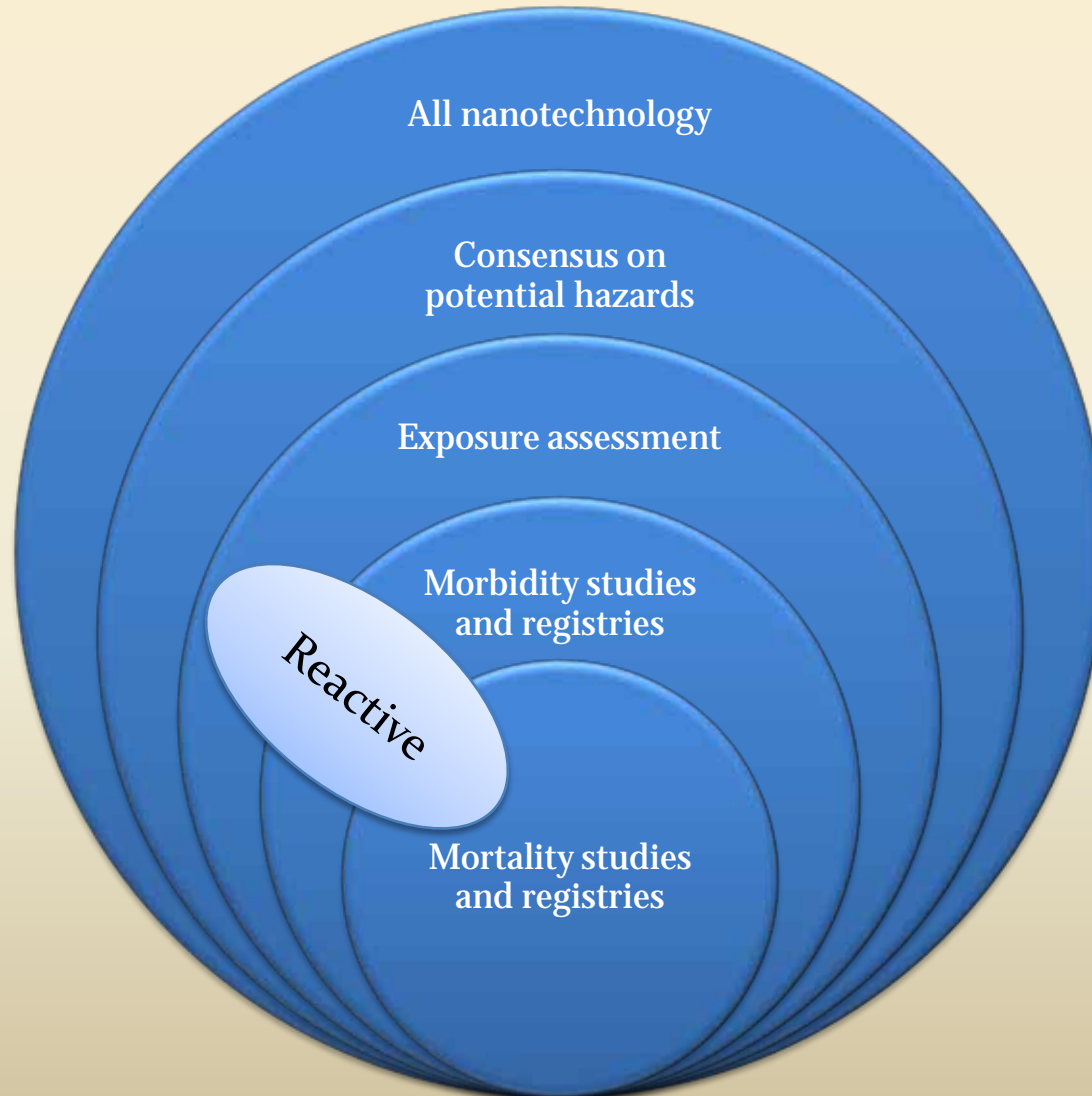
Methods development After Identifying Potentially Exposed

- **Biomonitoring**
 - For nanoparticles, in human samples
- **Medical monitoring and testing**
- **Epidemiologic methods**

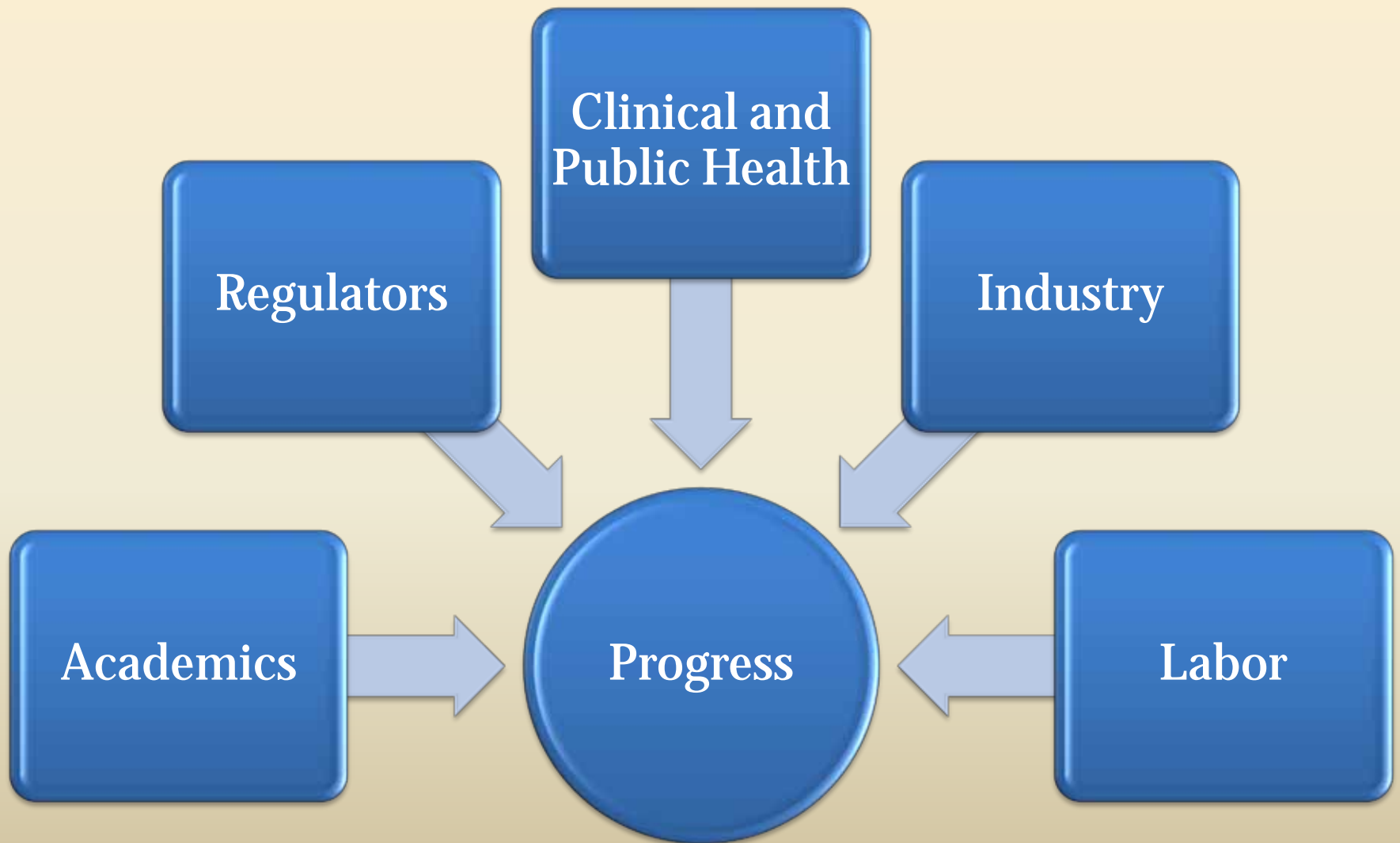
More on Limitations: Will Prototypical Surveillance Systems Work?

	NIOSH Preplanned Cohort Studies	CPSC Sentinel Hospitals (e.g. NEISS)	FDA Passive Post- market Surveillance	NIOSH Field Epidemiology and Investigation
Local Human – Occupational	+	-	-	+
Widespread Human – Environmental	+	+	+/-	+
Local Plant life	+	-	-	+
Local Non- human animal life	+	-	-	+

A Strategic Approach to Population-based Research



Organizing and Managing the Process





***TOGETHER* WE WIN**

Get behind your labor-management committee

Humility:

“Good surveillance does not necessarily ensure the making of the right decisions but it reduces the chances of wrong ones.”

- Alex Langmuir

Summary and Conclusions:

- A wave of beneficial new technology is coming
- There may be exposures and related hazards
- We need:
 - To be organized and inclusive
 - To be systematic and judicious
 - To be funded (set aside of 5-10% of funding)



THE

END

Literature: Review Articles

- Schulte P, Geraci C, Zumwalde R, Hoover M, Kuempel E. Occupational risk management of engineered nanoparticles. *J Occup Environ Hyg*. Apr 2008;5(4):239-249.
- Maynard AD. Nanotechnology: the next big thing, or much ado about nothing? *Ann Occup Hyg*. Jan 2007;51(1):1-12.
- Sng J, Koh D. Nanocommentary: Occupational and environmental health and nanotechnology--what's new? *Occup Med (Lond)*. Oct 2008;58(7):454-455.
- Wilson RF. Nanotechnology: the challenge of regulating known unknowns. *J Law Med Ethics*. Winter 2006;34(4):704-713.
- Warheit DB, Sayes CM, Reed KL, Swain KA. Health effects related to nanoparticle exposures: environmental, health and safety considerations for assessing hazards and risks. *Pharmacol Ther*. Oct 2008;120(1):35-42.

Literature: Basic Science Benefits

- Jordan A, Scholz R, Maier-Hauff K, et al. The effect of thermotherapy using magnetic nanoparticles on rat malignant glioma. *J Neurooncol*. May 2006;78(1):7-14.
- Lacoeyille F, Hindre F, Moal F, et al. In vivo evaluation of lipid nanocapsules as a promising colloidal carrier for paclitaxel. *Int J Pharm*. Nov 1 2007;344(1-2):143-149.
- Ochoa J, Irache JM, Tamayo I, Walz A, DelVecchio VG, Gamazo C. Protective immunity of biodegradable nanoparticle-based vaccine against an experimental challenge with *Salmonella* Enteritidis in mice. *Vaccine*. May 30 2007;25(22):4410-4419.
- Reddy GR, Bhojani MS, McConville P, et al. Vascular targeted nanoparticles for imaging and treatment of brain tumors. *Clin Cancer Res*. Nov 15 2006;12(22):6677-6686.

Literature: Clinical Trials Benefits

- Ernst CP, Brandenbusch M, Meyer G, Canbek K, Gottschalk F, Willershausen B. Two-year clinical performance of a nanofiller vs a fine-particle hybrid resin composite. *Clin Oral Investig.* Jun 2006;10(2):119-125.
- Yilmaz E, Borchert HH. Effect of lipid-containing, positively charged nanoemulsions on skin hydration, elasticity and erythema--an in vivo study. *Int J Pharm.* Jan 13 2006;307(2):232-238.
- Reis AF, Giannini M, Pereira PN. Long-term TEM analysis of the nanoleakage patterns in resin-dentin interfaces produced by different bonding strategies. *Dent Mater.* Sep 2007;23(9):1164-1172.
- Banchellini E, Macchiarini S, Dini V, et al. Use of nanotechnology-designed footsock in the management of preulcerative conditions in the diabetic foot: results of a single, blind randomized study. *Int J Low Extrem Wounds.* Jun 2008;7(2):82-87.

Literature: Nanotoxicology

- Morfeld P. Lung dosimetry and risk assessment of nanoparticles. *Inhal Toxicol.* Feb 2007;19(2):195; author reply 197-198.
- Niwa Y, Hiura Y, Sawamura H, Iwai N. Inhalation exposure to carbon black induces inflammatory response in rats. *Circ J.* Jan 2008;72(1):144-149.
- Oyabu T, Ogami A, Morimoto Y, et al. Biopersistence of inhaled nickel oxide nanoparticles in rat lung. *Inhal Toxicol.* 2007;19 Suppl 1:55-58.
- Roursgaard M, Poulsen SS, Kepley CL, Hammer M, Nielsen GD, Larsen ST. Polyhydroxylated C60 fullerene (fullerenol) attenuates neutrophilic lung inflammation in mice. *Basic Clin Pharmacol Toxicol.* Oct 2008;103(4):386-388.
- Veranth JM, Kaser EG, Veranth MM, Koch M, Yost GS. Cytokine responses of human lung cells (BEAS-2B) treated with micron-sized and nanoparticles of metal oxides compared to soil dusts. *Part Fibre Toxicol.* 2007;4:2.

Literature: Occupational Exposure Assessment

- Fujitani Y, Kobayashi T, Arashidani K, Kunugita N, Suemura K. Measurement of the physical properties of aerosols in a fullerene factory for inhalation. *J Occup Environ Hyg.* Jun 2008;5(6):380-389.
- Methner MM, Birch ME, Evans DE, Ku BK, Crouch K, Hoover MD. Identification and characterization of potential sources of worker exposure to carbon nanofibers during polymer composite laboratory operations. *J Occup Environ Hyg.* Dec 2007;4(12):D125-130.
- Peters TM, Elzey S, Johnson R, et al. Airborne monitoring to distinguish engineered nanomaterials from incidental particles for environmental health and safety. *J Occup Environ Hyg.* Feb 2009;6(2):73-81.
- Paik SY, Zalk DM, Swuste P. Application of a pilot control banding tool for risk level assessment and control of nanoparticle exposures. *Ann Occup Hyg.* Aug 2008;52(6):419-428.

Grants: Field Development

- **Career Development Component (\$66,268)**
- **Training for a New Interdisciplinary Research Workforce in Regenerative Medicine (\$331,407)**
- **Nanobiology Institutional Training Grant (RMI) (\$318,605)**
- **Priority Setting Stage (\$15,042)**

Grants: Basic Science Benefits

- **Use of Beta-lapachone for Lung Cancer Chemotherapy (\$341,159)**
- **Using Nanomaterials to Inhibit Mast Cell/Basophil-Associated Disease (\$297,814)**
- **Viral Detection Using Fluorescent Nanocrystals (\$330,353)**
- **Tumor targeted RNAi by novel nanovectors for molecular therapy of prostate cancer (\$127,680)**

Grants: Occupational Exp Assessment

- **Nontoxic Si Nanoprobes for Multiple Biomarker Imaging (\$323,280)**

Grants: Engineering

- **Atomic force microscope (\$275,000)**
- **Atomic Force-FRET Microscope Using Quantum Dot for Cell Mechanobiology (\$174,722)**

Grants: Exposure Registries

- **Development of methods and models for nanoparticle toxicity screening (\$127,015)**

Grants: Toxicology

- **Chemical, Structural, and Superstructural Determinants of Nanocarbon Toxicity (\$249,900)**
- **Nano-Biological Interactions and Toxicity of Engineered Metal Oxide Particles (\$346,500)**
- **Pharmacology and Toxicology Core (\$413,290)**
- **Remote Microvascular Dysfunction After Particulate Matter Exposure (\$477,202)**

Funding Opportunities: Field Development

- **Ethics Education in Science and Engineering (NSF)**
- **Science, Technology, and Society (NSF)**

Funding Opportunities: Basic Science Benefits

- **FY 2009 Multidisciplinary University Research Initiative (MURI) - For Proposal Submission to the Air Force (Air Force Office of Scientific Research)**
- **Metallic Materials and Nanostructures (NSF)**
- **Nanoscience and Nanotechnology in Biology and Medicine (R01) (NIDCR)**
- **Nanotechnology Undergraduate Education in Engineering (NSF)**

Funding Opportunities: Exposure Assessment

- **Environmental Implications of Emerging Technologies (NSF)**
- **Research to Action: Assessing and Addressing Community Exposures to Environmental Contaminants (R21) (NIEHS)**
- **Superfund Basic Research and Training Program (P42) (NIEHS)**

Cascade of Prevention

- Rutstein, D., Mullan, R., Frazier, T., Halperin, W., Melius, J., Sestito, J.: The sentinel health event (occupational): a framework for occupational health surveillance and education, JAPHA 73:1054-1062, 1983.
- Halperin WE. The role of surveillance in the hierarchy of prevention. Am J Ind Med 1996 Apr;29(4):321-3.
- Greife, A., Halperin, W., Groce, D., O'Brien, D., Pedersen, D., Myers, J., Jenkins, L. Hazard surveillance: Its role in primary prevention of occupational disease and injury. Appl.Occup. Environ. Hyg. 10:737-742, 1995
- Halperin, W., Ratcliffe, J., Frazier, T., Wilson, L., Becker, P., Schulte, P.: Medical screening in the workplace: proposed principles. JOM 28:547-552, 1986.
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