

# Nanotechnology: Medical Devices Science and Regulatory Aspects

**Subhas G. Malghan, PhD**

**Deputy Director**

**Office of Science and Engineering Laboratories**

**Center for Devices and Radiological Health**

**Food and Drug Administration**

**For presentation at the**

**ANH Workshop**

**March 10, 2008**

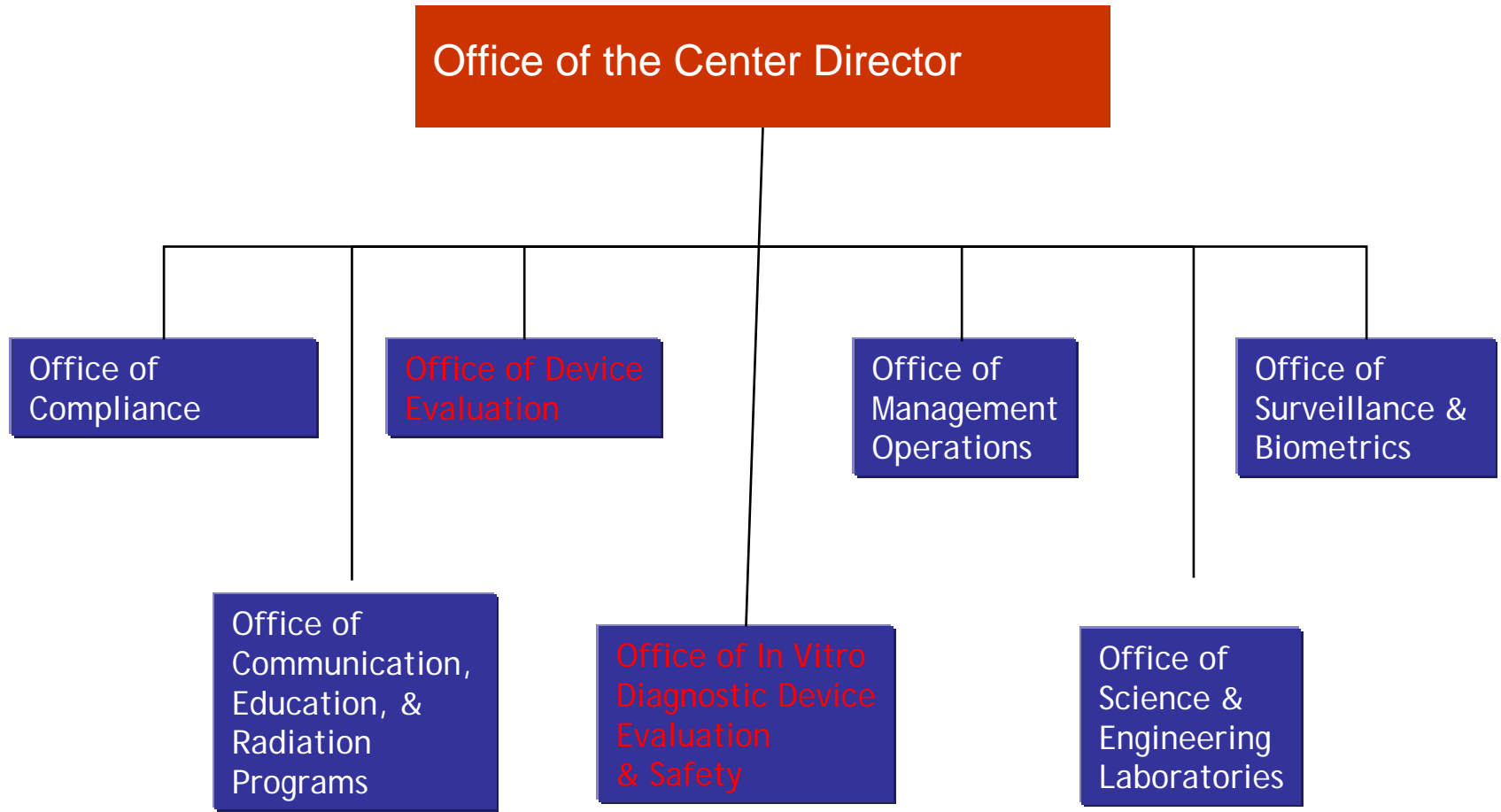
# Outline

1. Device specific issues
2. Science needs
3. Review aspects
4. Moving forward

# CDRH Mission

CDRH **promotes** and **protects** the health of the public by ensuring the safety and effectiveness of medical devices and the safety of radiological products

# CDRH Organization



# Medical Device Classification- Risk-Based Paradigm

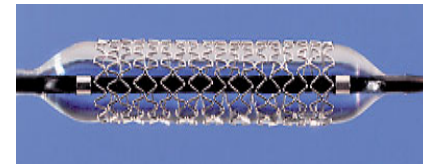
Medical devices are classified and regulated according to their degree of risk to the public



Class I



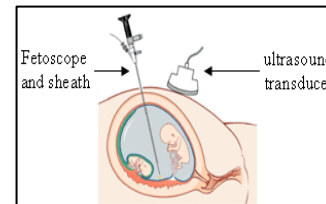
Class II



Class III



De Novo



HDE

# Device Specific Issues

- **Pathways for NT products to enter human body**
- **Materials and manufacturing**
- **Regulatory aspects**

# Device Specific Issues - - Pathways for nanoparticles to enter human body

## I. Devices in contact with human body

- Safety is an issue
- Wear debris from implanted devices
- Delivered - - e.g., implants, injected particles

## II. Devices not in contact with human body - -

### In-vitro diagnostic devices

- Safety of NT products is a lesser concern
- Accuracy and reproducibility of detection/measurement is a major concern

# Device Specific Issues - - materials science and manufacturing

- **NT in prevention, diagnosis, and treatment through innovations in:**
  - biosensors,
  - drug delivery,
  - molecular imaging,
  - surgery,
  - implants, ...
- **Uniqueness to medical devices: requirement of significant advances in**
  - + materials science (characterization, processing, ...)
  - + manufacturing (reproducibility, product quality, ...)

# Materials Science in NT Applications to Medical Devices

- **Richard Feynman, “principles of physics did not bar maneuvering things atom by atom.”**
- **Challenges**
  - **Lab innovation to Commercial product**
  - **Materials manufacturing, and scale-up**
  - **Production of medical grade materials**
  - **Multidisciplinary S&E expertise**
- **Easier path**
  - **Develop NT for existing applications to improve products; e.g., drug delivery**
  - **Simple to manufacture products come to market first; e.g., powders, colloids, coatings (catheters)**

# Waiting for a major breakthrough ... in device sector?

- **Scaffolding - - lattice material composed of nanomaterials- - help nerve cells regenerate; Tests conducted on mice by Dr. Samuel Stupp at Northwestern University**
- **Current consumer applications (tennis rackets, better golf balls, ...) are good for the long term view of medical devices**
- **Materials technology, scale up and manufacturing would benefit from such products development**

# We covered so far

## Device Specific Issues

- **Materials and manufacturing issues are major challenges, and require multidisciplinary approach**
- **First to come + simple to manufacture products**

# The following helped us shape our research directions

- Mechanistic understanding of how NP are retained in the tissue **is still evolving**
- Evidence of NP agglomerate within a short time of entering tissue (lungs, liver, spleen, ...)
  - presence and action of agglomerates of NP as a foreign body?
- Presence and ultimate disposal of NP from the body
- Physical, biological and chemical properties of particles play a major role

# CDRH Research Focus

**“Help CDRH address safety and efficacy of medical devices that incorporate NT” by developing knowledge and data.**

- **Mechanistic understanding of NP behavior from physical, chemical and biological aspects**
- **Advancing our knowledge regarding the characterization of NP.**
- **Knowledge and data help us address potential questions related to:**
  - **Available methods/technologies for characterization of NP and their limitations**
  - **Physico-chemical stability of NP**
  - **Physical, chemical and biological interaction of NP**
  - **Behavior of NP in in-vitro and in-vivo**
  - **Biocompatibility and Toxicity of NP**
  - **Guidance preparation**
  - **Participation in standards**

# CDRH Research Projects

1. **Stability of Nano-scale Constructs** (Saylor, Dair)
2. Hemolysis and Platelet Response to NP (Malinauskas)
3. **Critical Properties and Biological Effects of Nanoparticles** (Goering, Umbreit, Hitchins, Stratmeyer)
4. **Characterization of Optical Coherence Tomography (OCT)-Based Imaging Approaches** (Agrawal, Pfefer)
5. **Minimally Invasive Optical Imaging and Nanobiosensors for Biological Tissue** (Ilev)

# Are We Ready?

- **Current state**
  - Rate of arrival of NT-based products/devices has been slow ( as expected)
- **Future of NT products appears brisk**
  - **Freedonia Group projects 17% growth**
    - + \$53B in 2011 (\$5.2B for medical devices)
    - + \$110B in 2016 (\$16.2B for medical devices)

# Examples of Products Cleared by CDRH, supposedly contain nano(?)

Office of Device Evaluation (ODE)

- **NanoComposite -- Cosmedent Inc. (Dental filling material)**
- **Filtek Supreme -- 3M ESPE (Dental filling material)**
- **Simile Nano-Hybrid -- Pentron Labs (Dental filling material)**
- **NanOss -- Angstrom Medica (Orthopedic bone filler)**
- **On-Q Silver Soaker Catheter -- I-Flow Corp (Catheter)**
- **Silver Bandage -- Curad (bandage)**

# Examples of IVD Products Cleared by CDRH, supposedly contain nano

Office of Invitro-Diagnostic Device Evaluation and Safety (OIVD)

- 1) **Verigene Warfarin Metabolism Nucleic Acid Test, Nanosphere Inc. (Warfarin sensitivity)**
- 2) **The GeneSearch™ Breast Lymph Node Assay --- molecular diagnostics assay for breast lymph node testing, Veridex LLC**

# Regulatory Aspects

- Does the product contain NP?
- Under the existing authorities and procedures, CDRH has ability to assure product safety (?)
- Combination products likely to emerge first?
- Does the presence of NP affect product labeling?
- Does the presence of NP raise issues under the National Environmental Policy Act (NEPA)?
- Can existing QSR requirements for process validation address issues for manufacturing nanotechnology products?

# Current Review Process

- **Primary focus is on products safety and efficacy**
  - **No formal process to address/identify NT products**
  - **Case-by-case evaluation**
  - **Attention to NT issues addressed within review offices**
- **Difference in safety assessment of in-vitro diagnostic (IVD) and non-IVD devices**
- **IVD devices: main focus is on efficacy (accuracy) and less on safety**
- **NEPA compliance is an on-going issue**

# Some Issues from Reviewers

- **Science and Test Methods**
  - **Product specification**
  - **Functionalization of polymers used for coatings**
  - **Interference from materials impacting the endpoint or the signal**
  - **Evaluation of stability of nanoparticles**
- **Manufacturing**
  - **Particle manufacturing process**
  - **Lot to lot reproducibility**
  - **Shelf life conditions**

## We covered so far ...

- **Current knowledge gaps is the basis for our research**
- **Products are slowly emerging, but future appears brisk**
- **No major changes in the review process, at present**
- **Case-by-case review**

# Progress and Future Actions

- **Some activities in progress:**
  - **Formation of a CDRH-NanoTechnology Interest Group (NTIG)** - representation from all offices.
  - implementation of FDA Taskforce report,
  - communication among reviewers and other knowledge holders
  - coordinate FDA second workshop activities
  - **develop knowledge on combination products**
- **CP program funded a project to promote training, review and communication aspects - - focus on reviewers**

# Summary

- **Device issues: characterization/standards, materials development, and manufacturing**
- **CDRH/FDA research is focused on these issues**
- **Regulatory considerations: safety aspects, and lack of science and manufacturing data**