Medical Applications of Nanotechnologies: Challenges and Concerns for Technology Roadmaps, International Standards and Measurements

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Any opinions expressed in this presentation are my own and not necessarily those of NIST.

NIST

Outline

- Why Standards Are Important
- Technology Roadmaps
- International Standards

  Priorities for Medical Applications of Nano-electrotechnologies
- A Nanostructure Example: Bone Tissue Engineering
- Invitation to Contribute

Significance of International Standards for Nanotechnologies

- **Global competition is intense.**
- **Standards are significant enablers for commercial success at all stages of innovation - from R&D to recycling/disposal.**
- **Successful innovation in nanotechnologies requires standards based on the best of each nation's science and engineering.** Standards not so based may constrain innovation and entrench inadequate technologies.
- **Documents for standards on consensus specifications advance the field.**
- **Standards influence R&D and business models.**

"Standards enable innovative products and new markets." –
Patrick Gallagher, NIST Director, November 2009

Technology Roadmaps for Nanotechnologies

- **International Electronics Manufacturing Initiative (iNEMI). MEMS (Sensors/Actuators) Working Group – medical products enabled by nanotechnologies are within the scope of the 2010 roadmap. http://www.inemi.org/**
  Michael Gaitan, NIST, leads the iNEMI MEMS Working Group.
- **International Roadmap for Semiconductors (ITRS) now has more than Moore (MtM) applications of nanoelectronics such as RF and Analog/Mixed-Signal technologies, Energy (e.g., solar, photovoltaics, smart grid, and storage-batteries), Imaging (e.g., quantitative medical imaging), MEMS-Sensors/Actuators (e.g, biosensors), Bio-Chips (e.g., bioelectronics), and 3D Heterogeneous Integration.**
  http://itrs.public.net/
- **iNEMI and ITRS are discussing collaborations for MEMS (2010 iNEMI roadmap and 2011 ITRS roadmap).**
- **Semiconductor Research Corporation (SRC) Bioelectronics Roundtable Reports 2009 (BERT1) and 2010 (BERT2)**

IEC TC 113 Working Groups

- **JWG 1: Terminology and Nomenclature**

- **JWG 2: Measurement and Characterization**

JWG 1/JWG 2 are Joint Working Groups with ISO TC 229 on nanotechnologies.

- **WG 3: Performance Assessment**

WG3 Scope: To develop standards for the assessment of performance, reliability, and durability related to the nanotechnology-enabled aspects of components and systems in support of continuous improvement at all stages of the value adding chain. WG 3 considers market demand and technology pull with an emphasis on fabrication, processing and process control, disposal, and recycling.

IEC TC 113 Working Groups (continued)

- **WG 3: Performance Assessment**

Six stages of the linear economic model – technical research, technology development, initial deployment, commercialization (large-scale, high-volume manufacturing), end of first use, and end-of-life (disposing and recycling)

ISO TC 229 Working Groups

- **JWG 1: Terminology and Nomenclature**

- **JWG 2: Measurement and Characterization**

JWG 1/JWG 2 are Joint Working Groups with IEC TC 113

- **WG 3: Health, Safety and Environmental (HSE) Aspects of Nanotechnologies**

WG3 Scope: The development of science-based standards in HSE aspects of nanotechnologies. A key part of the strategy for WG3 is to develop a framework and roadmap. There are high-priority needs for standard methods for toxological screening, toxicity/hazard potential determinations, occupational exposure limits, etc. for nanoparticulates and other nanoscale materials; and protocols for inhalation testing, toxicology testing, safe handling, exposure determination and safe disposal of nanotubes.

ISO TC 229 Working Groups (continued)

- **WG 4:** **Material specifications**

WG4 Scope: (work in progress) The development of material specifications for about 40 distinct materials and four classes of materials. These include metallic nanoparticles, such as gold, silver and platinum; metal oxides nanoparticles such as zinc and titanium oxides; compound particles such as polymers and alloys; and functionalized nanoparticles and quantum dots. Works in closed collaboration with JWG2 to ensure coordination of measurement, characterization and test methods.

A GRAND CHALLENGE

Sustaining effective communication, cooperation, and collaboration among all the organizations working on international standards – essential for reducing the overload of overlaps or *who is doing what*? And optmizing limited resources

In nanotechnologies, TCs for ISO and IEC co-exist with:
OECD
JEDEC JC-14 Quality and Reliability – before 2001
ASTM International Committee E56 on Nanotechnology – 2005
IEEE Standard Test Methods for Measurement of Electrical Properties of Carbon Nanotubes - 2005
IEEE NTC Nanoelectronics Standards Roadmap – 2007
SEMI
ANF
CEN 352 on labeling
And this list goes on and on and on ……. .

Survey Results - Priorities

Survey on nano-electrotechnologies was online from May 10, 2008 to December 15, 2008. 459 respondents from 45 countries ranked in priority order the items listed below for the five taxonomy categories.

Products

1. Energy
2. Medical Products
3. Computers
4. Telecommunication
5. Security/Emergency
6. Consumer Electronics
7. Household Applications
8. Transportation

Cross-Cutting Technologies

1. Sensors (chemical, physical, mechanical, etc.)
2. Fabrication tools for integrated circuits
3. Nano-electromechanical Systems
4. Performance and reliability
5. Analytical equipment for properties
6. Environmental, Health, and Safety (bi-modal)
7. Instrumentation for Process Control
8. Optical Technologies

Properties

1. Electronic and Electrical
2. Optical
3. Biological
4. Chemical
5. Radio Frequency
6. Magnetic

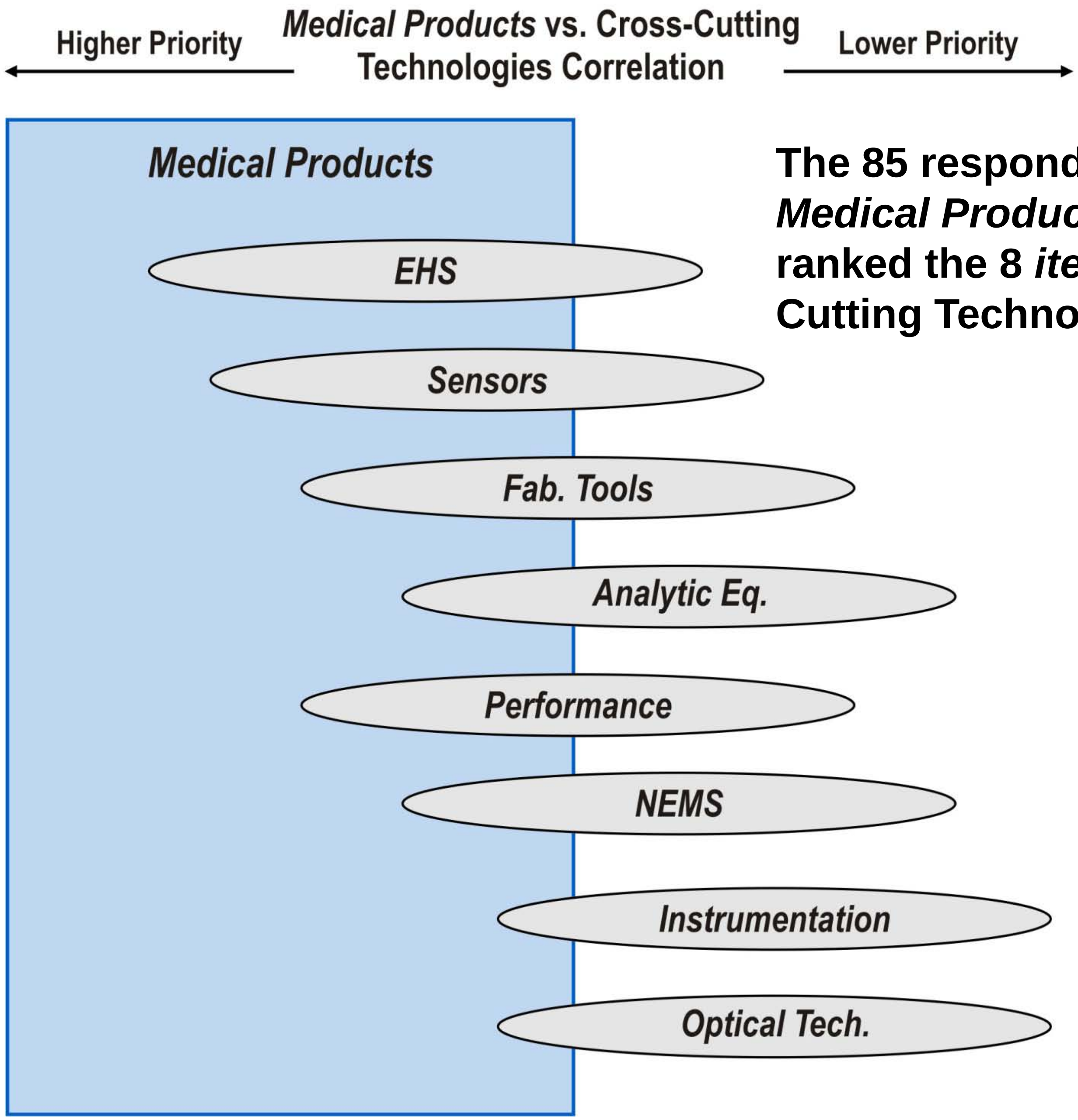
IEC Discipline Areas

1. Measurement /Performance
2. Design/Development
3. HSE
4. Dependability/Reliability
5. Electromagnetic Compatibility
6. Terminology/Symbols

Stages of the Economic Model

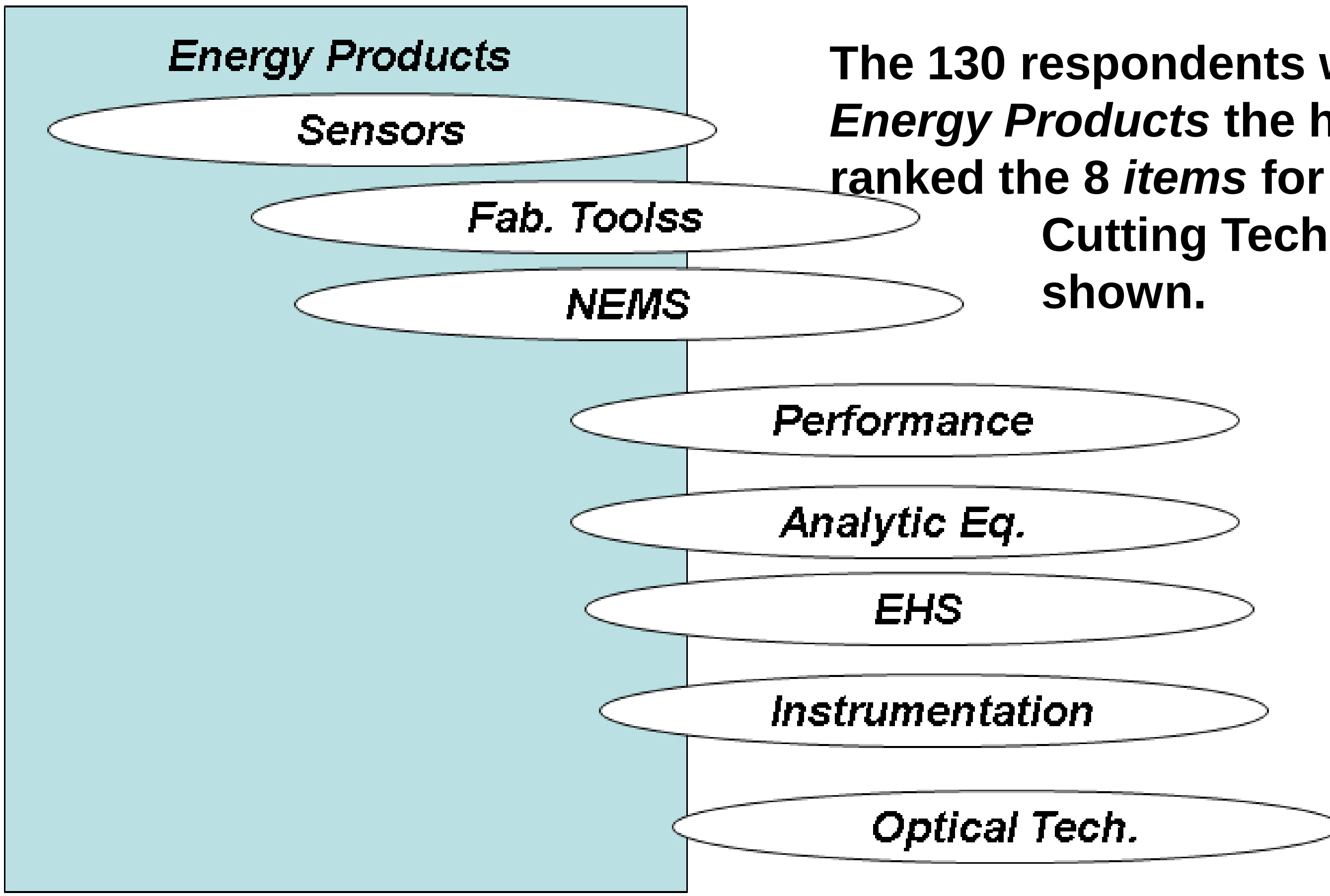
1. Basic Research
2. Technology Development
3. Initial Deployment
4. Commercialization
5. Initial End-of-Use
6. End-of-Life (Recycle/Disposal)

http://www.nist.gov/eeel/semiconductor/upload/NIST_Energetics_Survey.pdf



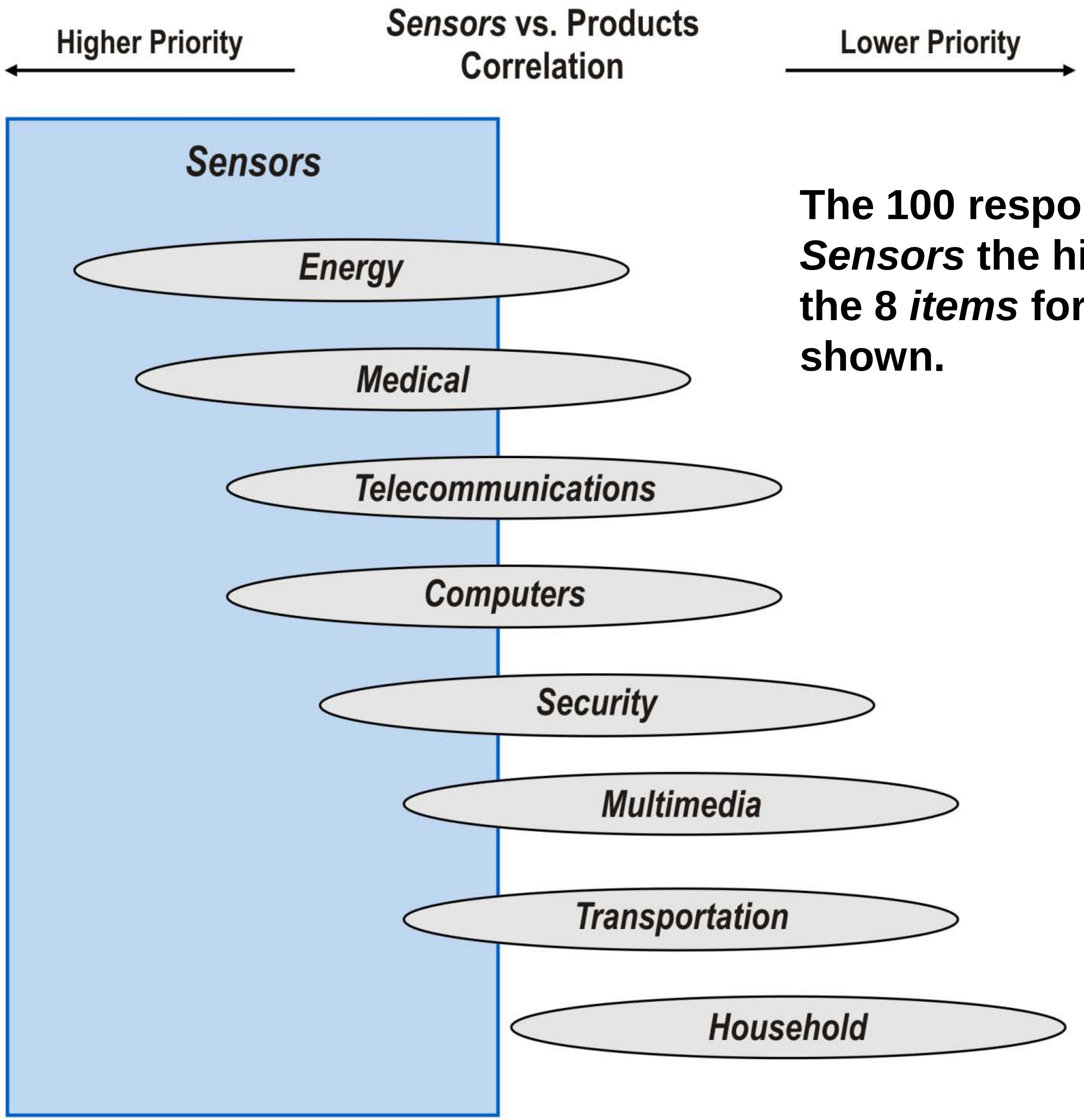
The 85 respondents who ranked *Medical Products* the highest also ranked the 8 *items* for Cross-Cutting Technologies as shown.

Higher Priority ← ***Energy Products* vs. Cross-Cutting Technologies Correlation** → Lower Priority



The 130 respondents who ranked *Energy Products* the highest also ranked the 8 *items* for Cross-Cutting Technologies as shown.

H. S. Bennett, et al., *Priorities for Standards and Measurements to Accelerate Innovations in Nano-electrotechnologies: Analysis of the NIST-Energetics-IEC TC 113 Survey*, NIST Journal of Research, Volume 114, Issue 2, March-April 2009, and on the Web at http://www.nist.gov/eeel/semiconductor/upload/NIST_Energetics_Survey.pdf



The 100 respondents who ranked *Sensors* the highest also ranked the 8 *items* for Products as shown.

Complete Analysis of the Survey

Priorities for Standards and Measurements to Accelerate Innovations in Nano-electrotechnologies: Analysis of the NIST-Energetics-IEC TC 113 Survey

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http://nvl.nist.gov/pub/nistpubs/jres/114/2/V114.N02.A03.pdf

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Bone Tissue Engineering [1]

Single-walled carbon nanotube scaffolds promote differentiation of progenitor osteoblast cells into functional mature osteoblast cells – increase bone mineral density in patients with osteoporosis

Carbon nanotubes promote bone cell proliferation, show excellent affinity for cell adhesions, carry neutral charge sustain the highest bone cell proliferation and production of hydroxyapatite crystals; and chemically functionalized SWCNTs with negatively charged surface control the orientation of the nuclei of hydroxyapatite and promote the crystal growth.

Establishes direct relationships among SWCNTs, their electronic charge distributions, and bone health biomarkers.

[1] Xiaomin Tu, et al., Department of Chemistry, University of Arkansas Little Rock, Paper presented at MRS Spring Meeting 2007, San Francisco

Environmental, Health, and Safety (EHS) International Opportunities and Challenges

One randomly selected example from *NanoToday*, October 2007, Volume 2, Number 5, page 10:

Carbon nanotubes show germ-fighting promise

Toxicology and Environment - Researchers from Yale University have provided the first direct evidence that highly purified single-walled carbon nanotubes (SWNTs) exhibit strong antibacterial activity [Kang et al., Langmuir (2007) 23, 8670]. This has implications for both useful antimicrobial filtering processes, tissue engineering scaffolds based on nanostructures, and possible harmful environmental effects. … contact with nanotubes results in the death of the bacteria. … After exposure, loose DNA and RNA were found floating in the solution, …., causing this genetic material to float out.
What is the mechanism that leads to leakage of genetic material? – local inflammation, puncturing, etc. ?

Environmental, Health, and Safety (EHS) International Opportunities and Challenges

In U.S. – no single agency has jurisdiction over nanomaterials and nanostructures

OSHA - during manufacture

FDA - drug and device

EPA - end use

Balance between proceeding with some innovations and not proceeding other innovations – How will society decide?

In other nations

In other regions - EU, Asia, and the like

Environmental, Health, and Safety (EHS) International Opportunities and Challenges

EHS at each stage of the Nanomaterials/Nanostructures Cycle

Raw and/or Recycled Material → Process → Subassembly
→ System Integration → Product → End Use
→ End-of-Life → (Disposing and Recycling)

Who is responsible for EHS at each stage?

Who determines measurements and standards for benefits and risk management at each stage?

Will they be traceable to national measurement institutes?

Invitation to Contribute

The quality of the those portions of roadmaps and international standards and labeling that pertains to medical products enabled by nanotechnologies will depend in part on the contributions from the medical community (e.g., healthcare providers, researchers, manufacturers, regulators, and insurers) for all stages of the economic cycle - from R&D to recycling and/or disposal.

THANK YOU