

# Regulatory Issues & Capacity

NIRT: Evaluating Oversight Models for Active  
Nanostructures and Nanosystems:  
Learning from Past Technologies in a Societal Context

SES-0608791

Susan M. Wolf, J.D. (PI)

Efrosini Kokkoli, Ph.D. (Co-PI)

Jennifer Kuzma, Ph.D. (Co-PI)

**Jordan Paradise, J.D. (Co-PI)**

Gurumurthy Ramachandran, Ph.D. (Co-PI)



UNIVERSITY OF MINNESOTA

# NIRT Research Goals & Methodology

1. Assessment of 6 oversight models utilizing criteria schooled by consensus (literature collection and analysis, expert elicitation, consensus):
  - drugs\*
  - medical devices\*
  - chemicals in the environment
  - chemicals in the workplace
  - gene transfer research (“gene therapy”)
  - genetically engineered organisms in the food supply
2. Application of oversight lessons to nanobiotechnology (mapping, consensus)
3. Development of oversight models for nanobiotechnology products and research (scenario analysis, consensus)

# Regulatory Issues & Capacity--Outline

1. Existing oversight frameworks & capacity--relevant federal agencies for 6 case studies
2. Regulatory criteria for evaluating oversight models
3. Case study: drugs & devices (FDA)
4. Regulatory issues & capacity in nano-bio

# 1. Relevant Federal Agencies for Case Studies

- **Environmental Protection Agency (EPA)**
  - Toxic Substances Control Act (TSCA), 15 U.S.C. §§2601-92
  - Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), 7 U.S.C. §§135-36
- **Food & Drug Administration (FDA)\***
  - Food, Drug & Cosmetics Act (FDCA), 21 U.S.C. §§301-99
- **Occupational Safety and Health Administration (OSHA)**
  - Occupational Safety & Health Act (OSHAct), 29 U.S.C. §§651-78
- **United States Department of Agriculture (USDA)**
  - Coordinated Framework for the Regulation of Biotechnology (with FDA & EPA)
- **National Institutes of Health (NIH)**
  - Recombinant DNA Advisory Committee (RAC), Human Gene Therapy Working Group

# 2. Regulatory Criteria for Evaluating Oversight Models

- A. Development
  - i. Impetus
  - ii. Legal grounding
  - iii. Empirical basis
  
- B. Attributes
  - i. Legal grounding
  - ii. Data requirements; stringency of the system
  - iii. Treatment of uncertainty
  - iv. Post-market monitoring
  - v. Compliance & enforcement
  - vi. Institutional structure; architecture of system
  
- C. Evolution
  - i. Extent of change in Attributes
  
- D. Outcomes

# 3. Case study: drugs & devices (FDA)

- FDA Institutional Structure:
  - Center for Drug Evaluation and Research (CDER)
  - Center for Devices and Radiological Health (CDRH)
  - Center for Biologics Evaluation and Research (CBER)
  - Office of Combination Products within the Office of the Commissioner:
    - Combination products: drug-device; drug-biologic; device-biologic.
    - Center coordination to determine how a product will be regulated depending on its primary mode of action. (Final rule and definition of PMOA effective November 2005, 21 CFR §3.2 (e).)
- Hierarchy:
  - U.S. Constitution
  - Statutes
  - Regulations
  - Guidance documents
  - Informal statements and advice

# Limitations of the FDA process

- Products regulated by the FDA each have a distinct regulatory framework. The policy approaches, definitional structures and basis for approval varies.
- Many provisions have become outdated, with amendments and definitions tacked on.
- FDA does not compare competing products, only determines whether safe and effective given data and using a risk/benefit approach.
- Measures of efficacy are context-specific and patient-specific and subject to changes over time.
- Many side effects are unknown before approval and only post-marketing surveillance can detect them.
- FDA recalls drugs or devices if they are unsafe, not because of evidence that they don't work.
- Unclear how best to balance benefits of making new products rapidly available with risks of unanticipated complications and recalls.
- Off-label use by doctors.

Richard A. Deyo, *Gaps, Tensions and Conflicts in the FDA Approval Process: Implications for Clinical Practice*, 17(2) *JABFP* 142-149 (2004).

## 4. Regulatory Issues & Capacity in Nanobio

- Recent agency efforts:
  - EPA: National Pollution Prevention and Toxics Advisory Committee (NPPTAC) Interim Ad Hoc Work Group on Nanoscale Materials formed in 2005 to develop voluntary nanoscale materials program & consider EPA review under TSCA.
  - FDA: Nanotechnology Task Force held first public meeting in October 2006 with findings slated for release in July 2007. Goal is to determine “regulatory approaches that encourage the continued development of innovative, safe and effective FDA-regulated products that use nanotechnology materials.”

## 4. Regulatory Issues & Capacity in Nanobio

- Nanobiotechnology crosses many product domains.
- Traditional definitions and methods of risk assessment are challenged by nanobio.
- Some agencies and regulatory frameworks regulate the products, some regulate claims of the manufacture. Many nanobio products fall into areas not regulated by the FDA as rigorously as others (e.g., cosmetics, dietary supplements).
- Uncertainty in how to define nanobiotechnology, and more specifically, how to distinguish from previous products:
  - Many products already approved by the FDA already fit into the definition(s) of “nano”.
  - Unclear how the “nano-ness” of a product matters to the FDA. How will the size matter for bioequivalence (drug), substantial equivalence (device), etc?