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NIST Analytical Chemistry Division (839)
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FY01 Division Overview

I. Introduction

The Analytical Chemistry Division is one of five Divisions in the Chemical Science and Technology Laboratory, National Institute of Standards and Technology. The Division has approximately 100 scientists, technicians, and administrative/clerical support staff and an annual budget of about \$15M of which about \$6M supports programs for other Federal and State Government Agencies and/or American industry on a cost reimbursable basis.

The Division serves as the Nation's reference laboratory for chemical measurements and standards to enhance U.S. industry's productivity and competitiveness, assure equity in trade, and provide quality assurance for chemical measurements used for assessing and improving public health, safety, and the environment. The Division maintains world-class metrologically based core competencies in:

- Analytical Mass Spectrometry
- Analytical Separation Science
- Atomic and Molecular Spectroscopy
- Chemical Sensing Technology
- Classical and Electroanalytical Methods
- Gas Metrology
- Nuclear Analytical Methods
- Microanalytical Technologies

These competencies provide the capability to carry out the Division's broad mission and the flexibility to respond to changing and evolving national priorities. These core competencies reside in five Groups: [1] Spectrochemical Methods, [2] Organic Analytical Methods, [3] Gas Metrology and Classical Methods, [4] Molecular Spectrometry and Microfluidic Methods and [5] Nuclear Analytical Methods. The skills and knowledge derived from laboratory-based research concerning the phenomena that underpin the measurement of chemical species in a broad spectrum of matrices are applied to the development and critical evaluation of measurement methods of known accuracy and uncertainty. These internationally-recognized reference methods support the Division's infrastructure for providing traceability of chemical measurements used in programs of National/International importance through:

- Standard Reference Materials
- NIST Traceable Reference Materials (NTRMs)
- Measurement Quality Assurance Programs in critical areas
- Comparisons of NIST chemical measurement capabilities and standards with other National Metrology Institutes.

II. Division Project Areas in Support of Chemical Science and Technology Laboratory Programs

Reference Methods and Standards for Healthcare

The objective of this project is to develop and maintain the measurements and standards infrastructure to facilitate accurate decision-making regarding the diagnosis, treatment, and prevention of diseases. Measurements are responsible for 10% - 15% of the \$1.3 T annual costs of healthcare in the United States. A significant portion (25% - 30%) of health-related measurements is performed for non-diagnostic reasons (re-tests, error prevention and detection). Even modest improvements in measurement accuracy and quality assurance will result in multi-billion dollar savings in health care costs. Project drivers are therefore, measurement reliability as it impacts healthcare costs and medical decision-making, regulatory requirements, and international trade and competitiveness-related issues.

Project components include [1] Reference Methods for selected health status markers (electrolytes, small organic markers, toxic and/or speciated metals, protein-based markers) [2] Standard Reference Materials (pure primary chemical standards, optical filter standards for instrument calibration/assessment, body fluid-based materials), [3] interactive measurement quality assessment activities, [4] strategic international comparison exercises

NIST works with other government agencies (e.g., CDC, NCI, NIH), professional organizations (e.g., AACC, CAP, NCCLS), and the private sector (e.g., AdvaMED, Mayo Clinic) to prioritize measurement and standards needs.

Measurement Methods and Standards for Forensic Analyses

Forensic chemical analyses have become important tools for solving crimes and assuring justice. Today, most forensic analysis techniques are qualitative and are used to identify or confirm the presence or absence of certain materials. However, in many cases applying quantitative analytical techniques can provide important additional information about material sources or the significance of material identifications.

Project activities address measurement method and standards issues related to alcohol and drugs of abuse testing, human identity testing (DNA and chemical profiles in hair), crime scene investigations (gunshot and explosive residues, teleforensics), and chemical and biological weapons detection.

Project priorities are driven by input from the U.S. Departments of Justice and Defense.

Measurement Methods and Standards for Nutrients, Contaminants, and Adulterants in Foods

The integrity of the nation's food supply is important for public health and safety. The development of reference methods and standards for nutrients, contaminants, and adulterants in foods is essential in this regard. Project components include measurement and standards issues related to nutrients in food products, contaminants and adulterants in food products, chemical composition and contaminants in herbal supplements/nutraceuticals, and detection of genetic modifications in food products

Project priorities are determined in consultation with the AOAC, FDA, NIH, and the National Food Processors Association.

Environmental Measurements and Standards

Responsible stewardship of the environment is facilitated when measurements of known accuracy are used in monitoring and decision-making. Activities in this project involves the development of reference methods, developing Standard Reference Materials and the provision of other measurement quality assurance services to address measurement problems associated with Drinking Water Quality, wastewater Chlorination/Dechlorination Mechanisms, Atmospheric Monitoring and Global Climate Change Assessment, Automotive Exhaust Emissions, Atmospheric Particulate Characterization, Contaminants in Sediments and Soils, Contaminants in Biological Fluids and Tissues, Specimen Banking Technology.

Activities of this project support directly and indirectly the federal agencies that have stewardship responsibility for the environment (EPA, NOAA, DOE, DOD), state laboratories, and the large, environmental testing service sector that consists of private laboratories, secondary standards producers and proficiency testing firms. Our environmental projects also support industries and their consortia (e.g., AIGER, EPRI, etc.) that require high quality and/or traceable measurements to respond in a cost-effective manner to changing regulatory mandates concerning emissions and waste disposal. Our activities also support basic studies and models that track the fate of pollutants over both time and space and their impact on quality of life.

Methods and Standards for Advanced Materials Characterization

Industrial and academic materials scientists often require accurate information regarding the chemical properties of advanced materials. These properties include chemical purity, trace element content, and the distribution of elements within the material. Such information not only allows optimization and control of production processes, but also facilitates a theoretic understanding of both chemical processes and material properties. As the Nation's reference laboratory for chemical measurements, CSTL must not only provide the fundamental basis of the nation's chemical measurement system, but also extend these capabilities to the real world. The Analytical Chemistry Division does this by direct measurements for customers and collaborators, by providing standard reference materials for instrument calibration and for measurement quality assurance, and by making the latest measurement techniques and data available to the advanced materials community.

The Division has a broad array of analytical measurement tools including unique capabilities like neutron activation analysis, prompt gamma activation analysis, neutron depth profiling to provide analytical data and reference measurements needed to provide answers to important measurement problems.

Methods and Standards for Commodities Characterization

The provision of accurate, accepted chemical characterization determinations is critical for those materials whose commercial value, properties, or suitability for use depend on their chemical composition. These characterizations may require measurement of major component(s), identification and quantification of contaminants, and/or determination of the spatial distribution of components. This project requires ongoing identification of those commodity areas with critical needs that can be addressed by NIST and strategic selection of project tasks from among these.

Current project activities focus on sulfur in diesel fuels, composition of metals/metal alloys (e.g., low carbon silicon steel, phosphorized copper), a series of cement SRMs, and an electronic scrap artifact material – the first of a new class of SRMs addressing industrial “green product” goals in which key decisions, with significant economic and ecological consequences, depend on the quality of analytical characterizations of materials to be recycled.

Microanalytical Technologies – Lab on a Chip

This project is focused on facilitating the design and development of commercial plastic microfluidic systems by developing techniques to achieve greater control of microflow and microchemistries performed in plastic microchannels. In both the analytical and biotech industries, there has been tremendous interest in recent years in the development of chip-based technologies incorporating microfluidics. It is predicted that miniaturization of chemical processes using these technologies will have a huge impact on rapid point-of-care screening as well as high throughput screening. For these devices to become commercially viable, the chemistries performed in microfluidic systems must be well-controlled to provide accurate and reliable results. In response to this need, the goal of our multi-year program is to develop novel methods to evaluate and control chemistries in microscale systems. First, we will develop methods to understand and manipulate microflow in a predictable manner since a lack of flow control can lead to misinterpretation of analytical results. We will also develop methods to accurately evaluate and control temperature profiles in microchannels since temperature is a critical parameter that has a profound effect on reaction kinetics. Finally, we will develop methods to fabricate and integrate components that allow for finer control of chemical reactions including passive micromixers and microarrays. Based on input from a young microfluidics industry, the fundamental control of chemical reactions performed in microchannels is the underpinning of a program designed to promote the commercial realization of plastic microfluidic systems.

Further discussions regarding the Division's core competencies, focused project areas, and products/services delivered to customers are provided in the Groups Section of this Overview and the Selected Technical Activity Reports.

III. SRMs: Tools for Providing Chemical Measurement Traceability

Increased requirements for quality systems documentation for trade and effective decision-making regarding the health and safety of the U.S. population have increased the need for demonstrating "traceability-to-NIST" and establishing a more formal means for documenting measurement comparability with standards laboratories of other nations and/or regions. Standard Reference Materials (SRMs) are certified reference materials (CRMs) issued under the National Institute of Standards and Technology trademark that are well-characterized using state-of-the-art measurement methods and/or technologies for chemical composition and/or physical properties. Traditionally, SRMs have been the primary tools that NIST provides to the user community for achieving chemical measurement quality assurance and traceability to national standards. Currently, NIST catalogs nearly 1300 different types of SRMs; in 2001 NIST sold over 32,000 SRM units to more than 6,500 unique customers. Approximately 16,000 of the units sold were from the ~700 different types of materials that are certified for chemical composition.

During the past year, measurements were made on ~140 SRMs. Fifteen high-priority renewals were completed along with twelve completely new SRMs. Other measurements were made for stability assessment and/or to address customer questions. In order to address questions from the international community concerning the quality of data provided on SRM certificates, NIST 260-136 "Definitions of Terms and Modes Used at NIST for Value-Assignment of Reference Materials for Chemical Measurements was developed. Completed in January 2000. In addition, a Division Quality Manual that summarizes and formalizes the Division's policies and approaches to addressing quality-related issues concerning the services that we provide was also completed and placed on the Division's internal website.

Since it has the world's leading, most mature, and most comprehensive reference materials program, most of the world looks to NIST as the de facto source for high quality CRMs to support chemical measurements. NIST has met the reference materials needs of U.S. industry and commerce for nearly 100 years. While our reference materials program has focused primarily on U.S. requirements, it is clear that these materials address international measurement needs as well. As demonstration of quality and "traceability" for chemical measurements have become increasingly global issues, the need for internationally recognized and accepted CRMs has increased correspondingly. Their use is now often mandated in measurement/quality protocols for analytical testing laboratories. Coupled with the fast pace of technological change and greater measurement needs, the demand for additional quantities and additional specific varieties of reference materials has mushroomed. NIST, by itself, does not have the resources to provide SRMs (exact sample types, unique compound combinations, concentrations, etc.) to meet all these needs. Without a significant shift in paradigm, we will not be able to address future needs for reference materials; neither nationally nor internationally.

IV. NTRM Programs for Leveraging NIST Resources and Efforts

The NIST Traceable Reference Materials (NTRM) program was created to partially address this problem of increasing needs for reference materials with a well-defined linkage to national standards. An NTRM is a commercially produced reference material with a well-defined traceability linkage to existing NIST standards for chemical measurements. This traceability linkage is established via criteria and protocols defined by NIST and tailored to meet the needs of the metrological community to be served. The NTRM concept was implemented initially in the gas standards area to allow NIST to respond to increasing demands for high quality reference materials needed to implement the "Emissions Trading" provisions of the Clean Air Act of 1990 (while facing the reality of constant human and financial resources at NIST). The program has been highly successful. Since its inception, 11 specialty gas companies have worked with NIST to certify over 8500 NTRM cylinders of gas mixtures that have been used to produce more than 500,000 NIST-traceable gas standards, with a market value of approximately \$110M, for end-users.

Operationally, in the Gas NTRM Program, candidate gas mixtures are prepared in batches of ten or more cylinders, analyzed, and data submitted to NIST. NIST selects 10% of the cylinders in the batch and analyzes them so that NIST can value assign the batch. The cylinders are returned to the SGC with Certification documentation for the batch. The cylinders are under control of the SGC and can be sold to end users to provide a NIST traceable gas or the NTRM mixtures can be used by the SGC to analyze other mixtures that are then sold to provide traceability. The qualifier on the part of NIST is that NIST must have the primary standards available to perform the NIST analyses. Thirty-six NTRMs were value-assigned for four Specialty gas Companies during FY01. According to Stephen Miller, Technical Director, Scott Specialty Gases, "the NTRM program has served as an excellent vehicle for production of the high quality standards - of known pedigree - required by both industry and the regulatory community in the implementation of Title IV [SO₂ emissions trading] of the 1990 Clean Air Act."

The NTRM concept has been expanded to our Optical Filter Standards Program. Currently, this program is just getting underway with three vendors. In the Optical Filters NTRM program, each vendor is certified by the National Voluntary Laboratory Accreditation Program (NVLAP) to produce visible filter standards. Traceability is provided by the use of NIST SRM optical filters to calibrate vendor spectrophotometers, and quality assurance is afforded by NIST review of all vendor calibration, certification, and recertification data, NIST measurements (one set from each vendor production batch), and blind spot checks. In addition to NTRMs, 176 sets (for 125 different companies) of optical filter standards were re-value assigned for wavelength and/or absorbance in the UV and NIR spectral region 12 during FY01.

We had previously planned to also develop NTRMs in the Elemental Standards area. Those plans are being re-evaluated. Our single element spectrometric solution standards program (SRM 3100 series) is now on its firmest footing since its inception. All elements are now in stock and the uncertainty model was updated to bring the certificates into full ISO GUM compliance. This uncertainty analysis includes incorporation of the new "Type B on Bias" method developed by the Statistical Engineering Division, as well as a different treatment for transpiration correction. This year the certification projects for 7 elements were completed (Th, Er, Pt, Co, Ni, and Ca)

and re-certifications for 6 additional elements initiated (Al, As, Cr, Cu, Pb, and Na), all of which anticipate replacement of in-stock materials. The certification of two very difficult elements, rhodium and rhenium, which have been out-of-stock for several years was also completed. Both projects involved considerable research before reliable results were achieved. Stability tests were also completed for five elements (Mn, P, Cs, Ho, Y). This testing was done to evaluate the extended shelf life of ampouled materials. The Plans for the coming year call for the initiation of a new class of elemental standards, NIST Primary Standards (NPS); these materials will be certified for amount of material, as opposed to concentration.

We recognize that the NTRM model is only applicable in selected areas. In the remaining areas, such as complex matrix standards, we have begun to leverage our resources through increased strategic collaborations with other National Metrology Institutes and selected U.S. laboratories. Additional details concerning our collaborative activities with both private sector U.S. laboratories and commercial reference material and proficiency testing service providers as well as other National Metrology Institutes worldwide are provided in Technical Activity Reports that follow.

V. International Standards Activities

International agreements and decisions concerning trade and our social well-being are increasingly calling upon mutual recognition of measurements and tests between nations. The absence of such mutual recognition is considered to be a technical barrier to trade and environmental and health-related decision-making. In recent years, mutual recognition agreements have been established related to testing and calibration services and in respect of the bodies accrediting such activities. All of these rest upon the assumption of equivalence of national measurement standards and reliability of the link between national measurement standards and the relevant testing services in each country. In October 1999, the Directors of National Metrology Institutes for the thirty-eight member states of the Meter Convention signed the mutual recognition arrangement on national measurement standards and calibration and measurement certificates issued by national metrology institutes (MRA). This MRA provides a framework for assessing the degree of equivalence between the measurement capabilities and standards issued by NMIs or NMI-designated labs throughout the world. NIST has taken a leadership role the International Committee of Weights and Measures-Consultative Committee on the Quantity of Material (CCQM) and the Chemical Metrology Working Group of the Interamerican System for Metrology (SIM) in order to assure the effective, fair and metrologically sound implementation of this MRA.

The CCQM has formed seven working groups: (1) gas analysis, (2) organic analysis, (3) inorganic analysis, (4) electrochemistry (5) Biometrology, (6) Surface Analysis and (7) Key Comparisons. These working groups are responsible for selecting and overseeing the operation of key comparisons that address chemical measurement-related issues important for international trade, environmental, health, and safety-related decision making. The Analytical Chemistry Division is currently leading various activities within all five of the seven working groups. During FY01, we participated in 25 CCQM comparison studies; serving as Pilot Laboratory in 13 of those. A summary report of results from CCQM K-6 that has been recently "Approved for Equivalence" is provided in the Technical Activities Reports section as Report # 26. A similar report is required for each key comparison upon its completion.

Participation in CCQM comparisons is available only to top-tier NMIs around the world. Within the Americas, only the U.S., Canada and Mexico have well-established programs in chemical metrology. In order to most effectively address the unique needs of the 34 countries within SIM whose capabilities in chemical metrology span a very broad range, we have initially focused the SIM program on training and capability assessment rather than participation in MRA- driven Key and Supplemental Comparisons. During the past year, six intercomparison exercises were developed to assess the proficiency of SIM NMI's and/or their designated collaborators for addressing chemical measurement problems within their regions and the Americas. While SIM is focussing entirely on training and capability assessment, Regional Chemical Metrology Working Groups in Europe and the Asian Pacific are forging ahead and conducting MRA-driven Key Comparison Studies. We have established agreements with the Chemical Metrology Working Group Leaders of both regions to allow non-CCQM member countries within SIM to participate in such studies as soon as they feel competent to do so.

We are also working with CITAC (Cooperation in International Traceability in Analytical Chemistry) to establish practical, yet metrologically sound, vertical traceability links between the NMIs and chemical testing labs in the various countries and regions around the world.

In addition to these global and regional activities, we are also establishing a limited number of strategic bilateral collaborations and intercomparisons with NMIs around the world. For example, our collaboration with the Netherlands Measurement Institute (NMI) for determining the equivalence of primary gas standards has resulted in a formal "Declaration of Equivalence" that is recognized by the U.S. EPA and European environmental regulatory bodies as documenting the equivalence between seven NIST and NMI primary gas mixture suites. Our formal agreement with NRC-Canada (via the NAFTA Treaty) for cooperation in marine environmental studies has fostered collaborations in the certification of a several certified reference materials important for trade and environmental decision-making between the U.S. and Canada. We have recently signed a Cooperative Arrangement with NIMC (Japan) for collaborative efforts in the area of pure volatile organic compound standards. These highly pure reference compounds will serve as primary references for many of our gas mixture SRMs and our quantitative reference database (SRD-79). Several additional strategic bilateral arrangements with other National Metrology Institutes /Standards laboratories are being discussed.

VI. Collaborations with Other Government Agencies and Professional Organizations

Providing chemical measurement quality assurance services in support of other Federal and State government agency programs (on a cost reimbursable basis) continues to be an important part of our measurement service delivery portfolio. During the past year, we were involved with 25 projects with eleven federal and state government agencies. We also had technical interactions that involve laboratory research and measurement activities with more than 20 professional organizations and societies including the American Industry/ Government Emissions Research consortium (AIGER), American Association for Clinical Chemistry (AACC), American Society for Testing and Materials (ASTM), Certified Reference materials Manufacturers (CRMMA), Association National Food Processors Association (NFPA), National Council on Clinical Chemistry (NCCLS), and the National Environmental Laboratory Accreditation Council

(NELAC) Specific details concerning many of these interactions are provided in the Groups Section of this Overview.

VII. Future Directions

We will continue our strategy of maintaining core competencies in chemical measurement science to address measurement problems in areas of national priority. All Division research and service projects will continue to be reviewed on an annual basis for match to mission, progress, quality and customer need.

Several new research activities will be initiated in the coming year. In the **Forensics Standards** area, we will be developing a collaborative program with CDC for providing quality assurance and measurement proficiency assessment for the “Chemical Counter-Terrorism Laboratory Network” which will initially be comprised of several state public health laboratories and the CDC. In the event of a chemical terrorism attack, samples (urine or blood) would be shipped to CDC for analysis to determine what agents were used, who was exposed, and how much exposure occurred. CDC would most likely not be able itself to handle so many samples in a short time that would need the help of the state labs in the analyses. NIST’s responsibility would be to work with CDC and the State Labs to assure the quality of results from such tests. Emphasis of our **Food and Nutrition Measurements** area will be shifted from population of the AOAC Food Triangle to address nutritional labeling issues to quality assurance for Nutraceutical products and detecting of genetic modifications in foods. Research will also begin in a new Competence area, **Single Molecule Measurements and Manipulations**. Additional details concerning research activities in these areas are provided in the Group Sections of this Overview that follow later.

Healthcare is a major focus area for NIST, the Chemical Science and Technology Laboratory and the Analytical Chemistry Division. In addition to the clinical measurement reliability and cost issues that have driven our measurement and standards for clinical diagnostic markers project over the past twenty years, a very significant commerce and competitiveness issue has recently emerged -- the European Directive 98/79/EC on *in vitro* diagnostic medical devices. By December 2003, manufacturers must declare that any new IVD product to be sold within the EU complies with all “essential requirements” of this Directive. One of these requirements is that IVD products be traceable to “standards of the highest order”, e.g., nationally and/or internationally recognized reference methods and/or certified reference materials. At present, IVD devices are used in clinical laboratories to measure more than 300 different chemical or biochemical species. Reference methods and/or materials exist for about 30. Approximately 60% of the IVD products currently on the European market are imported from the USA. Excluding home diagnostics, the overall world wide in-vitro diagnostic market ("IVD") is approximately \$20 billion.

In response to this need we have committed to develop new reference methods and blood/urine-based SRMs for several new health-status markers while maintaining previously developed reference systems for calcium, chloride, cholesterol, creatinine, glucose, lithium, magnesium, potassium, sodium, triglycerides, urea, uric acid, and vitamins A,C, E and beta carotene. Over the next two years, reference methods and standards will be developed for:

- **Bilirubin** (*liver function*)
- **Cardiac Troponin I** (*heart attack occurrence and damage*)
- **Cadmium** (*toxicity*)
- **Cortisol** (*endocrine function*)
- **Folates** (*neural tube defects*)
- **Prostate Specific Antigen** (*prostate*)
- **Glycated Hemoglobin** (*diabetes status*)
- **Homocysteine** (*heart attack risk*)
- **Ionized Calcium** (*important marker for diagnosis of various disease states such as skeletal resorption and stone formation in the urinary tract*)
- **Mercury** (*toxicity*)
- **Speciated Iron** (*anemia and hemochromatosis*)
- **Thyroid Stimulating Hormone, Triiodothyronine and Thyroxine** (*thyroid function*)
- **Total and Speciated Selenium** (*to support clinical monitoring in the relatively narrow range of beneficial effect*)

Over the next decade, driven by the availability of new sensor-based measurement technologies, more and more clinical testing will be done outside the traditional clinical laboratory. The annual U.S. market alone for this new form of clinical measurements, called point-of-care testing (POCT), is currently a billion dollars and is growing at an annual rate of 10%. POCT is expected to be used extensively in the home as part of a self-care trend, which is currently experiencing a 70% growth rate. Published studies have concluded that POCT provides at least the same level of diagnostic value as centralized testing, but at half the cost. The standards infrastructure that has supported clinical chemistry for the past two decades must adapt to support POCT. Collaborative efforts need to be established among National Standards Laboratories, in-vitro diagnostic device (IVD) manufacturers, and others in the medical professional community to develop appropriate technologies and non-biohazardous standards to facilitate the provision of data used in medical decision-making that are accurate and traceable to national/international standards. NIST leadership in developing traceable POCT standards will help assure continued U.S. dominance of the worldwide IVD market and foster more affordable healthcare both at home and abroad.

The most widely used home testing devices are for glucose. Diabetes affects more than 10 million Americans and its prevalence rose from ~5% to 7% during the 1990's. Although home blood glucose monitoring has clearly revolutionized diabetic care and changed both the therapy and outcome for this disease, use of these testing systems remains problematic. In the short term, we support will CDC and FDA in their investigations of the performance of home glucose monitors. We have been asked to provide the reference method and whole blood reference materials to support these studies. In the longer term, we will be developing optical artifact standards for non-invasive measurement technologies.

While focusing increased attention on the health-care/clinical measurements area over the next 3-5 years, we will still address critical measurements and standards needs in other areas. The following SRMs are scheduled for completion during the coming year:

- **Anode Tin** (to support lead and material purity measurements for this important steel coating material manufactured, used, and recycled worldwide; lead content of the recycled high-value tin is of particular importance for food safety, product liability, and environmental concerns)
- **Baking Chocolate** (to complement suite of SRMs developed in response to new nutritional labeling laws)
- **Drinking/Wastewater Standards** (to provide accuracy benchmark and measurement traceability for proficiency testing of >5000 environmental laboratories conducted by commercial providers) additional SRMs added to suite such as additional VOCs in methanol, renewals of needed SRMs such as pH, electrolytic conductivity, bromide and fluoride anion solutions, and selected elemental solution standards; Reissue of SRM 1643, Trace elements in Water, as testing laboratory benchmark
- **Fluorescein Fluorescence Intensity** (in collaboration with the Biotechnology Division for calibration of instrumentation widely used by clinical and biotechnology communities)
- **Gravimetric Elemental Primary Standards** (“Mole standards for metals”)
- **Gunpowder Composition** (to validate forensic methods used to identify gunpowder residues)
- **Low Sulfur and Mercury Coal** (to support lower EPA emissions regulations for sulfur and mercury)
- **NIR Transflectance/Reflectance** (wavelength standards suitable in form for calibration of single- and double-pass transmission in both wavenumber and wavelength)
- **Toxic Elements in Freeze Dried Urine** (to provide QA for toxic metal exposure measurements)
- **Phosphorus Implant in Silicon Depth Profile Standard** (with Div. Surface and Microanalysis Science Division, to complement recently issued boron and arsenic implant SRMs for critical calibration of SI mass spectrometers in support of the semiconductor industry)
- **Raman Spectroscopy Standard** (in collaboration with the Surface and Microanalysis Science and Process Measurements Divisions as second in suite of SRMs to calibrate Raman instruments used in pharmaceutical and agricultural industries and other process control applications)
- **TiAl Alloy for Microanalysis and XRF** (with the Surface and Microanalysis Science Division to provide benchmark for aerospace industry for Ti, Al, Nb, W in USAF-supplied alloy material)

Projects that are in progress with expected completion dates in FY 2003 include:

- **Additives in Smokeless Gunpowder** (for 3 propellant additives; to provide accuracy benchmark and support QA and proficiency testing for explosives-type measurements of state, local and federal forensic laboratories and US military propellant laboratories)
- **Low Nitric Oxide Standards** (to support measurements needed for development of very low emission vehicles and future automobile emissions regulations)
- **Peanut Butter**
and

- **Spinach** (*to complete population of AOAC Food Triangle with SRMs for quality assuring measurements made to monitor nutritional labeling compliance*)

We expect that the NTRM approach will continue to expand as the basis for allowing the commercial sector to provide reference materials to end-users with a well-defined traceability linkage to NIST. High quality SRMs will continue to be developed to address both national and international measurement problems, but they will be much more expensive and targeted for purchase primarily by other national metrology institutes and commercial producers/distributors. Increasingly, end-user needs will be met via NIST-traceable commercially produced reference materials.

The complex nature of chemical measurements coupled with the increasingly global nature of trade, health, and environmental issues speaks to the need for having the world make measurements using a common “meterstick”. The comprehensive nature of the NIST program in chemical measurements puts us in position to make a very significant contribution to the international chemical measurements community in this regard. In order to do this in both a cost-effective and internationally congenial manner, we are investigating opportunities for partnering with other highly qualified NMIs to provide high quality Certified Reference Materials in specific standards areas. Potential advantages of these proposed partnerships include increased supply, breadth and quality of reference materials for the worldwide chemical measurements community as well as less duplication of effort for more efficient use of limited resources.

This overview plus the Group-specific sections and Selected Technical Activity Reports that follow provide additional details concerning our work and reflect the high quality of our staff. This information also shows how our efforts are impacting U.S. industry's productivity and competitiveness as well as providing the measurement and standards infrastructural support for environmental quality and human health assessments. They also illustrate the critical synergistic relationships that exist among our research programs in chemical measurement science and the standards and quality assurance services that we provide to customers.

VIII. Group Overviews

Spectrochemical Methods

Research activities in the Spectrochemical Methods Group are directed toward the development, critical evaluation, and application of techniques for the identification and measurement of inorganic species using x-ray, optical, and mass spectrometries. The focus of this research is measurement accuracy and precision, benchmarking industry's needs for traceability, advanced materials characterization, and commodity value assignment and specification.

Development of a new Reference Method for mercury (Hg) was one highpoint of this past year's activities. The cold vapor isotope dilution inductively coupled plasma mass spectrometric method of measurement (CV-ID-ICP-MS) developed last year was refined and applied to a wide range of materials—commodities, as well as clinical and environmental matrices. Research and Development Magazine recognized this measurement technology as among the 100 most

innovative in the United States in its presentation of a 2001 R&D 100 award to its inventors W. Robert Kelly and Stephen E. Long.

The emission of mercury from coal-fired power plants is one of the most important regulatory issues for the electric power industry and prior to this year there were no NIST coal SRMs with mercury certified. Now, all seven of the NIST SRM coals have been certified for their mercury content. Because of its responsiveness to a major industry need, this work was nominated by the ACD for the FY 2001 CSTL Technical Achievement Award. In addition to the coals, the mercury content of crude and refined oils was surveyed. Although coal burning is believed to be the major anthropogenic source of mercury emissions, the refinement and combustion of liquid fossil fuels is a potential source for which sparse data exist. The NIST measurements will be extremely useful in this source term evaluation. Further information concerning our work in this area can be found in Technical Activities # 6.

Mercury is just one of a number of toxic elements for which environmental exposure is a worrisome health issue. In the last decade the major toxic element of concern was lead (Pb) and we have completed an extensive program of standards development and certification to benchmark accurate measurement of lead in environmental and clinical samples. Last year, certification of SRM 966 Toxic Metals in Bovine Blood was completed, which in addition to lead had mercury and cadmium certified. This material complements the previously (1998) certified SRM 955b Lead in Blood.

We are currently engaged in certifying the normal and elevated levels of analytes in a freeze-dried urine renewal material SRM 2670a. This SRM will expand the suite of toxic elements certified in a clinical matrix further—to elements such as arsenic, chromium, thallium, uranium, and thorium—in addition to lead, mercury, and cadmium. As the kidneys regulate elemental metabolism directly through urinary excretion, the concentration of toxic elements in urine has been recognized for some time as one of the most efficient means to biomonitor exposure. Some of the toxic elements of concern—such as arsenic, uranium and thorium—are naturally found at elevated concentrations in certain areas of the United States, such as the American Southwest. In addition, many of these elements have important roles in industrial processes and materials. In contrast to the original urine SRM (SRM 2670) where some of the elements were unrealistically high and exceeded clinically and biologically significant action levels, the levels of the toxic elements in SRM 2670a have been carefully chosen to help the clinical community accurately benchmark biological indices of exposure. This work is being done in collaboration with the CDC, and the SRM should help to benchmark the many measurements that CDC is making through its NHANES effort (<http://www.cdc.gov/od/oc/media/pressrel/r010321.htm>).

In contrast to toxic elements, iodine is an essential micronutrient that is used by the thyroid gland to synthesize the hormones thyroxine and triiodothyronine. Iodine deficiency causes an increased risk for metabolic disorders, goiter, and, in the case of infants, impaired neurological development. This risk is largely preventable by administration of iodine in consumed foodstuffs. Almost all of the iodine excreted in urine is present as iodide and this represents a good health marker for iodine loading and intake. The World Health Organization (WHO) has provided guidelines on iodine status as a function of urinary iodide levels, but this clinical measurement has not been supported by the availability of accurately certified reference

materials. This year a new analytical method employing isotope dilution inductively coupled plasma mass spectrometry (ID-ICP-MS) was developed. The method utilizes the addition of a long-lived radioactive isotope (^{129}I), which can be calibrated in the usual manner with a stable iodine primary standard. SRM 2670a Toxic Elements in Freeze-Dried Urine has also been analyzed for its iodine content. Iodine certification in this SRM will provide a traceability basis for clinical laboratory measurements of urinary iodine. Future measurements of iodine in human blood serum are also planned.

Iron is also an essential element for life and serum iron determination is an important clinical measurement. Low serum iron levels are indicative of diseases such as anemia, rheumatoid arthritis, and certain infections. High serum iron levels are also indicative of various diseases, including hemochromatosis, an inherited disorder that causes the body to absorb and store too much iron, often resulting in failure of the liver, heart, or pancreas. This year the Group collaborated with the Organic Analytical Methods Group to develop a reference method for speciated iron. Typically, for the purpose of medical diagnosis, the total serum iron concentration is measured. However, in many iron-related diseases, the distribution of iron bound to serum proteins is altered. For improved medical diagnosis, it would be beneficial to determine the distribution of iron among serum proteins as well as the total serum iron concentration.

The two important iron-containing proteins in serum are transferrin and ferritin. Transferrin is the most abundant iron-containing protein, and most clinical measurements involve transferrin determinations. The concentration of ferritin in serum is approximately one thousand times lower than that of transferrin. However, medical research is indicating that serum ferritin determination can often be a more selective diagnosis tool than determination using transferrin. Development of a quantitative method for serum transferrin using liquid chromatography coupled with mass spectrometry (LC/MS) and affinity chromatography is underway. To provide the information on the concentration of iron associated with the transferrin, we are using high-resolution inductively coupled plasma mass spectrometry (ICP-MS). High resolution is required because ^{56}Fe suffers a major interference from the $^{40}\text{Ar}^{16}\text{O}$ species produced in the Ar ICP. Together, the LC/MS and the ICP/MS measurements provide highly selective and high precision values for both serum transferrin and serum iron levels. The goal will be to produce a reference material for speciated iron in serum that will meet the needs of the majority of clinical iron measurements performed.

We continue to underpin the National Reference System for the Clinical Laboratory (NRSCL) through our development and application of mass spectrometric methods for isotope dilution analysis of electrolytes (calcium, chloride, lithium, magnesium, and potassium). In 2001, an isotope dilution procedure for the determination of potassium and calcium using ICP-MS in the cold plasma operational mode was explored. Thermal ionization mass spectrometry (TIMS) has traditionally provided the accuracy base for the determination of potassium and calcium, but ICP-MS is simpler and more widely available. Ratio measurement precision of ICP-MS can be comparable to TIMS when competently applied. The measurement of K and Ca isotopes by ICP-MS is hindered by the high background from the Ar plasma. However, low power or “cold plasma” conditions can significantly reduce Ar-based interferences, and commercial ICP-MS instruments can be configured to operate in this mode. The increased tendency to form polyatomic ions from the matrix in this mode of operation can affect accuracy, but cation

exchange chromatography was applied to completely remove matrix-induced interferences, thus allowing the determination. (Separations are also required by TIMS, for formation of a stable ion beam). The determination of Ca in serum was demonstrated and the results benchmarked against TIMS.

Calcium was determined in a frozen serum material as part of the CCQM Key Comparison P-14. SRM 956a Electrolytes in Frozen Serum was analyzed as a control. Isotope ratios were determined using both ICP-MS and TIMS. The ICP-MS/TIMS ratio of concentrations determined was 0.9999 ± 0.0016 (1s, N=5), illustrating the good comparability between the two techniques. The result for SRM 956a was +0.28 % relative to the certified value, which was well within the relative certified uncertainty of ± 0.63 %. These results again validate the inherent accuracy and stability of a measurement system based on IDMS.

One of the major occupational health issues for the Nation's construction and mining industries is silicosis. Nearly 2 million U.S. workers (and millions more worldwide) are potentially exposed to crystalline silica, which causes this debilitating and incurable, but entirely preventable lung disease. Silica is difficult to measure accurately, as demonstrated by the poor agreement in interlaboratory comparisons. One of the main reasons is that a suitable reference material for silica is unavailable. Consequently, private and public resources are diverted from correcting silica exposure problems to contesting enforcement cases. Thus, the Occupational Safety Health Administration (OSHA), National Institute for Occupational Safety and Health (NIOSH, a branch of CDC) and the Mine Safety Health Administration (MSHA) and industry representatives are working with NIST to develop a Standard Reference Material that is appropriate for silica calibration.

The creation of a stable silica-on-filter reference material has been investigated and the feasibility for commercial production explored. A certification plan for the reference material has been established and methods developed and validated for sample digestion and silicon determination. Silicon on prototype filters has been determined using both inductively coupled plasma optical emission spectrometry and high resolution ICP-MS with comparable results. The production and certification of the SRM is slated for the coming year.

Interface characterization and the analysis of thin layers and coatings is an important analytical problem in a wide variety of modern technologies. The need to develop better, faster, and more economical characterization methods to determine elemental composition quantitatively as a function of depth will surely grow. We have investigated glow discharge optical emission spectrometry (GDOES) for this purpose this year, with support from the CSTL Exploratory Research Program, and in collaboration with the Surface and Microanalysis Science Division. The initial research focused on the conditions that affect uniform sputtering during the glow discharge process. SRM 2135c Nickel Chromium Depth Profiling standard has been the principal test sample. This Ni/Cr multilayer stack has been thoroughly characterized using secondary ion mass spectrometry (SIMS) and Auger emission spectrometry. Encouraging depth profiles have been achieved (reported in an accompanying Technical Activity Report).

The glow discharge sputtering process was shown to depend on the both the physical and chemical nature of the sample. Samples of brass, monocrystalline silicon, and electrolytic nickel

were sputtered at various sets of discharge conditions, and the resulting craters were evaluated. Even in the single crystal Si, a flat crater was not formed—the edges sputtered faster than the center. Similar types of sputtering effects have been studied extensively in SIMS but have not been documented in GDOES. It is obvious that quantitative depth analysis will require better physical understanding and control of this sampling process.

The X-Ray Fluorescence (XRF) team continued to refine the development of a matrix-independent method based on borate fusion (reported in an accompanying Technical Activity Report). This method provides direct traceability to primary reference materials in combination with the speed and repeatability of XRF. The method has been applied to the certification of cements and zeolites. This year, its applicability to the analysis of metals and metal alloys was studied in depth. A direct comparison was made between calibrations from disk-form low alloy steels and fused, chip-form low alloy steels. Calibrations for 20 elements were created using a straight-line model for both fused and disk forms. The performance of bracket standard calibration for low alloy steel demonstrated matrix-independence with traceability to primary reference materials. The application of this calibration method was applied to the analysis of SRM 361 and resulted in excellent performance even for trace As, normally considered a volatile element. In general, this work demonstrates that XRF will no longer be limited to disk-form specimens, which is especially important for alloys that do not form homogeneous solids. In fact, the superior speed and repeatability of XRF can be used to great advantage for analysis of metals, alloys, ores and related materials with fewer certified reference materials.

The identification and measurement of elemental species is a prominent topic in many areas of science. This topic was central to a workshop at the most recent BERM meeting, and discussions have been held with EPA and other agencies about the need for environmental standards certified for species (e.g. arsenic, chromium, and mercury). As discussed above, we have initiated research for clinical iron species. This year we have also initiated a collaborative research effort in species measurement with Professor Christine Grant and her students (North Carolina State University). The use of calcium ion sequestrants as environmentally benign alternatives to strong acids for the cleaning of mineral deposits, typically calcium phosphate, calcium oxalate and calcium carbonate, on stainless steel surfaces is being explored. The research requires the identification and quantification of calcium and its species on-line under various mechanical cleaning conditions. This summer, a tandem technique was developed that incorporated size-exclusion chromatographic (SEC) separation of calcium species, spectrophotometry and inductively coupled plasma optical emission spectrometric (ICPOES) detection techniques. This problem, the formation and removal of mineral deposits (scale), is important for many industries.

The single element spectrometric solution standards program (SRM 3100 series) is now on its firmest footing, probably since its inception. All elements are now in stock and the uncertainty model was updated to bring the certificates into full ISO GUM compliance. This uncertainty analysis includes incorporation of the new “Type B on Bias” method developed by the Statistical Engineering Division, as well as a different treatment for transpiration correction. This year the certification projects for 7 elements were completed (Th, Er, Pt, Co, Ni, and Ca) and re-certifications for 6 additional elements initiated (Al, As, Cr, Cu, Pb, and Na), all of which anticipate replacement of in-stock materials. The certification of two very difficult elements,

rhodium and rhenium, which have been out-of-stock for several years was also completed. Both projects involved considerable research before reliable results were achieved. Stability tests were also completed for five elements (Mn, P, Cs, Ho, Y). This testing was done to evaluate the extended shelf life of ampouled materials. The Plans for the coming year call for the initiation of a new class of elemental standards, NIST Primary Standards (NPS); these materials will be certified for amount of material, as opposed to concentration.

The basis of the single element spectrometric solution standards' certification is high performance ICP-OES. The underpinning science in the application of this technique to the program was documented this year in *Analytical Chemistry* [Marc L. Salit, Gregory C. Turk, Abigail P. Lindstrom, Therese A. Butler, Charles M. Beck II, and Bruce Norman; "Single-Element Solution Comparisons with a High-Performance Inductively Coupled Plasma Optical Emission Spectrometric Method," *Analytical Chemistry*; 2001; 73(20); 4821-4829]. An alternative mechanism for technology transfer of HP-ICP-OES has also been pursued this year through the development of a software tool that guides an analyst through the measurement process. This tool was beta-tested with two commercial standards companies that wish to use HP-ICP-OES to perform traceability comparison measurements between their products and the SRM 3100 standards. The results are encouraging. With this capability, they can now value-assign their standards based on our SRMs with uncertainties that are nearly identical to the SRM uncertainties.

The Group participated in four pilot and key comparisons of the inorganic working group of the CCQM this year. CCQM K-13 key comparison of cadmium and lead amount content in sediment was a successor to the CCQM P-15 study (NIST did not participate). Satisfactory agreement of reported results among the NMIs was observed in K-13, although several laboratories did not adequately account for a Sn interference during Cd measurement—this was not a problem for the pilot material which had much lower Sn content. The median value was chosen as the key comparison reference value (KCRV) with the exclusion of two NMI results. NIST results were both within 0.24 % of the KCRV. NIST and NRC-Canada results agreed within 0.61 % for Cd and were the same for Pb. All of these results—NIST, NRC-Canada, and the KCRV—were indistinguishable within stated uncertainties.

CCQM P-12 was focused on measurement of the Pb content in wine. Fifteen NMIs reported results, which were in excellent agreement at the 25 ng/g level. NIST results were within 0.01 % of the median value. Twelve of the 15 laboratories agreed within 2 % of the median value. The consensus of the working group was that this comparison should have been instituted as a key comparison, not a pilot comparison.

CCQM P-26 Sulfur in Fuel was completed in June; the results have not yet been presented. This pilot comparison was sponsored by IRMM, using two materials that will be certified as BCR (European Community Bureau of Reference) CRMs. NIST and IRMM collaborated on the certification (in progress) of these CRMs (and a third material not distributed in the CCQM comparison). Previous BCR sulfur in fuel CRMs were certified by European interlaboratory exercises. For this certification, it was decided to deliver results directly traceable to the SI using "primary methods of measurement." Thus, the characterization measurements performed by NIST and IRMM were both the isotope dilution thermal ionization mass spectrometric (ID-

TIMS) method developed at NIST. This work was the first application of ID-TIMS by IRMM and they made a number of changes in their adoption of the method, including microwave dissolution instead of the Carius tube technique used at NIST. The results were not in as good agreement as we would have expected; there was a relative bias between 1 to 2 % between the two laboratories. This experiment and intercomparison gives us the opportunity to re-evaluate the primary nature of the ID-TIMS method.

CCQM P-14 Calcium in Serum was completed in July; the results have also not been presented. The measurements at NIST were made by both ID-TIMS and ID-ICP-MS as described above and benchmarked against SRM 956a Electrolytes in Frozen Serum. The precision and accuracy of the results provide good confidence in our capability for application of this definitive method.

The CCQM inorganic working group has one pilot comparison ongoing (CCQM-P29 Cadmium in Rice) and will be initiating further work at its first meeting in October 2001. The results for the completed pilot comparisons discussed above could lead to several new key comparisons in the coming year. These CCQM and other international interactions (CITAC, SIM)—comparative measurement programs, traceability and uncertainty discussions, and measurement capability assessments and claims—promote the development of a global infrastructure for chemical measurement, an infrastructure where NIST must represent the highest U.S. interest.

The above summary illustrates the wide range of research and measurement activities studied by the Group in the past year, using the spectrometric techniques available. The Group also made significant contributions to Division Standard Reference Material projects not mentioned above; inorganic constituents were determined in: Pine Needles, Inorganic Sediment, Mine Waste, Trace Elements in Water, Baking Chocolate, Peanut Butter, KDP, Steels, Anode Tin, Copper Alloys, Crude Oil, Coals, and more

Organic Analytical Methods

Research activities in organic analytical methods are directed toward the development, critical evaluation, and application of methods for the identification and measurement of organic and organometal species using mass spectrometry and analytical separations techniques. These separation techniques include gas chromatography (GC), liquid chromatography (LC), supercritical fluid chromatography (SFC) and extraction (SFE), capillary electrophoresis (CE), and capillary electrochromatography (CEC).

Recent research activities in organic mass spectrometry have focused on the development of techniques for characterization and quantitative determination of proteins in biological matrices. Levels of specific proteins and other biomolecules in blood are indicative of certain disease states. These so called “health status markers” often permit more rapid diagnosis of disease with greater certainty than is possible by other methods. Twelve health status markers have been identified as highest priority for immediate studies. This year efforts have been directed toward the development of reference methods for troponin I (a new marker of myocardial infarction), thyroxine (a marker for thyroid function), cortisol (a marker for endocrine function), speciated iron (how iron is associated with proteins is important for elevated or low iron levels), homocysteine (a risk factor for myocardial infarction), folic acid (an essential nutrient that reduces the risks of heart disease and neural tube defects), and prostate specific antigen (a marker

for prostate cancer). Because protein biomarkers occur naturally with considerable heterogeneity (i.e., with glycosylation, acetylation, phosphorylation), we have developed techniques for chemical characterization of the target species. For example, techniques have been developed for the characterization of purified troponin I preparations, thus providing a means for comparing the molecular structure with results from field studies involving immunoassays. An important aspect of the health status marker program is commutability. To be useful to the clinical community, biomarker levels in reference materials certified by primary and/or reference methods must be commutable to field methods. To this end, an interlaboratory comparison exercise of candidate troponin I reference materials was carried out in collaboration with the Troponin Subcommittee of the American Association of Clinical Chemists. Ten troponin I materials were evaluated by 13 manufacturers of immunoassays. A second interlaboratory comparison with the best candidate materials from the first study is being organized. The most suitable troponin I preparation from this second study will be identified for issuance as an SRM in the coming year.

Acquisition of an LC/MS/MS instrument during the past year increased our capabilities for the determination of analytes of health, nutritional, forensic, and environmental importance, as well as for structural studies of natural products. Another new instrument, a matrix assisted laser desorption time-of-flight mass spectrometer (MALDI-TOF) system, was obtained to further enhance our capabilities for characterizing biomolecules. This instrument was acquired with support from the Defense Threat Reduction Agency to begin development of protocols for generation of mass spectra from bacteria. The combination of proteins produced by one species of bacteria differs from that of another. Even different strains of the same species can generate significantly different combinations of proteins. The MALDI-TOF is used to generate a mass spectrum from the bacterial proteins. However, the patterns are affected by how the bacteria are treated and by the matrix compounds added to facilitate the MALDI-TOF process. Once protocols are established and agreed upon by researchers in this field, a searchable database will be created. Such a system will permit the identification of bacteria much faster than is now done by conventional approaches and will be applicable to counter terrorism activities as well as to other applications such as food safety. The MALDI-TOF system will also be used in characterizing health status protein markers as well as proteins expressed by genetic modification of foods.

Research activities in separation science continue to focus on investigations of the physical and chemical processes that influence retention in LC, GC, SFC, CE, and CEC. Results from these fundamental studies are used to design stationary phases tailored to solve specific separation and analysis problems, and to assist in method development and optimization. Recently we have explored a novel approach to the synthesis of LC stationary phases based on polymer immobilization. Polyethylene acrylic acid copolymers were immobilized on silica as an alternative to conventional silane surface modification chemistry. The resulting columns were evaluated for the LC separation of carotenoid isomers, and preliminary results indicate exceptional selectivity for this class of compounds. Further optimization of this promising stationary phase should result in improved measurement capability for carotenoids and related nutrients in food and tissue samples. Research in chiral separations is continuing in several areas using LC, CE, and GC. The determination of chiral drug species in hair samples using LC may permit environmental exposure to be distinguished from illicit use. Method development is in

progress for the determination of amphetamine and methamphetamine enantiomers in hair extracts. In other studies, functionalized cyclodextrins have been evaluated as chiral selectors in CE. Three commercially available sulfated cyclodextrins with similar degrees of sulfation were chosen for study. A capillary electrophoresis method with indirect detection was used to characterize the patterns of sulfate substitution of these materials. The selectors were then investigated as chiral additives in capillary electrophoresis. The electrophoretic results highlighted the importance of both the degree of substitution and the location of sulfate substituents on the cyclodextrin. The strongest analyte-selector interactions were observed for the randomly substituted material. These studies emphasize the importance of the use of well-characterized selectors for reproducible results in chiral CE.

Our research in organometal speciation has continued with improvements in the GC-atomic emission (AED) method for methylmercury and alkyltin species. The new approach involves derivatization and a solid phase microextraction (SPME) step to concentrate the analytes prior to GC-AED analysis. This approach has been used to provide data for certification of methylmercury in SRM 2977 Mussel Tissue, SRM 1566b Oyster Tissue, and SRM 1946 Lake Superior Fish Tissue. This same general approach has also been used to measure butyltin species in several of the sediment-matrix SRMs (i.e., SRM 1941b Organics in Marine Sediment, SRM 1944 New York/New Jersey Waterway Sediment, and SRM 1646a Estuarine Sediment). The butyltin results will be provided as reference values for these SRM.

Other separation science research has involved the development of multidimensional chromatographic approaches for isolation and quantification of nonortho-substituted polychlorinated biphenyl congeners (considered to be the most toxic congeners) in some of our existing SRMs (cod liver oil, sediment, and whale blubber). This method was applied for the certification of these nonortho congeners in SRM 1946 Lake Superior Fish Tissue, which will be the first natural matrix SRM to have certified values for these toxic PCB congeners. We also improved the methodology for the determination of nitro-substituted PAHs in environmental matrices using a normal-phase LC isolation of the nitro-PAHs prior to measurement by GC/MS with negative ion chemical ionization detection. An improved separation of the isomeric nitro-PAHs, particularly the nitropyrene and nitrofluoranthene isomers, was achieved using a 50% phenyl-substituted methylpolysiloxane. This improved methodology was used to assign values for concentrations of mononitro-PAHs and dinitrorene isomers in three diesel particulate-related SRMs (SRM 1650a, SRM 1975, and SRM 2975) and two air particulate SRMs (SRM 1649a and SRM 1648).

During the past year, measurements have been completed on a number of SRMs of importance to the clinical, environmental, and food and nutritional communities:

- Clinical Reference Materials
SRM 913a Uric Acid. SRM 913a is a standard used for calibrating assays for serum uric acid, a measurement used for diagnosis of gout. A variety of analytical techniques were used to detect and measure impurities in this material. These results were evaluated to determine the overall purity and uncertainty of this material.
- Environmental Reference Materials

Diesel Particulate SRMs. Three diesel particulate materials were issued during the past year. SRM 1650a Diesel Particulate Matter, first issued in 1985, was reanalyzed and issued with certified/reference values for ~56 PAHs and nitro-PAHs. SRM 2975 Diesel Particulate Matter (Industrial Forklift) is a contemporary diesel particulate material collected from an industrial forklift. SRM 1975 Diesel Particulate Extract is a solvent extract of the particulate material used to prepare SRM 2975. Both SRM 1975 and SRM 2975 were developed at the request of EPA to provide reference materials representative of emissions from modern diesel engines. Certified and reference values are provided for ~50 PAHs and nitro-PAHs. In addition, mutagenicity data provided by EPA is reported for SRM 1975.

SRM 1941b Organics in Marine Sediment. SRM 1941b is the third issue since 1989 of the popular marine sediment SRM for organic contaminants. Results from multiple analytical methods were combined to provide certified values for approximately 25 PAHs, 30 PCB congeners, and 10 chlorinated pesticides. The PAH, PCB, and pesticide concentrations are approximately 2 to 20 times lower than those in SRM 1944 New York/New Jersey Waterway Sediment, thus these two sediment materials will serve the needs of the marine environmental measurement community for both high and moderate levels of organic contaminants.

SRM 1946, Lake Superior Fish Tissue. SRM 1946 is a cryogenically homogenized fish fillet prepared from adult lake trout (*Salvelinus namaycush*). The fish tissue homogenate is indicative of urban contamination levels and will be beneficial to both the environmental and food/nutrition measurement communities. Certified values have been determined for 30 PCB congeners (including 3 non-ortho congeners), 13 chlorinated pesticides, methylmercury, and total mercury. This is the first SRM available with certified concentrations for the non-ortho PCB congeners, which are considered the most toxic, similar in structure to polychlorinated dibenzo-p-dioxins.

SRM 1974b, Organics in Mussel Tissue (*Mytilus edulis*). SRM 1974b is the third issue since 1990 of the mussel tissue SRM for organic contaminants. Certified values will be determined for approximately 40 PAHs, PCBs, and pesticides, as well as methylmercury and total mercury.

Instrument Calibration Standards. Six calibration solution SRMs to support measurements of contaminants in the marine environment were completed last year, including SRM 2269 and SRM 2270 Perdeuterated PAH Solution in Hexane/Toluene, SRM 2273 DDTs and Metabolites in Iso-octane, SRM 2275 Chlorinated Pesticide Solution-II in Iso-octane, SRM 2276 Three Planar PCB Congeners in Iso-octane, and SRM 2274 PCB Congener Solution-II in Iso-octane.

A suite of 26 organic calibration solution SRMs has been developed to support the recently externalized Water Performance Evaluation (PE) Studies Program orchestrated by the US Environmental Protection Agency (USEPA). These SRMs are intended to support the PE program; however, it is anticipated that widespread usage will result after issuance. These SRMs include: six Aroclor mixtures in methanol and in oil; chloral

hydrate, haloacetic acids, dioxin, endothall, chlorinated herbicides, toxaphene, chlordane, and adipate/phthalates in methanol; organochlorine pesticides in acetone; glyphosate and diquat dibromide in water; and vydate and carbamates in acetonitrile.

- Food Reference Materials

The composition of a food-matrix SRM should be matched closely to that of the test sample being analyzed. AOAC (Association of Official Analytical Chemists) International has developed a nine-sectored triangle in which foods are positioned based on their fat, protein, and carbohydrate content. AOAC's belief is that one or two reference materials within each sector should be representative of other foods within that sector and could be used for quality assurance and method validation when analyzing those other foods. NIST has been working with other government agencies and the food industry over the past several years to provide an increased array of SRMs with values assigned for proximates (procedurally defined values for fat, protein, carbohydrate, etc.), fatty acids, cholesterol, vitamins, elements of nutritional interest, etc. Concentration values in the food-matrix SRMs are assigned based on a combination of measurements from NIST and interlaboratory comparison exercises involving approximately 20 member laboratories of the National Food Processors Association's (NFPA's) Food Industry Analytical Chemists Subcommittee (FIACS).

SRM 2384 Baking Chocolate. SRM 2384 has values assigned for proximates, individual fatty acids, total dietary fiber, several vitamins, catechins, theobromine, caffeine, and elements of nutritional interest.

SRM 1946 Lake Superior Fish Tissue. SRM 1946 is described above as an environmental matrix SRM, but is also useful as a food-matrix. Therefore SRM 1946 also has values assigned for nutrients including proximates (fat, protein, etc.) and individual fatty acids, including several omega-3 fatty acids.

SRM 2385 Spinach and 2387 Peanut Butter. These two SRMs have been prepared and value assignment is in progress for nutrients, carotenoids, and pesticides in the spinach and for nutrients, allergens, aflatoxins, and amino acids in the peanut butter.

- Botanical SRMs

The U.S. 1998 market for nutraceuticals (i.e., herbal supplements and functional foods) was estimated at nearly \$26 billion; botanicals accounted for about \$3.5 billion of this market, and a continued growth rate of 10% to 20% was expected. However, in 1998 sales of botanical products began to level off, and by the end of 1999, overall sales had dropped 3% compared to 1998. Part of this decrease in sales may be attributed to a loss in consumer confidence in botanical products as a result of negative publicity. Reports of inaccurate labeling, adulteration, contamination (pesticides, heavy metals, or toxic botanicals), and drug interactions have all contributed to the decline in sales. Taxonomically authentic botanical reference materials with assigned values for active and/or marker compounds, as well as for contaminants such as pesticides, mycotoxins, and heavy metals, are necessary for verification of manufacturers' label claims and quality control during the manufacturing process.

We have developed a collaborative program with the Food and Drug Administration's (FDA's) Center for Food Safety and the National Institutes of Health's (NIH's) Office of Dietary Supplements to produce a number of authentic, well-characterized reference materials of botanical raw materials to support the needs of the dietary supplement community. Starting in FY02 ACD, FDA, and NIH will collaborate to prepare six to eight selected botanical-matrix SRMs from authentic raw materials during the next several years. FDA, with input from other agencies and organizations, will consult with NIST to identify the materials of high priority.

- **Instrument Performance Standards**
Insights gained from our research in separation mechanisms have provided us the knowledge to develop two new LC column performance test mixture SRMs. SRM 870 Column Performance Test Mixture has been developed to characterize LC column properties such as silica silanol activity, trace metal activity, and separation efficiency. SRM 877 Chiral Selectivity Test Mixture for Liquid Chromatography has been developed to facilitate prediction of the performance of columns for resolving enantiomers.

Gas Metrology and Classical Methods

Research activities within the Gas Metrology and Classical Methods Group are focused on gas metrology, classical wet chemical methods (gravimetry, titrimetry), coulometry, ion chromatography, and maintenance of the theoretical infrastructure for pH and conductivity measurements.

During FY01 the following SRMs were completed: 10 gaseous, 6 conductivity, 3 Volatile Organic Compound solutions and a titanium dioxide material. A total of 104 gas cylinder SRMs were recertified for 13 companies. While these certified reference materials are critically needed, their continuous production consumes considerable fiscal and human resources and limits our ability to address new standards needs. The gas NIST Traceable Reference Materials (NTRM) Program was created to address this concern. In FY01, we worked with 4 specialty gas vendors to certify 36 NTRM batches. The over 1000 individual gas cylinders in these certified batches will be used to produce approximately 100,000 NIST-traceable gas standards for end-users.

In the area of electrolytic conductivity, we continued our research into new packaging technology. The problem we face is that the packaging used in the past was not suitable for storage of conductivity solutions for more than one year. This has caused us problems in that each solution must be remade every year and uncertainties could not be lowered below 1%. During the past year we decided to package all conductivity solutions greater than 500 $\mu\text{S}/\text{cm}$ in 50 ml ampoules. We are still researching the problem for lower conductivity solutions. In sealed ampoules the transpiration problem, which has plagued us in the past, is solved and the solutions have multiyear self-lives. This should help us in the electrolytic conductivity program by reducing the SRM reissue rate so we can devote more time to low conductivity research, which is desperately needed to address needs in industry driven by regulations. Collaboration with the Netherlands (NMI) will help in this research. We have also benchmarked and compared

our capabilities in the area of electrolytic conductivity measurements with the National Metrology Institutes for Denmark and Hungary. The data from this benchmarking activity will appear in the journal of the BIPM, *Metrologia* in FY01. We are also participating in a CCQM pilot study on conductivity (CCQM-P22).

In the area of pH we continue to be very active in the international arena. In FY01 we participated in a pH Key Comparison (CCQM-K17), phthalate buffer (pH 4.0), and assisted the pilot laboratory (PTB) in preparing the solutions. We also completed a SIM pilot study on pH (SIM QM-P4) with 16 participating laboratories in South America, Mexico and the Caribbean. We also continue to be active in IUPAC commission V.5, completing revisions to the pH document that will define the traceability of pH to the Bates-Guggenheim convention, thus assuring continued traceability of pH to sound thermodynamic principals. This manuscript is now working its way through the IUPAC review process.

In collaboration with EPA and the remote sensing community, we have developed a quantitative database of infrared spectra, which is required for establishing remote IR-based technology as a reliable tool for real-time monitoring for airborne chemical contaminants along plant boundaries and within plant facilities. Because the spectra are being prepared using NIST primary gas standards, well-defined traceability to NIST can be established for any subsequent field measurements. These spectra will be required to be used in the new update of EPA method TO-16. At the present time we have released 40 compounds. We are working in collaboration with PNNL on an error affecting the higher wavenumbers, which deals with a fundamental problem with commercial instruments. This will result in an interesting paper that will detail needed changes in commercial instruments to resolve this systematic bias. In the near future we hope to increase user availability of this database on the Internet.

We continue to be very busy in the Ozone Program with completion of the upgrade of the EPA Standard Reference Photometer (SRP) network with new electronics. Many more countries have expressed interest in receiving an SRP to provide traceability in ozone measurements. New SRPs have been ordered by Portugal, Spain, BIPM, and Brazil. This presents a problem to NIST, in that we expend many resources to provide traceability to most of the world. It would be in NIST's interest to transfer this responsibility to another organization so we could shift those resources to areas of concern to U.S. industry. During the past year, we concluded talks, which will transfer the responsibility for world traceability for ozone to the BIPM in Paris, France. Over the next 5 years NIST will be working with BIPM to build two SRPs to act as the official ozone traveling standards, and a Primary Reference Photometer (PRP) to act as the stable international standard for ozone. Two PRPs will be constructed, one at NIST and one at BIPM. Work will be concluded in FY02 on construction of the two SRPs, and in design of the PRP. It is planned that construction of the PRP will begin in FY03. Plans for a CCQM key comparison on ozone are proceeding, and will be organized after BIPM has received their two SRPs.

We continue to promote U.S. industry through development of high priority standards, and through standards organizations such as ASTM. Over the past two years we have developed the capability to produce low concentration nitric oxide gas standards. These standards are need by the automotive industry in new car development and to meet new regulations in California. These standards also are required by Industry to meet new regulations covering stack gas

emissions. This research has resulted in two new nitric oxide gas SRMs in the coming years, one at 0.5 ppm (SRM 2737) and one at 1.0 ppm (SRM 2738).

In July 2001, a meeting was held at NIST with representatives from the American Industry/Government Emissions Research consortium (AIGER) to discuss research and standards needs to support emissions testing for the next generation of automobiles. AIGER is comprised of the California Air Resources Board, the US EPA, and the Automobile Industry (Daimler-Chrysler, Ford, General Motors). Critical new standards are needed for methane, propane, nitric oxide, and carbon dioxide that are significantly lower in concentration than SRMs currently available. These new standards will require research into new cylinder technology, and in new delivery systems in order to provide traceability. Without these new gas standards, delivery of lower emission automobiles will be impeded. We will be working closely with AIGER to develop the new standards, and to certify new NTRM lots that meet their strict requirements.

We also are continuing to assist the health industry with the task of safely implementing the inhaled nitric oxide therapy for newborns. Over the past year we have held another workshop to test clinical instruments, which measure nitric oxide and nitrogen dioxide. We have also assisted ASTM and industry draft a standard procedure to test these clinical instruments effectively before introduction into the hospitals and in continued operation.

Molecular Spectrometry and Microfluidic Methods Group

The MS&MM Group conducts research on the metrology of molecular spectrometry and develops standards for calibration, validation, and performance of instruments for measuring molecular spectra; conducts research on microfluidic devices, methods, and applications for chemical analysis including studies of materials and material properties affecting the flow of liquids in microchannels and the use of microchannel and other electrophoretic methods for forensic and toxicological applications and standards; has responsibility for the development and certification of optical transmittance and wavelength standards in the ultraviolet, visible, and near-infrared spectral regions; and works with users and manufacturers of analytical instruments to assess and measure the performance of analytical methods and to determine and address existing and future needs for analytical instrument standards ranging from device calibration and instrument performance through specifications for remote device control and data interchange.

In FY01, 68 solid absorbance filter SRMs were certified, and 176 optical filter sets were recertified. Continuing measurements were made on a number of other filter sets. In addition, 175 units of SRM 2034 (holmium oxide UV-Vis wavelength standard), 98 units of SRM 2065 (UV-Vis-NIR transmission wavelength standard), and 200 units of SRM 2241 (Relative Intensity Standard for Raman Spectroscopy with 785 nm Excitation) were certified. A new “just-in-time” filter certification process was instituted to solve the problem of filter certifications expiring prior to sale. We began to utilize the infrared laser marking system to etch identification numbers onto our optical filter glass and fused silica products—this year’s production run of SRM 2034 featured the SRM number and series identification etched into the fused silica cuvettes. We conducted a study to see if the laser etching would produce any measurable effect on the transmittance of our optical filters—it did not. The laser etcher was also utilized to label the anodized aluminum holders for SRM 2241.

Several new features were added to the high accuracy reference spectrometer (HAS-II) including capabilities to measure 50 mm (2 inch) square filters (useful for international intercomparisons), to determine filter transmittance at three height and multiple width positions on a filter (useful for filter homogeneity assessments), and to provide easy access to the data in the database for control chart generation. The effort to renovate the original high accuracy reference spectrometer (HAS-I) continued with the development of a new integrating sphere, new sample transport, new visible lamp controller, new shutter and controller, and automation to drive the monochromator and monitor its position. The goal for HAS-I renovation is to reach the level of automation and control currently available for HAS-II so that HAS-I can be used for research on spectrometric measurements. Since HAS-II is used for production (certification and recertification) activities, it cannot be (and should not be) used for research.

Research was carried out to develop an extended set of visible filters (0.1%, 0.3%, and 70% transmittance) to enlarge the range of transmittances covered and fill in a gap in our coverage. This is being done to make the range of our visible filter offerings more compatible with those of other NMIs (e.g., NPL) and to meet partially requests by CORM, our NTRM vendors, and others for broadening the range of our standards. Modifications to the HAS-II software will be required before we can actually certify these darker filters. Our studies into causes of the problems plaguing the production of our metal-on-fused-silica filters yielded some solutions. The spectral interference (fringe) problem was solved by purposefully making the filter substrate and cover plate different thicknesses. The aging process (filter drift) was improved considerably by heating the filters after the contacting step. The remaining two difficulties, coating inhomogeneity and spectral slope (decreasing transmittance with decreasing wavelength) remain under study.

The NVLAP assessments and accreditations were completed for the three participating NTRM certifiers of optical filters, although only one of the three has passed the post-accreditation phase involving our testing of their production filters. Going into this year, the traceability aspect of this program was vague as to the actual methodology of assigning uncertainties and/or bias correction equations to the NTRM certifiers. We designed and implemented computer macros to massage comparative measurements made on SRMs, proficiency-test (PT) samples, and NTRM production "batch-test" filters, resulting in a tighter traceability link and lower uncertainties than anticipated. It appears that we can maintain traceability through the use of the batch samples sent to us for approval and the SRM recertifications. This will streamline the proficiency testing requirements and simplify the process the certifiers and us. A fourth vendor has expressed a desire to join the program.

The NORAMET intercomparison of holmium oxide solutions for UV/Visible wavelength standards (see individual TAR) was expanded to participating SIM nations, and measurements were made in Trinidad and Tobago and Brazil this year. Although two participating countries remain for the SIM intercomparison, the NORAMET portion has been completed, and a draft of the report has been prepared. The analysis of the NORAMET data has very significant consequences for UV/visible wavelength standards. The first of these is the revision of our uncertainty estimates for SRM 2034. The second consequence is a decision to convert this standard from an artifact to an inherent (data) standard. The samples are now in Argentina, and we have scheduled the final shipments to Costa Rica when they return.

Progress was made on the creation of a NIR wavelength “transflectance” standard. Test samples from the production block of glass were cut, polished, and evaluated in transmission mode. The temperature coefficients of the material were determined. The next step is to mate the glass with the polyfluorocarbon diffuse reflector to create the reflectance/transflectance device that will be certified as the SRM.

The certification of first Ramen relative intensity correction standard for excitation at 785 nm was completed this year (see separated TAR on SRM 2241). Suitability studies were completed on the second material, a uranium glass for excitation at 488 nm to 532 nm. This paves the way for the certification of SRM 2242 in the upcoming year. Studies were also conducted on an europium-bearing glass for 1064 nm excitation (SRM 2243).

We continued our search for candidate materials for luminescence standards and examined several transition-metal-, rare-earth-, and actinide-doped glasses. Uranium- and manganese-bearing glasses look promising for fluorescence spectral emissivity standards. We are also studying glasses containing mixtures of rare-earth s as possible fluorescence wavelength standards. Unlike absorbance, mixed rare-earth glasses do not give fluorescence spectra that are simply the sum of the spectra of the separate element-doped glasses. With mixed elements, emission bands can decrease in intensity, grow in intensity, shift in wavelength, and/or disappear altogether. Elemental concentration, the type of glass matrix, and the glass making conditions all have effects on the final fluorescence spectra observed.

We continued to qualify the SPEX-JY fluorometer. We recently had a small integrating sphere/photodiode assembly calibrated in PL. This will allow us to quantify the light from the excitation monochromator. We fabricated several sample chamber devices to hold samples, to reflect light into the emission monochromator, to hold tritiated phosphor devices, etc. These will be used to further qualify the instrument and determine its stability, etc. A standard uniform light source has been constructed to calibrate the emission detection system. After further testing, it will be sent to PL for calibration.

Progress was made on linking the fluorometer to the dual diode array detector system that will allow us to obtain excitation-emission matrix spectra rapidly. Using the fluorometer’s built-in optics, the detected signals proved weaker than desired; accordingly, an alternate optical arrangement is being investigated. Devising the software to control both instruments simultaneously remains the biggest hurdle.

We continued to provide statistics and data representation studies for FBI, OLES, and other agencies investigating the use of DNA methods of forensic analysis including studies on various aspects of STR DNA typing, particularly related to how errors in the measurement of DNA quantity propagate into the detection of the STR profile and the recovery of DNA from aged stains; on the quantitative characterization of STR allelic signals and assignment of match thresholds; and on aspects of gunpowder residue analysis. We continued to provide computational, organizational, and philosophical support for the Micronutrients Measurement Quality Assurance Program including data analysis and feedback for reports on two fat-soluble and one vitamin C interlaboratory studies.

Our project, initiated through the Office of Law Enforcement Standards at NIST, to advance and support quantitative measurements for forensic analyses received a boost this year from the symposium we organized and chaired at PittCon. The program was both well received and well attended. A report about it was featured in a subsequent PittCon promotional brochure. Progress was made on the first gunpowder reference material (RM 8107). A single ball rifle powder has been selected as the material, and the procedure for extracting and quantifying the organic additives from this material was developed. Our OLES-sponsored forensic analysis fellowship program continued with support for two graduate students this year. The MECE procedure that we developed for gunpowder additives was recently used in criminal casework by the Washington State Patrol and has also been adopted by the Army Research Lab at the Redstone Arsenal for propellant additive determination.

This year was a banner year for our microfluidics projects resulting in eleven publications, five patent applications, and six invited talks (see separate TAR). Microfluidics funding, which had been largely from the Microscale Analytical Laboratory Competence, a small ATP grant, and STRS, received additional ATP sponsorship this year and will receive an additional boost from a new Single Molecule Manipulation and Measurement competence award. The joint program with Div. 836 continues to attract NRC postdocs, adding one more this year to bring the MS&MM total to three. One of them, Emanuel Waddell, won first prize in the student/postdoc poster contest at LabAutomation 2001.

We continue to study the parameters that affect flow in plastic microchannel devices. This year major progress was made in exploring applications of UV-laser ablation for fabricating microdevices, for studying parameters important to the post-machining properties of microdevices, and for carrying out both physical and chemical modifications to the surfaces of microdevices. New techniques were discovered for controlling surface charge and the spatial distribution of surface charge in channels made either by imprinting, laser ablation, or hybrid fabrication techniques using both methods. Extensive progress has been made in evaluating flow in microchannels using particle velocimetry and caged fluorescent dye imaging. Thanks to the availability of ITL-procured simulation software, we have begun to model flow in microchannels. These simulations have already been beneficial in new fluid mixer and flow steering designs. The microfluidics projects are rich in collaborations—across NIST and off-campus in both academe and industry. In one such collaboration with Cornell University, a liposome-based microfluidic assay was developed for detection of RNA/DNA in *Cryptosporidium parvum*, a difficult to kill environmental pathogen.

Working with Guest Researchers for the Fachhochschule in Wiesbaden Germany, we developed SpectroML a markup language for molecular spectrometry data that can be used as a “web-aware” mechanism for instrument-to-instrument, instrument-to-application, and application-to-application data interchange and archiving (see separate TAR). SpectroML was developed using XML (extensible mark up language), and its vocabulary was gleaned from the terminology, data dictionaries, and concepts embodied in existing standards, instrument software, and data interchange formats. Currently, we have created a SpectroML vocabulary, document type definition, schema, stylesheets, and some demonstration applications for UV-visible spectroscopy data; however, the structure and flexible data model embodied in SpectroML should make it easily adaptable to other spectroscopy techniques. We are currently developing

applications to utilize SpectroML in house for data interchange among our spectrometers and also those of our NTRM vendors.

Nuclear Analytical Methods

Research activities in this group are focused on the science that supports the identification and quantitation of chemical species by nuclear analytical techniques. Current laboratory research activities involve the full suite of nuclear analytical techniques, including instrumental and radiochemical neutron activation analysis (INAA and RNAA), prompt gamma activation analysis (PGAA), and neutron depth profiling (NDP). In addition, we are developing analytical applications of neutron focusing technology. The measurement capabilities that reside within this group provide an excellent complement to those in the Spectrochemical Methods Group in that they depend upon characteristics of the nucleus of the element rather than the electron shells, and therefore are insensitive to the chemical state of the analyte. In addition, the nuclear analytical methods are generally nondestructive and do not require sample dissolution, thus providing an independent assay.

INAA and RNAA are powerful reference techniques that have been used at NIST for many years. New developments continue to provide improvements in detection sensitivities, elemental specificity, precision, and overall accuracy that allow nuclear methods to address new measurement needs. We have recently developed new INAA procedures and applied them to homogeneity studies of SRMs at small sample sizes. Many analytical techniques used in industry and academia rely on the analysis of very small samples (i.e., 1 mg), typically in the solid (undissolved) form. Unfortunately most SRMs are certified with minimum sample sizes of 100-500 mg, and are therefore unsuitable for use as control materials for these techniques unless additional information is made available. Taking advantage of the sensitivity and nondestructive properties of INAA, the use of this technique for homogeneity studies of small samples has been evaluated and implemented for the determination of sampling characteristics for a number of environmental SRMs. The minimal analytical uncertainty associated with the INAA measurements allows extraction of the variability due to material inhomogeneity from the observed total variability within a given set of measurements. We have investigated three sediment materials that have shown the potential for a high degree of homogeneity at very small sample sizes for possible use as a future SRM aimed at solid-sampling analytical techniques. From the candidate materials a portion of sediment from the Baltimore Harbor, currently under certification for “normal” sample sizes (SRM 2102) was selected for further processing as an SRM for microanalytical techniques. Evaluation of the Ingamells model describing homogeneity has been initiated with the Statistical Engineering Division.

Instrumental neutron activation analysis has been used as a primary method for certification of the arsenic implanted dose in SRM 2134, Arsenic Implant in Silicon. This material has been a high-priority need of the semiconductor industry for a number of years. It was produced and characterized in collaboration with the Surface and Microanalysis Science Division and is intended for use as a calibrant for secondary ion mass spectrometry. The INAA results used for certification include the first complete, quantitative evaluation of all sources of uncertainty in an INAA measurement. The expanded relative uncertainty for the mean value of this SRM was 0.38 % and approximates the 95 % level of confidence.

In the course of our high-accuracy measurements of arsenic, we found that the most recently published and compiled half-life of ^{76}As did not describe our data as well as the earlier accepted value. We have redetermined this parameter using four Ge detector systems, and fitted an exponential to the decay data by two different nonlinear least-squares methods. We measured $t_{1/2} = 1.0938$ d with an expanded uncertainty $U = 0.0009$ d. This result is 1.5% higher than the recent value, and in agreement with the older, less precise, consensus value.

As part of our attempts to demonstrate that instrumental neutron activation analysis meets the CCQM definition of a primary ratio method of analysis, we are currently determining the concentration of Cr in a ferrous metal, SRM 1152a. We will provide a complete uncertainty evaluation as in the case of arsenic in silicon. Analysis of a metal matrix challenges the INAA measurement process in a totally different manner than does determination of arsenic in silicon. The high density of the metal increases the magnitude of both neutron and gamma ray self-shielding. The metal matrix also produces an elevated level of baseline radiation. An additional reason we have chosen to determine Cr in SRM 1152a is the small uncertainty in its certified value. Initial measurements were conducted using crystalline chromium metal as a comparator. The measurements were validated with weighed aliquots of SRM 3112a dried on filter paper pellets. The experimental results do not show deviations beyond the uncertainties of the SRMs (≤ 0.2 % relative), and the initial assessment of the uncertainty budget indicates that an expanded uncertainty of ≤ 0.3 % should be achievable.

Radiochemical neutron activation analysis has proven to be a powerful tool for measuring trace phosphorus in a variety of materials. An RNAA procedure has been developed to determine and value assign phosphorus in various SRMs. Phosphorus is quantified by beta counting of ^{32}P after radiochemical separation. Originally developed for the analysis of metals, the method was used to value assign phosphorus in SRMs 861 (Aircraft Superalloy) and 2175 (Refractory Alloy), both containing phosphorus at low mg/kg levels. Modifications to the procedure have allowed us to value assign phosphorus in two new SRMs: 1575a (Pine Needles) and 2702 (Inorganics in Marine Sediment). Plans are currently underway to develop an ion-implanted phosphorus in silicon SRM for the semiconductor industry, which will be value assigned by RNAA. The RNAA procedure has been modified for use in determining phosphorus in implanted silicon, critically evaluated, and applied to subsamples of an ion-implanted phosphorus in silicon wafer previously used for an interlaboratory comparison. Our RNAA results indicate that phosphorus can be determined at approximately 8.5×10^{14} atoms \cdot cm $^{-2}$ with an expanded uncertainty of 3 %.

Nearly thirty years ago a simple and rapid radiochemical procedure was developed at NIST, using oxygen combustion to separate mercury quantitatively from interfering radioactivities. Mercury was subsequently determined by counting the 64-hour ^{197}Hg with a low-energy Ge gamma detector. This method was used extensively for the certification of mercury in biological materials and other reference materials. However, the published combustion method suffers from problems due to high levels of activity from ^{82}Br , which elevates the baseline level under the peaks of interest. This radiochemical procedure is not optimum for determination of mercury via 47-day ^{203}Hg , because selenium follows mercury efficiently in the combustion (indeed, an almost identical procedure was developed for selenium determination). The sole ^{203}Hg gamma is interfered with by 120-day ^{75}Se , so correction for this interference is imprecise in high-selenium

matrices. In the present work selenium is removed by precipitating mercury as periodate. The chemical yield of each sample is measured gravimetrically. The procedure has been applied to the certification of mercury in SRMs 1632c Coal, 2702 Sediment, and 1575a Pine Needles. Expanded uncertainties of 2 to 3 % can be achieved via this method.

Pioneering research is conducted by the Nuclear Methods Group on the use of cold neutron beams as analytical probes for both PGAA and NDP. PGAA measures the total amount of an analyte present throughout a sample by the analysis of the prompt gamma rays emitted immediately following neutron capture. NDP, on the other hand, determines the concentrations of several important elements (isotopes) as a function of depth within the first few micrometers of the surface by energy analysis of the prompt charged particles emitted during neutron bombardment. Both of these techniques continue to make important contributions in the characterization of advanced materials, particularly with the enhanced sensitivities now available using cold neutrons from the NIST Reactor.

The cold neutron PGAA and NDP spectrometers, which are available to outside researchers as part of the NIST Center for Neutron Research “national users’ facility”, continue to provide high-quality measurements for outside scientists. Non-destructive, matrix-independent measurements of hydrogen by the cold neutron PGAA technique have become particularly valuable in view of the difficulties of accurate determination of this element by other techniques. Many of our current PGAA collaborations involve determining hydrogen in a wide variety of materials for different applications. These include: metal embrittlement studies, studies of materials for new types of lithium batteries and fuel cells, determination of hydrogen in porous thin films on silicon, and screening materials for H prior to neutron scattering measurements. Other measurements made at the PGAA facility this year include H, S, Ca, and K in Nafions, derivatives of Teflon which have potential use as membranes in electrochemical separations and in fuel cells; Dy in polymers with potential use in optical communications, Bi, Nb, and Zn in dielectric materials with potential in wireless communications, and La, Sr, Cu, and Zn in antiferromagnetic materials which are of interest to the superconductor industry. In a continuing project, cold neutron PGAA is being used in conjunction with crystallography to study the stoichiometry and arrangement of the atoms in zeolites, acid based catalysts used in production of gasoline. PGAA is being used to measure H, Al, and Si in these materials, and also to quantitatively measure deuterium/hydrogen exchange.

A method has been developed and apparatus built to produce titanium (and other metal) SRMs of known hydrogen concentration on the few-kilogram scale. The method is based on the controlled reaction of hydrogen with titanium in a closed system. After preparation, the hydrogen concentration is verified by cold-neutron prompt-gamma activation analysis and gravimetry. The first SRM, 2453 (Hydrogen in Titanium Alloy) has been prepared near the critical level of approximately 100 mg/kg. Cold neutron PGAA has been used to measure a hydrogen mass fraction of 114 ± 14 mg/kg, in agreement with the volumetric measurement. Two additional hydrogen in titanium SRMs will be prepared at bracketing levels. This apparatus has also been used to prepare standards for neutron-tomographic nondestructive analysis of turbine blades at McClellan Air Force Base.

We are currently developing and critically evaluating a second nondestructive technique for the quantitative determination of hydrogen based upon neutron incoherent scattering (NIS). This will serve as a complement to our PGAA measurements of this element. NIS has a limited overlap of error sources with PGAA, and agreement of results between the two techniques provides a high degree of confidence. In addition, by measuring the scattered neutrons using a position-sensitive detector, NIS may be used to determine the location of hydrogen within various metallic systems. Using a slit or aperture in the scattering geometry, we have demonstrated the imaging of hydrogen in layers of polypropylene sandwiched between sets of titanium plates, and in titanium standards containing known amounts of hydrogen. We have shown the ability to image hydrogen in titanium at the 100 $\mu\text{g/g}$ level as a function of location. Analysis of the images shows that the scattering from the hydrogen increases linearly with its mass fraction within the titanium.

In collaboration with the Reactor Radiation Division (856) and the US Food and Drug Administration, a new thermal neutron prompt gamma ray activation analysis instrument was designed and fabricated. This instrument became operational in FY01. A sapphire filter was placed in the neutron beam shutter assembly and all external components of the original system were replaced. The new beam tube is made of two sections constructed from aluminum lined with a lithiated polymer (lithoflex). Both sections are sealed at each end, and kept under vacuum. The sample chamber was also constructed of aluminum and lined with lithoflex. The chamber may be evacuated when necessary. The new Ge detector has a resolution of 2.0 keV (for the 1332.5 keV line from ^{60}Co) and 40% efficiency (relative to NaI). Experiments were performed to determine mass fractions of Cd in SRM 2702 Sediment, and B, K and Cl in SRM 1575a Pine Needles. Additional experiments were performed to determine the background count-rates during various operational conditions, to measure element sensitivities in this configuration, and to determine the optimum amount of neutron and gamma ray shielding that will be incorporated into the final design for the detection system. A variable-position detector support platform will be designed. Additional work will involve optimization the detection system and shielding configuration, and complete characterization of the new system.

A novel approach is under investigation to alleviate some persistent problems in PGAA. Detection sensitivities of this technique are often restricted by the following factors: poor signal-to-noise ratios, interferences from background signals, and, in some cases, overlapping energy lines from different origins, namely ultra-short lived decay lines interfering with prompt decay. Discrimination between prompt and delayed emissions from a sample source, as well as against background events, can be achieved by examining the timing between the gamma-ray acquisition with the actual capture events using a pulsed beam of cold neutrons. Coincidence gating is used to select the prompt gamma-ray emissions. Signals from background capture gamma rays are suppressed because of times at which gamma rays are measured can differentiate between the sources of background radiation, providing a reduction in direct gamma-ray interferences. Anti-coincidence gating allows measurement of only decay radiation that originates from short-lived activated states of the nuclides after capture. Spectra of decaying nuclides are free of interfering prompt activities, and also have lower continuum background from Compton scattering of high-energy prompt gamma rays in the detector. The measurements provide the opportunity to use ultra-short half-life nuclides for analytical purposes; no sample decay occurs during transfer

times, and repetitive activation and counting cycles are achieved with the use of pulsed neutron beams.

The neutron depth profiling facility continues to provide unique measurement capabilities directly to US industries. Current experiments of interest at the NDP instrument include the measurement of lithium concentration and distribution in thin films being studied for battery applications, studies of boron mobility in tungsten with the Army Research Laboratory, shallow-doped boron content in silicon in conjunction with Advanced Micro Devices, the study of lithium distribution in lithium niobate, and the measurement of nitrogen in layers such as TiN and GaN. As a recent example, we have used NDP to measure nitrogen distributions in GaN/GaAs bilayers with Corning. This material is a base material for construction of devices such as blue light emitting lasers. The N concentration, which we can determine quantitatively, is a crucial parameter for establishing the device characteristics.

As part of a continuing collaboration between NIST and Tufts University, we have employed NDP to measure elemental concentrations versus depth for different lithium ion battery materials. One goal is to rationally design the thermo-mechanical properties of amorphous lithium phosphorus oxynitride (lipon, a solid ionic conductor), particularly the thermal stress (thermal expansion coefficient). A part of this study is to relate the resulting thermal stress to starting composition and temperature of evaporant, and of the composition and pressure of the background gas during deposition. We are also studying LiCoO₂ films (a material that can be used as an electrode in batteries) to determine if the ion beam assisted deposition process being used has the capability of controlling not only the degree of crystallinity and orientation of crystallites, but also the Li/Co ratio.

We have just concluded an assessment of long-term stability of primary boron and lithium thin film standards for NDP. Results show that the lithium standards have not changed over a ten year period, while the boron standards have lost from 0.1 to 0.5% of their original value. This will guide us in the design parameters of the next set of boron standards.

Efforts continue within the group to develop the techniques and methodology of focusing cold neutron beams for analytical applications of PGAA and NDP. A monolithic lens consisting of a fused tapered bundle of polycapillaries that provides a smaller focus of about 0.15 mm (FWHM at the focal spot) has been installed in the NDP chamber. The chamber has also been modified to accept a separate lid on which the lens can be mounted for remote-controlled alignment. A new alignment system containing a CID neutron camera with vacuum capability has also been installed. It provides a spatial resolution of 12 μm (pixel size) and an 8 bit dynamic range for the neutron intensity, and provides the possibility for charged particle imaging. Together with the new vacuum-compatible motion stages, the alignment system permits measurements without breaking the vacuum. Furthermore, the lens can be retracted out of the beam for measurements on the same sample with normal NDP geometry. The new lens and focusing system now gives us the capability of measuring samples as small as ≈ 0.1 mm in diameter or, together with our current scanning system, of measuring concentrations in three dimensions with much improved spatial resolution. Previously, our three dimensional profiles were performed with beam spot sizes of 1 cm.

Neutron focusing lenses have been shown to enhance the measurement capabilities of prompt gamma activation analysis (PGAA) for small samples ($\approx 100 \mu\text{m}$ in size) using a reactor-based cold neutron beam. Previously, a cold neutron beam emerging from a ^{58}Ni -coated guide, cross section = $50 \text{ mm} \times 45 \text{ mm}$, has been compressed to a spot size of about 0.54 mm (FWHM). Recently, we have made preliminary prompt-gamma measurements using a monolithic capillary lens. The lens accepts a 10 mm (hexagon flat-to-flat) size beam and focuses it to a spot size of $< 100 \mu\text{m} \times 100 \mu\text{m}$ (FWHM), with a gain in neutron beam current density of > 40 . The smaller focal spot size enables better spatial resolution, but also makes sample alignment more challenging. We have added a neutron imaging technique to the sample positioning procedure that takes advantage of the converging and subsequent diverging nature of the focused beam. The measurement sensitivity for a $2.6 \mu\text{g}$ Gd sample has improved by a factor of 34. In addition to rastering samples in the lateral plane, we have also explored the possibility of profiling the inhomogeneity of the sample in the direction along the beam axis.

A neutron thermometer technique has been employed to characterize neutron beam spectra at various instruments. The idea is to measure the prompt gamma signals from a “thin” (negligible absorption) and a “thick” (total absorption) sample, and to deduce the effective absorption cross section with the average neutron wavelength. This information is useful for characterizing “white beam” measurements such as those used for NDP and PGAA, as well as when additional components are introduced in the beam (such a filter or a neutron lens), which alters the neutron spectrum.

A technique for performing pseudo-Laue neutron crystallography of small single crystals with large unit cells, such as proteins, has been investigated using polycapillary optics. Instead of using a broad wavelength band, the technique uses a broad angular bandwidth in order to increase the neutron current density on the crystal. The convergent beam results in elongated diffraction spots that require modified software for analysis. We have taken measurements to characterize the transmission of a monolithic focusing lens with a focal length of 100 mm that was later used for preliminary tests of the proposed neutron technique on a pulsed source. The alignment of the optic in the neutron beam is most critical.