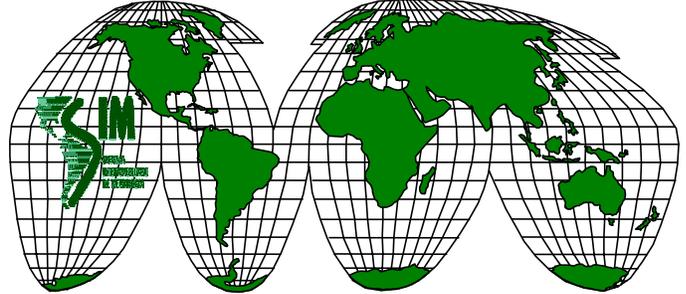


## 12. International Measurement Standards

National Metrology Institutes (NMIs) have been collaborating and carrying out international comparisons of their national measurement standards for more than one hundred years. As the NMI of the United States, NBS/NIST has represented the interests of our nation during the past century. However, the *ad hoc* recognition that resulted from these long-standing interactions is no longer considered sufficient to promote international trade and to ensure equity in trade. Virtually all aspects of our lives have become global in nature, and world-wide interdependence has never been more apparent. In this climate, it has become evident that non-tariff trade barriers rooted in measurement-related issues for standards maintained in the individual NMIs can limit international trade. Therefore, in addition to the less formal collaborations, the infrastructure for formal mechanisms to demonstrate comparability of measurements and standards has been developed by international committees.



**The EU/US Mutual Recognition Agreement** for international trade was negotiated at the highest level of national governments and requires mutual recognition of standards and conformance infrastructure. These include the capabilities of



***“The MRA ... facilitates bilateral trade between the United States and the European Community, ... and mutual recognition of conformity assessment activities as an important means of enhancing market access ...”***

calibration, verification, and test laboratories as well as those of laboratory accreditation bodies. The NMIs, NIST in the U.S., provide traceability to the SI required for these services, and thus mutual recognition of the capabilities of the NMIs is a prerequisite for the mutual recognition of metrology services in general.

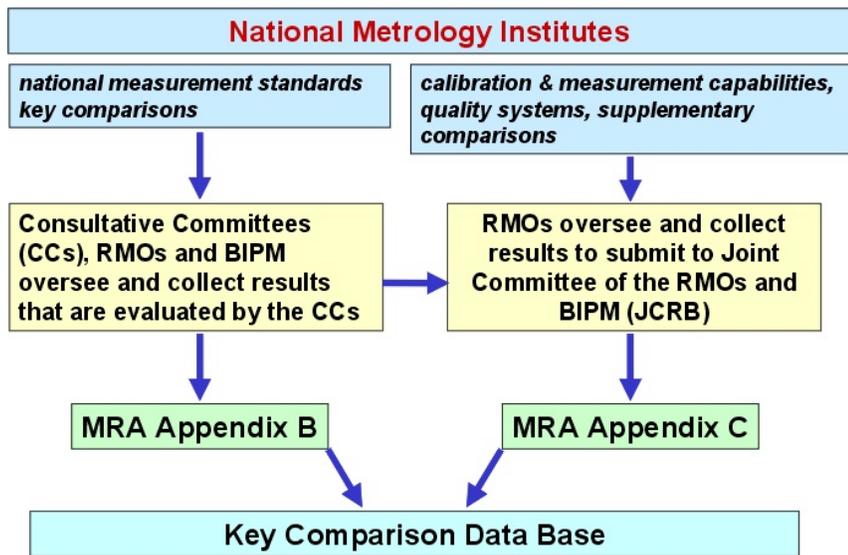


**The CIPM Mutual Recognition Arrangement (MRA)** was signed in October, 1999 by the directors of the national metrology institutes (NMIs) of thirty-eight member states of the *Metre Convention*, and representatives of two international organizations. The MRA provides the framework for “mutual recognition of national measurement standards, and of calibration and measurement certificates issued by National Metrology Institutes”.

The MRA has as its objectives: to establish the degree of equivalence of measurement standards maintained by NMIs; to provide for the mutual recognition of calibration and measurement certificates issued by NMIs; thereby, to provide governments and other parties

**Recognizing the necessity for international collaboration and agreement on metrological issues, the *Convention du Metr * was signed in Paris in 1875. The United States, while not a world power at the time, was one of the seventeen original signatory nations. The Convention remains the basis of all international agreement on units of measurement. Currently, there are fifty-one Member States, including all the major industrialized countries.**

with a secure technical foundation for wider agreements related to international trade, commerce, and regulatory affairs. Implementation of the MRA involves three aspects, these are: declaring and documenting calibration and measurement capabilities (CMCs) (MRA Appendix C), participating in relevant international comparisons to support the CMCs (MRA Appendix B), and documenting the existence of a system for assuring the quality of the measurement services provided by the NMI. Results of comparisons that underpin the claims of the CMCs are maintained in a database by the BIPM and are publicly available on the World Web Web at <http://kcdb.bipm.org/BIPM-KCDB>.



The implementation of the CIPM MRA is carried out by a Joint Committee of Regional Metrology Organizations (RMOs) and the BIPM (JCRB). The JCRB is made up of representatives from each RMO and the BIPM, and provides oversight for results included in the Key Comparisons Database (Appendix B of the MRA), as well as the determination of the degree(s) of equivalence of results from individual NMIs. The Key Comparisons Database was developed

jointly by NIST/CSTL and the BIPM and is now operated by the BIPM. The database contains results of key and supplementary comparisons, including individual values for each institute and their declared uncertainty, and for each institute its degree of equivalence, defined as the magnitude and uncertainty in the deviation from the key comparison reference value. In addition, the degrees of equivalence between the standards of each of the participating NMIs are provided. A given authority can use this database to determine if the equivalence demonstrated is sufficient for the purpose at hand.

Regional Metrology Organizations (RMOs) play an important role in the MRA. They have the responsibility for carrying out key comparisons within their regions. They also carry out supplementary comparisons and other actions to support mutual confidence in the validity of

calibration and measurement certificates through the Joint Committee of the RMOs and the BIPM (JCRB). They are also responsible for the entries into database for the calibration and measurement capabilities of their member NMIs.



<http://kcdb.bipm.org/BIPM-KCDB/>

Systema Interamericano de Metrologia (SIM) is the metrological regional organization (RMO) that includes the United States. The metrology organizations that make up SIM are known as: NORAMET (North America), CAMET (Central America), CARIMET (Caribbean), ANDIMET (Andes Region), and SURAMET (Southern America). Regional cooperation leads to a wider harmonization of measurements and standards, facilitates free flow of trade, and is a necessary first step to globalization. NIST and NRC Canada link SIM countries to the BIPM, and as such, provide greater opportunities for international trade and commerce. CSTL staff provides leadership for SIM by chairing the Chemical Metrology Working Group of SIM, and by serving as the U.S. representative to the JCRB, in order to assure the effective, fair and metrologically sound implementation of the MRA.



**Populating Appendix C of the BIPM Database:**  
 CSTL staff led the critical review of both SIM and international CMC data for Appendix C of the BIPM Database with the following results:

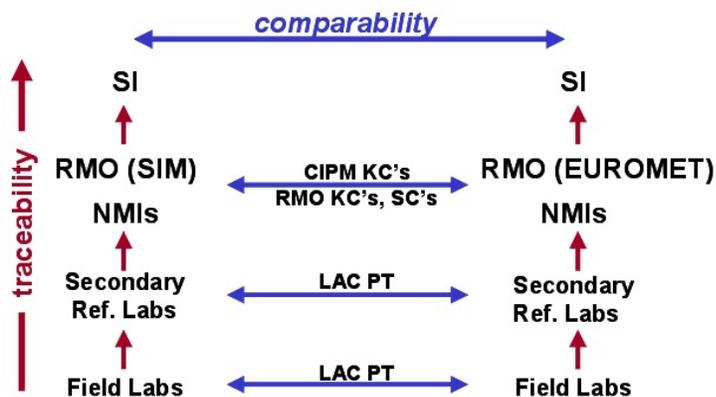
**The BIPM database currently includes:**  
 approximately 930 NIST CMCs for Chemistry  
     40 from CENAM  
     100 from NRC Canada

CSTL also has CMCs for Flow (14), Temperature and Humidity (99), Vacuum and Pressure (23)

**SIM has the most comprehensive list of CMCs in the BIPM Database, mostly from NIST.**

**Linking Vertical Systems of Traceability to Facilitate Global Comparability of Measurements**

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 the 34 countries within SIM whose capabilities in chemical metrology span a very broad range, we have initially focused the SIM program on training and capability assessment rather than participation in MRA-driven Key and Supplemental Comparisons. During the past year, six intercomparison exercises were developed to assess the proficiency of SIM NMIs and/or their designated collaborators for addressing chemical measurement problems within their regions and the Americas. An example of such a comparison follows.



The NIST **International Comparisons Database** (ICDB) was developed in CSTL and is now maintained in NIST's Technology Services. It serves the SIM Regional Metrology Organization with information from the BIPM Key Comparisons Database and other traceability issues that impact the United States and the Americas in particular.



<http://icdb.nist.gov>

**Comparison of pH of a Phosphate Buffer (SIM.8.P4)**  
**K.W. Pratt (839)**

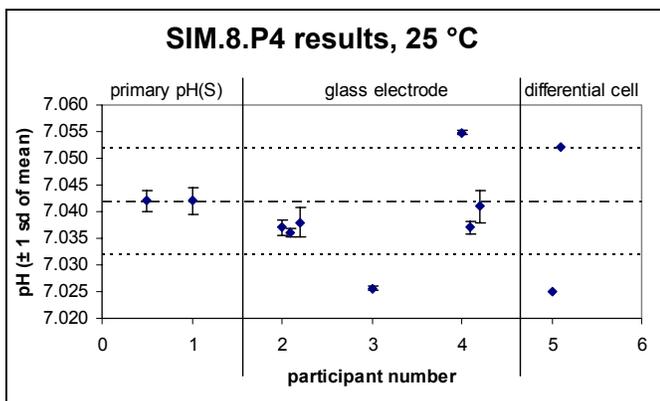
A valid comparison requires that each participant use identical calibrants and samples of buffer solution. To ensure uniformity in the calibrants, the pilot laboratory distributed samples of NIST pH Standard Reference Material (SRM) 1861f/11f to each participant. Each participant then prepared two calibrants using the two formulations of this SRM pair. The pH values of these two certified buffers bracketed the pH of the unknown buffer solution. To ensure uniformity of the unknown buffer, the pilot laboratory prepared and distributed samples of a single batch of phosphate buffer solution ("unknown buffer") to each participant.

***This comparison was designed to provide an evaluation of pH measurements with glass electrodes, as obtained with the procedures used at the participating institutions of SIM.***

**All the NMIs participating in CCQM comparisons use absolute pH cells (Harnet cells) and all agree to within 0.005 pH units. The SIM.8.P4 indicates the countries could deliver national standards through use of secondary pH devices (glass electrodes and differential cells) that are calibrated high quality NIST SRMs to 0.03 pH units.**

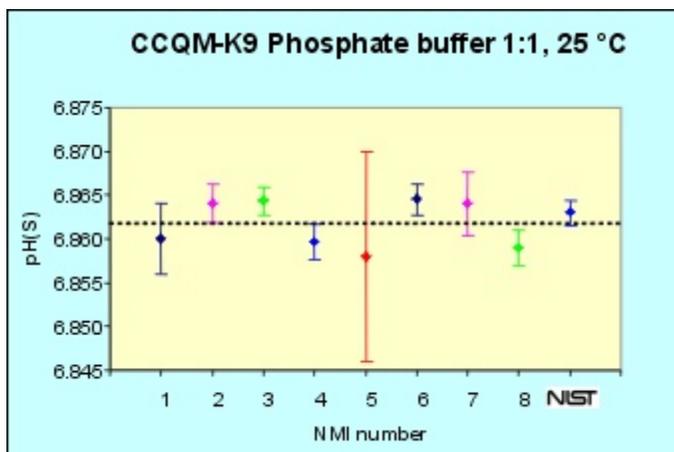
Reports were received from Argentina (INTI), Brazil (INT, IPT, and Oxiteno); Chile (INTEC); Costa Rica (ONNUM and the Universidad de San José); Mexico (CENAM, Cideteq, Productos Químicos de Monterrey); and the USA (NIST). Results were received from Jamaica (JBS) in May 2001, following distribution of the draft Summary to the remaining participants.

The SIM philosophy is to focus on training and capability assessment. However, some Regional Chemical Metrology Working Groups in Europe and the Asian Pacific are forging ahead and conducting MRA-driven Key Comparison Studies. Therefore, 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.



**Note that the SIM study was not intended to provide information regarding primary pH measurements, as is the CCQM study. However, NIST serves to facilitate integration of all SIM members into the larger global network.**

CSTL is 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.



## **Selected Examples of CSTL Activities for FY 2001**

Rooted in its rich 100 year history, CSTL continues to provide our customers services in areas such as amount of substance, flow, contact thermometry, pressure, and vacuum. These services provide the traceability required for U.S. companies to compete in the global market. NIST has increased activities in the international arena including transferring technology to other countries, to facilitate trade and accurate decision-making particularly in the areas of health and the environment.

### **Consultative Committee for the Amount of Substance (CCQM)**

***CSTL Provides Leadership for the CIPM CCQM: The CSTL Director serves as the NIST representative on the CCQM, and as chair of the Key Comparisons Working Group; Chief of the Analytical Chemistry Division serves as the chair of the Organic Analysis Working Group.***

NIST has taken a leadership role the International Committee of Weights and Measures-Consultative Committee on the Quantity of Material (CCQM).

The CCQM has formed seven working groups: (1) gas analysis, (2) organic analysis, (3) inorganic analysis, (4) electrochemistry (5) biometrology, (6) surface analysis and (7) key comparisons. These working groups are responsible for selecting and overseeing the operation of key comparisons that

address chemical measurement-related issues important for international trade, environmental, health, and safety-related decision making. CSTL's Analytical Chemistry Division is currently leading various activities within all five of the seven working groups. During FY01, we participated in 25 CCQM comparison studies; serving as Pilot Laboratory in 13. Because the field of chemical metrology is so diverse, broad and multidimensional (measurands, concentrations, matrices, etc.), it is estimated that the number of key comparisons that will be required to cover this field will certainly exceed the number of those for all of the physical metrology areas combined.

#### **CSTL Activities in FY 01 within the Framework for CCQM Key Comparisons and Pilot Studies**

<b>Health</b>	<b>Nine KCs completed or underway, NIST leads 7 of 9</b>
<b>Food</b>	<b>Seven KCs underway, NIST leads one</b>
	<b>Pesticide Residues, 7 completed or underway</b>
<b>Environment</b>	<b>Water, 1 underway</b>
	<b>Atmospheric Pollutants, 3 underway, NIST leads 2</b>
	<b>Point Source Emissions, 1 underway</b>
	<b>Primary Gas Standards, 16 underway, NIST leads 3</b>
	<b>Contaminants in soils/sediment, 6 underway, NIST leads 2</b>
<b>Advanced Materials</b>	<b>Semiconductors, one underway</b>
	<b>Metal Alloys, two underway, NIST leads one</b>
<b>Commodities</b>	<b>One underway, NIST lead</b>
<b>Forensics</b>	<b>Four underway</b>
<b>Pharmaceuticals</b>	<b>None Planned</b>
<b>Biotechnology</b>	<b>Five areas identified</b>
<b>General Analytical</b>	<b>Purity of materials, 7 underway, NIST leads 5</b>
	<b>Calibration Solutions, 4 underway, NIST leads one</b>
	<b>pH Standards, 4 underway</b>

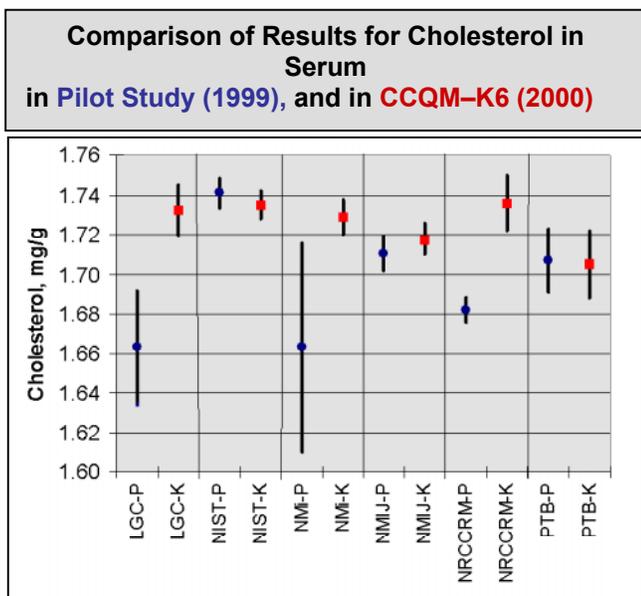
Key Comparison studies have been completed and international equivalence statements approved or drafted for: Natural Gas, Automobile Emission Gases, Acid Rain Precursors Gases, Ethanol in Air (for Breathalyzers), Volatile Organic Compounds, Cholesterol in Human Serum, pp'-DDE in Fish Oil, Elemental Standard Solutions, Lead in Drinking Water, and pH. Other completed Key Comparisons include: Glucose and Creatinine in Human Serum, Lead and

Cadmium in Sediment and pp' DDT in Fish Oil. CSTL is also participating in 14 Pilot Studies including Arsenic in Shellfish, Trace Metals in Food, PCBs and Tributyl Tin in Sediment, and LSD in Urine.

### **Key Comparison on the Determination of Cholesterol in Serum (CCQM-K6)**

**M.J. Welch, R. M. Parris, L.T. Sniegowski, and W. E. May (839)**

This Key Comparison was led by CSTL/NIST and utilized samples from two pools of human serum with significantly different concentrations of cholesterol for the participants to analyze using isotope dilution-gas chromatography/mass spectrometry. This followed a Pilot Study conducted in 1999. The results of both studies are shown in the figure to the left.



Two unfortified frozen serum materials, with concentrations unknown, except by the Pilot Laboratory, were sent on dry ice. For each material there were four vials included, one as a test sample to determine how much internal standard was needed and three vials for measurements of two aliquots per vial. Material A was a material prepared at NIST by thoroughly mixing sera from two volunteers known to have high blood cholesterol levels. Material B was SRM 965, Glucose in Frozen Human Serum. This SRM is not value assigned for cholesterol, but has a cholesterol level in the normal range for humans.

All of the laboratories followed the published ID/MS “definitive” method for serum cholesterol. This method involves adding a known mass of a cholesterol material with a stable isotope label to a known mass of serum. After equilibration, extraction, and derivatization, the sample is injected into a GC/MS, and the ratio between the native cholesterol and the isotope labeled material that was added is measured. By comparing this ratio with that of known mixtures of the same labeled cholesterol and unlabeled cholesterol of known purity (calibration material), it is possible to accurately and precisely determine the cholesterol content of the serum. This Key Comparison study demonstrated that the participating NMIs could successfully measure serum cholesterol for normal and elevated levels, using ID/MS-based methods, with interlaboratory expanded uncertainties of less than 1%. Comparison of results from the Key Comparison and the earlier pilot study demonstrated that laboratories previously inexperienced in the determination of serum cholesterol showed dramatic improvement as they gained experience and better understood potential sources of bias, such as incomplete hydrolysis.

To provide a more comprehensive measure of the capabilities of NMIs for measuring well-defined serum analytes, the CCQM also has conducted pilot studies for the determinations of serum glucose and creatinine, in addition to the cholesterol study recently completed. These two analytes were chosen because they present very different challenges than does cholesterol, thus providing a more complete picture of the

***The challenge that CCQM faces is to identify, design, and conduct a limited number of KCs to enable the assessment of measurement comparability among National Metrology Institutes across the entire chemical measurement universe. Ideally, an internationally recognized reference system should be established for all important health status markers, but that is not possible in any reasonable time frame.***

**Strategic design of KCs with broader analytical implications:**

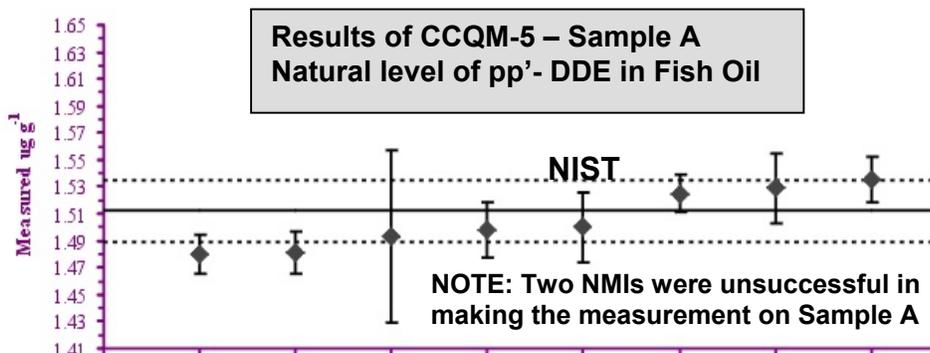
- CSTL led KC for glucose and Creatinine in Serum to complement the Cholesterol in Serum KC
- A unique set of challenges are provided
  - Glucose is highly water-soluble and also associates strongly with proteins.
  - Creatinine is very polar, and at concentrations at much lower levels than cholesterol, and requires challenging separation techniques.
- Overall performance in these three Key Comparisons is an indication of the capabilities of NMI for determination of other well-defined organic health status markers in human serum.

capabilities of participating NMIs. The CV among the results from the participating laboratories was less than 1% for glucose and less than 1.5% for the creatinine both at clinically significant levels. Key Comparisons for both of these additional measurands are underway. The combination of these three Key Comparisons may provide a basis for the evaluation of measurement capabilities of participating NMIs for other well-defined organic analytes present in serum at  $\mu\text{g/g}$  levels or higher, without having to actually conduct a Key Comparison for all such analytes.

**Key Comparison on the Determination of pp'-DDE in Fish Oil (CCQM-K5)**  
**M. M. Schantz and R.M. Parris (839)**

This compound is one of the major metabolites of the pesticide (pp'-dichlorodiphenyl) trichloroethane (pp'-DDT) and even though the use of pp'-DDT was discontinued many years ago it is extremely persistent and hence of environmental importance. There is much interest in this metabolite, particularly with reference to human fertility studies, since the metabolite is reported to be ten times more potent in its effect on male fertility than pp'-DDT. A fish oil matrix was selected for the key comparison since measurable levels of pp'-DDE are commonly found in such oils, and participants were asked to use ID/GC/MS as their method of analysis. The fish oil material used for this key comparison was a dogfish liver oil (gift from NRC, Canada) and contained a measurable concentration of pp'-DDE. An aliquot of this oil was also gravimetrically spiked with pp'-DDE. This enabled two samples to be sent to participants, Sample A (a natural level of pp'-DDE) and Sample B (a natural level plus fortification with pp'-DDE).

**A key comparison based on the determination of pp'-DDE in a fish oil matrix was lead by the LGC in the U.K., with NIST as one of the 10 participating laboratories.**

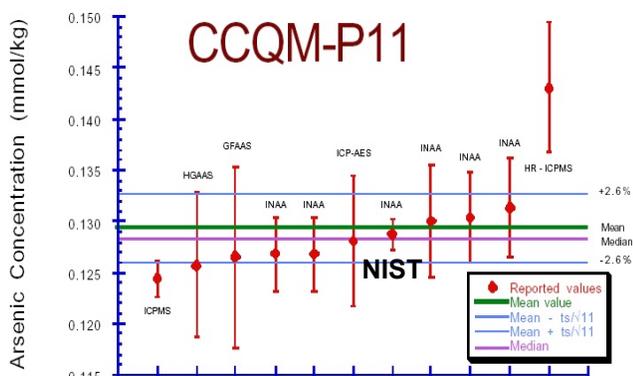


## Pilot Study on the Determination of Arsenic in Shell Fish (CCQM-P11)

R.R. Greenberg and E.A. Mackey (839)

The determination of arsenic, mononuclidic, volatile, and subject to a serious interferences with many widely-used analytical methods, served this purpose. The Oyster Tissue selected for this study was collected from several locations on the eastern coast of the United States and suitably prepared and sterilized at NIST. Eleven NMIs or their designates, participated in this study. No particular analytical method was prescribed, and variations were found among dissolution methods, as well as instrumental technique and calibration methods. Determination of natural

levels of arsenic in a complex matrix is quite challenging. Overall, the spread of data is better than expected from non-NMI or field laboratories.



**This study is one of eight studies conducted for inorganic constituents in natural samples in 2001.**

Based on the agreement among methods a decision was made to proceed with a key comparison for As in Fish.

## Strategic Bilateral Collaborations

W.E. May, F.R. Guenther, S.A. Wise, and R.R. Greenberg (839)

In addition to the global and regional activities described in this report, CSTL scientists have established a limited number of strategic bilateral collaborations and intercomparisons with NMIs around the world. For example, our collaboration with the Netherlands



Measurement Institute (NMI) for determining the equivalence of primary gas standards has resulted in a formal "Declaration of Equivalence" that is recognized by the U.S. EPA and European environmental regulatory

bodies as documenting the equivalence between seven NIST and NMI primary gas mixture suites. Our formal agreement with NRC-Canada (via the NAFTA Treaty) for cooperation in marine environmental studies has fostered collaborations in the certification of a several certified reference materials important for trade and environmental decision-making between the U.S. and Canada. We have recently signed a Cooperative Arrangement with NIMC (Japan) for collaborative efforts in the area of pure volatile organic



compound standards. These highly pure reference compounds will serve as primary references for many of our gas mixture SRMs and our quantitative reference database (SRD-79). Several additional strategic bilateral arrangements with other NMI standards laboratories are being discussed.



## Consultative Committee for Thermometry (CCT)

The participation in Key Comparisons is mandatory for a signatory National Measurement Institute (NMI) in the Mutual Recognition Arrangement (MRA) for physical measurements as well as chemical. In fact, international comparison of physical measurements dates back more than 100 years. The results of the Key Comparisons (Appendix B) are to be used to support the calibration and measurement capabilities [(CMCs), Appendix C] claims of each NMI. In turn, the validation of CMC claims is vital for international acceptance of NMI calibration services to customers and the resultant facilitation of global trade.

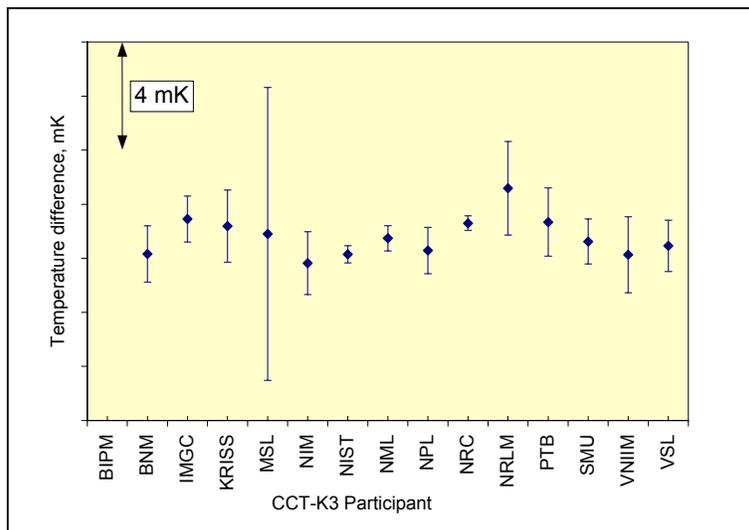
**NIST Thermometry Group is involved in four Comité Consultatif de Thermométrie (CCT) Key Comparisons in thermometry, one CCT Key Comparison in humidity, two preliminary SIM comparisons, and a bilateral comparison with NRC (Canada).**

### International Comparisons of Temperature and Humidity

**D.C. Ripple, C.W. Meyer, G.F. Strouse, W.L. Tew, C.D. Vaughn (836) and B.W. Mangum (Contractor)**

**Key comparisons establish levels equivalence of national measurement standards. KC results are maintained in the BIPM Key Comparison database. This equivalence, together with traceability within a nation to a single NMI, will promote the acceptability of measurements across national boundaries, thereby minimizing measurement-based barriers to international trade.**

Over the past year, the NIST Thermometry Group was active as the pilot of CCT-K3 (83.8 K to 933.5 K), as a participant in CCT-K2 (13.8 K to 273.16 K), and as a sub-pilot for CCT-K4 (933.5 K to 1234.9 K). Unanimous approval by the CCT was attained for the CCT-K2 Final Report and Appendix B and for the CCT-K3 Final Report. Results for CCT-K2 are now available on the BIPM Key Comparison Database (KCDB).



**Differences in the realizations of the Zn freezing point, measured in CCT Key Comparison 3.**

The CCT-K4 Report is currently a working draft and is awaiting approval by the participants before submission to the CCT. Within SIM, NIST initiated two SIM preliminary comparisons that are designed to be equivalent to CCT-K3. To verify the results of CCT-K3, a bilateral comparison was undertaken with NRC in the range 234.3156 K to 692.677 K. The measurements and a draft report for this comparison were completed. In the area of humidity, the NIST Thermometry Group led the task group that drafted a protocol for a KC of dew-point temperature.

The Thermometry Group will be focusing on the ongoing measurement phase of the SIM preliminary comparisons, and on publication of

the results of the bilateral comparison with NRC. In humidity, the NIST Thermometry Group has responsibilities as Chair of the CCT Working Group on Humidity and will participate in a CCT-K6 comparison of dew-point temperatures, which is planned to start in FY02.

## **Consultative Committee for Mass and Related Quantities (CCM)**

The purpose of the CCM is to establish the equivalence among the world's NMIs of pressure and vacuum standards for pressures between  $3 \times 10^{-6}$  Pa and 500 MPa. As with other physical and chemical measurements, international trade is, in part, based upon the equivalence of national measurement standards. Some of the largest segments of industrial measurements are in the areas of pressure and vacuum. To help alleviate technical trade barriers, the relative agreement of national pressure and vacuum measurement standards needs to be assessed, established, formally recognized, and maintained.

***NIST/CSTL participated in four CCM KCs and piloted three of them. An innovative, NIST-developed, transfer standard design was key to the success of two KCs. NIST also participated in a SIM comparison to 100 MPa, a bilateral comparison with Japan to 200 MPa, and a trilateral comparison with Japan and Egypt to 200 MPa.***

### **International Comparisons of Pressure Standards**

***D.A. Olson, R G. Driver, P.J. Abbott , J.P. Looney, A. Lee, A.P. Miiller (836 ), T. Kobata (National Metrology Institute of Japan), and A.A. Eltawil (National Institute of Standards, Egypt)***

The prevailing CCM Key Comparisons in pressure are listed in the table. Comparison CCM.P-K3 is piloted by NIST. The transfer-standard package that was developed by NIST consists of two spinning rotor gauges and three Bayard-Alpert ionization gauges NIST began circulation of the gauges in FY99. It is anticipated that participating laboratories will complete all measurements in FY02.

<b>Comparison Number</b>	<b>Pressure Range</b>	<b>Transfer Standard</b>	<b>Status</b>	<b>Pilot NMI*</b>
CCM.P-K1.a, b	0.05 -1 MPa (gauge)	Piston Gauge	Approved	PTB LNE
CCM.P-K1.c	0.08 -7 MPa (gauge)	Piston Gauge	Approved	LNE
CCM.P-K2	10 -120 kPa (absolute)	Piston Gauge	In process	NPL
CCM.P-K3	$3 \times 10^{-6}$ - $9 \times 10^{-4}$ Pa (absolute)	Spinning Rotor and Ion Gauges	In process	NIST
CCM.P-K4	1 - 1000 Pa (absolute)	Low Pressure Transducers	Draft B Complete	NIST
CCM.P-K5	1 -1000 Pa (differential)	Low Pressure Transducers	Draft B Complete	NIST
CCM.P-K6	10 -120 kPa (differential)	Piston Gauge	In process	NPL

Comparison CCM.P-K4 involved seven NMIs using two different principal techniques (liquid-column manometers vs. static expansion systems), and CCM.P-K5 involved four NMIs using two principal techniques (liquid-column manometers vs. double pressure balances).

**Participating NMIs were generally equivalent with some exceptions, and there did not appear to be any significant relative bias between the principal techniques. These two comparisons were also notable for being the first successful international comparisons in this pressure range (due to an innovative transfer standard design incorporating state-of-the-art MEMS-based sensors with traditional vacuum gauges).**

These comparisons, both piloted by NIST, encompass low to medium vacuum measurements, and are also important for accurate metering of low-speed air-flows and altimetry. Participants completed measurements in FY99, and Draft B reports were completed in late FY01. CCM.P-K4 and CCM.P-K5 have formally established the degree of equivalence between several NMIs in an industrially important pressure range.

### Other Strategic International Activities

#### Measurement and Analysis of Results Obtained on Biological Substances with Differential Scanning Calorimetry

F. P. Schwarz (831), and International Collaborators

**One of the objectives of IUPAC is “to study topics of international importance to pure and applied chemistry that need standardization or codification”.**



IUPAC

recommended procedures on the measurement and analysis of results obtained on biological substances with differential scanning calorimetry (DSC). DSC has been widely used to determine the thermodynamics of phase transitions and conformational changes in biological systems including proteins, nucleic acid sequences, and lipid assemblies.

An IUPAC Biophysical Chemistry Commission sponsored project headed NIST and PTB by F.P. Schwarz and H.-J. Hinz and consisting of a total working party of 10 scientists was formed to address the need for

recommended procedures on the measurement and analysis of results obtained on biological substances with differential scanning calorimetry (DSC). DSC

#### Collaborators:

**Hans-Jurgen Hinz (Institut für Physikalische Chemie, Germany)**  
**A. Ginsburg, R. Szczepanowski, and M. Gonzalez (NIH, USA)**  
**S. A. Potekhin (Institute of Protein Research, Russia)**  
**G. Rialdi and F. Attanasio (Istituto di Studi Chimico Fisici di Macromolecole Sintetiche e Naturali, Italy)**  
**J. M. Sanchez-Ruiz, and B. Ibarra-Molero (Facultad de Ciencias, Departamento de Quimica Fisica, Spain)**



The technique of DSC involves recording the energy necessary to establish a zero temperature difference between a substance and a reference material against either time or temperature as each specimen is subjected to an identical temperature program. Integration of the area under the heat flow curve yields the enthalpy change associated with the thermal event of interest.

This International Union of Pure and Applied Chemistry (IUPAC) report consists of recommendations for DSC measurement procedures, calibration procedures, procedures for testing the performance of the DSC instrument, analysis of the measurements, and the reporting

**Analysis of the data in terms of a two-state transition model yielded transition temperatures ranging from 329.4 K to 331.9 K and averaging 331.2 K, and transition enthalpies ranging from 377 kJ mol<sup>-1</sup> to 439 kJ mol<sup>-1</sup> and averaging 405 kJ mol<sup>-1</sup>. It is recommended that thermodynamic transition models only be applied to the analysis of the data if the model-derived transition temperatures and enthalpies are independent of the instrumental scan rate.**

of results. A test solution of (1-10) mg mL<sup>-1</sup> lysozyme in HCl-glycine buffer at pH = 2.5 is recommended to check the operating performance of differential scanning calorimeters used for biological substances. Samples of the protein solution were sent and tested successfully in six different international laboratories. The IUPAC report will help ensure international uniformity in the nomenclature, analysis, and reporting of results obtained on biological substances with differential scanning calorimetry.

## Standards for Calorimetry and Thermodynamics

D.R. Kirklin and D. G. Archer (838)

Details provided in the **Chemical and Biochemical Data** section.

## A NORAMET Evaluation of Holmium Oxide Solution Reference Materials for Wavelength Calibration in Molecular Absorption Spectrometry

J.C. Travis, D.L. Duewer, M.V. Smith, M.D. Maley, and G.W. Kramer (839)

**“UV/vis” spectrophotometers are widely used in clinical laboratories and the pharmaceutical and chemical industries. To provide accurate measurements, these instruments must be validated or calibrated – with regard to both their intensity (transmittance) and location (wavelength) axes. NIST supplies a suite of SRMs designed to help users ensure the validity of their measurements.**

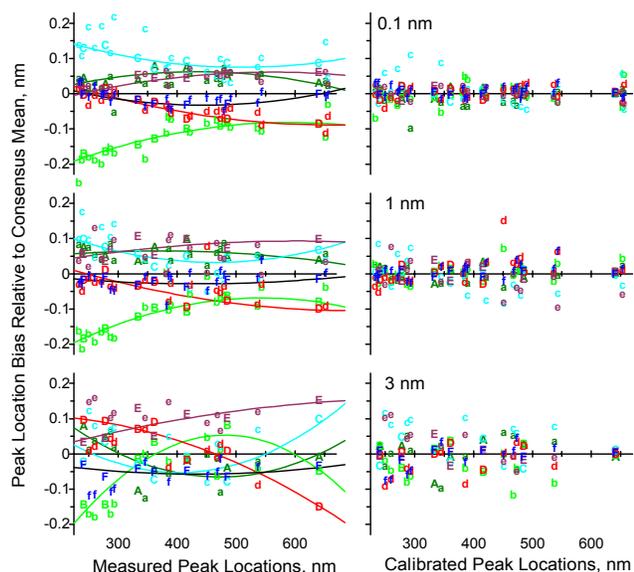
**noramet**



NIST conducted a study among five laboratories within the three NORAMET NMIs to assess the current degree of comparability of wavelength measurements for “UV/vis” spectrometry among these participants under “routine” operating conditions using commercial instrumentation and between the aqueous  $\text{Ho}_2\text{O}_3$  wavelength standard produced by NIST (SRM 2034) in the U.S. and that provided by CENAM (DMR 41) in Mexico. The study also produced  $\text{Ho}_2\text{O}_3$  solution spectral data from a variety of spectrometers for use in a NIST study of wavelength assignment algorithms and to provide a basis for a possible reassessment of the NIST-certified wavelength values.

The resulting data show a substantial level of comparability across laboratories, measurement events, CRM preparations, and peak location algorithms. At the same time, it demonstrated that the wavelength comparability of the five participating instruments actually could be improved by calibrating all of the instruments to the consensus band locations of  $\text{Ho}_2\text{O}_3$  solution. This finding supports the value of absorption-based wavelength standards for absorption spectrophotometers.

The three left-side segments of the figure display the among-set biases of the measured locations relative to the consensus mean for the 0.1 nm, 1 nm, and 3 nm spectral slit width (SSW) spectra. Biases are estimated as the location difference averaged over sets of eight spectra at each SSW. Quadratic polynomial calibration curves of the measured biases to the consensus locations are also displayed. The capital symbols denote the seven features used to define the calibrations. The three segments to the right display the bias data after adjustment to their calibration curve.



### ***International Cooperation on the Properties of Water and Aqueous Mixtures***

***D.G. Friend, A.H. Harvey, J.W. Magee, E.W. Lemmon, J.M.H. Levelt Sengers (838), and I.M. Abdulagatov (Dagestan Scientific Center of Russian Academy of Sciences)***



International standards for water properties are important, both for scientific studies involving this important substance and so that industry (especially the steam power industry) can have a “level playing field” for design and contracting. These standards are developed and promulgated through the International Association



for the Properties of Water and Steam (IAPWS). U.S. representation to IAPWS is through the Properties of Steam Subcommittee of the ASME Research and Technology Committee on Water and Steam in

Thermal Systems, which serves as the U.S. National Committee to IAPWS. NIST/CSTL participation in IAPWS activities serves to ensure that U.S. scientists and engineers have access to important international standards for properties of water and aqueous systems, and that they have a voice in developing those standards.

**In September 2001, the IAPWS annual meeting was held at NIST headquarters in Gaithersburg, Maryland. NIST research toward the goals of IAPWS includes a joint IAPWS project with scientists at the Dagestan branch of the Russian Academy of Sciences for calorimetric measurement of properties of water/methanol mixtures, and a project to produce an updated correlation for the vapor pressure of heavy water (D<sub>2</sub>O).**

### ***Methods and Standards for GMOs***

***W. E. May, K.E. Sharpless, S.J. Choquette, and D.M. Bunk (839)  
M.J. Holden, and V.L. Vilker (831)***

Currently, labeling of genetically modified products is ***not required*** in the U.S. unless the resultant product’s nutritional content or allergenicity differs from the “normal” product, therefore, FDA is currently developing ***voluntary*** guidelines for labeling. However, labeling is currently mandated in the European Union, Japan, Australia, and New Zealand, and labeling regulations in South America are pending. The GMO issue is becoming a significant barrier to trade. Market disruptions in the EU have impacted U.S. corporations attempting to do business there.

***Crops have been genetically modified to resist pests and disease, to tolerate chemical herbicides, to resist poor soil and weather conditions, or to possess improved nutritional content, food processing characteristics, ripening, texture, or flavor. Genetically modified seeds accounted for \$1.5 billion in sales in 1998, and genetically modified seeds were used to plant more than 70 million acres around the world (excluding China) approximately 50 million of these in the U.S.***

#### ***Needs Assessment:***

***NIST sponsored workshop was held in December 2001 with representation from the EU, Asia-Pacific Rim, and all five subregions within the Americas (SIM), to discuss:***

- Regulatory differences***
- Existing measurement methods***
- New methods and standards needs***
- Gap analysis***
- Plan of action***



CSTL staff responded to this pressing need by sponsoring and leading a “needs assessment” workshop. The workshop was held December 2001, and was attended by 63 public and private officials from 28 countries, including representatives from Australia, New Zealand, South Africa, Belgium, Germany, and the UK, as well as North and South America.

**Improvement of Value Assignments for NIST and IAEA Stable Isotope Reference Materials**  
**R.M. Verkouteren, D.B. Klinedinst (837), and M. Groening (IAEA)**



The intercomparison exercise was completed this year with the reporting of measurement data from Poland, Canada, and China. These data were merged with data from The Netherlands, Germany, Austria, and the United States, and were processed through a standard algorithm now available on a NIST web site. Results show significant shifts in most values and up to 3-fold improvements in uncertainties over prior exercises.

**Operational artifacts were recently discovered in isotope ratio mass spectrometers (IRMS). This prompted the International Atomic Energy Agency (IAEA) to convene a panel of experts to inspect the susceptible isotope metrology. One recommendation was a comparison exercise, led by NIST, of key isotope reference materials (RMs) designed to overcome the limitations of IRMS.**

<http://www.nist.gov/widps-co2>

**Global Impact:**

Researchers at IRMM in Belgium have realized the SI through absolute IRMS of the three NIST CO<sub>2</sub> isotope RMs. These determinations of the absolute ratios of CO<sub>2</sub> isotopomers now **give modelers of climate change more accurate information regarding the global carbon cycle.**

The NIES in Japan has used NIST RMs to value assign a CO<sub>2</sub> reference material produced especially for ocean studies. This material has an oxygen isotopic signature very close to ocean water, and will be **useful for detailed studies of ocean-atmosphere chemical exchange.**

Researchers at the Max-Planck Institute in Germany, under the European Network for Research in Global Climate Change (ENRICH, DG XII), have utilized the NIST web-based data processing system **to verify the accuracy of isotopic measurements used for extremely precise analysis of carbonaceous species in the atmosphere.**

Several international atmospheric monitoring networks and organizations (Asia-Pacific Network, CSIRO; INSTAAR/NOAA; AEROCARB; WMO) are searching for a solution to a long-standing measurement traceability problem. Biases in high-precision measurements of atmospheric CO<sub>2</sub>, including isotopic composition, exist across these networks. While the NIST isotope standards have been helpful to researchers in these networks, there are further needs to improve the commutivity of these standards and the reproducibility of the CO<sub>2</sub>-in-real air measurements. We are actively involved in international discussions to address these issues, which include the proposed GlobalHubs and BIPM/CCQM mechanisms.

**Autoradiography of Uranium Particles**

**C.J. Zeissler (837), G.P. Lamaze, and R.M. Lindstrom (839)**

Details provided in the **Chemical Characterization of Materials** section.

**Biothermodynamics**

**R.N. Goldberg and Y. Tewari (831)**

Details provided in the **Chemical and Biochemical Data** section.

**Development of an International Standard for the Evaluation of Microheterogeneity of Reference Materials for Microanalysis**

**R.B. Marinenko (837), S.D. Leigh (ITL), and M. Styles (British Standards Institute)**



CSTL researchers, and international collaborators prepared an ISO document titled *Microbeam analysis - Electron probe microanalysis - Guide to specification of certified reference materials (CRMs) ISO/CD 14595* to provide guideline procedures for the evaluation of candidate specimens as microanalysis reference materials for electron probe microanalysis (EPMA) and other microanalytical techniques. The document details the physical and chemical requirements of an EPMA reference material and provides procedures for testing the extent of heterogeneity of each element in a material with EPMA.



**INTERNATIONAL  
ORGANIZATION FOR  
STANDARDIZATION**

This document pertains primarily to flat, polished, solid specimens that exhibit long-term stability under normal environmental conditions as well as to the impact of an energetic (5 kV to 30 kV) electron beam with currents of 20 nA to 100 nA. It details these and other chemical and physical characteristics that are required of good quality microanalysis standards, including a detailed description of how to test candidate reference materials for the

**Although the procedures described in the document have to some extent been loosely followed in some parts of the microanalysis community in the past, a rigorous description of proper certification procedures has not heretofore been readily available to the microanalysis community. In fact, during the early stages of the preparation of this document, there was evidence of poor understanding and a general lack of rigor as to how to properly evaluate materials as reference materials for microanalysis.**

extent of microheterogeneity of each element present within each specimen and between specimens. A nested statistical scheme as described in ISO Standard Guide 35 is used, but is expanded from bulk specimen to specimen comparisons to comparisons from micrometer to micrometer within each candidate specimen. The statistics developed for the document are a combination of procedures used during the past 35 years of development of NIST Standard Reference Materials for microanalysis, contributions from the National Physics Laboratory, UK,

**This ISO document provides valuable guidelines to numerous laboratories performing quantitative microanalysis:**

- **high-tech industry where reference materials are important in determining the accurate composition of materials such as ceramics, semiconductors, or metal oxides**
- **geology and mineralogy communities where accurate evaluation of the compositions is needed**
- **laboratories with contract requirements specifying verification or *traceability* of reference materials.**

and suggestions from other country members of the Working Group. From a well-designed sampling procedure including replicate x-ray count readings from a single point, analysis of several points per specimen, and consistent sampling from specimen to specimen, the user can determine the uncertainty in mass fraction due to specimen heterogeneity taking into account the measured experimental counting uncertainty. The between-point and between-specimen uncertainties can be specifically calculated in this procedure. Since uncertainties are in mass fraction units, they can be combined with the uncertainties determined from a bulk quantitative analysis for certification.

**Central Analytical Database of the Organization for the Prohibition of Chemical Weapons (OPCW)**

**W.G. Mallard (838), E. White V (839), and E.S. Etz (837)**



The prohibition of Chemical Weapons has become increasingly important in light of recent events. CSTL researchers have leadership roles and are active members of the Validation Group for the Central Analytical

Database of the OPCW. In this capacity they are responsible along with representatives from other

countries for ensuring the quality of the data added to the OPCW Database. There are several working groups within the Validation Group devoted to different data types: infrared spectra data, retention data for gas chromatography; and mass spectral data. CSTL experts support the

**The DTRA is under the authority, direction, and control of the Assistant Secretary of Defense (International Security Policy), serves as the focal point within DoD for administering the DoD Technology Security Program. It is responsible for reviewing the international transfer of defense-related technology, goods, and services consistent with U.S. foreign policy and national security objectives.**

United States Delegation to the OPCW with technical assistance on the drafting of documents relating to the taking and transfer of samples at inspection sites under the Chemical Weapons Convention. The work of technical advisor has included briefings of the Bureau of Export Administration (BXA) and ongoing discussions with DoD Joint Staff and Department of State. In addition, CSTL researchers provide direct onsite support for the consultations in The Hague. The NIST efforts are funded by the Defense Threat Reduction Agency (DTRA).

**U.S. companies engaged in activities involving certain chemicals may be required to submit reports to the Department of Commerce and may be subject to inspection by the Organization for the Prohibition of Chemical Weapons (OPCW), the international body that administers the *Chemical Weapons Convention*.**

CSTL experts in mass spectrometric techniques have led evaluations of analytical methodologies for the analysis of chemical and biochemical weapons, including a joint U.S.-Finnish project to develop better methods for onsite sample preparation techniques for CW detection. MALDI-TOF detection of biological agents is a new project started this year with long-term goals of developing standards and protocols for the identification of microorganisms.

***Chemical Weapons Convention*: The United States is one of 143 signatory parties to the Chemical Weapons Convention (CWC), a global treaty that bans chemical weapons. Issued in August 1994 the Convention reaffirmed principles and objectives of and obligations assumed under the Geneva Protocol of 1925.**

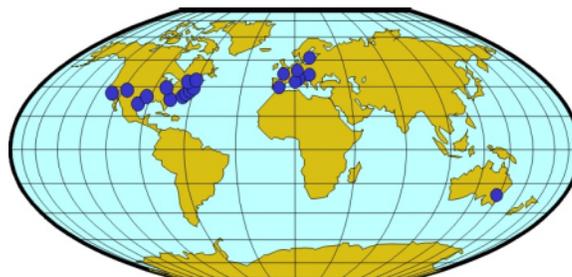
CSTL researchers have also developed a software system for automated and reliable detection and identification of chemical warfare agents, as well as tools for directed verification of compliance under the Chemical Warfare Convention. The NIST program compares GC-MS experimental data with a spectral library, using established and novel algorithms. CSTL staff members provide training in the use of their Standard Reference Databases (SRDs) and associated software systems. One such system, coupled to a GC-MS, is designed specifically for field detection and identification of chemical warfare agents, and will be utilized for verification of compliance to the global Chemical Weapons Convention.

## Establishing an International System for Primary Realization of Atmospheric Ozone Measurements

P.M. Chu, J.E. Norris, and F.R. Guenther (839)

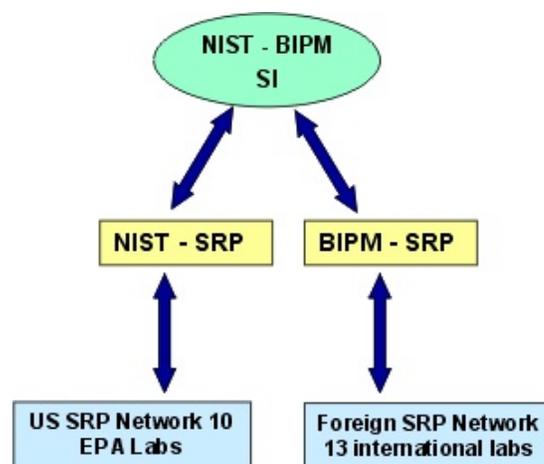


NIST has provided Standard Reference Photometers (SRPs) based on UV photometry to U.S. Environmental Protection Agency (EPA) facilities since 1983 to provide an infrastructure for the calibration and traceability of ozone measurements within the U.S. More recently, the international interest in ozone measurements has prompted eleven national laboratories to acquire NIST SRPs. To support the growing national and international need of improved ambient ozone measurements, NIST is partnering with BIPM to develop an advanced primary ozone reference standard and to share the dissemination of secondary or transfer standards. The basic project plan includes 1) Transfer the current ozone "national reference photometer" technology to BIPM. 2) Assess the performance of the current technology with respect to current and future ozone measurement requirements. 3) Provide recommendations for potential improvements of the SRPs and survey other candidate secondary standards. 4) Develop a primary reference standard with capabilities of SI-traceability verification.



**Ozone, at tropospheric levels, is a health concern and contributes to climate change as a greenhouse gas, while stratospheric ozone protects earth from harmful UV radiation.**

Success of this project, independent of the verification method, demands instrumentation with high sensitivity, accuracy, precision, and rapid time response for measuring chemical species at atmospheric levels (nmol/mol and lower). In fact, minimum detection sensitivities better than 1 nmol/mol will be required to maintain uncertainties at the 1% level for the current ground level ozone concentrations.



### **Global Network: Proposed**

As a collaborative project between NIST and BIPM, the advanced primary ozone photometer will provide an internationally validated ozone standard that can be used to anchor all ozone measurements through a defined traceability structure. The accuracy of the NIST SRP would be checked for consistency with the NIST SRM gas program and primary standards developed by BIPM.

