

Quality Management Program – Laboratory Services
2001 Review





QUALITY MANAGEMENT PROGRAM— LABORATORY SERVICES

VISION

To be the leading international accreditation and quality assessment agency for diagnostic laboratories.

THE PURPOSE

To serve health professionals and the public by promoting quality improvement of laboratory services through accreditation, assessment and education.

VALUES

- ✓ *Quality*
- ✓ *Collaboration*
- ✓ *Integrity*

QUALITY POLICY

To provide high quality laboratory accreditation, assessment and education services, QMP–LS commits to:

- ✓ Meet all customers' requirements; applicable regulatory, statutory and contractual requirements; and relevant national/international standards;
- ✓ Evaluate and continually improve the effectiveness of the service;
- ✓ Ensure this policy is communicated to and understood by all employees;
- ✓ Provide a process for establishment, review and modification of quality objectives;
- ✓ Review and modify this policy annually for continued suitability.

ACKNOWLEDGEMENTS

The success of an organization largely depends on the willingness of all involved parties to work co-operatively. We at QMP–LS acknowledge the supportive role that the Ontario Medical Association, and the Ministry of Health and Long-Term Care have played in the development and ongoing operation of QMP–LS. We acknowledge the leadership and counsel provided by Tom Magyarody, past Executive Director, Corporate Affairs & Administration, OMA. We wish him success in his new position.

We acknowledge the contributions of our client laboratories and the professional associations who allow their employees to serve as committee members, advisors and volunteers. Their support is invaluable.

Central to the operation of QMP–LS is the strength of its committees. Our committee members (Appendix A) devote considerable time, energy and skill to assist QMP–LS and we thank them for their service. This year, we would especially like to thank the following members who have retired from the committees:

- ✓ Dr. Reinhard Lohmann served for many years on the Hematology Committee and was the Chair of the Management Committee. Dr. J. Gilbert Hill served on the Chemistry Committee since its inception. Their wisdom, skills and dedication will be greatly missed.
- ✓ Dr. George Luxton, a longtime member of the Endocrinology Committee, served as a member and Chair, Mr. Sam Thomson served as a member and Chair of the Hematology Committee, Dr. William Brien served on the Hematology Committee and Ms. Carol Major, was a member and Chair of the Virology Committee. All have served on committees since the 1980s. We gratefully recognize their contributions.
- ✓ Dr. Donald Sutherland (Endocrinology), Dr. Darius Nazir (Enzymes, Lipids and Cardiac Markers), Ms. Susan Webb (MSS), Dr. Russell Price and Mrs. Edna Zuber (Transfusion Medicine), Ms. Susan Finn (Microbiology), Mrs. Linda Turner-Smith (Cytology), Ms. Martha Wood-Burgess (Genetics) and Dr. Martin Petric (Virology) have all provided valuable services to their respective committees.

The late Dr. Julius Kane served as a Special Advisor for mycology since 1996. His interest and enthusiasm will always be remembered.

A number of individuals volunteer their services to QMP–LS by providing technical and consultative assistance. Their names are listed in Appendix B. Their services are greatly appreciated.

Our staff (Appendix C) also deserve recognition and thanks. Ms. Kathleen McShane, Technological Consultant left QMP–LS in 2001 and we wish her well in her new post.

CONTENTS

Vision, Purpose, Values and Quality Policy of QMP-LS	i
Acknowledgements	ii
The Year in Review	1
Quality and Added Value	1
QMP-LS Structure	1
Development of Quality System	2
Office Relocation	2
Education	2
Information Services	3
Developing Global Relationships	4
Management Committee	6
Conjoint Committee	7
External Quality Assessment (EQA)	8
Provision of EQA Services	9
Monitoring Participant Performance	9
Chemistry Disciplines	11
Chemistry-General	11
Drug Monitoring	19
Enzymes, Cardiac Markers & Lipids	24
Enzymes & Cardiac Markers	24
Lipids	27
Endocrinology	30
Immunology	37
Maternal Serum Screening	38
Point-of-Care Testing (Glucose Meters)	41
Hematology Disciplines	43
Hematology-General	43
Hemoglobinopathy (Red Cell Disorders)	45
Detection of Fetal Cells	46
G6PD	47
Flow Cytometry	47
Bone Marrow Examination	49
Hematology-Coagulation	50
Hematology-Morphology	52
Transfusion Medicine	56
Microbiology Disciplines	61
Bacteriology	61
Mycology	69
Parasitology	71
Virology	74
Anatomic Pathology	79
Cytology	81
Genetics	85
Cytogenetics	85
Molecular Diagnostics of Inherited Human Diseases	87
Ontario Laboratory Accreditation (OLA)	89
Expanding our Quality Focus with Ontario Laboratory Accreditation	89
Proposed Accreditation Criteria	89
Operating Policies and Processes	90
Advisory Panel	90
Assessor Recruitment	91
Test Review Committee	91
Computer Databases	92
Next Steps in Development	92
Appendices	93
A. 2001–2002 QMP-LS Committees	93
B. Non-Committee Members Who Assisted QMP-LS (2001)	95
C. QMP-LS Staff as at March 31, 2002	96
D. External Quality Assessment Operating Principles	97
E. Ontario Laboratory Accreditation Operating Principles	98
F. Scientific Communications	99
G. Invited Presentations	100
H. Symposia & Workshops	101
I. Parameters Monitored by QMP-LS, by Discipline	102
J. EQA Decision Path	104
K. Summary of Committee Action in 2001	105
L. OLA Focus Group Presentation	106
M. OLA Proposed Accreditation Process	107

The reader is cautioned not to take any single item, or part thereof, of the *2001 Review* out of context.

Copyright © 2002 Quality Management Program — Laboratory Services, a Department of the Ontario Medical Association.

All rights reserved.

THE YEAR IN REVIEW

QUALITY AND ADDED VALUE

Throughout the world the practice of laboratory medicine is facing the challenge of a lack of human resources and fiscal restraint while, at the same time, the public becomes more informed and has greater expectations. Internationally, the need for quality systems and quality management of laboratories is increasingly recognized. QMP-LS, in its first full year of operation under its new name and mandate, has begun the development of its quality system. Over the next year or so, this development will be completed. At that time QMP-LS will seek accreditation by the Standards Council of Canada against ISO 17011 (previously Guide 58) and recognition that the external quality assessment program meets the requirements of ISO Guide 43-1 and ILAC (International Laboratory Accreditation Cooperation) G13. In the meanwhile, internal changes at QMP-LS serve to enhance the services for client laboratories and meet the obligations under the Memorandum of Agreement between the Ontario Medical Association (OMA) and the Ministry of Health and Long-Term Care (MOHLTC).

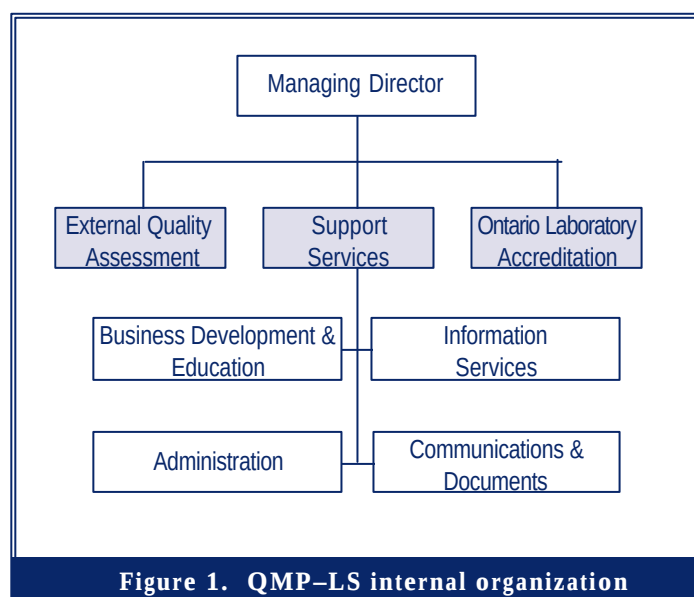
QMP-LS STRUCTURE

The current structure of QMP-LS is functionally organized (Figure 1). The two operational divisions, External Quality Assessment (EQA) and Ontario Laboratory Accreditation (OLA), are separate entities for day-to-day activities although mutually supportive through setting standards and evaluating laboratory performance. A support division provides information services, communication services, education services, and office administration in a multi-tasked horizontal matrix. The MOHLTC

Laboratories Branch requires and approves an annual workplan and budget request. Variance from the workplan and approved budget must be reported to the Branch as it occurs.

Figure 2 displays the QMP-LS committee structure. The scientific committees bring expert knowledge to the design of the assessment models and the evaluation of performance. The committees are composed of laboratory physicians, laboratory scientists, and medical laboratory technologists representing the geography and scope of practice of the participating laboratories. Committee terms of reference are in place and a codified system of committee member appointment established. All members sign a confidentiality agreement and make a conflict of interest declaration. In Ontario, all licensed medical laboratories are required to participate as the program acts as a deemed agent of MOHLTC under the provincial statutes.

The number of scientific committees has been reduced to 11 by consolidation of some of the chemistry committees. Among them, they provide models that examine and evaluate performance in 25 laboratory disciplines and sub-disciplines. A Committee Handbook provides members with key information on QMP-LS structure, process, and procedures.



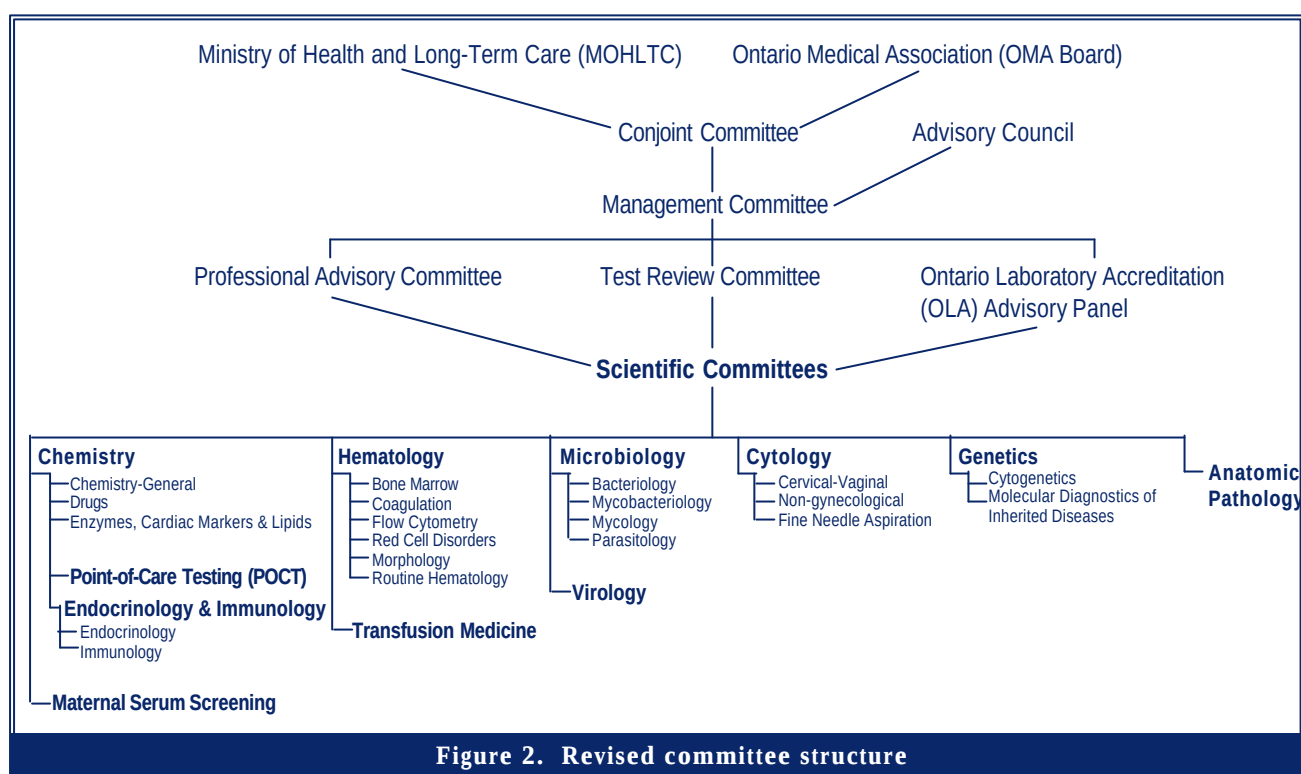


Figure 2. Revised committee structure

New senior committees have been established to support the reconstructed Management Committee. The Professional Advisory Committee (PAC) is made up of the Chairs of scientific committees. The PAC advises the Managing Director and staff on the implementation of the policies and directives of the Management Committee and on reports, policy options, and recommendations for consideration by the senior committees. The Ontario Laboratory Accreditation Advisory Panel reviews the accreditation requirements and makes recommendations on the accreditation policies, structure and process. An Advisory Council provides stakeholder input to the Management Committee with representation from government, the regulatory colleges, hospitals, laboratory and professional associations, and users.

The new Management Committee is smaller in size with membership from MOHLTC, OMA, College of Physicians and Surgeons of Ontario (CPSO), College of Medical Laboratory Technologists of Ontario (CMLTO) and the Chair of the PAC. The Management Committee makes recommendations for approval by the Conjoint Committee that has equal numbers from MOHLTC and OMA and is co-chaired by the Director, MOHLTC Laboratories Branch and the Managing Director, QMP-LS.

DEVELOPMENT OF QUALITY SYSTEM

QMP-LS has created an internal quality council to guide the development and implementation of a quality system designed

to meet or exceed client expectations. Jane Gun-Munro, Director of EQA, acts as the Quality Manager. The statement of purpose has been revised to reflect the vision, values, and quality policy as shown in the preface. Policy revisions, process mapping and procedure documentation is underway. An active review of all EQA models, evaluation strategies and communication templates has begun. Operating principles for the EQA and OLA have been developed and approved by the Management Committee (Appendices D and E).

OFFICE RELOCATION

Faced with the expiry of the office space lease in early 2002, a lease amendment agreement was negotiated with Manulife Financial. This required relocating to a newly renovated area on the fifteenth floor. The move was completed by the end of September. The square footage remains as before but by the use of work stations and fewer offices it has been possible to accommodate the additional staff of the OLA division.

EDUCATION

Information sharing with participating laboratories is key in supporting quality improvement. Survey Reports (111) and Committee Comments (83)

provided participants with timely analysis, feedback and interpretation of the survey data. The bi-weekly QMP–LS News provides comment on significant developments in the medical and scientific literature and information on upcoming activities and events. Broadsheets are distributed on topics of general interest. Increasingly, browser-enabled Web-based public access and secure site postings are used to make educational information available.

Scientific publications and presentations at national and international meetings (Appendices F and G) are an integral and important part of QMP–LS' educational activities and are discussed below.

Symposia, Workshops and Courses

In January 2001, the newly released Ontario Quality Assurance Program in Gynecologic Cytology was available in an electronic format on the QMP–LS Web site. The electronic version allows laboratories to download and customize the quality assurance forms from the Laboratory Workbook. A confidential Web site access password was required for access. In March, QMP–LS hosted a one-day cytology continuing medical education event entitled *Integrating GYN Cytology QA into Daily Practice* (Appendix H). Approximately 230 pathologists and cytotechnologists from all regions of Ontario participated.

In November, over 300 participants attended the Chemistry Symposium jointly sponsored by QMP–LS with the Ontario Society of Clinical Chemists and the Sunnybrook & Women's College Health Sciences Centre.

The proceedings of both symposia are available on videotape.

In 2001, QMP–LS continued its collaboration with CMLTO and the Ontario Society of Medical Technologists (OSMT) to deliver workshops across Ontario. Three Gram Stain workshops were hosted in Thunder Bay, Windsor and Kingston. These workshops were presented by Lindsay Wilcox, Technical Specialist from the Hamilton Laboratory Medicine Program and were attended by 69 participants.

We continue to offer two Internet-based educational courses— *Introduction to Hematology: The Erythrocyte*

and *Erythrocyte Disorders: Detection and Diagnosis*. These courses are eligible for continuing education credits. Registrants can proceed at their own pace and leisure, participate in interactive tutorials and self-assessment exams, and can e-mail their questions or queries to the instructor. Both courses continue to be popular.

To raise awareness of our expanded role in developing an enhanced quality management program, we displayed information about QMP–LS and addressed queries regarding OLA at various symposia and regional meetings.

INFORMATION SERVICES

Reorganization and Relocation

To support the expanded QMP–LS mandate, the structure of Information Services was modified and the Data Officers and Receptionist joined the team. The mid-September office relocation provided an opportunity to consolidate the QMP–LS servers in a restricted area with minimal floor space, reducing costs and increasing security. All workstations were provided with High-Speed Network access. Improved data projection capabilities were installed in the meeting rooms.

Collaboration

We conducted a virtual committee meeting by combining our Internet-based file-sharing capabilities with teleconferencing. The cost-savings and productivity gains from this approach will be expanded in 2002.

Our Document Server gave authorized Ontario participants access to digital images of cases for assessment in EQA challenge surveys. We continued to provide an electronic workspace that was accessed over the Internet by members of the Interprovincial Quality Assurance (IPQA) Information Technology Working Group.

In partnership with North York General Hospital and Mount Sinai Hospital we used a grant from The Change Foundation to develop and implement an Internet-based interactive genetics service to health care providers in Ontario. The site, www.OnGene.ca (Figure 3) will serve as the provincial resource centre for education, consultation and referral for genetic tests (cytogenetic and molecular) available in Ontario.

Point-of-Care Testing Application

We conducted our first computer-assisted point-of-care testing (POCT) survey for Ontario hospitals in March 2001. The enhanced application developed to support POCT provides for:

- ✓ Procedure-based testing in addition to discipline-based testing.
- ✓ Restructuring caused by regionalization and consolidation of laboratory services.
- ✓ Graphic reporting capabilities (Figure 4) not previously available in our EQA applications.

Anatomic Pathology Application

The software applications required to support EQA surveys in anatomic pathology was developed in 2001 (Figure 5). Pilot challenge surveys are scheduled for 2002.

OLA Application

We began development of functionality to support the OLA division, including the maintenance of requirements, roster of assessors, and scheduling of accreditation visits (Figure 6).

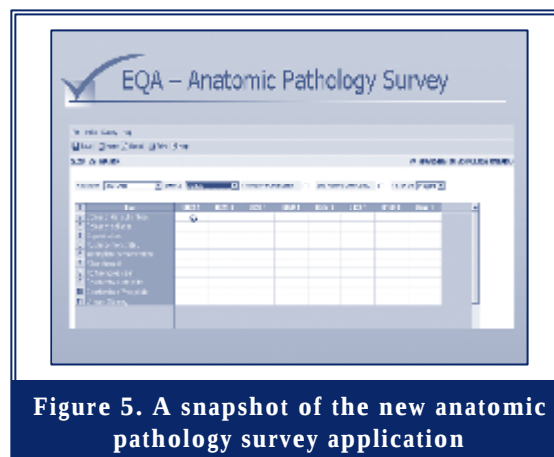


Figure 5. A snapshot of the new anatomic pathology survey application

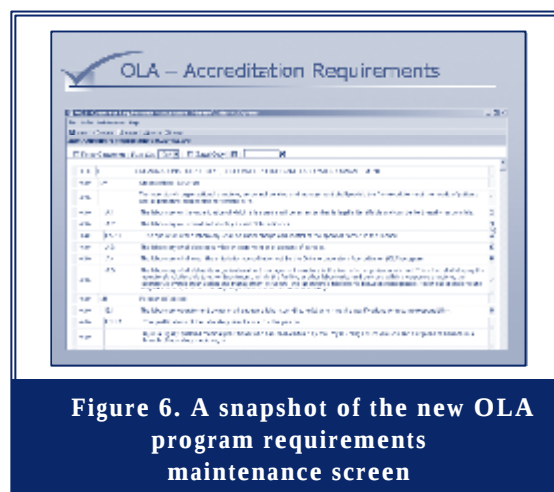


Figure 6. A snapshot of the new OLA program requirements maintenance screen

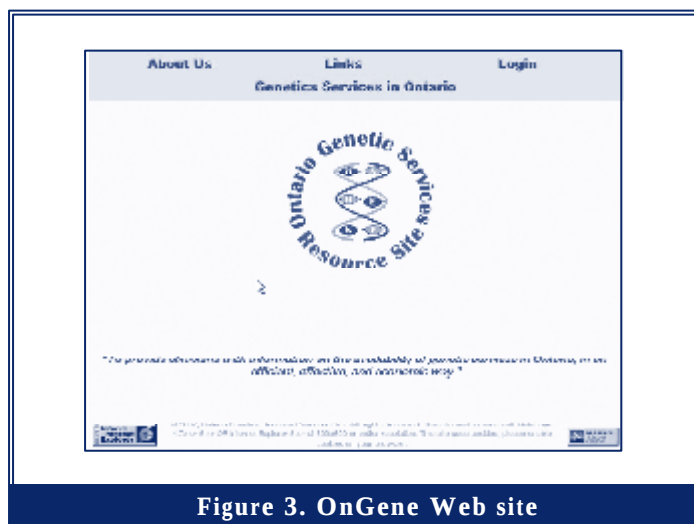


Figure 3. OnGene Web site

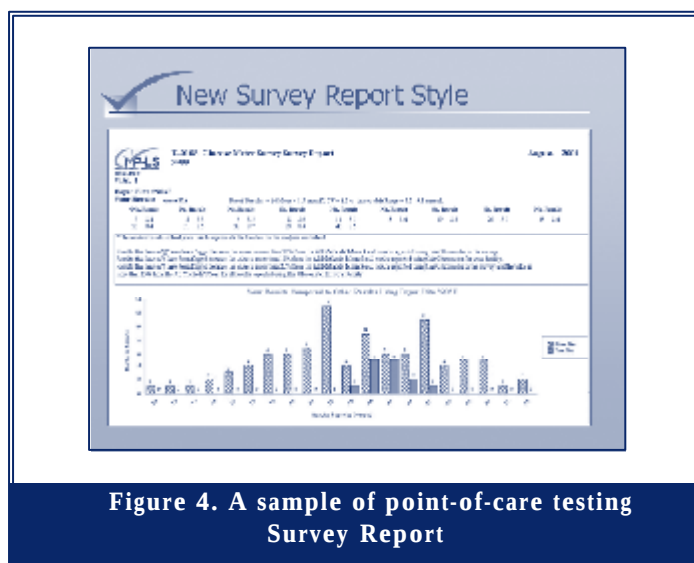


Figure 4. A sample of point-of-care testing Survey Report

DEVELOPING GLOBAL RELATIONSHIPS

Sharing Experience Nationally and Internationally

Eight scientific presentations were made at national and international meetings following the submission and acceptance of abstracts (Appendix F). Three papers were published in peer-reviewed journals and a further six were invited publications in local and national journals. Thirteen invited presentations were made at local and Canadian national meetings and two at meetings in the United States (Appendix G).

QMP-LS assisted the OMA in preparing its briefs to the Walkerton Inquiry. Dr. Richardson met with Counsel to the Commission and appeared twice at the Hearings before Mr. Justice O'Connor. Of interest is the requirement that all water-testing laboratories in the province must now be accredited and undergo external quality assessment by the Canadian Association of Environmental Analytical Laboratories (CAEAL) in partnership with Standards

Council of Canada (SCC). QMP–LS is exploring a partnership with SCC.

Visitors to QMP–LS during the year included Linda Cash of The Change Foundation, Alf Dolan and Bob White of BRI International, Paul Gould of OAML, Dr. Jean Joly of the Laboratoire Santé Publique du Québec, Lynne Belle-Isle of Health Canada and Peggy Stupca from the Mayo Clinic to discuss QMP–LS activities and potential collaboration.

QMP–LS Managing Director was appointed to the Organizing Committee of the Center for Disease Control (CDC) International Conference on Proficiency Testing. Originally Global Odyssey was planned for September 2001 but was deferred until February 2002. Five QMP–LS abstracts were accepted for presentation with Dr. Richardson acting as a working group leader and sub-group leader. Dr. Richardson was invited to present on *Information Management and PT data—What Now?* at the CDC Global AIDS Program Workshop—Proficiency Testing: from Concept to Reality that followed the Global Odyssey.

Linda Crawford is a member of the Education Committee of the Trillium Chapter of Clinical Laboratory Management Association, which delivered a two-part series of seminars titled *The Roadmap to Quality* in 2001.

Dr. Richardson was appointed to the Organizing Committee for the June 2002 *Quality Management in Laboratory Medicine Symposium* to be held at the Michener Institute in conjunction with *Quality is Key*.

Collaboration with Partners in Health Care

Once again, we actively participated in the Ontario Cervical Screening Collaborative Group and its sub-committees. Logistical, technical and secretarial support was provided to the Quality Assurance Committee. Details of the workshop conducted in March have been provided in the education report. Continued collaboration with Cancer Care Ontario is planned as an update to the quality assurance guideline to reflect the recent changes to the Bethesda System.

We continue to participate in the Ontario Consultative Group for Maternal Serum Screening. Plans to add additional analytes to the biochemical screen are in place and discussions continue with the CPSO regarding integrated first trimester screening.

The IPQA held its annual meeting in Regina in June. At that time it was decided to explore a more formal structure for IPQA including incorporation and by-laws. Proposals have been circulated for discussion under the leadership of Saskatchewan. A definitive proposal will be considered at the 2002 meeting in Calgary in May. QMP–LS holds the Chair of the Hematology and the Laboratory Information Systems Working Groups. We participate actively in the Transfusion Medicine, Microbiology, Chemistry and Anatomic Pathology Working Groups. We host the Web page for IPQA and its working groups.

QMP–LS provides a cytology EQA program to the Alberta Laboratory Proficiency Testing Program under contract. Out-of-province participants are included in Ontario surveys, on a cost-recovery basis in various disciplines as discussed in the EQA report. Transfusion medicine EQA materials are provided to Thistle QA in South Africa.

We continue as an active member of NCCLS. We have the opportunity to review and comment on proposed guidelines at the draft stage, to vote on tentative standards and to suggest members of sub-committees. Dr. Phil Wyatt has been appointed Chair of the subcommittee on Maternal Serum Screening. Linda Crawford and Dr. Richardson participated in the annual leadership conference in Washington, DC.

Some years ago the Pan American Health Organization established a cervical cytology quality assurance program for Central and South America called the Red-Pac Network. QMP–LS acts as an external referee for the panel of slides to be distributed by the program. The network is operated from a base in Chile.

The partnership between QMP–LS and the Canadian Public Health Association provides support to the Caribbean Epidemiology Centre (CAREC) and to Laboratory Services in Kosovo. The CIDA funded HIV/AIDS project in the Caribbean has ended although a new project has been funded. The modular multi-media training program on laboratory management was completed during the visit of Dr. Richardson in March. Initially, this program will be distributed to all laboratories supported by CAREC in paper format, but other modalities such as CD-Rom are in preparation. Seven modules span the spectrum of

laboratory management while the eighth module consists of self-assessment exercises. Additionally, by a separate cost-recovery arrangement, QMP-LS provides CAREC with an external quality assessment program in bacteriology and immunology. Two surveys are conducted each year with challenges requested by CAREC. Material is shipped in bulk to CAREC for forwarding to laboratories throughout the Caribbean. Worksheets are analysed by QMP-LS for review and comment. The primary support to Kosovo has been to the microbiology laboratories of the Institutes of Public Health. Donna and Steve Thompson have spent extended periods in Pristina enhancing bench knowledge and skills of the medical microbiologists and technicians. A QMP-LS team conducted a wet lab one-week workshop in Pristina during the summer on quality control of antimicrobial susceptibility testing. Twenty-eight microbiology staff from across Kosovo participated in the workshop.

Joanne Miyazaki represented QMP-LS on the Provincial Advisory Committee on Predictive Genetic Services and the Laboratory Sub-committee. She also participated in the Federal Government stakeholders meeting on the development of a surveillance system on genetic testing. The development of the OnGene Web site on genetic services in Ontario in partnership with the North York General and Mount Sinai Hospitals and funded by a grant from The Change Foundation is well advanced. QMP-LS has been funded by Health Canada to develop a Web site for genetic services throughout Canada.

The Canadian Standards Association (CSA) Technical Committee Z252 and the Canadian Advisory Committee to ISO Technical Committee 212 were harmonized some time ago under the aegis of CSA. The harmonized committee has been named the National Committee for Medical Laboratory Quality Systems. Dr. Richardson is Vice-Chair of this committee that will seek national consensus on standards for medical laboratory practice in Canada.

ISO (International Organization for Standardization) TC212 continues its work on developing international standards for medical laboratories. Dr. Richardson is one of four delegates of SCC to this technical committee. Three working groups are addressing quality laboratory systems, reference methods and materials, and *in vitro* diagnostic system standards. The long awaited ISO 15189 on Medical Laboratories: Requirements for Quality and Competence should be finalised by the summer of 2002.

QMP-LS provides support to the Michener Institute in its continuing education programs in the Lebanon, the Quality Management in Laboratory Medicine Symposium and the evolving certificate course in Laboratory Management.

The reporting pathway to the Laboratories Branch, MOHLTC regarding non-participation in QMP-LS surveys has been clarified. All laboratories have been notified of the requirements.

MANAGEMENT COMMITTEE

The Management Committee met twice in the year. The term of the previous Management Committee ended in March 2001 and the new committee has been struck with representation from MOHLTC, CPSO, CMLTO, OMA, the Chair of PAC and the Managing Director of QMP-LS. The Management Committee held its first meeting on October 15, 2001 along with the newly formed PAC, comprising the Chairs of the QMP-LS scientific committees. Membership of the Management and PAC is listed in Appendix A. A stakeholder Advisory Council (Appendix A) has been established to provide input to the Management Committee.

Regular agenda items included:

- ✓ Updates from the EQA division.
- ✓ Matters of policy arising from the committee updates.
- ✓ Progress reports on laboratory performance, and decisions on actions to be taken where required.
- ✓ QMP-LS staff reports on budget and operational matters.
- ✓ Reports on educational initiatives.
- ✓ Updates from OLA division.

Special Issues for 2001 included:

- ✓ Update on three POCT surveys for glucometers.
- ✓ An update on the establishment and initiatives of the Test Review Committee.
- ✓ Existing process for QMP-LS Information Sharing with LLIS—Late and non-reporting

laboratories. A process has been developed and shared with laboratories through the QMP–LS News No. 21 of November 13, 2001, that will more effectively capture non-participation.

- ✓ Need to develop a policy and process to limit disclosure of quality assessment when this would jeopardize or identify a laboratory professional.
- ✓ To speed up communication pathway for non-proficient laboratories.
- ✓ Utilization of tests regarding folate testing
- ✓ Address the need for new elements in the enhanced prenatal screening program.
- ✓ QMP–LS' findings on excessive cytologist workload.

CONJOINT COMMITTEE

The Conjoint Committee (Appendix A) met on two occasions during the year, co-chaired between Ms. Ogram and Dr. Richardson. Non-proficient laboratories being monitored regarding performance were reviewed and further appropriate actions determined, when required. Laboratories of concern that are being monitored

for other reasons were also reviewed, discussed and advice given where applicable. One laboratory was taken off the non-proficient list for Transfusion Medicine. No laboratories were declared non-proficient during the year.

Other matters of interest included:

- ✓ Status reports of the POCT Pilot study
- ✓ Advisory Group on HER2/neu Testing
- ✓ QA Cytology Program
- ✓ Human resources shortfall of physicians, scientists and technologists on the quality of laboratory testing
- ✓ QMP–LS information sharing with LLIS including late and non-reporting laboratories
- ✓ Mailing of correspondence, specimens and other material according to site licence
- ✓ Affiliation with a competitor or a companion laboratory—Conflict of Interest
- ✓ Assessing performance of individuals versus laboratories
- ✓ Process for consideration of non-proficient laboratories
- ✓ Utilization of tests regarding folate testing
- ✓ Proposed Enhanced Maternal Serum Screening Program
- ✓ Anatomic Pathology Committee
- ✓ Test Review Committee
- ✓ Ontario Laboratory Accreditation.



EXTERNAL QUALITY ASSESSMENT

2001 was a year of review for the External Quality Assessment (EQA) division of QMP–LS. The expanded mandate of QMP–LS, the decision to seek external accreditation and the need to integrate activities with those of Ontario Laboratory Accreditation (OLA) have required an extensive review of current EQA processes and development of plans for an improved structure that will support future growth. The planned structure is a quality management system that meets international requirements established for performance of external quality assessment. Laboratory information obtained through EQA and OLA activities will be maintained separately with established criteria for sharing. Enhancements to the EQA database will enable the storing and reporting of results by laboratory and/or region, by survey or test.

In short, significant changes are required to the existing structure for external quality assessment processes. It is anticipated that much of the planning that was accomplished in 2001 will be implemented in 2002 and 2003.

New initiatives within EQA also confirmed the need for change. Development of a slide circulation scheme for anatomic pathology raised concerns about assessment of individual performance and confidentiality of QMP–LS information. A major tenet of the EQA program is to assess laboratory performance, not that of the individual. However, in smaller laboratories, where there may only be a single practitioner, assessment of laboratory performance may be considered synonymous with individual assessment. Also, current legislation does not provide to QMP–LS the same information protection as is provided to hospital quality assurance activities i.e. protection from discovery. This fact prompted the OMA legal counsel to seek inclusion of such protection under the draft legislation for *Quality of Care Information Protection Act, 2002*.

The issues raised about the current performance assessment process will be addressed through the review of EQA processes in accordance with international accreditation

requirements as well as other established EQA schemes. This includes the following proposed actions:

- ✓ Development of a set of operating principles for EQA (Appendix D) to use as a framework for assessing validity and objectivity of models used.
- ✓ Review of the EQA models to bring about compliance with the operating principles. Particular attention will be paid to those models that assess only part of the laboratory practice and have an interpretive component.
- ✓ Revision of the error assignment process to ensure that it is fair and equitable, complies with the operating principles, is comparable to other EQA schemes and meets international standards.
- ✓ Revision of the correspondence templates to ensure clarity and to provide participants with an opportunity to investigate and determine corrective action to address unacceptable or discordant results.
- ✓ Clarification of EQA assessment processes with regard to performance of laboratories and individuals.

These actions will be completed during 2002. Until then, and pending enactment of the draft legislation, surveys in which the major component is interpretation will not be assigned errors. However, clarification of unexpected or discordant results will still be required from laboratories as standard practice.

Another EQA initiative during 2001 was the introduction of surveys for point-of-care testing (POCT) of glucose meters in Ontario hospitals. This project was initiated with input from the Ontario Hospital Association and extended QMP–LS activity

beyond the doors of the traditional laboratory for the second time—the first being provision of surveys for blood gas instruments. Preparation for POCT surveys required significant changes to the QMP–LS database to accommodate data from sites with multiple instruments. These surveys were voluntary, and although they required considerable coordination by laboratory participants, were well received. Challenges that arise from surveys for POCT include improving the coordination of EQA POCT within an institution, correlation of results obtained using EQA testing material to patient samples, understanding the calibration of glucose meters and determination of clinical decision points, and sharing EQA survey information with non-laboratory POCT end-users. QMP–LS will continue to develop pathways to assess use of POC tests.

In addition to the three surveys evaluating point-of-care use of glucose meters in Ontario hospitals, the scope of testing continues to expand to reflect evolving technology and test/analyte demand in other areas. Pilot surveys were conducted in hematology for glucose-6-phosphate dehydrogenase (G6PD), circulation of unstained blood films for morphology, and use of data on CD ROM instead of fresh patient

samples as challenge material for flow cytometry instrumentation. Plans for testing in anatomic pathology progressed with two patterns-of-practice surveys being conducted in preparation for pilot challenge surveys in 2002. New analytes tested for the first time included respiratory syncytial virus (RSV) antigen detection in virology (Appendix I).

PROVISION OF EQA SERVICES

As Ontario hospital and community laboratories progressed with their own amalgamation and restructuring activities, the number required to participate in the program declined from 266 in 2000 to 254 in 2001 (See Tables 1 and 2).

Table 1. Comparison of Types of Ontario Laboratories Participating in QMP–LS

Laboratory Facility Type	Number of Laboratories			
	1991	1999	2000	2001
Private	173	61	62	53
Hospital	211	185	183	181
Public Health	12	11	11	11
Psychiatric	5	1	1	0
Canadian Blood Services	5	6	6	6
Federal Government	3	3	2	2
Other	7	1	2	1
Total	416	268	266	254

Provision of services outside of Ontario is conducted on a cost-recovery basis. External participants were included in Ontario surveys for chemistry-general, coagulation, cytology, drug monitoring, endocrinology, enzymes and lipids, genetics, hematology-general, hematology-morphology, flow cytometry, immunology, maternal serum screening, mycology, parasitology, and virology (Table 2). Distinct programs were supplied to other jurisdictions in bacteriology and cytology. Testing materials were provided to an external program in South Africa.

Overall, in 2001, 114 routine challenge surveys, 14 patterns-of-practice surveys and 6 questionnaires were conducted. Patterns-of-practice surveys and questionnaires—major tools used to evaluate pre- and post-analytical phases of laboratory service and develop best practice guidelines—increased over previous years.

MONITORING PARTICIPANT PERFORMANCE

QMP–LS' scientific committees evaluate survey results and assess errors based on the clinical significance of discordant results. Lesser errors are assessed for results that exceed the established acceptable limits, and significant errors for results that have the potential to

Table 2. Number of Participating Ontario Laboratories in 2001 vs. Out of Province

Discipline	Ontario	Out of Province
Anatomic Pathology	80	0
Chemistry-General	215	11
Drug Monitoring	167	22
Endocrinology	122	2
Enzymes, Cardiac Markers & Lipids	206	3
Immunology	108	1
Maternal Serum Screening	7	2
Hematology-General	227	15
Coagulation	212	1
Hematology-Morphology	218	1
Transfusion Medicine	179	0 *
Bacteriology	127	39
Mycology	27	2
Parasitology	28	1
Virology	73	4
Genetics	10	12
Cytology	86	13
Point-of-Care Testing	196	0

* Testing material is provided to one external program with 20 laboratories.

cause mistreatment or misdiagnosis. Committees correspond with laboratories regarding all errors assessed. Unacceptable or incomplete participant responses may prompt further communication, continued monitoring of survey performance or a letter of concern and/or an offer of an on-site consultation. The decision path for the EQA of laboratories is shown in Appendix J. The number of errors assessed in 2001 is shown in Appendix K. Error rates as calculated by individual committees are discussed within this *Review* in subsequent scientific committee reports. The number of on-site consultations conducted in 2001 increased to 14 from 13 in 2000. (Table 3). No laboratories were declared non-proficient in 2001 (Table 4).

As part of the EQA survey process, QMP-LS, through its scientific committees, provided on-

going education to promote improvement in the quality of laboratory performance. This included the following in 2001:

- ✓ 83 Committee Comments
- ✓ 2 Broadsheets
- ✓ 6 best practice guidelines

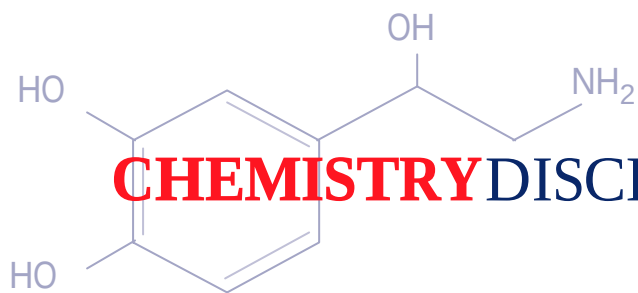
Committee Comments review the objectives of a survey, discuss participant performance and provide supporting educational information. Broadsheets provide educational information on specific topics (not necessarily regarding survey activities). Best practice guidelines are usually developed through a consensus process initiated by a patterns-of-practice survey. In this process, current practice information is presented and discussed, best practice is recommended and participants are invited to comment. After a defined period (usually six months), the comments are revised as required and published in Committee Comments or as Guidelines as a consensus document for Ontario.

Table 3: QMP-LS On-site Consultations that Occurred During Each Year, 1991–2001

Discipline	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001
Bacteriology	5	3	2	4	0	5	3	2	0	4	0
Parasitology	0	0	3	2	0	1	0	3	1	0	0
Virology	0	3	2	3	2	1	0	0	1	0	0
Microbiology Total	5	6	7	9	2	7	3	5	2	4	0
Chemistry	7	14	7	11	14	5	2	1	1	0	2
Endocrinology	3	0	3	1	1	0	0	0	0	0	0
Enzymes & Lipids	0	1	0	0	0	0	0	0	1	2	0
Immunology	0	1	2	1	0	0	0	0	0	0	0
MSS	0	0	0	0	0	0	0	0	1	0	0
Chemistry Total	10	16	12	13	15	5	2	1	3	2	2
Hematology	0	1	0	0	0	1	0	0	0	2	0
Morphology	3	2	1	0	0	0	0	1	1	0	4
Coagulation	0	1	0	0	0	0	0	0	0	0	0
Bone Marrow	0	0	0	0	0	0	0	0	0	0	1
Transfusion Medicine	3	1	3	1	1	5	1	3	1	3	6
Hematology Total	6	5	4	1	1	6	1	4	2	5	11
Genetics	0	0	0	0	1	1	0	0	0	0	0
Genetics Total	0	0	0	0	1	1	0	0	0	0	0
Cytology	3	1	2	3	0	0	1	1	0	2	1
Cytology Total	3	1	2	3	0	0	1	1	0	2	1
Grand Total	24	28	25	26	19	19	7	11	7	13	14

Table 4: Number of Newly Named Non-proficient Laboratories by Discipline, 1991–2001

Discipline	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001
Chemistry	0	0	0	2	0	0	0	0	0	0	0
Hematology	0	0	0	0	0	1	0	1	0	0	0
Microbiology	0	0	0	3	0	0	0	1	0	0	0
Other	0	0	0	0	0	0	0	0	0	0	0
Total	0	0	0	5	0	1	0	2	0	0	0



CHEMISTRY DISCIPLINES

CHEMISTRY-GENERAL

TESTING MODEL

Four surveys were distributed to test routine chemistry analytes. Surveys C-0101, C-0105 and C-0110 contained two vials of previously frozen serum supplemented with some of the analytes. Five vials of supplemented serum were distributed for survey C-0103. Participants were requested to test the vials on specific days. There were two sets of replicates to test between-run precision. One of each of the replicate vials was distributed in the October survey for a between-survey precision study. The analytes tested are shown in Appendix I (p. 102).

One blood gas survey using commercially-prepared aqueous material was conducted to test pH, pCO₂, pO₂, sodium, potassium, glucose and ionized calcium. Sufficient material was distributed to test all of the blood gas instruments within an institution including point-of-care devices.

Three HbA_{1c} surveys were distributed, each containing two whole blood samples from single donors.

One urine chemistry survey occurred that included testing for protein sodium, potassium and creatinine. Participants were required to calculate the 24-hour results using the urine volume indicated on the analysis worksheet.

Three albumin excretion rate (AER) surveys were conducted. Each survey contained four samples of patients' urine. Participants were required to measure albumin and creatinine and calculate the ratio.

The survey schedule was as follows:

C-0101	Routine chemistry, HbA _{1c} and AER
C-0103	Routine chemistry and urine chemistry
C-0105	Routine chemistry and blood gases
C-0107	HbA _{1c} and AER
C-0110	Routine chemistry, HbA _{1c} and AER

Chemistry (Routine, Quantitative Urine Chemistry, Albumin Excretion Rate, HbA_{1c}, Blood Gases)

No. of Participants (Dec. 2001)	215
No. of Participants (Dec. 2000)	222
No. of Surveys Conducted in 2001	13

Drug Monitoring (Routine, Cyclosporine, Drugs of Abuse)

No. of Participants (Dec. 2001)	167
No. of Participants (Dec. 2000)	171
No. of Surveys Conducted in 2001	13

Enzymes, Cardiac Markers & Lipids

No. of Participants (Dec. 2001) Enzymes	206	Lipids ...	148
No. of Participants (Dec. 2000) Enzymes	210	Lipids ..	155
No. of Surveys Conducted in 2001	10		

Endocrinology

No. of Participants (Dec. 2001)	122
No. of Participants (Dec. 2000)	125
No. of Surveys Conducted in 2001	6

Immunology

No. of Participants (Dec. 2001)	108
No. of Participants (Dec. 2000)	120
No. of Surveys Conducted in 2001	5

Maternal Serum Screening

No. of Participants (Dec. 2001)	7
No. of Participants (Dec. 2000)	7
No. of Surveys Conducted in 2001	4

Point-of-Care Testing (Glucose Meters)

No. of Participants (Dec. 2001)	196
No. of Participants (Dec. 2000)	NA
No. of Surveys Conducted in 2001	3



ASSESSMENT OF RESULTS

The computer flagging rules used for chemistry-general routine, urine chemistry, AER, HbA_{1c} and blood gas surveys remained the same as those reported in the 2000 Review. These rules are used as a screening tool to bring outliers to the attention of the committee. Before the committee recommends action for outliers, laboratory performance, peer group results and concentration of the analyte in question are taken into consideration.

LABORATORY PERFORMANCE

Analytical Systems in Use

Information about the use of analytical systems has been published in previous Reviews in order to help readers keep

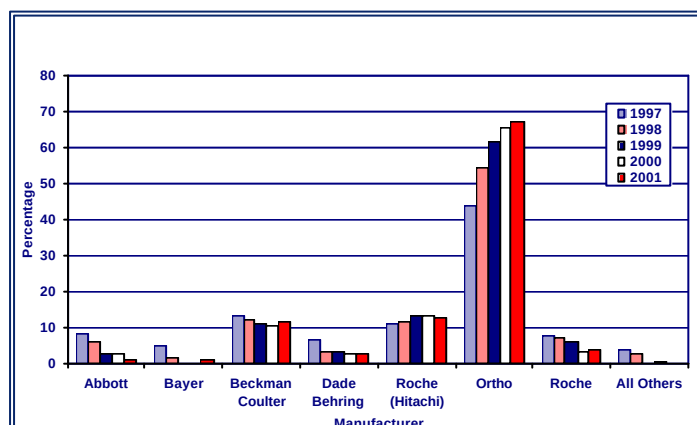


Figure 7. Measurement systems used for glucose

abreast of changing practices. Using glucose as the analyte likely to indicate the principal chemistry analyzer in a laboratory, Figure 7 provides a snapshot of the market, comparing methods used during the last five years. Ortho Diagnostics continues to dominate instrumentation used in Ontario laboratories. Ortho Diagnostics and Beckman Coulter analyzer numbers have increased in 2001 compared to the previous year, whereas all other manufacturers have either experienced a decline in the number of analyzers in use or the number has remained the same.

Bias in Analytical Systems

Some analytical systems continue to demonstrate significant biases in survey results. Table 5 provides a summary of the number of laboratories flagged for bias and the number receiving correspondence for surveys C-0103 and C-0110. Assays exhibiting the greatest number of bias flags over the two surveys include albumin, creatinine, magnesium and urea.

A large number of the bias flags are occurring because one analytical system is influencing the all-methods' mean (AMM). The Ortho Vitros instruments tend to produce lower results than the other instruments when measuring albumin,

Table 5. Summary of Laboratories Flagged for Bias and the Number Receiving Correspondence by Analyte for Surveys C-0103 and C-0110

Analyte	C-0103			C-0110		
	No. of Laboratories	No. of Laboratories Flagged	No. of Memos	No. of Laboratories	No. of Laboratories Flagged	No. of Memos
Bicarbonate	159	8	3	158	1	1
Chloride	210	4	2	208	3	2
Sodium	213	11	1	211	4	2
Potassium	213	4	1	211	1	1
Glucose	215	4	0	212	0	0
Urea	209	32	1	207	23	2
Creatinine	209	33	11	206	18	8
Calcium	195	7	2	194	3	2
Phosphate	177	3	2	177	3	3
Total Protein	186	7	3	186	8	0
Albumin	184	14	1	185	22	1
Urate	185	2	0	185	0	0
Magnesium	131	23	5	133	18	5

magnesium and urea. The committee takes this into consideration before taking action on the results from other instrument systems as evidenced by the small number of memos compared to number of computer flags. The committee is corresponding with Ortho representatives regarding the results reported for these analytes.

Bias in the Measurement of Creatinine

Target creatinine values continue to be obtained on survey samples from a reference laboratory¹ using a high performance liquid chromatography (HPLC) reference method. Table 6 shows the QMP–LS AMMs, the HPLC results, and the means and coefficient of variations (CVs) for survey results, grouped by reagent supplier for survey vials distributed in 2001. Only groups with five or more users are included.

In Figure 8 we have shown the mean creatinine values, by reagent supplier compared to the AMM and HPLC results for two representative vials—one of which was unaltered (C-0101-A) and the other was supplemented with creatinine (C-0105-A). The mean of Roche (BMC) users is the closest to the reference value for both vials, whereas the mean of Ortho users is the farthest away from the reference value for both vials.

¹ Reference Laboratory, Ortho-Clinical Diagnostics, Inc., Rochester, New York.

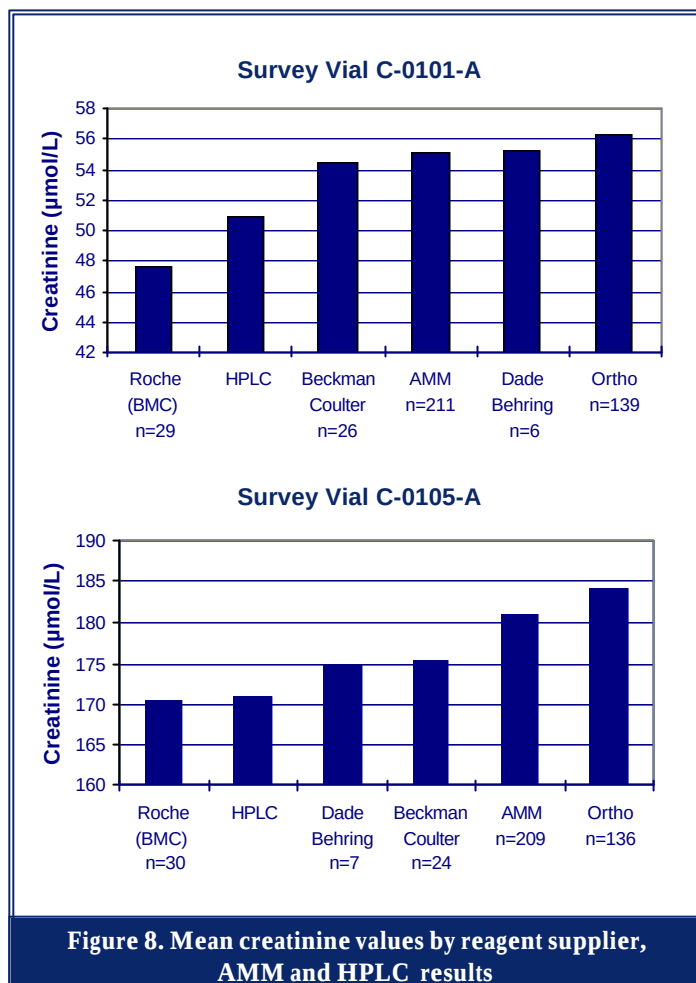


Figure 8. Mean creatinine values by reagent supplier, AMM and HPLC results

Precision Studies

Five vials of serum were distributed for survey C-0103 to conduct between-run precision studies. One pool of serum was used as the base to prepare all five vials. Vials C-0103-A, -C, -E were supplemented to 12 mmol/L glucose and 2.9 mmol/L calcium. Vials C-0103-B, -D were supplemented to 1.8 mmol/L magnesium.

Table 6. Creatinine AMMs, HPLC Results and Means by Reagent Supplier for the 2001 Survey Vials

	AMM	HPLC	Beckman Coulter			Roche (BMC)			Dade Behring			Ortho			Roche		
			No.	Mean	CV(%)	No.	Mean	CV(%)	No.	Mean	CV(%)	No.	Mean	CV(%)	No.	Mean	CV(%)
C-0101-A	55.2	51	26	54.5	7.3	29	47.6	8.1	6	55.3	5.8	139	56.4	3.7	4	NSQ	...
C-0101-B	50.0	51	23	43.8	27.3	29	37.0	11.9	6	43.0	11.9	139	52.5	4.2	4	NSQ	...
C-0103-A	84.4	84	25	86.4	6.9	30	79.3	4.2	7	86.6	8.5	136	84.9	2.4	4	NSQ	...
C-0103-B	84.1	80	24	84.3	6.1	30	77.6	5.1	7	84.3	7.7	137	85.2	2.6	4	NSQ	...
C-0105-A	180.9	171	24	175.4	3.1	30	170.3	3.2	7	174.7	2.4	136	184.3	1.8	5	165.2	4.5
C-0105-B	77.6	73	24	79.4	5.2	30	73.1	5.1	7	81.1	5.2	137	77.9	2.3	5	75.6	10.1
C-0110-A	86.0	81	25	79.2	7.3	27	78.4	6.5	6	80.7	3.8	133	89.0	2.0	7	78.7	4.9
C-0110-B	86.0	81	25	81.6	7.1	27	80.0	5.0	6	85.0	2.8	134	88.3	2.2	7	80.0	6.3



Each of the five vials was to be tested on different days. The testing schedule was specified on the analysis worksheet. At least 25 laboratories did not follow the instructions and tested all vials in the same test run.

Two vials of serum were distributed for survey C-0110 to conduct between-survey precision studies. Vial C-0110-A was a replicate of vials C-0103-B and 0103-D. Vial C-0110-B was a replicate of vials C-0103-A, -C and -E.

A summary of the number of laboratories whose results were flagged by the computer for imprecision when the difference in results was greater than 10%, and the number of laboratories receiving correspondence, by analyte, for both surveys is shown in Table 7.

The performance on these two precision studies was very good with only a few laboratories receiving correspondence. The precision flagging limit of 10% was used for all analytes and is quite generous for many of them. The committee intends to revise the precision flagging limits based on the overall performance on past precision studies for each analyte.

URINE CHEMISTRY (SURVEY C-0103-UC)

Urine Protein

The number of laboratories reporting this analyte has declined slightly from 2000 and the distribution of methods employed continues to change. The Ortho pyrocatechol violet method is

utilized by 45% of surveyed laboratories. Pyrogallol red represents the next largest method group at 33% followed by benzethonium chloride at 21%. Only one laboratory is using a coomassie blue application in 2001 and the sulfosalicylic acid methods have disappeared. Table 8 provides a summary of the statistics collated for urine protein performance by analytical principle in surveys C-0003-UC and C-0103-UC.

The Ortho pyrocatechol violet method continues to demonstrate excellent precision, however, it also continues to demonstrate a positive bias relative to other systems.

Urine Sodium and Potassium

One hundred seventeen laboratories reported values for urine electrolytes. Ortho technology represents the largest single user group (52%), followed by Beckman Coulter (18%) and Roche (BMC) (17%). Acceptable precision was observed in all method groups studied, with an all-methods' CV of 4.5% (sodium) and 3.1% (potassium) for vial C-0103-UC-1 and 4.6% (sodium) and 3.6% (potassium) for vial C-0103-UC-2. Table 9 summarizes the performance of urine sodium and potassium in 2000 (C-0003-UC) and 2001 (C-0103-UC).

Table 7. Summary of Laboratories Flagged for Imprecision (difference in results >10%) and the Number Receiving Correspondence by Analyte for Surveys C-0103 and C-0110

Analyte	C-0103 Between-day Precision			C-0110 Between-survey Precision		
	No. of Laboratories	No. of Laboratories Flagged	No. of Memos	No. of Laboratories	No. of Laboratories Flagged	No. of Memos
Bicarbonate	159	4	1	158	17	1
Chloride	210	0	0	208	0	0
Sodium	213	0	0	211	0	0
Potassium	213	0	0	211	0	0
Glucose	215	0	0	212	0	0
Urea	209	5	0	207	5	4
Creatinine	209	7	1	206	13	4
Calcium	195	0	0	194	0	0
Phosphate	177	0	0	177	7	4
Total Protein	186	0	0	186	1	0
Albumin	184	1	1	185	2	1
Urate	185	0	0	185	0	0
Magnesium	131	2	2	133	6	2

Table 8. Comparison of Urine Protein Statistics for Surveys C-0003-UC and C-0103-UC

Analytical Principle	C-0003-UC								C-0103-UC							
	Vial 1				Vial 2				Vial 1				Vial 2			
	n	Mean (g/L)	SD	CV	n	Mean (g/L)	SD	CV	n	Mean (g/L)	SD	CV	n	Mean (g/L)	SD	CV
BenzethoniumChloride	18	0.05	0.028	56.0	19	0.55	0.024	4.4	16	0.048	0.013	26.0	19	0.223	0.033	15.0
PyrocatecholViolet	38	0.07	0.006	8.6	38	0.64	0.031	4.8	40	0.060	0.005	8.3	41	0.300	0.016	5.3
Pyrogallol Red	33	0.05	0.025	50.0	33	0.57	0.056	9.8	29	0.060	0.024	40.0	30	0.240	0.034	14.2
Coomassie Blue	4	0.04	0.025	62.5	4	0.59	0.092	15.5	1	0.030	N/A	N/A	1	0.220	N/A	N/A
3% SSA+Sod. Sulphate	1	<0.05	N/A	N/A	1	0.49	N/A	N/A	...	...	...	...	...	...	...	...
AllMethods	94	0.06	0.023	38.3	94	0.59	0.057	36.3	86	0.060	0.016	26.7	91	0.267	0.045	16.7

Urine Creatinine

In contrast to previous years, there were no apparent calculation errors made by the participants. Analytical performance for this analyte was good. Table 10 summarizes the performance by reagent source in 2000 and 2001.

Based on the performance in 2001 surveys, the committee has recommended lowering the computer flagging limits in future surveys for urine sodium and potassium to >15% from the AMM and urine protein to >15% from the peer group mean. The urine creatinine flagging limit remains unchanged.

Albumin Excretion Rate

Three surveys were completed in 2001. Each consisted of four vials of urine from diabetic patients. Participants (n=30) were asked to report albumin (mg/L), creatinine (mmol/L) and the albumin:creatinine ratio (mg albumin/mmol creatinine). No significant change in the distribution of instruments or methods in use was observed when compared to previous years.

Performance data illustrated a wide range of sensitivity, precision and bias between methods for albumin. Sensitivity limits ranged from 0.1 to 6.0 mg/L albumin. Laboratories employing nephelometric or radioimmunoassay technologies for determination of this analyte reported superior sensitivity capabilities compared to immunoturbidimetric assays. Results reported from immunoturbidimetric methods were positively biased and consistently gave higher CVs compared to nephelometric technologies. Table 11 summarizes the albumin statistics for three of the vials distributed in survey C-0101-AE.

Table 9. Summary of Laboratory Performance for Urine Sodium and Potassium in 2000 and 2001

Analyte	2000		2001	
	Vial C-0003-1	Vial C-0003-2	Vial C-0103-1	Vial C-0103-2
Sodium				
N	125	125	117	117
Mean (mmol/L)	48.6	75.0	101.7	115.8
SD (mmol/L)	1.7	2.4	4.6	5.3
CV (%)	3.5	3.2	4.5	4.6
Potassium				
N	125	125	117	117
Mean (mmol/L)	40.6	30.8	35.7	25.3
SD (mmol/L)	1.6	1.0	1.1	0.9
CV (%)	3.9	3.2	3.1	3.6

Table 10. Summary of Performance by Reagent Source for Urine Creatinine in 2000 and 2001

Reagent Source	2000					2001				
	Vial C-0003-1			Vial C-0003-2		Vial C-0103-1			Vial C-0103-2	
	n	Mean (mmol/L)	CV	Mean (mmol/L)	CV	n	Mean (mmol/L)	CV	Mean (mmol/L)	CV
All Methods	158	5.71	4.2	4.28	4.2	149	7.12	4.6	8.42	4.5
Ortho	91	5.70	3.2	4.24	3.1	88	7.06	4.6	8.35	4.5
Roche (BMC)	28	5.62	6.8	4.30	6.3	24	7.25	3.8	8.56	4.9
Beckman Coulter	22	5.95	3.2	4.30	6.3	22	7.34	2.9	8.67	2.3
Dade Behring	7	5.61	1.3	4.16	1.9	6	7.05	2.8	8.48	3.5
Other	10	5.69	8.1	4.42	10.4	9	6.88	6.8	8.09	7.3



Table 11. Urine Albumin Statistics for Survey C-0101-AE

Albumin	C-0101-2			C-0101-3			C-0101-4		
	n*	Mean (mg/L)	CV	n*	Mean (mg/L)	CV	n*	Mean (mg/L)	CV
Rate Nephelometry	17	11.5	4.2	17	125.1	7.1	17	27.1	7.6
Immunoturbidimetry	12	12.1	22.6	12	133.2	4.5	12	30.3	28.5
Radioimmunoassay	3	15.4	...†	2	154.2	...†	3	30.8	...†
All Methods	32	12.0	17.8	30	128.2	6.8	31	29.4	13.9

* Note that all results are included in the data set used for the calculation of the AMM and CV, and for the identification of outliers for the All-methods data set. This included some items, which were outliers for their specific method, but that turned out not to be outliers for the larger group, and vice versa. Thus the "n" for All methods may not equal the sum of the "n" for the individual methods.

† Not applicable because of sample size.

The challenges were designed to evaluate a range of clinically important albumin concentrations (2.0–128.3 mg/L). A total of 59 (16%) of 360 results reported in the three surveys exceeded the 15% from the all-methods' median computer flagging limit for bias.

Although creatinine results were good without exception, the performance of this important indicator in diabetic patients was disappointing overall. The albumin:creatinine ratios reported to QMP–LS would have been, in several cases, misleading to the physician and could potentially result in inappropriate treatment of the patient.

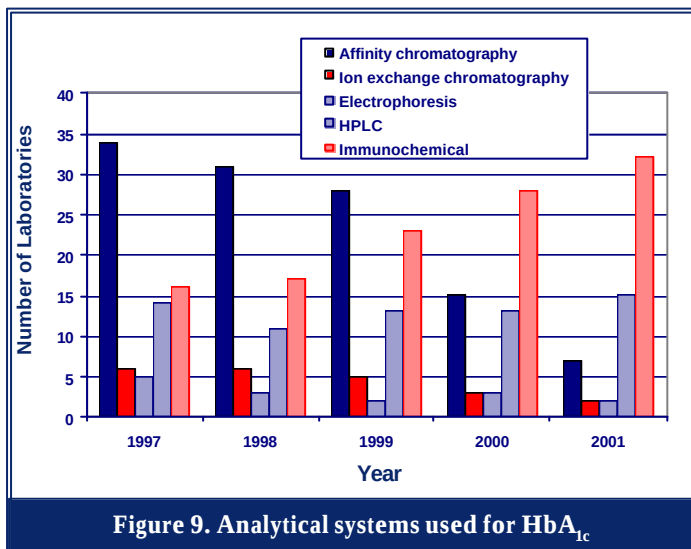


Figure 9. Analytical systems used for HbA_{1c}

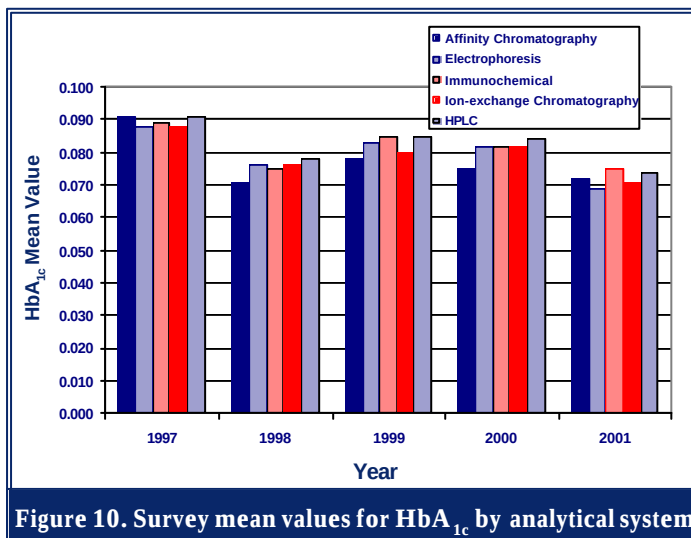


Figure 10. Survey mean values for HbA_{1c} by analytical system

Hemoglobin A_{1c}

Surveys were distributed in January, July and October. Each included two fresh whole blood samples obtained from single donors. All laboratories (59) now report results as HbA_{1c}. Figure 9 displays the methods used by the participants from 1997–2001. The use of immunochemical methods has increased dramatically since 1997 whereas usage of affinity chromatography methods has declined from 34 users in 1997 to seven in 2001. Reference values were obtained from the Central Primary Reference Laboratory of the National Glycohemoglobin Standardization Program (CPRL-NGSP) at the University of Missouri. The AMMs were within 0.001 units of the reference values for all challenges this year. Figure 10 displays the mean values by analytical system for a typical survey vial from 1997 to 2001. The negative bias previously seen with the Abbott affinity chromatography method was not evident in the 2001 surveys.

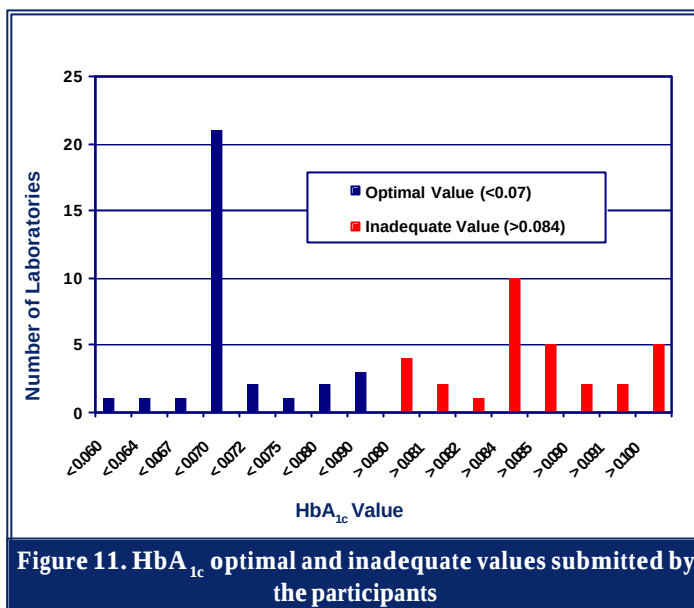
Thirty-nine (11%) of 350 results received for the three surveys were >10% from the reference laboratory's values. Memos were sent regarding 33 of these results. Overall, there was no

consistent bias or ongoing difficulty in remaining within the recommended total error of 10% of the reference laboratory's value.

Patterns-of-Practice Survey

In April 2001, the 59 laboratories licensed to perform HbA_{1c} completed this survey. At that time 22 (37%) laboratories were not using a method certified by the NGSP. It is recommended that only certified methods be used by Ontario laboratories. A quarterly update on certified methods is available at <http://www.missouri.edu/~diabetes/ngsp.html>.

The use of reference intervals and interpretations is still somewhat variable. According to the 1998 clinical practice guidelines for the management of diabetes in Canada (CMAJ 1998; 159 [suppl 8], pp. s1–29), optimal (target) HbA_{1c} concentrations for patients with diabetes are <0.070, suboptimal (may require action) are 0.07–0.084, and inadequate (action required) are >0.084. Non-diabetic individuals should have HbA_{1c} concentrations between 0.040–0.060. Figure 11 displays the optimal and inadequate values submitted by the participants. Only 12 of the 32 laboratories with guidelines for diabetic patients are using the current recommended levels; 37 laboratories only indicate the non-diabetic reference range on their patient reports. All laboratories should be using the current guidelines as stated.



Almost 1.5 million HbA_{1c} tests are performed annually in Ontario.

In summary, all laboratories are now reporting HbA_{1c}, as opposed to glycated hemoglobin. The precision of many methods has improved substantially and is now well below the recommended level of 5%. Laboratories need to review the concentrations of their HbA_{1c} controls to ensure adequate coverage over the reporting range. It is recommended that only NGSP certified methods be used, which would then justify the global adoption of the 1998 Canadian clinical practice guidelines for optimal, suboptimal and inadequate HbA_{1c} action limits.

Blood Gases

A blood gas challenge consisting of two ampoules of aqueous material was circulated to participating laboratories in May (C-0105-BG). Participants were asked to report results for pH,

Table 12. Summary of Results for pH, pCO₂ and pO₂ in Blood Gas Survey C-0105 (Range of Results is in Brackets)

Method	n	Vial X			Vial Y		
		pH	pCO ₂ mm Hg	pO ₂ mm Hg	pH	pCO ₂ mm Hg	pO ₂ mm Hg
All	274	7.16 (7.10–7.28)	68.1 (48–84)	68.7 (51–146)	7.41 (7.14–7.55)	43.0 (34–51)	103.8 (88–173)
Radiometer	147	7.15 (7.11–7.19)	68.3 (48–73)	71.2 (55–146)	7.41 (7.14–7.47)	43.0 (38–46)	105.8 (91–128)
Nova	57	7.18 (7.14–7.24)	67.6 (61–74)	62.6 (53–77)	7.43 (7.41–7.47)	43.1 (39–47)	99.6 (91–154)
Bayer	33	7.17 (7.10–7.19)	71.2 (65–84)	68.7 (51–92)	7.43 (7.45–7.55)	44.1 (39–51)	100.2 (88–120)
iSTAT	22	7.20 (7.19–7.28)	64.7 (52–69)	79.2 (73–129)	7.47 (7.45–7.55)	40.6 (34–46)	105.7 (97–173)
IL	11	7.15 (7.14–7.17)	69.1 (62–75)	64.2 (56–72)	7.39 (7.38–7.42)	43.3 (40–45)	104.6 (98–108)



**Table 13. Summary of Results for Sodium, Potassium, Glucose and Ionized Calcium in Blood Survey
(Range of Results is in Brackets)**

Method	n	Vial X				Vial Y			
		Sodium mmol/L	Potassium mmol/L	Glucose mmol/L	Ionized Calcium mmol/L	Sodium mmol/L	Potassium mmol/L	Glucose mmol/L	Ionized Calcium mmol/L
All	66	112.6 (103–114)	1.93 (1.6–2.2)	4.32 (3.8–4.8)	1.438 (1.23–1.65)	132.9 (128–137)	4.37 (4.2–4.8)	10.78 (9.5–11.6)	1.098 (1.00–1.19)
Nova	31	112.9 (112–114)	2.02 (1.9–2.2)	4.53 (4.2–4.8)	1.452 (1.23–1.65)	133.3 (129–136)	4.47 (4.2–4.8)	11.10 (10.6–11.6)	1.100 (1.02–1.16)
Radiometer	13	112.8 (111–114)	1.97 (1.9–2.1)	3.88 (3.8–4.0)	1.501 (1.32–1.56)	131.2 (129–133)	4.28 (4.2–4.3)	9.70 (9.5–10.1)	1.131 (1.00–1.19)
iSTAT	13	112.4 (112–113)	1.80 (1.8–1.9)	4.02 (4.0–4.1)	1.330 (1.30–1.36)	135.6 (135–137)	4.32 (4.3–4.4)	10.70 (10.5–10.9)	1.078 (1.07–1.09)
Bayer	9	109.4 (103–113)	1.81 (1.6–1.9)	4.23 (4.1–4.4)	1.405 (1.38–1.48)	130.1 (128–131)	4.33 (4.3–4.4)	10.90 (10.6–11.2)	1.073 (1.04–1.11)

pCO₂, pO₂, as well as sodium, potassium, glucose and ionized calcium from all instruments in use within their institution.

Results from 274 blood gas analyzers were generated from 160 hospitals. A maximum of 24 participants provided electrolyte, glucose and ionized calcium data. Tables 12 and 13 summarize the results of this survey. Twenty participants received correspondence requesting investigation of analytical performance, primarily of pO₂ measurement. Sample handling

issues appeared to be the principal underlying cause of these analytical errors.

Glucose data generated using Radiometer technologies illustrated a negative bias compared to other instruments and the AMM. Calibration of this instrument is based upon plasma standards, hence the aqueous materials used in the survey are subject to a matrix effect.

DRUG MONITORING

TESTING MODEL

The material used for the challenges in the five 2001 surveys continued to be, for the most part, previously frozen serum supplemented with specific drugs. Two urine pools were distributed for the “Drugs of Abuse” surveys. Whole blood samples were distributed for cyclosporine. Two samples were distributed for the drugs tested in each of the surveys. The drugs tested were:

D-0101	gentamicin, tobramycin, vancomycin, cyclosporine, tacrolimus
D-0103	ethanol, lithium, cyclosporine, drugs of abuse
D-0105	carbamazepine, phenobarbital, phenytoin, theophylline, valproic acid, digoxin, cyclosporine
D-0107	ethanol, acetaminophen, salicylate, lithium, cyclosporine
D-0110	carbamazepine, phenobarbital, phenytoin, theophylline, salicylate, digoxin, cyclosporine, tacrolimus, drugs of abuse

ASSESSMENT OF RESULTS

Computer flagging rules remained the same as in previous years (see 1998 Review). Before acting on any flagged result, the committee carried out a peer group assessment to examine contributing factors such as biases between methods. Reference results were provided for the drugs of abuse surveys.

LABORATORY PERFORMANCE

Carbamazepine, Phenobarbital, Phenytoin, Theophylline and Valproic Acid

Table 14 summarizes the results for carbamazepine, phenobarbital, phenytoin, theophylline, and valproic acid for surveys D-0105 and D-0110.

Overall performance of these tests appears to be good. However most laboratories are using similar methodology. Fluorescence polarization continues to be the method of choice for analysis of these drugs. Significant method biases were observed in some of these surveys with enzyme immunoassay results for phenytoin continuing to be higher than results from other technologies. Theophylline results for survey D-0110 were dramatically different from those observed in survey D-0105.

Table 14. Summary of Results for Carbamazepine, Phenobarbital, Phenytoin, Theophylline and Valproic Acid in Surveys D-0105 and D-0110

Survey	Analyte	No. of Labs	AMM (μmol/L)	SD	CV (%)	No. of Flags	No. of Letters
D-0105-A	Carbamazepine	71	41.6	3.0	7.1	3	1
D-0105-B	Carbamazepine	71	10.1	0.70	7.0	3	1
D-0110-A	Carbamazepine	71	37.9	2.1	5.5	2	0
D-0110-B	Carbamazepine	71	44.2	2.2	5.0	1	1
D-0105-A	Phenobarbital	61	184.3	7.5	4.1	2	2
D-0105-B	Phenobarbital	61	98.1	4.9	5.0	1	1
D-0110-A	Phenobarbital	58	101.3	5.6	5.5	5	2
D-0110-B	Phenobarbital	58	211.3	8.8	4.2	2	2
D-0105-A	Phenytoin	110	75.5	4.6	6.1	11	4
D-0105-B	Phenytoin	110	40.8	1.7	4.1	5	4
D-0110-A	Phenytoin	108	86.3	3.8	4.4	3	2
D-0110-B	Phenytoin	108	53.2	3.4	6.4	12	6
D-0105-A	Theophylline	79	122.9	5.2	4.2	4	2
D-0105-B	Theophylline	79	66.0	4.0	6.1	7	2
D-0110-A	Theophylline	76	69.7	6.9	9.9	20	2
D-0110-B	Theophylline	76	143.6	14.4	10.0	31	4
D-0105-A	Valproic Acid	54	415.0	20.0	4.8	0	0
D-0105-B	Valproic Acid	54	909.2	42.5	4.7	0	0



The results in Table 14 demonstrate that the interlaboratory CVs vary from 4%–7%. This indicates that a precision goal of 5% and a flagging limit of >10% is reasonable.

Digoxin

The results of surveys D-0105 and D-0110 are summarized in Table 15. The overall performance of digoxin testing is somewhat disconcerting. The large interlaboratory variability and significant method biases make it difficult to evaluate the results of these surveys.

Acetaminophen, Salicylate

Table 16 summarizes the performance of acetaminophen (survey D-0107) and salicylate in surveys D-0107 and D-0110. In general, testing of acetaminophen and salicylate is performed well.

Lithium

After years of observing significant method biases for lithium, the problem has apparently been resolved. The survey material is now serum based rather than plasma based. This change appears to have eliminated the positive bias observed for colorimetric methods and the negative bias for ISEs relative to flame photometry and atomic absorption (see Table 17).

Ethanol

The results of two ethanol supplemented samples distributed to 106 participants in two surveys are presented in Table 18. Performance was satisfactory.

Table 15. Summary of Results for Digoxin in Surveys D-0105 and D-0110

Survey	Analyte	No. of Labs	AMM (nmol/L)	SD	CV (%)	No. of Flags	No. of Letters
D-0105-A	Digoxin	133	0.88	0.15	16.7	42	5
D-0105-B	Digoxin	133	1.48	0.18	12.0	22	5
D-0110-A	Digoxin	133	1.24	0.22	18.3	58	8
D-0110-B	Digoxin	133	2.41	0.21	8.7	26	4

Table 16. Summary of Acetaminophen and Salicylate Results for Surveys D-0107 and D-0110

Survey	Analyte	No. of Labs	AMM	SD	CV (%)	No. of Flags	No. of Letters
D-0107-A	Acetaminophen	134	619.2 µmol/L	24.4	3.9	2	2
D-0107-B	Acetaminophen	134	215.0 µmol/L	8.5	4.0	14	7
D-0107-A	Salicylate	140	0.74 mmol/L	0.064	8.6	34	6
D-0107-B	Salicylate	140	1.42 mmol/L	0.082	5.8	21	6
D-0110-A	Salicylate	141	1.50 mmol/L	0.057	3.8	5	4
D-0110-B	Salicylate	141	2.25 mmol/L	0.086	3.8	6	4

Table 17. Summary of Lithium Performance in Surveys D-0103 and D-0107

Survey	Analyte	No. of Labs	AMM (mmol/L)	SD	CV (%)	No. of Flags	No. of Letters
D-0103-A	Lithium	89	1.11	0.052	4.7	2	0
D-0103-B	Lithium	89	0.83	0.056	6.7	9	1
D-0107-A	Lithium	88	1.06	0.04	3.9	2	2
D-0107-B	Lithium	88	1.59	0.05	3.4	2	2

Table 18. Summary of Ethanol Performance in Surveys D-0103 and D-0107

Survey	Analyte	No. of Labs	AMM (mmol/L)	SD	CV (%)	No. of Flags	No. of Letters
D-0103-A	Ethanol	106	29.3	1.02	3.5	5	5
D-0103-B	Ethanol	106	17.5	0.64	3.7	1	1
D-0107-A	Ethanol	106	38.3	1.8	4.6	5	3
D-0107-B	Ethanol	106	64.6	3.0	4.6	5	4

Table 19. Summary of Gentamicin, Tobramycin, Vancomycin Performance in Survey D-0101

Survey	Analyte	No. of Labs	AMM (mg/L)	SD	CV (%)	No. of Flags	No. of Letters
D-0101-A	Gentamicin	77	4.60	0.24	5.2	4	3
D-0101-A	Tobramycin	35	1.85	0.18	9.5	6	3
D-0101-A	Vancomycin	28	14.14	0.71	5.0	2	2
D-0101-B	Gentamicin	77	1.61	0.10	6.3	5	3
D-0101-B	Tobramycin	35	5.22	0.39	7.5	5	4
D-0101-B	Vancomycin	28	28.42	1.89	6.7	4	3

Gentamicin, Tobramycin, Vancomycin

The overall performance of gentamicin, tobramycin, and vancomycin testing is good (see Table 19). However attention should be paid to lowering the CVs around the concentrations corresponding to pre-dose or “trough” levels of these aminoglycosides.

Precision Goals

Precision goals for drug monitoring were published in June 2001 (Table 20). A patterns-of-practice

survey was distributed in December to find out if laboratories have adopted these precision goals. The information from the survey is currently being analyzed. Thirty-two participants indicated that they had changed the target SDs on one or more of the drugs analyzed in their laboratory.

Cyclosporine, Tacrolimus

QMP–LS offers cyclosporine surveys to Ontario laboratories as well as out-of-province laboratories. In 2001, there were 26 laboratories participating, 8 in Ontario, 4 in Quebec, 9 in British Columbia, and 1 each in Alberta, Saskatchewan, Manitoba, Nova Scotia, and New Brunswick. There are four analytical methods being used. Twelve laboratories use the Abbott TDx/TDxFLx, 8 use the Abbott AxSYM, 5 use EMIT reagents and 3 use Diasorin Cyclo-Trac. The group %CVs for each survey are given in Table 21. The number of participants is shown in brackets. Vial D-0101-1 is not included as the cyclosporine concentration was too low. The % biases of each method relative to the TDx/TDxFLx group (largest number of users) are given in Table 22. Surveys D-0107-1 and D-0107-2 had target amounts of cyclosporine weighed in. The % bias relative to these targets is given in brackets.

Fourteen laboratories participated in the tacrolimus surveys. There were 6 laboratories in Ontario, 1 in Alberta, 1 in Saskatchewan, 2 in British Columbia and 4 in Quebec. All use

Table 20. Precision Goals for Drug Monitoring

Drug	CV %
Acetaminophen	5.0
Carbamazepine	5.0
Digoxin	5.0
Ethanol	5.0
Gentamicin	5.0
Lithium	3.0
Phenobarbital	5.0
Phenytoin	5.0
Salicylate	5.0
Theophylline	5.0
Tobramycin	5.0
Valproic Acid	5.0
Vancomycin	5.0



Table 21. Group %CVs for Cyclosporine

Survey	TDx/TDxFLx		AxSYM		EMIT		Diasorin	
	CV %	(No.)	CV %	(No.)	CV %	(No.)	CV %	(No.)
D-0101-2	5.3	(12)	7.4	(8)	5.2	(5)	10.9	(3)
D-0103-1	3.9	(12)	7.4	(5)	6.5	(4)	24.6	(3)
D-0103-2	5.2	(12)	7.1	(7)	5.9	(4)	5.7	(3)
D-0105-1	5.4	(12)	11.4	(8)	12.7	(5)	3.2	(3)
D-0105-2	4.9	(12)	12.5	(8)	14.0	(5)	9.0	(3)
D-0107-1	13.2	(11)	16.6	(7)	4.0	(3)	7.5	(3)
D-0107-2	2.9	(11)	12.2	(6)	6.2	(4)	4.2	(3)
D-0110-1	4.9	(9)	5.6	(7)	7.8	(6)	2.3	(3)
D-0110-2	4.6	(9)	6.0	(7)	6.8	(6)	7.4	(3)

Table 22. Per cent Biases in Cyclosporine Results by Group Compared to TDx/TDxFLx Group

Survey	TDx/TDxFLx	AxSYM	EMIT	Diasorin
D-0101-2	0	-10.7%	-17.6%	-4.1%
D-0103-1	0	-16.1%	-3.1%	-2.7%
D-0103-2	0	-7.5%	-4.5%	-12.5%
D-0105-1	0	-14.6%	-18.2%	-22.2%
D-0105-2	0	-16.3%	-17.2%	-21.3%
D-0107-1	0 (+7.4%)	-12.7% (-6.2%)	-20.0% (-14.0%)	-10.6% (-4.0%)
D-0107-2	0 (+8.5%)	-11.1% (-3.6%)	-7.8% (0.0%)	+5.1% (14.1%)
D-0110-1	0	-13.3%	-17.5%	+0.5%
D-0110-2	0	-12.7%	-16.2%	-7.8%

the Abbott IMx method. The %CVs for the two survey vials are given in Table 23.

DRUGS OF ABUSE

Two drugs of abuse surveys were distributed in 2001. Urine drug screen samples were prepared from combined patient samples. The results are summarized in Table 24. Overall, performance is good for the testing of amphetamine, barbiturates, cocaine metabolites, opiates, and phencyclidine. A high rate of discrepant results was observed for benzodiazepines, cannabinoids, methadone, and tricyclic antidepressants.

Table 23. Precision for Tacrolimus Results

Survey	Mean	CV %
D-0101-1	10.87 µg/L	15.8
D-0110-1	7.13 µg/L	12.5

Table 24. Summary of Performance for Drugs of Abuse Surveys D-0103 and D-0110

Survey	Analyte	No. of Labs	Reference Result	No. of Positives	No. of Negatives
D-0103-DA-X	Amphetamine	80	Negative	0	80
D-0103-DA-Y	Amphetamine	80	Negative	0	80
D-0110-DA-X	Amphetamine	82	Positive	81	1
D-0110-DA-Y	Amphetamine	82	Negative	2	80
D-0103-DA-X	Barbiturates	85	Negative	0	85
D-0103-DA-Y	Barbiturates	85	Negative	1	84
D-0110-DA-X	Barbiturates	87	Negative	0	87
D-0110-DA-Y	Barbiturates	87	Negative	0	87
D-0103-DA-X	Benzodiazepines	84	Negative	10	74
D-0103-DA-Y	Benzodiazepines	84	Positive	63	21
D-0110-DA-X	Benzodiazepines	86	Positive	12	74
D-0110-DA-Y	Benzodiazepines	86	Positive	85	1
D-0103-DA-X	Cannabinoids	80	Positive	71	9
D-0103-DA-Y	Cannabinoids	80	Positive	73	7
D-0110-DA-X	Cannabinoids	82	Positive	79	3
D-0110-DA-Y	Cannabinoids	82	Negative	2	80
D-0103-DA-X	Cocaine Metabolites	84	Negative	0	84
D-0103-DA-Y	Cocaine Metabolites	85	Positive	85	0
D-0110-DA-X	Cocaine Metabolites	87	Negative	1	86
D-0110-DA-Y	Cocaine Metabolites	87	Positive	86	1
D-0103-DA-X	Methadone	20	Positive	14	6
D-0103-DA-Y	Methadone	20	Positive	14	6
D-0110-DA-X	Methadone	15	Positive	14	1
D-0110-DA-Y	Methadone	15	Negative	0	15
D-0103-DA-X	Opiates	82	Positive	81	1
D-0103-DA-Y	Opiates	81	Positive	1	80
D-0110-DA-X	Opiates	84	Positive	84	0
D-0110-DA-Y	Opiates	84	Positive	84	0
D-0103-DA-X	Phencyclidine	68	Negative	0	68
D-0103-DA-Y	Phencyclidine	68	Negative	0	68
D-0110-DA-X	Phencyclidine	69	Negative	0	69
D-0110-DA-Y	Phencyclidine	69	Negative	1	68
D-0103-DA-X	Tricyclic Antidepressants	63	Negative	4	59
D-0103-DA-Y	Tricyclic Antidepressants	63	Positive	14	49
D-0110-DA-X	Tricyclic Antidepressants	63	Negative	1	62
D-0110-DA-Y	Tricyclic Antidepressants	63	Negative	0	63

ENZYMES, CARDIAC MARKERS & LIPIDS

ENZYMES & CARDIAC MARKERS

TESTING MATERIAL

The survey material for amylase, lipase, and cardiac markers continued to be supplemented previously frozen fresh human serum. Reconstituted lyophilized human serum was used to test alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma glutamyl transferase (GGT) and lactate dehydrogenase (LD). EDTA plasma from single donors was distributed for the homocysteine surveys.

Fresh serum obtained from volunteer donors continues to be used for the lipid surveys.

The survey samples for enzymes, cardiac markers and lipids are packed with an ice-pack and distributed by overnight courier. Participants are instructed to analyze them within 24 hours of receipt and are permitted to include all samples in the same test run.

TESTING MODEL

Two enzyme and two cardiac marker surveys were conducted in 2001. Two of these surveys included challenges for myoglobin, troponin I and homocysteine. The enzymes and cardiac markers tested were as follows:

Z-0101	ALP, ALT, AST, GGT and LD
Z-0104	Total CK, CK-2, myoglobin, troponin I and homocysteine
Z-0106	Amylase and lipase
Z-0110	Total CK, CK-2, myoglobin, troponin I and homocysteine

Some of the computer flagging rules for accuracy and imprecision of enzyme results were changed this year and are shown in Table 25. The results reported for serum myoglobin, troponin I and homocysteine were reviewed manually for bias by the committee due to the small number of results reported.

LABORATORY PERFORMANCE

Total Creatine Kinase

Total CK results were received from 200 laboratories in survey Z-0104 and 199 laboratories reported in survey Z-0110. Ortho Diagnostics Vitros analytical systems are used by 67% of the participants to assay total CK. The next most popular instrument systems are Beckman Coulter and Hitachi systems.

The CVs for results from all methods ranged from 3.5%–5.3% for the ten challenges.

The reagent source means were within 10% of each other. Within-laboratory precision was excellent. Only six laboratories had a difference of >5% in the results between the duplicate vials in the two surveys.

The performance of total CK has remained stable. It is a reasonably robust assay, performed well in most of the laboratories. As long as it remains a cardiac marker, it will be monitored by QMP–LS.

CK-2

In October 2001 (survey Z-0110), 146 participants reported CK-2 results. Of these, 105 (72%) have followed the recommendation to use a mass method to measure CK-2. In October 2000, 66% of the participants used a mass method. Forty participants used the Vitros activity method and one laboratory used a Beckman Coulter CX4 system.

The CK-2 assays are not nearly as precise as the total CK assays. For example the CVs for the Ortho Vitros assay ranged from 7.5%–26.0% for the results on the ten challenges. The results reported from Abbott's microparticle enzyme immunoassay were lower with CVs ranging from 7.3%–13.3%.

In conclusion, the performance of the participating laboratories has been stable, representative of that of a mature assay. Although



CK-2 is becoming less important in the diagnosis of cardiac damage, it will be monitored by QMP-LS in the foreseeable future.

Serum Myoglobin

The number of participants measuring myoglobin increased in 2001. Twenty-one laboratories reported myoglobin results in October 2000. In the October 2001 survey results were received from 31 laboratories including six users of the Triage point-of-care device.

The instrument system means and diagnostic cutoffs are quite different, suggesting poor standardization across methods. Table 26 shows the upper limit of the reference range quoted for the various instrument systems.

Figure 12 displays the results reported for vial Z-0110-C. Four laboratories in the Triage group reported values below their diagnostic threshold of 170 µg/L for vial C, which is in disagreement with all other laboratories. The imprecision in the Triage results may be due to the survey samples being serum based rather than plasma based.

Six laboratories had a difference of >10% in the results reported for the set of duplicate vials in each of the two surveys.

The expansion of myoglobin testing is much slower than troponin I, consistent with the non-specificity of the test for cardiac damage. There continues to be significant differences among methods and in the decision thresholds.

QMP-LS will continue to monitor this assay closely. If the difference among methods continues, the effect on patient care must be questioned.

Troponin I

The number of laboratories reporting Troponin I has increased from 50 in October 2000 to 72 in October 2001. This represents a 44% increase. The Abbott AxSYM is used by 50% of the participants. The next largest group (20 participants)

Table 25. Revised Bias and Imprecision Flagging Rules

Analyte	Bias
Total CK	>10% from the Reagent Source Mean
Within-Run Precision	
ALP, AST, ALT, GGT, LD	Difference in results >5% or >4 U/L whichever is greater
Total CK	Difference in results >5%
CK-2, Amylase, Lipase	Difference in results >8%
Myoglobin, Troponin I	Difference in results >10%

Table 26. Myoglobin Upper Limit of Reference Range Quoted for the Instrument Systems

Instrument System	Upper Limit of Reference Range (µg/L)
Abbott AxSYM	116
Bayer ACS 180	110
Bayer ADVIA Centaur	110
Beckman Coulter Access	70
Biosite Triage	170
DPC Immulite	100
Hitachi 911	72
Roche Elecsys 2010	72

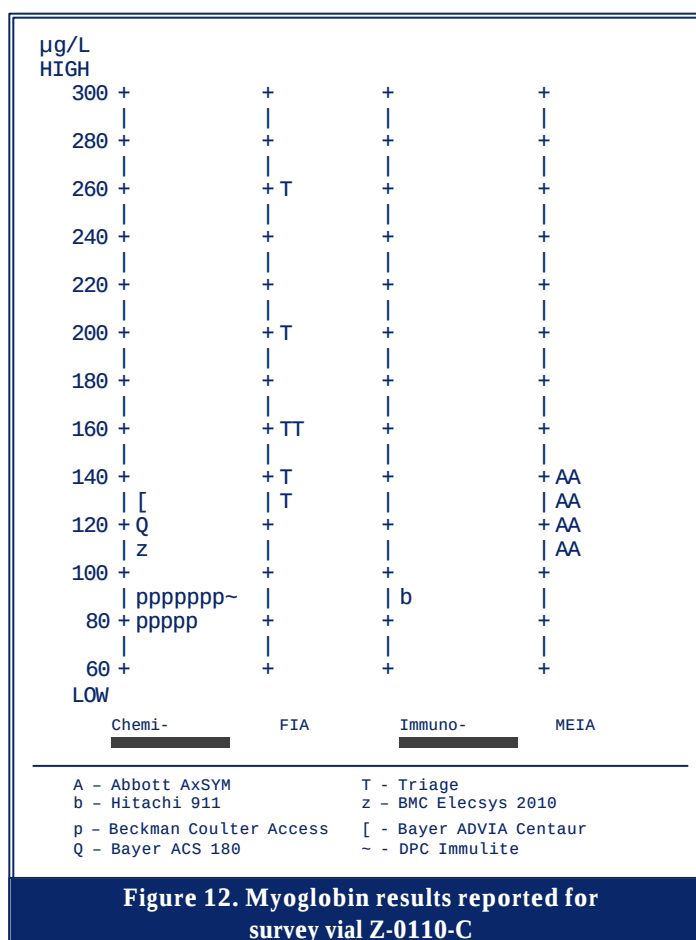


Figure 12. Myoglobin results reported for survey vial Z-0110-C

used the Beckman Coulter Access. The remaining 16 laboratories used six other analytical systems.

Within an analytical system, there was fair agreement in the results; however, the between-method agreement was poor as has been observed in the past and is largely due to the lack of a reference standard.

The concentration of troponin I in the duplicate vials in survey Z-0104 was low so it was difficult to judge precision. The duplicate vials in survey Z-0110 had higher levels. Fourteen laboratories had differences >10% in these results. Six of these received correspondence regarding imprecision.

Troponin I (and troponin T) is becoming the diagnostic test for cardiac damage. In January 2001, ten laboratories indicated they were testing troponin T and two others indicated that they were implementing troponin T in 2001. QMP-LS will continue to monitor troponin I. It continues to be a goal to have troponin T surveyed.

Homocysteine

Two surveys were conducted for homocysteine in April (Z-0104-HS) and October (Z-0110-HS). Two precision studies were included in the surveys. Vials Z-0010-HS-X and Z-0104-HS-X and vials Z-0010-HS-Y and Z-0110-HS-Y were the two sets of duplicates. The survey samples are EDTA plasma from single donors.

Ten laboratories participate in the surveys. Four different methods are used by the participants with five using the Abbott IMx method. The other methods used are high-performance liquid chromatography (HPLC) (3 users), DPC Immulite 2000 (1 user) and Tandem mass spectrometry (MS/MS) (1 user).

Figure 13 displays the results reported for vial Z-0110-HS-X. Variability in the results is greater amongst the HPLC users.

Three laboratories' results for the duplicate vials Z-0010-HS-Y and Z-0110-HS-Y differed by >10% although the AMMs were in agreement (10.1 mmol/L, 10.4 mmol/L).

The static number of participants suggests that demand for the test may have stabilized. If clinical trials on intervention show benefits to the patient, the workload may increase substantially. QMP-LS will continue to monitor the assay unless there is decline in the number of participants.

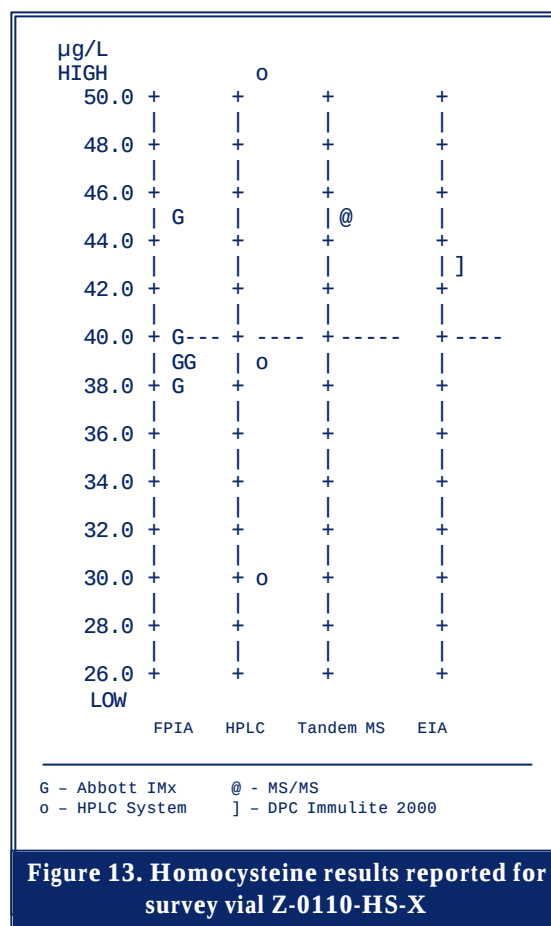


Figure 13. Homocysteine results reported for survey vial Z-0110-HS-X

AST, ALT, ALP, LD and GGT

Five vials containing AST, ALT, ALP, LD and GGT in reconstituted lyophilized human serum were sent to each participating laboratory for analysis in January (Z-0101). This included one set of duplicate vials for a precision study. Results were received from 212 participants for one or more of the enzymes tested in this survey.

Overall, performance on these enzymes has improved significantly over the years. Most laboratories were able to achieve a difference within 5% on both duplicate vials. On the basis of excellent year after year performance, the committee recommended lowering the imprecision flagging limits from >10% to >5% in future surveys.

As has been the picture for the last several years, Ortho Clinical Diagnostics, Beckman Coulter and Roche (BMC) systems seem to dominate the above enzyme analysis in the Ontario laboratories. More than 50% of the participating laboratories

use an Ortho Vitros analyzer. We continue to see wide variation in activity values of these enzymes between various systems (between-system variation) that is not always reflected in the reference range. Variation of results within the system is on acceptable level for most analyzers.

In general, error rates on all of the above enzymes were quite low with only nine laboratories receiving correspondence regarding performance. However, the committee has expressed concerns over varying reference ranges and has suggested that participants validate vendor or literature published reference ranges with their own data collected over time from healthy individuals.

Amylase and Lipase

Five vials containing previously frozen human serum supplemented with amylase and lipase were distributed in June (Z-0106). This survey included two sets of duplicate vials for precision studies. Amylase was reported by 192 laboratories and lipase by 38 participants.

The precision results were quite impressive. Ninety-nine per cent of the laboratories achieved a difference of <8% in the amylase results reported for the duplicate vials. Only one laboratory had a difference of >8% in the lipase results reported for one set of duplicates.

The Ortho Vitros systems dominated the amylase analysis with 127 of the total 192 laboratories using this method. Beckman Coulter (27) and Hitachi (22) systems were the second most commonly used methods for amylase. One laboratory reports results for pancreatic amylase rather than total amylase.

Lipase is a less commonly used assay with only 38 laboratories reporting in the survey. Of the 38 laboratories, 23 (61%) used the Ortho Clinical Diagnostics Vitros assay. Of the remaining 15 laboratories, 8 used Hitachi systems and the remaining 7 laboratories used one of the Beckman Coulter (4) or Dade Behring (1) and Roche Cobas

Integra (2) systems. All laboratories used lipase reagents supplied by their instrument vendor except one Beckman user who used DCL reagents. All but one of the laboratories used rate reaction methods for lipase.

Just like other enzymes, we continue to see between-system variation in values of both amylase and lipase, that is not always reflected in the reference range. Amylase results by Beckman and Roche methods were 2 times and 1.5 times the Ortho values, respectively. However, this difference was not seen in the upper reference limits, which were quite similar for all three systems.

LIPIDS

TESTING MATERIAL

Fresh human serum was collected from four donors for each survey. To closely duplicate the samples analyzed in Ontario laboratories, the samples were shipped on ice (not frozen) by overnight courier. All laboratories received the samples within two days of shipment.

Two reference laboratories (Wadsworth Center for Laboratories and Research, New York State Department of Health, Albany, New York and the Reference Laboratory, Ortho Clinical Diagnostics Inc., Rochester, New York) analyzed aliquots of each sample for cholesterol and HDL-cholesterol. Triglycerides were determined at only one reference laboratory.

TESTING MODEL

Three lipid surveys were carried out, in January, June and October. Each laboratory received samples from two donors. The groups were evenly divided so that each group contained approximately equal numbers of laboratories measuring cholesterol and triglycerides only, and those measuring cholesterol, triglycerides and HDL-cholesterol (and subsequently calculating LDL-cholesterol)

LABORATORY PERFORMANCE

Tables 27 and 28 present the results of the three surveys. These tables include:

- ♦ the AMM calculated from the results submitted
- ♦ the AMM calculated without the results from laboratories using Ortho instruments
- ♦ the AMM from laboratories using Ortho instruments
- ♦ the reference laboratories' values

Table 27. Comparison of the Reference Laboratories' Results and the Various Means (mmol/L) for Cholesterol and HDL-cholesterol for the 2001 Survey Samples

	Z-0101				Z-0106				Z-0110			
	Group 1		Group 2		Group 1		Group 2		Group 1		Group 2	
	Vial 1	Vial 2	Vial 1	Vial 2	Vial 1	Vial 2	Vial 1	Vial 2	Vial 1	Vial 2	Vial 1	Vial 2
Cholesterol												
Reference Lab. A	...	...	...	...	5.03	7.79	5.12	5.07	6.06	4.13	4.12	5.69
Reference Lab. B	6.48	5.69	5.49	4.89	4.95	7.76	5.10	5.05	5.95	4.03	4.06	5.61
All-methods' Mean	6.60	5.72	5.41	4.92	4.98	7.72	4.92	5.02	6.06	4.07	4.11	5.78
All-methods' Mean (w/o Ortho)	6.58	5.72	5.53	4.91	5.06	7.92	5.06	5.05	6.02	4.15	4.14	5.76
Ortho Mean	6.62	5.72	5.34	4.92	4.91	7.58	4.85	5.01	6.09	4.02	4.09	5.80
HDL-cholesterol												
Reference Lab. A	...	...	...	...	0.99	2.34	2.67	1.21	1.01	1.77	1.30	0.76
Reference Lab. B	1.21	1.11	1.84	0.96	1.14	2.44	2.76	1.21	0.94	1.72	1.23	0.68
All-methods' Mean	1.25	1.09	1.81	1.00	1.01	2.43	2.57	1.24	1.02	1.78	1.30	0.75
All-methods' Mean (w/o Ortho)	1.23	1.09	1.79	0.97	1.02	2.34	2.57	1.19	1.00	1.75	1.27	0.73
Ortho Mean	1.27	1.09	1.83	1.03	1.00	2.53	2.58	1.27	1.04	1.80	1.33	0.77

Table 28. Comparison of the Reference Laboratory Results and Various Means (mmol/L) for Triglycerides for the 2001 Survey Samples

	Z-0101				Z-0106				Z-0110			
	Group 1		Group 2		Group 1		Group 2		Group 1		Group 2	
	Vial 1	Vial 2	Vial 1	Vial 2	Vial 1	Vial 2	Vial 1	Vial 2	Vial 1	Vial 2	Vial 1	Vial 2
Triglycerides												
Reference Lab. B	2.31	2.19	1.23	2.90	3.33	1.07	0.95	1.77	1.35	1.08	1.59	2.99
All-methods' Mean	2.33	2.00	1.24	2.87	3.39	1.06	0.92	1.76	1.37	1.12	1.70	3.06
All-methods' Mean (w/o Ortho)	2.28	2.00	1.19	2.76	3.34	1.01	0.87	1.68	1.32	1.05	1.61	2.96
Ortho Mean	2.36	2.00	1.26	2.93	3.43	1.08	0.94	1.79	1.40	1.16	1.74	3.10

The AMMs with and without the Ortho values are presented because a skewing of the AMM is occasionally noted as a result of the large number of Ortho systems.

The committee has recommended that for the 2002 surveys, the mean of the two results of the reference laboratories will

be used for flagging cholesterol and HDL-cholesterol if the two agree within 3%. In cases where the difference is greater than 3%, the AMM will be used. The reference laboratory values for triglycerides will also be used in the 2002 surveys.

Figure 14 presents the percentage of cholesterol, triglycerides, and HDL-cholesterol results that were flagged from 1991 to 2001 against the AMMs. The flagging percentages for 2001 are, cholesterol: 4.2%, triglycerides: 7.4%, and HDL-cholesterol: 9.8%. These percentages are similar to previous years' although triglyceride flags increased from 5.6% in 2000 to 7.4% in 2001.

In July 2001, the committee conducted a lipids patterns-of-practice survey. This survey was designed to gather information with respect to instruments in use, guidelines for interpretation of results, workload, patient report format and

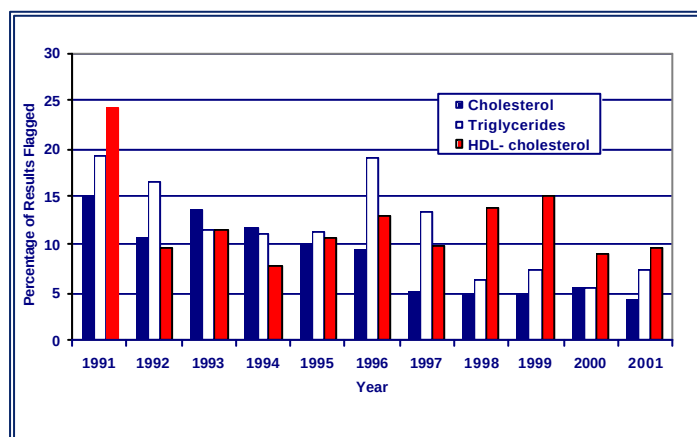


Figure 14. Comparison of the percentage of results flagged for cholesterol, triglycerides and HDL-cholesterol from 1991–2001

content, and quality control (QC). One hundred fifty-two participants responded to this questionnaire.

Table 29 tabulates the different methods in use in the province for the measurement of lipids. Ortho Vitros instruments are used in nearly two thirds of the laboratories measuring lipids. A direct method is used to measure HDL-cholesterol by 56% of the laboratories.

The testing volume for lipids in Ontario laboratories ranges from three to over one hundred thousand per month. The approximate annual volumes of lipid tests in Ontario are cholesterol: 4 255 000, triglycerides: 4 067 000, and HDL-cholesterol: 3 530 000. Private laboratories perform 85% of the lipid testing in Ontario.

Slightly over half of Ontario laboratories (55%) report reference intervals or target values only, without interpretive guidelines, on their patient reports, while 45% include interpretive guidelines. The Canadian Working Group on Hypercholesterolemia and Other Dyslipidemias and the United States' National Cholesterol Education Program have both recently released new guidelines for lipid interpretation. Both of these groups have

Table 29. Instrument Systems Used for Lipid Analysis

Instrument System	Cholesterol	Triglycerides	HDL-cholesterol
Hitachi 717, 911, 917, 902 and Modular	23	23	18
Beckman Coulter CX4, LX20	24	24	22
Ortho Vitros 250, 500, 700, 750, 950	94	94	59
Dade Behring AR, RxL	5	5	5
Roche Integra 700	3	3	4
Abbott Aeroset	1	1	1
Bayer ADVIA	1	1	1
Bayer RA	1	1	1
Total	152	152	111

recommended the use of target values based on an individual's risk factors as opposed to reference values for the general population. Laboratories will need to re-examine their reporting practices in the light of these two documents. Those that continue to report reference intervals should consider the use of target values.

Improvement was noted in the percentage of laboratories using QC material with concentrations near clinical decision points for triglycerides and HDL-cholesterol. Less improvement was noted for the cholesterol QC material.

ENDOCRINOLOGY

TESTING MODEL

Five surveys were distributed in 2001. Each included two vials of lyophilized human serum and two fresh serum donor samples in order to test a specific clinical state. The analytes tested are shown in Appendix I (p. 102). Beginning with the September 2001 (R-0109) survey, DHEA-S was removed from the testing menu due to lack of suitable testing material.

One patterns-of-practice survey on serum ferritin was distributed in August.

The analytes tested using the fresh serum by survey are shown in Table 30. Surveys R-0102 and R-0111 contained the same samples.

ASSESSMENT OF RESULTS

The computer flags for bias and imprecision remained the same as in previous years. However, during 2001 the committee reviewed the intersurvey precision flagging rules and plans to introduce changes in 2002. The committee reviews all results flagged by the computer before any action is taken.

ANALYTICAL PERFORMANCE

The number of laboratories participating decreased by 2.4% in 2001. Table 31 displays the number of participants reporting for each analyte tested in the last survey of 2000 and 2001 and the instrument systems in use.

It is noteworthy that:

- ✓ The use of radioisotopic methods has decreased for testosterone and has been phased out for cortisol.

- ✓ The use of the Abbott IMx continues to decrease while there is increased usage of the Abbott Architect, Roche Elecsys, Beckman Coulter Access and Bayer ADVIA Centaur instrument systems.
- ✓ The number of laboratories testing total PSA has increased by 11%. The same is evident with free PSA where the number of participants increased by 56%.

ACCURACY (BIAS)

The number of computer flags for accuracy on the lyophilized samples and the number of laboratories receiving correspondence are shown in Table 32. Vitamin B₁₂ and serum folate results received the most flags, but very few warranted correspondence from the committee.

There was a total of 8156 challenges during 2001 with 60 (0.7%) results flagged by the computer for bias. Correspondence was sent regarding 47 (0.3%) of the flagged results.

INTERSURVEY IMPRECISION

Each survey contained at least one intersurvey imprecision study in 2001. Six studies were conducted using the lyophilized material and two used fresh serum samples. On the whole performance was satisfactory.

Steroid and Pituitary Hormones

This area of testing was challenged on two occasions (R-0102 and R-0111) using duplicate

Table 30. Analytes Tested Using Fresh Serum in 2001 and the Clinical Histories

Survey	Clinical History	Analytes Tested
R-0102-1 & R-0111-1	59-year-old healthy postmenopausal female	Total testosterone, FSH, LH and estradiol
R-0102-2 & R-0111-1	53-year-old healthy male	Total testosterone, FSH, LH and estradiol
R-0104-1	Biopsy-proven prostate cancer	Total and free PSA
R-0104-2	Mild benign prostatic hypertrophy	Total and free PSA
R-0106-1	Euthyroid donor	TSH
R-0106-2	Female	Ferritin
R-0109-1	Untreated hyperthyroid disease	TSH, total T ₃ , free T ₄ and free T ₃
R-0109-2	Untreated hypothyroid donor	TSH, total T ₃ , free T ₄ and free T ₃

Table 31. Instrument Systems Used by Participants in 2000 and 2001*

Analyte	Abbott AxSYM		Abbott IMx		Abbott Architect		Bayer Immuno 1		Bayer ACS 180		Bayer Advia Centaur		Beckman Coulter Access		Gamma Counter		Ortho Vitros Eci		Roche Elecsys		Others†		No. of Participants	
	2000	2001	2000	2001	2000	2001	2000	2001	2000	2001	2000	2001	2000	2001	2000	2001	2000	2001	2000	2001	2000	2001	2000	2001
AFP	4	3	1	1	1	1	7	5	...	...	1	2	1	1	...	...	...	...	1	3	1	1	16	17
CG	42	43	8	5	3	4	3	1	1	1	1	1	15	17	...	...	3	3	2	4	1	1	80	80
Cortisol	...	...	...	...	...	...	4	2	3	1	1	2	6	5	1	...	1	1	...	3	11	10	27	24
Estradiol	6	4	1	...	...	...	2	...	...	...	1	1	...	...	5	5	1	1	1	6	3	...	21	20
Ferritin	29	28	12	6	3	4	5	2	2	1	3	5	15	16	...	...	4	3	3	6	4	4	80	75
Folate	14	15	11	5	...	...	2	2	1	...	1	1	12	11	6	6	...	...	1	2	4	3	52	45
FT ₄	37	32	11	7	2	4	5	3	2	1	4	5	11	13	...	...	4	3	6	9	1	3	83	80
FT ₃	10	8	1	...	2	3	...	...	4	1	1	3	...	...	...	...	...	...	1	3	...	...	19	19
FSH	11	8	4	1	3	4	4	2	2	1	2	4	2	3	...	...	3	3	3	4	3	3	37	33
LH	11	8	3	1	3	4	4	2	2	1	2	4	2	3	...	...	3	3	3	4	3	3	36	33
Progesterone	...	...	...	...	3	4	2	...	...	...	1	1	...	1	2	2	...	...	3	5	3	3	14	16
Prolactin	12	8	2	...	3	4	4	2	1	1	2	3	...	...	...	...	2	3	2	4	3	3	33	31
Total PSA	19	21	6	6	...	...	5	3	1	1	1	1	7	8	...	...	...	...	3	5	2	3	44	49
Free PSA	3	4	...	...	...	...	...	...	1	1	...	...	1	1	...	...	...	...	1	3	3	3	9	14
Testosterone	...	...	...	...	3	3	4	2	2	1	1	2	...	...	5	2	1	1	1	4	1	1	18	17
TT ₃	11	8	1	1	3	4	1	1	...	...	...	...	1	...	...	...	2	2	2	2	1	1	22	19
TSH	43	37	26	19	2	4	5	3	2	1	3	4	17	20	...	...	3	4	8	10	5	5	114	107
Vitamin B ₁₂	22	18	11	6	3	4	2	2	...	...	2	2	20	21	3	3	...	...	1	3	4	4	68	63

* Figures are taken from the last survey in 2000 and 2001.

† The "Others" column includes Abbott TDx, DPC Immulite & Immulite 2000, Dade Behring Dimension Rxl & xL, Wallac Autodelphia and Hitachi Systems.

Table 32. Number of Accuracy Computer Flags and Committee Correspondence for the 2001 Surveys (Lyophilized Material)

Analyte	No. of Participants		Total No. of Challenges	Flags		Correspondence	
	R-0102	R-0111		No.	(%)	No.	(%)
TT ₃	20	19	240	1	0.4	1	0.4
TSH	110	107	1411	2	0.1	4†	0.3
FT ₄	81	80	966	1	0.1	...	...
FT ₃	19	19	228	...	...	1†	0.4
Vitamin B ₁₂	65	63	647	23	3.6	3	0.5
Folate	51	45	478	11	2.3	4	0.8
Ferritin	78	75	840	8	0.9	6	0.7
Cortisol	26	24	248	...	...	...	...
Testosterone	17	17	172	...	...	...	...
FSH	35	33	356	1	0.3	1	0.3
LH	35	33	356	5	1.4	2	0.6
Prolactin	32	31	324	...	...	...	...
CG	77	80	796	8	1.0	...	...
Progesterone	15	16	154	...	...	...	...
AFP	17	17	322	...	...	1†	0.3
Estradiol	21	20	534	...	...	1†	0.2
DHEA-S	14	...	84	...	...	...	...

* DHEA-S was removed from the testing menu beginning with survey R-0109.

† Results are reviewed manually by the committee when there are <10 results in a peer group and correspondence may be recommended.

material (Table 30). Laboratories were requested to assay testosterone, FSH, LH and estradiol levels.

The steroid hormones (testosterone and estradiol) showed marked variation among different methods, particularly estradiol. Figure 15 displays the testosterone results reported for the female sample R-0111-1. The testosterone results reported by the three Abbott Architect users (3.9–4.4 nmol/L) demonstrate a positive bias compared to results from other methods. This bias was also apparent when this sample was tested in February 2001 (R-0102-1), but is not evident with the male sample. There were no testosterone intersurvey precision flags on the two samples.

Twenty laboratories reported estradiol results using nine different instrument systems. The performance on the estradiol assay is of concern to the committee. Figures 16A and 16B display the estradiol results reported on the lyophilized serum vial R-0111-A (AMM 93.5 pmol/L) and the fresh serum vial R-0111-1 (AMM 73.5 pmol/L). The results on the fresh serum sample are no better than the results on the lyophilized serum, indicating the performance is not a function of the testing material.

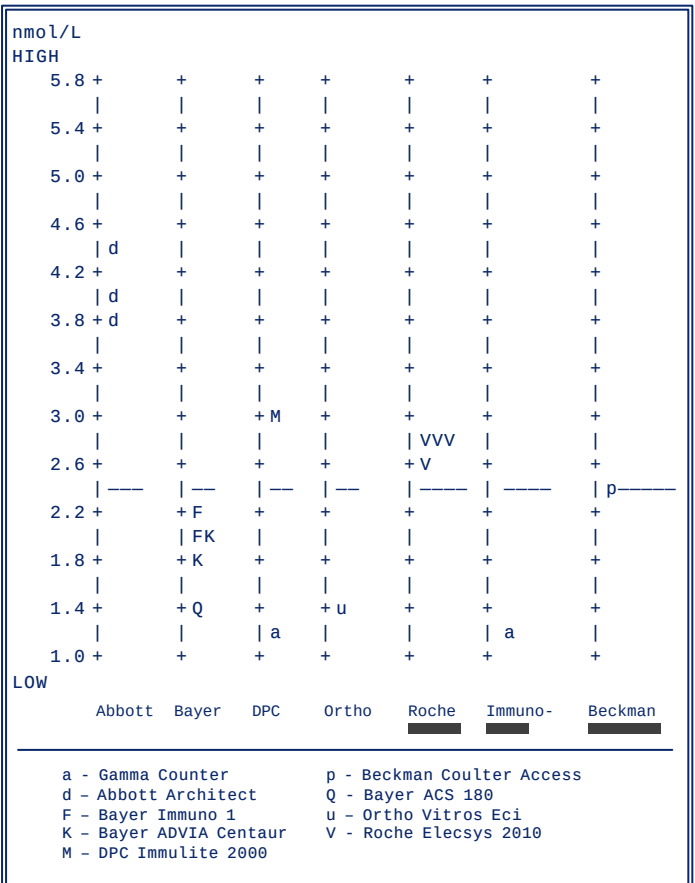


Figure 15. Testosterone results reported for vial R-0111-1

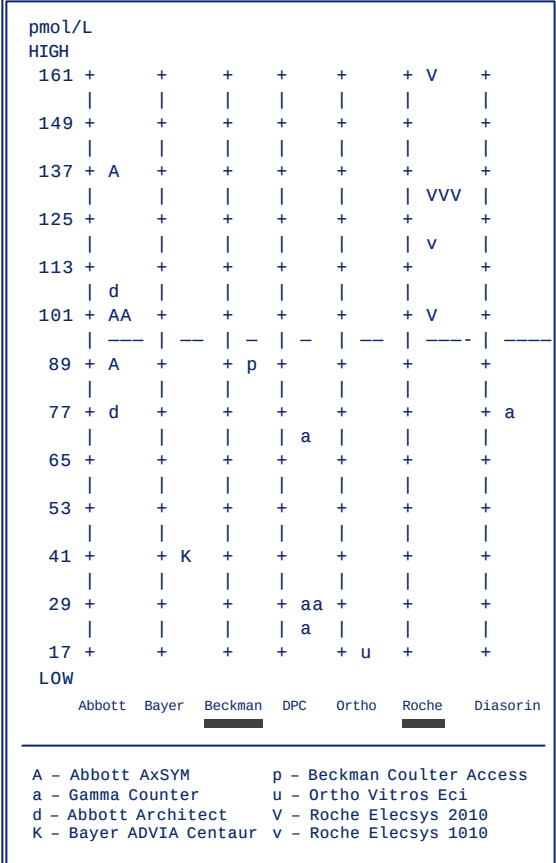


Figure 16A. Estradiol results reported for vial R-0111-A

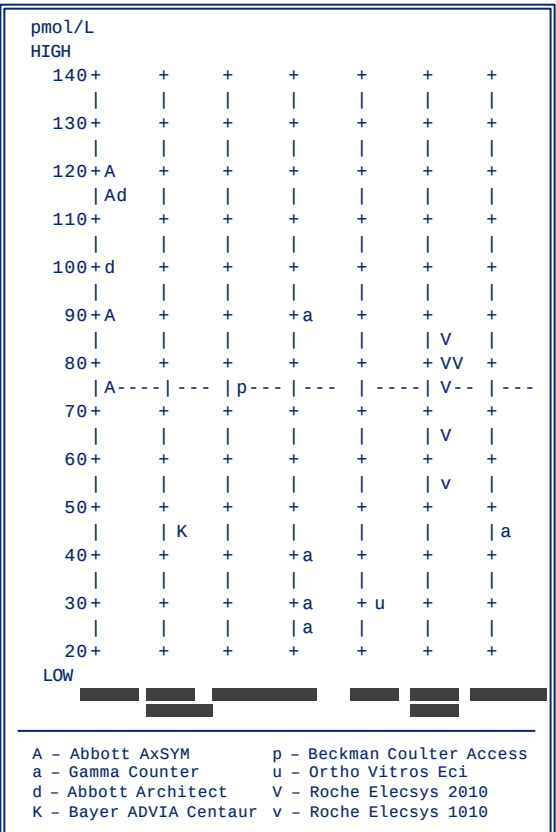


Figure 16B. Estradiol results reported for vial R-0111-1

Five laboratories received correspondence for imprecision of the estradiol results reported on the fresh serum samples R-0102-2 and R-0111-2. The committee will continue to evaluate estradiol performance in the 2002 testing cycle.

The pituitary hormones, FSH and LH, demonstrated almost perfect agreement between methods on the fresh serum samples. Figure 17 displays the FSH results for survey vial R-0111-1 that had an AMM of 46.0 IU/L. The results were all within the postmenopausal reference range.

Thyroid Hormones

In 2001, there were two surveys (R-0106 and R-0109) in which fresh donor sera were distributed for thyroid testing. Survey vial R-0106-1 was a specimen from a euthyroid female donor and was tested for TSH by 109 laboratories. The all-methods' median (AMM) was 2.9 mU/L.

As shown in Table 33 there are significant method differences, although the results within individual methods appear to be in good agreement. Abbott, Beckman Coulter and Roche – the main systems used – appear to give similar results. Bayer, Ortho and Dade Behring results were higher, while the DPC Immulite

2000 results were lower. These differences are not reflected in the reference ranges quoted by the participants as most report an upper limit of 5.0 mU/L.

Of the 458 results submitted only four (0.9%) were flagged, a testimony to the high standard of performance shown in thyroid function testing. Of interest was the group of three Abbott Architect analyzers that reported lower free T₃ results (range 7.7–7.9 pmol/L) for vial R-0109-1. The range of results for the other methods was 9.7–12.4 pmol/L (Table 34). Although these low results are consistent with the patient's clinical status, the bias was significantly different from other Abbott systems and was not apparent in the results for the lyophilized material. An explanation has been sought from the manufacturer. Of note is that 12 out of 38 AxSYM users continue to report TSH results as <0.1 mU/L even though the analyzer is capable of reporting down to a level of <0.05 mU/L.

Table 33. Range of TSH Results Reported by Instrument Manufacturer for Survey Vial R-0106-1

Instrument Manufacturer	Number of Results	Range of Results (mU/L)
Abbott	62	2.3–3.2
Bayer	8	3.1–3.8
Beckman Coulter	20	2.7–3.3
Dade Behring	3	3.1–3.5
Diagnostic Products (DPC)	2	2.1–2.3
Ortho	4	3.3–3.5
Roche	10	2.6–3.3

Table 34. Summary of Results for Survey Vials R-0109-1 and R-0109-2

Analyte	Reporting Units	No. of Results	No. of Instrument Systems	Vial	All-methods' Median	Range of Results	No. of Results Flagged
TSH	mU/L	108	12	1	0.02	0.0–0.37	2
		108	12	2	37.4	29.2–60.3	1
FT ₄	pmol/L	82	12	1	27.0	21–32	...
		82	12	2	5.0	2–7	...
FT ₃	pmol/L	19	6	1	10.2	7.7–12.4	1
		19	6	2	2.3	1.5–2.8	...
TT ₃	nmol/L	20	7	1	2.8	2.2–3.4	...
		20	7	2	0.6	0.4–1.0	...



Thyroid Precision Studies

In 2001 there were six duplicate sets of lyophilized material distributed for the assessment of intersurvey imprecision in thyroid function testing:

R-0102-A and R-0004-B

R-0111-A and R-0102-B

R-0104-B and R-0009-A

R-0104-A and R-0109-A

R-0106-A and R-0006-A

R-0106-B and R-0011-A

Results from four of these studies are shown in Table 35.

It is clear from Table 35 that the number of flags for thyroid tests was low attesting once again to the high standard of performance that was noted with fresh material. Based on the current flagging rules there were 2 flags for TSH and free T_3 , 3 for free T_4 and 1 for total T_3 . The current precision flagging rules may be outdated and may be incompatible with the improving standard of performance for thyroid tests. A review of past performance for several analytes suggests that laboratories can now easily meet these rules. In 2002 new rules will be established in keeping with the analytical goals defined by current technology.

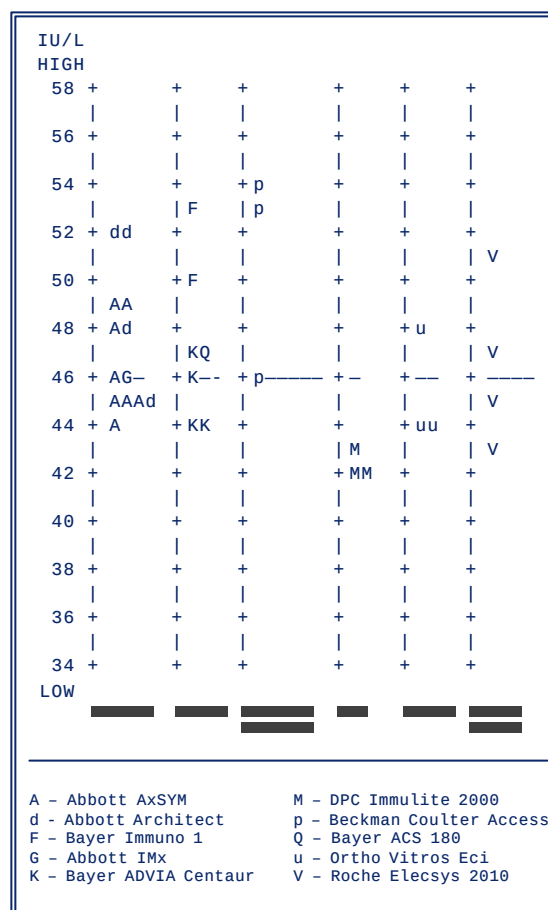


Figure 17. FSH results reported for vial R-0111-1

Table 35. Results of Four Precision Studies for Thyroid Tests Using Lyophilized Serum

Precision Studies	Units	TSH mU/L	FT ₄ pmol/L	FT ₃ pmol/L	TT ₃ nmol/L
R-0102-A, R-0004-B	Median	16.1	31	17.9	3.6
	(No. of Results)	(96)	(71)	(14)	(19)
	Difference Flagged	4.0	8	4.5	0.7
	No. of Flags	2	3	0	0
R-0111-A, R-0102-B	Median	0.12	5	3.9	1.5
	(No. of Results)	(96)	(69)	(14)	(17)
	Difference Flagged	0.25	5	1.0	0.5
	No. of Flags	0	0	1	0
R-0104-B, R-0009-A	Median	0.40	6	2.3	0.9
	(No. of Results)	(91)	(66)	(15)	(20)
	Difference Flagged	0.25	5	1.0	0.5
	No. of Flags	0	0	0	0
R-0104-A, R-0109-A	Median	2.4	12	11.2	4.0
	(No. of Results)		(78)	(17)	(19)
	Difference Flagged	0.60	5	2.8	0.8
	No. of Flags	0	0	1	1

Ferritin

Survey R-0106 contained two lyophilized serum vials (vials A and B) and a fresh serum vial (vial 2). Seventy-six laboratories reported results. The AMMs were: vial A—137 µg/L, vial B—48.5 µg/L and 40.0 µg/L for vial 2, the fresh serum vial. The spread in results among the five most common methods (Abbott, Beckman Coulter, Bayer, Roche and Diagnostic Products Corporation) was around 20%, 30% and 30% for the three vials respectively. Between-method differences were very similar for vial B (lyophilized) and vial 2 (fresh serum), which indicates no matrix affect with the lyophilized material. Differences were more marked for vial A, the higher concentration, suggesting that calibration differences may be the main cause.

Precision was also assessed in this survey. R-0106-A was a repeat of R-0006-A. The flagging level was 34 µg/L (medians 137 µg/L and 135 µg/L), and only one laboratory exceeded the allowed limit with results of 94 µg/L and 129 µg/L. This was the result of failure to notify QMP-LS of a change of instrument between surveys. R-0106-B was a repeat of R-0011-A (AMM 49 µg/L and 48 µg/L respectively), and no laboratory exceeded the flagging level of 12 µg/L.

FERRITIN PATTERNS-OF-PRACTICE SURVEY

In August 2001, Ontario clinical laboratories were surveyed about ferritin patterns of practice, and 75 responses were obtained. The results of this survey confirm the high standard of good laboratory practice in the province. Concerns were raised in only relatively few instances, which are discussed. The committee has concerns over maintaining proficiency in the few laboratories reporting workload as low as five patient samples per month. The estimated annual test volume for ferritin based on the data submitted on the questionnaire is 1 232 000 patient tests.

The shift to fully automated, non-isotopic detection methods has probably led to better reproducibility within each laboratory. Most

laboratories use quality control (QC) materials from companies other than their instrument manufacturer. However, only 20 of 75 laboratories (27%) reported using QC material with a mean value ≤ 20 µg/L — an important clinical decision area. Most laboratories, therefore, do not meet the earlier QMP-LS recommendation in this area (see Endocrinology Binder, Committee Comments, August 1994).

Analytical precision was generally good, with median between-day CVs for three levels of QC being less than 6.5%. However, the range of these CVs went from excellent (around 2%) to unacceptable (15%–20%). Those laboratories with CVs >10% need to review their practices.

Only seven laboratories used an elevated MCV to “trigger” a ferritin measurement, and their trigger points were quite different. Most (38) reported population-based reference intervals quoted in the manufacturers’ literature. Only 20 laboratories reported reference intervals for pediatric samples. More disturbing was the fact that lower and upper reference limits were often very different within the same method, which is a cause for concern.

TOTAL PROSTATE-SPECIFIC ANTIGEN (PSA) AND FREE PSA

Two vials of fresh serum were distributed in survey R-0104 for measurement of total and free PSA. Results were reported by 49 participants. Vial R-0104-1 was previously analyzed in survey R-0002 (vial R-0002-2). The total PSA AMMs for this sample were 11.2 µg/L (February 2000) and 10.8 µg/L (April 2001). The AMM for vial R-0104-2 was 1.5 µg/L. Figure 18 displays the results reported for vial R-0104-1.

The spread in results for this vial was almost as much for the most common method (Abbot AxSYM) as it was for all methods except one. The Beckman Coulter Access results for this sample continue to be the highest of all as a group even though the Hybritech method has been adapted to the Access. However, the spread in the results is smaller at 1.7 µg/L compared with 2.5 µg/L for the Abbott AxSYM results. There were no flags for imprecision in the results reported for the duplicate vials. A difference in the results of ≤ 1.8 µg/L was achieved by 35 of the 36 laboratories in the precision study.

Free PSA results were reported by 14 laboratories. The AMM (0.9 µg/L) for vial R-0104-1 did not change between February 2000 (vial R-0002-2) and April 2001. The AMM for vial



R-0104-2 was 0.20 µg/L. The results for vial 1 ranged from 0.7 to 1.1 µg/L. The range of results reported by the largest user group (Abbott) was almost as wide (0.8–1.1 µg/L). Five laboratories that reported results on the duplicate vials achieved a difference of ≤0.2 µg/L in the results.

In general, total PSA and free PSA are performed reasonably well by the different methods. However, the committee has some concerns about the between-method differences for total PSA. Universal adoption of the World Health Organization calibrator (90:10 total:free PSA) may assist in reducing these differences.

In 2002, the committee will introduce revisions to the precision flagging rules and investigate the estradiol assay further.

µg/L						
HIGH						
14.0 +	+	+	+	+	+	+
13.5 +	+	+ pp	+	+	+	+
13.0 +	+	+ p	+	+	+	+
12.5 +	+	+ pp	+	+	+	+
		p				
12.0 +	+	+ pp	+	+ V	+	+
A	F					
11.5 + GGd	+	+	+	+	+	+
AAAAA						
11.0 + d	+ FF	+	+	+ Vv	+	+
AA--	---	----	---	---	c--	---
10.5 + AAAAAAGG	+	+	+ M	+	+	+
AAAG						
10.0 + A	+	+	+	+	+	+
AA	K			V		J
9.5 + AG	+	+	+	+ v	+	+
A						
9.0 +	+	+	+	+	+	+
8.5 +	+	+	+	+	+	+
8.0 +	+	+	+	+	+	+
LOW						
	Abbott	Bayer	Beckman Coulter	DPC	Roche (BMC)	Hybritech Wallac
A - Abbott AxSYM c - Hybritech Photon ERA d - Abbott Architect F - Bayer Immuno 1 G - Abbott IMx K - Bayer ADVIA Centaur M - DPC Immulite 2000 p - Beckman Coulter Access v - Roche Elecsys 1010 V - Roche Elecsys 2010 J - Wallac Autodelphia						

Figure 18. Total PSA results reported for vial R-0104-1

IMMUNOLOGY

TESTING MODEL

The analytes tested (see Appendix I, p. 102) remained the same as in 2000. Five surveys, each containing one vial of serum were distributed over the year. All samples were fresh serums obtained from a commercial source. The disease state samples distributed this year were:

L-0102	IgM kappa monoclonal protein
L-0104	Positive ANA, centromere pattern
L-0106	IgM kappa monoclonal protein, positive ANA (speckled pattern) and RF
L-0109	ANA positive, speckled pattern, DNA positive
L-0111	Duplicate of sample for L-0102

The samples had varying levels of specific proteins (IgG, IgM, IgA, IgE, C3,C4) and serum protein fractions by protein electrophoresis, (albumin, alpha-1, alpha-2, beta and gamma globulin).

The number of participants testing each analyte in 2001 (L-0111) compared to 2000 (L-0011) is shown in Table 36.

Again there are further reductions in the number of participants, with the exception of IgE.

ASSESSMENT OF RESULTS

The flagging rules for Immunology remain the same as reported in previous *Reviews*.

LABORATORY PERFORMANCE

Laboratory performance was essentially the same as in 2000. However, the committee is concerned with the failure of some laboratories to identify the presence of a monoclonal band when interpreting protein electrophoresis results.

Seven laboratories failed to detect the presence of an abnormal band in the beta region for sample L-0102. One of the seven, plus another laboratory, failed to identify this abnormal band when the same sample was distributed for the November survey (L-0111). A review of the submitted gels demonstrated that in the majority of cases, the band was readily apparent. All of these laboratories were assigned a significant error.

The number of lesser and significant errors assigned during the year can be reviewed in Appendix K (p. 105).

OTHER ACTIVITIES

A questionnaire was distributed in June 2001 requesting information regarding testing for anti-glomerular basement membrane (GBM), cytoplasmic antineutrophil cytoplasmic antibodies (c-ANCA) and perinuclear antineutrophil cytoplasmic antibodies (p-ANCA). Nine laboratories indicated that they were testing these analytes. The annual test volume for GBM is approximately 1600, c-ANCA: 9800 and p-ANCA: 8900.

Table 36. Number of Participants Testing Immunology in Survey L-0111 Compared to L-0011 by Analyte

Analyte	L-0011	L-0111	% Difference
ANA	38	30	-21.0
Anti-DNA	21	19	-9.5
IgE	16	16	0
C3, C4	29	28	-3.4
CRP	36	35	-2.8
RF	100	98	-2.0
MAH	19	16	-15.8
IgG, IgA, IgM	36	34	-5.6
PEP* serum	50	44	-12.0

* Protein electrophoresis





MATERNAL SERUM SCREENING

TESTING MODEL

Overall, the external quality assessment model remained unchanged in the number of surveys and analytes monitored—Alpha Fetoprotein (AFP), Chorionic Gonadotropin (CG) and Unconjugated Estriol (uE_3). However, the type of serum survey material was changed to address the lyophilized material matrix effect that was exhibited at the end of 2000. Each serum sample was distributed to participants with the requisite “patient” demographic and clinical information required to generate a complete interpretive report. A facsimile of the Ontario MSS program requisition was utilized to transmit the demographics to the laboratories. The laboratories were required to submit their results on the QMP-LS survey material in the same format, as they would report patient results to physicians.

The MSS serum testing model was designed to monitor analytical, quality assurance (QA) indicator and interpretive performance. To determine within-laboratory variations (imprecision), identical testing materials were submitted to participants on two or more occasions.

The survey model included two challenges of amniotic fluid for AFP testing. The demographic and clinical data were provided on a facsimile of the Ontario MSS requisition. The laboratories were required to submit their results in the same format used for patient reports to physicians.

As an added feature, patterns-of-practice surveys continued. Since the MSS program requires close liaison between clinical and laboratory service providers, the completion of these surveys often requires close collaboration.

QMP-LS has a mandate to monitor the Ontario MSS Database of patient results. Each of the seven regional laboratories transfers their patient results to the database on a monthly basis. QMP-LS conducts a monthly performance review of the medians (AFP, CG and uE_3) and positive rates (Trisomy 21, Open Neural Tube Defects and Trisomy 18). The monthly volumes are also monitored.

LABORATORY PERFORMANCE

Each challenge was assessed for analytical accuracy and appropriate clinical interpretation. Within Ontario, analysis of specimens for the three markers — AFP, CG and uE_3 — has been

within acceptable limits. An investigation was launched to determine whether or not the inter-laboratory variation demonstrated with analytical performance on uE_3 could be attributed to material matrix effects. Single donor 2nd trimester samples were compared to the prepared serum materials. In Table 37, the fresh sera in vials 3 and 4 demonstrate better performance with a reduced CV as compared with that of the prepared materials in vials 1 and 2.

Fresh serum from a single donor was used instead of the prepared sera. This has resulted in increased material costs and, hence, a reduction in the number of challenges. The September survey was cancelled. This change should not unduly limit the assessment of the laboratories. It will only affect the frequency and type of 2002 survey challenges.

The laboratories continue to perform well on the quality assessment indicators and interpretive component of the MSS challenges.

For each survey, Committee Comments regarding the analytical and interpretive performance are published and histograms provided to enable peer comparison.

Adjunct surveys were conducted to determine performance on imprecision, amniotic AFP and patterns of practice on any of the new prenatal screening markers.

A patterns-of-practice survey was conducted in July to assess the use of new prenatal screening markers. The laboratories were at various stages of planning, evaluation and implementation. The data were published in Committee Comments and shared with the Ontario MSS Consultative Group for planning purposes.

ONTARIO MSS DATABASE

The MSS Database provides outcome assessment on the basis of calculated positive rates (PR). As shown in Figure 19, the fluctuation (error bars) for Trisomy 21 PR has remained fairly constant.

Table 37. Survey S-0102 Statistics

Constituent Concentration or MOM	Coefficient of Variation (CV) % per Vial			
	Vial 1	Vial 2	Vial 3	Vial 4
AFP, µg/L	7.5	6.4	3.7	4.0
AFP MoM	8.2	7.3	4.6	4.1
uE ₃ nmol/L	45.0	48.9	8.6	11.1
uE ₃ MoM	35.1	42.5	10.6	7.8
CG kIU/L	5.3	8.4	5.5	9.2
CG MoM	4.9	6.3	4.4	6.1

The mean actual positive rate for 2001 was 8.4%. This closely approximates the 2001 theoretical PR of 8.1%.

The utilization rate has remained constant and is shown in Figure 20.

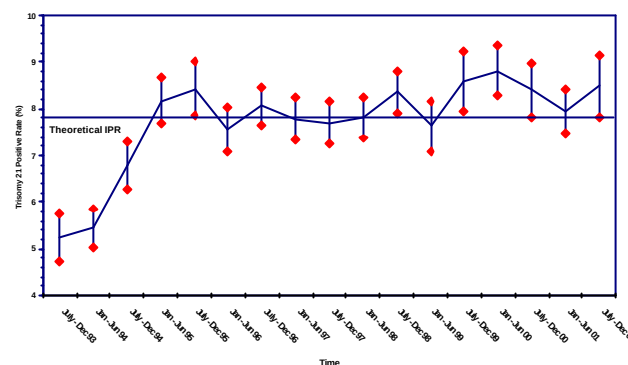
The changes in workload volume illustrate the changes in prenatal screening (Figure 21). In late 1999, Integrated Prenatal Screening (IPS) was introduced in Ontario and since then, MSS utilization has slightly increased to 48.1% (Figure 20).

The impact of the IPS on the Trisomy 21 positive rate has also been monitored since January 2001. Over the two-year period, the IPS has a decreased positive rate as compared with MSS (Figure 22).

An evaluation of the current MSS external quality assessment model has been initiated. QMP-LS is proactively addressing the requirements of the new screening modalities in relation to the current survey and database assessment models.

ENHANCED PRENATAL SCREENING

The transition from 2nd trimester triple marker screening to new screening modalities is being closely monitored. The new markers are biochemical and ultrasound based. The reported advantages of these new modalities are that they will decrease the false positive rate associated with screening while possibly increasing the detection rate. These changes should result in improved patient care. This shift in practice is likely to have an impact on the QMP-LS external quality assessment program.



Source: Ontario MSS Database

Figure 19. Ontario performance (N=7) on trisomy 21 Initial Positive Rate (IPR), July 1993 to December 2001

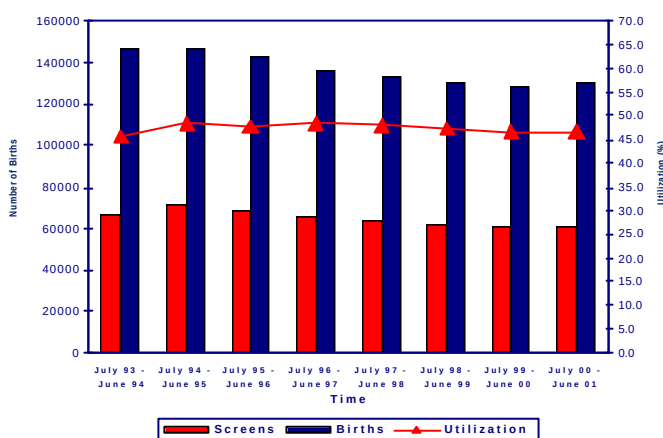


Figure 20. Utilization of maternal serum screening in Ontario, July 1993 to June 2001

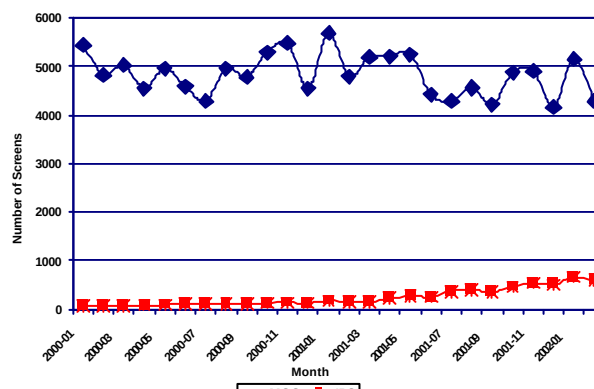


Figure 21. Prenatal screening volumes in Ontario, January 2000 to 2002

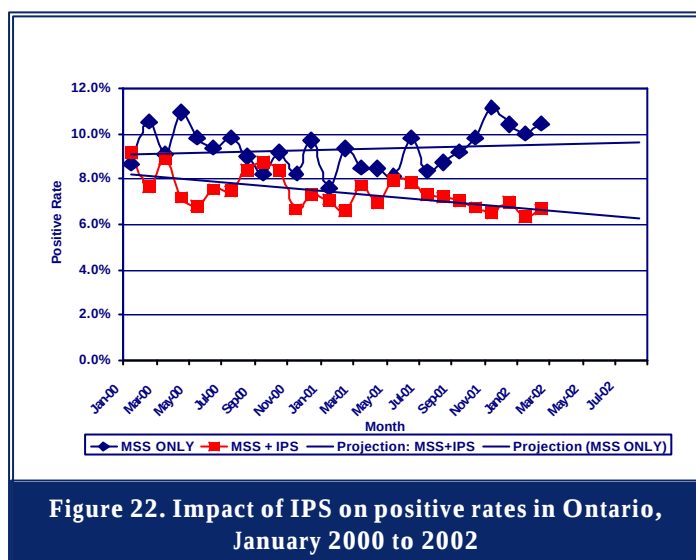


Figure 22. Impact of IPS on positive rates in Ontario, January 2000 to 2002

Ultrasound markers involve another sector of diagnostic medicine. Therefore, discussions have been initiated with the Ontario Medical Association and the College of Physicians and Surgeons of Ontario regarding the need for quality assurance of ultrasound measurements used in prenatal screening. It was agreed to collaborate on addressing this issue.

OTHER ACTIVITIES

QMP-LS is represented on the Ontario MSS Consultative Group assigned by the Ministry of Health and Long-Term Care to oversee the Ontario MSS program. This group meets semi-annually.

The Ontario MSS Consultative Group has a Chemistry Subcommittee. To enhance communications between QMP-LS and this subcommittee, a representative of the subcommittee is invited to each QMP-LS MSS committee meeting to share information. Since 1998, the provincial MSS Chemistry Subcommittee has tabled a report at each meeting.

The QMP-LS MSS program includes both the clinical and laboratory components as they are intertwined. The program evaluates the patterns of practice on both clinical and technical issues within the provincial program. Publishing the survey results in Committee Comments enables a unique opportunity for MSS staff to discuss and review their practices compared to provincial peers and implement changes.

POINT-OF-CARE TESTING

GLUCOSE METERS

TESTING MODEL

Pilot glucometer surveys were distributed in March, May and August 2001. Participation in the surveys is voluntary, as point-of-care testing (POCT) is not legislated in Ontario. Institutions with and without licensed laboratories in Ontario participated in the surveys.

Each survey included three vials of a commercially prepared material. One vial was considered to contain sufficient material to test 15 glucometers. Participants were instructed to test each glucometer within their institution. The users of the glucometers were expected to perform the testing. Compliance was generally good in this regard.

Results were compared to the glucometer model mean rather than an all-methods' mean as there are matrix effects with the commercial material.

In preparation for these surveys, a new database was developed and a new analysis worksheet and Survey Report was designed. A sample of the Survey Report is displayed on page 4 of this *Review*.

ASSESSMENT OF RESULTS

Results were not flagged by the computer for the March survey, however, the Chemistry Committee reviewed the results and recommended the following computer flagging rules:

Bias

Glucose ≤ 5.0 mmol/L: results >1.0 mmol/L from specific glucometer model mean

Glucose >5.0 mmol/L: results $>20\%$ from the glucometer model mean

If a result is $>15\%$ from the mean of the results reported from within an institution for a specific glucometer model, it will be flagged.

Imprecision

$>15\%$ difference in results reported on duplicate vials

These rules were applied to the May and August surveys.

GLUCOMETER PERFORMANCE

There were approximately 196 institutions participating in the surveys. Several respondents were from institutions without on-site laboratories. There were approximately 2400 to 2600 meters tested in each of the three surveys and 27 different meters were utilized by the participants.

The top five meters in use based on number of meters are: Precision PCx, Glucometer Elite 3903A, AccuData GTS/ Advantage, One Touch II Hospital and the Precision G.

Some meters can be referenced to whole blood or plasma/serum results. Glucose results for whole blood are usually 10% to 12% lower than plasma/serum results.

In the March survey (U-0103), each facility was asked to indicate whether their glucometers were referenced to whole blood or plasma/serum. The responses suggested that many participants are uncertain about the calibration of their glucometers.

Survey U-0105

This survey included one set of duplicates with a mid-range concentration (glucometer means 6.4–10.6 mmol/L) of glucose and one vial in the high range (glucometer means 16.2–26.9 mmol/L). Table 38 indicates the number of results that were flagged for bias and imprecision in the May survey. Twenty-two institutions with differences $>20\%$ in the results for the duplicate vials were notified of the imprecision in the results. The Survey Report alerted institutions to results flagged for bias.

Table 38. Number of Results Flagged for Bias and Imprecision for Survey U-0105

	No. of Results $>20\%$ From glucometer Mean	No. of Results $>15\%$ From Site Mean	No. of Precision Flags on Duplicate Vials 1 and 3
U-0105			
Vial 1 (mid-range)	16 (0.6%)	30 (1.2%)	67 (3.8%)
Vial 2 (high range)	22 (0.9%)	30 (1.2%)	...
Vial 3 (mid-range)	23 (0.9%)	35 (1.4%)	...



Survey U-0108

Three different concentrations of glucose were included in this survey. The glucometer means ranged from 7.9–10.7 mmol/L for vial 1, from 1.5–4.2 mmol/L for vial 2 and 14.1–24.3 mmol/L for vial 3. Sixteen institutions received correspondence notifying them of the bias in some of their results.

These surveys demonstrated that there is considerable variation in test results within the same glucometer model.

Variation in meter performance may be the result of a number of factors, including: technical performance of the meter, lot-to-lot variation of reagent strips, changing environmental conditions, insufficient sampling and variation in user technique. Inadequate mixing of survey material in the vials could also potentially give lower or higher results than expected.

LABORATORY PARTICIPATION

Comments have been forwarded to QMP–LS from participants regarding the staff time and the cost required to test all meters. In some cases the Medical Laboratory Technologists have performed the testing rather than the actual users. A few large institutions have not participated due to the labour intensity of the surveys. However, with the introduction of accreditation, participation in an EQA scheme will be necessary.

FUTURE ACTIVITIES

Two surveys are planned for 2002. A questionnaire will be distributed in the fall to update information received previously from a similar questionnaire on POCT for other analytes.

Testing Material Suppliers

Chemistry

Bio-Rad Laboratories Diagnostics Group, Montreal, Quebec, Ontario
Hamilton Regional Laboratory Medicine Program, Hamilton, Ontario
The Credit Valley Hospital, Mississauga, Ontario

Drug Monitoring

Centre for Addiction and Mental Health, Toronto, Ontario
Toronto General Hospital, University Health Network, Toronto, Ontario

Endocrinology

Bio-Rad Laboratories Diagnostics Group, Montreal, Quebec
Randox Laboratories, Mississauga, Ontario
Toronto General Hospital, University Health Network, Toronto, Ontario

Enzymes, Cardiac Markers & Lipids

Hamilton Regional Laboratory Medicine Program, Hamilton, Ontario
The Credit Valley Hospital, Mississauga, Ontario

Immunology

Hamilton Regional Laboratory Medicine Program, Hamilton, Ontario
Biomedical Resources, Hatboro, Pennsylvania

Maternal Serum Screening

Toronto General Hospital, University Health Network, Toronto, Ontario
North York General Hospital, Toronto, Ontario

Point-of-Care Testing (Glucose Meters)

Hematronix Inc., Plano, Texas



HEMATOLOGY DISCIPLINES

HEMATOLOGY-GENERAL

TESTING MODEL

Testing material for challenge surveys is chosen to mimic bona fide clinical samples. A whole blood product with human erythrocytes and mammalian leukocytes and thrombocytes in a plasma-like fluid, manufactured by R&D Systems, Inc. of Minneapolis, Minnesota was used for complete blood count and automated leukocyte differential testing. Target results covered the complete spectrum of low, normal and high values. The variety of blood cell analyzers used in Ontario continues to pose a challenge for this survey with respect to automated leukocyte differential counting, as there is no single testing material that is compatible with all instruments in use. To address this, each laboratory received automated leukocyte differential counting material that was compatible with the instrument last reported in use. The Hamilton Regional Laboratory Medicine Program supplied fresh K₃EDTA whole blood for the reticulocyte count surveys. Samples with increased reticulocyte counts were obtained from healthy individuals with well-compensated hemolytic syndromes.

The parameters monitored are shown in Appendix I (p. 102).

Of the 227 laboratories participating in routine surveys at the end of 2001 all but eight performed automated leukocyte differential, 181 laboratories participated in reticulocyte counting surveys compared to 187 in 2000.

LABORATORY PERFORMANCE

Challenges were conducted in May and November. Each challenge consisted of 4 vials for routine complete blood count (CBC) parameters and 3 vials (May) and 2 vials (November) for reticulocyte counting. Two additional vials were distributed for CBC and automated leukocyte differential counts. Computer flagging rules are displayed in Table 39. A comparison of the error rate obtained on Hematology-General surveys in 2000 and 2001 is shown in Table 40.

Hematology (General, Hemoglobinopathy, Detection of Fetal Cells, G6PD, Flow Cytometry, Bone Marrow)

No. of Participants (Dec. 2001) (General)	227
No. of Participants (Dec. 2000) (General)	236
No. of Surveys Conducted in 2001	7

Hematology-Coagulation

No. of Participants (Dec. 2001)	212
No. of Participants (Dec. 2000)	222
No. of Surveys Conducted in 2001	5

Hematology-Morphology

No. of Participants (Dec. 2001)	218
No. of Participants (Dec. 2000)	228
No. of Surveys Conducted in 2001	5

Transfusion Medicine (Set A and Set B)

No. of Participants (Dec. 2001)	179
No. of Participants (Dec. 2000)	179
No. of Surveys Conducted in 2001	4



Table 39. Hematology-General Flagging Limits Used in 2001

Parameters	Deviation Allowed From Mean (%)
Leukocyte	20
Erythrocyte	10
Hemoglobin	10
Hematocrit	10
MCV	5
Thrombocyte	20
Automated Leukocyte Differential	40

Table 40. Error Rates in Hematology-General (CBC, Leukocyte Differentials and Reticulocyte Surveys) in 2000 and 2001

		Significant	Lesser	Total	Error Rate %
H-0005	CBC and LD	8	4	12	0.1
	Reticulocyte	3	6	9	2.3
H-0011	CBC and LD	7	11	18	0.17
	Reticulocyte	10	4	14	2.5
H-0105	CBC and LD	5	1	6	0.10
	Reticulocyte	5	0	5	0.3
H-0111	CBC and LD	5	5	10	0.11
	Reticulocyte	15	0	15	1.4

CBC and Automated Leukocyte Differentials

Overall performance was excellent. Survey error rates for combined CBC and automated differential were 0.10% and 0.11% in May and November 2001 respectively, compared with 0.1% in April and 0.17% in November 2000.

Reticulocyte Counting

As in 2000, surveys focused on the ability of laboratories to differentiate samples with increased reticulocyte counts from those with normal counts. In addition, in May we conducted an intra-laboratory precision study on increased reticulocyte count by sending two vials of blood from the same donor. The May survey consisted of 3 vials—1 from a healthy individual with a normal reticulocyte count and 2 from an individual with hemoglobin (Hb) SC disease with an increased reticulocyte count.

The November survey contained 2 samples — 1 from a normal donor and 1 from an individual with an elevated reticulocyte count. In these surveys participants were required to report their measured erythrocyte count, the reticulocyte count in per cent, and their calculated absolute reticulocyte count. The error rates were 0.3% and 1.4% respectively in May and November 2001, compared to 2.3% and 2.5% in 2000. While the error rates appear lower than those in 2000 the method of error rate calculation was altered in 2001 to more closely reflect errors in all three parameters and not simply in the absolute reticulocyte count. The error rate calculation in 2002 will follow the same format.

The trend from manual methods towards automated methods continues (Table 41). Results indicate there is slightly better intra-laboratory and interlaboratory precision with automated methods. The majority of laboratories can reliably distinguish between samples with normal and increased reticulocyte counts, although coefficients of variation (CV) remain wide.

Two routine challenge surveys will be conducted in 2002.

Table 41. Reticulocyte Counting Methods in Use for 2000–2001 Surveys

Method	Reported Number per Survey			
	H-0005-R	H-0011-R	H-0105-R	H-0111-R
Manual Assessment	129 (67%)	120 (64%)	117 (63%)	106 (59%)
Hematology Cell Analyzer	58 (30%)	61 (33%)	63 (34%)	68 (38%)
Flow Cytometry	5 (3%)	5 (3%)	6 (3%)	7 (3%)
Total	192	186	186	181



HEMOGLOBINOPATHY (RED CELL DISORDERS)

TESTING MODEL

Three surveys utilizing fresh whole blood and one utilizing a dry laboratory challenge were distributed in 2001. Eighty-five laboratories in Ontario participated in the Hb S screening surveys and 24 laboratories (including one out of province) submitted results for the Hb fraction quantitation/hemoglobinopathy investigation challenges. Surveys focused on the ability of participants to detect α -thalassemia trait and to identify normal specimens.

LABORATORY PERFORMANCE

Table 42 provides a summary and the reference diagnosis of surveys conducted in 2001.

The Hb S screening survey contained one sample from a normal healthy volunteer and all participants obtained the correct result. Table 43 shows the various Hb S screening methods currently in use in Ontario. The solubility screening methods are recommended by QMP-LS and it is encouraging to see that only two laboratories continue to use the slide-sickling test.

The April Hb fraction quantitation/hemoglobinopathy investigation survey contained a sample from a donor with α -thalassemia trait who was heterozygous for the Southeast Asian ($-\text{SEA}/$) α^0 -thalassemia mutation. Six laboratories were unable to identify the case as α -thalassemia trait for a missed diagnosis rate of 24%. Three of these laboratories recommended referral to a reference laboratory and were not assigned errors. The remaining three reported no hemoglobinopathy detected and were assigned significant errors for an error rate of 12%. Table 44 shows the missed diagnosis rate on SEA α^0 -thalassemia trait samples submitted from 1994 to 2001. These figures reflect the difficulty laboratories have in identifying this important hemoglobinopathy. Committee Comments addressed the detection and diagnosis of α -thalassemia trait.

Table 42. Hemoglobinopathy Reference Diagnoses Submitted in 2001

Survey	Month	Test Monitored	Reference Diagnosis
H-0104-X	April	Hb S	Normal
H-0104-Y	April	Hb Fraction	α -thalassemia trait ($-\text{SEA}/\alpha\alpha$)
H-0109-Y	September	Hb Fraction	Normal
H-0109-PP	September	Patterns of Practice	Acquired α -thalassemia

Table 43. Hb S Screening Methods Currently in Use in Ontario

Method	No. of Laboratories
Solubility Methods	
Ortho Sickledex	49
In-house sodium dithionite solubility	20
Mich Clone Heme/Sickle Cell	10
Dade Behring Sickle-Sol	2
Other solubility	2
Sickling Methods	
In-house sodium metabisulfite slide-sickling	2

Table 44. Missed Diagnosis Rate on SEA α^0 -Thalassemia Trait Samples 1994–2001

Year	Diagnosis	% of Participants Missed Diagnosis
1994	α^0 -thalassemia trait	16
1999	α^0/β -thalassemia trait	85
2001	α^0 -thalassemia trait	24

The September Hb fraction quantitation/hemoglobinopathy investigation survey contained a sample from a normal donor. All participants reported the correct result of no hemoglobinopathy detected. No errors were assigned on this survey.

The September patterns-of-practice survey involved an unusual case of acquired α -thalassemia secondary to acute leukemia. Responses to the questions on this survey were good, with an overall correct answer rate of 88%.

In October, the committee released Good Practice Guidelines for the Laboratory Investigation of Hemoglobinopathies. These guidelines were prepared in an effort to address recurrent errors in the diagnosis of hemoglobinopathies detected on surveys conducted between 1990 and 2000.

DETECTION OF FETAL CELLS

TESTING MODEL

Surveys utilized whole blood, obtained from an Rh-negative adult donor that had been spiked with ABO compatible Rh-positive cord blood to simulate a fetal maternal hemorrhage. Surveys in 2001 focussed on the reliability of detecting a fetal-maternal hemorrhage when present, then quantifying the volume of hemorrhage accurately. As of September 2001 there were 49 participants in this survey.

LABORATORY PERFORMANCE

Two surveys were conducted in 2001. Each three-vial survey contained a sample simulating:

- ✓ 45-mL fetal-maternal hemorrhage where additional Rhlg immune prophylaxis would be required with either the 120 µg or 300 µg standard post-partum Rhlg dose.
- ✓ 20-mL fetal-maternal hemorrhage where additional Rhlg immune prophylaxis would be required with the 120 µg but not the 300 µg standard post-partum Rhlg dose.
- ✓ 0-mL fetal-maternal hemorrhage where additional Rhlg immune prophylaxis would not be required with either the 120 µg or 300 µg standard post-partum Rhlg dose.

Table 45 shows the various screening and quantitative techniques employed in the province. Two laboratories now use flow cytometry, the remaining 44 continue to use some form of acid elution technique. Table 46 shows the Rosette test results for surveys H-0104-Z and H-0109-Z. Table 47 summarizes the quantitative statistics per vial for % fetal cells and mL fetal blood. As in 2000, results from the 2001 surveys demonstrate that the Rosette test and the acid elution techniques are reliable screening tools to identify samples requiring fetal-maternal hemorrhage quantification, but the acid elution techniques lack adequate precision for the reliable quantitation of fetal-maternal hemorrhage. Due to the unacceptable precision obtained on these surveys, errors were assigned for blatantly discordant findings only. Two lesser errors were assessed on H-0104-Z and one lesser error was assessed on H-0109-Z for a total error rate of 1.0%.

Fetal-maternal hemorrhage detection will be scaled back to a single two-vial survey in 2002.

Table 45. The Fetal-maternal Hemorrhage Screening and Quantitative Techniques Employed in Ontario

Manufacturer	No. of Laboratories
Rosette Test	
Gamma Biological	8
Ortho	5
In-house	1
Kleihauer Stain at 37°C	
ENG	1
Sigma	9
Simmler	1
In-house	9
Sure-Tech	1
Kleihauer Stain at Room Temperature	
ENG	4
Sigma	2
Simmler	2
In-house	13
Nierhaus Stain at Room Temperature	
	4
Flow Cytometry	
	2

Table 46. Rosette Test Results for Surveys H-0104-Z and H-0109-Z

Level of Hemorrhage	No. of Laboratories			
	H-0104-Z		H-0109-Z	
	Positive	Negative	Positive	Negative
45 mL	14	0	14	0
20 mL	14	0	14	0
0 mL	1	13	0	14

Table 47. Statistics Per Vial for % Fetal Cells Detected and mL Fetal Blood for Surveys H-0104-Z and H-0109-Z

Level of Hemorrhage	Mean (% Fetal Cells)		CV (%) (% Fetal Cells)	
	H-0104-Z		H-0109-Z	
	H-0104-Z	H-0109-Z	H-0104-Z	H-0109-Z
45 mL (0.9%)	1.15	1.14	44.2	46.4
20 mL (0.4%)	0.54	0.56	40.6	44.5
0 mL (0.0%)	0	0	n/a	n/a

Level of Hemorrhage	Mean (mL Fetal Bleed)		CV (%) (mL Fetal Bleed)	
	H-0104-Z		H-0109-Z	
	H-0104-Z	H-0109-Z	H-0104-Z	H-0109-Z
45 mL	56.2	57.2	45.5	47.1
20 mL	26.8	27.9	41.5	45.4
0 mL	0	0	n/a	n/a



GLUCOSE-6-PHOSPHATE DEHYDROGENASE (G6PD) DEFICIENCY DETECTION

TESTING MODEL

One pilot survey (H-0109-G6) containing two vials of whole blood as well as a patterns-of-practice questionnaire was conducted in 2001.

LABORATORY PERFORMANCE

Thirty-two laboratories participated in this survey, 28 reported G6PD screen results and 10 reported G6PD assay results. Vial A contained blood from a normal individual and all participants reporting G6PD screen results achieved a correct result of normal. Six participants reported G6PD assay results within their reference interval, two reported decreased results and one reported increased results. Vial B contained blood from a normal individual that had been stored for four days to induce borderline G6PD deficiency. Twenty-two laboratories reported normal and six laboratories reported decreased G6PD screen results. Five participants reported normal G6PD assay results, three reported decreased results and two reported markedly increased results. As this was a pilot survey no errors were assessed.

Analysis of the questionnaire yielded valuable data regarding the investigation of G6PD deficiency in Ontario. Key findings were:

1. Ten laboratories do not have a mechanism for the performance of a G6PD assay when screen results indicate a deficiency.
2. Only four laboratories run both normal and abnormal controls with their G6PD screens and only six laboratories run both normal and abnormal controls with their G6PD assays.
3. Six laboratories have extremely low workload for this test, i.e. less than two G6PD screens per month.
4. Three laboratories perform large numbers of G6PD assays, e.g. 26 to 54 per month, without first performing a G6PD screen. This is an inefficient means of screening for G6PD deficiency.

The pilot survey revealed some incongruities and deficiencies. Of particular concern were erroneously high G6PD assay results, the omission, in many laboratories, of both normal and abnormal controls for the screen and assay, and the performance of large numbers of assays without prior G6PD screening. The first G6PD deficiency detection survey will be conducted in the fall of 2002.

FLOW CYTOMETRY

TESTING MODEL

Two surveys were conducted in 2001, each consisting of samples of whole blood for HIV investigation and samples accompanied by blood films for the investigation of neoplastic hematologic disorders. Samples for CD34+ progenitor cell enumeration were also distributed. Testing material is sent by overnight courier to allow participating laboratories to conduct their analyses within three days of distribution. Results are submitted on the computer compatible reporting form that also allows limited textual comment. The reporting form for the hematologic neoplasm investigation allows correlation of blood film morphology with analytical results for diagnostic interpretation. Laboratories are also required to submit sample preparation data, all light scatter and fluorescence histograms and laboratory-generated reports.

LABORATORY PERFORMANCE

Lymphocyte Immunophenotyping for HIV

Samples from a negative donor and a positive donor were distributed to 21 participants—18 Ontario and 3 out of province. All but one laboratory utilized CD45 as gating agent as recommended by the committee. Few laboratories continue to correct the lymphocyte percentage for purity while using CD45 as gating agent. Correcting for lymphocyte purity along with CD45 gating may result in falsely elevated results. An error will be assessed in future if this practice continues. The majority of laboratories used dual platform, but the number of laboratories that used single platform has gradually increased from two in March 1999 to six in the August 2001 survey. Surveys for HIV testing have been conducted since 1995 and the performance is summarized in Table 48. There were no significant errors in 2001, but a total of 3 lesser errors were assessed—2 in March and 1 in August.



Table 48. Performance on 1995–2001 Surveys, Lymphocyte Phenotyping for HIV Investigation

Survey	Reference Result	Lesser Errors	Significant Errors	Error Rate %
H-9509-FC	Normal	0	0	0
H-9603-FC-A	Normal	3	1	22.2
H-9603-FC-B	HIV	8	2	27.8
H-9703-FC-A	HIV	1	2	15.0
H-9803-FC-A	HIV	1	0	14.3
H-9808-FC-A	HIV	0	0	0
H-9903-FC-A	Normal	0	0	0
H-9908-FC-A	HIV	1	0	5.3
H-0003-FC-A	HIV	2	0	11.1
H-0008-FC-A	HIV	2	0	11.1
H-0103-FC-A	Normal	2	0	10.5
H-0108-FC-A	HIV	1	0	4.8

Leukocyte Phenotyping for Neoplastic Hematological Disorders

Two clinical cases were distributed (March and August) to 26 participants (15 Ontario and 11 out of province). Participants were expected to include the following in their submissions:

- ✓ Blood film morphology
- ✓ Flow cytometry analysis results
- ✓ Interpretation of results
- ✓ Laboratory-generated reports showing interpretation of results.

The first sample was from a patient with a B-cell disorder, splenic marginal zone lymphoma with villous lymphocytes. All 26 laboratories reported B-cell disorder. Eight lesser errors were assessed for failure to identify or suggest splenic lymphoma with villous lymphocytes. Two lesser errors were assessed for incorrectly identifying isotypic light chain restriction.

The second sample was from a lymphoproliferative disorder of granular lymphocytes, T-cell type. One significant error was assigned for incorrectly identifying the abnormality as a reactive process. Correspondence was sent to several laboratories for failing to submit the required blood film morphology and the internally generated laboratory reports recording their results. This correspondence indicated that this oversight may result in error assessment on future surveys.

A patterns-of-practice survey, which included a compact disc with listmode data files, patient data sheets and photomicrographs of three separate cases of leukemia or lymphoma, was initiated in November. Fifteen laboratories

submitted results. All participants correctly identified the first case as an acute myeloid leukemia. Fourteen laboratories correctly identified the second case as a B cell lymphoproliferative disorder other than CLL. One participant reported an unacceptable diagnosis. The third case was the most challenging and contained both a monoclonal plasma cell population and a small CD19 lambda B cell monoclonal population. Fourteen participants identified the plasma cell population, while only seven participants detected the secondary B cell population. As this was a pilot survey, no errors were assessed.

Some participants expressed concerns about the new testing format. Some of these concerns will be addressed on future surveys. However, it is the committee's view that the continued use of this format will facilitate external quality assessment of cases that would otherwise not be available. Interestingly, the College of American Pathologists (CAP) is now considering adding this format to their flow cytometry quality assurance program.

CD34+ Progenitor Cell Enumeration

There were two surveys for CD34 analysis in 2001. A total of fifteen laboratories participated, approximately half of which were out of province. The first survey consisted of one blood and one diluted apheresis sample. The second survey consisted of two blood samples. All laboratories use the combination of CD45 with CD34 and the majority follow the ISHAGE guidelines for analysis. This survey continues to be challenging for participants, partly due to the low number of CD34+ cells found in the samples. In one of the blood samples with a high CD34+ level (approximately 1.7%), all participants performed well. However, many of the challenge samples have CD34+ levels in the range of 0.2%–0.5% making them more difficult to assess. Several laboratories failed to include the dilution factor in their calculations for the apheresis samples. Overall, these surveys were analyzed well. Most errors were due to dilution and/or calculation problems.



BONE MARROW EXAMINATION

TESTING MODEL

QMP–LS conducted two bone marrow surveys in 2001. We continued with the distribution of cases on a rotational basis that was established in 1999. For each survey, five rotations of the material, over an approximate 15-week period were carried out. Each laboratory received four cases. Each case included appropriate clinical and laboratory data, a peripheral blood film and bone marrow material (aspirate or biopsy) relevant to the case. The cases used covered a variety of primary hematological disorders including anemia of chronic disease/normal, acute leukemia (M1), acute leukemia (M5a), and a bone marrow biopsy submitted for evidence of lymphoma (Table 49).

Computer flagging was based only on the clinical interpretation, but the committee considered all aspects of the uniform reporting format. Any laboratory that did not report the reference diagnosis was flagged for review. In addition, any laboratory that reported additional diagnoses, along with the reference interpretation, was also flagged for review.

LABORATORY PERFORMANCE

The overall performance of laboratories in bone marrow evaluation was excellent with an error rate of 2.9% for the March survey (H-0103-BM). Only two lesser and two significant errors were identified. The committee did not assess errors for the September survey (H-0109-BM). Survey interpretive results that were unexpected were identified as discordant findings. In total, eight memos of clarification, together with the original slides, were sent to participants for further review and asking for an explanation of discrepancies.

The cases distributed are intended to be clear-cut examples of a normal or a disease process, and are not intended to represent difficult differential diagnostic problems. Therefore, laboratories should attempt to indicate only one or two main diagnoses in their responses.

Also, with bone marrow biopsy material it is difficult to make statements regarding specific elements of the marrow, other than to recognize hyperplasia/hypoplasia of various marrow elements. It is also difficult to comment on specific cytological details, as these are much more apparent in aspirate material. For this reason, in 2002 the analysis worksheet will be specific to the sample distributed, i.e. biopsy versus aspirate material.

The committee is still faced with the problem of acquiring suitable material for testing. In 2002, two further surveys will be conducted, again using the rotational model.

Table 49. Summary of Survey Results for H-0103-BM and H-0109-BM

Diagnosis	No. of Participants	No. of Labs Reporting Reference Diagnosis	No. of Diagnostic Flags	No. of Lesser Errors	No. of Significant Errors	No. of Memos of Clarification
Anemia of Chronic Disease/Normal	35	31	8	0	2	2
Normal Bone Marrow	34	33	1	0	0	0
Acute Leukemia (FAB M1)	35	35	3	0	0	0
Acute Leukemia (FAB M5a)	34	28	6	2	0	0
Anemia of Chronic Disease/Normal	34	23	11	0	0	3
Acute Leukemia (FAB M5a)	35	32	3	0	0	2
Normal Bone Marrow Biopsy	63*	51	18	0	0	3

* Six participants did not respond



HEMATOLOGY-COAGULATION

TESTING MODEL

Three coagulation surveys were conducted in 2001, utilizing testing materials chosen to represent a variable, but clinically meaningful range of results. Prothrombin Time/International Normalized Ratio (PT/INR) testing was monitored with lyophilized coumadinized plasmas and artificially depleted plasmas supplied by the Thrombosis Reference Centre, Manchester, UK, and Organon Teknika. The Activated Partial Thromboplastin Time (APTT) testing survey also utilized artificially depleted plasmas. Factor VIII analysis was performed on material obtained from Organon Teknika. A questionnaire on the use of D-dimer in the province was included with survey K-0106. An Activated Protein C (APC) resistance testing survey was undertaken in conjunction with survey K-0110.

The flagging rules, designed to bring laboratory results to the attention of the committee for review are noted in Table 50.

In 2001, the committee decided to discontinue the use of the all-methods' mean to evaluate the performance of IL Test PT/Fibrinogen Recombinant reagent used on the ACL coagulation instrument. This change was due to the continuing observation that lyophilized Thrombosis Reference Centre survey material, when analyzed with this reagent/instrument combination, yielded INR values that were significantly higher than those obtained from other reagent/instrument combinations. Centres using this machine/reagent combination will now be evaluated against their peers, until the source of this deviation is ascertained. All other machine/reagent combinations will continue to be evaluated using the all-methods' mean.

LABORATORY PERFORMANCE

PT/INR

PT/INR testing was conducted on all surveys using either lyophilized coumadinized plasmas or artificially depleted plasmas (Table 51). In survey K-0102, 10 lesser errors and 1 significant error were assessed; in K-0106 only 1 significant and one lesser error were assessed and in K-0110 only 1 significant and 3 lesser errors were assessed. While overall the number of errors is low, the committee has some ongoing concerns with INR testing. These include the variations in INR reported by different machine/reagent combinations as discussed above, the apparent lack of careful review and revision of reference intervals as indicated by the reporting of an INR "reference interval" of 2.0 to 3.0 and continued problems with reconstitution of test reagents. To address these issues, a number of steps are planned for 2002. These include a frozen warfarin plasma survey to a limited number of centres, increased review of normal ranges, and a comprehensive patterns-of-practice survey regarding hemostasis and thrombophilia testing in the province.

APTT

APTT testing took place in all surveys on lyophilized, artificially depleted plasmas. A total of one significant and four lesser errors were assessed on the three surveys. It is difficult to assess the results of proficiency testing samples, since there is considerable variation between reagent groups due to different sensitivities to depleted plasmas, heparinized plasmas and lupus anticoagulant plasmas. Because of this limitation, the committee compares the results within reagent groups and often only flags results if normal is identified as abnormal and vice versa. The committee will attempt to explore some of these issues in 2002 by sending out a lyophilized human heparinized survey to determine the variation in APTT within- and between-machine/reagent combinations when compared to a reference centre.

Table 50. Coagulation Flagging Limits Used in 2001

Tests	Deviation Allowed From Mean (%)
PT (Prothrombin Time)	15% of reagent mean
INR (International Normalized Ratio)	20% of all-methods' mean*
APTT (Activated Partial Thromboplastin Time)	20% of reagent mean
Factor VIII Assay	20% of all-methods' mean

* Until further notice, participants using IL Test PT/Fibrinogen Recombinant reagent and an ACL coagulation instrument will be evaluated against their peers



Factor VIII

Factor VIII analysis was carried out on an immuno-depleted factor VIII sample (reference VIII:C level of less than 0.01 U/mL) and a sample with a normal factor VIII (reference VIII:C level of 1.12 U/mL). Two significant and four lesser errors were assessed to laboratories whose results did not reflect a severe factor VIII deficiency. Unfortunately, an unknown problem with the normal factor VIII survey material caused instability of the product, and, therefore, no errors were assessed on this survey. A total of 21 laboratories are licensed to perform factor assays. Factor VIII and IX assay surveys are planned for 2002.

D-dimer

A D-dimer patterns-of-practice survey was carried out in June 2001. This questionnaire documented a number of very concerning observations, most importantly the widespread use of non-validated D-dimer tests in diagnostic strategies for deep vein thrombosis (DVT) and pulmonary embolism (PE). Use of inappropriate assays in this setting could result in falsely negative test results, with inappropriate exclusion of the diagnosis of DVT/PE. Committee Comments published on this survey (Coagulation Binder) provide additional information and recommendations. This area will be explored further with a pilot D-dimer survey of spiked, lyophilized plasma in June 2002.

Thrombophilia—Activated Protein C Resistance

APC Resistance analysis was carried out in October 2001. Three samples were sent to participants—a normal, a known factor V Leiden heterozygote, and another known factor V Leiden heterozygote on oral anticoagulants. Testing was uniformly done well with all participants being able to distinguish the normal sample from the abnormal samples. The Molecular Diagnostics of Inherited Diseases Committee, in conjunction with the Hematology Committee, sent the same samples for factor V Leiden assessment. The findings of the two surveys using different

Table 51. INR Target Values and Flagging Rules

Vial	Material	Target INR	All Mean Methods	Range Flagged Outside
Survey K-0102				
A	Coumadinized plasma	2.0	2.3	1.8–2.8
B	Coumadinized plasma	4.2	4.6	3.7–5.5
C	Artificially depleted	1.0	1.0	0.8–1.2
Survey K-0106				
A	Coumadinized plasma	3.1	3.4	2.7–4.1
B	Coumadinized plasma	2.0	2.3	1.8–2.8
C	Artificially depleted	4.1	4.2	3.4–5.0
D	Artificially depleted	1.0	1.0	0.8–1.2
Survey K-0110				
A	Coumadinized plasma	3.1	3.4	2.7–4.1
B	Coumadinized plasma	4.2	4.5	3.6–5.4
C	Artificially depleted	4.1	4.2	3.4–5.0

technologies but the same challenge material will be published in 2002.

A patterns-of-practice survey on hemostasis is scheduled for June 2002. It will assess the “state of the art” of provincial testing for congenital and acquired hemostasis and thrombophilia disorders. Using this information, a comprehensive pilot thrombophilia survey will be distributed in October 2002. This survey will assess protein C, protein S, antithrombin III and APC resistance.



HEMATOLOGY-MORPHOLOGY

TESTING MODEL

In 2001, 4 routine surveys, 1 educational and 1 patterns-of-practice survey were conducted. One of the surveys (M-0102) was distributed across Canada as an inter-provincial survey and another (M-0105-E) was distributed as an educational survey to enhance the laboratories' hematology blood film collection and give technologists the opportunity to investigate a disorder rarely seen in Canada.

To reflect current practice, the policy allowing the referral of survey blood films for the purpose of examination and/or confirmation, interpretation and reporting was continued if a patient's blood film of similar complexity would normally be referred out.

The Hematology Committee evaluates laboratory performance by comparing the participant's results to reference results and scoring rules as defined by designated referees. The reference results and the final scoring rules on a survey are the majority or consensus of referees' submitted results. Each flagged result is classified as either no error, a lesser error or a significant error. Lesser errors are unexpected results yielding a low score but if reported in a clinical setting would not compromise patient care. Significant errors are assessed if the results reported have the potential to lead to clinical decisions that may be harmful to the patient.

LABORATORY PERFORMANCE

Survey M-0102

This blood film was from an asymptomatic 40-year-old male with normal hematologic indices and known Hb SC disease. The

principal findings were large numbers of target cells (Figure 23), some fragments and sickle cells, increased polychromasia, as well as folded or oat cells typical of Hb C or SC conditions. This constellation of findings was highly indicative of an underlying hemoglobinopathy.

Although 95% of participants reached a diagnosis of Hb C, Hb SC or other hemoglobinopathy, only a minority of laboratories reported the presence of sickle and/or oat cells. Many participants utilized the "Comments" section to report the presence of the folded cells while many may have reported their presence as "spherocytes" (71% of participants) indicating a degree of uncertainty of the significance of these cells. Fifteen significant errors were assigned on this survey, 11 for not reporting the above diagnoses and four for not including a statement that would result in hemoglobin electrophoresis. This survey was distributed across Canada and performance was excellent.

An interesting finding was the different rates of blood film referral reported by each province (Figure 24) with a mean of 50% laboratories referring the blood film for review. This rate varied from as low as 8% to 85% indicating significant differences in the way in which laboratories develop their criteria for slide reviews. A case of Hb SC with sickle cells present on the blood film would be highly significant clinically if the diagnosis was unknown at that time and the patient required emergency surgery. This area is further examined in the patterns-of-practice survey, H-0107-PP (see below).

Survey M-0105

This blood film was from a patient with the May-Hegglin Anomaly (MHA). This is the most common type of an inherited giant platelet disorder and may result in a mild bleeding tendency depending on the degree of associated thrombocytopenia although some patients are completely asymptomatic. The presence of Döhle bodies with a mild to moderate degree of thrombocytopenia and giant platelets are the characteristic findings.

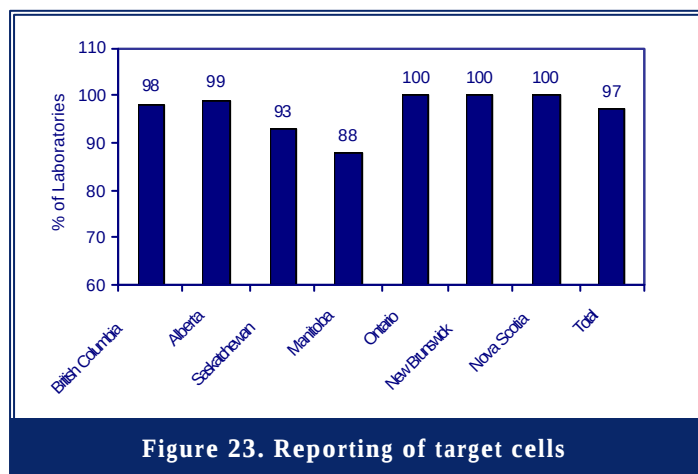


Figure 23. Reporting of target cells

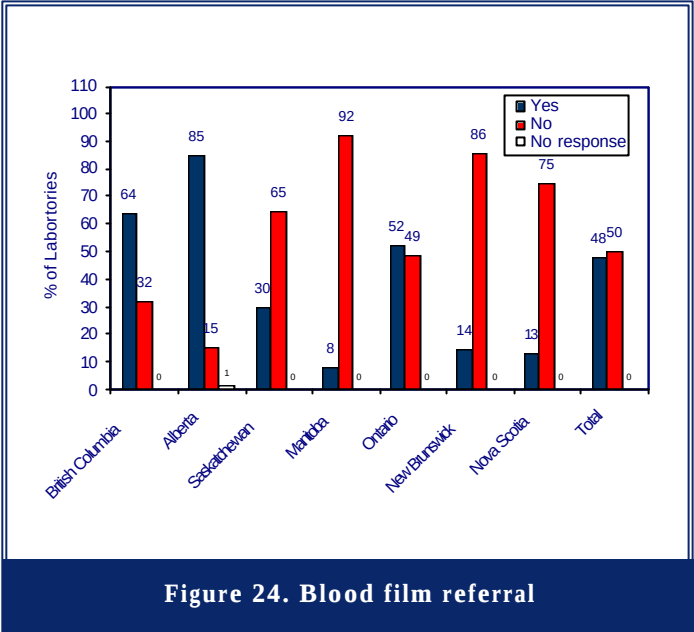
This was the first time that this anomaly had been used for a morphology survey assessment and the results were excellent with 98% of laboratories correctly identifying the anomaly. Only one significant error was assessed for failure to identify the key morphological findings and four lesser errors were assessed for failure to make the correct clinical diagnosis subsequent to noting the key morphological findings.

Survey M-0105-E

This was a very challenging survey and was included as an educational slide to illustrate a parasite that is rarely seen in Canada. The case was that of an immunocompromised patient with a T-cell malignancy who had received multiple blood transfusions during his treatment. The principal educational finding was the presence of a blood-borne parasite, *Trypanosoma cruzi* also known as Chagas’ disease, acquired through a blood transfusion. This is a major health problem in South America and has been found in the southern United States with extremely rare cases reported in Canada. It is important for laboratorians to consider this possibility when encountering unusual findings on a blood film suggestive of a parasitic infestation. This blood film was distributed as an educational exercise, participants were not asked to submit results and errors were not assessed.

Survey M-0108

This blood film—a case of iron deficiency anemia—resulted in an unexpectedly high number of errors (42) even though 99% of respondents provided the correct diagnosis. Fifteen significant and 27 lesser errors were assessed based primarily on the over-reporting of potentially clinically misleading findings. These included reporting of sickle cells, Hb S condition, myeloproliferative condition, and erythrocyte enzymopathy. The problem of over-reporting of both morphologic and clinical findings has not been systematically examined and based on the current scoring system, laboratories do not lose marks for reporting any findings identified by the referees as not being clinically significant. In



some cases, these “false-positive” findings may convey to the physician the possibility of other diagnoses that may have no bearing on the case, and may cause harm or discomfort to the patient should they be inappropriately investigated or treated. It is not known as to what extent this is a function of proficiency testing models and the implied need to provide every “possible” or “consistent with” diagnosis as opposed to daily clinical practice.

Survey M-0111

This pilot survey used an unstained blood film from a patient with Chronic Lymphocytic Leukemia (CLL) that demonstrated significant numbers of normal-appearing small lymphocytes characteristic of this relatively common entity. The majority of participants (99%) correctly identified the primary diagnosis of CLL. The stated Hb value for the patient was 62 g/L and while 74% of respondents reported the presence of spherocytes, only 66% of respondents commented on the finding of an immune hemolysis as the cause of the anemia. This may reflect a degree of uncertainty of the significance of this finding in this clinical setting, which has a strong association with immune hemolytic anemias. The ongoing problem of quantitating or otherwise ranking morphologic findings is a diagnostic challenge for laboratorians. This issue is particularly relevant in the context of uncertainty inherent to this testing model, i.e., one cannot obtain additional clinical or other diagnostic information before rendering a morphological diagnosis.

SUMMARY OF PERFORMANCE

Table 52 compares the error rates since 1998. The challenging nature of the 2001 surveys is reflected in the comparative error rates over the past four years.

Table 52. Comparison of Morphology Error Rates 1998–2001

	Average No. of Significant Errors	Average No. of Lesser Errors
1998	10	10
1999	3	19
2000	7	9
2001	31	31

PATTERNS-OF-PRACTICE SURVEY

Survey H-0107-PP was to ascertain the practice in Ontario laboratories regarding instrumentation flagging protocols and criteria for making and reviewing blood films. Of 234 laboratories expected to participate, 231 returned the questionnaires.

The results indicated that 94% of laboratories were capable of generating either a five-part (63%) or three-part differential (31%) and that based on flagging criteria established by each laboratory, the vast majority proceeded to a microscopic examination of the blood film. This was either by a scanning blood film technique (microscopic assessment with no comments unless significant abnormalities are detected) or a manual blood film review (microscopic assessment with manual leukocyte differential, erythrocyte morphology and thrombocyte assessment) if needed. Sixty-three per cent of laboratories used the scan technique as their primary step and based on their findings, either reported any abnormalities detected or proceeded to a manual blood film review.

A number of other specifications were used including the presence of a positive sickle cell screen, positive monostest, and leukocyte differential with inverse neutrophil/lymphocyte ratio or at the discretion of the technologist or physician. The average percentage of blood films reviewed in hospital laboratories was 27% with the corresponding figure for private laboratories being 29%. Blood films are prepared on only specified samples by 87% of participants; the remainder prepare and stain blood films

on every CBC sample. It would appear that the scanning technique is underutilized with 37% of the laboratories not performing this abridged version of a manual blood film review. Of the participants who have automated differential capability and statistically differentiate the method of blood film review, only 42% of private laboratories use the scanning format compared to 64% of the hospital laboratories. Interestingly, 6% of laboratories still perform a manual blood film review on all patients requiring a complete blood cell count (CBC). These data suggest that there are opportunities for further workflow efficiencies in the Ontario laboratory community without compromising patient care. Ninety-four per cent of laboratories had a set of written criteria for blood film abnormalities requiring review by a laboratory physician. Only 51% of Ontario laboratories had the capability of performing this review on site and only 45% reported an achievable turnaround time of 24 hours or less. This slow turnaround time has clinically significant implications particularly in cases where there is a time dependent prognostic determinant, for example, malaria diagnosis and speciation.

Figures 25 and 26 summarize the number of CBCs and scan and manual differentials performed monthly by hospital and private laboratories in Ontario.

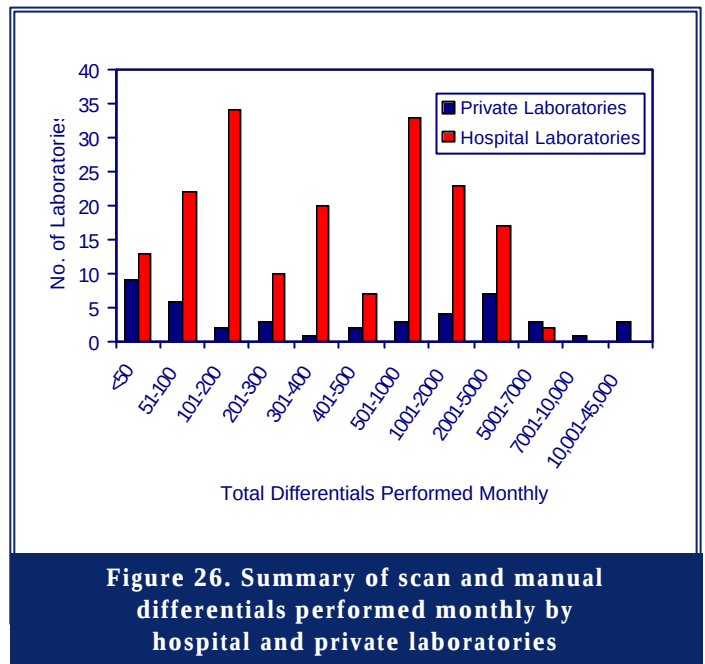
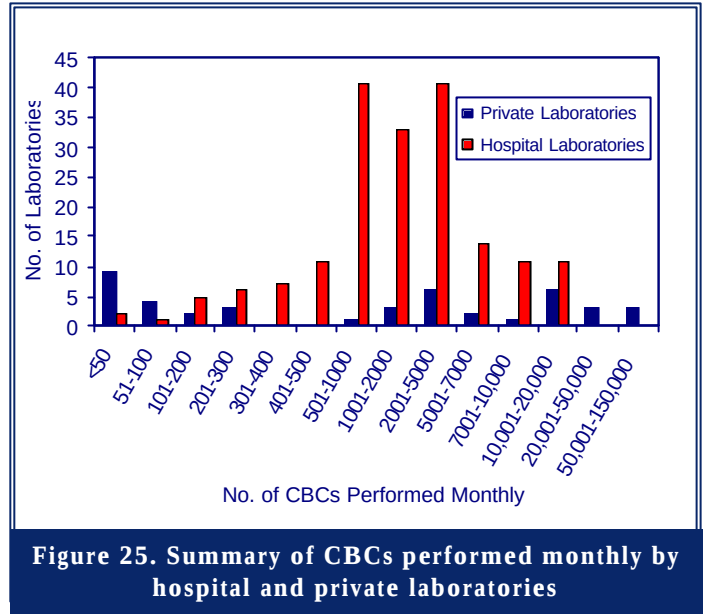
SUMMARY OF ACTIVITIES

- ✓ Issued Good Practice Guidelines for the Laboratory Investigation of Hemoglobinopathies and for Reporting of Smudge Cells.
- ✓ Supported continuing education in northwestern Ontario by sponsoring a morphology workshop at the Kenora-Rainy River 2001 Annual Fall Symposium.
- ✓ Supported distance continuing education by offering two on-line self-study courses, *Introduction to Hematology: The Erythrocyte* and *Erythrocyte Disorders: Detection and Diagnosis*.



FUTURE INITIATIVES

- ✓ Investigating a persistent positive bias in INR survey results with participants using a specific reagent/instrument combination.
- ✓ Conducting a D-dimer pilot survey to assess the sensitivity and accuracy of current methods.
- ✓ Conducting a patterns-of-practice survey to assess current practices in the investigation of thrombophilia and hemostasis.
- ✓ Supporting continuing education in northeastern Ontario by sponsoring a morphology workshop at the NORONT conference in Timmins.
- ✓ Supporting continuing education by providing a beginner to intermediate level flow cytometry workshop.



TRANSFUSION MEDICINE

TESTING MODEL

Four wet surveys were conducted in 2001 (Table 53). As in previous years, challenges were based on the laboratory licence, using two sets of material from different sources:

- ✓ Set A is procured from a US supplier and is distributed to laboratories with licences that include antibody identification. The number of participants in this category ranged from 94–95.
- ✓ Set B is procured from a Canadian supplier and is distributed to laboratories with licences that include antibody detection, but not identification. The number of participants in this category was 84.

This tiered approach continues to provide an appropriate level of challenge to all laboratories, while permitting cost containment.

Routine assessment of all participants includes ABO and Rh grouping, antibody detection, direct antiglobulin testing and crossmatching.

Set A participants were challenged with:

- ✓ A variety of ABO and Rh groups for typing and interpretation.
- ✓ Pre-natal samples from two Rh-negative women at different gestational periods, requiring titrations to detect rise in antibody titre.
- ✓ A possible transfusion reaction requiring detection and identification of a clinically significant antibody, assessment of a positive direct antiglobulin test, phenotyping and follow-up investigations of a possible transfusion reaction.
- ✓ Detection of mixed field agglutination in ABO grouping.
- ✓ Identification of a clinically significant antibody and selection of appropriate units for transfusion by crossmatch.

Set A participants completed a Titration Questionnaire on a survey with prenatal samples to assess methodology, serum/cell ratio, titration end point/interpretation and reporting.

Table 53. Samples Distributed in 2001

Set A		Set B	
I-0103-1	O Rh negative	I-0103-7	O Rh positive, antibody in the serum
I-0103-2	O Rh negative	I-0103-8	O Rh positive, donor unit for crossmatch
I-0103-3	O Rh negative, anti-D in serum	I-0103-9	O Rh negative, donor unit for crossmatch
I-0103-4	O Rh negative, anti-D in the serum	I-0103-10	O Rh positive, donor unit for crossmatch
I-0104-1	O Rh positive, Jk(a–)	I-0104-7	AB Rh positive
I-0104-2	O Rh positive, DAGT positive, anti-JK ^a in the serum and on the cells	I-0104-8	A Rh negative, antibody in the serum
I-0104-3	O Rh positive, Jk(a–)	I-0104-9	A Rh negative, antibody in the serum
I-0104-4	O Rh positive, Jk(a+)	I-0104-10	AB Rh positive
I-0109-1	AB Rh positive	I-0109-7	AB Rh positive
I-0109-2	B Rh positive. Mixed field B and O cells (50% B and 50% O)	I-0109-8	B Rh positive
I-0109-3	O Rh positive, anti-K and anti-Fy ^a in the serum	I-0109-9	AB Rh positive
I-0109-4	B Rh positive	I-0109-10	A Rh positive, antibody in serum
I-0111-1	A Rh negative, Jk(b–) and anti-Jkb	I-0111-7	A Rh? Mixture of 75% O Rh negative and 25% A Rh positive
I-0111-2	A Rh negative, Jk(b+), RBCs only	I-0111-8	A Rh positive, antibody present
I-0111-3	A Rh positive, Jk(b+), RBCs only	I-0111-9	AB Rh negative
I-0111-4	O Rh positive, Jk(b–), RBCs only	I-0111-10	B Rh positive

Set B participants were challenged with:

- ✓ A variety of ABO and Rh groups for typing and interpretation.
- ✓ Detection of a clinically significant antibody and performing crossmatching.
- ✓ Detection of three separate moderate-to-strongly reactive antibodies.
- ✓ Detection of mixed field agglutination in ABO and Rh groups.

Set B participants completed a Crossmatch Questionnaire to assess their ability to interpret crossmatch results and make appropriate decisions to select red cell units for transfusion.

ASSESSMENT OF RESULTS

Surveys were designed to be challenging, but were representative of scenarios commonly encountered in Transfusion Medicine laboratories. Clinical information was provided with each survey and directions were given on how to proceed with testing.

The Committee's assessment of errors for 2001 for Set A and B is displayed in Tables 54 and 55, and a five-year review of error rates is displayed in Table 56. The total number of significant errors is less than last year (21 in 2000 and 14 in 2001). Comparing Set A and Set B groups (Tables 54 and 55), Set A significant errors were similar to last year (7 in 2000 and 5 in 2001) and Set B significant errors were improved (14 in 2000 and 9 in 2001). There was only one ABO interpretation error in Set A, none in Set B, and no Rh interpretation errors in either set. Of most concern were the three laboratories in Set B, on sample I-0103-9, which failed to detect an incompatible donor unit on crossmatch and would transfuse the unit.

The total number of lesser errors increased from last year (133 in 2000 and 154 in 2001). Again, failure to detect mixed field reactions in ABO grouping was the main reason for the continuing large number of lesser errors for both Set A and Set B. The clinical significance of this reaction pattern was re-emphasized in Committee Comments.

Table 54. Committee Assessment of Errors for 2001 Surveys, Set A Only

Error Type	I-0103		I-0104		I-0109		I-0111		Total 2001*	
	Significant	Lesser	Significant	Lesser	Significant	Lesser	Significant	Lesser	Significant	Lesser
ABO	0	0	0	0	0	18	1	2	1	20
Rh	0	0	0	0	0	7	0	2	0	9
DAGT	0	0	1	8	0	1	2	1	3	10
Ab Detection	0	4	0	1	0	3	0	5	0	12
Ab Identification	0	2	1	0	1	1	0	0	1	3
Phenotype	0	0	0	0	0	8	0	1	0	17
Crossmatch	0	0	0	8	0	0	0	2	0	2
Total	0	6	2	16	1	38	3	13	5	73

* Ontario data only

Table 55. Committee Assessment of Errors for 2001 Surveys, Set B Only

Error Type	I-0103		I-0104		I-0109		I-0111		Total 2001*	
	Significant	Lesser	Significant	Lesser	Significant	Lesser	Significant	Lesser	Significant	Lesser
ABO	0	0	0	1	0	1	0	21	0	23
Rh	0	2	0	4	0	0	0	42	0	48
DAGT	0	0	0	0	0	0	0	1	1	1
Ab Detection	0	2	2	0	2	2	0	5	4	9
Phenotype	0	0	0	0	0	0	0	0	0	0
Crossmatch	4	0	0	0	0	0	0	0	4	0
Total	5	4	2	5	2	3	0	69	9	81

* Ontario data only

Table 56. Committee Assessment of Errors, 1997–2001

Error Type	1997		1998		1999		2000		2001*	
	Significant	Lesser	Significant	Lesser	Significant	Lesser	Significant	Lesser	Significant	Lesser
ABO	2	110	4	10	0	6	3	45	1	43
Rh	22	139	5	17	1	4	2	66	0	57
DAGT	1	0	0	2	0	8	0	6	4	11
Ab Detection	5	6	9	2	5	5	3	13	4	21
Ab Identification	1	6	4	7	13	1	5	3	1	3
Phenotype	0	21	0	22	0	11	0	0	0	17
Crossmatch	7	3	6	0	2	1	8	0	4	2
Total	38	285	28	60	21	36	21	133	14	154

* Ontario data only

ABO AND RH

Forty-three lesser errors were assessed in ABO grouping, mainly due to missing mixed field reactions in the clinical setting of a Group A or Group B patient receiving varying proportions of transfused Group O cells (50% O and 50% B for Set A, and 75% O and 25% A for Set B).

Table 57 shows the results of similar 50/50 mixed field surveys for Set A participants in 1997, 2000, and 2001. The improvement in mixed field detection seen in 2000 (96%), compared to 1997 (69%), has not been sustained in 2001 (81%). The failure to detect a mixed field pattern in ABO typing by 36 of 84 Set B laboratories was also of concern to the Committee. The clinical significance and laboratory investigation of this reaction pattern was again emphasized in Committee Comments.

Except for mixed field detection problems, however, there was only one ABO misinterpretation error in 2001 (a Set A laboratory) and none in Set B compared to three in 2000.

DIRECT ANTIGLOBULIN TESTING

Four significant, and 11 lesser errors were assessed in 2001. Although this is an increase from 2000 (six lesser errors), eight errors occurred on the sample involved in a transfusion reaction by failure to detect a weak positive DAGT. Proper DAGT technique has been addressed in Committee Comments.

ANTIBODY DETECTION AND IDENTIFICATION

For antibody detection and identification, five significant and 24 lesser errors were assessed in 2001, similar to 2000. There were four significant and 21 lesser errors in antibody detection and one significant and three lesser errors in antibody identification. Both Set A and Set B participants committed errors. As in previous years, these errors included detection of antibodies that were not present, failure to detect some that were, and incorrect antibody identification. Participants were reminded to record in the results column on the Analysis Worksheet only those antibodies that are identified. When antibodies are suspected, or if a particular antibody cannot be ruled out, this should be recorded in the Comments section.

CROSSMATCHING

Four significant errors were recorded in the Set B group. One laboratory found a unit incompatible

Table 57. Participants Detecting Mixed Field in Survey I-9703-2, I-0008 and I-0109

Vial	ABO (MF)	50/50 Mix	
	%	No. Detected Mixed Field	Total No. of Laboratories
I-9703-2	69	79	114
I-0008-3	96	94	98
I-0109-2	81	77	95

and three laboratories found units compatible when a significant antibody was present. Again the clinical significance of failing to detect an incompatible crossmatch was identified in Committee Comments.

CORRECTIVE ACTIONS

The questionnaire on antibody titration was analyzed and summarized in Committee Comments. Recommendations to enhance management of prenatal samples included emphasis on the importance of a high serum/cell ratio to promote sensitivity in antibody detection and use of a standard end-point for antibody titration.

Committee Comments also dealt with the importance of a disciplined approach to transfusion reaction investigation and the principles behind the selection of test methods to be employed.

Despite several observations in previous surveys on the difficulty encountered by many laboratories in detection of mixed field reactions, with significant impact on ABO and Rh grouping, this difficulty was again obvious in 2001. Committee Comments have again focused on the importance of detecting mixed field reactions, and emphasized its potential clinical significance.

FUTURE ACTIVITIES

A questionnaire was distributed in 2001 to determine the extent of automation in transfusion medicine. Since new techniques are becoming more widespread, in 2002, plans will be initiated to develop a pilot survey of laboratories using automated technology.

OTHER ACTIVITIES

Two articles, *Licensing, Accreditation and Quality Assurance of Transfusion Medicine Laboratories* and *Provincial Consensus Requirements for External Transfusion Medicine Quality Assessment Programs* were published in the CSTM Bulletin.

Testing Material Suppliers	Reference Laboratories
Hematology-General Hamilton Regional Laboratory Medicine Program, Hamilton, Ontario R&D Systems, Inc., Minneapolis, Minnesota	
Hemoglobinopathy and Fetal Cell Detection Hamilton Regional Laboratory Medicine Program, Hamilton, Ontario	Hamilton Regional Laboratory Medicine Program, Hamilton, Ontario
Flow Cytometry Hamilton Regional Laboratory Medicine Program, Hamilton, Ontario London Health Sciences Centre, University Campus/ R&D Systems, Inc., Minneapolis, Minnesota	
Coagulation Hamilton Regional Laboratory Medicine Program, Hamilton, Ontario Organon Teknika, Scarborough, Ontario Thrombosis Reference Centre, Manchester, UK	
Hematology-Morphology and Bone Marrow Various laboratories throughout the province	The Credit Valley Hospital, Mississauga, Ontario Toronto General Hospital, Toronto, Ontario Sunnybrook and Women's College Health Sciences Centre, Toronto, Ontario
Transfusion Medicine Gamma Biologicals, Inc., Houston, Texas London Health Sciences Centre, University Campus/ Canadian Blood Services, London, Ontario	The Credit Valley Hospital, Mississauga, Ontario Royal Victoria Hospital, Barrie, Ontario Sunnybrook and Women's College Health Sciences Centre, Toronto, Ontario





MICROBIOLOGY DISCIPLINES

BACTERIOLOGY

TESTING MODEL

Table 58 provides an overview of the 2001 testing model. Sixteen samples for isolation and identification were distributed. Antimicrobial susceptibility testing was expected to be performed on nine of these specimens. Twelve cultures were lyophilized and three were simulated “fresh” specimens. One-third (5/16) of the challenges contained a mixture of organisms:

- ✓ sputum specimen with *Moraxella catarrhalis*, *Staphylococcus epidermidis* and viridans streptococci (B-0102-1);
- ✓ “fresh” simulated faecal sample with *Escherichia coli* O157:H7 and mixed faecal flora (B-0104-2);
- ✓ urethral swab with *Neisseria cinerea* and *Staphylococcus epidermidis* (B-0106-1);

Bacteriology

No. of Participants (Dec. 2001).....	127 *
No. of Participants (Dec. 2000)	137 *
No. of Surveys Conducted in 2001	12

Mycology

No. of Participants (Dec. 2001)	27
No. of Participants (Dec. 2000)	29
No. of Surveys Conducted in 2001	2

Parasitology

No. of Participants (Dec. 2001)	28
No. of Participants (Dec. 2000)	29
No. of Surveys Conducted in 2001	2

Virology

No. of Participants (Dec. 2001)	73
No. of Participants (Dec. 2000)	60
No. of Surveys Conducted in 2001	16

* Includes laboratories licensed for Gram stain only.

Table 58. 2001 Bacteriology Surveys

B-0102	4 lyophilized cultures
B-0102-G	1 smear for Gram staining
B-0104	3 lyophilized cultures
	1 “fresh” simulated faecal specimen
B-0104-G	1 smear for Gram staining
B-0104-MB	1 smear for acid-fast bacilli (AFB) staining
B-0106	4 lyophilized cultures
B-0106-G	1 smear for Gram staining
B-0106-MB	1 smear for acid-fast bacilli (AFB) staining
B-0109	2 lyophilized cultures
	1 “fresh” simulated blood culture specimen
	1 “fresh” simulated faecal specimen for VRE screening
	Patterns-of-practice survey: Protocols for VRE surveillance specimens
B-0109-G	1 smear for Gram staining
B-0109-MB	1 smear for acid-fast bacilli (AFB) staining
B-0111-PP	Patterns-of practice survey: Blood cultures



- ✓ swab from hand, dog bite with *Pasteurella multocida* and *Staphylococcus intermedius* (B-0106-3);
- ✓ “fresh” simulated faecal sample for vancomycin resistant *Enterococcus* (VRE) screening with vancomycin-resistant *Enterococcus faecalis* and mixed faecal flora (B-0109-1).

Four smears for Gram staining and interpretation were distributed to laboratories licensed for either bacteriology or Gram stain and three unstained smears for detection of acid-fast bacilli (AFB) were distributed to those laboratories licensed to perform this testing.

Two patterns-of-practice surveys were conducted:

- ✓ Survey B-0109, which included a specimen for VRE screening, assessed laboratory protocols for performing this testing;
- ✓ Survey B-0111-PP was a patterns-of-practice survey that assessed all aspects of blood culture practice including blood collection protocols and quality indicators.

SURVEY ASSESSMENT

Participants' results for identification, antimicrobial susceptibility testing, Gram stain interpretation and AFB detection were assessed against the consensus results determined by eight reference laboratories. Results were flagged when they did not agree with the reference results or when an antimicrobial agent was reported that was not appropriate for the specific organism or site of isolation in the clinical data provided. Errors were assessed according to the potential impact a similar error would have on patient care, with a significant error assigned for results that were considered potentially clinically misleading.

OVERALL PERFORMANCE

Isolation and Identification

Overall performance in identification was very good with greater than 90% accuracy in identification to species level (i.e., excellent) achieved for 9/16 (56.3%) organisms distributed (Table 59).

The bacteriology program continues to reflect QMP-LS' commitment to quality improvement of laboratory services through education. Three organisms were distributed solely for their educational value—*Candida dubliniensis* (B-0102-3), *Staphylococcus intermedius* (B-0106-3B) and *Helicobacter cinaedi* (B-0106-4). No errors were assessed for these challenges.

Not surprisingly, the majority of laboratories (69/106, 65.1%) identified *C. dubliniensis* as *Candida albicans*, since these two species are closely related phylogenetically and share similar phenotypic characteristics, including germ tube production. The significance of *C. dubliniensis* (first described in 1995), particularly its potential to develop resistance to fluconazole, was discussed in Committee Comments with a recommendation that this organism be considered when treatment failure of a suspected *C. albicans* infection occurs. Ten laboratories (9%) identified *C. dubliniensis* correctly to species level, probably alerted by the clinical information provided with this sample (AIDS patient failing to respond to therapy with fluconazole).

Laboratory performance in identification of *S. intermedius* was better than anticipated. Almost one-third of laboratories recognized that the coagulase-positive staphylococcus, present in conjunction with *Pasteurella multocida* in a dog bite specimen, was *S. intermedius*. As expected, approximately 50% of laboratories identified the organism as *S. aureus* because most laboratories rely solely on a positive tube coagulase test for identification of *S. aureus*. While this is appropriate practice, laboratories were advised to consider *S. intermedius* in canine-inflicted wounds particularly when oxacillin resistance is detected in coagulase-positive isolates.

Helicobacter cinaedi was by far the most difficult organism to both isolate and identify. The major educational focus of this challenge was to provide guidance to laboratories on the use of supplementary stains (i.e., basic fuchsin, acridine orange) when a Gram-stained preparation of a positive blood culture does not yield visible microorganisms, and to reinforce the fact that selective media (in this case selective *Campylobacter* media) are not required, nor are they appropriate for subculture of positive blood cultures.

Other than these educational challenges, laboratories experienced some difficulty in isolation and/or identification with only three organisms:

- ✓ 6/105 (6%) failed to grow *Fusobacterium nucleatum* either because their anaerobic culture medium was not sufficiently

enriched to grow this organism or because their anaerobic conditions were not stringent enough;

- ✓ 11/103 (11%) misidentified *Neisseria cinerea* as *Neisseria gonorrhoeae*, seven of which used Gonocheck II (B-0106-1);
- ✓ 8/108 (7%) reported 'No growth obtained' with the "fresh" simulated blood culture containing *Corynebacterium jeikeium* because their automated system failed to flag positive; all that failed to detect growth used the BacT/Alert FAN bottle. No errors were assessed because a matrix effect with the simulated sample could not be excluded at the time of the survey. Subsequent studies using whole blood seeded with *C. jeikeium* confirmed that the FAN medium did not perform as well as the BacT/Alert standard aerobic medium for this particular organism. A significant decrease in the ability of laboratories to identify this organism to species level was noted compared with that in 1990 when this

organism was last used in a QMP-LS survey [28/109 (26%) in 2001 versus 153/225 (68%) in 1990].

As noted in the 1999 Review, identification of enterococci to species level is continuously improving. The year 2001 saw the best performance yet with 91% of laboratories identifying B-0109-1 as *Enterococcus faecalis* (compared with 85% in 1999).

Antimicrobial Susceptibility Testing

A reference result was available for 4029 antimicrobial susceptibility results and 99 (2.5%) results were flagged (Table 60). This is excellent performance.

While susceptibility testing of Gram-negative organisms was the major focus in 2000, susceptibility testing of Gram-positive organisms was the main emphasis in 2001 and there were several notable successes:

- ✓ all laboratories correctly reported *S. aureus* (B-0102-2) as oxacillin-resistant; this is the second time in a row that 100% of laboratories have identified an oxacillin-resistant strain;

Table 59. Organisms Distributed in 2001 and Performance in Identification

Survey	No. of Laboratories Reporting	Organism	%Correct* Identification (Excellent)	% Partial† Identification (Acceptable)	% Incorrect‡ Identification (Unacceptable)
B-0102-1	107	<i>Moraxella catarrhalis</i>	97.2	2.8	0.0
B-0102-2	107	<i>Staphylococcus aureus</i>	100.0	0.0	0.0
B-0102-3	106	<i>Candida dubliniensis</i>	9.4	89.6§	0.0
B-0102-4	107	<i>Serratia marcescens</i>	99.1	0.9	0.0
B-0104-1	104	<i>Streptococcus pneumoniae</i>	97.1	0.0	2.9
B-0104-2	113	<i>Escherichia coli</i> O157:H7	94.7	2.7	2.7
B-0104-3	105	<i>Fusobacterium nucleatum</i>	22.9	61.9	15.2
B-0104-4	105	<i>Acinetobacter baumannii</i>	61.9	36.2	1.9
B-0106-1	103	No <i>Neisseria gonorrhoeae</i> isolated¶	56.3	32.0	11.7
B-0106-2	102	<i>Staphylococcus aureus</i>	100.0	0.0	0.0
B-0106-3A#	103	<i>Pasteurella multocida</i>	96.1	3.9	0.0
B-0106-3B#	103	<i>Staphylococcus intermedius</i>	29.1	69.9**	1.0
B-0106-4	103	<i>Helicobacter cinaedi</i>	1.9	31.0	64.1††
B-0109-1‡‡	98	<i>Enterococcus faecalis</i>	90.8	8.2	1.0
B-0109-2	103	<i>Streptococcus pneumoniae</i>	100.0	0.0	0.0
B-0109-3	103	<i>Staphylococcus hominis</i>	24.3	72.8	2.9
B-0109-4§§	108	<i>Corynebacterium jeikeium</i>	25.9	60.2	13.8

* Identified correctly to species level

† Identified to genus level (without naming a species) or to correct Gram stain characteristics (e.g., Gram-positive bacillus)

‡ Identified incorrectly

§ An identification of *Candida albicans*, although technically incorrect, was considered an acceptable identification for this educational challenge

|| "Fresh" simulated faecal specimen with normal faecal flora and *E. coli* O157:H7

¶ *Neisseria cinerea* mixed with *Staphylococcus epidermis*, urethral swab

Mixed culture (swab from hand, dog bite)

** An identification of *Staphylococcus aureus*, although technically incorrect, was considered an acceptable identification for this educational challenge

†† Educational challenge

‡‡ "Fresh" simulated faecal specimen for VRE screening

§§ "Fresh" simulated blood culture specimen



- ✓ only 10/84 (12%) laboratories reported clindamycin as susceptible for B-0106-2 compared with 86/99 (87%) in 1998 for this strain of *S. aureus* that was susceptible to clindamycin by *in vitro* testing but should have been reported resistant because it was erythromycin-resistant due to the presence of the *erm* gene; this practice was recommended in Committee Comments for the 1998 survey;
- ✓ 48/103 (46%) laboratories reported a levofloxacin result for *Streptococcus pneumoniae* (B-0109-2) compared with only 15/109 (14%) in 2000; this practice was recommended in Committee Comments for the 2000 survey;

- ✓ only 5/99 (5%) laboratories failed to detect oxacillin-resistance in *Staphylococcus hominis* (B-0109-3) compared with 28/101 (28%) that failed to do so in 2000.

An exception to otherwise excellent performance was with *Streptococcus pneumoniae* ATCC® 49619. This strain, recommended by NCCLS for quality control of disk diffusion and dilution methods for streptococci, was sent as a blind challenge (B-0104-1). Zone diameter and MIC results were requested in addition to the interpretation of these results. The proportion of

Table 60. Antimicrobial Susceptibility Testing Interpretive Error Flags for 2001

Antimicrobial Agent	Gram Negative Organisms Interpretive Error Flags					Gram Positive Organisms Interpretive Error Flags				
	No. of Tests Reported	Very Major*	Major†	Minor‡	Total Flags (%)	No. of Tests Reported	Very Major*	Major†	Minor‡	Total Flags (%)
Amikacin	19	1	0	3	4 (22.2)	0	...	...	...	...
Amoxicillin/clavulanate	4	0	0	0	0 (0.0)	0	...	...	...	...
Ampicillin	95	1	0	0	1 (1.0)	0	...	...	...	...
Cefazolin	68	0	0	1	1 (1.5)	0	...	...	...	...
Cefotaxime	17	0	0	4	4 (23.5)	18	0	0	0	0 (0.0)
Cefoxitin	4	0	0	0	0 (0.0)	0	...	...	...	...
Cefotetan	4	0	0	0	0 (0.0)	0	...	...	...	...
Ceftazidime	80	2 §	0	30 §	32 (40.0)	0	...	...	...	...
Ceftriaxone	35	2 §	0	3 §	5 (14.3)	18	0	0	0	0 (0.0)
Cephalothin	18	0	0	0	0 (0.0)	0	...	...	...	...
Ciprofloxacin	186	0	0	0	0 (0.0)	20	0	0	1	1 (5.0)
Clindamycin	0	...	...	...	...	351	10	0	0	10 (2.8)
Erythromycin	0	...	...	...	...	498	0	1	1	2 (0.4)
Gentamicin	104	0	0	0	0 (0.0)	74	0	0	0	0 (0.0)
Imipenem	92	0	0	1	1 (1.1)	0	...	...	...	...
Levofloxacin	2	0	0	0	0 (0.0)	76	0	0	0	0 (0.0)
Meropenem	8	0	0	0	0 (0.0)	0	...	...	...	...
Ofloxacin	0	...	...	...	...	10	0	0	0	0 (0.0)
Oxacillin	0	...	...	...	...	402	5 ¶	1	1	7 (1.7)
Penicillin	0	...	...	...	...	449	0	0	21 #	21 (4.7)
Piperacillin	82	0	0	0	0 (0.0)	0	...	...	...	...
Piperacillin/tazobactam	6	0	0	0	0 (0.0)	0	...	...	...	...
Rifampin	0	...	...	...	...	15	0	0	0	0 (0.0)
Tetracycline	0	...	...	...	...	76	0	0	1	1 (1.3)
Ticarcillin	9	0	0	0	0 (0.0)	0	...	...	...	...
TMP/SMX	154	2	1	0	3 (1.9)	463	3	0	0	3 (0.6)
Tobramycin	5	0	0	0	0 (0.0)	0	...	...	...	...
Vancomycin	0	...	...	...	...	334	0	1	1	2 (0.6)
β-lactamase	94	0	0	1	1 (1.1)	139	0	0	0	0 (0.0)
Total	1086	8	1	43	52 (4.8)	2943	18	3	26	47 (1.6)

* Reporting an antimicrobial result as susceptible (S) when the reference result is resistant (R) (i.e. falsely susceptible)

† Reporting an antimicrobial result as R when the reference result is S (i.e. falsely resistant)

‡ Reporting an antimicrobial result as S or R when the reference result is intermediate (I) or reporting an I when the reference result is S or R.

§ All for *Acinetobacter baumannii* (B-0104-4)

|| All for *Staphylococcus aureus* (B-0106-2)

¶ All for *Staphylococcus hominis* (B-0109-3)

All for *Streptococcus pneumoniae* (B-0104-1)

zone diameter results outside the published acceptable QC range was unacceptably high (14.5%). MIC results were somewhat better, with 7.1% being flagged for falling outside the acceptable range. This is strikingly similar to the performance seen with *Pseudomonas aeruginosa* ATCC® 27853 (1998 Review). It is difficult to determine the reasons for such a high level of discordant results when QC strains are tested blindly compared to when tested for QC purposes. Subsequent to the survey, laboratories were asked to submit their QC data for *S. pneumoniae* ATCC® 49619 for each antibiotic reported. Review of submitted QC data showed that the most significant factor contributing to poor performance on this survey was that laboratories were not performing QC on the particular antibiotic that had out-of-range results. This practice is unacceptable. Twenty of the 21 minor flags for penicillin (Table 60) were for reporting penicillin as resistant based on an oxacillin result of ≤ 19 mm. While oxacillin can be used to screen for increased resistance to penicillin in *S. pneumoniae*, the level of penicillin resistance must be determined by an MIC method.

Performance in susceptibility testing of Gram-negative organisms was also remarkably good with the exception of a substantial number of interpretive error flags for ceftazidime for a multi-drug resistant strain of *Acinetobacter baumannii* (B-0104-4). All flagged results were determined using an automated system. Laboratories using automated systems must be aware of their shortcomings, including the failure to detect some inducible or subtle resistance mechanisms, and implement appropriate measures to ensure that the patient results they report are accurate.

Gram Stain Smear Interpretation

Performance on staining and interpretation of Gram smears is shown in Tables 61 and 62. Overall performance improved considerably compared with the previous two years (see 1999 and 2000 Reviews). Interpretation of the microorganism component for the simulated vaginal smear

(B-0102-G) was problematic for some laboratories. The smear contained moderate to large numbers of *Candida glabrata*, which was reported by all laboratories. However, several bacterial morphotypes were also present (i.e., few Gram-positive cocci, few Gram-positive bacilli and few Gram-negative bacilli). Consequently, 11 laboratories reported that the smear was suggestive of bacterial vaginosis, despite the fact that the bacterial morphotypes present were not those typically found in bacterial vaginosis (i.e., *Gardnerella*, *Mobiluncus*). As a result, it was

Table 61. Performance in Microscopic Identification of Microorganisms for Gram Stain Smears Distributed in 2001

Survey	No. of Laboratories Reporting	Microorganism Component	%Correct* Identification (Excellent)	% Incorrect† Identification (Unacceptable)
B-0102-G‡	132	Yeast	88.6§	11.4§
B-0104-G	131	Gram-negative bacilli	90.8	9.2
B-0106-G¶	129	Gram-positive cocci/diplococci	92.2	7.8
B-0109-G#	127	Gram-negative cocci/diplococci	74.8	25.2

* Correct morphology and Gram reaction of microorganism component

† Failure to report microorganism morphotype(s) present or reporting microorganism or morphotype(s) not present in the smear

‡ Simulated smear of vaginal swab for Gram staining (moderate to large numbers of *Candida glabrata*), few Gram-positive cocci, few Gram-positive bacilli and few Gram-negative bacilli were also present but were not evaluated

§ Although all laboratories correctly reported yeast cells, 11 also reported that the smear was suggestive of bacterial vaginosis and 3 reported Gram-negative diplococci (on physician reports)

|| Simulated smear of splenic abscess for Gram staining (moderate to large numbers of *Fusobacterium nucleatum*)

¶ Simulated smear of CSF (moderate to many *Streptococcus pneumoniae*)

Simulated smear of sputum for Gram staining (large numbers of *Moraxella catarrhalis*)

Table 62. Performance in Microscopic Identification of Cells for Gram Stain Smears Distributed in 2001

Survey	No. of Laboratories Reporting	Cellular Component	%Correct* Identification (Excellent)	% Incorrect† Identification (Unacceptable)
B-0102-G‡	132	Epithelial cells	64.4	35.6
B-0104-G§	131	Pus cells/white blood cells	95.4	4.6
B-0106-G	129	Pus cells/white blood cells	97.7	2.3
B-0109-G¶	127	Pus cells/white blood cells & epithelial cells	92.1	7.9

* Correct identification of cellular component of smear

† Failure to report cellular morphotype(s) present or reporting cellular morphotype(s) not present in the smear

‡ Simulated smear of vaginal swab for Gram staining (moderate to many epithelial cells)

§ Simulated smear of splenic abscess for Gram staining (moderate to many pus cells/white blood cells)

|| Simulated smear of CSF (many pus cells/white blood cells)

¶ Simulated smear of sputum for Gram staining (large numbers of pus cells and few epithelial cells)



recommended that laboratories adhere to a numerical scoring system for diagnosis of bacterial vaginosis in Gram-stained smears. The simulated smear of sputum containing large numbers of *Moraxella catarrhalis* also caused significant difficulty. Under-decolourization was the major cause of discordant results, not unexpected given that *Moraxella* species resist decolourization.

AFB Smear Interpretation

Performance on the three prepared smears of concentrated sputa for acid-fast stain and interpretation improved slightly over previous year (see 2000 Review) (Table 63).

There has been a marginal increase in the proportion of Ontario laboratories that used a fluorochrome method (e.g., auramine-rhodamine) to stain their slides [36/45 (80%) compared with (39/53)(74%) in 2000].

Patterns-of-Practice Surveys

A patterns-of-practice survey to determine current laboratory practice in processing of surveillance specimens for VRE investigation was carried out in conjunction with the “fresh” simulated faecal sample for VRE screening (B-0109-1). Laboratories were asked to submit their laboratory protocols for this testing. Results showed that practice with VRE surveillance specimens was much more standardized with respect to the selective isolation media used compared to 1997 when this practice was last reviewed.

A patterns-of-practice survey on blood cultures was also conducted (B-0111-PP). Laboratories were asked to submit:

- ✓ copies of the requisitions, workcards and reports for the last ten patients with at least one a positive blood culture;
- ✓ a completed questionnaire on quality indicators for blood cultures;

- ✓ their institution's current instructions on blood culture collection;
- ✓ their bench manual protocols for processing and examining blood cultures specifically for fungi.

Results showed:

- ✓ most laboratories do not measure, record, summarize and analyze in a systematic fashion, quality process indicators for blood cultures (e.g., transit time, volume of blood collected, number of blood culture sets per patient, transit time, positivity and contamination rates);
- ✓ blood collection protocols were highly variable;
- ✓ most laboratories do not have specific protocols for fungal blood cultures.

A set of “best-practice” recommendations for all aspects of blood culture testing was issued with extensive Committee Comments. Feedback on the recommendations was invited.

ERROR RATES

The overall errors assessed in 2001 for identification and susceptibility testing are shown in Table 64. Errors for incorrect identification, incorrect antimicrobial susceptibility testing results and inappropriate antimicrobial agents are detailed in Tables 65, 66 and 67, respectively. Total significant errors decreased to 52 from 92 in 2000, and similarly total lesser errors also decreased (to 179 from 298). The sizable increase in lesser errors over 2000 for incorrect susceptibility test results was due almost exclusively to *S. pneumoniae* ATCC® 49619 as discussed earlier in this report. Although down from last year, 52 lesser

Table 63. Performance in Microscopic Identification of AFB for Smears Distributed in 2001

Survey	No. of Laboratories Reporting	Quantity of Acid-Fast Bacilli	%Correct* Identification (Excellent)	%Partial† Identification (Acceptable)	% Incorrect‡ Identification (Unacceptable)
B-0104-MB	48	Few to moderate AFB present	81.3	16.7	2.1
B-0106-MB	48	Scarce to few AFB present	85.4	2.1	12.5
B-0109-MB	45	No acid-fast bacilli present	100.0	0.0	0.0

* Correct quantity of AFB reported

† Presence or absence of AFB correctly identified but quantity reported differed from expected quantity

‡ Presence or absence of AFB incorrectly identified

errors were assessed for inappropriate antimicrobial reports, mainly due to reporting results for *Pasteurella multocida*, an organism for which NCCLS interpretive criteria do not exist.

Errors for Gram stain interpretation decreased almost three-fold compared with 2000 (Table 68). While significant errors continue to be proportionately higher for laboratories that are licensed for Gram stain only, the variance was not as marked as in 2000 (Figure 27).

Errors for AFB interpretation were down slightly in 2001 (Table 69) as were transcription errors, while survey errors attributable to testing the wrong sample remained constant (Table 70).

Table 64. Overall Errors Assessed for Identification and Susceptibility Testing in 2001

Survey	No. of Laboratories	Total Flags	No. of Significant Errors	No. of Lesser Errors
B-0102	107	19	2	15
B-0104	113	159	20	119
B-0106	103	68	13	32
B-0109	108	45	17	13
Total	...	291	52	179

Table 65. Errors Assessed for Identification

Survey	No. of Laboratories	No. of Significant Errors	No. of Lesser Errors
B-0102	107	1	1
B-0104	113	16	5
B-0106	103	11	2
B-0109	108	7	5
Total	...	35	13

Table 66. Errors Assessed for Incorrect Antimicrobial Susceptibility Results

Survey	No. of Laboratories	No. of Significant Errors	No. of Lesser Errors
B-0102	107	1	3
B-0104	113	4	101
B-0106	103	2	4
B-0109	108	10	6
Total	...	17	114

Table 67. Errors Assessed for Reporting Inappropriate Antimicrobial Agents (for Organism and/or Site)

Antimicrobial Agent	No. of Significant Errors	No. of Lesser Errors	Organism
Not applicable	0	3	<i>Moraxella catarrhalis</i> *
	0	24	<i>Pasteurella multocida</i> *
	0	2	<i>Escherichia coli</i> O157:H7†
Ampicillin	0	3	<i>Acinetobacter baumannii</i> §
Amoxicillin/clavulanic acid	0	3	<i>Acinetobacter baumannii</i> §
Cefazolin	0	2	<i>Acinetobacter baumannii</i> §
Cephalothin	0	1	<i>Acinetobacter baumannii</i> §
Ciprofloxacin	0	3	<i>Staphylococcus aureus</i> †
Gentamicin (high-level)	0	2	<i>Staphylococcus aureus</i> †
Tetracycline	0	3	<i>Staphylococcus aureus</i> †
	0	1	<i>Acinetobacter baumannii</i>
Levofloxacin	0	1	<i>Staphylococcus aureus</i> †
	0	1	<i>Acinetobacter baumannii</i>
β-lactamase	0	1	<i>Serratia marcescens</i>
	0	2	<i>Corynebacterium jeikeium</i>
Total	0	52	

* No NCCLS interpretive criteria for this organism

† Inappropriate to report for 8-year-old

‡ Inappropriate to report antimicrobial results since antibiotic therapy may increase the risk of hemolytic uremic syndrome (HUS)

§ No NCCLS interpretive criteria for this antibiotic/organism combination

|| Interpretive criteria are for urine isolates only

†† Appropriate only for *Enterococcus* species

Table 68. Errors Assessed for Incorrect Gram Stain Interpretation

Survey	No. of Laboratories	Total Flags	No. of Significant Errors	No. of Lesser Errors
B-0102-G	132	104	4	15
B-0104-G	131	17	12	4
B-0106-G	129	22	7	7
B-0109-G	127	42	24	24
Total	...	185	47	50

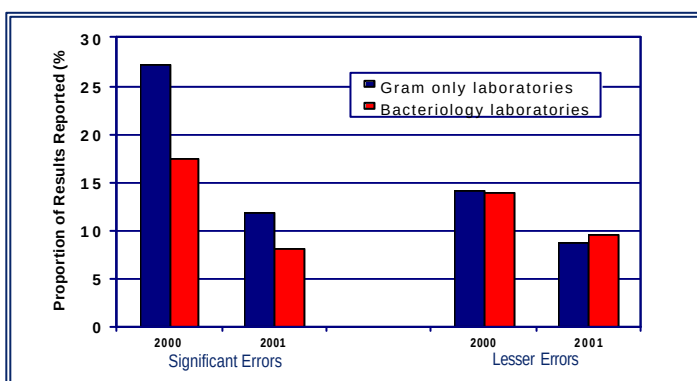


Figure 27. Significant and lesser errors assessed for Gram stain interpretation by laboratory type as a proportion of total results reported

Corrective Actions

All errors assessed to a laboratory result in correspondence (i.e., memorandum of clarification) from QMP-LS. While this is usually somewhat disconcerting to the laboratory receiving it, correspondence is an integral component of the external quality assurance process. It is the only way to assure that a laboratory has thoroughly investigated a discordant result and implemented appropriate corrective action(s) as necessary.

Corrective actions most frequently undertaken in 2001 included the following:

- ✓ updated antibiotic susceptibility testing protocols in accordance with the most recent NCCLS guidelines;
- ✓ revised antibiotic reporting protocols in accordance with NCCLS and QMP-LS recommendations;
- ✓ not accepting identification provided by testing systems when confidence levels are below 90% probability;
- ✓ instituted testing of *Streptococcus pneumoniae* ATCC® 49619 for QC of susceptibility testing for streptococci;
- ✓ instituted testing of *Staphylococcus aureus* ATCC® 25923 for testing the oxacillin disk used for screening for increased resistance of *Streptococcus pneumoniae* for penicillin;
- ✓ added Brucella agar for culturing specimens for anaerobes;
- ✓ changed identification system or implemented additional testing for *Neisseria gonorrhoeae*;
- ✓ revised scoring and reporting protocols for bacterial vaginosis in accordance with QMP-LS recommendations;
- ✓ changed decolourizer for Gram stain procedure;
- ✓ changed positive control for Gram stain procedure to *Streptococcus pneumoniae*;

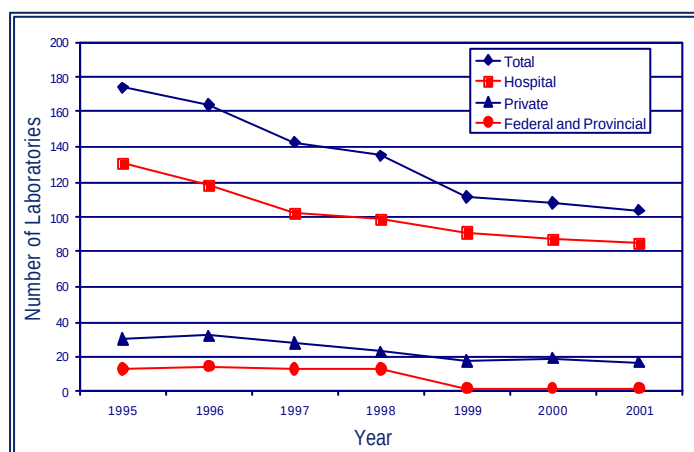


Figure 28. Number of bacteriology laboratories in Ontario by facility type

Table 69. Errors Assessed for Incorrect AFB Interpretation

Survey	No. of Laboratories	Total Flags	No. of Significant Errors	No. of Lesser Errors
B-0104-MB	48	1	1	0
B-0106-MB	48	6	3	3
B-0109-MB	45	0	0	0
Total	...	7	4	3

Table 70. Type of Errors

Type of Error	Number
Wrong sample	4
Transcription error	12

- ✓ changed Gram stain reagent supplier;
- ✓ staff attended QMP-LS Gram stain workshop;
- ✓ dropped Gram stain from testing menu due to low volume.

NUMBER OF PROVIDERS

The number of laboratories that provide a comprehensive testing menu in bacteriology has remained relatively stable over the last three years (Figure 28). Ten laboratories that were licensed for Gram stain only have dropped this test since 1999 (Figure 29). Many of these laboratories were having difficulty in maintaining proficiency in Gram stain interpretation because of low testing volumes. Similarly, fourteen laboratories have discontinued AFB smear examination during this same period of time (Figure 29).

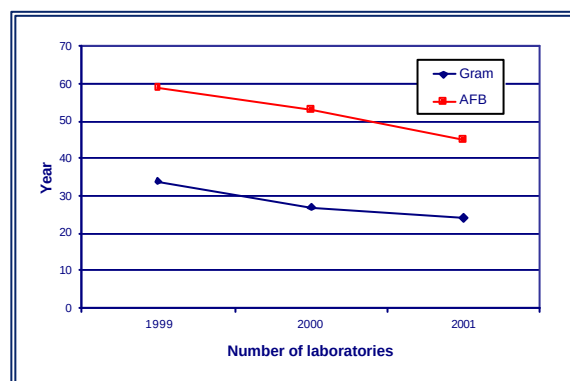


Figure 29. Number of laboratories performing Gram stain and AFB smear examination

MYCOLOGY

TESTING MODEL

Two challenge surveys were conducted in 2001. Each survey consists of four samples. As before, the challenges were selected from the three groups of medically significant fungi—dermatophytes, yeasts and moulds. Testing material was distributed to laboratories as live cultures on agar slants. The type of specimen and a limited clinical history was provided to participants on the analysis worksheets. Survey W-0108 also provided microscopic information. Laboratories were required to process the cultures as if they were patient specimens. Laboratories' licences for mycology vary in the type of specimens processed and the extent to which isolates are identified (Table 71). All challenge samples are sent to all laboratories, but assessment of survey results is based on each laboratory's stated level of practice.

Although the reported identification of organisms according to the Ontario System for Identification of Medically Important Bacteria (OSIMIB) code is the only component of the survey that is scored, all information provided by participants on the analysis

worksheets in terms of isolation media used, macroscopic and microscopic findings as well as other identification features are reviewed for appropriateness. In addition to the requirement to report the identity of the organism according to OSIMIB, participants are encouraged to comment on how each organism would be reported to the physician. Hypothetical direct microscopy results for each sample are now provided on the analysis worksheet to facilitate participant interpretation of the potential clinical significance of each organism. Errors are classified as lesser or significant, depending on their potential impact on patient care.

Comprehensive Committee Comments for each organism include a review of the identification of the organism and its clinical significance as well as a review of participant performance.

LABORATORY PARTICIPATION

There has been a reduction in the number of laboratories licensed to perform mycology since the program started in 1997, when 52 laboratories participated in the initial pilot survey. By the end of 2001, there were 28 laboratories performing mycology (Figure 30).

Although the number of participants has dropped, the level of practice has not changed significantly. Most laboratories identify yeasts as part of their routine microbiology practice. However, some of these may not attempt to isolate yeasts associated with systemic infection and choose to refer out such specimens. In

Table 71. Level of Practice by Laboratories Licensed for Mycology (n=28)*

	2001 No. of Laboratories
Yeast	
Identify most yeast to species level	27
Perform minimal identification tests	2
Practice with yeast not specified	...
Dermatophytes	
Culture for dermatophytes and identify most isolates	20
Culture for dermatophytes and refer all isolates	5
Refer all dermatological mycology specimens	3
Systemic Fungi	
Culture systemic specimens and identify most isolates	15
Culture systemic specimens and refer all isolates	9
Culture systemic specimens, perform preliminary identification and refer for confirmation	1
Refer all systemic specimens for mycology	3

* No laboratories participating at end of year; includes two out-of-province laboratories that participate in the mycology program as reference laboratories—Wadsworth Centre for Laboratories and Research, Albany, New York, and Laboratoire de Santé Publique du Québec.

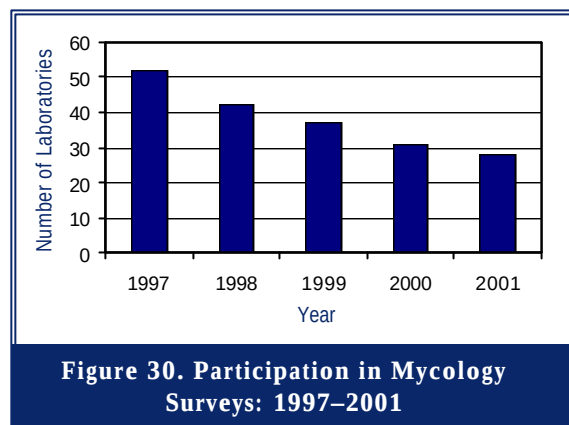


2001, 69.0% of laboratories identified most dermatophyte fungi from superficial skin specimens, while only 51.7% of licensed laboratories cultured and identified fungi from systemic specimens.

OVERALL PERFORMANCE

Overall, performance on surveys W-0103 and W-0108 was excellent (Table 72), with most laboratories performing satisfactorily to their stated level of practice.

There were two misidentifications in survey W-0103. Two laboratories misidentified *Trichophyton tonsurans* as *Trichophyton mentagrophytes* based on micromorphological features. *T. tonsurans* was previously sent to laboratories in March 1997 (B-9703-MY-2). At that time, only 37.5% of laboratories were able to identify this organism to species level, compared to 68.0% of reporting laboratories in this survey. This indicates a significant improvement in ability to recognize this organism. Laboratories had little difficulty in recognizing *Aspergillus fumigatus* (W-0103-2), with 96.2% of laboratories able to identify this organism to the species or genus level. Similarly, most laboratories were able to identify *Curvularia* NOS to the genus level. Identification of *Trichosporon beigeli*/*cutaneum* complex was also very good with 85.2% achieving identification to the species or genus level. There have been recent taxonomic changes within the *Trichosporon* genus and the strain provided to participants is actually now classified as *T. asahii*. However, there still exists considerable confusion with



the taxonomy, and it is preferable at this time for laboratories to identify to the genus level and refer isolates from sterile sites to reference laboratories for full identification.

There were also very few problems encountered in survey W-0108. Laboratories had little difficulty with recognition of *Rhizopus*, NOS (W-0108-1) at the genus level. One laboratory failed to grow *T. verrucosum* (W-0108-2). This organism grows more slowly than other members of its genus. Although *T. verrucosum* is a dermatophyte rarely encountered in routine practice, 69.2% of laboratories were able to identify this organism to species level and more than 86% provided an acceptable identification. One laboratory misidentified *Trichoderma* NOS (W-0108-3) as *Acremonium* species based on micromorphological

Table 72. 2001 Organism Distribution and Survey Performance

Survey	No. of Labs Reporting	Organism	% Correct* Identification (Excellent)	% Partial † Identification (Acceptable)	% Incorrect ‡ Identification (Unacceptable)
W-0103-1	25	<i>Trichophyton tonsurans</i>	68.0	24.0	8.0
W-0103-2	26	<i>Aspergillus fumigatus</i>	76.9	23.1	0.0
W-0103-3	26	<i>Curvularia</i> , NOS	84.6	15.4	0.0
W-0103-4	28	<i>Trichosporon cutaneum/beigeli</i> complex	85.2	14.8	0.0
W-0108-1	27	<i>Rhizopus</i> , NOS	77.8	22.2	0.0
W-0108-2	26	<i>Trichophyton verrucosum</i>	69.2	26.9	3.9
W-0108-3	26	<i>Trichoderma</i> , NOS	65.4	30.7	3.9
W-0108-4	27	<i>Geotrichum candidum</i>	92.6	7.4	0.0

* Identified correctly to species level (or to genus level when appropriate)

† Identified genus level (without naming a species) or correct to general classification (e.g., yeast, mould, filamentous fungi, dermatophyte)

‡ Identified incorrectly

findings. Recognition of *Geotrichum candidum* (W-0108-4) to the genus level was excellent (92.6%), with many laboratories using some form of commercial identification system to supplement macroscopic and microscopic findings.

Error Rate

There were a total of five errors assessed for the two surveys in 2001 (see Table 73). This compares favourably with a total of four errors assessed in 2000 in which there was only one challenge survey, and nine errors in 1999.

Table 73. Errors Assessed in 2001

Survey	No. of Labs Reporting	Total Flags	No. of Significant Errors	No. of Lesser Errors
W-0103	27	5	0	2
W-0108	27	4	1	2
Total	54	9	1	4

PARASITOLOGY

TESTING MODEL

Two surveys, each consisting of three vials of SAF-preserved faecal suspension for concentration and preparation of stained smears by laboratories, were conducted in 2001. Testing material consisted of unpooled specimens from patients in Ontario and was generously provided by the Regional Parasitology Laboratory, Hamilton Regional Laboratory Medicine Program—St. Joseph’s site, Hamilton, Ontario. Material was distributed by London Health Sciences Centre, London, Ontario.

Performance is assessed by comparing participants’ results to the consensus results of ten referee laboratories, selected from their peers. The ten laboratories with the highest average score over the preceding four surveys were selected as the referee group for the survey being evaluated. Results from these laboratories were collated and used to determine the scoring scheme and flagging criteria. The referee group represented approximately one-third of participating laboratories. A result was scored if more than one-half of the referee laboratories reported it. Full marks were awarded for each correct stage and quantity of parasite species reported. Partial marks were awarded if the quantity reported fell outside the expected range. Marks were deducted for reports of parasite species not present in the sample. Errors were assigned only when a parasite was not reported in both the concentrate and stained smear or if a parasite not actually present in the specimen was reported in either the concentrate or stained smear. Errors were not assessed for failing to report a parasite unless there was at least 90% agreement among the referee laboratories. A significant error was not assessed for failing to report helminth ova or larvae that were present in very small quantities unless consensus was achieved by all referee laboratories.

LABORATORY PERFORMANCE

An overview of performance on the two surveys conducted in 2001 is shown in Table 74. Detection of A quantities of parasites (i.e. 1–4 per coverslip for helminths and 1–5 per coverslip for protozoa) continues to be a challenge for laboratories. Notably, only 54% of participating laboratories reported *Chilomastix mesnili* trophozoites in survey T-0105-3S, 52% reported *Endolimax nana* cysts in T-0110-1C and 52% reported *Entamoeba hartmanni* trophozoites in T-0110-1S, while 90% of the referee laboratories did so. It is difficult to determine exactly what factors account for

Table 74. Overall Performance of Referee and Participating Laboratories in 2001*

Survey	Expected Parasite	Quantity	Referee Agreement (%)	Participant Agreement (%)†
T-0105-1C (Concentrate)	<i>Schistosoma mansoni</i> ova	A	100	89
	<i>Strongyloides stercoralis</i> larvae	A	90	61
T-0105-1S (Stained slide)	<i>Schistosoma mansoni</i> ova	A	90	71
	<i>Strongyloides stercoralis</i> larvae	A	60	61
T-0105-2C (Concentrate)	No parasites seen	...	100	96
T-0105-2S (Stained slide)	No parasites seen	...	100	96
T-0105-3C (Concentrate)	<i>Entamoeba histolytica/dispar</i> cysts	B/C	100	100
T-0105-3S (Stained slide)	<i>Chilomastix mesnili</i> trophozoites	A	90	54
	<i>Entamoeba histolytica/dispar</i> cysts	B	100	100
	<i>Entamoeba histolytica/dispar</i> trophozoites	C	100	100
T-0110-1C (Concentrate)	<i>Endolimax nana</i> cysts	A	90	52
T-0110-1S (Stained slide)	<i>Endolimax nana</i> cysts	A	60	45
	<i>Endolimax nana</i> trophozoites	C	100	100
	<i>Entamoeba hartmanni</i> trophozoites	A	90	52
T-0110-2C (Concentrate)	<i>Entamoeba histolytica/dispar</i> cysts	D	100	100
T-0110-2S (Stained slide)	<i>Entamoeba histolytica/dispar</i> cysts	D	100	100
	<i>Entamoeba histolytica/dispar</i> trophozoites	C	100	100
	Unidentified flagellate trophozoites (no cysts present to identify species)	B	100	72
T-0110-3C (Concentrate)	<i>Strongyloides stercoralis</i> larvae	A	100	100
T-0110-3S (Smear)	<i>Strongyloides stercoralis</i> larvae	A	100	86

Helminths: A-occasional, 1–4 per coverslip; B-few, 5–20 per coverslip; C-moderate, 11–20 per coverslip; D-many, 1 per low power field; E-numerous, 1 or more per high power field

Protozoa: A-occasional, 1–5 per coverslip; B-few, 6–25 per coverslip; C-moderate, 1 per low power field; D-many, 1 per high power field; E-numerous, 1 or more per oil immersion field

* Includes one laboratory in New Brunswick

† All laboratories including referee laboratories

the differences in performance between referee and participating laboratories (in which the referee laboratories are also included). However, based on feedback and/or review of slides from laboratories that have experienced difficulties detecting small quantities of organisms, there are a couple of recurring themes. One is that some laboratories hold back an aliquot of material for retesting. There is no doubt that this practice leads to sub-optimal performance. As well, review of

submitted slides has on occasion shown either poor slide preparation and/or staining techniques, which have interfered with detection or accurate identification of organisms.

Performance was excellent when larger numbers of organisms were present. Once detected, most Ontario laboratories are able to identify the parasites to species level with a high degree of accuracy.

As part of the evaluation process, laboratories were routinely required to report results on their laboratory report form as they would normally report to a physician, in addition to submitting the routine analysis worksheets. These reports were reviewed to assess whether laboratories were following the QMP–LS guidelines distributed in 2000 for reporting enteric parasitology specimens. All but five laboratories were adhering to the recommendations to not report non-pathogenic protozoa and to not report the stage of parasite (except *Strongyloides stercoralis*). All but six laboratories include a comment concerning the pathogenicity, or lack thereof, for *Entamoeba histolytica* or *Entamoeba dispar*, respectively.

ERROR RATES

Table 75 shows the number of significant and lesser errors assessed in 2001. The total errors were down from last year, primarily due to a substantial decrease in the number of significant errors (Figure 31).

Table 75. Errors Assessed in Parasitology in 2001

Survey	No. of Laboratories	Total Flags	No. of Significant Errors	No. of Lesser Errors
T-0105	28 *	58	8	19
T-0110	29 *	78	4	26
Total	...	136	12	45

* Includes one laboratory in New Brunswick

NUMBER OF PROVIDERS

The number of parasitology laboratories in Ontario decreased by one since 2000 (hospital laboratory) leaving a total of 28 testing facilities (Figure 32).

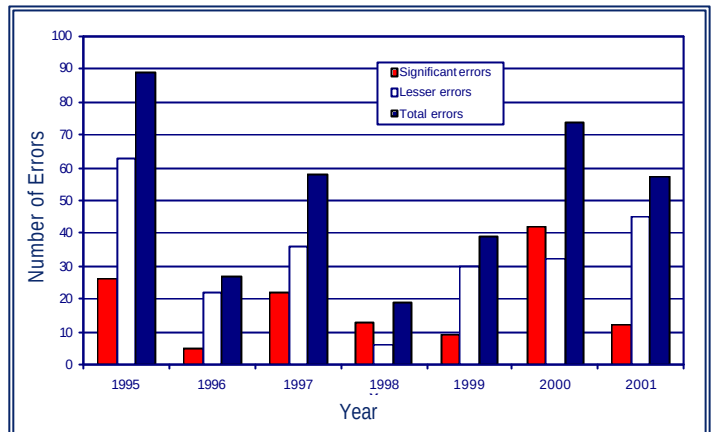


Figure 31. Errors in parasitology (1995–2001)

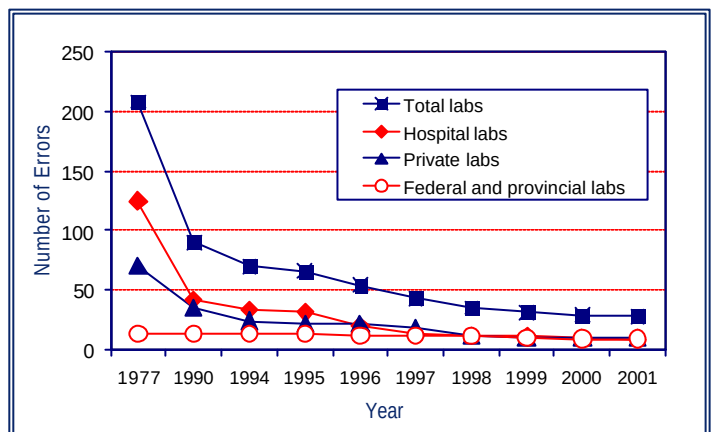


Figure 32. Number of parasitology laboratories by facility type



VIROLOGY

TESTING MODEL

Sixteen surveys were conducted during 2001. Of these, there were 14 challenge surveys, one patterns-of-practice survey for chlamydia, and a pilot challenge survey for respiratory syncytial virus (RSV) antigen detection. Table 76 shows the number of samples in the survey and the number of laboratories participating.

The testing material used for hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV) and rubella/varicella-zoster virus surveys was either serum or plasma. The plasma used for hepatitis and HIV testing was kindly provided by the Canadian Blood Services. In previous years, testing material for HIV was heat-inactivated. This was the first year that heat-inactivation was discontinued.

Serum for rubella and Varicella-Zoster virus (VZV) testing was obtained from volunteers selected on the basis of their immune status. In addition, since it is becoming increasingly difficult to find donors who test negative for rubella antibody or positive for rubella IgM antibody, material for rubella must also be sought from commercial sources. When material from a potential commercial source is identified, a sample is procured and pre-tested before purchase to ensure that it meets the required testing specifications and demands for quality.

Material for chlamydia testing was prepared at the Regional Virology Laboratory of the Hamilton Regional Laboratory Medicine Program where strains of *Chlamydia trachomatis* are grown in tissue culture, harvested and then adjusted in strength to simulate clinical specimens containing defined numbers of

elementary bodies. Participants are instructed to place the chlamydia samples into collection tubes of their respective testing systems immediately upon receipt. Similarly, material for the pilot RSV survey was prepared by the Virology Laboratory of the Hospital for Sick Children where RSV is grown in tissue culture, harvested and adjusted to simulate clinical specimens.

Packaging and shipping of all samples complies with federal regulations for transportation of dangerous goods. Participants are instructed to process the samples as they would handle routine clinical specimens. In addition, participants are reminded that serum and plasma samples have been previously frozen and they should observe manufacturer's instructions for processing such material.

In addition to the Ontario laboratories participating in the surveys, three out-of-province laboratories also participate in the virology surveys.

SURVEY ASSESSMENT

Participant results were compared with those obtained from reference laboratories using similar methodology and manufacturers' assays, and where applicable, with peer groups (participants using identical methodology). The amount of the analyte present in the specimen was also taken into consideration when assays of different sensitivity were assessed. Results were flagged when they did

Table 76. Number of Ontario Participating Laboratories Performing Viral or Chlamydial Challenges During 2001*

Survey	Samples per Survey	Hepatitis A and B	HCV	HIV	Rubella IgG	Rubella IgM	VZV	<i>C. trachomatis</i>	RSV
V-0101	12	...	...	4/20	4/30	4/4	4/14	4/27	...
V-0103	15	4/49	3/26	4/20	...	...	...	4/26	...
V-0108	15	4/49	3/26	4/19	4/30	4/4	4/13	...	...
V-0110	15	4/48	3/26	...	4/30	4/4	4/13	...	4/48

* Number of samples/number of participants reporting results. The numbers include out-of-province laboratories (1 chlamydia, 1 rubella/VZV, 2&3 HP, 1&2 HC, 1 HV)

not agree with the reference results. Errors were assessed as being either significant or lesser errors, depending on the potential impact of the results on patient outcomes or the potential risk for disease transmission. Errors were further classified as analytical or interpretative.

OVERALL PERFORMANCE

Chlamydia trachomatis

Performance for chlamydia continued to improve in 2001 with only one significant error assigned (in Ontario), giving an overall error rate of 0.47%. Precision of chlamydia test results continued to be excellent.

Hepatitis A and B

Overall, improvement in hepatitis A and B testing continues, with error rates declining from 1.1% in 2000 to 0.5% in 2001. The number of false positive HBsAg results also declined in 2001 (Table 77). Lack of standardization regarding the assessment of Hepatitis B antibody and immune status was apparent in the surveys in 2001. The internationally accepted definition of immunity is equal to or greater than 10 mIU/mL of anti-HBs. However, antibody can be present at levels lower than 10 mIU/mL. It is clearly a challenge for laboratories to assess antibody levels and immune status independently with 16 of 41 laboratories reporting a low level anti-HBs positive specimen as negative.

Hepatitis C (HCV) Antibody Detection

Errors for HCV testing have only been assessed since June of 2000. In 2000, the rate was low at 0.8%. In 2001, the error rate increased to 2.1% when the

committee began to assess errors for failure to confirm positive HCV screening test results. The committee continues to have concerns about the quality of HCV testing in Ontario.

HIV Antibody Detection

The HIV error rate remained low (0.4%) with only one lesser error for a false positive screen result.

Rubella Antibody Detection

The error rate for Rubella decreased from 1.6% in 2000 to 0.3% (representing one significant error) in 2001. This year, the committee was interested in the ability of participants to appropriately interpret the immune status of samples. This activity raised awareness of the variability of interpretation of test results, particularly in samples containing lower levels of antibody.

VZV Antibody Detection

No errors were assessed for varicella antibody testing. Surveys demonstrated that different methods varied in sensitivity. For the most part, latex and fluorescent assays were more sensitive than enzyme immunoassays. The same problem with standardized interpretation of immune status exists for VZV as it does for hepatitis B and rubella antibodies.

RSV Antigen Detection

A pilot survey for RSV antigen detection was conducted in 2001. Participants were asked to test the fluid samples provided as if they were patient samples. Unfortunately the tissue culture in which the RSV was grown contained factors that interfered with one particular RSV test used by some laboratories. It is hoped that this problem will be solved for surveys in 2002. As with all pilot surveys, this survey was considered to be educational and no errors were assessed.

Patterns-of-Practice Survey

A patterns-of-practice survey was conducted to assess how laboratories report positive chlamydia results. In addition to reporting results on the analysis worksheet as routine practice for challenge surveys, for one positive sample V-0103-C, laboratories were asked to submit the results on a routine laboratory report. This survey revealed some significant issues related to reporting practices, which were addressed in the Committee Comments. The committee also developed a sample laboratory report to demonstrate recommended data elements.

There were no on-site consultations recommended in 2002.

Table 77. False Positive HBsAg Results in Surveys Conducted From 1994–2001

Year	Error Rate (%)
1994	5.5
1995	1.09
1996	1.01
1997	0.62
1998	1.17
1999	0.5
2000	1.4
2001	0.17



ERROR RATE

The numbers and types of errors assessed are shown in Table 78. To calculate the overall error rate in virology, a significant error is given a weight of three times a lesser error. The total errors in

Table 78. Error Assessment for Ontario Laboratories in 2001

Analyte	Significant Errors	Lesser Errors	Opportunities for Error	% Error
Chlamydia	2	-	212	0.9
Hepatitis A and B	2	1	584	0.5
Hepatitis C	2	1	234	2.1
HIV	...	1	236	0.4
Rubella	1	...	360	0.3
Varicella-Zoster	...	...	160	0.0
Total	7	3	1786	0.56

Table 79. Number of Ontario Participants Testing Virology in 2001 Compared to 2001 by Constituent and/or Marker

Constituent/Marker	2000	2001
Hepatitis (V-0010/V-0110)		
HBSAg	50	44
anti-HBs	43	39
Anti-HBc	32	31
Anti-HBc IgM	13	13
HbeAg	11	11
Anti-HBe	10	10
Anti-HAV	20	20
Anti-HAV IgM	23	22
Hepatitis C (V-0010/V-0110)		
HCV Screening Tests	26	24
HCV Supplementary Tests	4	6
Rubella (V-0010/V-0110)		
Rubella Ab	29	29
Rubella IgM	4	4
VZV (V-0010/V-0110)		
VZV Ab	13	13
HIV (V-0008/V-0108)		
HIV Ab/Interpretation	21	19
Chlamydia (V-0010/V-0103)		
<i>C. trachomatis</i> Ag or NA	26	26
RSV (V-0108)		
RSV Direct Antigen	...	48

Note: The last survey in each year was used for comparison for each of the constituents. The numbers relate to Ontario participants only and do not include markers tested by the out-of-province laboratories

2001 were $(3 \times \text{No. of significant}) + (1 \times \text{No. of lesser}) = (3 \times 6) + (1 \times 3) = 21$. Therefore, the weighted overall error rate for virology in 2001 was 0.5% (excluding out of province results). This represents a continuing decrease in error rate from 2.3% in 2000 and 3.7% in 1999.

CORRECTIVE ACTIONS

All errors assessed to a laboratory result in correspondence from QMP-LS. Laboratories are required to respond and provide specific information regarding the error and their own assessment of the situation and assurance that internal corrective action has been taken. If the committee is not satisfied with the response, further correspondence is undertaken with additional responses until the committee is satisfied that the laboratory understands the nature and cause of the error and has undertaken appropriate corrective action.

For the benefit of all laboratories, Committee Comments are used to address general issues that arise as a result of each survey:

- ✓ Committee Comments addressed the issue of determination of immune status for Hepatitis B and requested all laboratories to report results using International Units so that interpretive guidelines for immune status cut-offs could be developed.
- ✓ Issues regarding the determination of immune status for rubella highlighting the difference between test cut off values and immunity levels established by international standards were discussed in Committee Comments. Laboratories have been requested to report results in International Units of antibody.
- ✓ The committee outlined the issue of various technologies and their differing sensitivities for VZV antibodies in Committee Comments.
- ✓ A sample laboratory report with recommended data elements was included in Committee Comments to provide laboratories with an appropriate template for creating an acceptable laboratory report.

A Broadsheet on HCV testing is in preparation to assist laboratories in improving the quality of HCV testing. The most important aspect of HCV testing is the need for confirmation of screen test positive results.

LABORATORY PARTICIPANTS

Table 79 shows the number of laboratories participating in respective surveys by constituent. The number of laboratories testing for virology constituents/markers in 2001 has continued to decline. The largest decline in testing is for hepatitis B surface antigen (12% drop). This reflects the continued trend of hospital laboratory mergers and amalgamation of private laboratories.

OTHER ACTIVITIES

The committee published an article in the *QMP-LS News* on the status of point-of-care testing assays for HIV.

Testing Material Suppliers

Bacteriology

London Health Sciences Centre, London, Ontario

Gram Smears

Clinical Microbiology Proficiency Testing Program (CMPT),
Vancouver, British Columbia

AFB Smears

Central Public Health Laboratory, Toronto, Ontario

Mycology

Central Public Health Laboratory, Toronto, Ontario

Parasitology

Hamilton Regional Laboratory Medicine Program—
St. Joseph's Site, Hamilton, Ontario

Virology

The Canadian Blood Services
and selected volunteer donors
Hamilton Regional Laboratory Medicine Program, Hamilton, Ontario
Hospital for Sick Children, Toronto, Ontario
London Health Sciences Centre, London, Ontario

Reference Laboratories

Central Public Health Laboratory, Toronto, Ontario
London Health Sciences Centre, London, Ontario
Lakeridge Health, Oshawa, Ontario
Mount Sinai Hospital, Toronto, Ontario
Kingston General Hospital, Kingston, Ontario
The Credit Valley Hospital, Mississauga, Ontario
The Ottawa Hospital – General Campus, Ottawa, Ontario
Hamilton Health Sciences Corporation – General Division, Hamilton, Ontario

Central Public Health Laboratory, Toronto, Ontario
Wadsworth Centre for Laboratories and Research, Albany, New York
Laboratoire de Santé Publique du Québec, St-Anne-de-Bellevue, Quebec

Canadian Blood Services, National Testing Laboratory, Ottawa, Ontario
Central Public Health Laboratory, Toronto, Ontario
Health Canada—Federal Laboratories, Winnipeg, Manitoba
Hamilton Regional Laboratory Medicine Program, Hamilton, Ontario
Hospital for Sick Children, Toronto, Ontario
Sunnybrook and Women's College Health Sciences Centre, Toronto, Ontario
Toronto Medical Laboratories, Toronto, Ontario





ANATOMIC PATHOLOGY

QMP–LS has made considerable progress in developing an external quality assessment (EQA) program for Ontario anatomic pathology laboratories in 2001. The Anatomic Pathology Committee met four times over the course of the year to discuss the issues related to this endeavour. A clearer picture of the proposed program has emerged and we have put forward proposals for histotechnology and surgical pathology diagnosis EQA survey models.

QMP–LS hired a consultant pathologist to complete a literature review and to evaluate the various peer-review accreditation and EQA programs for anatomic pathology throughout the world. This included extensive discussions with participants and organisers of these programs. The consultant pathologist made recommendations on the design, structure and operation of the QMP–LS program that were subsequently endorsed by the Anatomic Pathology Committee.

The difficulties in developing an EQA program for anatomic pathology that adequately tests the whole diagnostic process of the laboratory are well known. By utilizing patterns-of-practice surveys, best practice guidelines and other types of surveys, a program will be developed that is holistic in its scope. Both the pre- and post-analytical, as well as the analytical, phase of testing can be evaluated.

SURVEY MODELS

After reviewing reports from the consultant pathologist and other information, the following types of models for EQA surveys have been proposed:

- ✓ Histotechnology EQA surveys (hematoxylin and eosin, special stains and immunohistochemistry)
- ✓ Surgical pathology diagnosis EQA surveys
- ✓ Patterns-of-practice surveys and questionnaires.

Planning is well underway for the first two pilot histotechnology surveys scheduled for 2002. The proposed surveys will be circulated for hematoxylin and eosin stain and conventional special stains as well as immunohistochemistry.

Anatomic Pathology

No. of Participants (Dec. 2001)	80
No. of Participants (Dec. 2000)	NA
No. of Surveys Conducted in 2001	2

Participants will receive unstained sections, stain the material and return it for assessment. Participants will also receive the assessment criteria and procedures. Multiple assessors will apply the criteria to determine the score. In addition, a questionnaire will accompany the survey, querying technical details of the participant's staining methods.

Participants will receive a Survey Report indicating their assessed score for each criterion by each assessor and a final overall score following the surveys. Committee Comments will discuss overall performance and correlate the technical variables from the questionnaire with the assessed scores to produce best practice guidelines.

The development of the surgical pathology diagnosis EQA model has not progressed as quickly. The Anatomic Pathology Committee and the pathology community have concerns that require attention. These include:

- ✓ Limited manpower and resources in anatomic pathology laboratories to accommodate an EQA program.
- ✓ Need for protection of confidentiality for individuals participating in QMP-LS quality assurance activities.
- ✓ Clarification of QMP-LS assessment processes with regard to slide circulation models that have an interpretive component.

We will address these issues by seeking input and consensus from the committee and the pathology community. Submissions have been made for the proposed legislation to protect QMP-LS' quality assurance data from discovery in legal proceedings. The EQA Report (p. 8) discusses some of these issues.

We have proposed and discussed the model for surgical pathology and headway has been made. The model is based on those widely employed in the United Kingdom and includes the following:

- ✓ Assessment method must be clearly defined and shared with participants.
- ✓ Participants themselves will decide the "correct" diagnosis and what constitute acceptable diagnoses.
- ✓ Cases should be indicative of routine practice and not rarities.

However, more work needs to be done, following which initial surveys will be distributed as educational pilot surveys.

We distributed two patterns-of-practice surveys in 2001. Survey P-0106 was distributed to Ontario anatomic pathology laboratories in June. The Committee Comments from this survey were distributed in October of 2001 and contained summary data on laboratory personnel, demographics and operations. The data provide an opportunity for laboratories to compare their practice to that of their peers and provide QMP-LS with information to aid in the development of the anatomic pathology program.

In October, survey P-0110 was distributed. This survey dealt with the issues pertaining to surgical pathology reporting and quality assurance activities. The Committee Comments will be distributed early in 2002.

COMMITTEE ACTIVITIES

An important objective for 2001 was to share the proposed models for an EQA program with the anatomic pathology community of Ontario. We are committed to encouraging full participant involvement in the development of these models. QMP-LS liaised with the anatomic pathology community through several means, including the *QMP-LS News* and Web site and the newsletters of other anatomic pathology professional associations. In addition, QMP-LS Anatomic Pathology Committee members have made presentations at meetings for medical laboratory technologists and the Ontario Association of Pathologists to share information and to receive input. Other communications will be forthcoming as the survey models develop.

PLANS FOR 2002

Two pilot histotechnology surveys will be distributed in 2002, one for hematoxylin and eosin and conventional special stains, and another survey for immunohistochemistry. Further development of the surgical pathology diagnosis EQA survey model will take place in consultation with the anatomic pathology community.



TESTING MODEL

The combined gynecologic and non-gynecologic cytology external quality assessment (EQA) survey Y-0009 was completed in 2001. Relatively minor changes were made to the survey model introduced for survey Y-9710 in 1997. Each participating laboratory again received a total of 20 slides, ten gynecologic plus eight non-gynecologic challenges. Two slides on fine needle aspiration (FNA) cytology of head and neck were included as an educational survey. The evaluation procedure for the gynecological and non-gynecologic components of this survey and tables cross-referencing participant and committee consensus diagnoses were previously shared with participants and remained unchanged. A turnaround time of approximately three weeks was again used for this survey. This allows time for review and discussion of results following their submission thus enhancing the educational aspect of the survey. Committee Comments for survey Y-0009 contained full colour photomicrographs as a further enhancement of the educational value of the surveys.

A fourth cytology patterns-of-practice survey was distributed in 2001. This survey focused on personnel and laboratory demographics, laboratory operations, screening and reporting practices, and quality assurance procedures. This type of survey provided participants with an opportunity to compare their practice in these areas to those of their peers, as well as to compare data with the previous years’.

PERFORMANCE ASSESSMENT

Committee consensus diagnoses are based on an independent review of the slides with agreement of at least two committee members. Slides in which diagnostic disagreements arise are rescreened and reviewed by a consensus panel. Participant results are assessed by degrees of deviation from the committee consensus diagnosis for each slide. All discordant results were flagged by computer and manually reviewed by the committee. Diagnoses that were discordant from the committee reference diagnosis were

Cytology	
No. of Participants (Dec. 2001)	86
No. of Participants (Dec. 2000)	84
No. of Surveys Conducted in 2001	2

classified as lesser or significant discordances based mainly on the implications for patient management.

REVIEW OF PERFORMANCE

Gynecologic Cytology

Survey Y-0009 was the fourth to use the modified Bethesda terminology system. Table 80 compares some parameters between Y-0009 and the previous surveys Y-9710, Y-9812 and Y-9911. The number of laboratories participating in the gynecologic slide survey has decreased from 85 to 79. There have been decreases in the number of both lesser and significant discordances. In addition, 32 laboratories (40.5%) had no discordances on survey Y-9911 as compared with thirteen (15.3%) for survey Y-9710. The continued improvement in performance over the previous surveys may represent an increased level of comfort with the testing model and terminology, as well as the improved quality of the slide material.

Table 80. Ontario Laboratories Gynecologic Cytology Slide Survey Results

	Gynecologic Cytology Survey			
	Y-9710	Y-9812	Y-9911	Y-0009
No. of participants	85	81	78	79
No. of lesser discordances	143	102	86	69
No. of significant discordances	4	1	2	4
No. of laboratories with no discordances	13	15	27	32

Non-Gynecologic and Fine Needle Aspiration Cytology

The combined slide survey Y-0009 contained ten non-gynecologic challenges, two each of urine, serous body cavity fluid, sputum or bronchogenic material, FNA of breast and FNA of head and neck. Table 81 compares performance in the different areas of non-gynecologic cytology between surveys Y-9710, Y-9812, Y-9911 and Y-0009. As was the case with gynecologic cytology, there has been a decline in the number of participating laboratories. However, there has been a proportionately larger decrease in the overall number of significant discordances. The most notable decrease was for serous body cavity fluids that saw a reduction from 23 to eight significant discordances over the last four surveys.

Fine needle aspiration cytology of the head and neck was included in survey Y-0009 for the first time. Two slides were sent to each laboratory, aspirated sites included the thyroid gland, salivary glands and lymph nodes. Results of the survey were encouraging: 71 laboratories participated in the survey; there were eight lesser discordances and 11 significant discordances. In the next survey FNA of head and neck will be incorporated as a component of the regular survey.

Table 81. Comparison of Ontario Laboratories Non-Gynecologic and Fine Needle Aspiration Cytology Performance for Surveys Y-9710, Y-9812, Y-9911 and Y-0009

		Y-9710	Y-9812	Y-9911	Y-0009
Urinary	No. of participants	83	74	70	67
	No. of significant discordances	5	3	2	2
Body Cavity Fluid	No. of participants	83	73	69	66
	No. of significant discordances	23	10	8	8
Exfoliative Bronchogenic	No. of participants	85	77	71	68
	No. of significant discordances	7	4	7	4
Fine Needle Aspiration of Breast	No. of participants	83	74	70	67
	No. of significant discordances	0	5	2	1

PATTERNS-OF-PRACTICE SURVEY

A fourth cytology patterns-of-practice survey Y-0103 allowed for comparison with the previous surveys Y-0003, Y-9904 and Y-9806. Fifty-eight hospital and 25 private laboratories completed the survey. Table 82 shows the number of gynecologic and non-gynecologic cases and the percentage reported in private and hospital laboratories. Other points of note from the patterns-of-practice survey include: all laboratories now use the Bethesda terminology system for reporting cervical-vaginal cytology; all laboratories include a statement of adequacy in each gynecologic cytology report; and no Ontario laboratories report that they continue to use the Papanicolaou terminology for reporting gynecologic cytology.

SUMMARY OF ACTIVITIES

In 2001 QMP-LS coordinated the implementation of the Ontario Quality Assurance Program—Gynecologic Cytology. The Ontario-specific standards and key indicators of performance were developed based on a review of existing guidelines for gynecologic cytology laboratory performance. The program was distributed to all Ontario cytology laboratories in December 2000 and was to be implemented by laboratories over the course of 2001. To monitor the implementation of the program QMP-LS distributed a gynecologic cytology quality assurance questionnaire in September of

2001. Results of the questionnaire indicated that all laboratories had received the program and started its implementation. Progress will again be surveyed in the next cytology patterns-of-practice survey in 2003.

Two slide surveys were conducted and reviewed for the Laboratory Proficiency Testing Program of the College of Physicians and Surgeons of Alberta in 2001. Negotiations were completed with Alberta regarding the provision of future EQA testing in cytology.

During 2000, QMP-LS has provided support for the Pan American Network of Cytology RED-PAC. QMP-LS continues to provide expertise and advice to assist in the development of a cytology EQA program for five Latin American countries. The program is based in Chile and utilizes the QMP-LS testing model.

The distribution of the second edition of the monograph *Adequate Pap Smears—A Guide for Sampling Techniques and Screening for Abnormalities of the Uterine Cervix* by Dr. Donald Thompson and the laminated reference card with Ontario Pap smear guidelines continues.

PLANNED INITIATIVES FOR 2002

- ✓ To incorporate fine needle aspiration cytology of the head and neck as a regular component of the slide surveys.
- ✓ To incorporate bronchial washings and brushings in the respiratory portion of the slide survey.
- ✓ To revise the non-gynecologic cytology analysis worksheets to decrease the number of pages from ten to six.
- ✓ To continue to monitor and support the implementation of the Ontario Quality Assurance Program in Gynecologic Cytology.

Table 82. Number of Cytology Specimens Performed by Private and Hospital Laboratories from Survey Y-0103 (% Performed in Different Laboratory Types)

	Private Laboratories		Hospital Laboratories		Total
Cytology cases	1 649 684	(80.8)	392 721	(19.2)	2 042 405
Gynecologic cases	1 600 431	(86.5)	250 622	(13.5)	1 851 053
Non-gynecologic cases	49 253	(25.7)	142 099	(74.3)	191 352

Testing Material Suppliers

Cytology

Various participating laboratories



GENETICS

The Genetics committee membership reflects the activities within both cytogenetics and molecular genetics. There are four members representing each sub-discipline.

CYTOGENETICS

TESTING MODEL

The cytogenetics external quality assessment model remains essentially unchanged. Three challenge surveys were conducted in 2001 with a participating laboratory supplying the testing material for each survey. The ongoing involvement of participating laboratories in survey development is an important feature of the program. This involvement enabled the test challenge to be a bona fide clinical specimen of human whole blood or tissue culture obtained from a single donor. Participants are required to culture, process, karyotype and provide an interpretive report on the case provided. The laboratories submitted their results on QMP–LS survey material in the same format used to report patient results to physicians. Laboratories that do not perform long-term culturing received fixed culture survey material.

All results, karyotypes and photographs submitted by each laboratory were reviewed and evaluated. Each laboratory was assessed on the technical procedure and interpretive report. One of seven assessment levels was assigned and errors were classified as either “lesser” or “significant” the latter considered potentially misleading for clinical management.

For each survey, Committee Comments were published and included the clinical case report provided by the supplying laboratory, the committee’s expectations and minimum requirements for assessment, karyotypes submitted and a model report.

The fourth routine survey G-0111 was cancelled due to a material problem. As a result, a new process was developed to validate and pre-screen the survey material prior to shipment to the participants.

Genetics	
No. of Participants (Dec. 2001)	10
(plus 12 out-of-province laboratories)	
No. of Participants (Dec. 2000)	10
(plus 12 out-of-province laboratories)	
No. of Surveys Conducted in 2001	4

LABORATORY PERFORMANCE

Table 83 outlines the types of challenges, karyotypes, levels of difficulty and average numbers of cells analyzed in 2001, as compared with the previous two years.

The performance of the Ontario laboratories over the past three years (11 surveys) is presented in Tables 84 and 85. The cytogenetics laboratories continue to perform well and the results were within acceptable limits.

Table 86 provides an overview of participants' performance in relation to the difficulty of the survey. The failure rate remains low for all levels of difficulty, yet has increased as compared to previous years. In particular, the failure rate on the difficult surveys (level 3), of which there were four in the past three years, was 9% as compared to the previous rate of 2% per interval.

Table 83. Average Number of Cells Analyzed, Level of Difficulty, Type of Material and Karyotype (1999–2001)

Survey	Average No. of Cells Analyzed	Level of Difficulty*	Type of Material	Karyotype
G-9902	18	3	Whole blood	46,XY,der(1)(3pter->3p21::3q27->3q13::1p31->1qter), der(3)(1pter->1p31::3q13->3p21::3q27->3qter)
G-9905	47	1	Whole blood	46,XX
G-9908	18	2	Amniocyte culture	46,XX,t(1;19)(p34.1;q13.2)
G-9911	N/A	2	Bone marrow photographs	46,XX,t(9;11)(p22;q23)
G-0002	24	3	Fixed bone marrow aspirate	49-52,XY,add(2)(p25),del(3)(q26),add(4)(q35),+7,+i(8)(q10),t(8;22)(q24;q11),+12,t(14;18)(q32;q21), der(14)t(14;18)(q32;q21),+18,+22[cp10]
G-0005	21	2	Whole blood	46,XX,ins(14;11)(q24.1;q23.1q24.3)
G-0008	35	2	Whole blood	46,X,der(X)t(X;Y)(p22.3;p11.2).ish der(X)t(X;Y)(p22.3;p11.2)(SRY+,wcpY+)
G-0011	19	2	Fixed lymphocyte culture	46,XX,t(15;16)(q13;q12.1)
G-0102	32	3	Whole blood	46,XX,der(4)(4pter->4q13.2::16q22.3->16q13::4q31.2->4q13.2::16q22.3->16qter), der(16)(16pter->16q13::4q31.2->4qter)
G-0105	49	2	Fibroblast culture	46,XY,r(19)(p13.3q13.4)[14]/46,XY[36]
G-0108	26	3	Fixed cell culture from a solid tumour	46,XY,der(1)t(1;1)(q12;p36),t(10;11)(q24;p13), del(11)(p13p13)[24]/46,XY[1].ish t(10;11)(wcp11+;wcp11+)
G-0111	N/A	N/A	Fixed metaphase cell suspension from a blood culture	46,X,I(y)(p10)(WCPY+, SRY++)

* 1 = easy; 2 = moderately difficult; 3 = difficult

Table 84. Performance Summary, by Survey, Over Three Years (1999–2001, 11 Surveys)

Survey	No. of Participants	No. of Participants Not Assessed (Including Reference)	Correct Technical Procedure	Minor Technical Problem	Major Technical Problem	Misleading or Incomplete Interpretation
G-9902	13	2	11	...	...	...
G-9905	13	0	12	...	1	...
G-9908	13	3	10	...	...	...
G-9911	13	1	8	4	...	...
G-0002	13	1	11	...	1	...
G-0005	12	1	11	...	...	...
G-0008	11	1	8	...	...	2
G-0011	11	1	10	...	...	...
G-0102	11	0	11	...	...	...
G-0105	11	1	10	...	...	...
G-0108	11	0	1	7	1	2

Table 85. Performance Summary, by Laboratory, Over Three Years (1999–2000, 11 Assessed Surveys)

Assessment Level	Reference Laboratory	Assessed Surveys	*Correct Technical Procedure (1, 2)	Minor Technical Problem (3)	Major Technical Problem (6)	Misleading or Incomplete Interpretation (4, 5, 7)
Ontario Laboratory						
A	...	11	10	1	...	...
B	...	11	10	1	...	...
C	...	11	9	...	...	2
D	1	10	9	1	...	...
E	1	10	9	1	...	...
F	1	10	9	1	...	...
G	1	10	8	2	...	...
H	1	9	8	1	...	...
I	2	9	8	...	...	1
J	...	10	7	...	1	2
K	...	6	6	...	...	...
L	...	5	3	1	1	...
M	...	4	3	1	...	...

* Sorted by correct technical procedure

Table 86. Performance Summary, by Survey Difficulty, Over Three Years (1999–2001, 11 Assessed Surveys) as Compared to the Previous Three Year Intervals 1996–98, 1997–99, 1998–2000 and 1999–2001

1998-2001						1996–98	1997–99	1998–2000	1999–2001
Survey Level of Difficulty	Number of Surveys	Average No. of Cells Analyzed	Pass (Assessment Level 1–3)	Fail (Assessment Level 4–7)	No. of Assessments	Failure (%)	Failure (%)	Failure (%)	Failure (%)
1	1	47	12	1	13	4	2	4	8
2	6	28	61	2	63	0	0	4	3
3	4	25	41	4	45	2	2	2	9

MOLECULAR DIAGNOSTICS OF INHERITED HUMAN DISEASES

The development continued on the testing model for molecular diagnostics of inherited human diseases. A pattern-of-practice survey (N-0104-PP) focused on the staffing and quality assurance processes. The data was released for review and comment from the community. Tables 87, 88 and 89 summarize some of the data submitted by participants on this survey.

A further survey was developed in conjunction with the Hematology Committee to test for Hemachromatosis and Factor V Leiden. This voluntary survey utilized extracted DNA as testing material, which was distributed with the necessary clinical information. All documentation pertaining

Table 87. Number of Molecular Genetics Staff in Each Category Reported by Participants on Survey N-0104-PP

Category	No. of Positions	No. of Laboratories
Laboratory Directors N=17	1	11
	2	4
	2.1	1
	3	1
Laboratory Manager/Coordinator N=10	0.25	1
	1	9
Laboratory Resource/Head Technologist N=10	1	9
	2	3
Laboratory Technologists N=17	1	1
	2	4
	3	3
	4	2
	5	1
	5.5	2
	6	1
Administrative Staff N=8	7	3
	0.25	1
	0.5	2
	1	3
	2	1
	2.5	1



to the cases were returned for assessment, including the report, worksheets and images of gel electrophoresis. As a pilot challenge survey, participant's results were not assessed, however, an assessment model based on technical and interpretive components was evaluated. A complete review was conducted in conjunction with the Hematology Committee.

OTHER ACTIVITIES

QMP-LS continues to provide an external quality assessment service to 12 out-of-province cytogenetics laboratories. One laboratory participates in the oncology challenges only. Interest has been expressed by out-of-province molecular genetic colleagues to participate in the surveys for molecular diagnostics of inherited human diseases. This will be explored further as the survey model is developed.

The application of new techniques to support cytogenetics analysis of samples submitted as QMP-LS surveys continues to be monitored. Techniques such as fluorescence *in situ*

hybridization (FISH) and spectral karyotyping (SKY) have been used on QMP-LS surveys. It has become evident that in cytogenetics laboratories across Canada on-site FISH techniques are a standard of care in order to issue timely reports for patient care.

QMP-LS participated on the Laboratory Subcommittee, Ontario Provincial Advisory Committee on New Predictive Genetic Technologies that contributed to the report *Genetic Services in Ontario, Mapping the Future*.

QMP-LS also participates on the Predictive Cancer Genetics Implementation Steering Committee for breast, ovarian and colon cancer programs and the respective sub-committees (laboratory and data).

QMP-LS in collaboration with Health Canada, Centre for Chronic Disease Prevention and Control is developing the Canadian Genetic Quality Network (CGQN). The network of genetic services providers (clinical and laboratory) will collect and share information through a Web site. The aim of the project is to promote networking and sharing of resources to obtain accurate and timely information regarding genetic services in Canada.

Table 88. Elements on Molecular Genetics Final Report Provided by Participants on Survey N-0104-PP

Elements on Final Report	Number of Laboratories (N=17)
Date of report	17
Name of patient	17
Date of birth	14
Unique laboratory identifier	17
Referring physician(s)/counselor	17
Reason for referral/test done	11
Appropriate summary of the methods used	12
Loci or mutations tested	15
Test limitations/sensitivity	10
Patient results	16
Clinical interpretation	14
Appropriate recommendations	10
Signature of Laboratory Director	15

Table 89. Elements Included in the Molecular Genetics Test Reports Provided by Participants on Survey N-0104-PP

Test Reports Include the Following:	Number of Laboratories (N=17)*
Risk estimates for samples tested by linkage analysis	8
Risk estimates for samples tested for multiple mutations	7
Limitations of findings and clinical implications, including recurrence risk, penetrance, severity and other aspects of genotype-phenotype correlations	9

* No reply = 6

Testing Material Suppliers

Genetics

Various participating laboratories



ONTARIO LABORATORY ACCREDITATION

EXPANDING OUR QUALITY FOCUS WITH ONTARIO LABORATORY ACCREDITATION

The Ontario Laboratory Accreditation (OLA) program continued to be developed in 2001. We focused on establishing the framework for a peer-group accreditation program and sharing it with participating laboratories and interested stakeholders. In 2001, we achieved the following objectives:

- ✓ Drafting accreditation criteria and seeking input from laboratory personnel and stakeholders.
- ✓ Developing operating policies and processes.
- ✓ Establishing an Advisory Panel and seeking its counsel.
- ✓ Recruiting interested personnel to become assessors.
- ✓ Creating and managing a Test Review Committee.
- ✓ Designing computer databases for use in the program.

OLA subscribes to the following definition of accreditation:

A peer-review process by which an authoritative body ensures that laboratories meet explicit quality management criteria, in order to give formal recognition that the laboratory is competent to carry out examinations.

One of our major goals is to align Ontario accreditation with the principles endorsed in international initiatives. The assessment will be process-oriented rather than procedural-based. A set of defined criteria (program requirements) was drafted using the ISO Draft Standard: *Medical Laboratories—Particular Requirements*

for Quality and Competence as a primary reference. This Draft International Standard endorses a quality management system (QMS). The OLA requirements apply to all aspects of laboratory practice. They are organized into sections that represent the path of workflow (Table 90).

Table 90. Table of Contents for the OLA Consensus Universal Requirements

- I. Organizational Structure, Personnel Policies and Laboratory Management
- II. Quality Management System
- III. Physical Facilities
- IV. Equipment, Reagents and Supplies
- V. Pre-Analytical Process
- VI. Analytical Process
- VII. Quality Assurance of Laboratory Examinations
- VIII. Post-Analytical Process (Reporting)
- XI. Laboratory Information System
- X. Safety
- XI. Point-of-Care Testing

PROPOSED ACCREDITATION CRITERIA

Considerable time was spent in 2001 developing accreditation criteria, sharing program requirements with participating laboratories and stakeholder groups, and gathering feedback. As mentioned above, the OLA program requirements are largely based on international initiatives. An attempt was made to substantiate each requirement with a supporting reference so that interested individuals can determine the basis on which that requirement is included. Suitable references include international, national or provincial standards and/or consensus guidelines, Ontario and Canadian law.

Proposed requirements were released to laboratories and identified stakeholder groups in September 2001. Twenty-one focus group sessions (Appendix L) were scheduled around the province to:

- ✓ Familiarize Ontario laboratory professionals with QMP-LS.
- ✓ Introduce the concept of accreditation and explain the principles and process of OLA.
- ✓ Provide a stimulating forum to explain and discuss OLA's proposed program requirements.
- ✓ Reach all laboratory professionals employed in licensed clinical laboratories by scheduling sufficient sessions to provide access within a reasonable travel distance, free of charge.
- ✓ Personalize the program by introducing OLA staff and advisors.

The response was overwhelming with 1022 individuals attending. Feedback was also welcomed directly and was received by mail, fax, e-mail and telephone. Recommendations, where appropriate, were incorporated into program requirements and final consensus requirements representing substantial agreement by the majority were released early in 2002 (Figure 33). This set of accreditation criteria includes 680 requirements that will apply to the pilot assessments in 2002

and for the initial assessments to be conducted after April 1, 2003. These requirements are considered essential for the accurate, reliable and timely provision of laboratory results, the design of a QMS, the safety of employees and patients, the protection of employee and patient rights, and to meet legal requirements.

OPERATING POLICIES AND PROCESSES

The framework for operation of OLA was established in 2001. A set of operating policies was drafted and processes defined that represent the flow of work in preparing for accreditation assessments, conducting accreditation assessment visits, and follow-up after visits (see Appendix M, p. 107). Information about this framework was shared with participating laboratories and stakeholder groups in September, and by means of a publication titled *Frequently Asked Questions* the accreditation process was explained. Through the fall 2001 focus group sessions, valuable advice was received on the process and operation of assessments. These policies and processes will be refined in 2002, and individual procedures drafted and tested during the pilot phase.

ADVISORY PANEL

The OLA Advisory Panel was constituted in March 2001, for the purpose of providing counsel to staff on all aspects of OLA. Members on the panel are individuals of stature from the laboratory community who have broad knowledge of laboratory operations and quality assurance practices and possess management skills. Some are experienced accreditation assessors. They represent a cross-section of laboratory professionals (technologists, scientists and physicians) from across the Province of Ontario. A total of ten professionals serve on the panel (Appendix A, p. 93). We would like to thank Dr. Rocke Robertson for his service to the panel before additional commitments precluded his continuing participation. The panel met five times in 2001. Through the efforts of the panel, a set of values was established for the program that ensures OLA is fair and objective, impartial and non-discriminatory, open

OLA ACCREDITATION PROGRAM - LABORATORIES
July 2001

I. ORGANIZATIONAL STRUCTURE, PERSONNEL POLICIES AND LABORATORY MANAGEMENT

II. ORGANIZATIONAL STRUCTURE

1. The laboratory shall have a clear organizational structure that is consistent with the scope of the laboratory's accreditation.

2. The laboratory shall have a clear organizational structure that is consistent with the scope of the laboratory's accreditation.

3. The laboratory shall have a clear organizational structure that is consistent with the scope of the laboratory's accreditation.

4. The laboratory shall have a clear organizational structure that is consistent with the scope of the laboratory's accreditation.

5. The laboratory shall have a clear organizational structure that is consistent with the scope of the laboratory's accreditation.

III. PERSONNEL POLICIES

1. The laboratory shall have a clear personnel policy that is consistent with the scope of the laboratory's accreditation.

2. The laboratory shall have a clear personnel policy that is consistent with the scope of the laboratory's accreditation.

3. The laboratory shall have a clear personnel policy that is consistent with the scope of the laboratory's accreditation.

4. The laboratory shall have a clear personnel policy that is consistent with the scope of the laboratory's accreditation.

5. The laboratory shall have a clear personnel policy that is consistent with the scope of the laboratory's accreditation.

IV. LABORATORY MANAGEMENT

1. The laboratory shall have a clear laboratory management policy that is consistent with the scope of the laboratory's accreditation.

2. The laboratory shall have a clear laboratory management policy that is consistent with the scope of the laboratory's accreditation.

3. The laboratory shall have a clear laboratory management policy that is consistent with the scope of the laboratory's accreditation.

4. The laboratory shall have a clear laboratory management policy that is consistent with the scope of the laboratory's accreditation.

5. The laboratory shall have a clear laboratory management policy that is consistent with the scope of the laboratory's accreditation.

Figure 33. Final Program Requirements

and transparent, flexible and adaptable. The panel spent considerable time reviewing and revising accreditation requirements and it offered valuable advice on operating policies and processes.

ASSESSOR RECRUITMENT

Recruitment of qualified individuals to serve as assessors began in fall 2001. Individuals who practice or who have recently retired are ideally suited to serve on assessment teams because they are in tune with current practices and can objectively assess laboratories' compliance with accreditation requirements. Assessors needed are technologists, scientists and physicians, whose experience represents both community and hospital service, and who are from all regions of Ontario. A wide range of expertise will be required to adequately cover all aspects of laboratory service. All assessors will be trained and certified in advance. To date, 160 individuals have applied. In 2002, the selection process will continue. Training and certification will be designed and delivered in accordance with international guidelines. All assessors will be remunerated for time and reimbursed for expenses.

TEST REVIEW COMMITTEE

The Test Review Committee (TRC) was constituted in January 2001 to advise Laboratories Branch, MOHLTC, on the quality requirements for tests that are not currently listed in the Schedule of Benefits for laboratory services.

Six members were appointed for a three-year term by QMP–LS/OMA. Members are laboratory physicians, laboratory scientists and medical laboratory technologists of stature in the province (see Appendix A, p. 93). The Chair was named by and from the members. An OMA Board representative (with voting rights) and the Managing Director QMP–LS are ex-officio members.

Following identification of a candidate test by Laboratories Branch, the TRC conducts a quality review, seeks expert opinion and arranges for critical appraisal of the medical and scientific literature.

When applicable, it then refers the expert opinion to the QMP–LS scientific committee(s) for review and input. The final step is to report its findings to Laboratories Branch and recommend the quality requirements for the test.

The quality review criteria include the following components:

- ✓ The clinical utility of the examination or test.
- ✓ The health care cost implications.
- ✓ Analytical policy and technical procedures including analytic principle, analytical methods, available instruments and reagents, special considerations, and process to establish reference intervals.
- ✓ Quality management system required by the testing laboratory, i.e. patient preparation, collection and handling of specimen, quality assurance process, quality control procedures, and quality indicators.
- ✓ External quality assessment through interlaboratory comparisons.
- ✓ Available and/or required practice guidelines.

The interaction between Laboratories Branch, the Laboratory Licensing and Inspection Service (LLIS) and the TRC was changed during the year by defining processes to appeal the recommendations. Appropriate correspondence channels have been determined to facilitate the prompt exchange of information.

External advisors and current or former scientific committee members have willingly shared their knowledge and expertise in the review and preparation of expert opinion reports on referred tests. Their contribution has been invaluable to committee activities.

Summary of Referred Tests for which quality requirements for testing have been completed are:

- ✓ PSA (Prostate Specific Antigen)
- ✓ Homocysteine
- ✓ Troponin
- ✓ Myoglobin
- ✓ HPV (Human Papilloma Virus) report
- ✓ Monolayer cell methodology report

At the request of Laboratories Branch, clinical guidelines were subsequently provided on homocysteine and HPV testing. Both guidelines will be forwarded to the Guideline Advisory Committee (MOHLTC/OMA) for endorsement.

Quality requirements for the following tests were requested and were under development in 2001:

- ✓ Bone metabolism related tests (crosslinked telopeptides of type 1 collagen, deoxypyridinoproline crosslinks, osteocalcin)
- ✓ Coagulation related tests (protein C, protein S, active protein C resistance, von Willebrand multimeric assay, anti-cardiolipin antibody, factor V Leiden, prothrombin variant)
- ✓ High-sensitivity C-reactive protein (hsCRP)
- ✓ Therapeutic monitoring of caffeine
- ✓ Cancer antigen 19-9
- ✓ Drugs:
 - ◆ Alprazolam
 - ◆ Clobazam
 - ◆ Clozapine
 - ◆ Gabapentin
 - ◆ Sirolimus
 - ◆ Tacrolimus
- ✓ Neuron-specific enolase (NSE)
- ✓ Trace elements

Formal submission of these tests will take place early in 2002.

COMPUTER DATABASES

OLA will require customized computer databases to manage the accreditation process. Separate databases are needed for the maintenance of program requirements and standards for volunteer assessors, and for scheduling of accreditation assessment visits. Preliminary development of these was completed in 2001, and they will be tested and implemented in 2002.

NEXT STEPS IN DEVELOPMENT

Development of OLA will continue in 2002. Our focus will be:

- ✓ Sharing of information with participating laboratories.
- ✓ Assisting laboratories in preparing for accreditation.
- ✓ Drafting operational procedures.
- ✓ Training and certifying assessors.
- ✓ Conducting pilot assessment visits to determine the success of the program model.
- ✓ Identifying the quality requirements for candidate tests

identified by the MOHLTC.

Final program requirements for accreditation were released early in 2002. Participants in the focus sessions delivered the message that laboratory personnel would appreciate assistance in preparing for accreditation—understanding of the principles of a QMS, tools and templates to assist them in establishing a QMS, a clearer understanding of laboratory information system requirements and assistance with documentation. Education modules to assist laboratories in the interpretation of program requirements will be developed for implementation after April 1, 2002. Guidance documents (“what to look for”) will be drafted for the benefit of assessors and laboratories in preparing for assessments. Assessor training and certification will commence in mid 2002. Pilot accreditation assessments will be conducted in the fall of 2002, followed by an impact analysis. Implementation of accreditation will occur after April 1, 2003.

APPENDICES

Appendix A

2001–2002 QMP–LS Committees

CONJOINT

MOHLTC Representatives:
Ms. Dawn Ogram
 Ms. Joanne Bishop (to February 2002)
 Ms. Leela Prasaud

OMA Representatives:
Dr. Harold Richardson
 Dr. G.J. Flynn
 Dr. M. Thoburn (from October 2001)

MANAGEMENT

Dr. Gregory J. Flynn
 Dr. Daniel Klass
 Ms. Dawn Ogram
 Ms. Leela Prasaud
 Dr. Michael Thoburn (ex-officio)
 Mrs. Kathy Wilkie
 Dr. Philip R. Wyatt

ADVISORY COUNCIL

College of Physicians & Surgeons of Ontario

Dr. Daniel Klass

College of Medical Laboratory Technologists of Ontario

Mrs. Kathy Wilkie

Association of Medical Microbiologists of Ontario

Dr. Alicia Sarabia

Ontario Association of Medical Laboratories

Mr. Don Kerr

Ontario Association of Pathologists

Dr. Frank E. Thompson

Ontario Hospital Association

Mr. Glen Dietz

Ontario Society of Clinical Chemists

Dr. Lynn Allen

Ontario Medical Association
 Section on Laboratory Medicine

Dr. Barry W. Sawka

Ontario Society of Medical Technologists

Mrs. Blanca McArthur

PROFESSIONAL ADVISORY COMMITTEE

Dr. Philip R. Wyatt
 Dr. Robert M. Barr
 Dr. C. Mark Cheung
 Mr. Mark Donahoe
 Mrs. Suba Krishnan
 Mr. John Lafferty
 Dr. Donald E. Low
 Dr. James B. Mahony
 Dr. Catherine M. (Meg) McLachlin
 Dr. Murray E. Treloar

ONTARIO LABORATORY ACCREDITATION ADVISORY PANEL

Mrs. Sheila Woodcock
 Mr. Kurt Davis
 Dr. Joel Goodman
 Dr. Denis Macdonald
 Mr. Gaman Modi
 Dr. John Penswick
 Dr. Sandip Sengupta
 Dr. Brian Sheridan
 Ms. Dawn Ogram*
 Ms. Leela Prasaud*

TEST REVIEW COMMITTEE

Dr. Robert Moore
 Dr. Kenneth Arnold (OMA Representative)
 Dr. David E.C. Cole
 Dr. Gregory J. Flynn
 Dr. Sandip Sengupta
 Dr. Frank E. Thompson
 Mr. Sam Thomson
 Ms. Dawn Ogram,* or
 Ms. Leela Prasaud*

POINT-OF-CARE TESTING ADVISORY PANEL

Dr. Harold Richardson
 Dr. Daniel Klass
 Mrs. Cathie McCallum
 Ms. Leela Prasaud
 Mrs. Kathy Wilkie

* Ex-officio member with voting rights
 Note: Names in italics identify Chairs

CHEMISTRY-GENERAL & ENZYMES

Dr. C. Mark Cheung
 Dr. Vipin Bhayana
 Dr. Sheila Boss
 Dr. Christine Collier
 Dr. Stephen A. Hill
 Ms. Maureen MacDonald
 Drug Monitoring Advisor:
 Dr. Edward Dunn
 Point-of-Care Testing Advisor:
 Ms. Cathie McCallum

ENDOCRINOLOGY & IMMUNOLOGY

Mr. Mark Donahoe
 Dr. Peter S. Bunting
 Dr. Mario D'Costa
 Dr. V. M. Prabhakaran
 Dr. Lois E. Shepherd
 Ms. Marguerite Zeale
 Immunology Advisor:
 Mrs. Brenda Roberge
 Endocrinology Advisor:
 Dr. P.Y. Wong

MATERNAL SERUM SCREENING

Mrs. Suba Krishnan
 Dr. Jo-Ann Johnson
 Mrs. Andrea O'Donnell
 Dr. Jennifer Raymond
 Dr. Anne M. Summers
 Dr. P.Y. Wong
 MSS Database Consultant:
 Mr. Chris Meier

HEMATOLOGY

Mr. John Lafferty
 Dr. Mark Crowther
 Dr. J. Timothy Feltis
 Mr. Michael Keeney
 Dr. Denis MacDonald
 Technical Advisors:
 Dr. George R. Massarella
 Mr. Praniti Soamboonsrup

TRANSFUSION MEDICINE

Dr. Robert M. Barr
 Dr. Jeannie Callum
 Mrs. Laura J. Harrison
 Mrs. Debbie Lauzon
 Ms. Wendy Owens

MICROBIOLOGY

Dr. Donald E. Low
 Dr. Frances B. Jamieson
 Ms. Candy Rutherford
 Ms. Marilyn Sarina
 Dr. Baldwin W. Toye
 Dr. Dick E. Zoutman
 Parasitology Advisory:
Dr. Donald E. Low
 Dr. Kevin Kain
 Dr. Douglas W. MacPherson
 Ms. Rose McQueen
 Mycology Advisory:
Dr. Donald E. Low
 Mrs. Ursula Bunn
 Dr. Susan E. Richardson
 Dr. James Scott

VIROLOGY

Dr. James B. Mahony
 Dr. Margaret Fearon
 Dr. Tony Mazzulli
 Dr. Martin Petric

ANATOMIC PATHOLOGY

Dr. Murray E. Treloar
 Dr. Geoffrey W. Gardiner
 Dr. Ola A. Kassim
 Ms. Laurie Mason
 Dr. David Murray
 Dr. A. Rocke Robertson
 Dr. Sandip Sengupta
 Dr. John R. Srigley
 Dr. Frank E. Thompson
 Technical Advisor:
 Mr. Bryan R. Hewlett

CYTOLOGY

Dr. Catherine M. (Meg) McLachlin
 Dr. Yvan C. Bedard
 Dr. Scott L. Boerner
 Mrs. Sue Clipsham
 Dr. Linda Kapusta
 Mr. Marvin K. Maclean

GENETICS

Dr. Philip R. Wyatt
 Dr. Nancy Carson
 Dr. Yao-Shan Fan
 Mrs. Viola Freeman
 Ms. Dara Kennedy
 Dr. Peter Ray
 Dr. Sherry Taylor
 Dr. Ikuko E. Teshima

Appendix B

Non-Committee Members Who Assisted QMP–LS (2001)

Ms. Jennine Anderson
Ms. Nancy Angus
Ms. Diane Armstrong
Ms. Aimee Axler
Ms. Jackie Barten
Mr. Guy Beauparlant
Ms. Linda Borycheski
Mr. Joe Bottos
Dr. William Brien
Ms. Shirley Brown
Ms. Virgincita Bryan
Ms. Jessica Caron
Dr. Rabindra Chaudhary
Ms. Pam Chedore
Dr. William Chodirker
Ms. Gail Clifton
Mr. Ahmed Coovadia
Mr. David Core
Dr. Dennis Delaney
Mr. Diaram Deokharan

Ms. Kathy Eckert
Ms. Jean Falagario
Mr. Shaker Farhat
Dr. Margaret Fearon
Ms. Elnora Fleming
Dr. John Freedman
Ms. Judy Frisina
Ms Kathleen Gagliardi
Ms. Esther Giesbrecht
Ms. Chitra Ghosh
Ms. Karen Green
Ms. Michelle Henry
Mr. Dan Jang
Dr. Robert Lannigan
Dr. Wendy Lau
Ms. Theresa Mahany
Ms. Laurie Malloch
Dr. Allison McGeer
Mr. Ken McMillan
Dr. Matthew McQueen

Ms. Donna Meckel
Mrs. Sue Mimmagh
Ms. Lisa Morris
Mrs. Connie Pletch
Mr. Jim Roberts
Ms. Gwen Rosenfield
Ms. Olive Russell
Mr. Vito Scalia
Ms. Jane Ann Schroeder
Mr. Glen Small
Ms. Dina Suchak
Ms Linda Sunisloe
Ms. Carol Swanti
Dr. Mary Vearncombe
Ms. Liese Walchuk
Ms. Lai Ling Wat
Ms. Carol Wenzel
Mr. Lindsay Wilcox
Ms. Barbara Willey
Ms. Wendi Woods

Harold Richardson	Managing Director
Joanne Bishop	Staff Technologist, OLA
Darlene Cameron	Data Officer
Jason Chard	Systems Analyst
Julie Coffey	Staff Technologist, OLA
Linda Crawford	Director, OLA
Cheryl D'Souza	Office Administrator
Ruby Dubash	Supervisor, Communications and Documents
Christine Fleming	Consultant Technologist, EQA—Bacteriology, Mycobacteriology and Parasitology
Beverley Glenday	Administrative Assistant, Special Projects
Jane Gun-Munro	Director, EQA
Neela Khatri	Senior Systems Analyst
Maritess Koerner	Communications Assistant
Emily Lee	Receptionist
Alex Lesniara	Senior Systems Analyst
Scott MacDonald	Consultant Technologist, EQA—Cytology and Anatomic Pathology
Dan MacFayden	Director, Information Services
Carol Major	Consultant Technologist, EQA—Mycology and Virology
Joanne Miyazaki	Manager, Business Development and Education, and Consultant Technologist, EQA—Genetics and Maternal Serum Screening
Matt O'Connor	Clerk, Expediting
Astrid Petersons	Consultant Technologist, EQA—Transfusion Medicine
Anne Raby	Consultant Technologist, EQA—Hematology, Coagulation, Morphology, Bone Marrow, Flow Cytometry and Red Cell Disorders
Shelly Rowe	Senior Systems Analyst
Maureen Singh	Senior Administrative Assistant, EQA
Miralla Soares	Senior Administrative Assistant, OLA
Brenda Todd	Senior Administrative Assistant, EQA
Susan Varga	Senior Administrative Assistant, EQA
Betty Waltenberry	Data Officer
Sharon Webb	Consultant Technologist, EQA—Chemistry-General, Drug Monitoring, Endocrinology, Immunology, Enzymes, Cardiac Markers and Lipids and Point-of-Care Testing (Glucose Meters)
Margaret Hall Yousefi	Web site Officer
Emmanuel Zamora	Assistant, Expediting Services

The principal function of external quality assessment is performance improvement through assessment and education.

External quality assessment is one essential component of an overall participating laboratory quality management system.

Scientific committees of Ontario laboratory physicians, scientists and medical laboratory technologists will oversee specific assessment models.

The assessment process will be transparent, objective, and capable of distinguishing between good and poor performance.

Challenge materials will assess routine practice, reflect real patient samples as far as possible, be homogeneous, stable and free from interfering substances that cause matrix effect. In some disciplines, the limited availability of material allows only for partial processes, e.g. interpretative slide rotation surveys. The assessment process for partial surveys will consider the limitation or artificial environment of the model.

Pilot surveys or challenges that address new or evolving medical or scientific issues and technologies are considered educational and performance assessment will not include assignment of errors.

Participants will be provided with information and instructions to process challenge samples and report results in a similar manner to patient samples.

The specified disease/state/reference value of the challenge samples will be validated.

The assessment models will be scientifically valid and statistically sound.

The assessment process will recognise that sub-standard performance in an EQA survey can have many causes and may not reflect substandard performance in routine practice.

Investigation of performance will focus on performance improvement through education but will protect standards of patient care as necessary.

Feedback to participants will include reports of individual laboratory performance, a summary of overall performance and educational comments.

The confidentiality of all information that serves to directly identify individual laboratories will be protected.

A process to handle complaints or other feedback from participants will be maintained.

A process for participants to appeal the assessment of their performance will be maintained.

The principal function of accreditation is to help laboratories deliver high-quality, efficient laboratory services by achieving full accreditation. Full accreditation requires the laboratory to show objective evidence of its quality goals, management commitment, communication within and outside the laboratory, client satisfaction, continual improvement through effective QC/QA/quality management and sound reporting practices.

The accreditation program will include periodic surveillance (e.g. follow-up, self-assessment) and re-assessment, and will be linked to external quality assessment monitoring of performance.

Accreditation will operate within the context of a quality system and the documentation requirements thereof. Accreditation policies, processes and procedures will be documented and accessible.

Consultants will advise on all accreditation policies, processes and procedures.

All consultants and staff will adhere to conflict of interest rules.

Accreditation will ensure that laboratories meet explicit quality management criteria and will recognize the laboratory's competency and integrity.

Accreditation requirements and the methods of assessment will be defined.

Accreditation requirements define quality expectations, set the desired standards of best practice, and serve as the benchmark against which laboratory quality and competency are assessed.

Criteria for granting full and provisional accreditation will be established, along with guidelines to recommend withdrawal of accreditation.

The assessment process will be non-discriminatory and impartial.

Qualified assessors will be contracted, and records maintained of their qualifications and expertise including conflict of interest declarations.

Applicant laboratories will confirm that assessors appointed, including the team leader, do not have conflicts that may compromise their impartiality.

Assessors will undergo training to ensure their familiarity with requirements, assessment methods, operating policies and processes, and to enhance their communication skills.

Assessors will be provided with tools to ensure that comprehensive and correct assessments are conducted.

Laboratory information manuals will contain relevant information about the requirements, assessment process, criteria for assessment and necessary information/documentation to be provided by the applicant.

The assessment date will be mutually agreed upon by QMP-LS and the applicant laboratory.

Assessment reports will be provided in a timely fashion, and shall document the findings along with any explanation of non-compliance and conditions for corrections.

Accreditation will be granted according to established protocol, certificates will be issued and policies regarding the sharing of this information will be defined.

Staff will aid in defining and promoting standards-of-practice guidelines, assisting laboratories with utilization management.

Opportunities for improvement of the program will be identified and monitored.

Davidson R, Cavalcanti R, Brunton JL, Bast DJ, de Azavedo JCS, Kibsey P, Fleming C and Low DE. *Levofloxacin Treatment Failures of Pneumococcal Pneumonia in Association with Resistance*. N Engl J Med. (in press)

Fleming CA, Green K, Richardson H, Saginur M, Low DE and McGeer A. *Evolution of Antimicrobial Resistance in Nosocomial Gram Positive Pathogens in Ontario*. 2001 Conjoint Meeting of Canadian Association for Clinical Microbiology and Infectious Diseases (CACMID), Community and Hospital Infection Control Association (CHICA) & Canadian Infectious Diseases Society (CIDS). Victoria, British Columbia. November 2001.

Fleming CA, Palmer J, Kain KC, MacPherson DW, Mackenzie AMR, Richardson H and the Microbiology Committee. *Does Concentration Method Affect Performance on Enteric Parasitology Proficiency Samples? – A Five Year Review*. 2001 Conjoint Meeting of Canadian Association for Clinical Microbiology and Infectious Diseases (CACMID), Community and Hospital Infection Control Association (CHICA) & Canadian Infectious Diseases Society (CIDS). Victoria, British Columbia. November 2001.

Fleming CA, Green K, Richardson H, Saginur M, Low DE and McGeer A. *Evolution of Antimicrobial Resistance in Nosocomial Gram Positive Pathogens in Ontario, Canada*. 2001 41st Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC). Chicago, Illinois. December 2001.

Fleming CA, Jamieson F, Finn SJ, Richardson H and the Microbiology Committee. *Mycobacterial Smear Microscopy and Interpretation by Ontario Laboratories: An External Quality Assessment using Prepared Smears of Concentrated Sputum*. 101st General Meeting of the American Society for Microbiology. Orlando, Florida. May 2001.

Hill JG and Webb S. *Hemoglobin A_{1c}: Proficiency Testing in Ontario, Canada*. American Association for Clinical Chemistry (AACC) Annual Meeting. IL: Chicago. July 2001.

Lafferty J. *Good practice guidelines for the laboratory investigation of hemoglobinopathies*. Hamilton Regional Laboratory Medicine Program Newsletter No. 59, October 2001.

McShane K and the Inter-provincial Quality Assurance (IPQA) Transfusion Medicine Working Group. *Licensing, Accreditation and Quality Assurance of Transfusion Medicine Laboratories*. CSTM Bulletin, Fall 2001.

McShane K and the Inter-provincial Quality Assurance (IPQA) Transfusion Medicine Working Group. *Provincial Consensus Requirements for External Transfusion Medicine Quality Assessment Programs*. CSTM Bulletin, Fall 2001.

Miyazaki JH, MacDonald S, McLachlin CM and Richardson H. *Ontario Gynecological Cytology Patterns-of-Practice*. 14th International Congress of Cytology. Amsterdam, The Netherlands. June 2001.

Miyazaki JH, McLachlin CM and Richardson H. *Development of Consensus Standards of Practice Guidelines in Gynecologic Cytology in Ontario*. 14th International Congress of Cytology. Amsterdam, Netherlands. June 2001.

Richardson H, Flynn GJ and Dubash R. *Enhanced quality management for Ontario medical laboratories: OMA-administered QMP–LS program under way*. Ontario Medical Review March 2001;68(3):22-24.

Richardson H and Dubash R. *Introducing QMP–LS*. Advocate Spring 2001;8(1):9–10.

Richardson H and Dubash R. *New Direction for Quality Management Program—Laboratory Services*. CLMA Trillium Chapter: The Trillium Gazette May 2001;8.2:4.

Richardson H. *L'assurance de la qualité en biologie médicale dans l'État de l'Ontario (Canada)*. Les Enjeux du Labo 2001;3/4:39–40.

Thompson DS, Thompson JS, Richardson H, Zoutman D, and Fleming CA. *Canadian Involvement in Microbiology Laboratory Services in Kosovo*. 2001 Conjoint Meeting of Canadian Association for Clinical Microbiology and Infectious Diseases (CACMID), Community and Hospital Infection Control Association (CHICA) & Canadian Infectious Diseases Society (CIDS). Victoria, British Columbia. November 2001.

Zoutman D, Fleming C, QMP–LS Microbiology Committee, Richardson H. *Compliance with NCCLS approved standard M22-A2 for bacteriologic media quality assurance: a survey of 124 Ontario microbiology laboratories*. Diagn Microbiol Infect Dis. (in press)

EVENT/TOPIC	DATE	LOCATION	QMP-LS REPRESENTATIVE
St. Joseph's Hospital <i>Quality Management Systems</i>	February	Hamilton, ON	Dr. H. Richardson
Ontario Hospital Association <i>Laboratories Accreditation Process and Requirements</i>	March	Toronto, ON	Dr. H. Richardson
OAML Board Meeting <i>Ontario Laboratories Accreditation Process and Requirements</i>	March	Toronto, ON	Dr. H. Richardson
OHA Convention <i>Quality Laboratory Services – Where Are we Headed?</i>	March	Toronto, ON	Dr. H. Richardson
Hospital for Sick Children <i>Laboratory Medicine Rounds on Quality Management and Molecular Diagnostics</i>	April	Toronto, ON	Dr. H. Richardson Ms. J. Miyazaki
OMA Section on Laboratory Medicine <i>Quality Management Program-Laboratory Services</i>	April	Toronto, ON	Dr. H. Richardson
Hospital for Sick Children <i>Medicine Rounds: Quality Management and Molecular Diagnostics</i>	April		Dr. H. Richardson
Michener Institute <i>Total Quality Management Symposium Quality Planning 1: ISO in the Medical Laboratory. From Principles to Practice</i>	May	Toronto, ON	Dr. H. Richardson
<i>Cost Effectiveness of Urinalysis Screening for Urinary Tract Infection</i>	July	Chicago, IL	Dr. H. Richardson
Ontario Association of Pathologists <i>Development of an External Quality Assurance Program in Anatomic Pathology</i>	October	Alliston, ON	Dr. D. Murray
Kenora-Rainy River Regional Laboratory Program 2001 Annual Fall Symposium (October 23–25): <i>Let's Get Together! Keys to successful teamwork</i>	October 24	Dryden, ON	Mrs. L. Crawford
CACMID <i>Microbiology Quality Assurance Symposium Activities of the Interprovincial Quality Assurance Program Microbiology Working Group (IPQA)</i>	November 6	Victoria, BC	Mrs. C. Fleming
CACMID <i>Microbiology Quality Assurance Symposium Canadian International Activities in Laboratory Quality Assurance</i>	November 6	Victoria, BC	Dr. H. Richardson

TOPIC	DATE	LOCATION	PLANNERS/ PRESENTERS/ MODERATORS
Integrating GYN Cytology QA into Daily Practice	March 31	Toronto, ON	
Morning Workshop <i>A User's Guide – Implementing the Ontario Gynecologic Cytology QA Program into Daily Practice</i>			Dr. C. Meg McLachlin Ms. Linda Turner-Smith Ms. Sue Clipsham
Afternoon Symposium <i>Update on the Ontario Cervical Screening Program Quality Management Program – Laboratory Services Ontario Gynecologic Cytology Quality Assurance Program Pap Smear QA: Interlaboratory Comparison Studies Emphasizing Quality Assessment of ASCUS and SIL</i>			Dr. Terence J. Colgan Dr. Verna Mai Dr. Harold Richardson Dr. C. Meg McLachlin Dr. Diane D. Davey
Joint OSCC/QMP–LS Annual Scientific Meeting <i>Quality Assurance: Troponin I and T New Guidelines for Myocardial Infarction Homocysteine Quality Assurance: POCT POCT - Requirements for Quality and Competence ISO 22870 Hemoglobin A_{1c}</i>	November 7	Toronto, ON	Dr. Stephen Hill Dr. David Fitchett Dr. David E. C. Cole Dr. Christine Collier Dr. Harold Richardson Dr. C. Mark Cheung
Joint QMP–LS/OSMT/CMLTO Workshop <i>Troubleshooting the Gram Stain</i>	September 15 October 27 December 8	Thunder Bay, ON Windsor, ON Kingston, ON	Mr. Lindsay Wilcox
OTHER PRESENTATIONS			
On-line education courses			
<i>Introduction to Hematology: The Erythrocyte</i>	(Introduced in 1997)		Mr. John Lafferty
<i>Erythrocyte Disorders: Detection and Diagnosis</i>	September 1		Mr. John Lafferty

Appendix I

Parameters Monitored by QMP-LS, by Discipline

Chemistry**Chemistry-General**

Albumin
 Albumin Excretion Rate (AER)
 Bicarbonate
 Bilirubin, Total
 Blood Gases (pH, pCO₂, pO₂, Na⁺, K⁺, Glucose, Ionized Calcium)
 HbA_{1c}
 Calcium, Total
 Chloride
 Creatinine
 Glucose
 Magnesium
 Phosphate
 Potassium
 Protein, Total
 Sodium
 Urate
 Urea
 Urine Chemistry (Quantitative Protein, Sodium, Potassium, Creatinine, Osmolality)

Drug Monitoring

Acetaminophen
 Carbamazepine
 Cyclosporine
 Digoxin
 Drugs of Abuse
 Ethanol
 Gentamicin
 Lithium
 Phenobarbital
 Phenytoin
 Salicylate
 Tacrolimus
 Theophylline
 Tobramycin
 Valproic Acid
 Vancomycin

Endocrinology

Total Triiodothyronine (TT₃)
 Thyrotropin (TSH)
 Free Thyroxine (FT₄)
 Free Triiodothyronine (FT₃)
 Vitamin B₁₂
 Serum Folate
 Ferritin
 Cortisol
 Total Testosterone
 Follicle Stimulating Hormone (FSH)
 Luteinizing Hormone (LH)
 Progesterone
 Prolactin
 Chorionic Gonadotropin (CG)
 Alpha Fetoprotein (AFP)
 Estradiol
 Prostate Specific Antigen (PSA)
 Free PSA

Enzymes, Cardiac Markers & Lipids

Alkaline Phosphatase (ALP)
 Alanine Aminotransferase (ALT)
 Amylase
 Aspartate Aminotransferase (AST)
 Gamma Glutamyl Transferase (GGT)
 Homocysteine
 Lactate Dehydrogenase, Total (LD)
 Lipase
 Total Creatine Kinase (Total CK)
 CK-2

Serum Myoglobin
 Serum Troponin I
 Cholesterol
 Triglycerides
 HDL-cholesterol (HDL-C)
 Calculated LDL-cholesterol (LDL-C)

Immunology

ANA (Antinuclear Antibody)
 RF (Rheumatoid Factor)
 MAH (Antimicrosomal Antibody)
 CRP (C-reactive Protein)
 High Sensitivity CRP
 Anti-DNA
 Specific Proteins:
 IgG
 IgA
 IgM
 IgE
 C3
 C4
 Serum Protein Fractions:
 Albumin
 Alpha 1 Globulin
 Alpha 2 Globulin
 Beta Globulin
 Gamma Globulin
 Urine Protein Electrophoresis
 Urine Light Chain Detection (Bence Jones Protein)

MATERNAL SERUM SCREENING

Serum Analytes:
 Alpha Fetoprotein (AFP)
 Chorionic Gonadotropin (CG)
 Unconjugated Estriol (μE₃)
 Multiple of Median (MoM):
 AFP, CG, and μE₃
 Initial Positive Rate (IPR):
 Trisomy 21
 Open Neural Defect
 Trisomy 18

Hematology**Bone Marrow**

Aspirate and Biopsy

Coagulation

Prothrombin Time (PT)
 International Normalized Ratio (INR)
 Activated Partial Thromboplastin Time (APTT)
 Factor VIII
 Factor IX
 D-dimer
 Thrombophilia Investigation
 APC Resistance
 Antithrombin III
 Protein C
 Protein S

Flow Cytometry

Lymphocyte Immunophenotyping (HIV)
 Leukocyte Immunophenotyping
 (Hematological Investigation)
 CD34⁺ Stem Cell Enumeration

Red Cell Disorders

Hemoglobin S Screen
 Hemoglobin Fraction Quantitation
 Fetal Cell Detection
 G6PD

Morphology

Blood Film Morphology and Differential

Routine Hematology

Leukocytes
Erythrocytes
Hemoglobin
Hematocrit
Mean Corpuscular Volume
Thrombocytes
Reticuloctyes
Automated Leukocyte Differential

Transfusion Medicine

ABO and Rh Grouping and Interpretation
Antibody Detection
Antibody Identification
Direct Antiglobulin Testing (DAGT)
Crossmatching
Phenotyping
Elutions
Titrations

Microbiology**Bacteriology**

Aerobic and anaerobic isolation and identification of organisms from:

Blood
Genital specimens
Throat swabs
Body fluids
Other swabs/pus
Sputum
Stool samples

Serological grouping and identification
Quantitative urine cultures
Interpretation and reporting of cultures
Antimicrobial susceptibility testing
Interpretation and reporting of susceptibility findings
Gram stain interpretation
Special stains

Mycobacteriology

Detection of acid-fast bacilli from direct smears
Quantification of acid-fast bacilli

Mycology

Isolation and identification of:
Dermatophytes
Moulds
Yeasts
Wet preparations for fungal elements

Parasitology

Wet preparation examination of stool samples
Preparation of faecal concentrates
Staining of samples for gastrointestinal parasites
Identification and quantification of parasites
Use of special stains

Virology

Antibody detection
Cytomegalovirus
Hepatitis A and B
Hepatitis C
HIV
Rubella
VZV
Chlamydia trachomatis
Respiratory Syncytial Virus

GENETICS

Cytogenetics
Blood
Bone Marrow
Tumour
Tissue
Amnion Cells

Molecular Diagnostics of Inherited Diseases

ANATOMIC PATHOLOGY

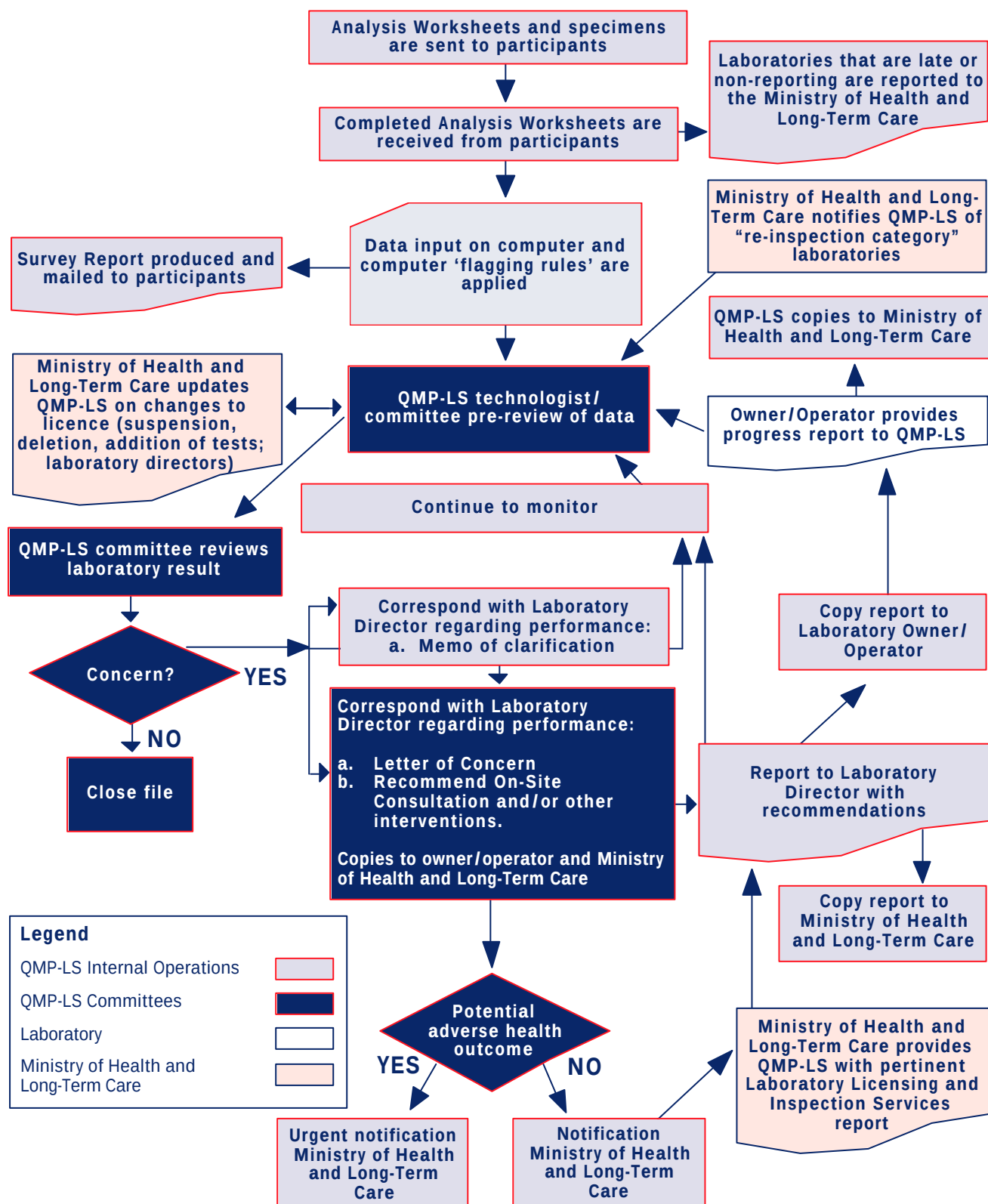
Histopathology

Histotechnology

Cytopathology
Gynecological
Non-Gynecological
Respiratory
Sputum
Bronchial washings
Bronchial brushings
Urinary
Body fluids
Fine needle aspiration of breast
Fine needle aspiration of head and neck
Thyroid
Lymph node
Salivary glands

OTHER**Point-of-Care Testing**

Glucose Meters



Appendix K

Summary of Committee Action in 2001

	Chemistry					Drug Monitoring					Endocrinology				
	C0101	C0103	C0105	C0107	C0110	D0101	D0103	D0105	D0107	D0110	R0102	R0104	R0106	R0109	R0111
Total receiving survey	221	219	218	63	214	80	143	141	157	161	123	123	122	121	121
Total number of labs presented	128	114	155	67	92	32	37	80	75	129	30	39	35	32	31
Significant error	18	20	14	9	24	5	5	10	7	14	2	5	2	2	4
Lesser error	6	22	19	4	10	4	6	3	10	14	11	8	9	9	7
Correspondence	32	46	43	25	36	10	12	17	21	29	15	16	12	12	12
OSC recommended	1	1	0	0	0	1	1	0	0	0	0	0	0	0	0

	Enzymes				Lipids			Immunology					Maternal Serum Screening		
	Z0101	Z0104	Z0106	Z0110	Z0101	Z0106	Z0110	L0102	L0104	L0106	L0109	L0111	S0102	S0104	S0112
Total receiving survey	210	201	198	200	155	151	148	120	115	114	112	112	7	7	7
Total number of labs presented	46	101	32	83	64	72	60	23	20	29	28	34	0	0	1
Significant error	1	4	1	2	7	4	18	6	0	2	1	2	0	0	0
Lesser error	8	13	1	13	11	10	9	2	8	12	9	10	0	0	0
Correspondence	15	21	4	16	24	21	29	9	8	23	10	12	0	0	0
OSC recommended	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

	Hematology								Coagulation		
	H0103BM	H0103FC	H0104XYZ	H0105	H0108FC	H0109BM	H0109XYZ	H0011	K0102	K0106	K0110
Total receiving survey	69	19	97	234	19	69	60	227	221	220	214
Total number of labs presented	15	12	38	93	8	8	6	49	50	43	50
Significant error	2	1	3	10	1	0	0	21	3	2	1
Lesser error	2	15	2	1	4	0	1	6	16	2	4
Correspondence	6	25	6	19	10	8	2	34	19	4	18
OSC recommended	1	0	0	0	0	0	0	0	0	0	0

	Transfusion Medicine			
	I0103	I0104	I0109	I0111
Total receiving survey	179	179	179	179
Total number of labs presented	49	47	64	88
Significant error	5	4	3	4
Lesser error	8	21	24	85
Correspondence	28	31	39	58
OSC recommended	2	1	0	0

	Bacteriology					Mycology		Parasitology		Virology			
	B0102	B0104	B0106	B0109	B0111PP	W0103	W0108	T0105	T0110	V0101	V0103	V0108	V0110
Total receiving survey	136	132	131	129	108	30	28	29	28	42	54	53	75
Total number of labs presented	81	100	99	92	66	14	9	21	24	20	15	20	11
Significant error	6	33	23	41	0	0	1	6	4	0	2	2	1
Lesser error	29	123	42	39	0	2	2	18	25	0	2	0	1
Correspondence	51	83	66	78	11	6	3	15	20	10	7	4	9
OSC recommended	0	0	0	0	0	0	0	0	0	0	0	0	0

	Cytology	Genetics		
	Y0109	G0102	G0105	G0108
Total receiving survey	86	10	10	10
Total number of labs presented	73	1	0	10
Significant error	19	0	0	0
Lesser error	115	0	0	10
Correspondence	43	1	0	10
OSC recommended	1	0	0	0

DATE	LOCATION	PRESENTER(S)
September 24, 2001	CMLTO Toronto, Ontario	Mrs. L. Crawford
October 11, 2001	Wingham and District Hospital Wingham, Ontario	Mrs. L. Crawford, Mrs. J. Coffey
October 17, 2001	The Ottawa Hospital, Ottawa, Ontario	Mrs. L. Crawford, Mrs. J. Coffey, Mr. K. Davis
October 19, 2001	CLMA Trillium Chapter Burlington Convention Centre Burlington, Ontario	Mrs. L. Crawford, Mrs. J. Coffey, Mrs. S. Woodcock
October 23, 2001	Kenora-Rainy River Fall Symposium Best Western Motor Inn, Dryden, Ontario	Mrs. L. Crawford
October 29, 2001	London Health Sciences Centre London, Ontario	Mrs. J. Coffey, Mr. K. Davis
October 30, 2001	Southlake Regional Health Centre Newmarket, Ontario,	Mrs. L. Crawford, Mrs. J. Coffey, Mr. G. Modi
November 2, 2001	Timmins & District Hospital Timmins, Ontario	Mrs. L. Crawford
November 5, 2001	Ontario Hospital Association Convention and Exhibition Metro Toronto Convention Centre Toronto, Ontario	Mrs. L. Crawford, Mrs. J. Coffey, Dr. H. Richardson, Mrs. S. Woodcock
November 8, 2001	Public General Campus of Chatham, Ontario	Mrs. L. Crawford, Mrs. J. Coffey
November 12, 2001	Quality Management Group, GTA Chapter Toronto, Ontario	Mrs. L. Crawford
November 12, 2001	Sudbury Regional Hospital Sudbury, Ontario	Mrs. J. Coffey, Mr. G. Modi
November 15, 2001	QMP-LS (POCT only) Toronto, Ontario	Mrs. L. Crawford, Mrs. J. Coffey
November 16, 2001	Hamilton Health Sciences Chedoke Campus Hamilton, Ontario	Mrs. L. Crawford, Mrs. J. Coffey, Dr. H. Richardson
November 20, 2001	Delta Hotel Toronto East MDS Inc. Toronto, Ontario	Mrs. L. Crawford, Mrs. J. Coffey, Dr. B. Sheridan
November 23, 2001	Peterborough Regional Health Centre Peterborough, Ontario	Mrs. L. Crawford, Dr. D. Macdonald
November 29, 2001	OAML Board, North York	Mrs. L. Crawford, Dr. H. Richardson
November 29, 2001	St Michael's Hospital Toronto, Ontario	Mrs. L. Crawford, Mrs. J. Coffey
December 3, 2001	Kingston General Hospital Kingston, Ontario	Mrs. L. Crawford, Mrs. J. Coffey
December 5, 2001	Thunder Bay Regional Hospital Thunder Bay, Ontario	Mrs. L. Crawford
December 6, 2001	QMP-LS (Genetics only) Toronto, Ontario	Mrs. L. Crawford, Mrs. J. Coffey

