

NIST Analytical Chemistry Division (839)

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Chemical Science and Technology Laboratory
Analytical Chemistry Division

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FY03 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 90 scientists, technicians, and administrative/clerical support staff and an annual budget of about \$17M of which about \$7M 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 core competencies reside in five Groups [Spectrochemical Methods; Organic Analytical Methods; Gas Metrology and Classical Methods; Molecular Spectrometry and Microfluidic Methods; Nuclear Analytical Methods] and provide the capability to carry out the Division's broad mission and the flexibility to respond to changing and evolving national priorities. 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 underpin all of the Division's measurement service to the chemical measurements community through:

- Standard Reference Materials and Data
- 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 Clinical Diagnostics

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 \$1.5 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 healthcare 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) and the international community through the recently formed Joint Committee on Traceability in Laboratory Medicine to prioritize measurement and standards needs.

Measurement Methods and Standards for Forensics and Homeland Security

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 involve the development of reference methods, the development of 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, and Specimen Banking Technology.

Activities in this area support directly and indirectly the federal such as, EPA, NOAA, DOE, DOD agencies that have stewardship responsibility for the environment, 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 providing 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 such as neutron activation analysis, prompt gamma activation analysis, and 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 focuses 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 Group Sections 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 1440 SRMs; in FY03 NIST sold approximately 30,400 SRM units to more than 6,500 unique customers. Approximately 24,000 of the units sold were from the ~700 different types of materials that are certified for or support measurements of chemical composition.

During the past year, measurements were made to support our value assignments for ~100 SRMs. Approximately 45 high-priority renewal SRMs were issued and measurements were completed for the certification of 46 completely new SRMs. This does not include 137 gas SRMs recertified for 14 Specialty Gas Companies nor the approximately 200 sets of optical filter standards that were re-value assigned for wavelength and/or absorbance in the UV and NIR spectral region for more than 125 companies during 2003. The following narrative descriptions of six of these new SRMs completed during the past year illustrate the diversity of the industries and societal segments impacted by the SRM services delivered by the Division:

- In 2002, a collaborative effort was initiated with the Office of Dietary Supplements within the National Institutes of Health (NIH) and the Food and Drug Administration (FDA) Center for Food Safety and Applied Nutrition to develop SRMs for use in validating analytical methods for measurement of both “active ingredients” and contaminants in dietary supplements. This year, a suite of five ephedra-related SRMs was completed. The priorities for future Dietary Supplement SRMs are ginkgo, saw palmetto, St. John’s wort, and green tea.
- Fifteen elements were determined in a Suite of six Aluminum Alloy SRMs in which Glow Discharge Optical Emission Spectrometry was used for the first time for NIST certification measurements. Final completion of the certification project awaits results from cooperating laboratories. These SRMs are benchmark materials for several important aluminum alloys: 3004 (SRMs 853a and 1240c), 5182 (SRMs 854a and 1241c), and 356 (SRM 1255b, and 380 (SRM 1256b). All of these alloys have varied infrastructural uses; for example, their use ranges from body parts to engine components in automobile manufacturing. The aluminum industry has sophisticated in-house reference materials programs to supply their plants and customers with well-characterized materials for product quality control and business transactions. These SRMs serve as the benchmarks to underpin these industry reference materials.

- SRM 1946, Lake Superior Fish Tissue, has certified concentration values for 30 PCB congeners, 15 chlorinated pesticides, 13 fatty acids, total and methylmercury as well as reference concentrations for an additional 35 constituents. This is the world's first certified reference material with assigned-values for coplanar PCB congeners (the most toxic congeners) and omega-3 fatty acids. This SRM was requested by both the nutritional labeling and environmental measurements communities. Due to the required development and validation of measurement methods for this components as well as the complexity of certifying this wide range of types of constituents in this natural sample, the certification of this SRM was selected as the top technical achievement within the Chemical Science and Technology Laboratory in 2003.
- SRM 2242, Relative Intensity Correction Standard for Raman Spectroscopy: 532 nm Excitation, provides relative intensity correction for Raman spectrometers using the popular 532 nm lasers. Proper use of the SRM will enable "normalization" of Raman spectra and removal of instrument dependent effects on the appearance of Raman spectra. This will enable the creation of universal Raman spectral libraries which will greatly enhance the utility of Raman based technologies.
- SRM 2387, Nutrients in Peanut Butter, has certified values for total fat, selected fatty acids, selected minerals, and tocopherols. Information values are provided for mycotoxins. This SRM falls into Sector 3 in the AOAC food triangle, where no previous SRMs were available. With the completion of SRMs 1946 and 2387, we have now provided SRMs for all nine sectors of this triangle.
- SRM 2670a, Toxic Elements in Urine, which was completed with the cooperation of CDC and the Mayo Clinic, provides Certified or Reference Values for 23 elements at one or two levels of concentration. The concentrations of some of the elements are among the lowest ever certified by NIST in a clinical material; for example, Thorium at 5.3 ng/L \pm 1.4 ng/L. This SRM will be used by CDC as a QA tool for their ongoing measurements of human exposure to toxins via their National Health and Nutrition Examination Survey (NHANES).

Additional examples are provided in the Group Overviews and Technical Activity Reports that follow.

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 completed in January 2000. In addition, the Division's Quality Manual that summarizes and formalizes the Division's policies and approaches to addressing quality-related issues concerning the services that we provide is being updated to assure appropriate compliance with ISO/EC 17025 and ISO 34.

IV. NTRM Programs for Leveraging NIST Resources and Efforts

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.

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, 12 specialty gas companies (SGC) have worked with NIST to certify over 9000 NTRM cylinders of gas mixtures that have been used to produce more than 500,000 NIST-traceable gas standards. A recent study conducted by RTI International estimates that the “net benefits” of this NTRM program projected through 2007 will be between \$50M and \$63M with a social rate of return of about 225%.

Operationally, in the Gas NTRM Program, a specialty gas company prepares candidate gas mixtures in batches of ten or more cylinders, analyzes these, and submits the data 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 in the analysis of 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. Eighteen NTRMs were value-assigned for three specialty gas companies during FY03. These included the first 5 mmol/mol and 10 mmol/mol nitric oxide in nitrogen NTRMs. An additional fifty-three NTRM batches for five companies were recertified this year to extend their certification period by four years. 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 where three vendors have been 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.

We had previously planned to 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 compliance with the ISO Guide to Uncertainty of Measurements (GUM). This uncertainty analysis includes incorporation of the new “Type B on Bias” method developed by the NIST Statistical Engineering Division, as well as a different treatment for transpiration correction. Improvements in packaging instituted several years ago are now paying off with longer shelf lives and larger lot sizes that have reduced the need for replacement of expired or sold out SRMs. Two years ago, over 20 SRMs in the series needed to be produced and certified over the course of a year. This year only three SRMs needed to be replaced. Emphasis has shifted to stability testing of SRMs in stock, and working with commercial standards producers to develop strong and defensible claims of traceability between their CRM products and the SRM 3100 Series. Toward that end, we have developed a method for the rigorous comparison of single element solutions standards to the SRM 3100 Series that has been accepted for publication in *Analytical Chemistry*. The paper includes, as supplemental information, a software tool to help laboratories outside NIST implement the method to establish their claim of traceability to the SRM. 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 element or compound, 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 are provided in Technical Activity Reports that follow concerning our collaborative activities with both private sector U.S. laboratories and providers of commercial reference materials and proficiency testing services as well as other National Metrology Institutes worldwide.

V. Intrinsic Standards

Intrinsic standards “based on well characterized laws of physics, fundamental constants of nature, or invariant properties of materials” (ANSI/NCSL Z540) have many uses in physical and chemical metrology. Such standards can reduce the need for (1) labor-intensive artifact standard production by National Metrology Institutes (NMIs) and (2) repeated costly laboratory measurement comparisons associated with mutual recognition agreements.

For more than three decades the Division has provided a suite of Optical Filter Standards for validating the absorbance/transmittance scale and calibrating the wavelength scale of spectrophotometers from the near infrared through the ultraviolet spectral region. Current efforts are directed to developing a more cost-effective steady-state support structure for customers. The approach is to shift the burden of support for the mature technologies to the commercial sector and intrinsic standards in order to dedicate limited Division resources to emerging

applications of near infrared and Raman technologies (to process chemistry) and fluorescence spectroscopy (to biotechnology). A paradigm is envisioned in which appropriate SRMs are not supported in perpetuity, but are produced through enough cycles to establish the material as an intrinsic standard or transfer the continued production to the private sector with an acceptable traceability strategy. A specific step in this direction is the imminent publication of internationally determined band positions of dilute acidic holmium oxide solution as an intrinsic wavelength standard. In a related development, CSTL researchers have developed an algorithm to implement holmium oxide solution wavelength calibration and a proposed extended use of the material as a universal simultaneous standard for both wavelength and absorbance.

VI. 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 an open, transparent, and comprehensive framework for obtaining reliable quantitative information on the comparability of metrological services provided by the signatory NMIs. It also provides governments and other parties with a secure technical foundation for wider agreements related to international trade, commerce, and regulatory affairs. Signatories to this MRA have some very special responsibilities:

- declaring and documenting their calibration and measurement capabilities (CMCs in Appendix C of the MRA)
- participating in relevant international comparisons to benchmark the claims made in the CMCs (MRA Appendix B)
- documenting the existence of a system for assuring the quality of the measurement services provided.

NIST has taken a leadership role in 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 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. Analytical Chemistry Division staff are leading various activities within five of the seven working groups and Chairing the Organic Analysis Working Group.

During the past five years, approximately 96 comparison studies have or are being conducted under the auspices of the CCQM. The Analytical Chemistry Division has participated in 75 of these, serving as Coordinating Laboratory in 31. Over 25 additional studies are planned to be conducted over the next two years and NIST has already committed to coordinate at least seven of these.

Analytical Chemistry Division staff have led the critical review of CMC data for Appendix C for the BIPM Database. SIM has approximately 1140 CMC entries scheduled for inclusion in the BIPM database. By the beginning of 2004, the BIPM database will include approximately 3000 CMCs for chemical measurements. About 1000 will be from NIST.

Participation in CCQM Key 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 all 32 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 three years, 16 intercomparison exercises were carried out to assess the proficiency of SIM NMIs and/or their designated laboratories. Four additional exercises are planned for 2004. While SIM is focusing 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. Once self-assessed capabilities of SIM member states are at an appropriate level, as determined based on performance in the SIM capability assessment studies, they can also request permission to participate in CCQM Comparisons.

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 between the U.S. and Canada in the certification of a several certified reference materials important for trade and environmental decision-making. 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.

VII. 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 about 25 projects with 11 federal and state government agencies. The most prominent of these other agencies programs, based on level of funding, are described below:

- National Institutes of Health/Food and Drug Administration – In 2002 a collaborative effort was begun with the Office of Dietary Supplements (ODS) within the National Institutes of Health (NIH) and the Food and Drug Administration (FDA) to develop SRMs for use in validating analytical methods for chemical characterization of dietary supplements. This program is a multi-year effort (six years minimum) designed to provide SRMs for 8-10 selected dietary supplement materials such as ephedra, ginkgo biloba, St. Johns wort, saw palmetto, and green tea. NIH-ODS and FDA have identified high-priority dietary supplement materials for which SRMs will be developed, and NIST will prepare the reference materials and certify the concentrations of the active and/or marker compounds as well as contaminants in plant material, commercial extract, and finished product SRMs.
- National Oceanic and Atmospheric Administration (NOAA) – The Division has had a long history of involvement with NOAA related to environmental specimen banking and quality assurance activities. For example, we have coordinated quality assurance programs for organic and trace metal contaminants in the marine sediments and tissue for more than ten years. In FY03, a new quality assurance project was initiated to focus on the development of methods and protocols for the determination of contaminants in marine mammal blood.

Because of our past involvement with NOAA in quality assurance activities, we have been asked to provide quality assurance for measurements being used to assess the efficacy of remediation efforts in the Hudson River area of New York State and the Montrose Chemical damage assessment project in Southern California. In the Hudson River project, polychlorinated biphenyl (PCBs) are being monitored in fish, mink, river otter liver, and sediment. DDT and its metabolites are being monitored in the Montrose Chemical Damage Assessment Project as a result of extensive input of DDT into the ocean in Southern California.

- Department of Justice through NIST Office of Law Enforcement Standards (OLES) – In FY03 we had several projects supported by OLES including the development of forensic SRMs (ethanol in water, arson test mixture, and drugs of abuse in serum), and the evaluation of drug spray reagent test kits. In late FY03 OLES requested assistance from the Division in the physical and chemical testing of pepper spray canisters. This effort will continue in FY04.

In a totally separate activity for the National Institute of Justice, the Division's Microfluidics Team is designing an automated miniaturized DNA analysis system based

on microfluidic technology that will be capable of simultaneously analyzing 16 individual samples for forensic applications.

- Environmental Protection Agency (EPA) – In 2000, a new program was initiated with EPA to provide quality assurance and reference materials to support measurements of organic components in air particulate matter less than 2.5 μm in diameter (PM_{2.5}). As part of this program, a third NIST QA program for contaminants was initiated, the NIST/EPA Intercomparison Program for Organic Contaminants in PM_{2.5} Air Particulate Matter. This program currently has 25 laboratories participating in two interlaboratory studies for organic constituents in air particulate matter. This program will continue through FY04. For development of an SRM for organic contaminants on PM_{2.5} we have started a collection of PM_{2.5} at a site in Baltimore MD. The goal is to collect approximately 200 g of material by late 2004 for the SRM. Because the collection and production of a PM_{2.5} SRM will require several years, an “interim reference material” has been prepared from 20g of PM_{2.5} collected at the same site in Baltimore. Characterization of the organic and toxic metal content of this material is currently in progress with measurements at NIST and as part of the intercomparison exercise described above.

The U.S. EPA has plans to publish a regulation that requires analysis of coal fired power plant emissions to determine adherence to a maximum emission rate. This regulation begins to go into effect in December of 2003. EPA has funded the Division’s Gas Metrology team to develop a suite of primary standards for mercury in air to underpin measurements of mercury measurements and to facilitate “fair trading” of these emissions in the future.

- Defense Threat Reduction Agency (DTRA) – The Division and CSTL have had a long-term association (~10 years) with this agency to provide chemical consultation and peer-review of analytical methods and data to support chemical weapons treaty verification.

We also had technical interactions that involve laboratory research and measurement activities with more than 20 professional organizations, trade groups, 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 Association (CRMMA), the International Federation of Clinical Chemistry (IFCC), 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 Group Sections of this Overview.

VIII. Future Measurement and Standards Activities

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 match to customer needs. Projects in several new areas are being initiated or expanded.

In the **Forensics Standards** area, we are working with CDC to provide 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 itself would most likely not be able to handle so many samples in a short time and would need the help of the state labs in the analyses. NIST’s responsibility would be to provide Reference Materials and QA samples to assist CDC in assuring the quality of results from such tests. In addition, Division activities concerning detection of toxins in the water supply and the establishment of a mass spectral database to facilitate rapid and unambiguous identification/detection of pathogens are being expanded to address Homeland Security issues.

The primary focus of the Division’s component of CSTL’s **Food Safety and Nutrition Program** is being shifted from populating the AOAC Food Triangle with food-matrix reference materials (to address nutritional labeling issues) to reference methods and standards to address consumer safety and truth-in-labeling issues associated with Nutraceuticals/Herbal Supplements. More than 50% of the U.S. population uses dietary supplements, accounting for roughly \$10 billion in sales every year. A variety of botanical-containing products are marketed as dietary supplements; common examples include St. John’s wort, ephedra, and ginkgo. Taxonomically authentic botanical reference materials with assigned values for active and/or marker compounds are needed for quality assurance of analytical measurements associated with the manufacturing process and for the verification of manufacturers’ label claims for the dietary supplement industry. Assigned values for contaminants and adulterants are also necessary to address public health and safety concerns. Priorities for activities in this new project area are being set in consultation with the U.S. Food and Drug Administration, and the National Institutes of Health’s Office of Dietary Supplements.

Our research project on **Microfluidic Devices**, methods, and applications for chemical analysis including studies of materials and material properties affecting the flow of liquids in microchannels will begin to focus more on the use of microchannel and other electrophoretic methods for forensic and toxicological applications and standards. Research in our new Competence area, **Single Molecule Measurements and Manipulations** will be expanded. Additional details concerning the latter two research activities are provided in the Group Sections of this Overview that follow.

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 (IVD). 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. Excluding home diagnostics, the overall world-wide *in vitro* diagnostic market is approximately \$20 billion. The total IVD market in Europe was about \$5.6 billion in 1998 and has shown growth of about 4% per year over the past five years (data from www.edma-ivd.be). Approximately 60% of the IVD products currently on the European market are imported from the US. One of these EU

requirements is that IVD products must 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. To facilitate the identification of “higher order” reference methods and reference materials that are currently available, the Joint Committee on Traceability in Laboratory Medicine (JCTLM) was created at a meeting held at the International Bureau of Weights and Measures (BIPM) in early June 2002.

NIST is leading the activities of JCTLM Working Group-I, charged with establishing the process for identifying the “higher order” Certified Reference Materials and reference measurement procedures that will be required for IVD industry compliance with the EU IVD Directive. Three meetings were held this year to review nominations for more than 80 Reference Methods and 435 Reference Materials for Electrolytes, Enzymes, Drugs, and Metabolites and Substrates Coagulation Factors, Non-Peptide Hormones, Nucleic Acids, and Proteins. The higher order standards endorsed by this process will be published in a database maintained by the International Bureau of Weights and Measures (BIPM) and will be publicly available on the BIPM website in February 2004 with links to the NIST CSTL and other relevant websites.

NIST has also 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 as well as several therapeutic drugs and drugs of abuse. Over the next two years, reference methods and/or new reference materials will be developed for:

- **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*)
- **Triiodothyronine and Thyroxine** (*thyroid function*)
- **Total and Speciated Selenium** (*to support clinical monitoring in the relatively narrow range of beneficial effect*)

While focusing increased attention on the health-care/clinical diagnostics area over the next 3-5 years, we will still provide renewals of existing SRMs that support measurements in areas critical to the global community and address critical measurements and standards needs in new high priority areas such as:

- **Biotech Foods** (*reference methods and materials for detecting genetic modification of whole grains using transgenic proteins as markers in collaboration with the CSTL Biotechnology Division — that will be developing reference methods and materials for direct detection of DNA modifications*)
- **Detection of Chemical Agents in Body Fluids** *to support CDC's Chemical Counter Terrorism Network*
- **Fluorescence Intensity Standards** *for calibration of microarray scanning instrumentation in collaboration with CSTL Biotechnology Division*
- **Gunpowder Composition** *to support NIST Office of Law Enforcement Standards programs for validating forensic methods used to identify gunpowder residues*
- **Low Sulfur and Mercury Coal** *to support lower EPA emissions regulations for sulfur and mercury*
- **Near Infrared Transflectance/Reflectance** *for calibration of single- and double-pass transmission instruments finding increasing use in sensing applications for both wavenumber and wavelength*
- **Botanical Dietary Supplements** *in collaboration with FDA and NIH to address consumer safety and truth-in-labeling issues*
- **Raman Intensity Correction SRMs** *in response to priorities established by ASTM E13.08 Raman Spectroscopy Subcommittee for a suite of standards for providing relative Raman intensity corrections for Raman spectrometers at the commercially important excitation wavelengths. SRM 2241 at 785 nm has been completed. SRMs for excitation at 532 nm, 488 nm/514 nm, and 1064 nm remain.*

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 Division 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. The Overview and Reports 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.

IX. Group Overviews

Spectrochemical Methods

Research activities in spectrochemical methods 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.

A significant portion of the Group's research and measurement activities help maintain the Nation's healthcare measurement infrastructure by developing and maintaining reference methods and materials for electrolytes and toxic metals in clinical matrices. After several years in the making, NIST has issued SRM 2670a, Toxic Elements in Freeze Dried Urine, a much improved replacement SRM that includes vials at both normal and elevated levels. In contrast to the original SRM 2670, which was certified for only two non-electrolyte metals at the normal level and seven at the elevated level, the new SRM is certified for 10 non-electrolyte metals at both the normal and elevated levels, including concentrations as low as 5 pg/mL. The new SRM also includes reference values for an additional eight elements. This SRM was developed in collaboration with the Centers for Disease Control and Prevention and the Mayo Clinic, and will serve as an important quality assurance tool for CDC population surveys of toxic element exposure.

Metal speciation will be a major research activity within the Group for the next several years, with a variety of healthcare and environmental projects planned. At the request of CDC, we have developed a NIST reference method to determine the inorganic fraction of mercury in blood, which when coupled with the measurement of total mercury serves as an indirect measure of highly toxic organic mercury. The method does not require chromatographic separation but rather is based on the selective reduction of the inorganic mercury fraction to mercury "cold vapor," which can be swept into an ICP mass spectrometer for selective matrix free detection. Detailed studies revealed several critical issues in achieving accurate selectivity between organic and inorganic components. Accuracy of the method is further enhanced by using isotope dilution for quantitation. The method was used to determine inorganic mercury in SRM 966, a frozen whole blood, and a certified value based on this measurement will now be added to the Certificate of Analysis for this SRM. Continued speciation research will be greatly enhanced by the installation this year of two new LC-ICPMS systems to allow sensitive metal specific detection of separated species. The new instruments are located in both our Gaithersburg and Charleston facilities. Planned projects include studies of arsenic, chromium, iron, tin, mercury and selenium speciation systems. We are also in the process of developing an interface for a GC-ICPMS system.

In the area of homeland security we have completed and implemented the development of an isotope dilution GC-MS method for the determination of cyanide in blood. This project was undertaken to enable the development of quality assurance and measurement proficiency standards for the Chemical Counter-Terrorism Laboratory Network developed by CDC to provide rapid measurement support in the event of a terrorist chemical attack. This new method has been adopted by CDC, and an interagency agreement between NIST and CDC has been put in place to value assign and test the stability of commercially prepared proficiency testing samples of frozen human blood spiked with cyanide at various concentrations.

Two years ago researchers within the Group achieved a breakthrough in the area of high-accuracy measurement of mercury at both trace and elevated levels with the development of an isotope dilution cold vapor ICPMS methodology. This work was recognized with the R&D Magazine award for being one of 100 notable innovations in 2001. After seeing the announcement of this award, NIST was contacted by the Department of Energy to help provide data that could affect impending regulation of mercury concentrations in crude oil at U.S. petroleum refineries. As it turns out, information regarding typical concentrations of mercury in crude oil is scant, and the levels are low enough that the accuracy of existing measurements can be considered questionable. As a means of assessing the typical concentrations of crude petroleum streams which find their way into U.S. refineries, we were asked to undertake a study of mercury concentrations in samples selected from the U.S. Strategic Petroleum Reserve. Thus far nearly 100 samples have been studied, and the results indicate that levels are an order-of-magnitude or more lower than estimates based on older measurements. This new information is likely to impact decisions regarding the need for regulation of mercury in crude oil. The Department of Energy is planning to continue and expand this project in FY04.

The Group maintains strong ties within many U.S. industrial sectors through its active participation in various committees of ASTM and ISO. Contacts and interactions developed through these activities help guide decisions regarding the development of new SRMs and the renewal of existing SRMs. Listed below are brief summaries of several SRM certification projects that took place in FY03 to provide national standards to underpin important measurements in aerospace, automotive, agriculture, food packaging, steel, cement, construction, and mining industries. Most of these certifications projects will be finalized in FY04 when NIST measurement data will be combined with data to be supplied by industry group laboratories to generate the final certified values and uncertainties.

- Suite of Six Aluminum Alloy SRMs. (SRM 853a, SRM 854a, SRM 1240c, SRM 1241c, SRM 1255b, SRM 1256b). A total of 15 elements were determined in these SRMs using Glow Discharge Optical Emission Spectrometry for the first time for NIST certification measurements. These SRMs are benchmark materials for several important aluminum alloys: 3004 (SRMs 853a and 1240c), 5182 (SRMs 854a and 1241c), 356 (SRM 1255b, and 380 (SRM 1256b). All of these alloys have varied infrastructural uses and are represented in automobile manufacture, for instance, from body parts to engine components. The aluminum industry has sophisticated in-house reference materials programs to supply their plants and customers with well-characterized materials for product quality control and business transactions. These SRMs serve as the benchmarks to underpin industry reference materials.

- SRM 173c, Titanium Alloy. This alloy is one of a small list of high value, high production Ti alloys that are important products of the US and world titanium industry.
- SRM 1d, Limestone. Argillaceous limestone is a basic commodity that is used in the production of steel (roughly 50 kg is added per 1000 kg of steel). The chemistry of the added limestone is an important factor in the quality of the steel production. Limestone also finds important uses in agriculture and building materials, and the renewal of this SRM was strongly advocated by several industrial sectors via ASTM.
- SRM 2696, Silica Fume. Silica fume imparts resistance to corrosion and adds strength to concrete; it has an estimated billion-dollar impact on our national infrastructure. Once an expensive waste byproduct of silicon and ferrosilicon production, it also has an environmental impact. Every ton used in concrete reduces the greenhouse gas output of the cement industry which releases CO₂ during cement manufacture. A number of national standard specifications for silica fume are being implemented in the United States, Canada, Europe, Japan and Australia. The silica fume SRM will be used by the construction industry, silica fume producers and over 60 state and federal agencies (mostly state highway administrations) to verify specifications of silica fume before it is admixed into concrete. Demand for this SRM is driven by its unique physical and chemical properties as well as its economic impact. Quantitative XRF analyses were completed at NIST using a matrix-independent methodology developed a few years ago.
- Crystalline Silica on Filter SRMs. A series of SRMs undertaken at the request and with funding provided by NIOSH and OSHA to provide a basis for the comparability of results from various laboratories to monitor mine safety conditions.

The group has a small but potentially important research effort to utilize our High Performance ICP-OES capabilities to determine the stoichiometry of crystalline materials with high accuracy and precision. Aluminum gallium arsenide (AlGaAs), used in optoelectronic applications, was studied in a collaboration with EEL. In collaboration with the Surface and Microanalytical Research Division we have also studied SiGe, a material that is being applied in wireless communication and computer applications. In the latter project, the major effort was the development of an accurate means of dissolving the sample for ICP-OES analysis.

Throughout the world spectrochemical instrumentation is calibrated using elemental solution standards that most laboratories purchase from commercial suppliers. In most, if not all, cases these commercial standards assert traceability to NIST, which translates to traceability to the SRM 3100 Series of 69 single-element solution standards certified for the mass fraction of the element in solution. This SRM series therefore plays a key role in the overall calibration infrastructure for elemental analysis, and these SRMs directly affect the results of millions of analyses performed around the world. The ability to maintain this large and critical suite of SRMs certified and in stock has been a challenge for many years, and a key element in making this task feasible is the shelf life of the SRM. For the past two years the main activity in the maintenance of this SRM series has revolved around testing the stability of the existing SRM stock, looking to extend certification periods rather than discarding and replacing stock. New

data on the transpiration of water through the walls of the plastic containers used for many of the SRMs collected over the past three years indicates that the rate of transpiration is negligible when the containers are sealed in aluminized mylar pouches, as they have been for several years. Since transpiration results in a change of the element mass fraction, this new evidence of the lack of transpiration has allowed us to extend the certification period.

The Group's activities at the Hollings Marine Laboratory in Charleston, SC have expanded with the addition of new staff. Activities are centered around providing a quality assurance infrastructure for marine environmental monitoring projects, often in collaboration with state and other federal government agencies. As part of our collaboration in the Seabird Tissue Archival Monitoring Project with the U.S. Fish and Wildlife Service, the Alaska Maritime National Wildlife Refuge, and USGS we have analyzed a set of 27 sea bird eggs collected in Alaska for mercury concentration using our high accuracy isotope dilution method. Another activity is the Dolphin Health Assessment Project in collaboration with the National Marine Fisheries Service, the Mote Marine Laboratory, and the Chicago Zoo, for which we have developed blood sampling protocols for trace element determinations and are working to develop accurate high throughput methods for the determination of trace elements in marine animal blood. The second round of the NIST National Marine Analytical Quality Assurance Program for trace metal analysis has begun with the preparation, value assignment, and distribution of new whale liver homogenate QC materials to 31 participating laboratories.

Many of the above Group activities have been benchmarked against the measurement capabilities of other national metrology institutes through our participation in the Inorganic Analysis Working Group of CCQM. Our capability to perform clinical measurements of electrolytes at the highest metrological level was nicely demonstrated through Key Comparison K-14 for the measurement of calcium in un-modified frozen human serum. NIST results were excellent, with the NIST value virtually identical to the reference value. More industrially oriented measurements were tested through a pilot study (P-34) on the determination of constituent elements in aluminum alloy. We are presently piloting the Key Comparison K-35 on the measurement of low sulfur in diesel fuel that is being run concurrently with a pilot study (P26.1) on the measurement of very low (~10 ppm) sulfur in kerosene. Both of these studies are designed to demonstrate NMI measurement capabilities needed to meet current and near-future regulatory limits on low sulfur concentrations in fuels. The regulatory push to lower sulfur concentrations is needed in order to enable extremely efficient and long-lived after-treatment emission technologies, primarily catalytic converters. The need for these after-treatment systems is being nationally and internationally mandated by regulatory actions seeking to reduce the level of nitrogen oxides and non-methane organic gases, which are the primary emission pollutants from internal combustion engines. We are also developing a pilot study that will compare the primary elemental solution standards of participating NMIs.

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 nuclear analytical methods 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 methods are generally nondestructive and do not require sample dissolution, thus providing an independent assay. NDP and focused beam PGAA provide unique capabilities at NIST for location sensitive analysis and elemental mapping.

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. During the last several years, we have been attempting to demonstrate that instrumental neutron activation analysis meets the CCQM definition of a primary ratio method of measurement. Our first step was to characterize all sources of uncertainty for INAA measurements and develop the tools to establish a complete uncertainty statement in terms of SI units. We next applied INAA as a primary method for certification of the arsenic content of SRM 2134, Arsenic Implant in Silicon. The INAA results used for this certification included 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 certifying SRM 2134, 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. Methods developed in this work, in parallel with ion chamber measurements in the Physics Division, have also been applied to the accurate redetermination of other crucial half-lives. Half-life measurements of ^{24}Na , ^{42}K , and ^{198}Au have been completed, validating the consensus values that had been put in question by a 1994 publication. As a result of our work, the process for evaluating published nuclear data have become more robust.

In our continuing effort to demonstrate the metrological capabilities of the nuclear analytical methods, we have determined the concentration of Cr in a ferrous metal, SRM 1152a, and provided a complete uncertainty evaluation, as a test of our capabilities in a difficult matrix. Analysis of a metal 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, which provides a good test of our analytical values. Measurements were conducted using crystalline chromium metal as a comparator standard, and were validated with weighed aliquots of SRM 3112a solution dried on filter paper pellets. The INAA results agree with the certified value within the stated uncertainty of this SRM ($\leq 0.2\%$ relative), and the complete assessment of the uncertainty budget indicates a relative expanded

uncertainty of 0.2%. This work is now being expanded to a participation in the CCQM P-25 pilot study for the determination of Cr, Mn, Ni, and Mo in low-alloy steel.

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 small 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. Based on the evaluation of three sediment materials that previously have shown the potential for a high degree of homogeneity at very small sample sizes, we have processed a portion of sediment from the Baltimore Harbor, previously certified for "normal" sample sizes (SRM 2702) to develop SRM 2703, Sediment for Microanalytical Techniques. We have achieved a finely powdered sample with a median particle size of 3.5 μm with no particles exceeding 20 μm in diameter. The excellent homogeneity that had been expected from this processing has been confirmed with INAA determinations of minor and trace elements in 0.8 mg samples. We have observed relative standard deviations of 0.9% for Al and 1.8% for V, for example, in 22 samples of this material. Compositional results are nearing completion for all critical elements by NIST and collaborating laboratories using small sample techniques. The certification should be completed by the end of December 2003.

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). The radiochemical method for phosphorus has been critically evaluated, and shown to have the necessary sensitivity, chemical specificity, matrix independence, and precision to certify phosphorus at ion implantation levels in silicon. This year, RNAA has been used for the first time as a primary method to certify the ion implanted phosphorus dose in SRM 2133, Phosphorus Implant in Silicon. This material has been a continuing high-priority need of the semiconductor industry for many years, and is intended for use as a calibrant for secondary ion mass spectrometry (SIMS). This work was done in collaboration with the Surface and Microanalysis Science Division.

Often radiochemical separation is the most effective way of optimizing NAA determinations because it yields lowest detection limits and lowest uncertainty. A new RNAA method has been developed for low-level determination of Si in biological materials, which is based upon the $^{30}\text{Si}(n,g)^{31}\text{Si}$ nuclear reaction with thermal neutrons. The radiochemical separation consists of an alkaline-oxidative decomposition followed by distillation of SiF_4 . Nuclear interferences,

namely that of the $^{31}\text{P}(n,p)^{31}\text{Si}$ with fast neutrons, have been examined and found negligible only when irradiation is carried out in an extremely well-thermalized neutron spectrum, such as available at the NIST reactor. The RNAA procedure yields excellent radiochemical purity of the separated fractions, which allows the measurement of the β^- activity of the ^{31}Si by liquid scintillation counting. It was concluded that with the employment of the inherent quality properties of NAA the challenging task of accurate low-level determination of Si in biological materials can be resolved. Interference-free detection limits achieved were 150 mg g⁻¹ for irradiation of 200-mg samples in the NIST reactor RT-4 channel for 30 minutes, and 0.5 mg g⁻¹ for irradiation of 500-mg samples in the RT-5 channel for 10 h. Initial values have been established for SRM 1549 and SRM 1577b. This work will have significant impact. It demonstrated that the use of this RNAA procedure, for samples irradiated at the NIST reactor, can provide detection limits for Si in biological materials that are fit for value assignment of Si in benchmark SRMs.

In order to quantify amounts of arsenic typically found in body fluids that contain sodium, phosphorous, and bromine, INAA detections limits must be reduced by about one order of magnitude. The potential of improving arsenic detection limits for biological samples was investigated using two approaches. The first approach involved the use of a dissolution procedure to volatilize bromine. This simple volatilization procedure did not yield sufficient improvement to detect levels of arsenic present in fractions of biological fluids. The second approach involved use of electronics capable of processing high count-rates without degraded resolution so that counting could be started earlier in the decay. Use of a more sophisticated detection system was successful but requires longer counting times, thereby limiting throughput. Future research will involve investigating the use of more aggressive digestion procedures, using ion-exchange separations, liquid extractions, or a combination of these.

During FY03, work on the new thermal neutron PGAA instrument was completed. This instrument was built at the Center for Neutron Research to replace the original PGAA instrument that was built in the late 1970's. A new external beam tube, sample chamber, beam stop, and support structure were built and a new detection system installed. The new beam tube is made of two cylindrical aluminum sections lined with a lithiated polymer. The sample chamber was also fabricated from aluminum and lined with lithiated polymer, and may be evacuated to minimize the number of neutrons scattered and absorbed by air. The detection system shield consists of lead surrounded by borated and lithiated polyethylene, placed on a table attached to the support structure. The new, more compact beam stop is welded to the support structure. The improved detection system, positioned closer to the sample, increased element sensitivity by 5% to 50%. This new instrument provides better detection limits, and much lower background radiation and is easier and safer to assemble for use.

Delayed Neutron Activation Analysis (DNAA) is being established at NIST for the measurement of small quantities of fissionable nuclides such as ^{235}U and ^{239}Pu . DNAA is rapid, specific, matrix independent, nondestructive, and sensitive. The system being built at NIST is calculated to have a detection limit for either of these species about 10 picograms, based on a straightforward extrapolation from published practice. After testing uranium standards in two shielding configurations, a final detection system has been designed. This consists of ten neutron detectors in a 30 x 30 cm cylindrical moderator of polyethylene, lined with 2 cm of lead to

absorb gamma radiation. The design incorporates the existing pneumatic rabbit assembly for irradiation control. The system is able to move the sample rapidly to the neutron detector through a polyethylene flight tube. The analysis time is less than 2 minutes per sample. On completion and verification, the Nation will have a readily accessible, rapid means of measuring traces of fissionable U and Pu in samples of forensic interest. In addition, the specificity and sensitivity of this method of analysis will be put to use in certifying trace uranium in Standard Reference Materials.

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, neutron incoherent scattering, volumetry and gravimetry have been used together to certify a hydrogen mass fraction of 114 ± 5 mg/kg. Two additional Hydrogen in Titanium SRMs have been prepared at bracketing levels, and are in the final stages of certification. This method has also been used to prepare standards for neutron-tomographic nondestructive analysis of turbine blades at McClellan Air Force Base.

Transmutation of silicon by nuclear reactions has become well established for the production of high-power rectifiers and other electronic devices. In this application, phosphorus is created by the capture of neutrons by ^{31}Si to make ^{32}Si , which decays to ^{32}P . The same process as used for elemental silicon is applicable to 1:1 compound semiconductors. Recently, neutron transmutation doping (NTD) has been explored in two additional systems. In collaboration with North Texas State University and the NIST Center for Neutron Research, samples of $\text{Hg}_{0.8}\text{Cd}_{0.2}\text{Te}$ films on $\text{Cd}_{0.95}\text{Zn}_{0.05}\text{Te}$ substrates have been subjected to neutron irradiation. The goal is to transmute both Hg to Au and Te to As. A first experiment using neutron fluences of $1\text{--}2 \times 10^{16} \text{ cm}^{-2}$ showed that transmutation is feasible. To study the effects of irradiation quantitatively, additional samples have been exposed to a pure thermal neutron flux for fluences from 3×10^{16} to $1.3 \times 10^{17} \text{ cm}^{-2}$; these specimens are now under study at NTSU. Gallium nitride is of great current interest for high-temperature devices, and is the subject of a large national research project coordinated by DARPA. The opportunity exists for uniform doping of this material, by transmuting both ^{69}Ga and ^{71}Ge to the corresponding Ge isotopes. In collaboration with IEEL, a sample of bulk GaN was obtained from ATMI, Inc. and irradiated with $1.0 \times 10^{18} \text{ neutrons/cm}^2$, for a calculated uniform doping of $2.5 \times 10^{16} \text{ atoms Ge/g Ga}$, or $1.3 \times 10^{17} \text{ atoms Ge/cm}^3$. This material is has been returned to ATMI for characterization.

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 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 recent examples, we have collaborated with Corning Laboratories on analyses of several high technology materials. One measurement was of nitrogen concentrations measured in GaN/GaAs bilayers. 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. However, there are processing issues in the introduction of N at high levels without causing phase separation. An important need towards that goal is a reliable, accurate method for N concentration as a function of depth in GaAs-based alloys. Two other types of samples with Corning have been analyzed: (1) Boron profiles are measured in glasses to determine B loss due to its volatilization during manufacturing. Surface depletion of B is a key characteristic of borosilicate materials for both chemical vapor deposition and conventional melting processes; and (2) lithium niobate where a quantitative measure of Li concentration was able to differentiate congruent and stoichiometric compositions and any surface depletion in commercial wafers.

We have also measured the nitrogen concentration of MnN/ScN in conjunction with scientists from the NCNR and Ohio University. MnN is a metallic anti-ferromagnetic material that can be used with ferromagnetic semiconductors to make spintronic devices for data storage systems. The magnetic transition point of thin films made with this material is different from that of the bulk material. To measure this transition, which occurs at an elevated temperature, annealing is required. However, the annealing process is suspected of causing the nitrogen to escape, which in turn changes the transition temperature. Using NDP, we have determined that the original films were indeed nitrogen-deficient. Subsequent films were then made with a ScN layer and were again measured with NDP. These measurements show that this problem has been corrected. A joint publication on this work is in preparation. The total film thickness was determined (330 nm) and the total nitrogen concentration to a precision of better than 1% relative.

Members of the Nuclear Methods Group have also worked on a number of high priority PGAA projects with more than 20 “outside clients” as part of our responsibility for supporting the NIST Center for Neutron Research “National Users’ Facility. Many of our current PGAA collaborations involve determining hydrogen in a wide variety of materials for different applications. PGAA has been used for elemental analysis of cattails, which are being used as biomonitors of environmental conditions in Florida. C, N, P, and H were measured in the plant tissues in order to monitor the levels of various nutrients. PGAA has also been used to measure hydrogen in potential hydrogen storage materials (carbon nanotubes and ZrBe₂H_x), and to screen a variety of other materials (nanocrystalline iron, MgB₂, DxCoO₂, BaTiO₃, and

[(CD₃)₂SO]CuCl₂) for hydrogen prior to their characterization by neutron scattering techniques. PGAA has also been used to measure native boron in silicon as part of a CCQM study. Boron mass fractions near 50 ng/g were measured.

In collaboration with scientists at Johns Hopkins University, PGAA was used to perform an efficiency calibration of a gamma-ray detector that will be used on an upcoming NASA mission to map the composition of the crust of the planet Mercury. The detector will measure gamma rays emitted by elements in the planet's crust upon capture of cosmic ray induced neutrons. Efficiency was calibrated as a function of energy up to 9 MeV using prompt gamma rays emitted from NaCl and chromium targets, along with gamma rays emitted by calibrated radioisotope sources mounted in the same configuration. The results will allow the spacecraft to obtain an accurate compositional map.

We are also collaborating with Jefferson Laboratory to monitor the hydrogen content of niobium that is used in the construction of the accelerator for the Spallation Neutron Source at Oak Ridge National Laboratory. The presence of interstitial hydrogen in niobium is believed to have a detrimental effect on its mechanical and superconducting properties. It is suspected that chemical polishing (acid treatment) used to remove surface defects from the niobium introduces hydrogen, while vacuum heating may be used to remove it. We have used prompt gamma-ray activation analysis (PGAA) and neutron incoherent scattering to study the effects of these two processes on the hydrogen content of the niobium. The measurements indicated that both processes can significantly alter the metal's hydrogen content. The results of these and future studies should lead to significant improvement in the methods for manufacturing and processing the high purity niobium used in these cavities.

PGAA with a focused beam has been used to determine the spatial distribution of chlorine in high-purity quartz for an industrial customer. Chlorine is a key element in the removal of OH whose presence is detrimental to optical applications that transmit light in the 1.3 to 1.5 μm wavelength range. Focused beam PGAA has the advantage over bulk INAA and PGAA measurements in that it provides spatial information, and has been employed as a calibration technique for micro-XRF measurements of test samples.

Organic Analytical Methods

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 separation science-based methods. These methods are applied to the development and/or provision of reference methods, SRMs, and other quality assurance program in the clinical, food and nutritional, environmental, forensic, and homeland security areas.

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 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.

Recent investigations of alkyl bonded phases for LC involved the synthesis of a series of consecutive length alkyl phases ranging from C13 through C18, with three different bonding chemistries (monomeric, polymeric, and self-assembled monolayer) at each phase length. The phases were characterized in terms of methylene selectivity, shape selectivity, and band broadening. It has been concluded that the performance of stationary phases in LC is influenced in different ways by the bonding chemistry, surface coverage, and alkyl chain length of the sorbent. No significant chromatographic differences were found to result from the synthetic routes, except that the different bonding chemistries provide a different range of bonding densities. The approach used in bonded phase synthesis limits the density of the alkyl chains that can be achieved. For bonding densities ranging from 2 mmol/m² to 8 mmol/m², a linear increase in methylene selectivity was observed with increasing bonding density. In general, retention behavior towards nonpolar solutes was most strongly influenced by the density of the alkyl chains at the silica surface. Dramatic changes in shape selectivity were observed, however, as a function of temperature for alkyl phases that differ by only one carbon in length.

The conformational structure of alkyl stationary phases has been investigated by infrared and Raman spectroscopy. Stretching and bending vibrational modes in normal alkanes have been correlated with specific alkyl conformational states. In a collaborative research effort with Klaus Müller (Universität Stuttgart, Germany), infrared spectra of alkyl stationary phases have been acquired for a series of C22 phases prepared on silica, alumina, titania, and zirconia substrates. Liquid crystalline-like ordering of the alkyl chains were observed for densely loaded stationary phases. A complementary study utilizing Raman spectroscopy was carried out in collaboration with Jeanne Pemberton (University of Arizona). Consistent results were obtained with the two approaches, which indicate that alkyl stationary phases represent highly ordered states of matter.

The conformational structure of stationary phases has also been studied by computational chemistry. Models of alkyl modified surfaces (containing up to 8000 atoms) have been simulated for a broad range of conditions and stationary phase types. Monomeric and polymeric surface modification approaches have been modeled with surface coverages of 1.6 mmol/m² to 6 mmol/m². Models have also been constructed to correspond to actual materials prepared in previous studies. The influence of temperature on conformational structure has been carefully evaluated. Trends for these computational studies are consistent with experimental observations: (1) alkyl chain order increases with increased surface coverage; (2) monomeric and polymeric phases with similar loadings give rise to similar degrees of alkyl chain order (although subtle differences exist); (3) the portion of the alkyl chain closest to the substrate surface is disordered (primarily gauche conformations) and the opposite end is most ordered (trans conformations); (4) longer chain length phases (e.g., C30 chains) exhibit significantly more order than C18 phases; and (5) alkyl chain ordering is significantly enhanced at lower temperature.

These varied approaches to the study of alkyl stationary phases (synthesis, chromatographic characterization, spectroscopic characterization, and simulations) are providing a consistent and detailed picture of the molecular structure of covalently modified surfaces. It is anticipated that insight gained from this work will facilitate the development of improved materials with cross-cutting application to the fields of separation science, material science, and biotechnology.

During the past year, research in chiral separations focused primarily on the use of capillary electrophoresis (CE) for enantioselective separations. A detailed investigation of the applicability of CE for quantitative measurements was performed in conjunction with efforts to develop ephedra-based SRMs. Three CE methods were developed for the separation of ephedrine and pseudoephedrine enantiomers. Determination of the enantiomeric composition of these two compounds is of interest because only (-)-ephedrine and (+)-pseudoephedrine occur naturally in ephedra plants. Each of the three methods provided slightly different selectivity, and each method was used to quantify ephedrine and pseudoephedrine enantiomers in ephedra plant material, plant extracts, and dietary supplements. The CE results compared favorably with those from LC and LC-MS analyses of the same samples.

Results of our research efforts in separation science have been applied to development of improved methodology for the determination of nitro-substituted polycyclic aromatic hydrocarbons (nitro-PAHs) and high molecular weight PAHs in environmental matrices. For the nitro-PAHs a normal-phase LC isolation of the nitro-PAHs was implemented 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 25 mononitro-PAHs and three 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). Improved separation of PAHs isomers of MW 302 has resulted from the use of a 50% phenyl methylpolysiloxane phase instead of the common 5% phenyl phase. GC/MS analysis of several environmental matrix SRMs (air and diesel particulate matter, two sediments, and coal tar) provided identification and reference values for 23 MW 302 isomers. Both the nitro-PAH and the MW 302 PAH studies resulted in the most extensive characterization of these groups of compounds in any environmental matrix and have provided reference values for these SRMs.

Recent research activities in organic mass spectrometry have focused on the development and critical evaluation of new approaches to the quantitative determination of biomolecules (e.g., proteins) in biological matrices. The recent acquisition of a LC with tandem mass spectrometry (LC/MS/MS) system and a matrix assisted laser desorption time-of-flight mass spectrometer (MALDI-TOF), has significantly increased our capabilities for the determination of trace-level analytes of health, nutritional, forensic, and environmental importance, as well as for structural studies of natural products. The MALDI-TOF has greatly enhanced our capabilities for structural characterization of biomolecules.

A new generation of health status markers shows great promise from the clinical diagnostic perspective, but offers new and more difficult challenges for standardization. Many of the new markers are proteins, peptides, or other large biomolecules and are usually present at very low

concentrations. Most are thermally labile, very polar, and heterogeneous, both in conformation and in other molecules attached or otherwise associated with them. With a vast potential market for tests for these new markers, many different approaches are being developed in a short time frame and these approaches often provide different “answers.” These differences can lead to erroneous diagnoses and/or the need for retesting – both very costly. Recent efforts have been directed toward the development and critical evaluation of reference methods for troponin I (a new marker of myocardial infarction), triiodothyronine (thyroid function), cortisol (a marker for endocrine function), speciated iron (Anemia and Hemochromatosis), homocysteine and C-reactive protein (risk factors for myocardial infarction), folic acid (an essential nutrient that reduces the risks of heart disease and neural tube defects), and prostate specific antigen (PSA) for prostate cancer.

The LC/MS/MS method for T3 along with an LC/MS/MS method for tetraiodothyronine (T4) were used in an international comparison with good agreement with laboratories in Europe. The LC/MS/MS method for cortisol has been thoroughly tested and it provides unrivaled precision and specificity for this low-level hormone. Because of the extensive use of the LC/MS/MS in the development of these methods, we have purchased a second instrument that will be available in the coming year. Certification will begin in FY 04 for a human serum-based SRM for homocysteine and folates, and development will begin for an SRM for T3, cortisol, and several other important hormones.

A proteomics approach using LC and MS is being investigated for the determination of C-reactive protein (CRP). Peptides liberated from this protein using a tryptic digest can be isolated and measured by LC/MS with use of an isotope labeled peptide as an internal standard. The research to date has found that the tryptic digest is far from quantitative for breaking down the CRP. Research in collaboration with scientists at LGC in the UK and PTB in Germany is ongoing to address this problem.

The Analytical Chemistry Division has been involved in environmental specimen banking and marine analytical quality assurance programs for over two decades; these activities are collaborative efforts supported by both NIST resources and by funding for the other federal agency partners (see below for Other Agency Activities). We currently maintain the National Biomonitoring Specimen Bank (NBSB) at two locations, the NIST Gaithersburg campus and the Hollings Marine Laboratory (HML) in Charleston, SC. The NBSB is a cryogenic environmental specimen bank that resulted from the pilot Environmental Specimen Bank Program, which was established in 1979 with support from EPA, to develop collection and banking protocols for human liver specimens and to cryogenically store these specimens for retrospective contaminant analysis. Since 1982, the specimen bank has grown in number and types of specimens (e.g., sediments, fish tissues, mussels, oysters, human diet samples, marine mammal tissues, and seabird eggs) collected as part of several monitoring and research programs. The National Oceanic and Atmospheric Administration (NOAA), Minerals Management Service (MMS), and the U.S. Geological Survey (USGS) have been major consistent supporters since the mid-1980's. A major expansion in environmental specimen banking occurred in 1995 with an agreement between NOAA and NIST to establish an environmental specimen bank in Charleston, SC, specifically designed for marine specimens. ACD currently has seven permanent staff members, two post-doctoral fellows, as well as several students working in the HML on specimen banking,

development of analytical protocols, and marine quality assurance activities. Presently the primary specimen banking activities involve tissues collected from marine mammals throughout the U.S., including Alaska, and seabird eggs collected from seabird colonies in Alaska. There are presently 2,182 marine mammal tissue specimens banked in the NBSB, representing 784 individual animals and 35 species, and 321 seabird eggs from 3 species. These banked specimens represent a resource that has the potential for addressing future issues of marine environmental quality and ecosystem changes through retrospective analyses. In 2002, NIST began the development of collection and storage protocols for marine mammal serum, plasma and whole blood as part of a blood banking program for NOAA's Marine Mammal Health and Stranding Response Program, and in the last quarter of 2003 began the banking of eggs and feathers for USFWS' peregrine falcon monitoring plans. As part of the specimen banking and marine QA activities, analytical methods are developed and implemented for the measurement of organic contaminants in marine mammal tissues (including blood) and seabird eggs. Specimen bank samples are regularly analyzed for both organic (PCBs and pesticides) and inorganic contaminants. These analyses also include compounds of more recent concern, such as toxaphene, polybrominated diphenyl ethers (PBDE), and polychlorinated naphthalenes (PCNs).

During the past year, significant efforts were expended toward the development of high priority SRMs in several important CSTL Program areas:

- Healthcare/Clinical Diagnostics

SRM 2921 Troponin I. After evaluating of six different candidate reference materials using two round robin studies, a single reference material has been selected. More than 20 different commercial cTnI assays, made by 12 different manufacturers, from the US, Europe, and Japan, were used to evaluate the candidate materials. This choice was made after evaluation of the troponin preparation for purity, stability, its ability to provide harmonization of assay results, and the commutability of the material among the 20 commercial cTnI assays used in the study. A solution of this cTnI has been prepared and the concentration of cTnI determined using two independent methods, one involving LC-UV measurement of the intact protein and the other involving measurement of certain amino acids in the sequence of this protein. The material will be completed in late 2003.

SRM for homocysteine (Hcy) and tetrahydrofolic acid (Fol) in human serum. Hcy is implicated as a risk factor for heart disease and other diseases associated with oxidative damage. Fol is an important vitamin that is known to reduce the risk of neural tube defects but is also thought to reduce Hcy levels. This SRM will consist of three levels, one having high Hcy with low Fol, one with normal levels of each, and one with high Fol and low Hcy. Certification will be completed in FY 04.

SRM 965a Glucose in Frozen Human Serum and SRM 1951b Lipids in Fresh-frozen Human Serum. The renewal of these two important clinical SRMs is in progress and will be completed in late 2003.

- Environmental Monitoring

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 24 PAHs, 29 PCB congeners, and seven chlorinated pesticides. Reference values are also provided for 60 additional PAHs, PCBs, 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), 15 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. Results from multiple analytical methods were combined to provide certified values for 22 PAHs, 31 PCB congeners, and seven chlorinated pesticides. Reference values were also provided for 30 additional PAHs, PCBs, chlorinated pesticides, methylmercury, total mercury, and selected trace elements.

SRM 1650b Diesel Particulate Matter. SRM 1650b is a renewal of the popular SRM 1650 which was first issued in 1985. When issued in early 2004, SRM 1650b will have values assigned for over 40 PAHs and nitro-PAHs.

SRM 2260a PAHs in Toluene and SRM 1491a Methyl-PAHs in Toluene: SRMs 1491a and 2260a are redesigned renewals of two organic solution SRMs first issued in the late 1980s with values for 22 PAHs at two different concentrations levels. The new SRM 2260a will contain 35 PAHs and SRM 1491a will contain 17 methyl-substituted PAHs, both in toluene. Because of the expanded number of constituents, these two SRMs will now be much more useful to analysts measuring PAHs and methyl-PAHs.

- Instrument Calibration Standards (SRMs 3061-3086).

A suite of 26 organic calibration solution SRMs has been completed to support the recently externalized Water Performance Evaluation (PE) Studies Program orchestrated by the US Environmental Protection Agency (U.S. EPA). 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, endothal, chlorinated herbicides, toxaphene, chlordane, and adipate/phthalates in methanol; organochlorine pesticides in acetone; and glyphosate and diquat dibromide in water.

- Food Safety and Nutrition

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 25 fatty acids, including several omega-3 fatty acids.

SRM 2387 Peanut Butter. SRM 2387 was issued with values assigned for nutrients, allergens, aflatoxins, and amino acids.

SRM 2385 Slurried Spinach. SRM 2385 was completed with certified and reference values for proximates (solids, fat, protein, carbohydrate), nine elements, and four vitamins and carotenoids. With the completion of SRM 2385 Slurried Spinach and SRM 2387 Peanut Butter, NIST now has SRMs/RMs in all nine of the sectors of the AOAC Fat-Protein-Carbohydrate triangle which is used to describe food matrices.

SRMs 3240-3244 Ephedra-related Dietary Supplements. As part of the multi-year NIST/NIH/FDA collaboration to develop SRMs for use in validating analytical methods for dietary supplements, we are nearing completion of a suite of ephedra-related SRMs consisting of ground plant material, two extracts, and two finished products (powdered oral dosage form and protein powder). Measurements of the ephedra alkaloids using LC-UV, LC/MS, LC/MS/MS, and CE-UV have been completed. Values will also be assigned for toxic metals (Hg, As, Cd, and Pb).

- Forensics

Drugs of Abuse in Hair SRMs. Two new SRMs for drugs of abuse in hair were developed to replace the previous RMs: SRM 2379 Cocaine, Benzoyllecgonine, Cocaethylene, Amphetamine, Methamphetamine, and PCP in Hair and SRM 2380 Codeine, Morphine, Monoacetylmorphine, and THC in Hair. Both of these SRMs were value assigned using GC/MS and newly developed LC/MS methods.

SRM 1828b Ethanol in Water. SRM 1828b Ethanol in Water is intended for blood- and breath-alcohol testing, and it will replace SRM 1828a (currently four levels) with a set of nine solutions that will cover the concentration ranges of importance to both the blood and breath alcohol testing. The development of this expanded SRM 1828 was supported in part by the Department of Justice through the NIST Office of Law Enforcement Standards (OLES).

SRM 2285 Arson Test Mixture. The development of SRM 2285 was supported in part by the Department of Justice through the NIST Office of Law Enforcement Standards (OLES) and consists of a mixture of even carbon number straight chain hydrocarbons, toluene, p-xylene, o- and m-ethyltoluenes, and 1,2,4-trimethylbenzene in dichloromethane. This SRM is intended for use in the calibration of instrumentation to determine accelerants in arson investigations.

Gas Metrology and Classical Methods Group Overview

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

During the past year, nine gas mixture standards, six conductivity solution standards, two pH materials, and a Sodium Oxalate Reductometric standard were completed. In addition, we recertified 139 gas mixture standards for various clients. We also worked with three Specialty gas Companies in development of 18 batches of NTRMs. The over 400 individual gas cylinders

that comprised these 18 NTRM batches will be used to produce approximately 40,000 NIST-traceable gas standards for end-users.

In the area of electrolytic conductivity, we continued our investigations of new standards packaging technology. The packaging used in the past was not suitable for storage of conductivity solutions for more than one year. Each conductivity solution standard has to be remade every year and uncertainties can not be lowered below 1%. For the past two years all conductivity solutions greater than 500 $\mu\text{S}/\text{cm}$ have been packaged in 50 ml glass ampoules. In sealed ampoules the transpiration problem, which has plagued us in the past, is solved and the solutions have multiyear self-lives. The leaching problem is minimal since the solutions have high ion concentrations already. This reduces the reissue rate for these high conductivity standards and allows us to devote more time to the development of low conductivity standards being requested by the pharmaceutical industry to address new water purity specifications. However there is no simple solution for the low conductivity standards. Leaching from glass is the limiting problem and will require some exotic containers to solve. Until this issue is resolved, electrolytic conductivity standards will continue to increase in price, and perhaps outstrip the ability of our customers to pay. We benchmarked our capabilities for the preparation and delivery of electrolytic conductivity standards with that of other National Metrology Institutes through participation in an international comparison carried out under the auspices of the CCQM Electrochemistry Working Group (CCQM-P47), the results, to be published in early 2004.

In the area of pH 2003 was very busy for SRM certifications; however it was very quiet for International Comparisons. There were no international comparisons completed in 2003. However significant progress was made in our comparability with other NMIs. In the past a very small bias has been evident, along with a larger uncertainty, when compared with other NMIs. Research in FY03 yielded significant improvements in the Type A uncertainty ("scatter"), associated with measurement replication, of the NIST pH SRMs. These pH SRMs provide the primary benchmarks to establish the traceability of pH measurements. The decreased uncertainty results from the elimination of transient mixed potential phenomena within the Ag|AgCl electrodes, used in the primary measurement, after they are transferred from the storage solution (0.01 mol kg⁻¹ HCl) to the pH SRM buffer being certified. The mixed potential decays to a negligible level if the electrodes are stored in the given buffer solution for at least 12 h prior to performing the primary measurement. A corresponding pre-equilibration step was incorporated into the NIST procedure for primary pH measurements. This new protocol yielded a 3-fold improvement for the carbonate buffer (pH 10). Smaller improvements were noted for the phthalate buffer (pH 4). Typical Type A uncertainties with the new protocol are less than 0.0005 pH for each buffer with overnight equilibration. This uncertainty now equals or exceeds that of other NMIs that currently perform similar measurements. A model, based on modern mixed-potential theory, was developed and tested to explain the observed transient potentials at these Ag|AgCl electrodes.

Two years ago, we made the difficult decision to shut down our future production of anion solution standards. This decision was not easily nor hastily made, and we realize that there are many clients that have come to rely on these SRMs. However, we are not abandoning our responsibility or our customers in this area. We will maintain the capability of making world-class measurements in this area and there is currently a 1+ years supply for all of the six

individual SRMs in this series. Many of the anion SRMs could be easily prepared directly by customers using available pure chemical SRMs. We will be evaluating whether a NIST published procedure will assist customers in preparing these solutions. In addition, in a recent CCQM study several NMIs demonstrated capabilities for making and value-assigning anion solution standards that are comparable to NIST. We plan to establish strategic partnerships with one or two of them whereby they would provide anion solution CRMs to U.S. customers and we would make any measurements required to assure U.S. quality and traceability requirements.

We have continued the development of a quantitative database of infrared spectra for calibration of IR-based technology used for real-time monitoring for airborne chemical contaminants along plant boundaries and within plant facilities. The spectra are being prepared using NIST primary gas standards. These standards have been critically evaluated at NIST and compared internationally. The use of SRD-79 to establish traceability of open-path IR measurements is required in the update of EPA method TO-16. SRD-79 currently has data for 40 compounds. During the upcoming year, we plan to increase the number of compounds available and to place all the data on the internet for free access by all.

Improved analytical tools for real-time measurement of trace-level vapors in the atmosphere are critical for evaluation of new technologies for reduction of hazardous industrial emissions. Towards this end, fourier-transform microwave (FTMW) spectroscopy is being investigated as a means for quantitative real-time measurements. Briefly, FTMW spectroscopy combines the high spectral resolution of microwave spectroscopy and the high sensitivity of molecular beam and cavity-enhanced methods creating a technique that can provide unambiguous identification of vapor phase analytes that possess permanent electric dipole moments. The principal goal of the present program is to critically evaluate the technique's potential as a sensitive, reliable, and robust tool for quantitative measurements of trace gases. Current work has focused on improving the sensitivity of the detection system and characterizing the effects of species such as water and carbon dioxide present in the sample gas.

The concentration of ozone (O₃) in the atmosphere remains a significant issue from both scientific and political perspectives. At tropospheric levels, O₃ is a health concern and contributes to global climate change as a greenhouse gas, while stratospheric O₃ protects earth from harmful UV radiation. Since 1983, NIST has provided Standard Reference Photometers (SRPs) based on UV photometry to ten U.S. Environmental Protection Agency (EPA) facilities to provide an infrastructure for the calibration and traceability of ozone measurements within the U.S. More recently, the international interest has prompted sixteen foreign laboratories to acquire SRPs. Current efforts focus on further anchoring the SRP through international comparisons, comparisons with NIST's primary nitric oxide (NO) gravimetric standards and a nitrogen dioxide (NO₂) permeation tube system, and the development of an advanced primary reference standard. Additionally, NIST and BIPM have been collaborating to transfer the responsibility of international O₃ measurement traceability to the BIPM.

In continued support of our collaboration with the BIPM on ozone, James Norris completed training of BIPM staff in construction and maintenance of the Standard Reference Photometer (SRP). Philippe Moussay, a BIPM technician responsible to the SRPs at the BIPM worked at NIST for ten weeks to construct SRPs 31 and 32. After Philippe returned to Paris, James Norris

traveled to the BIPM and worked in their laboratory for eight weeks to complete the training of Philippe and other staff members, and oversee the construction of SRP 33. James Norris also completed a comparison of SRP 2 to the BIPM SRPs as part of CCQM-P28, the pilot study on ozone comparability. This completes our present interactions with the BIPM on transferring the infrastructure for international ozone traceability. The BIPM now has five SRPs to anchor their program, and have had sufficient training to build and maintain SRPs. Collaborations on the CCQM pilot study and on the advanced ozone instrument will continue.

The NIST SRP network continues to expand. Many more countries have requested NIST SRPs for establishing traceability for their atmospheric ozone measurements. New SRPs have been constructed and delivered to the BIPM (3) in France, Taiwan Environment Protection Administration, Kaohsiung, Taiwan R.O.C., and Hong Kong S.A.R. Environment Protection Department Air Services Group.

We also continue to support U.S. industry through development and dissemination of high priority reference materials based on input from organizations such as the American Industry Government Emissions Research (AIGER) consortium and ASTM. Stakeholders in the AIGER group are working together to facilitate the automobile industry meeting more stringent 2003 Federal Tier II and California LEV II emission regulations. AIGER members include the U.S. EPA, California Air Resources Board (CARB), General Motors, Ford, and Daimler-Chrysler. In 1998, NIST worked with a Specialty Gas contractor to blend two cylinders each of low NO standards at concentrations of 0.5 $\mu\text{mol/mol}$, 0.75 $\mu\text{mol/mol}$, 0.95 $\mu\text{mol/mol}$, 1.05 $\mu\text{mol/mol}$ and 1.25 $\mu\text{mol/mol}$. The ten new standards were prepared employing a newly developed cylinder pretreatment, a NIST SRM 2629a as the parent NO source and a diluent balance gas of specially gettered nitrogen ($\text{O}_2 < 2 \text{ nmol/mol}$). The new standards have been analyzed periodically against NIST dynamic permeation standards and have exhibited excellent NO concentration stability for more than four years. In 2001, AIGER provided direct funding to NIST's contractor to expedite the development of two new NO SRMs at the lower concentrations of 0.5 $\mu\text{mol/mol}$ and 1.0 $\mu\text{mol/mol}$. NIST and its contractor used the same pretreatment etcetera to blend forty cylinders of 0.5 $\mu\text{mol/mol}$ and forty cylinders of 1.0 $\mu\text{mol/mol}$ NO in nitrogen candidate SRM mixtures. The ownership of 27 candidate cylinders of each new SRM (54 total) was transferred from AIGER to NIST; who is certifying twenty-five (25) stable cylinders of NIST SRM 2737 (0.5 $\mu\text{mol/mol}$) and twenty-five (25) stable cylinders of NIST SRM 2738 (1.0 $\mu\text{mol/mol}$), to be completed by January, 2004. Additionally, thirteen cylinders of each concentration were recently analyzed by NIST and returned to AIGER members for their interim use – until the new SRMs become available in March, 2004.

One way to meet the increasing needs of industry for standards at much lower concentrations is through dynamic dilution technology. Over the past two years we have collaborated with the United Kingdom's National Physical Laboratory (NPL) on the critical evaluation of a binary network dilution device that they patented in 2001. This dilutor consists of six mass flow controllers (MFC) arraigned in series. Each MFC, or bit, is adjusted to deliver precisely twice the flow of the preceding MFC. Thus calibration consists of matching flows precisely, and does not rely on absolute flow calibration. The binary network behaves like a binary number, and dilution is easily adjusted through switching the MFCs between the dilution gas and the standard gas. We have been working to further develop this concept into a "primary" dilutor. Work using

Mol Bloc flow measurement technology and new state of the art mass flow controllers, shows great promise for reducing the uncertainty in the composition of gas mixtures delivered

We participated in three gas mixture comparison studies during FY03. We were a participant in a CCQM key comparison on Natural Gas composition. Our results were in good agreement with those from other NMIs considerable experience in gas metrology. NIST also participated in CCQM-P41 pilot study on global warming gases. In this study participants prepared primary standards containing atmospheric levels of methane and carbon dioxide, and sent the standards to the pilot laboratory in the Netherlands. In a second part of that study, the pilot laboratory sent a cylinder to each participant for analysis. NIST demonstrated excellent agreement for both methane and carbon dioxide. The general conclusion was that for carbon dioxide, most NMIS agreed to well within 0.1%, and for methane the agreement was within 0.5%. The main conclusion was that most NMIs need to do a better job at purity analysis for trace levels of methane.

Other activities in international comparison of gas standards included; (1) NIST piloted a pilot study on automobile emission gas measurements within SIM. The comparison included relevant concentrations of carbon dioxide, carbon monoxide, nitric oxide, and propane. The comparison is in progress at the time of this report, and results are no expected until early 2004. (2) NIST continued with the bilateral comparison program with the Netherlands Measurement Institute (NMI). Gases compared this last year included, sulfur dioxide, hydrogen sulfide, nitric oxide, and nitrogen dioxide. Generally, all comparisons with NMI have shown agreement to within 0.5% or better. The lone exception has been hydrogen sulfide, where a 2% agreement has been demonstrated. (3) NIST will be piloting a SIM study on industrial emission in FY2004. The comparison will be on emission levels of sulfur dioxide. (4) NIST has committed to piloting two CCQM comparisons, one on high and low concentration oxygen in nitrogen, and the second on 10 ppm hydrogen sulfide. Preparation for these comparisons will start in FY2004.

During the past year, we have had discussions with EPA on traceability of mercury measurements from coal fired power plants. EPA is publishing a regulation, which requires analysis of coal fired power plant emission for mercury emission, and adherence to a maximum emission rate. This regulation begins to go into effect in December of 2003. To meet this deadline, EPA funded the Gas Metrology team to establish a traceability link for mercury gas standards. This work started in March 2003, with the deadline of December 2003 for traceable gas standards. Although NIST will not be able to establish the ultimate traceability protocols by December 2003, NIST will be able to deliver to EPA gas standards, which have been highly characterized by NIST, with a provisional certified value. Of course NIST will continue to work with EPA past the December 2003 date to better establish traceability and to evaluate the stability of the gas standards. EPA will also be funding NIST to work on HgCl in FY2004, with a goal of establishing traceability for HgCL standards. The ultimate traceable artifact may or may not be gas cylinder standards. For HgCL, it most likely will be a dynamic generation system, which will have traceable linkages to flow, mass, temperature, and pressure. This program will be one of the high priority items for the coming year.

Molecular Spectrometry and Microfluidic Methods

The Molecular Spectrometry and Microfluidic Methods 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, of Raman intensity correction standards, and of fluorescence wavelength and intensity standards; 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 FY03, 42 sets of solid absorbance filter SRMs were certified, and 176 optical filter sets were recertified. Continuing measurements were made on a number of other filter sets. The certificates were completed for SRM 2036 (UV-Vis-NIR transfection wavelength standard), and SRM 2242 (Relative Intensity Standard for Raman Spectroscopy with 532 nm Excitation). Certificate measurements were made on SRM 2243 (Relative Intensity Standard for Raman Spectroscopy with 488 nm and 514 nm Excitation), but revealed that the material (a uranium glass) under went a small, but reversible amount of photobleaching. We will try making the artifact in a slightly different glass matrix to see if this cures the problem; however, this will set back the anticipated completion of this SRM by several months and will adversely impact the timely development and certification of the remaining artifacts in the series (for 1064 nm excitation and 633 nm excitation).

Software renovations intended for the upgrading of the original high accuracy reference spectrometer (HAS-I) were made instead directly to the HAS-II instrument. Since these were not vetted as originally intended on the HAS-I, there has been some impact on the availability of the HAS-II for production work. The new upgrades mostly work, but we are still suffering from some work-arounds and tracking down some software bugs.

The SpectroML project for the optical filters program was completed. Data may now be automatically converted from the HAS-II, PerkinElmer 900, and Hewlett Packard 8453 spectrometers to SpectroML and directly imported into the optical filters database with. Several new features have been added to the optical filters database to improve our tracking of filter and customer information. This will make it easier to respond to both customer requests and to queries from our AO.

Work continued on the development of an extended set of visible filters (0.1%, 0.3%, and 70% transmittance) to enlarge the range of transmittances covered and to make the range of our visible filter offerings more compatible with those of other NMIs (e.g., NPL) and to meet requests by CORM, our NTRM vendors, and others for broadening the range of our standards. Testing of the instrumentation and methods for certifying these filters is complete, and certification measurements have been completed on half of the production batch, with the final

measurements on the remainder to be complete early in FY04. The major task remaining to complete this SRM is the estimation of the Type B uncertainties and the drafting of the certificate. Both are expected to be complete in the first quarter of FY04.

The Optical Filters NTRM Program continues to hang on with two vendors. It is likely that both will drop out of the program prior to the next round of NVLAP assessments. The economic model for this program is not sufficiently positive to sustain the program.

The report for the SIM intercomparison of holmium oxide solutions for UV/Visible wavelength standards was completed. We have proposed that the spectrum of holmium oxide may be useful as an “intrinsic” standard – a standard whose purity can be assessed inherently and whose wavelength “peak” values at given spectral slit widths can be certified independently and published as standard reference data. Therefore, a given artifact, independent of source, can be accurately assessed and, if found suitable, can be utilized as a standard. To substantiate this concept, we need to assess the extent of the international agreement on the wavelength assignments for holmium oxide solutions. Accordingly, we conducted a holmium oxide wavelength intercomparison with several NMIs around the world. Although the data are still being analyzed, we are confident that this material can serve as an intrinsic UV/vis wavelength standard, allowing us to cease production of SRM 2034. However, prior to this we must publish the data and several articles to educate our customers about this intrinsic standard and its use. We had hoped to accomplish this by the end of FY03; however, this did not happen, and we will have to produce at least one additional batch of SRM 2034.

We continued our development of candidate materials for luminescence standards. We selected a uranium-based glass and a manganese-bearing glass that appear useable for fluorescence spectral emissivity standards in the green and yellow spectral regions respectively. Test samples of the materials were produced, and at the end of the FY were being cut and polished in the glass shop for final testing. The composition of the uranium glass had to be changed, as the original melt was quite viscous and entrapped small gas bubbles. A lower viscosity glass melt seemed to solve this production problem. We have developed two additional fluorescence emissivity candidate materials for the blue and violet spectral regions and continue to search for a suitable candidate in the red.

We continued to qualify fully the SPEX-JY fluorometer as a reference instrument. We determined that occluders (devices that precisely limit the height of the beam) were needed for both the excitation and emission beams. Once these were constructed and fitted into the instrument, it was possible to determine the beam area, which is necessary to relate the measured optical signal to the irradiance of the light). Last year, we utilized our PL-calibrated small integrating sphere/photodiode assembly to quantify the light from the excitation monochromator and to calibrate the internal photodiode/beamsplitter assembly that relates the fluorescence signal to the excitation output. By using a highly diffuse reflective material (Spectralon) of known reflectance in the sample position to reflect light from the excitation monochromator to the emission monochromator/detector, we can calibrate the whole system with traceability to the SI. This year we began to attach our PL-calibrated dual-integrating-sphere light source to the spectrometer to calibrate the emission monochromator/detector assembly. We can utilize either the sphere source’s radiance calibration and a mirror in the sample position or its irradiance

calibration and Spectralon in the sample position to calibrate the emission monochromator/detector assembly. This will provide an independent, SI-traceable calibration check.

The certificate for SRM 1932, Fluorescein Solution was completed, and around 300 units were delivered to SRMP, placed into stock, and made available for sale. We contributed measurements to the determination of the fluorescence intensity of SRM 1933, Fluorescein-Labeled Microbeads. This SRM developed primarily by Division 831 is used with SRM 1932 in the calibration of flow cytometers by the MESF method.

Our Smokeless Powder Reference Material proposal for was funded, and the certification of our existing material is well in hand. By improving the extraction with earlier addition of internal standard the uncertainty for CE results have gone down by a factor of three. In addition, we developed a completely new LC method to determine all four analytes. Both methods give good agreement for the four components in the powder.

Our proposal for developing a High Explosives Reference Material was funded. This allowed the purchase of an MSD detector to go with our new liquid chromatograph. The acquisition of this gear is important not only for the development of a method for certifying this reference material, but because it gives us analytical capabilities comparable to that used in the better forensic labs around the country. LC-MS methods will be better appreciated by our customers because they will be a lot more familiar than the CE methods that we have used in the past.

The Edgewood Arsenal requested that NIST develop a QA and traceability program for purity assessment of surety agents. This morphed into completion of a “reviewable draft” of a NISTIR with the working title “Approaches to the Metrologically Sound Traceable Assessment of the Chemical Purity of Organic Reference Materials.” The initial version was delivered as promised at the end of June for review by a number of ACD staff with particular expertise in various aspects of the material—to generally positive responses. A second draft suitable for broad within-ACD and selected outside-NIST review was completed.

In conjunction with Division 831, we continue to provide statistics and data representation studies for FBI, OLES, and other agencies investigating the use of DNA methods of forensic analysis. The first of a series of reports (DNA quantitation) on the Mixed Stain Study #3 was prepared and has been published. Two more are in various stages of preparation: intrinsic imbalances in the commercial STR multiplexes and types and causes of STR profiling “errors.” We have been working on a number of new and ongoing projects, including a DNA quantitative SRM, creation of a DNA repository (both physical and database) for evaluating new profiling technologies, and evaluation of a new commercial mitochondrial typing method using the repository.

This year was another banner year for our microfluidics projects. This was the final year of the Microscale Analytical Laboratory Competence and the ATP intramural grant. Our efforts at understanding microflow and tailoring microflow through chemical reactions on the surface of microchannels were finally recognized with funding from DARPA, and a former NRC Post Doctoral was hired to develop this project. Late in the year, the Microfluidics Team was

contacted by the NIJ to assist MIT in completing a DNA separation-on-a-chip device to be used for forensic determinations. This program area with collaborations in the Process Measurements Division, the Biotechnology Division, the Optical Technology Division, the Semiconductor Electronics Division, and NIH continues to attract students and NRC Post Doctorals. We acquired a multiple optical tweezers microscope device for the Single Molecule Manipulation and Measurement Competence this year.