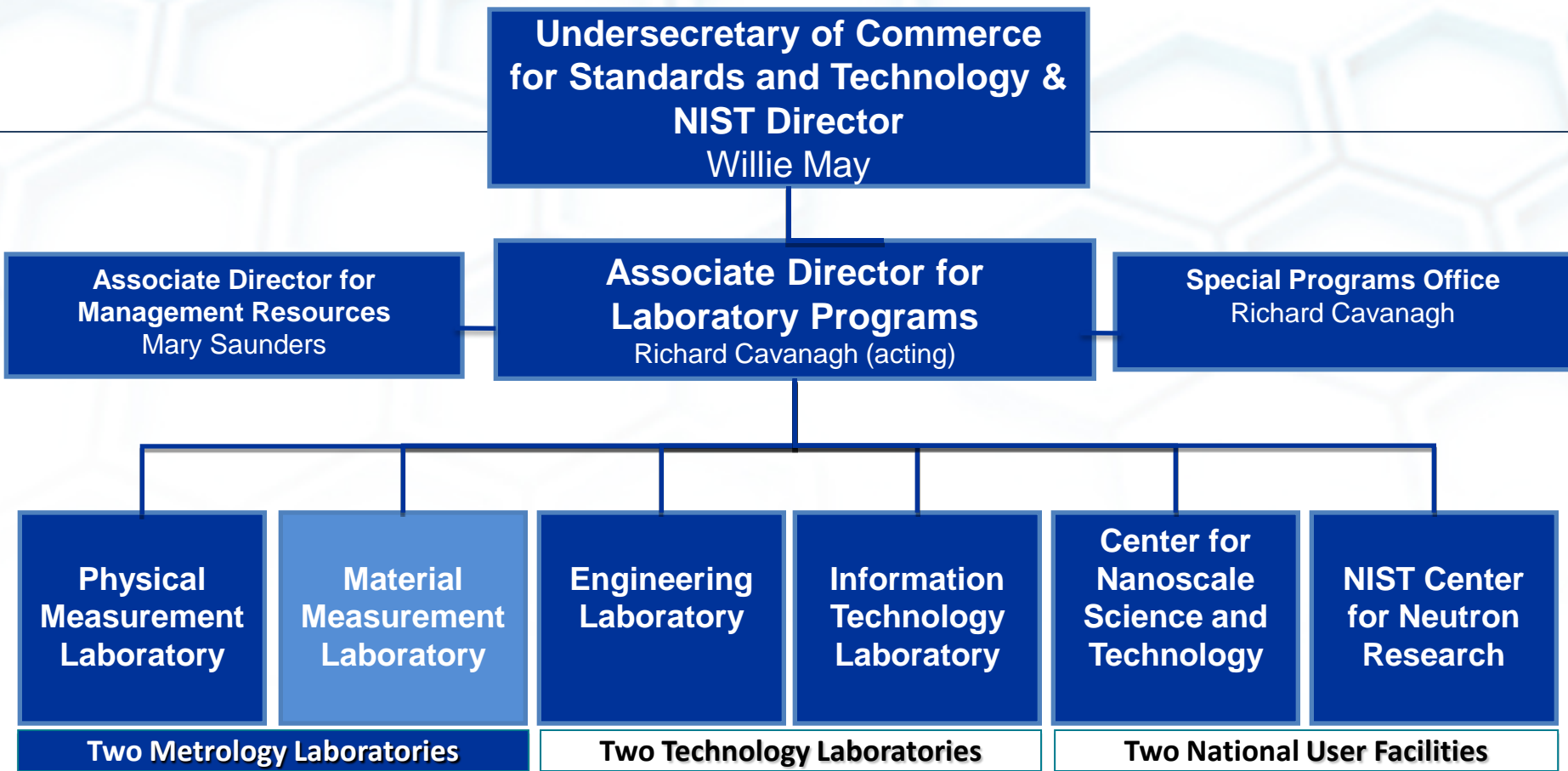




## Overview of NIST's JCTLM Activities: *Past, Present, and Future*

**Karen W. Phinney**  
Biomolecular Measurement Division

# Structure of NIST's Laboratory Programs



# Material Measurement Laboratory

National reference laboratory for measurements in the

## chemical, biological, and material sciences

MML serves a broad range of industry sectors ranging from transportation to biotechnology and provides research, measurement services, and measurement quality assurance tools for addressing problems of national importance such as:

- assessment of climate change
- renewable energy
- the nation's aging infrastructure
- environmental quality
- food safety and nutrition
- forensics and homeland security
- health care measurements
- manufacturing (ranging from advanced materials to photovoltaics to biologic drugs)

MML is also responsible for coordinating the NIST-wide **Standard Reference Materials** and **Standard Reference Data** programs

# Material Measurement Laboratory



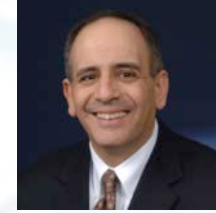
R. Watters, Assoc Dir for Measurement Services



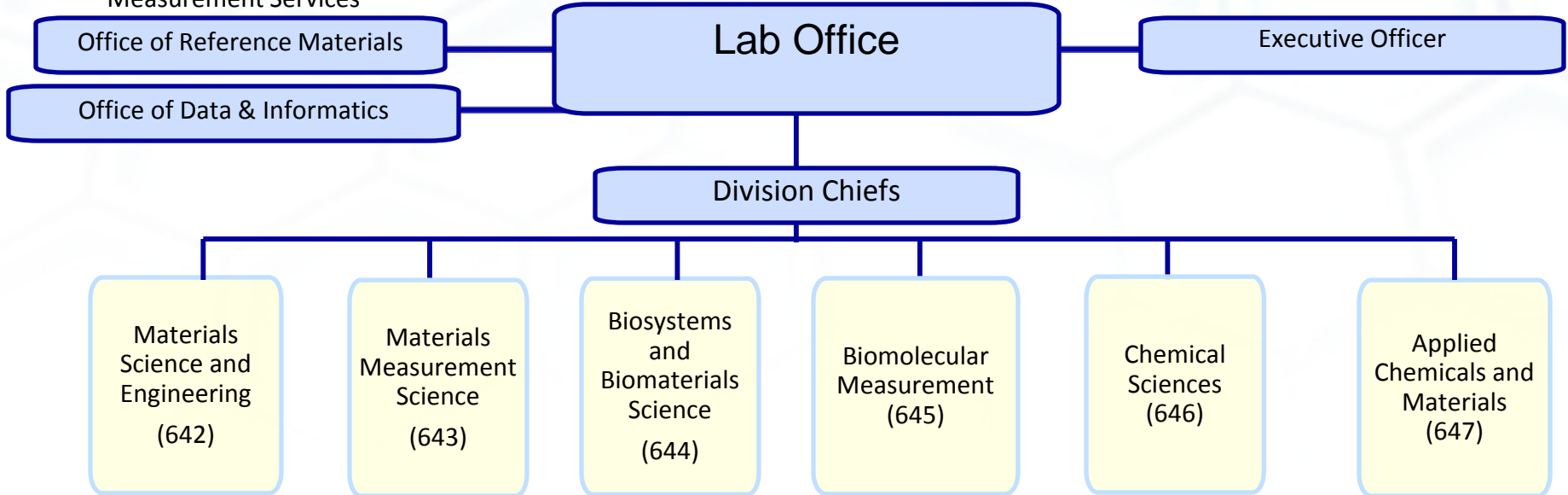
L. Locascio, Director



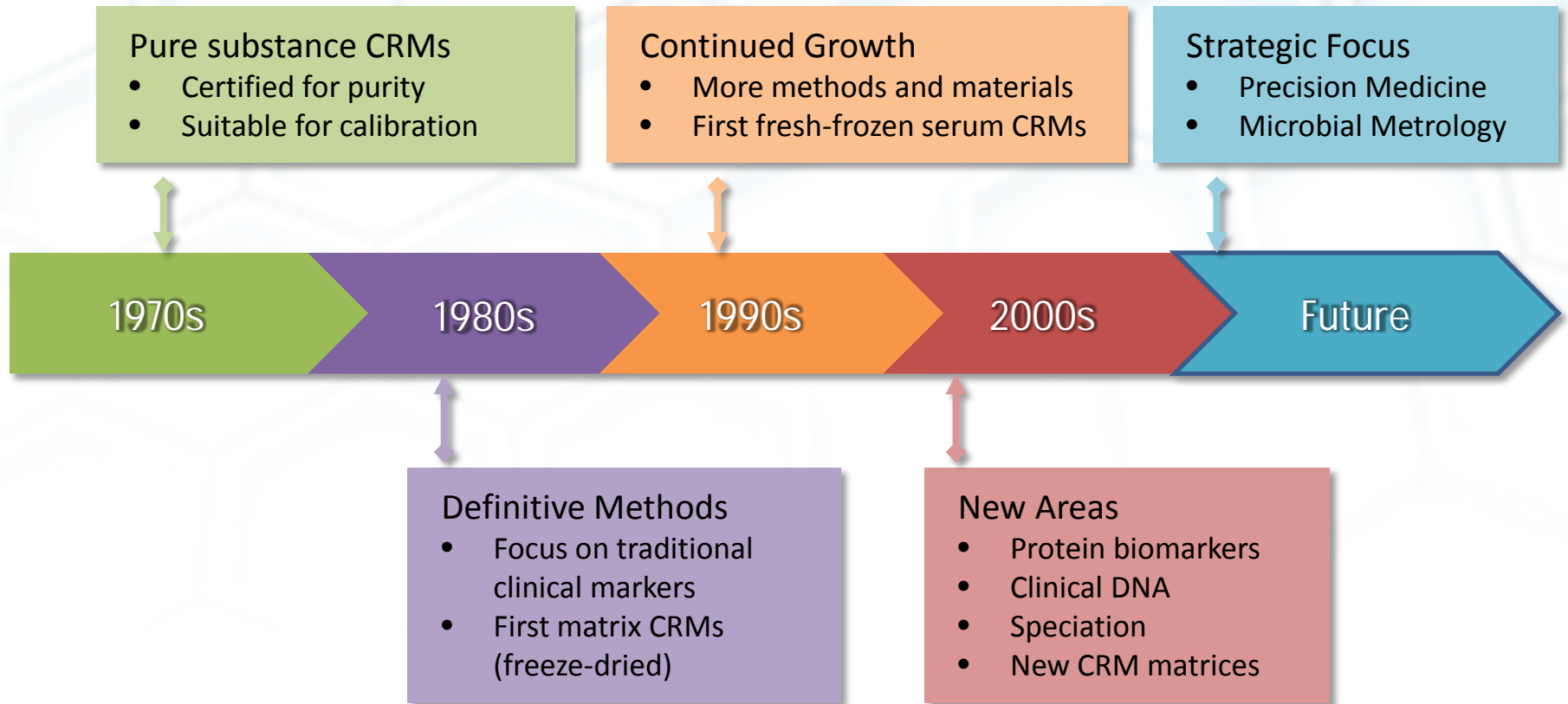
M. Fasolka, Deputy Director



N. Alderoty, Exec Officer



# NIST Involvement in Laboratory Medicine



# NIST JCTLM Database Listings

Category	Reference Materials	Reference Methods
Blood cell counting	0	0
Blood gases	0	0
Blood groupings	0	0
Coagulation factors	0	0
Drugs	16	4
Electrolytes	24	16
Enzymes	0	0
Metabolites and substrates	32	14
Microbial serology	0	0
Non-electrolyte metals	43	15
Non-peptide hormones	1	8
Nucleic acids	0	0
Proteins	2	0
Vitamins and micronutrients	9	2

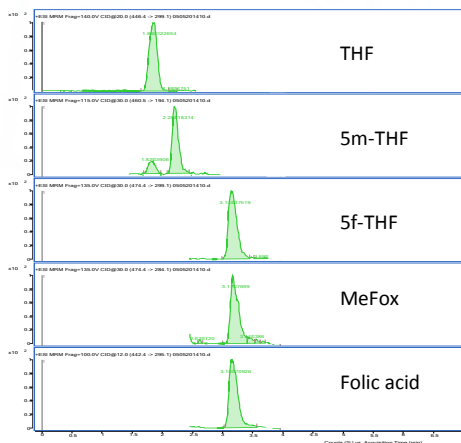
# Evolution of CRM Approaches

## SRM 1955 Homocysteine and Folate in Human Serum



- Three level reference material
- Low level achieved by dilution with PBS
- High level achieved by spiking
- Certified value for 5-methyltetrahydrofolate
- Reference value for folic acid

## SRM 3949 Folate Vitamers in Human Serum



- Screening and blending of donor serum units
- Wider range of folate values
- Some donors given a folic acid supplement
- Stabilization of minor folate species
- Improvements in analytical methods
- Will replace SRM 1955 (mid-2016)

# Evolution of CRM Approaches

- SRM 900 Antiepilepsy Drug Level Assay Standard issued in 1978
- Lyophilized material with 3 levels (plus a blank) of phenytoin, ethosuximide, phenobarbital, and primidone
- Value assignment by gas and liquid chromatography

## What changed?

- Development of next generation of antiepilepsy drugs
- Changes in treatment practices
- Customer preference for fresh-frozen serum
- Development of ID LC-MS and ID LC-MS/MS methods



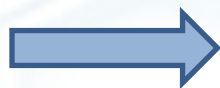
## SRM 900a Antiepilepsy Drugs in Human Serum

Analyte	Level 1 ( $\mu\text{g/mL}$ )	Level 2 ( $\mu\text{g/mL}$ )
Phenobarbital	17.1 (3.5)	70.2 (3.3)
Phenytoin	11.9 (3.4)	47.0 (3.2)
Lamotrigine	4.02 (3.2)	14.9 (3.4)
Topiramate	7.05 (3.3)	19.7 (4.1)

Concentrations of antiepilepsy drugs in new SRM 900a. Concentrations determined by ID LC-MS and ID LC-MS/MS. Relative expanded uncertainties given in parentheses.

# Prioritization of Reference Method and Reference Material Development

Support for national or international standardization efforts



Cholesterol  
Creatinine  
Hormones  
Cardiac troponin I  
Urine albumin



Need identified by another government agency



Vitamin D metabolites  
Toxic elements  
Iodine  
Folates  
Fatty acids



Needed to aid full realization of diagnostic test potential



Genome sequencing  
Proteomics  
Metabolomics



# Updates and CRMs in Development

RM/SRM Name	Comments
RM 8398 Human DNA for Whole-Genome Variant Assessment	New, Genome in a Bottle Consortium
SRM 2373 Genomic DNA Standards for <i>HER2</i>	New
SRM 2378 Fatty Acids in Human Serum	New
SRM 956d Electrolytes in Human Serum	Now includes value for phosphorus
SRM 909c Frozen Human Serum	Values added for electrolytes
SRM 2972a 25-Hydroxyvitamin D Calibration Solutions	Additional concentrations added, now includes 3-epi-25(OH)D <sub>3</sub>
SRM 972a Vitamin D Metabolites in Human Serum	Values added for total 25(OH)D and 24R,25(OH) <sub>2</sub> D <sub>3</sub>
SRM 971 Hormones in Human Serum	Values for T3 and T4 to be added in 2016
SRM 2924 C-Reactive Protein Solution	Expected release mid-2016
SRM 2925 Human Serum Albumin Solution	Expected release in 2016
SRM 3666 Albumin and Creatinine in Human Urine	Candidate materials being acquired

# Looking Ahead

## **Engineering biology**

Develop the measurements and models for engineering biology to map out the fundamental principles that drive development of next generation bio-based products (high tech manufacturing, health)

## **Microbial Measurements**

Develop measurement infrastructure for microbial measurements (health, environment)

**Data and Informatics** Provide validated data and informatics tools to support confident decision-making (all sectors)

## **Quantitative Tools for Characterization of Complex Biologics**

Define complex biomolecules/biologics through quantitative measurements to enable prediction of biological function in healthcare applications (manufacturing, health)

**Precision Medicine** Develop measurement science and standards to ensure confidence in clinical decision-making, and ultimately enable adoption of precision medicine (health)

# Looking Ahead



- MML recently issued a five year strategic plan
- Outlines priorities in biological, chemical, and materials sciences
- Includes a focus on precision medicine, microbial metrology
- Available online: [mmlstrategy.nist.gov](http://mmlstrategy.nist.gov)

- **Goal 1a: Measurement Science Excellence: Biological Sciences Strategies**



### **Complex Biotherapeutics**

Develop measurement science, standards and tools to support the quantitative definition of complex biologic therapeutics and correlation of their structural differences with clinical outcomes.

### **Engineering Biology**

Develop the measurements and models for engineering biology to map the fundamental principles that drive the development of the next generation of bio-based products.

### **Reproducibility of Biomedical Research**

Establish NIST as the agency for measurement assurance to enable reproducibility of biomedical research results.

### **Microbial Metrology**

Develop measurement infrastructure for microbial measurements in health and environmental applications.

### **Precision Medicine**

Develop measurement science and standards to ensure confidence in clinical decision-making, and ultimately enable adoption of precision medicine.

# For More Information

- NIST Office of Reference Materials: [www.nist.gov/srm](http://www.nist.gov/srm) or [srminfo@nist.gov](mailto:srminfo@nist.gov)
- Material Measurement Laboratory: <http://www.nist.gov/mml/>
- [karen.phinney@nist.gov](mailto:karen.phinney@nist.gov)