New Opportunities for NIST in Bioscience and Health: Defining the Sweet Spots

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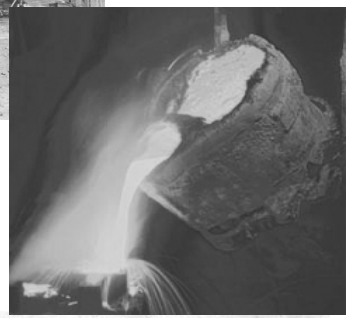
March 2007

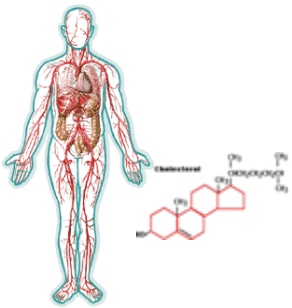
Outline

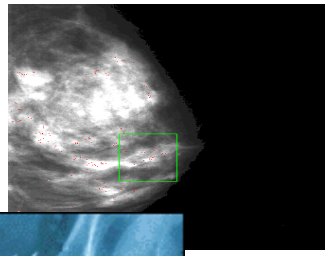
- Brief History of Healthcare Standards Program
- Formal NIST Commitment to the Emerging Biotechnology Industry
  - *Formation of Biotechnology Division*
- Expansion of Bio Activities throughout NIST in the late 1990's and 2000's
- Development of NIST-Wide Strategic Vision for Bio and Health Activities

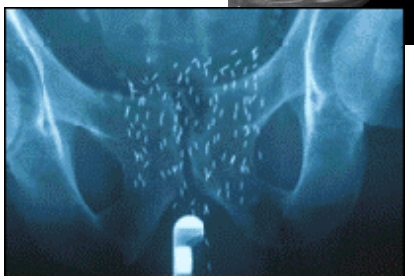
Since its inception NIST has focused its research and measurement standards program on addressing contemporary societal needs.



1901 → **2007**



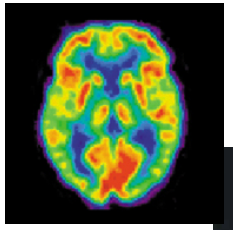


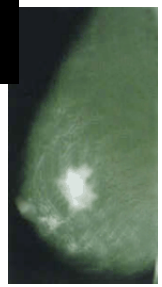


Examples of Healthcare Activities

1928 - Today: NIST & the American Dental Association

- Led to the development of mercury-free amalgams and the air-driven turbine drill now found in virtually all dentist offices





1920s - Today: NIST and Radiation Physics

- Critical program in dosimetry initially involving X-ray calibration and now standards for mammography and brachytherapy
- Radionuclide standardization for radiopharmaceuticals

1970's - Today: Standards for Clinical Diagnostics

- Primary references for electrolytes and metabolites
- Serum based standards for electrolytes and metabolites
- New Protein, peptide or DNA-based biomarkers

Biotechnology Emerges as a Market Sector

In the 1980's and 1990's, biotechnology emerged as a new market sector with predictions that biotech would become a major player in world markets

- this presented a new challenge and opportunity for NIST

The State of Biotechnology in 1991

- pre- "omics" era and the Human Genome had not been sequenced
- bioprocess engineering, biomedical engineering, biochemical engineering were becoming established as scientific disciplines
- New tools and applications for bio measurements were being developed at a rapid pace
  - e.g., CE, PCR, bio MS, high field NMR

Establishment of Biotechnology Division

At the request of the U.S. Senate, NIST prepared a plan for development of a measurements and standards program to support the emerging Biotech Industry.

- The Biotechnology Division was created in 1991 as a part of a NIST-wide reorganization.
- Scientists with “bio-related expertise” from seven divisions were brought together to assess needs and begin developing the generic measurements, models, data, and standards needed to accelerate the commercialization of biotechnology.

Biotechnology Division

In 1991 …

Efforts focused on:

- Bioanalytical Separations
- Sensor Technologies
- Biophysical Chemistry
- Structural Biology
- Bioprocess Engineering

We estimate the initial NIST investment in the Biotechnology Division budget to be approx. $3M (STRS).

In 2007 …

Efforts focused on:

- Biospectroscopy
- Cell and Tissue Measurements
- DNA Technologies
- Structural Biology

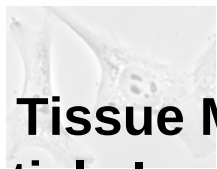
Biochemical Science Division's budget in 2007 is $9.5M (STRS), and a total budget of $14M.

Bio-Related Activities Have Expanded and Morphed … Within CSTL

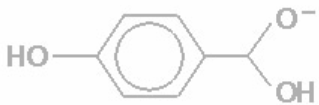
DNA and RNA Science
Metrology for Gene Expression
Nanobiotechnology

Marine Bioscience and Health
Metrology for Drug Delivery Systems
Standards for Food Safety and Nutrition

Cell and Tissue Measurements
Nanoparticle Imaging in Tissue
Quantitative Cell Biology

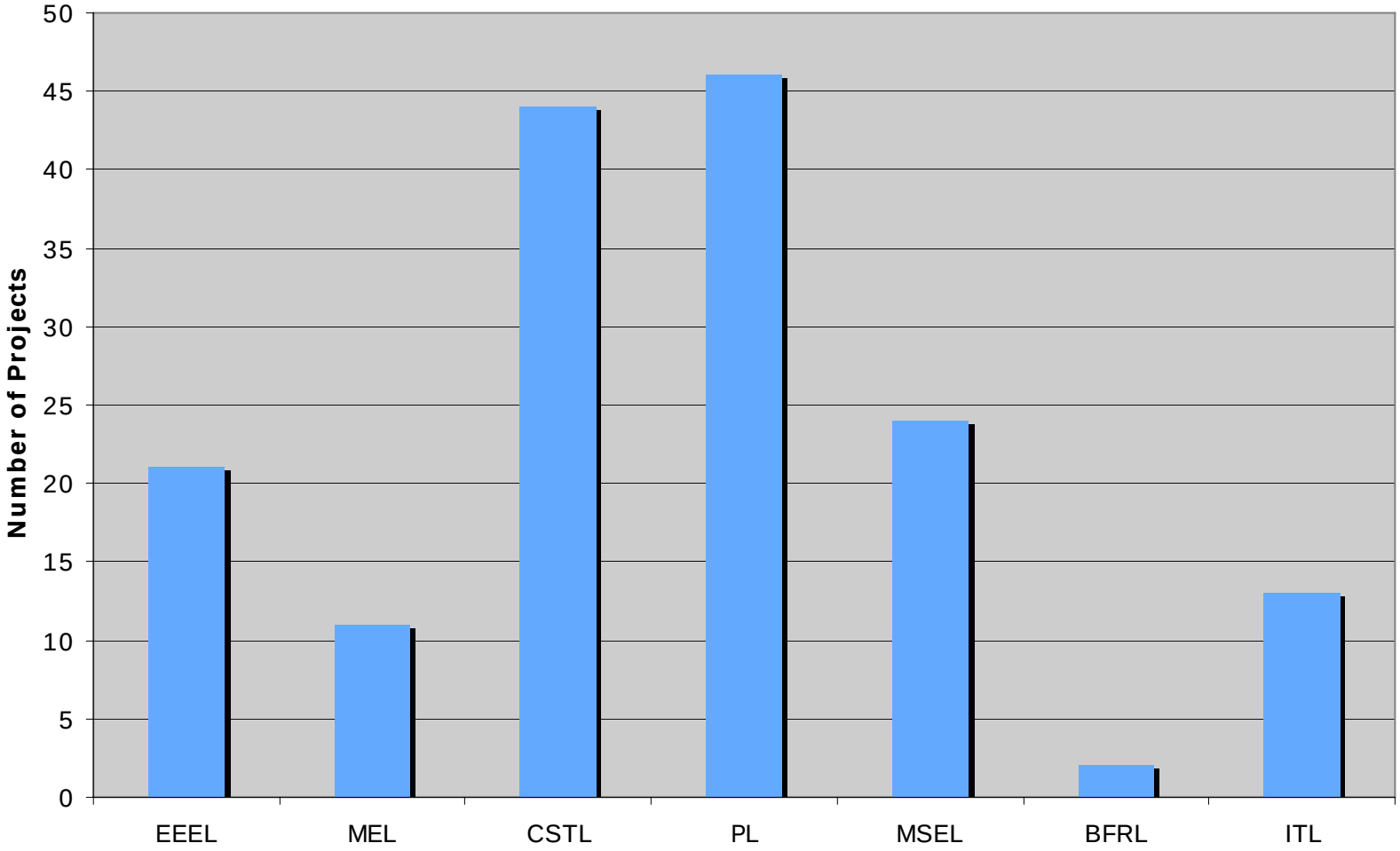


Structural Biology
Standards for Clinical Proteomics



Standards for Metabolomics

…and Throughout NIST



161	Projects in the Measurement and Standards Laboratories
66	Projects in the Advanced Technology Program

Total Project by Funding Level	Total Funding					
Core Competency	1 - $0K to $100K	2 - $101K to $500K	3 - $501K to $1M	4 - > $1M	Grand Total	Total Est $$$
01-Optical measurements and microscopy for biosensing, imaging and therapeutics	6	13	3	0	22	$ 6,550,000
02-Radiation metrology for diagnostic and therapeutic applications	2	11	4	0	17	$ 5,900,000
03-Optical measurements for structure, dynamics and function of biomolecules	3	13	2	1	19	$ 5,850,000
04-Electromagnetic fields and magnetic markers for bio/healthcare applications	8	6	0	0	14	$ 5,800,000
05-Electromechanical measurements and chemical microsensing for biosystems	3	7	0	1	11	$ 3,750,000
06-Mechanical and Structural Properties of Tissue Engineering Materials	0	8	2	0	10	$ 3,500,000
07-Neutron and X-Ray Measurements of Biomolecular Structures & Dynamics	3	7	0	0	10	$ 2,900,000
08-Chemical and Biological Measurements - Biological Markers	1	10	4	1	16	$ 2,850,000
09-Biothermodynamics	0	6	0	0	6	$ 1,900,000
10-Cell Metrology	0	3	1	0	4	$ 1,900,000
11-Chemical and Biological Measurement Standards	0	1	2	2	5	$ 1,500,000
12-Chemical and Biological Measurement Data	0	3	1	0	4	$ 1,500,000
13-Standards for medical, biological, and healthcare information systems	7	4	2	0	13	$ 1,500,000
14-Dimensional and Functional metrology for medical devices	3	2	0	0	5	$ 800,000
15-Mathematical models and software for bio-regulatory networks, protein patterns and image improvements	3	0	0	0	3	$ 650,000
16-Statistical metrology for bioimages and bioinformatics	1	2	0	0	3	$ 550,000
17-Environmental Measurements for Air and Water Quality	1	3	0	0	4	$ 150,000
Grand Total	41	99	21	5	166	$ 47,550,000

Of listed projects/programs:

26 have > $500K total funding

with only 5 of the 166 projects > $1M

Strategic Working Group on Biosystems and Health Established in 2003

Charge:

- identify areas of highest impact for biosystems and health
- identify the measurements, standards, and data requirements
- define NIST's role and strategies

Accomplishments:

- NIST activities related to Bioscience and Health catalogued
- Cross-NIST communications and collaborations increased

Process was designed from the bottom-up and lacked a clear statement/vision/ understanding of NIST's role in this area vs. other agencies such as NIH.

New "Biovision Team" Established in FY07

Charged with:

- Establishing a statement that clearly articulates NIST's role in Bio and Health
- Developing resource allocation plan for FY07 Bioimaging Initiative
- Identifying high priority areas for program expansion and/or redirection
- Overseeing coherent development on new initiatives to support the program expansion

NIST Mission

To promote U.S. **innovation** and industrial **competitiveness** by advancing **measurement science, standards, and technology** in ways that enhance *economic security* and improve our *quality of life.*

NIST Role in the Biosciences

To leverage our vast expertise in the **quantitative physical and informational sciences** to provide the measurement infrastructure to underpin increased **innovation in the biosciences.**

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We do this by

- *Establishing new and strengthening existing external partnerships*
- *Recruiting staff with expertise and interest in working as part of interdisciplinary teams*
- *Informing stakeholders in the federal and private sectors of our broad array of measurement capabilities that could impact the bio and health arena.*

How should we prioritize?

Administration Input

Understanding Complex Biological Systems

"Agencies should target investments toward the development of a deeper understanding of complex biological systems through collaborations among physical, computational, behavioral, social and biological researchers and engineers, who will, among other things, need to develop the data management tools and platforms necessary to facilitate this research."

June 23, 2006
John H. Marburger III, Director, Office of Science and Technology Policy
Rob Portman, Director, Office of Management and Budget

How should we prioritize?

Other Agency Input

Proteomics Today – The Problem

"In order for proteomics to be accepted as a valid science in clinical medicine, it is vital that the experimental results be reliable and reproducible within the scientific community. The absence of these standards… is a barrier to innovation… and … delays the discovery and transfer of proteomic technologies into clinical applications."

-- Anna Barker, Deputy Director, NCI

NIST

How should we prioritize?

Input from VCAT

Consider radical changes to how it (NIST) supports the biotechnology and health care industries

Dr. Thomas M. Baer, Executive Director, Stanford Photonics Research Center, Stanford University - NIST VCAT Meeting, June, 2006

Provide measurements and standards to support next-generation clinical diagnostics

- Technologies for detection organ-specific proteins in blood – e.g., global proteomics, microfluidics, and nanotechnology measurement technologies
- Single cell analyses
- Technologies for the capture, storage, analysis, integration, and modeling of global data sets

Dr. Leroy Hood, President, Institute for Systems Biology - NIST VCAT Meeting, September, 2006

Barriers to Innovation in cancer screening and diagnosis which NIST could help overcome:

- Measurement methods to distinguish benign from malignant tissue and determine appropriate therapies
- Automated software algorithms to measure tumor size accurately
- Calibration procedures to assure instrument reproducibility over time
- CT and molecular analysis platform interoperability
- Methods to validate, analyze, and share huge 3-dimensional datasets

Dr. Thomas M. Baer, Executive Director, Stanford Photonics Research Center, Stanford University - NIST VCAT Meeting, June, 2006

Potential Bio-related Program Expansion Areas

- ***Meeting the Nation's most immediate needs***
  - Standards for Bioimaging
  - Standards and Technology to Enable the Transition to Biofuels as Major Automotive Fuel Source
  - Health and Environmental Effects of Nanomaterials
  - Improving Health Care Quality

- ***High Risk – High Payoff New Technologies***
  - Technologies and Standards for Next Generation Clinical Diagnostics and Therapies; A Systems Approach

Challenge: Defining the Sweet Spots

Standards for Bioimaging – New 07 Program

Examples of Year 1 Activities

A. Quantitative Medical Imaging

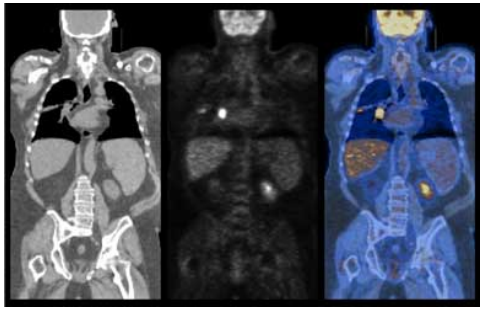
- Metrology for MRI contrast agents over a broad range of field and frequency
- Establish MRI standards such as NIST-traceable T1, T2 relaxation time standards.
- 3D phantom models for CT/PET

B. Quantitative Imaging of Cells and Tissues: Tissue and Cell-Based Measurements

- First reference materials for intensity standardization of fluorescence microscopy
- Determine mass detection limits of broadband CARS

C. Standards and Validation for Software

- Develop statistical methodology for annotating lung cancer CT images
- Develop standard methods and technologies for combining, interpreting, registration, and visualizing data from various imaging techniques for RIDER, LIDC, and other related image data sets



Source: MayoClinic
Positron Emission Tomography (PET) Scanning
http://www.mayoclinic.org/pet/

$3M in FY 07
$4M in FY 08

Technologies and Standards for Next Generation Clinical Diagnostics and Therapies: A Systems Approach

A. Measurement and Informatics Tools for Accelerating Innovation of *New Biomarker and Therapeutics Discoveries*

- **Develop and critically evaluate new biochemical measurement technologies and standards**
- **Develop new quantitative cellular imaging tools and standards**
- **Develop new computational technologies to enable the interpretation of thousands of biomeasurements and inter-molecular interactions.**

B. Technologies and Standards to Support Multiplex Clinical Diagnostic *Measurements of Organ-Specific Biomarkers*

- **Develop and critically evaluate new measurement methods/technologies for detecting organ-specific proteins and protein patterns/signatures**
- **Develop and provide measurement services (e.g., SRMs and SRD) to support the IVD industry in development of reliable measurement devices and the clinical laboratory community in performing multiplex blood protein biomarker determinations and analysis.**

C. Measurements and Standards for *Advanced Medical Imaging*

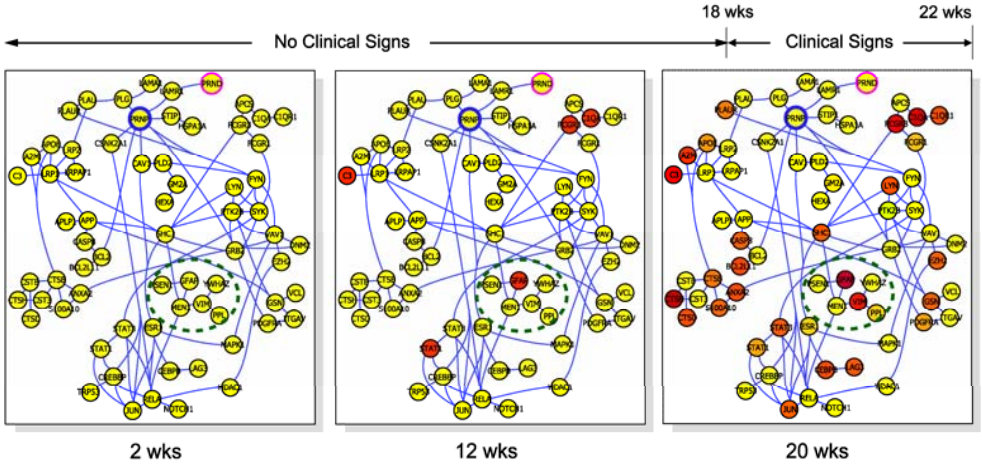
- **Identify, evaluate, and minimize sources of variability and sources of error, for MRI, PET/CT, XCT and Spiral CT imaging**
- **Measure the physical performance of different medical imaging platforms and agents (MRI relaxation times, radionuclide properties, contrast agents, etc.)**
- **Work with the manufacturer and user communities to develop and share open-source tools**

Where Could We Have the Highest Impact: Is this the Sweet Spot for NIST?

Applying our world-class expertise in:

- **physical and chemical measurement science**
- **computer science, mathematics and statistics**

To develop infrastructural technologies and standards that enable comparable measurement results and facilitate sound interpretation of complex data from - and images of - diverse biological systems



This infrastructure would impact a wide array of application areas such as:

- ***next generation healthcare***
- ***biofuel conversion and feedstock development technologies***
- ***health and environmental effects of nanomaterials***

Metrology and Standards for Understanding Complex Biological Systems

1. **Biochemical Metrology Technologies**
   - **Develop and critically evaluate new multiplex biochemical measurement technologies and standards**
   - **Develop new quantitative cellular imaging tools and standards**
   - **Characterization and establishment of minimum performance requirements for current biomeasurement systems**

2. **Heterogeneous-Data Management and Visualization Systems**
   - **Develop new quantitative computational methods for identifying and extracting diverse biological features - cataloguing, archiving, integrating, testing, manipulating, and visualizing divergent data sets to enhance experimental insight**
   - **Develop standards for SB language**
   - **Integrate new and existing SB software tools**

3. **Computational Biological Modeling**
   - **Develop new computational technologies to enable the practical utilization of the data to make scientific decisions - interpretation of thousands of biomeasurements and inter-molecular interactions.**

NBS → NIST Mission

NBS Mission 1901: To aid U.S. manufacturing and commerce

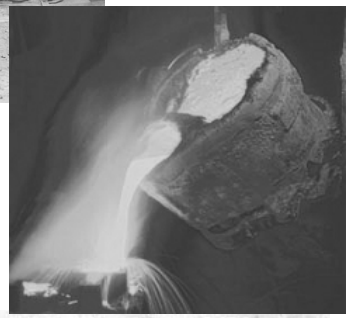
NIST Mission 2006:

To promote U.S. **innovation** and industrial **competitiveness** by advancing measurement science, standards and technology in ways that enhance economic security and promote our quality of life

Our original mission and our mission today call for us to conduct research and provide standards to address new areas related to commerce and quality of life as they emerge

NIST

Since 1901, NIST has reacted to and solved highly complex measurement problems that are important to the Nation



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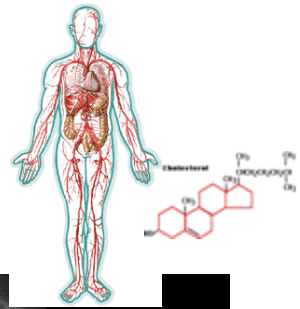
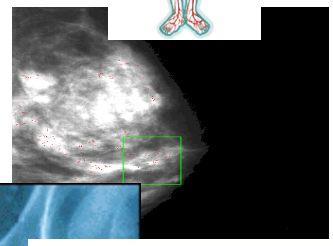
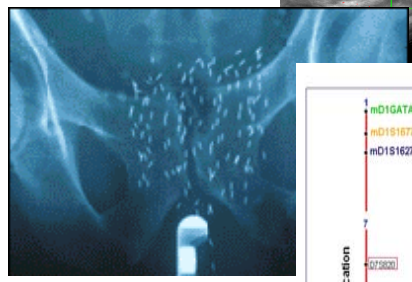
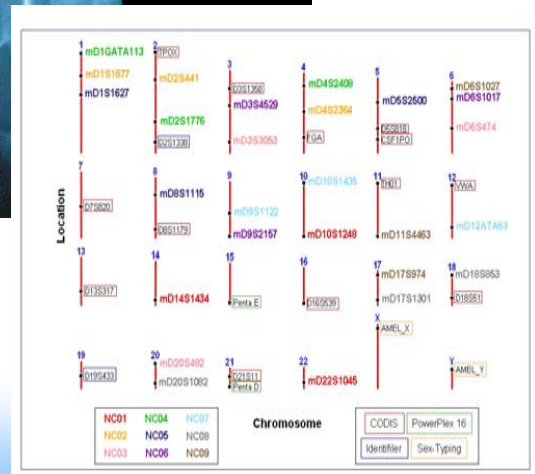




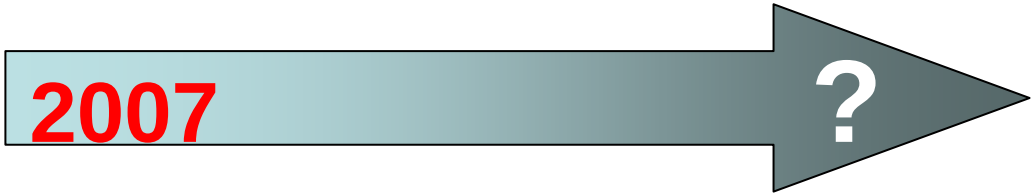




NIST

To most effectively facilitate innovation in the biological sciences, NIST should take a proactive approach and focus its existing expertise in the physical, chemical and computational sciences to develop infrastructural technologies and standards that enable a better understanding of the functioning of complex biological systems

Surprise



Wisdom

Expectations of VCAT Regarding Biosystems and Health

We'd like your thoughts concerning:

- our articulation of **NIST's role** versus that of other agencies, such as NIH, **in** the broad area we're calling **"Biosystems and Health"**
- focus and adequacy of our new "Standards for Bioimaging program"
- appropriateness of areas suggested for potential program expansion and/or funding redirections
- considering expectations, national needs and within the constraints of fiscal reality, is

  "Metrology and Standards for Understanding Complex Biological Systems"

  really the "sweet spot" for a NIST level program expansion at this time?