



2005 REVIEW

Quality Management Program—Laboratory Services



VISION

To be a world-class provider of accreditation, quality assessment and supports to laboratories and related services for diagnosis and treatment of disease, and the promotion of health.

PURPOSE

To promote quality improvement of laboratories and other related services for the public good and the benefit of health professionals.

VALUES

- Quality
- Collaboration
- Integrity

QUALITY POLICY

QMP-LS commits to provide high quality laboratory accreditation, assessment and education services, that:

- Meet all customers' requirements; applicable regulatory, statutory and contractual requirements; and relevant national/international standards;
- Evaluate and continually improve the effectiveness of the services;
- 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 QMP–LS *Review* encapsulates the yearly operation of the Quality Management Program—Laboratory Services (QMP–LS), and also serves as a valuable tool for capturing QMP–LS’ yearly activities and its key priorities.

QMP–LS continues to provide world-class external quality assessment, accreditation and education services, with the tireless support of many expert individuals who serve as committee members (Appendix A) and volunteers (Appendix B). We acknowledge their commitment and dedication to our program.

We thank the following committee members who retired during 2005/2006 year:

Dr. Robert Barr	Mrs. Viola Freeman
Dr. V. Bhayana	Dr. Joel Goodman
Dr. Scott Boerner	Dr. Doug Macpherson
Dr. Malcolm Carlson	Mr. Gaman Modi
Dr. Nancy Carson	Dr. Ken Onuska
Ms. Anna Chan	Dr. Peter Ray
Dr. William Chapman	Dr. Brian Sheridan
Dr. Christine Collier	

We are grateful to the Ontario laboratories and institutions that allow their staff to serve on our committees. We also thank Mr. Dan Tholen, our statistical consultant and Mr. Jim Moran, our assessor trainer, for their invaluable advice and guidance as we strive to meet applicable international standards.

Lastly, our staff (Appendix C) are commended for their constant support. Mrs. Ruby Dubash, Managing Editor, Communications and Documents and Ms. Dawn Earle, Senior Administrative Assistant, OLA left during 2005/2006. We wish them well.

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The reader is cautioned not to take any single item, or part thereof, of the 2005 Review out of context.

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INTRODUCTION

Quality Management Program—Laboratory Services (QMP–LS), a department of the Ontario Medical Association, is committed to provide high quality laboratory accreditation, external assessment and education services. The External Quality Assessment (EQA) division provides relevant, state-of-the-art programs in laboratory medicine that have heightened awareness of the need for quality management. The Ontario Laboratory Accreditation (OLA) division assists laboratories in delivering high-quality, efficient laboratory services to recognized international standards through achieving full accreditation.

Laboratory quality assessment is complex in nature and international in scope and we are proud that QMP–LS is recognized and respected internationally as a leader in this field. To this end, we collaborate with partners in health care and share our experiences nationally and internationally.

NURTURING QUALITY—BEGINNING AND ENDING WITH THE PATIENT

To deliver quality laboratory services we must constantly bear in mind the primary role of any medical laboratory. It is to generate information that allows a physician to practice good medicine having optimal health benefit for the patient. The information must be clinically relevant and correctly interpreted to achieve this benefit. The goal should be the best achievable quality in all laboratory results and reports.

In 1995, the Report of the Laboratory Restructuring Advisory Committee under Dr. Diane Schatz recommended the creation of a province-wide laboratory quality management program to help achieve the above quality goal. Consequently, the Minister of Health introduced medical laboratory accreditation to Ontario and invited the Ontario Medical Association to develop and implement the program. Over the past five years, all laboratories have undergone a self-assessment and just over half have had a peer-group on-site assessment visit against the OLA accreditation requirements. The majority has clearly shown their commitment to continue to meet the goal of best achievable quality. These laboratories have shown a high level of conformance to the internationally-based accreditation requirements developed by the OLA division. Their commitment to develop and implement a quality system has been impressive to say the least. However, not all have been as successful as the majority, indeed some have struggled. The same can be said about laboratory performance on the EQA challenge surveys; most perform to a high level but some do have difficulty in meeting expectations.

As laboratories have continued their quest for quality, QMP–LS itself has evolved with the intent that it shall operate in support of improving medical laboratory services across the province. At the same time there have been significant international developments in both accreditation approaches and in external quality assessment lead by ILAC (International Laboratory Accreditation Cooperation) and ISO (International Organization for Standardization). In this international arena of laboratory accreditation, QMP–LS is unusual but not unique in that it provides both accreditation and external quality assessment (a.k.a. proficiency testing). International acceptance requires that the two divisions are operated separately but with linkages as QMP–EQA must provide information to OLA on participating laboratory performance. This linkage supports the monitoring and surveillance that OLA must carry out to conform to the international standard (ISO 17011:2004) for accreditation bodies.

The fundamental differences between OLA and EQA are substantive. An OLA assessment determines that a laboratory has developed and implemented a management system of

interlinked processes to meet its quality goals and the OLA requirements. In other words it is a process-based accreditation model. EQA on the other hand uses clinically relevant challenge surveys with materials that mimic patient samples to verify that the laboratory processes are working and that the procedures produce expected results. Feedback on performance in the EQA challenge surveys allows the laboratory management to investigate discordant findings and implement corrective actions to ensure quality within the laboratory and to meet a fundamental condition of its accreditation certificate.

As I reflect on these recent and continuing demands in the way in which a laboratory is expected to be structured and operate, the key requirement is **quality** that meets not only local, provincial, and national, but also international standards. **Globalization is the current day norm!**

ISO defines quality, as “the totality of characteristics of an entity that bear on its ability to satisfy stated and implied needs.” Because of the difficulty of understanding what this means, for QMP-LS purposes we have defined **quality in the medical laboratory as a system for the collection, examination and reporting of human samples that:**

- supports the prevention, diagnosis and management of disease states;
- generates information having clinical utility and optimal impact on health outcomes;
- meets pre-determined targets for trueness, precision and traceability;
- strives to minimize error;
- is timely, efficient and cost-effective and;
- focuses on client satisfaction and continual improvement.

Attention to all activities throughout the pre-, analytical, and post-examination phases of all testing is needed to reach this quality goal. Most Ontario medical laboratories have a clear recognition of this need but as we move to the future and the quality “bar” is raised through increasing public awareness and media attention we as a laboratory community will need to respond. As Dr. Michael Noble of the University of British Columbia says, “Where are the OFIs?” The greatest potential for “Opportunities for Improvement”—OFI—lies in the pre- and post-examination phases but we need to pay attention to the analytical phase itself. **If the output of the analytical phase of examination is not accurate and precise then no amount of improvement in the pre-examination and post-examination phases will be able to correct for it.**

For decades the cornerstone of quality in the analytical phase has been calibration and quality control of the instrument/reagent systems. Although most Ontario laboratories have a good understanding of these activities, quality control (QC) data submitted to QMP-LS indicate that some still have work to do. This is illustrated throughout the Review where you will find reference to the investigation of discordant findings on the EQA challenge surveys. A recurrent theme is that enhancing the ability to carry out root cause analysis is a real OFI as well as:

- increasing awareness of the principles and practices of effective quality control;
- understanding random versus systematic error—precision versus bias;
- appreciating the impact of biological variation on the meaning of the result obtained;
- understanding the pitfalls of reference intervals as currently used by most laboratories and;
- knowing about uncertainty of measurement and the many factors that may contribute to this uncertainty.

A recent question to QMP-LS illustrates why we still have a way to go in bridging the gap between the laboratory and the patient. The question from a well-established geriatrician was, “When I send a blood sample from the same patient to two laboratories within a day or so for a hemoglobin level I get two different results 75 from one and 85 from the other. Which result is correct and why aren’t they the same?” Obviously this physician expected every result to be the same or very close. Like many physicians he did not recognize that variation in the result is to be expected. At least, he questioned the result because of the impact on the well-being of his patient. If the result was 80 or under the patient was transfused, if over 80 then no blood transfusion. I think we can all

appreciate his dilemma and frustration. This physician, like many others, had little understanding of what the real limitations are in the laboratory.

If we are to help physicians have a better understanding of what happens then we must continue to develop a better understanding of (i) why results vary in the same patient from laboratory to laboratory and from time to time (ii) is the variation significant in terms of health outcome? (iii) does the variation indicate an early or latent disease state? We all know that results do vary depending on the method used in the laboratory, operator experience and skill, as well as patient preparation, sample handling and biological variation itself but we do not share this information readily with our clinical colleagues. Another OFI?

In a further attempt to help physicians, many laboratories publish so-called reference intervals (normal ranges in older terminology) to assist them in determining whether a particular result is “normal” or “abnormal.” Is this really useful? To a limited degree! Just because a result falls within the reference interval does not mean that the result is “normal” for that patient. Consider the patient who had values for a given analyte over time that were consistently toward the low end of the reference interval and with a narrow standard error and then has a determined value that is towards the high end but still within the limits. This may mean merely that the patient has changed his/her homeostatic set point for some reason but it may also indicate that an early disease state has developed. Probably the best that any laboratory can do is to follow the recommendations of IFCC (International Federation of Clinical Chemistry and Laboratory Medicine) and the CLSI (Clinical and Laboratory Standards Institute) Guideline on establishing reference intervals.

Although most laboratories in the province produce high quality results, some of the other OFIs that might further enhance quality are:

- Establish quality indicators to be applied to patient preparation, specimen collection, handling and transport. You might wish to monitor the Institute for Quality in Laboratory Medicine Web site for suggestions (www.iqlm.org).
- Continue to be vigilant that your laboratory methods are free of bias and imprecision of the determined value.
- Monitor your internal quality control and ensure that it confirms that the laboratory procedures meet your pre-determined analytical requirements. Have the appropriate Westgard rules been applied and have the Levey-Jennings charts been constructed and interpreted correctly?
- Be aware of the concepts of measurement uncertainty. Some European authorities are pushing hard to have the degree of uncertainty published along with any result.

This is my last contribution to the *Review* as I plan to retire at the end of this coming June. It has been my privilege to participate in LPTP (Laboratory Proficiency Testing Program) and now QMP-LS since 1975. Ontario medical laboratories have good cause for pride and satisfaction with their work but as I was told as a young man about to enter medical school “aim for the stars and you might just hit the top of the trees.” Thank you for the support you have given me and the QMP-LS staff. I acknowledge without reservation the many laboratory professionals who give so freely of their time and expertise as committee members, advisors and expert consultants, without their input QMP-LS would be a shadow. I wish you all every success in your ongoing quest to be the best.

EDUCATION

QMP-LS’ philosophy in the delivery of education is to focus on problem areas identified through our EQA or OLA activities. We continue collaborating with partners in health care and sharing our experiences nationally and internationally (Appendices D–F). In addition, specific educational activities are detailed in the EQA and OLA Reports.

In 2005, we published articles on significant developments in the medical and scientific literature (Appendix D). Three invited presentations were made at international meetings and four at local and Canadian national meetings

(Appendix E). QMP-LS News highlights developments in laboratory medicine, details operational changes at QMP-LS and provides information on upcoming activities and events. QMP-LS News is posted once a month on our Web site where additional information on products and services is also available. Supplementary EQA and OLA information is provided to participants electronically via secure, password-protected access.

QMP-LS continued to provide education and professional development to its staff.

Symposia and Workshops

In 2005, QMP-LS continued its collaboration with the College of Medical Laboratory Technologists of Ontario (CMLTO) and the Ontario Society of Medical Technologists (OSMT) to deliver workshops across Ontario. Hematology is the topic of the workshop series that will continue into 2006.

In November, QMP-LS co-sponsored a symposium entitled *Quality Matters* with the Ontario Society of Clinical Chemists.

Several collaborative workshops and symposia are under development for 2006.

Information Services

In 2005, Information Services achieved a number of significant operational objectives in alignment with the QMP-LS quality system:

Customer Service

- Introduced enhanced survey reports for all quantitative survey types (Figure 1).
- Generated the OLA Accreditation Requirements Version 3.1 reports (Figure 2).
- Conducted a survey of 265 Ontario laboratories as well as 25 out-of-province participants for a total of 290 sites. The purpose was to help QMP-LS understand the level of satisfaction with access to our Document Server and use of electronic messaging and reports. The information received will be used in process improvement initiatives. A summary report of participant responses was posted on the QMP-LS Web site in January 2006. A sample question and participant responses appear in Figure 3.

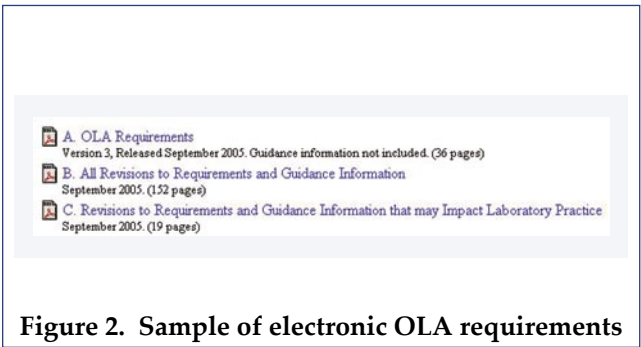


Figure 2. Sample of electronic OLA requirements

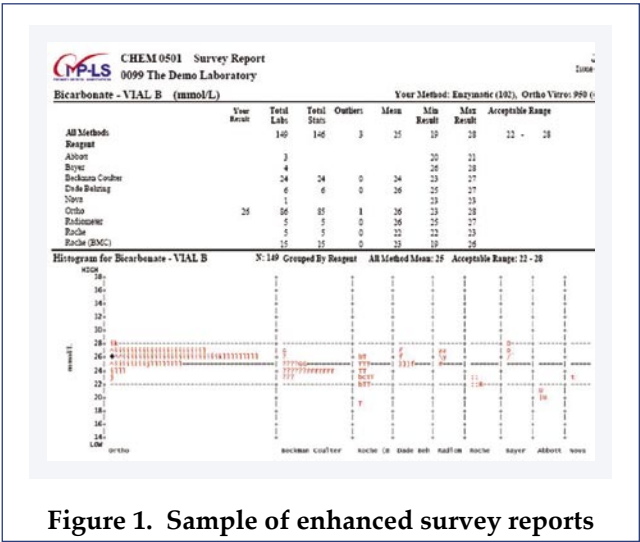


Figure 1. Sample of enhanced survey reports

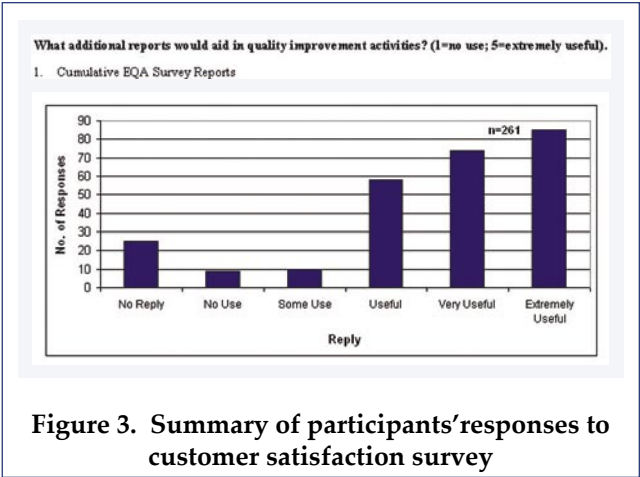


Figure 3. Summary of participants' responses to customer satisfaction survey

Management Responsibility—Document Management

- Evaluated alternatives to our existing Document Server resulting in the development of Q-View (Figure 4), the next generation QMP-LS document server and data collection portal, continuing through the 1st quarter of 2006. Implementation is planned for the 2nd quarter of 2006.

Resource Management

Identified and made recommendations for several critical equipment replacements including the replacement of obsolete file and print servers, the network backup system, multiple staff workstations and an obsolete phone system. These recommendations received funding approval in November 2005 and will be implemented in the 1st quarter of 2006.

Service Realization

OLA Accreditation Software Application Enhancements and Support

- The mobile assessor component of the Q-Accredit![®] software (Figure 5) used by our OLA assessors to collect OLA visit response data on-site now includes flexible version-specific and focused scope assessment reporting capability.

EQA Software Application Enhancements and Support

- Migration of EQA surveys from Ingres® to SQL-server-based LEQA application. Hewlett Packard will discontinue support for its proprietary HP3000 computer in 2007. All quantitative EQA surveys have been moved from the Ingres® relational database on the HP3000 onto a SQL-server-based application we call LEQA (Lab-EQA). The remaining disciplines' surveys will be moved into LEQA in 2006.
- Performed data entry and analysis, and generated participant Survey Reports, for 100 Ontario challenge surveys. 4 questionnaires. 5 patterns-of-practice and 5 dry or Web-based surveys.

Measurement and Analysis

- Integrated a Client Contact form into the QMP-LS Help Desk application to capture information on what our clients think about QMP-LS products and services. This information will be utilized to effectively make decisions on quality improvement opportunities (Figure 6).

MANAGEMENT COMMITTEE

The Management Committee consists of members appointed according to the Ministry of Health and Long-Term Care (MOHLTC)/Ontario Medical Association (OMA) Agreement. Membership includes representation from MOHLTC, the OMA, the College of Physicians and Surgeons of Ontario, the College of Medical Laboratory Technologists of



Figure 4. Sample home page of Q-View

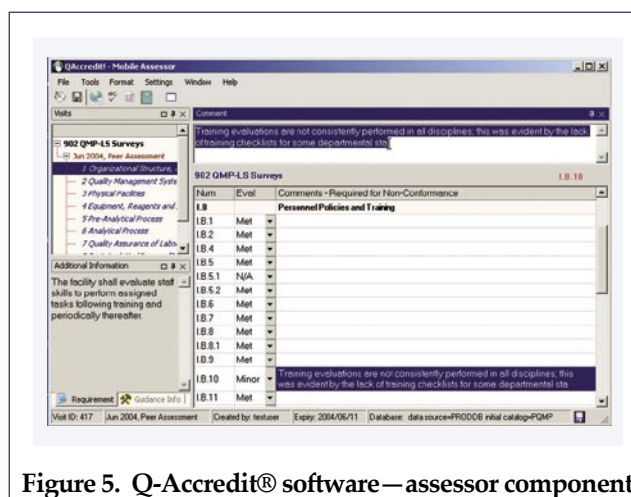


Figure 5. Q-Accredit® software—assessor component



Figure 6. QMP-LS HelpDesk client contact form

Ontario, the respective Chairs of the Professional Advisory Committee and the OLA Advisory Panel and the Managing Director, QMP-LS (Appendix A). The Advisory Council, with representation from the stakeholder organizations (Appendix A), continues to provide input to the Management Committee on the development of policies, processes and procedures. Members of the Advisory Council are invited to attend Management Committee meetings.

In 2005, Management Committee met four times in the year and convened a conference call meeting to review a referral from the OLA Advisory Panel as a result of a decision not to grant an accreditation certificate.

Regular agenda items included:

- QMP-LS work plan, budget and operational matters
- Policy issues
- Progress reports on laboratories under review
- Resolution of issues brought forward by the Professional Advisory Committee, OLA Advisory Panel and operational divisions
- Updates from the EQA, OLA and Information Services divisions on operational objectives
- Report on educational and communication activities.

Special issues for 2005 included:

- Review of policies in accordance with the quality system requirements
- EQA operating principles
- Revised terms of reference for the Professional Advisory Committee
- Update on OLA self-assessment and peer assessments
- Quality of Care Information Protection Act
- Point-of-Care Testing project and Advisory Committee
- Guidelines Advisory Committee.

CONJOINT COMMITTEE

The Conjoint Committee (Appendix A) met on four occasions and convened a conference call meeting to review a recommendation from Management Committee on a referral from the OLA Advisory Panel as a result of a decision not to grant an accreditation certificate. The Conjoint Committee is co-chaired between Ms. Marnie Cooper and Dr. Harold Richardson. Laboratories being monitored for poor survey performance by the scientific committees and brought forward on the recommendation of the QMP-LS' Management Committee were reviewed and actions determined. In particular, reports of follow-up on-site consultation visits conducted in a Parasitology and a Flow Cytometry laboratory were reviewed. Other issues concerning specific laboratories were also addressed as and when requested by Management Committee.

Issues addressed were:

- Point-of-Care Testing: compliance with EQA surveys mandatory or voluntary
- Late and non-reporting laboratories
- QMP-LS reporting quarterly instead of monthly to MOHLTC
- Enhanced information sharing
- Quality of Care Protection Act
- New model for cytological, hematological, morphology and histopathology
- Biological safety cabinets
- Supply of survey material
- Criteria for repeat OLA peer assessment visits
 - Protocol for a new laboratory
- Utilization management initiatives
- OLA certificate turnaround time issue
- Provincial Auditors' report
- Changes to memorandum of understanding between MOHLTC and OMA
- Meeting at the request of the Ministry of Labour and Health Care Health and Safety Association (HCHSA)
- Agreement with Standards Council of Canada
- Review of quality system policies in accordance with the quality system requirements
- Point-of-Care Testing Advisory Committee and project
- Updates on laboratory testing guidelines
- Activities of the Test Review Committee

INTRODUCTION

Change management and process improvement continued to be driving forces for the External Quality Assessment (EQA) division in 2005. The framework for the quality system is now in place. Aligning technical requirements of the program with international standards is the current focus.

Interaction with Peer and Stakeholder Organizations

As we move to compliance with international standards, it is important to communicate with like-minded peer organizations to share knowledge and collaborate when feasible. Activities that occurred during 2005 included:

- Meeting with peer Canadian organizations at the annual meeting of Canadian Coalition for Quality in Laboratory Medicine;
- Collaborating with Royal College of Pathologists of Australia EQA program in Chemical Pathology for procurement of endocrinology testing material and sharing of survey data;
- Membership of Advisory Committee to Caribbean Epidemiology Centre, Trinidad on a European funded project Strengthening Microbiology Laboratory Services in the Caribbean;
- Attending an inaugural meeting of the International Laboratory Accreditation Collaboration Proficiency Testing (PT) Consultative Group;
- Membership of Clinical Laboratory Standards Institute working group to revise GP27-A—Using PT to Improve the Clinical Laboratory.

QMP-LS Scientific Committees and Volunteers

In 2005, we again hosted more than 70 committee members at more than 40 committee meetings to plan and assess performance in EQA surveys. These meetings are always lively and a source of satisfaction and learning for all involved. We are grateful for the dedication and commitment of our scientific committee members who bring depth of knowledge and understanding of laboratory discipline issues to our program and ensure continued relevance. The names of individuals who served on committees or volunteered their time to our program in some way are listed in Appendices A and B. Their contribution to the program is greatly appreciated.

2005 PLANNED ACTIVITIES

Each year, the EQA division plans activities for the following year. This happens at two levels: in the early spring, QMP-LS management and staff plan annual goals and objectives in accordance with QMP-LS overarching quality management system goals. In the early fall, the scientific committees plan the survey models for the following year.

Scientific Committee Review

Execution of surveys is the major service realization function for EQA. Planning is largely an activity of the scientific committees, who review the outcome of the current year's surveys and plan the survey models for the following year. During this process, each committee considers the following in the selection and recommendation of challenges:

- Strengths and weaknesses of previous year's program;
- Opportunities for improvement and education;
- Current scientific or medical issues relevant to laboratory practice;
- Design of survey model in accordance with accepted standards and;
- Reliable supply of high quality testing material.

Plans for the various discipline surveys are reviewed and endorsed by the Professional Advisory Committee, the senior EQA advisory committee comprised of all scientific chairpersons. The QMP-LS Senior Management Group approves availability of resources for the survey plans.

During 2005, we administered 100 challenge surveys, 5 dry or Web-based surveys, 5 patterns-of-practice surveys and 4 questionnaires. Summaries of findings from these surveys are provided in the discipline reports.

Internal Review

Accomplishments for 2005 include:

CUSTOMER SERVICE

Customer Satisfaction Survey: Access and Format of Electronic Documents

Client satisfaction with access to QMP-LS reports and documents was surveyed through focus group meetings with five volunteer laboratories as well as a questionnaire issued to 290 participant laboratories. The objective was to understand the level of satisfaction with access to and design of the QMP-LS electronic document file structure and use of electronic messaging and documents. The response rate to the survey was 75%. In general, the following was identified:

- All but one respondent have Internet access and 80% of respondents have high speed access.
- The majority of respondents have computers in the laboratory. However, information from focus groups revealed that access to Internet sites, including the QMP-LS Web site may only be available to management or supervisory technologists.
- Almost all (97%) of respondents are aware of the e-mail notification system used when documents are posted to the Document Server. Suggested recommendations for improvement included identifying more contacts for each facility and providing a link to the documents within the e-mail message.
- Over 90% of respondents were satisfied with the current password system. Others found it to be cumbersome and preferred a password management system with greater flexibility.
- More than 80% of respondents were satisfied with the content and format of EQA reports and Committee Comments. File sizes of these documents were the major reason for dissatisfaction. In general, respondents still prefer to view hard copy reports.

The feedback has proved to be valuable for QMP-LS to understand the current capability of laboratory personnel to access and use QMP-LS electronic documents. This information has been used by the Information Services staff to develop an improved communication platform and new EQA reports (see page 4 of The Year in Review). Full results of the questionnaire are posted on the Document Server in the QMP-LS General Information folder, accessed through the QMP-LS Web site.

Improve Participant Access to EQA Information Through the QMP-LS Web site

The information received from the questionnaire is being used to develop a new portal or extranet, known as Q-View, for improved access, as discussed in the Information Services report within The Year in Review (page 5).

In addition to survey output, EQA-related publications and presentations are now available through the QMP-LS Web site.

Publication of Educational Material

Two articles on EQA were published in the *QMP-LS News* during 2005. The objective of these articles was to remind participants how to use EQA to optimize their quality assurance processes. The first article (No. 93, August 2005) describes the role and importance of EQA in the laboratory's quality management system.

The second article (No. 95, October 2005), focuses on the application of root cause analysis to the investigation of EQA discordances, and how this process optimizes process improvement.

MANAGEMENT RESPONSIBILITY

Review and Coordinate EQA Reporting Practices with OLA and MOHLTC

Prior to the implementation of the OLA program, the EQA program was responsible for monitoring several activities for which laboratories are now considered to be accountable to OLA through its accreditation requirements. These include:

- satisfactory participation in EQA surveys;
- satisfactory performance in EQA surveys and;
- satisfactory implementation of corrective action for EQA performance.

The EQA division is working closely with OLA and the MOHLTC, Laboratory Services Branch to provide reports that allow coordinated and continued surveillance of performance.

RESOURCE MANAGEMENT

To Identify Reliable Supply of EQA Testing Material

A major strength of the QMP-LS EQA program is the use of fresh or frozen human testing material wherever possible. This provides participants with reliable challenges closely resembling patient samples that are free of interfering factors sometimes associated with non-human material. Use of human material also allows a dependable comparison of instruments and methods not always obtained otherwise. A major disadvantage of using human material is sourcing a reliable supply. QMP-LS has depended very heavily in the past on committee members to identify sources of material, an onerous burden. During this year efforts were made to identify alternate sources of material. These include:

- commercial sources;
- collaboration with other EQA/PT providers and;
- Ontario laboratory participants.

In early 2006, a call for patient material was issued to Ontario laboratories for donations of material for certain laboratory disciplines, including:

- Cytology: Gynaecological and non-gynaecological preparations
- Parasitology: Human feces preserved in Sodium Acetate Fixative
- Histology: Fixed blocks of human tissue

Each material type has specific requirements that will be made available to interested parties.

SERVICE REALIZATION

To Complete Review and Revision of EQA Survey Models

Finalize Statistical Model for Quantitative Surveys

A major undertaking has been to review and revise the use of statistics for quantitative surveys. This was made possible this year as part of the migration of these surveys to the new database. After a rigorous validation process during 2005, a robust statistical algorithm recommended in ISO/EN 13528 Statistical Methods for

Interlaboratory Comparisons will be implemented for 2006 surveys. This will impact any chemistry, hematology or virology surveys where the mean and standard deviation of participant results are estimated for use as assigned values and calculation of allowable limits. All such surveys now have appropriate statistical estimates in accordance with international standards. Description of the statistics will be available in the General Information folders of each discipline.

Develop Mechanisms for Measurement of Cumulative Performance

In association with the implementation of robust statistics is the development of mechanisms to track survey performance over time. Mechanisms were developed during 2005 and will be validated during 2006 for full implementation with 2007 surveys.

Compliance of Healthcare Facilities with the MOHLTC 1999 Point-of-Care Test (POCT) Policy

In 2005, the Ministry of Health and Long-Term Care requested QMP-LS to facilitate a project to review and recommend quality requirements for POCT in Ontario healthcare institutions. To accomplish this, QMP-LS initiated an advisory committee comprised of thought leaders from all relevant stakeholder sectors to work on this project, scheduled for completion in the second quarter of 2006.

Provision of EQA Services

The parameters monitored by discipline are listed in Appendix G. The number and types of laboratories required to participate in the program are shown in Tables 1 and 2. The testing material suppliers for each discipline and the reference laboratories are shown in Appendix H.

In addition to services provided to Ontario laboratories, we provide services to other jurisdictions on a cost-recovery basis. The surveys most commonly provided are listed in Table 1. In addition, we provide separate microbiology surveys to 22 member countries of CARICOM and separate cytology surveys to Alberta laboratories.

Laboratory Performance

The scientific committee evaluation of survey results includes assessment of error based on the clinical significance of discordant findings. Lesser errors are assessed for results that exceed the established acceptable limits and significant errors for results that have the potential to cause mistreatment or misdiagnosis. Scientific committees correspond with the participating laboratories regarding the discordant

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

Laboratory Facility Type	Number of Laboratories				
	2001	2002	2003	2004	2005
Community	53	54	47	44	40
Hospital	181	182	180	182	182
Public Health	11	12	12	12	12
Psychiatric	0	0	0	1	1
Canadian Blood Services	6	6	6	6	5
Federal Government	2	1	1	1	1
Other	1	2	2	1	1
Total	254	257	248	247	242

Table 2. Number of Participating Ontario Laboratories in 2005 vs. Out of Province

Discipline	Ontario	Out of Province
Anatomic Pathology	76	0
Chemistry-General	199	6
Drug Monitoring	162	1
Endocrinology	130	1
Enzymes, Cardiac Markers	193	2
Lipids	134	0
Immunology	66	2
Maternal Serum Screening	NA	NA*
Hematology-General	209	2
Flow Cytometry	23	10
Red Cell Disorders	84	3
Coagulation	195	0
Hematology-Morphology	200	0
Transfusion Medicine	168	0
Bacteriology	107	0
Mycology	22	2
Parasitology	19	0
Virology	75	3
Genetics	11	10
Cytology	78	0
Point-of-Care Testing	192	1

* No surveys conducted in 2005

findings, requesting feedback on the cause and corrective action. Unacceptable or incomplete participant responses may prompt further communication, continuing to monitor performance and/or an offer of an on-site consultation. Two on-site consultations were conducted during 2005 (Table 3). No laboratories were declared non-proficient (Table 4).

Table 3. QMP-LS On-site Consultations that Occurred During Each Year, 1996–2005

Discipline	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
Bacteriology	5	3	2	0	4	0	0	0	0	0
Parasitology	1	0	3	1	0	0	1	1	1	0
Virology	1	0	0	1	0	0	0	0	0	0
Microbiology Total	7	3	5	2	4	0	1	1	1	0
Chemistry	5	2	1	1	0	2	1*	1*	0	0
Endocrinology	0	0	0	0	0	0	0	0	0	0
Enzymes and Lipids	0	0	0	1	2	0	0	0	0	0
Immunology	0	0	0	0	0	0	0	0	0	0
MSS	0	0	0	1	0	0	1	0	0	0
Chemistry Total	5	2	1	3	2	2	2	1	0	0
Hematology	1	0	0	0	2	0	1	0	0	0
Flow Cytometry	...	...	...	...	...	...	0	1	0	1
Morphology	0	0	1	1	0	4	0	0	0	0
Coagulation	0	0	0	0	0	0	0	0	0	0
Bone Marrow	0	0	0	0	0	1	0	0	0	0
Transfusion Medicine	5	1	3	1	3	6	2	3	1	0
Hematology Total	6	1	4	2	5	11	3	4	1	1
Genetics	1	0	0	0	0	0	0	0	0	0
Genetics Total	1	0	0	0	0	0	0	0	0	0
Cytology	0	1	1	0	2	1	1	0	0	0
Cytology Total	0	1	1	0	2	1	1	0	0	0
Grand Total	19	7	11	7	13	14	7	6	2	1

*Included enzymes

Table 4. Number of Newly Named Non-proficient Laboratories by Discipline, 1996–2005

Discipline	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
Chemistry	0	0	0	0	0	0	0	0	0	0
Hematology	0	1	0	0	0	0	0	0	0	0
Microbiology	0	1	0	0	0	0	0	1*	0	0
Other	0	0	0	0	0	0	0	0	0	0
Total	0	2	0	0	0	0	0	1	0	0

*Parasitology

Reports to Participants

Reports provided to participants include preliminary reports of the reference or consensus results, summary information of all participant results as well as reports of individual laboratory performance. In addition, the scientific committees provide educational feedback in the form of Committee Comments, Broadsheets and Practice Guidelines. During 2005, the following were provided to participant laboratories:

- 96 Provisional Reports
- 125 Survey Reports
- 92 Committee Comments
- 5 Broadsheets

INVESTIGATION OF DISCORDANT FINDINGS

This is the third year that participants have been requested to complete an investigation of discordant findings form. Summary information of cause analysis for the Chemistry, Hematology and Microbiology surveys is included in Figure 7.

The overall discordance rate has increased slightly this year over last year from 1.2% to 1.3%. This is largely associated with method (automated system) biases identified in the Chemistry disciplines. As with previous years, the most common categories of discordance are associated with methodology (64%) related issues involving automated systems, inappropriate use of quality control (QC) limits or control material and use of inadequate or out-dated procedures or reporting protocols. The percentage of technological causes remained the same as 2004 (27%) and includes inadequate response to QC results, failure to follow written procedures and sample handling issues. See the individual discipline reports for more information.

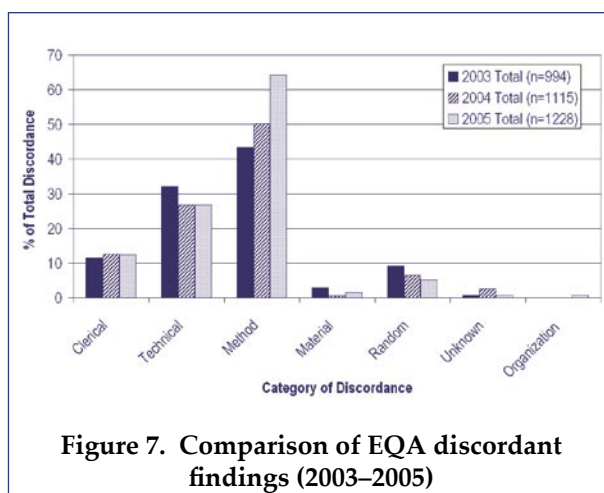


Figure 7. Comparison of EQA discordant findings (2003–2005)

CHEMISTRY COMMITTEE ACTIVITIES

Two Broadsheets were published in 2005. Topics included *Recommendations for management of dyslipidemia and prevention of cardiovascular disease* and *Laboratory support in the management of individuals with Diabetes Mellitus*.

The committee completed a review of precision goals and flagging criteria used for all chemistry analytes and communicated updated precision goals based on analytical performance, biological variation and quality specifications in November 2005 at the Ontario Society of Clinical Chemists Annual Scientific Day, which was jointly hosted by QMP-LS. The within-laboratory precision goals and changes in the computer flagging rules were released on the secure, password-protected Document Server of the Web site in January 2006. Quality control graphs submitted with responses to discordant results will be reviewed based on the new and updated precision goals.

In 2006, the committee anticipates the release of cumulative reports to aid participant interpretation of trends. A modified comprehensive scoring system will be piloted to support utilization of an objective long-term, cross-discipline review of individual laboratory performance.

CHEMISTRY-GENERAL

TESTING MODEL

Surveys for routine serum analytes, HbA_{1c}, blood gases (including sodium, potassium, glucose and ionized calcium), iron (total iron, unsaturated iron binding capacity [UIBC], total iron binding capacity [TIBC] and transferrin saturation), urine chemistry and albumin excretion rate were distributed in 2005.

ASSESSMENT OF PERFORMANCE

Routine Serum Analytes

Three surveys were circulated to participating laboratories. Each survey included three vials of previously frozen serum that were supplemented to produce concentrations in ranges of analytical or clinical interest. Duplicate vials were included in the CHEM-0501 and CHEM-0510 surveys to assess between-run precision for each analyte studied. A total of 13 analytes were included in each challenge survey. Testing for bilirubin was added to survey CHEM-0501.

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

No. of Participants (Dec. 2005)	199
No. of Participants (Dec. 2004)	203
No. of Surveys Conducted in 2005	14

Drug Monitoring (Routine, Drugs of Abuse)

No. of Participants (Dec. 2005)	162
No. of Participants (Dec. 2004)	167
No. of Surveys Conducted in 2005	7

Enzymes, Cardiac Markers & Lipids

No. of Participants (Dec. 2005)	Enzymes	193
	Lipids	134
No. of Participants (Dec. 2004)	Enzymes	195
	Lipids	135
No. of Surveys Conducted in 2005		9

Endocrinology

No. of Participants (Dec. 2005)	130
No. of Participants (Dec. 2004)	126
No. of Surveys Conducted in 2005	4

Immunology

No. of Participants (Dec. 2005)	66
No. of Participants (Dec. 2004)	65
No. of Surveys Conducted in 2005	3

Maternal Serum Screening

No. of Participants (Dec. 2005)	NA
No. of Participants (Dec. 2004)	NA
No. of Surveys Conducted in 2005	NA

Point-of-Care Testing (Glucose Meters)

No. of Participants (Dec. 2005)	192
No. of Participants (Dec. 2004)	195
No. of Surveys Conducted in 2005	2

Survey CHEM-0510 included a hemolysed specimen (vial A, 5.4 g/L hemoglobin) to survey the interpretive comments that would be reported by the participants. The computer generated flags were removed from this survey vial for the individual analytes. The committee reviewed the interpretative comments noted on the Analysis Worksheets for assays evaluated on this sample for consistency, validity and comprehensiveness. This review identified patterns of practice and associated issues in reporting due to a common laboratory interferent. Five laboratories failed to indicate that the sample was hemolysed. Laboratory participants are encouraged to review manufacturers' data describing the effect of select interferents on individual results. In some cases, QMP-LS survey data indicated that the influence of select, common interferents is more significant than previously understood. The need for concise but informative comments on patient reports in such a circumstance is clear. A review of the analytes, comments and sample rejection criteria by all laboratories is warranted.

Committee Comments were published for each survey to aid in the interpretation of the data and to describe method related trends noted in the data.

Table 5 provides a summary of the number of laboratories participating by survey and analyte, the number of computer generated flags and the number of laboratories receiving correspondence. Survey CHEM-0501 generated the largest number of computer flags due to the interference from bilirubin in some glucose, creatinine, phosphate and urate methods. The largest number of computer generated flags in the two other surveys were associated with results reported for magnesium, total protein and urea. Continued method related bias was observed with creatinine and magnesium.

Table 5. Summary of Results Flagged in Surveys CHEM-0501, CHEM-0505 and CHEM-0510

Analyte	CHEM-0501			CHEM-0505			CHEM-0510		
	No. of Labs	No. of Computer Flags	No. of Labs Receiving Correspondence	No. of Labs	No. of Computer Flags	No. of Labs Receiving Correspondence	No. of Labs	No. of Computer Flags	No. of Labs Receiving Correspondence
Bicarbonate	149	14	2	147	9	2	148	6	0
Chloride	198	4	0	197	1	0	195	3	1
Sodium	200	16	0	200	21	0	198	6	2
Potassium	200	3	1	200	0	0	198	2	1
Glucose	199	17	0	198	3	3	196	6	1
Urea	196	36	3	195	14	1	193	25	2
Creatinine	199	26	4	198	12	1	196	16	3
Bilirubin	189	2	1	N/A	N/A	N/A	N/A	N/A	N/A
Calcium	189	12	0	188	14	0	185	11	4
Phosphate	170	28	1	170	2	2	165	2	1
TP	183	32	0	182	22	2	181	26	2
Albumin	182	6	1	181	16	0	180	15	1
Urate	171	66	0	170	2	1	167	7	2
Magnesium	132	35	7	132	47	2	129	20	2

Magnesium

Review of the year illustrated that 102 computer flags were generated for magnesium results compared to 133 in 2004.

The all-methods' means (AMM) were compared to atomic absorption data generated by a reference laboratory. In all surveys, the AMMs were found to be in good agreement with the atomic absorption results. The majority of flags were recorded for CHEM-0505, which included two vials supplemented with increased concentrations of magnesium. These samples were also supplemented with increased levels of glucose, urea, creatinine and phosphate. As in previous years, Dade Behring and Beckman Coulter technologies continue to demonstrate consistent biases relative to the reference method data.

Urea

In general, urea assay performance was acceptable in 2005. Beckman Coulter users' results reported from the LX20 series of instruments continued to demonstrate a negative bias on samples with urea concentrations within the lower limit of the reference range.

Total Protein

A total of 80 computer generated flags were reviewed for total protein analyses. A continued positive bias was observed with Roche (BMC) users' group data. Method related biases were also noted in Ortho peer group (positive bias) while Beckman Coulter and Dade Behring technologies demonstrated negative biases.

The hemolysis in vial CHEM-0510-A generated a marked positive interference on total protein results reported using Ortho and Abbott technologies.

Urate

An increased number of flags were observed in CHEM-0501 due to the influence of bilirubin on assay performance of a number of methods currently in use. Bilirubin supplements in the two vials generated flags in approximately 25% of participating laboratories. Participants should investigate the influence of this interferent on routine assay performance for patients with increased concentrations of bilirubin. With the exception of the hemolysed specimen, all other surveys conducted in 2005 produced acceptable performance for this analyte. Beckman Coulter and Abbott results demonstrated a strong positive bias due to the interference of hemolysis.

Creatinine

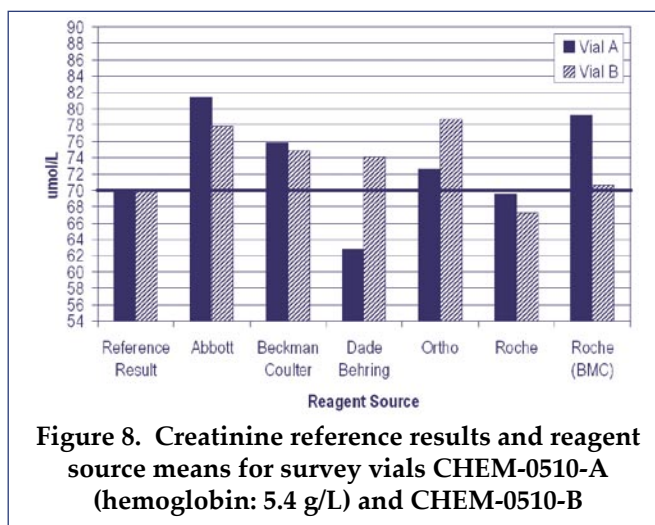
Challenge concentrations ranging from 70–830 $\mu\text{mol/L}$ (high performance liquid chromatography [HPLC] results) produced 40 flagged results resulting in eight memoranda for discordant results. In addition to comparing results to an HPLC reference method, primary analysis was separated into Ortho Clinical Diagnostics Vitros methods (which account for approximately two-thirds of Ontario instrumentation), and all "other" methods. The "other" methods, referred to as the "kinetic" group, included Jaffe reactions and enzymatic methods available from other manufacturers.

Creatinine assays in Ontario demonstrated both between method biases and random "outlier" results. As a group, the Vitros methods tend to be approximately 10% higher than the kinetic methods. Interference from bilirubin and hemolysis demonstrated method specific biases of various magnitudes when challenged within increased concentrations of either interferent. The Roche Integra and Abbott methods appeared to be the most susceptible to interference from high concentrations of bilirubin in survey CHEM-0501.

Figure 8 demonstrates the effect of hemolysis (hemoglobin 5.4 g/L) interference on creatinine methods (CHEM-0510-A). As most creatinine methods are based on the relatively non-specific Jaffe colorimetric assay, both endogenous and exogenous interferences may be important interpretation considerations. This situation is further confounded as the relative contribution of these interferences may vary in a patient's serum over time. Figure 8 also demonstrates the variation in results between methods and method bias relative to the reference values (CHEM-0510-B).

Reliability of creatinine results is of heightened importance with the emergence of clinical practice guidelines recommending laboratories automatically provide a calculated estimate of glomerular filtration rate (eGFR) on serum creatinine requests. Calculation of the eGFR has been found to facilitate early detection of chronic kidney disease (CKD) through serial monitoring and detection of an accelerated rate of decline in eGFR. The accuracy of creatinine and the eGFR calculation are critical for correct assessment and interpretation against established global decision limits.

The importance of creatinine method and gender-specific population reference ranges were highlighted



in 2004. The committee would like to emphasize the importance of assessing and reporting the presence and effects of common interferences such as bilirubin and hemolysis. Many drugs are also known to interfere with assay results.

The development of a more comprehensive evaluation process for creatinine assays in Ontario is in progress at QMP-LS. It is known that manufacturers will be moving towards standardizing their creatinine methods to isotope dilution mass spectrometry traceability and that some laboratories may opt to use enzymatic assays, which are inherently less susceptible to common interferences. The committee has proposed expansion of the QMP-LS program in 2006 to include calculation and monitoring of eGFR. Publication of educational materials in the form of a laboratory Broadsheet is also projected.

Urine Chemistry

Two vials of urine without preservative were sent to each participating laboratory for surveys CHEM-0503-UC and CHEM-0507-UC. The results for these challenges indicated that urine chemistries are being performed well across the province. The survey results are summarized in Table 6.

The discordant results in both surveys were mainly due to post analytical problems that included transcription and calculation errors. The protein results reported using the pyrocatechol violet method showed a positive bias compared to the benzethonium chloride and pyrogallol red method results in three of the four survey samples.

Table 6. Summary of Discordant Results

Analyte/Method	CHEM-0503-UC		CHEM-0507-UC	
	No. of Participants	No. of Discordant Results	No. of Participants	No. of Discordant Results
Protein Benzethonium Chloride	21	0	23	5
Protein Pyrocatechol Violet	37	3	33	0
Protein Pyrogallol Red	30	3	28	3
Sodium	106	7	104	1
Potassium	106	4	104	0
Creatinine	133	5	129	3
Osmolality	66	0	69	0

Blood Gases

Two blood gas surveys, CHEM-0504-BG and CHEM-0508-BG, were conducted in 2005. Sufficient vials of samples from commercially prepared aqueous material were distributed to participating laboratories to evaluate all blood gas instruments including point-of-care devices within an institution. Vial X of survey CHEM-0504-BG and vial Y of survey CHEM-0508-BG were duplicate specimens permitting assessment of inter-survey precision. As well as blood gas determinations, participants were requested to report data for sodium, potassium, glucose and ionized calcium if patient results were routinely reported from any of the blood gas instruments used within their institution.

As in previous years, the survey results showed acceptable performance by blood gas instruments in the province. The survey data is summarized in Table 7.

Table 7. Summary of Performance on the Blood Gas Surveys CHEM-0504-BG and CHEM-0508-BG

Analytes	CHEM-0504-BG			CHEM-0508-BG		
	No. of Results	No. of Discordant Results	%	No. of Results	No. of Discordant Results	%
pH	562	6	1.1	563	1	0.2
pCO ₂	560	11	2.0	563	1	0.2
pO ₂	558	11	2.0	562	8	1.4
Sodium	195	5	2.7	222	0	0
Potassium	197	1	0.5	226	0	0
Glucose	153	1	0.6	164	0	0
Ionized Calcium	193	7	3.6	210	1	0.5
Total (%)	2418	42	1.7	2510	11	0.4

The majority of flagged results for pH, pCO₂ and pO₂ were related to specimen handling problems, especially for pO₂.

Duplicate vials CHEM-0504-X and CHEM-0508-Y, which contained a low concentration of ionized calcium proved to be a challenge for some analyzers resulting in imprecision flags for some institutions. Inter-survey imprecision was drawn to the attention of two participants for sodium, two other participants for glucose and one participant for ionized calcium levels reported on the duplicate vials.

Hemoglobin A_{1c}

Three HbA_{1c} surveys were conducted in 2005. Each survey consisted of two aliquots of whole blood obtained from diabetic donors. Reference values for the survey samples were obtained from the National Glycohemoglobin Standardization Program (NGSP) at the University of Missouri-Columbia's Diabetic Diagnostic Laboratory.

The number of laboratories participating increased from 59 in the January survey (CHEM-0501) to 63 in the October survey (CHEM-0510). In the October survey, 23 laboratories used an HPLC method and 40 used an immunochemical method.

HPLC continues to provide better precision but does exhibit a positive bias to the reference values on all three surveys. Although bias is also a crucial performance issue for HbA_{1c}, a laboratory precision goal of ≤3% is recommended. The results of the three surveys are summarized in Table 8. Nine laboratories received memoranda for reporting results that were >7.5% from the reference result. Two of these laboratories' results were due to a reporting error.

Table 8. Summary of Performance of HbA_{1c} in the 2005 Surveys

Survey	Vial 1							Vial 2						
	Reference	AMM	%CV	HPLC		Immuno-		Reference	AMM	%CV	HPLC		Immuno-	
	Result			Mean	%CV	chemical	%CV	Result			Mean	%CV	chemical	%CV
CHEM-0501-HB	0.074	0.075	6.0	0.079	3.2	0.072	5.3	0.059	0.059	4.9	0.061	3.4	0.058	4.7
CHEM-0505-HB	0.066	0.066	4.2	0.068	2.4	0.066	5.1	0.078	0.078	5.0	0.082	2.5	0.076	5.4
CHEM-0510-HB	0.062	0.062	4.5	0.064	3.3	0.061	4.6	0.062	0.062	4.2	0.064	3.0	0.062	5.2

ALBUMIN EXCRETION RATE

Three surveys, each with three samples of urine, were distributed in January, May and October. There were 28–30 participants in each survey.

Urine Albumin

Three methodologies are currently in use in Ontario to quantitate urine albumin. In survey CHEM-0510-AE, 17 participants used turbidimetry, 11 used nephelometry and 2 used an enzyme immunoassay method. Nephelometric methods provide the laboratory with improved precision compared to the turbidimetric methods most notably at lower concentrations of albumin. For example, a coefficient of variation (CV) of 19.8% was obtained by the turbidimetric methods compared to a CV of 12.9% for the nephelometry assays at a urine albumin concentration of 17.6 mg/L in survey CHEM-0501-AE.

Creatinine

The flagging limit of >15% from the AMM is achievable by all of urine creatinine methods in use in Ontario. Only one laboratory's results exceeded the acceptable limits. This was due to a misidentification of samples during analysis.

Albumin:Creatinine Ratio

Participants were requested to interpret albumin creatinine ratios generated from the survey data based on the clinical information provided on the Analysis Worksheet. In the January survey the AMM for vial 1 was 2.3 and the sample was described as originating from a 50-year-old female (70 kg). Nineteen of 25 laboratories with ratios <2.8, correctly interpreted the ratio as normal, which is consistent with the Canadian Diabetes Association's (CDA) recommendations. Four laboratories with ratios ranging from 2.2–2.6 indicated the ratio was abnormal.

In the May survey, the clinical information indicated the sample was from a 55-year-old male. The CDA recommended normal albumin:creatinine ratio for a male is <2.0. Nine laboratories reporting ratios ranging from 2.0–2.9 incorrectly interpreted the ratio as normal. Through correspondence it was determined that the laboratories were not using the CDA guidelines or had not entered the gender information into their laboratory information systems (LIS).

DISCORDANT RESULTS

Table 9 displays the number of results reported for the chemistry surveys (routine, blood gases, HbA_{1c}, iron, albumin excretion rate and urine chemistry), the number of results generating memoranda and the 2005 error rate. The error rate has improved slightly in 2005 compared to 2004 (1%).

Figure 9 displays contributing factors for the 250 discordant results. The distribution of causes are very similar to those reported in 2004. Manufacturer related problems, inappropriate quality control concentrations or acceptance limits accounted for 54% of the methodological causes. Fifty-six per cent of the technical causes were attributed to inadequate response to quality control (QC) results and sample handling problems.

Table 9. Summary of Discordant Results Reported for 2005 Chemistry-General Surveys

Discipline	No. of Results Reported	No. of Discordant Results	Error Rate (%)
Chemistry General	31 782	250	0.79

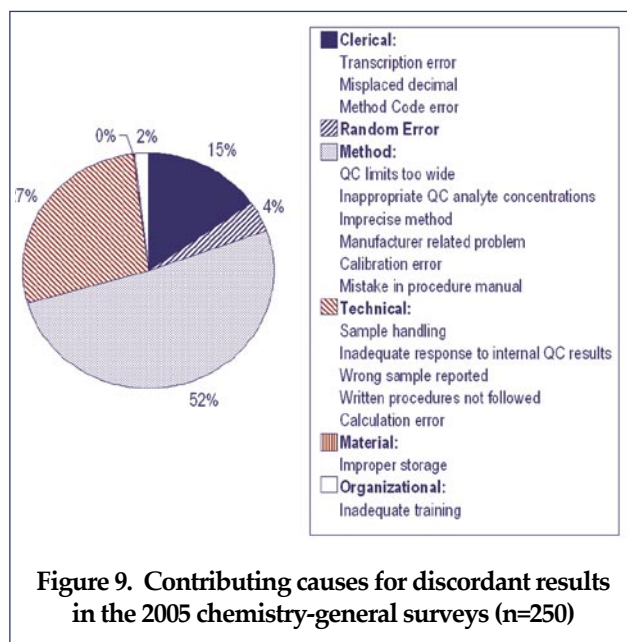


Figure 9. Contributing causes for discordant results in the 2005 chemistry-general surveys (n=250)

DRUG MONITORING

TESTING MODEL

Previously frozen serum supplemented with specific drugs was used for four routine drug surveys. Samples of pooled urine were distributed for each of the three drugs of abuse surveys.

The drugs tested were:

DRUG-0501-A	Ethanol, Acetaminophen, Salicylate, Digoxin, Lithium
DRUG-0501-B	Carbamazepine, Phenobarbital, Phenytoin, Theophylline, Valproic Acid
DRUG-0501-C	Gentamicin, Tobramycin, Vancomycin
DRUG-0501-DA	Drugs of Abuse
DRUG-0505-A	Ethanol, Acetaminophen, Salicylate, Digoxin, Lithium
DRUG-0505-B	Carbamazepine, Phenobarbital, Phenytoin, Theophylline, Valproic Acid
DRUG-0505-C	Gentamicin, Tobramycin, Vancomycin
DRUG-0505-DA	Drugs of Abuse
DRUG-0507-A	Ethanol, Acetaminophen, Salicylate, Digoxin, Lithium
DRUG-0507-B	Carbamazepine, Phenobarbital, Phenytoin, Theophylline, Valproic Acid
DRUG-0507-C	Gentamicin, Tobramycin, Vancomycin
DRUG-0510-A	Ethanol, Acetaminophen, Salicylate, Digoxin, Lithium
DRUG-0510-B	Carbamazepine, Phenobarbital, Phenytoin, Theophylline, Valproic Acid
DRUG-0510-C	Gentamicin, Tobramycin, Vancomycin
DRUG-0510-DA	Drugs of Abuse

ASSESSMENT OF LABORATORY PERFORMANCE

With the exception of digoxin, routine drug results were flagged for committee review when results exceeded >10% from the AMM. Digoxin results were flagged if 0.2 nmol/L from the AMM of <1.5 nmol/L or >10% from an AMM of ≥ 1.5 nmol/L. Data reported for drugs of abuse were compared to results reported by a reference laboratory.

Ethanol, Lithium, Carbamazepine, Phenobarbital, Phenytoin, Theophylline and Valproic Acid

Overall performance appears to be satisfactory for these analytes in each of the four surveys. No major method biases were observed in the four surveys containing these drugs.

Acetaminophen

Turbidimetric immunoassay methods have, for the past couple of years, demonstrated a positive bias when compared to the AMM in the surveys. Enzyme assays demonstrate a negative bias when compared to the AMM (Figure 10).

Salicylate

As reported in the 2003 and 2004 Reviews the Dade Behring method data have demonstrated a significant positive bias relative to the AMMs (Figures 11A and 11B, 11C and 11D). There has been some reluctance on the part of the manufacturer to acknowledge this problem. Participants continue to receive correspondence regarding these errors.

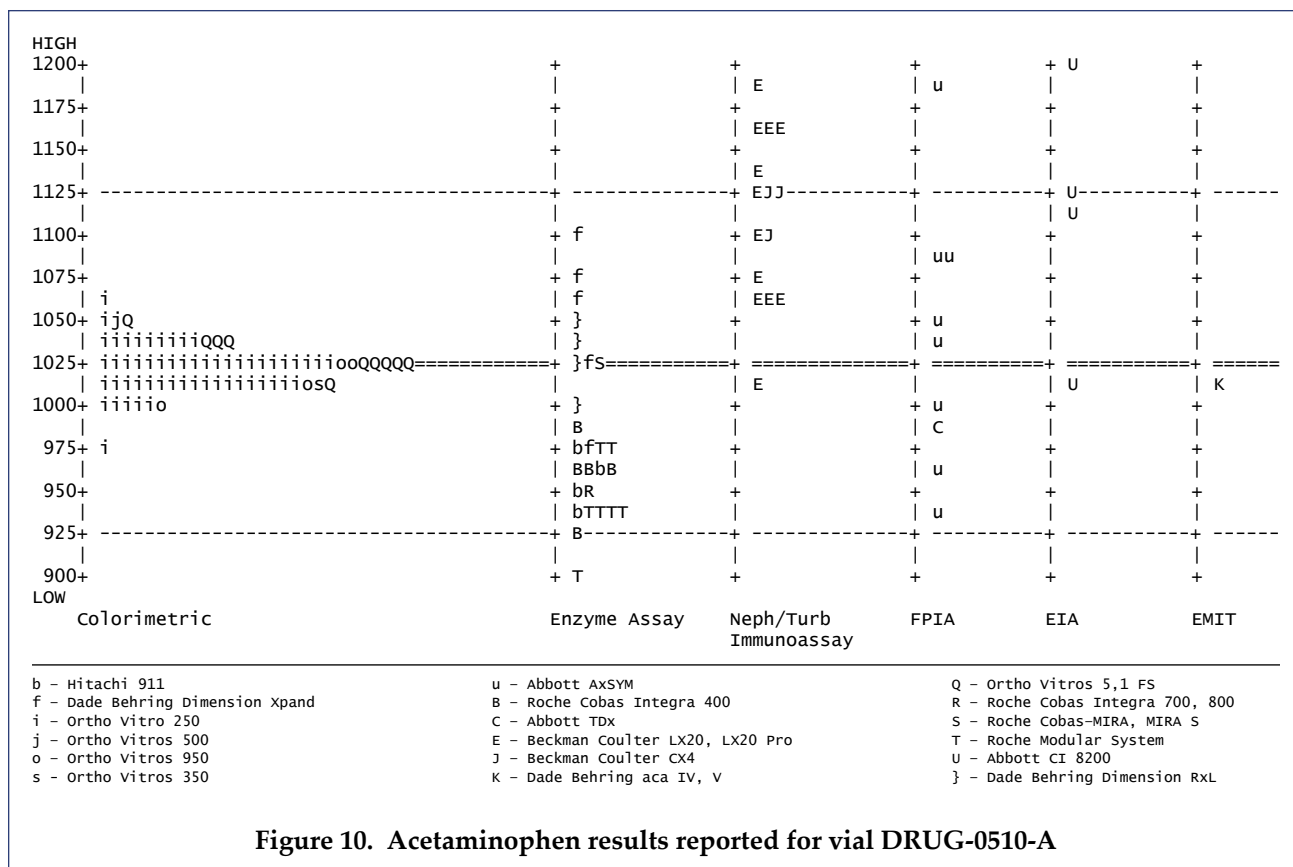


Figure 10. Acetaminophen results reported for vial DRUG-0510-A

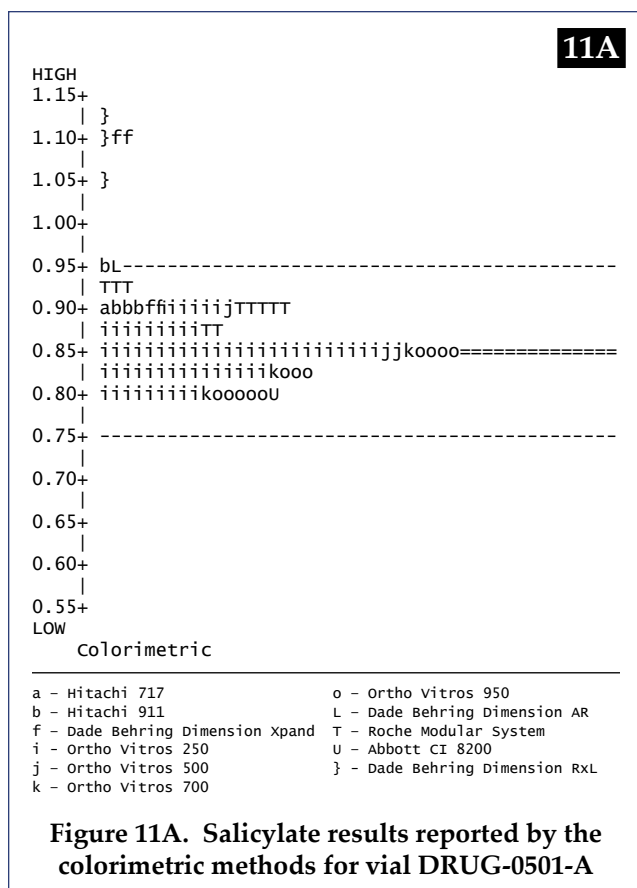


Figure 11A. Salicylate results reported by the colorimetric methods for vial DRUG-0501-A

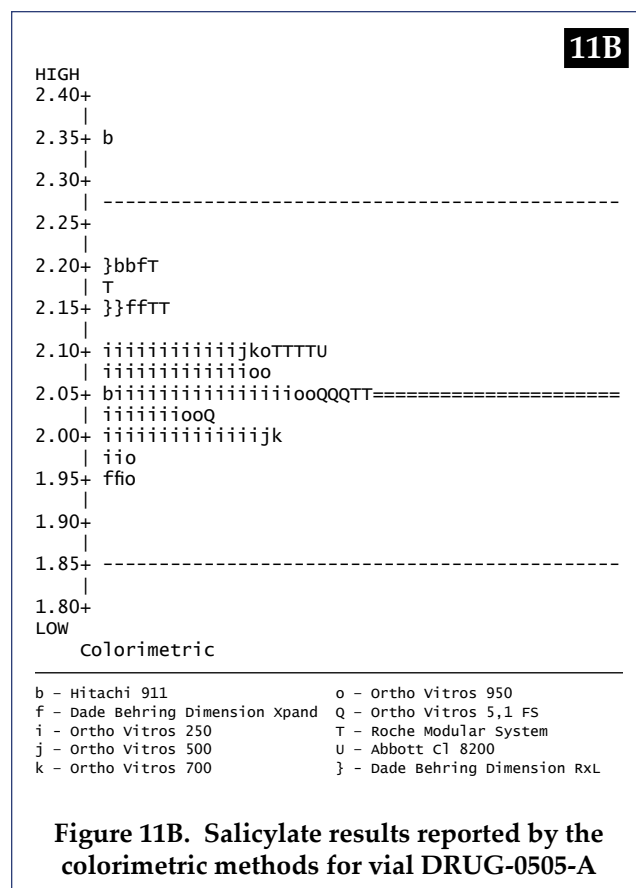
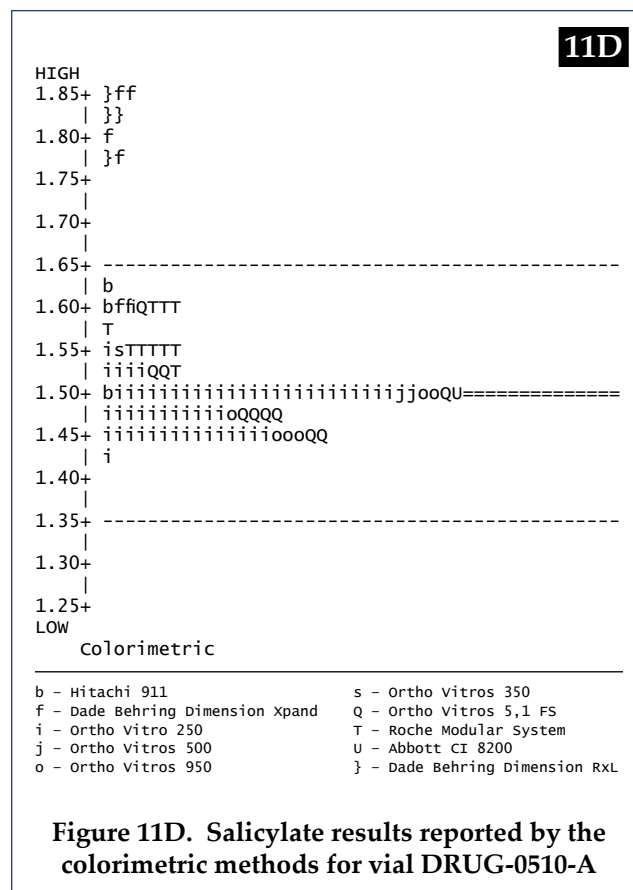
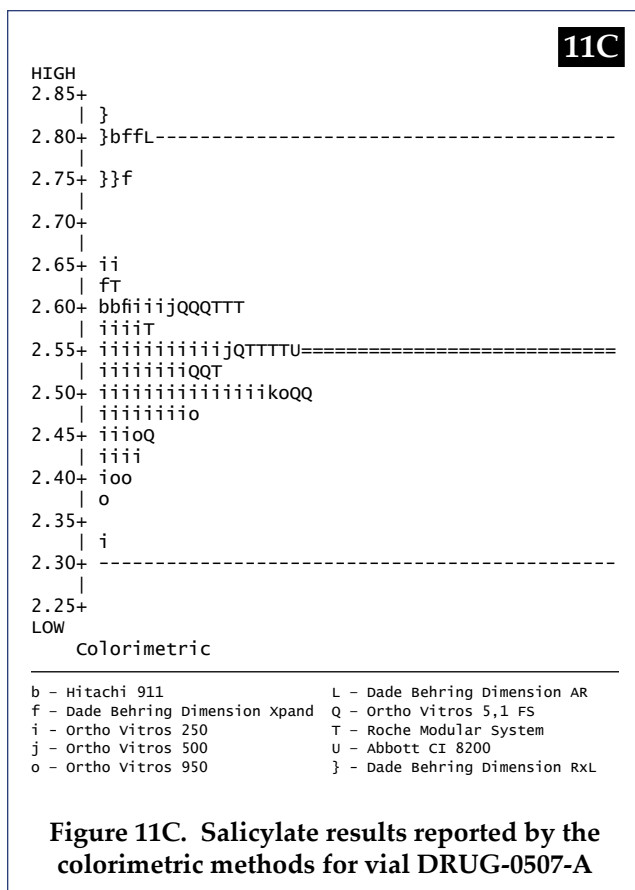


Figure 11B. Salicylate results reported by the colorimetric methods for vial DRUG-0505-A



Digoxin

Digoxin assays continue to demonstrate poor precision in the clinical range as shown in Table 10.

Table 10. Summary of Performance of Digoxin in the 2005 Surveys

Survey Vial	AMM (nmol/L)	Range of Results (nmol/L)	SD	%CV	No. of Computer Flags	No. of Memoranda
DRUG-0501-A	1.97	1.5–2.6	0.25	12.5	44	4
DRUG-0505-A	0.76	0.4–1.0	0.13	16.3	8	1
DRUG-0507-A	1.30	0.7–1.9	0.20	15.4	23	5
DRUG-0510-A	1.61	1.2–2.1	0.18	11.2	18	9

Gentamicin, Tobramycin, Vancomycin

The overall performance of vancomycin testing is good. Since the beginning of 2005, the nephelometric/turbidimetric methods, particularly the Beckman Coulter assays for gentamicin and tobramycin, have demonstrated a positive bias relative to the AMM. Figures 12A and 12B display results reported for survey vial DRUG-0510-C.

12A

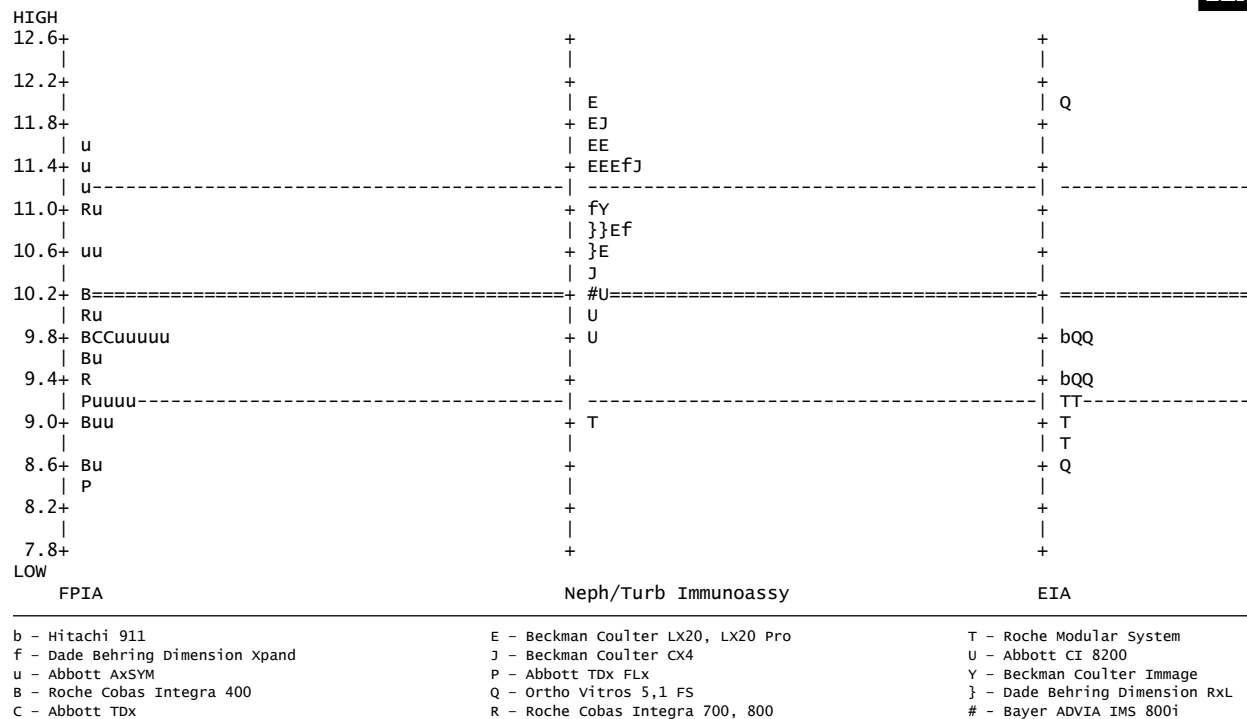


Figure 12A. Gentamicin results reported for vial DRUG-0510-C

12B

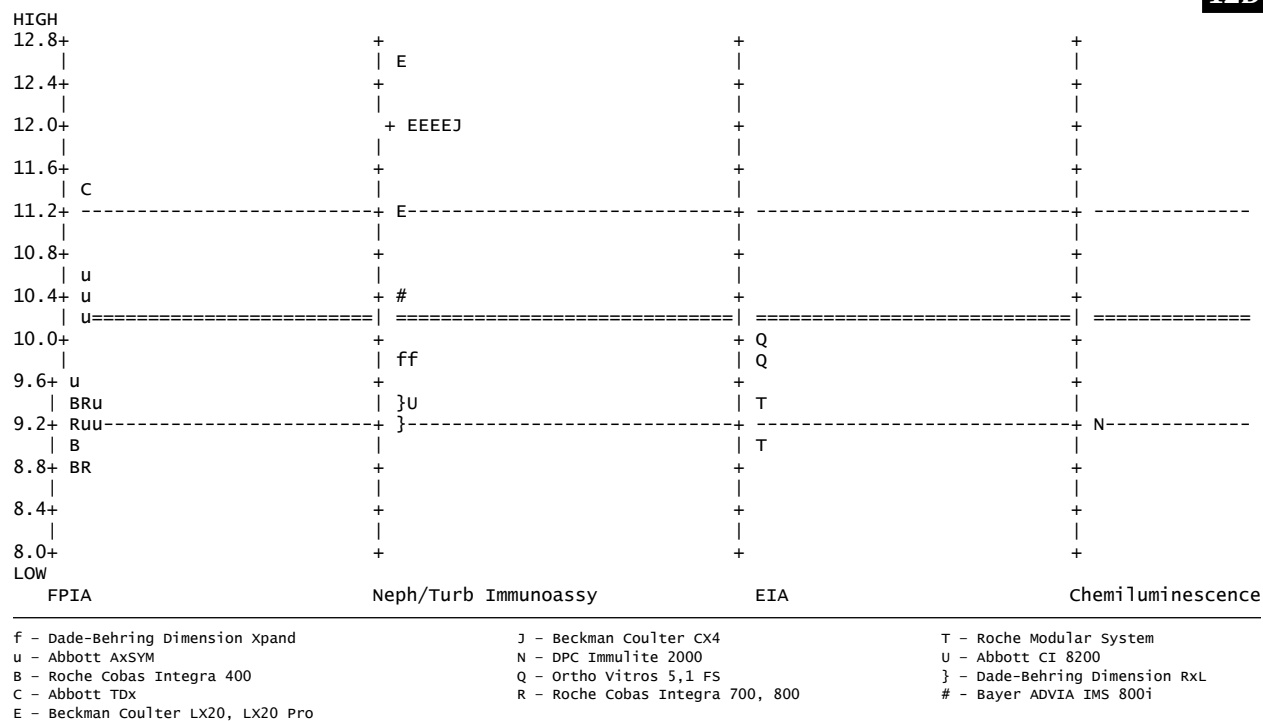


Figure 12B. Tobramycin results reported for vial DRUG-0510-C

DRUGS OF ABUSE

Three drugs of abuse surveys containing two urine samples were distributed in 2005. Urine drug screen samples were prepared from combined patient samples.

The following observations were noted:

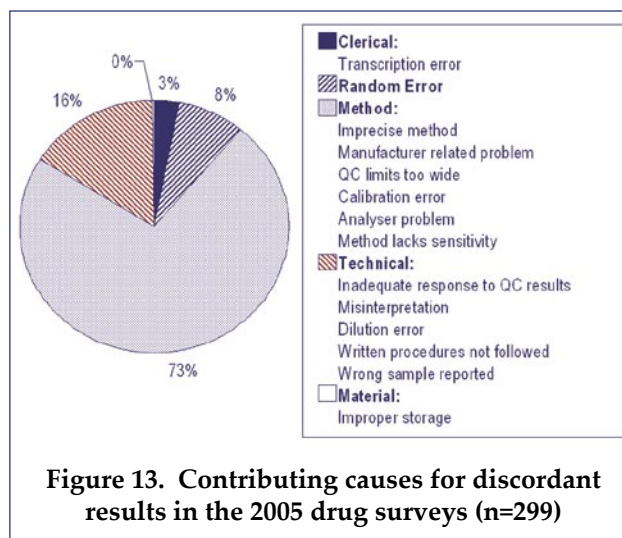
- Barbiturates, benzodiazepines and tricyclic antidepressants:
Surveys DRUG-0501-DA and DRUG-0510-DA demonstrate the variability in reactivity of different products to these groups of drugs and their metabolites. Laboratories should be aware of the specificity (which drugs and metabolites cross-react) and the sensitivity (cut-off concentration and degree of cross-reactivity) of the products. Clinicians should be made aware of the limitations of the drug screening methods used by the laboratory.
- Ecstasy (MDMA/MDA), methadone metabolite (EDDP), and oxycodone:
Screening for these drugs and metabolites has become more prevalent in the last couple of years. In response, QMP-LS added these analytes beginning with the DRUG-0510-DA survey.

DISCORDANT RESULTS

Table 11 summarizes the number of results reported for the drug surveys (routine and drugs of abuse), discordant results and the error rate for 2005. The error rate has increased from 2004 (2.2%). Figure 13 illustrates the contributing causes by percentage for the discordant results. The methodological causes have increased from 58% in 2004 to 73% in 2005. Manufacturer related problems accounted for 46% of the methodological issues. Sixteen per cent were attributed to QC limits being too wide and inappropriate QC material. Within the technical causes, 44% were attributed to an inadequate response to QC data.

Table 11. Summary of Discordant Results Reported for 2005

Discipline	No. of Results Reported	No. of Discordant Results	Error Rate (%)
Drug Monitoring	9491	299	3.2



ENZYMES AND CARDIAC MARKERS

TESTING MODEL

Two enzymes and two cardiac marker surveys were conducted in 2005. Four vials of reconstituted human lyophilized serum were utilized for each enzyme survey. Previously frozen supplemented serum samples were distributed for the cardiac marker surveys. Participants were requested to analyze the samples within 24 hours of receipt.

Surveys included the following:

ENZY-0501	Alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma glutamyl transferase (GGT), lactate dehydrogenase (LD), amylase and lipase
ENZY-0503	Total creatine kinase (CK), CK-2, myoglobin, troponin I (cTnI) and troponin T (cTnT)
ENZY-0506	Alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma glutamyl transferase (GGT), lactate dehydrogenase (LD), amylase and lipase
ENZY-0510	Total creatine kinase (CK), CK-2, myoglobin, troponin I (cTnI) and troponin T (cTnT)

ASSESSMENT OF LABORATORY PERFORMANCE

Enzymes

Where peer groups had ten or more participants, results were compared to a peer group median (reagent source). The committee manually reviews those results not meeting flagging rules based on this criterion. Performance was acceptable on the two surveys examining enzymes (ENZY-0501 and ENZY-0506). Four participants received memoranda for results reported in survey ENZY-0501 and another four for ENZY-0506 results.

Variability in quoted reference ranges by participants using the same method for enzymes continues to be an issue. Figure 14 displays the upper limit of the reference range (ULRR) for ALT for an adult male quoted by the 114 Ortho Vitros users (the largest group) on the ENZY-0501 Analysis Worksheet. In their published instrument data, Ortho indicates that an ULRR of 72 U/L may be expected for an adult male. The Ortho Vitros results for vial B survey ENZY-0501 ranged from 56–72 U/L. The 14 laboratories quoting an ULRR ranging from 40–55 U/L reported ALT results for vial B ranging from 59–68 U/L, all of which would be indicated as elevated on a patient report.

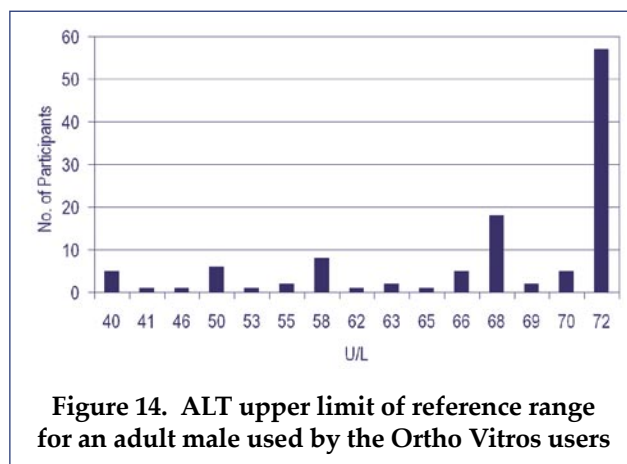


Figure 14. ALT upper limit of reference range for an adult male used by the Ortho Vitros users

Participants are encouraged to review their reference ranges to ensure that they are appropriate.

Cardiac Markers

The samples used for total CK, CK-2, myoglobin and cTnI were previously frozen serum supplemented with CK-2, CK-3, myoglobin and troponin I. Separate previously frozen serum samples supplemented with troponin T were distributed for the cTnT surveys. Computer flagging was performed by peer group comparison.

Total CK

Results were reported by 182 laboratories in the March survey (ENZY-0503-CM) and 184 in the October survey (ENZY-0510-CM). The number of laboratories reporting total CK has decreased slightly from 194 in October 2004.

Performance for this analyte was satisfactory on both surveys. There is wide variation in the ULRR reported for total CK within method groups. For example, the ULRR reported by the Ortho Vitros users ranged from 150–240 U/L for an adult male. Ortho reports an ULRR of 170 U/L in their manual. Once again, participants are encouraged to review their reference ranges.

CK-2

The number of laboratories testing CK-2 has decreased from 123 in October 2003 to 102 in October 2005. It is expected that the number will continue to decline as laboratories replace this assay with quantitation of troponin. Performance was satisfactory in the March survey (ENZY-0503). In the October survey (ENZY-0510), three participants failed to submit notification of a method change and their results were compared to the wrong peer group. Four participants received memoranda regarding imprecision in data reported for duplicate samples included in the survey.

Myoglobin

Thirty-five laboratories reported myoglobin results in the ENZY-0510 survey, which represents a slight decrease since October 2004. Eight different methods are used for myoglobin analysis. The ULRRs quoted for this analyte by the participants, appear to be more consistent within a method group with the exception of the Beckman Coulter Access users who quote ULRRs ranging from 70–106 µg/L.

Troponin I

Results were reported by 109 participants in the October survey. This represents an increase of 19 laboratories since October 2004. Performance was satisfactory for this cardiac marker.

Troponin T

There were 34 laboratories reporting results for cTnT in the October survey, which represents a slight increase since October 2004 when 31 sites reported cTnT. As previously noted, the wide range of results reported for the survey samples is disappointing. Table 12 summarizes the data generated for survey ENZY-0510-TT.

Table 12. Summary of Troponin T Results Reported for Survey ENZY-0510-TT

Vial	Median (µg/L)	Minimum Result (µg/L)	Maximum Result (µg/L)	%CV
ENZY-0510-1	0.64	0.47	0.77	7.0
ENZY-0510-2	1.20	0.85	1.36	9.6
ENZY-0510-3	0.060	0.03	0.08	15.0
ENZY-0510-4	0.130	0.09	0.16	10.8

Cardiac Markers Patterns-of-Practice Survey

A patterns-of-practice survey was distributed in October to determine if there were any changes in laboratory practice since the questionnaire was distributed in 1998. A preliminary analysis indicated that five laboratories are still providing AST as a cardiac marker and three of these also offer LD. This is an improvement over 1998 when 35 sites included AST and/or LD as cardiac markers. A cardiac assessment algorithm is in routine use in 111 institutions; whereas in 1998, only 44 laboratories reported having an algorithm available. Nineteen institutions offer point-of-care testing for one or more cardiac markers. Detailed Committee Comments summarizing the findings of this survey will be issued in 2006.

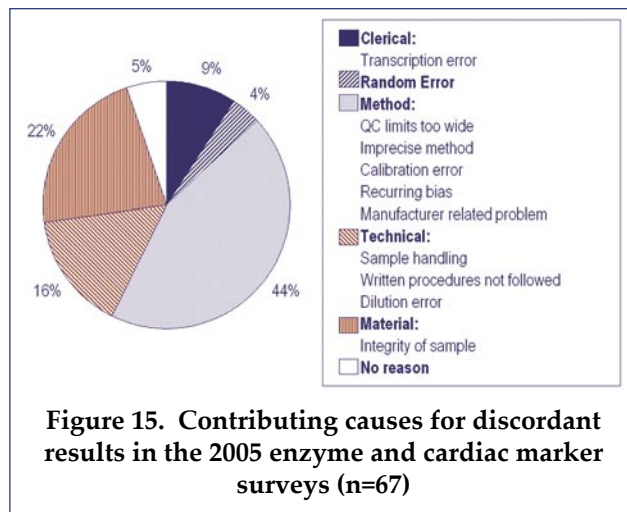
DISCORDANT RESULTS

Table 13 summarizes performance of enzyme and cardiac marker surveys in 2005. The error rate has increased slightly from 2004 (0.45%). Figure 15 displays the contributing causes for the discordant results. Method related errors have decreased from 63% in 2004 to 44% in 2005. Thirty-four per cent of the method issues were due

to inappropriate QC limits while 15% were associated with method imprecision. Not following written procedures caused 42% of the technical errors. Material problems were related to delays in delivery of survey material or delayed testing.

Table 13. Summary of Discordant Results Reported in 2005

Discipline	No. of Results Reported	No. of Discordant Results	Error Rate (%)
Enzymes and Cardiac Markers	12 548	67	0.53



LIPIDS

TESTING MODEL

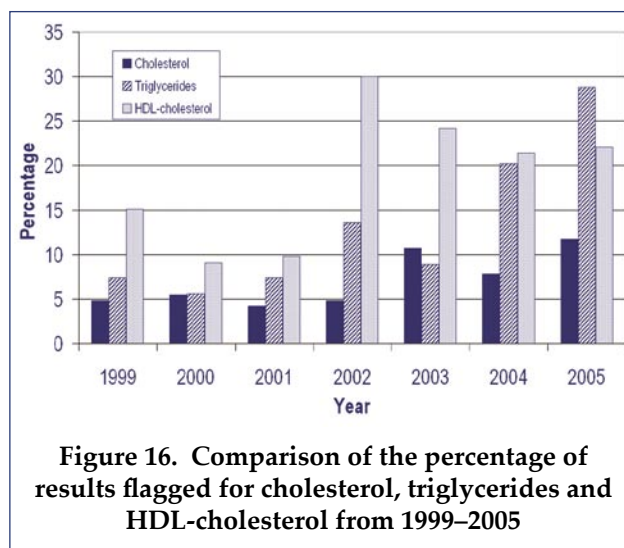
Three lipid surveys were conducted using fresh human serum from four donors for each survey. The 132 participants were split into two groups and each group received two of the samples. Specimens closely mimic samples analyzed in Ontario laboratories, and artefacts due to freeze/thaw cycles, pooling of samples, or lyophilization are avoided. Samples were shipped by overnight courier service; the majority of laboratories received the samples within 48 hours of collection.

ASSESSMENT OF LABORATORY PERFORMANCE

Expert recommendations, from Canada and abroad, provide common decision points and target values for lipids that should be used by all physicians for the diagnosis and management of dyslipidemia. Small differences in values have significant implications with respect to risk categorization of patients, treatment plans and potential outcomes. As a result, laboratories must be able to provide values that are independent of laboratory, method, instrument manufacturer, or analytical variability over time. The laboratory community, both the diagnostic manufacturers and the clinical laboratories, have made considerable effort, to standardize the measurement of lipids in Canada. Because lipid results should be independent of method or manufacturer, QMP-LS uses target values rather than participant consensus values (AMM or peer group mean) for analysis of performance. These target values are set by having the survey samples analyzed in certified reference laboratories, using techniques traceable to definitive methods.

The committee attempts to have all lipid survey samples analyzed by three reference laboratories to obtain target values for cholesterol and HDL-cholesterol, and two reference laboratories for triglycerides. On one occasion (survey LIPS-0506), one reference laboratory was unable to provide reference service. Participant results for triglycerides on this survey, were compared to the target value and the laboratory's peer group results.

Figure 16 presents the percentage of cholesterol, triglycerides and HDL-cholesterol results flagged for the years 1999–2005. The flagging rules have remained the same for this period. The increased flags since 2002 reflect the move to comparison of values against target values as opposed to peer group means.



Total Cholesterol

Performance of cholesterol testing across the province is generally good. The percentage of flagged results remained approximately the same (11.7%) as in previous years. Memoranda were sent to 21 laboratories for performance on cholesterol. This is slightly less than 2004 when 23 memoranda were sent.

HDL-cholesterol

Again in 2005, this remains an analyte of concern for the committee. Roche (BMC) users' results continue to display a positive bias compared to the reference method data (in 10 of 12 survey samples). Ortho Vitros users' results displayed evidence of multiple populations in two of the samples and both positive and negative biases. Beckman Coulter assay results displayed a negative bias on the four samples used in the LIPS-0506 survey.

Forty-eight memoranda were sent for performance on this analyte. Over half were sent for survey LIPS-0501. Performance improved as the year progressed. The percentage of results flagged was 22.1% compared to 21.4% in 2004.

Triglycerides

This analyte has become an area of concern over the past year due to the negative bias apparent in the results for the 12 survey samples assayed in 2005. This bias is noted across most of the manufacturer groups, but is most apparent amongst Beckman Coulter and Ortho Vitros assay results. The percentage of triglyceride results flagged increased from 20.2% in 2004 to 28.8% in 2005. Table 14 shows the per cent bias of the AMMs compared to the reference values on the 12 samples distributed in 2005. Table 15 displays the bias by manufacturer group. The root cause of this bias is an area of active investigation by the committee.

Table 14. Triglyceride Bias on the 2005 Lipids Surveys

Survey	Vial	Reference Value (mmol/L)	AMM (mmol/L)	% Bias
LIPS-0501	Group 1 Vial 1	0.930	0.892	-4.09
	Group 1 Vial 2	1.370	1.237	-9.71
	Group 2 Vial 1	1.370	1.277	-6.79
	Group 2 Vial 2	2.140	1.976	-7.66
LIPS-0506	Group 1 Vial 1	1.220	1.140	-6.56
	Group 1 Vial 2	1.690	1.563	-7.51
	Group 2 Vial 1	1.470	1.402	-4.63
	Group 2 Vial 2	1.870	1.767	-5.51
LIPS-0510	Group 1 Vial 1	2.970	2.751	-7.37
	Group 1 Vial 2	1.020	0.935	-8.33
	Group 2 Vial 1	3.450	3.289	-4.67
	Group 2 Vial 2	2.100	1.982	-7.67
Mean Bias				-6.71

Table 15. Triglyceride Bias on the 2005 Lipids Surveys by Manufacturer

Survey	Vial	Reference Value (mmol/L)	Beckman Coulter Mean (mmol/L)	% Bias	Dade Behring Mean (mmol/L)	% Bias	Ortho Mean (mmol/L)	% Bias	Roche (BMC) Mean (mmol/L)	% Bias
LIPS-0501	Group 1 Vial 1	0.930	0.805	-13.44	0.904	-2.80	0.924	-0.65	0.858	-7.74
	Group 1 Vial 2	1.370	1.240	-9.49	1.304	-4.82	1.222	-10.80	1.288	-5.99
	Group 2 Vial 1	1.370	1.211	-11.61	...	...	1.296	-5.40	1.278	-6.72
	Group 2 Vial 2	2.140	1.904	-11.03	...	...	1.997	-6.68	1.976	-7.66
LIPS-0506	Group 1 Vial 1	1.220	1.063	-12.87	1.146	-6.07	1.145	-6.15	1.158	-5.08
	Group 1 Vial 2	1.690	1.527	-9.64	1.631	-3.49	1.543	-8.70	1.621	-4.08
	Group 2 Vial 1	1.470	1.335	-9.18	...	...	1.428	-2.86	1.391	-5.37
	Group 2 Vial 2	1.870	1.718	-8.13	...	...	1.781	-4.76	1.782	-4.71
LIPS-0510	Group 1 Vial 1	2.970	2.817	-5.15	2.926	-1.48	2.671	-10.07	2.907	-2.12
	Group 1 Vial 2	1.020	0.909	-10.88	0.947	-7.16	0.935	-8.33	0.973	-4.61
	Group 2 Vial 1	3.450	3.205	-7.10	...	...	3.302	-4.29	3.371	-2.29
	Group 2 Vial 2	2.100	1.877	-10.62	...	...	2.012	-4.19	2.002	-4.67
Mean Bias				-9.93		-4.30		-6.07		-5.09

LIPID PATIENT REPORTS

The *Lipid Update* Broadsheet provided a summary of the 2003 recommendations of the Canadian Working Group on Hypercholesterolemia and Other Dyslipidemias and discussed the reporting difficulties that this document may present to laboratories in the province.

In survey LIPS-0510 the participants were requested to submit an actual patient report for lipids (with identifiers removed), along with any interpretive comments that would normally accompany that report, to examine the lipid reporting strategies of laboratories in the province. This is an area that presents difficulties, especially with

computer generated reports that do not present multiple lines of text or are unable to print customized reports based on the lipid results.

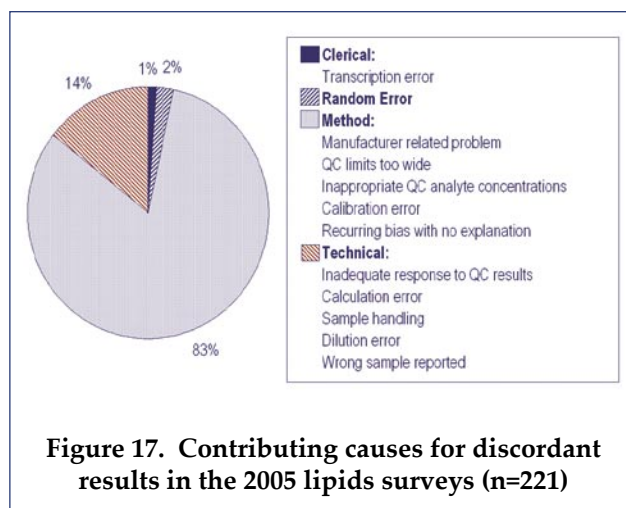
Fifty of 128 laboratories include a reference to a published interpretive guideline in their report; 23 to the Canadian Medical Association Journal report of the Canadian Working Group on Hypercholesterolemia, 5 to the National Cholesterol Education Program in the United States, 2 to the recent guidelines published by the OAML, and 20 to another guideline or interpretive scheme. The 78 laboratories that do not refer to interpretive guidelines for lipids also failed to make the distinction between reference intervals and target values.

With regard to reference intervals, 29 laboratories quote an upper reference range for cholesterol greater than 5.2 mmol/L, 39 quote an upper reference range for LDL-cholesterol greater than 3.4 mmol/L, 72 quote an upper reference range for triglycerides greater than 1.7 mmol/L, and 80 laboratories quote a lower reference range for HDL-cholesterol less than 1.0 mmol/L. This suggests that many laboratories in the province need to revisit their reference intervals and reporting strategies for lipids.

DISCORDANT RESULTS

The number of results reported in 2005, discordant results generating memoranda and the error rate are displayed in Table 16. The increase in the error rate over 2004 (4.8%) is due to the increase in the number of triglyceride results flagged. Figure 17 displays the contributing causes by percentage for the 221 discordant results. Problems associated with the manufacturer were responsible for 67% of the method causes

Discipline	No. of Results Reported	No. of Discordant Results	Error Rate (%)
Lipids	2930	221	7.5



ENDOCRINOLOGY

TESTING MODEL

Four surveys were conducted with each containing four to five samples. Three lyophilized serum samples and one or two previously frozen serum samples (for specific analytes) were distributed in February, April and August. The November survey contained four lyophilized serum samples. The analytes assessed using the lyophilized serum are listed in Appendix G.

The analytes assessed using previously frozen serum were:

Estradiol	ENDO-0502
Prostate specific antigen (PSA) and Free PSA	ENDO-0504
Vitamin B ₁₂	ENDO-0508

Seven inter-survey precision studies were conducted during the year using the lyophilized serum samples. The duplicate samples were:

ENDO-0408-B and ENDO-0502-A
ENDO-0502-B and ENDO-0504-C
ENDO-0502-C and ENDO-0508-A
ENDO-0504-B and ENDO-0511-A
ENDO-0504-A and ENDO-0511-B
ENDO-0508-B and ENDO-0511-C
ENDO-0508-C and ENDO-0511-D

ASSESSMENT OF LABORATORY PERFORMANCE

Survey results were compared to the instrument peer group median if there was a minimum of ten users. Performance was generally acceptable on the 15 analytes reported using the lyophilized serum for both bias and precision. Four Abbott users' LH results were flagged for imprecision in the November precision studies as they failed to update their LH method code after Abbott recalibrated the method to the World Health Organization (WHO) 2nd IS 80/552 standard. The November (ENDO-0511) results were 30%–40% lower than the results reported when the same samples were tested in previous surveys.

Estradiol

Eleven different instruments/methods were used by 23 laboratories reporting estradiol in 2005. Results for estradiol continue to be unsatisfactory on lyophilized serum studies. The CVs of the lyophilized serum sample results ranged from 20%–30%. As reported in the 2004 Review, a similar variation in results has been noted with fresh serum samples in previous surveys.

A fresh serum recovery study was included in the ENDO-0502 survey. Vial 1, obtained from a post-menopausal female, was the baseline sample. Vial 2 was prepared by adding 500 pmol/L of estradiol to the serum used for vial 1.

Table 17 shows a summary of the results of this estradiol recovery study. The majority of the Roche Elecsys and Modular System users, the Abbott Architect, CI 8200 and AxSYM users and the Bayer ADVIA Centaur user recovered over 80% of the added estradiol. Other methods such as the Beckman Coulter Access, Ortho Vitros Eci and the DPC RIA method recovered less than 50%.

The committee will work with an Ontario laboratory to develop the estradiol liquid chromatography/tandem mass spectrometry (LC/MS/MS) method in order to obtain reference results.

Total and Free PSA and PSA Ratio

One previously frozen serum challenge for total and free PSA (ENDO-0504-1) was distributed in 2005. This sample was from a male patient with confirmed benign prostatic hypertrophy (BPH). It was a duplicate of survey sample ENDO-0402-1.

The total PSA results reported by 65 laboratories ranged from 6.1–9.3 µg/L with an all-methods' median of 7.9 µg/L. These results are similar to the results reported for the duplicate vial tested in 2004 (6.7–10.1 µg/L) and are consistent with the donor's diagnosis of BPH.

Table 17. Summary of the Results of the Estradiol Recovery Study in Survey ENDO-0502

Method	Vial 1 pmol/L	Vial 2 pmol/L	Difference pmol/L	% Recovery
Beckman Coulter Access	229	456	227	45
DPC Immulite 2000	<73	358	285	57
	<100	362	262	52
Ortho Vitros Eci	37	249	212	42
BMC Elecsys	<55	407	352	70
	59	503	444	89
	45	423	378	76
	78	488	410	82
	71	484	413	83
	<50	486	436	87
	39	468	429	86
	66	1088*	1022	204
Abbott Architect	<90	458	368	74
	<37	440	403	81
	79	472	393	79
Roche Modular System	49	507	458	92
	43	487	444	89
Abbott CI 8200	55	488	433	87
Abbott AxSYM	<90	508	418	84
Bayer ADVIA Centaur	<40	556	516	103
Diasorin RIA	48	373	325	65
DPC RIA	30	261	231	46
	23	249	226	45

* Committee considered this result to be discordant

The Beckman Coulter and Ortho assays continue to have a positive bias compared to the other methods' results as they are calibrated to the original Hybritech method rather than the WHO standard.

There were 29 laboratories reporting free PSA and the PSA ratio. The free PSA results ranged from 1.0–1.9 µg/L. The Roche (BMC) users' results continue to show a negative bias compared to the results reported using the Beckman Coulter, Abbott and Wallac assays.

The free/total PSA ratio values ranged from 0.13–0.27. Roche (BMC) users reported the lowest ratios (0.13–0.18) while the Abbott users reported the highest ratios (0.19–0.27). It was felt that the range of the ratios reported is too wide as some laboratories may be reporting ratios suggestive of cancer rather than BPH.

Vitamin B₁₂

Sixty laboratories reported vitamin B₁₂ results on the previously frozen fresh serum vial (ENDO-0508-1) distributed in August 2004. The all-methods' median was 250 pmol/L and the results ranged from 199–360 pmol/L. It was disappointing to see between-method differences on the fresh serum sample similar to those seen in the results reported for the lyophilized serum samples.

The committee is still experiencing difficulty in obtaining a low-level fresh donor sample for vitamin B₁₂, but will continue to pursue this in 2006.

DISCORDANT RESULTS

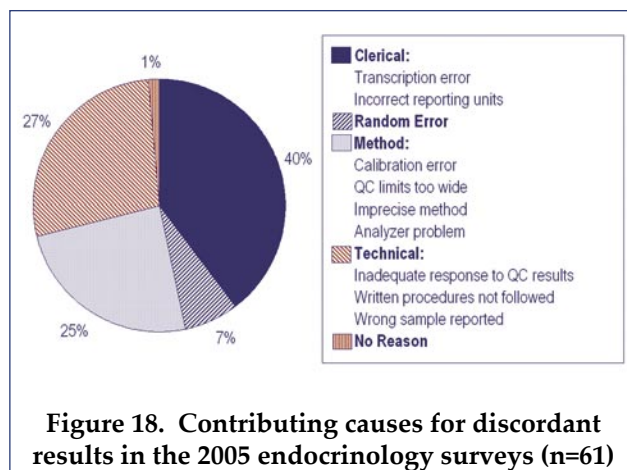
Table 18 summarizes the number of results reported, the number of discordant results generating memoranda and the error rate for 2005. The error rate remained the same as the rate reported for 2004.

Figure 18 displays the contributing causes by percentage for the 61 discordant results. Clerical errors have increased from 21% in 2004 to 40% in 2005. Failure to report a change in method, erroneous reporting units

and transcription errors were responsible for these clerical errors. Imprecise methods, calibration errors and inappropriate QC limits contributed to 56% of the methodological causes. Written procedures not followed, a mix up in samples and an inadequate response to QC results caused the technical problems.

Table 18. Summary of Discordant Results Reported for 2005

Discipline	No. of Results Reported	No. of Results Generating Memoranda	Error Rate
Endocrinology	10 821	61	0.56



IMMUNOLOGY

TESTING MODEL

Three surveys, each containing two serum samples were distributed in 2005. The six samples were from three commercial serum preparations with different clinical conditions:

- Presence of monoclonal proteins
- Elevated rheumatoid factor (RF)
- Positive antinuclear factor (ANA)

Each serum preparation was distributed twice for the assessment of precision. The analytes tested in the surveys are listed in Appendix G.

Beginning with survey IMGY-0511, it was decided to only include high-sensitivity CRP in the Immunology surveys due to the shift in laboratory diagnostics to the high-sensitivity assay.

Protein Electrophoresis

All 41 laboratories detected the presence of monoclonal protein when the serum sample from a myeloma patient was distributed on two occasions (vials IMGY-0502-2 and IMGY-0511-1). The 32 participants performing immunofixation electrophoresis (IFE) on vial IMGY-0502-2 identified the monoclonal band as IgA kappa. Nine also detected the presence of a free kappa light chains. Thirteen indicated the presence of free kappa light chains in the November survey. The possible reason for not detecting the free kappa light chains by the majority of laboratories is that the two monoclonal bands might have migrated to the same position in some electrophoresis systems. Additional IFE employing antisera against free light chains would have revealed the free kappa band. One laboratory erroneously reported the monoclonal protein as IgA lambda in survey IMGY-0511. It could have been a typing error or a mix-up in antisera during the performance of IFE.

Two flags were generated on a non-myeloma sample (IMGY-0508). One laboratory suggested testing alpha-1 antitrypsin due to an elevated alpha-1 fraction, which should be reserved for low alpha-1 levels. Another laboratory reported the presence of an IgM lambda monoclonal band.

Rheumatoid Factor

On the serum sample with elevated RF, all laboratories reported RF as abnormal on both surveys (IMGY-0502-1 and IMGY-0508-2). Since the RF level of this sample was very high, additional dilutions would be required to reach the end point on most assay systems. Depending on the patient population of each institution, laboratories might not dilute serum samples beyond a certain concentration. Two laboratories received memoranda regarding imprecision in their titre values. Both responded indicating the RF titre had been reported as a quantitative result for survey sample IMGY-0502-1 rather than the reciprocal of the dilution.

Antinuclear Factor

The ANA was reported as positive by all participants performing ANA screening and titre tests when the ANA sample was distributed in August and November. All reported the pattern as speckled. One laboratory reported a homogenous pattern in addition to speckled in survey IMGY-0508.

A consensus in results was not reached for ANA on the serum sample with elevated RF in both IMGY-0502 (59% positive) and IMGY-0508 (43% positive).

ANA Patterns-of-Practice Survey

In 2005, the committee conducted a patterns-of-practice survey which covered some of the laboratory aspects surrounding testing for antinuclear antibodies as well as the reporting of these tests. Twenty-seven laboratories responded, and it was apparent that there is a wide variation in practice for this assay. The majority of laboratories use an immunofluorescence technique at a screening dilution of 1/40. However, there is considerable variation in the endpoint titres as well as the titre that is considered to indicate a positive result. Some variation was noted in the number and variety of patterns reported, and the majority of laboratories do not provide an interpretive comment. The clinical utility of ANA testing was not addressed in this survey.

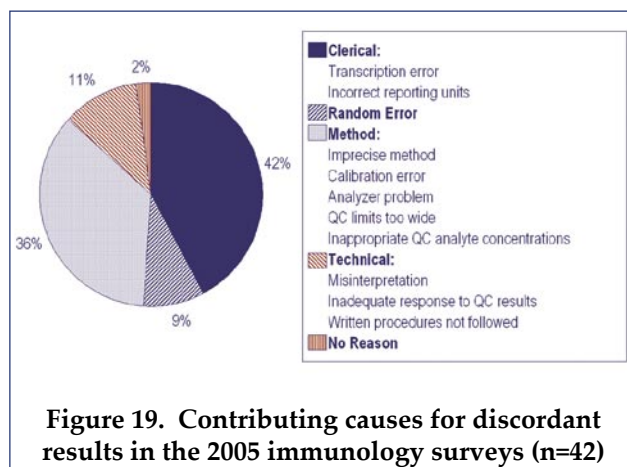
DISCORDANT RESULTS

Table 19 displays the number of results reported in 2005, the number of discordant results generating memoranda and the error rate. The error rate has increased slightly compared to 2004 (1%).

Figure 19 displays the contributing causes by percentage for the 42 discordant results. Clerical errors were responsible for 19 discordant results. Six of these were due to participants using incorrect reporting units. Method causes included inappropriate QC limits or material, method imprecision and analyzer problems. Misinterpretation, not following written procedures and inadequate response to QC results contributed to the technical causes of the discordant results.

**Table 19. Summary of Discordant Results
Reported in 2005**

Discipline	No. of Results Reported	No. of Discordant Results	Error Rate (%) 2005
Immunology	2020	42	2.1



MATERNAL SERUM SCREENING

TESTING MODEL

Since 1993, QMP-LS has provided second-trimester serum and amniotic fluid prenatal screening external quality assessment challenges. The testing model was designed to monitor quality assurance (QA) indicators and analytical and interpretive performance. QMP-LS also has an expanded mandate to monitor the performance of laboratories based on data provided by the Ontario Maternal Serum Screening Database (OMSSD).

Since 1999, QMP-LS has been aware of the transition from second-trimester triple marker screening to enhanced screening modalities. The new markers are biochemical and ultrasound based. The reported advantages of these new modalities are that they will decrease the false positive rate (PR) associated with screening while possibly increasing the detection rate (DR). These changes should result in improved patient care and this shift in practice will have an impact on the QMP-LS EQA program.

In the fall of 2003, The Ontario Women's Health Council (OWHC) awarded a grant to QMP-LS, through the Ontario Medical Association, to develop a QA program for both the new biochemical markers and the ultrasound marker nuchal translucency (NT), which comprise the enhancements included in enhanced prenatal screening. The final report of the project was submitted on February 28, 2005. Some of the recommendations regarding the biochemistry and database EQA were applied in 2005. The issue of monitoring an ultrasound marker is extremely complex and will require further work including linkage with several professional organizations before implementation.

Since 2004, during the QA project for enhanced screening, and as the three markers analyzed by the committee over the preceding ten years had remained stable, all wet challenges and patterns-of-practice surveys were suspended. The individual marker levels and the false positive rates for Down syndrome, Trisomy 18, and open neural tube defect (ONTD) testing were monitored on a monthly basis using data from the OMSSD. The laboratory monthly volumes are also monitored.

BIOCHEMISTRY MARKERS

In 2005, the laboratories were enrolled in the United Kingdom National External Quality Assessment Service (UK NEQAS) program for Down Screening in the First and Second Trimester. This was an extension of the OWHC project and the goal was to validate the OMSSD as the sole EQA model to be used in the future. The data will be evaluated in the spring of 2006.

ONTARIO MSS DATABASE

One outcome of the OWHC project is that, in 2005, the MSS Committee started monitoring the three new biochemical markers—pregnancy-associated plasma protein A (PAPP-A) and free beta human chorionic gonadotropin (free-hCG) in the first trimester; and dimeric inhibin A (DIA) in the second trimester. These markers were monitored using data from the OMSSD.

A second outcome of the OWHC project is the revised monthly reports.

The MSS Database provides outcome assessment on the basis of the PR. As shown in Figure 20, the fluctuation (error bars) for Trisomy 21 PR has remained fairly constant. The decrease in PR over the past two years may reflect the increasing use of enhanced screening modalities for older “high risk” women and, thus, the younger age group of those women undergoing MSS. As maternal age is a factor in the Down syndrome risk calculation, the higher the proportion of younger women in the population, the fewer positive results.

Since the introduction of enhanced screening, the overall uptake of prenatal screening as a function of live births has increased and, likewise, the proportion of screened patients who elect to undergo enhanced screening versus traditional MSS has increased (Figure 21). Figure 22 illustrates the introduction of enhanced screening as compared to 2nd trimester triple marker screening (MSS) alone. The changes in screening practice within Ontario, based on the type of screening method are illustrated in Figure 23.

Table 20, provides a summary of the Ontario screening modalities and volumes for 2005. Five marker Integrated Prenatal Screen (AFP, uE₃, hCG, PAPP-A and NT) represents 35 429 screens (47.3%) of the Ontario volume (74 916) with a positive rate of 2.4%. This is well within accepted international performance standards as published in the literature.

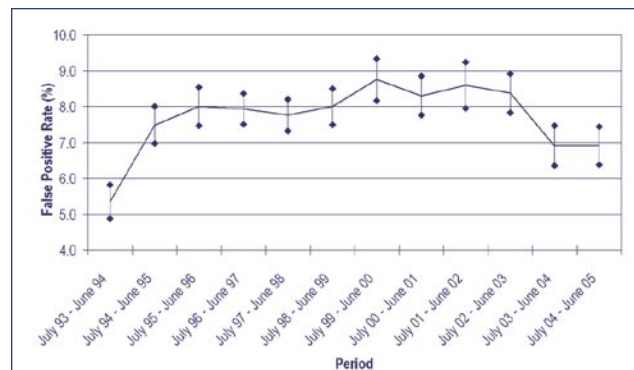


Figure 20. Ontario MSS performance on trisomy 21 adjusted positive rate (IPR) based on MSS 2nd trimester triple marker screening, July 1993–June 2005

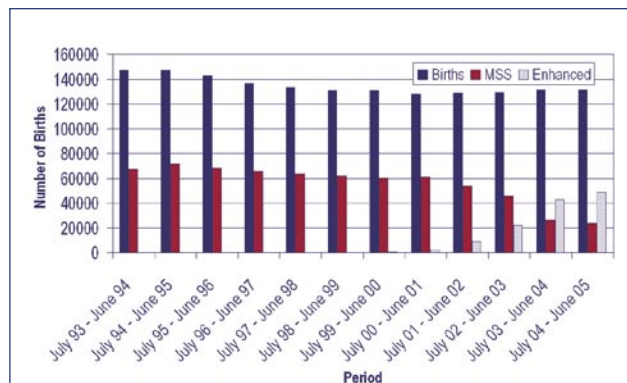


Figure 21. Birth, MSS and enhanced screening volumes in Ontario, July 1993–June 2005



Figure 22. Utilization of MSS and enhanced screening in Ontario, July 1993–June 2005

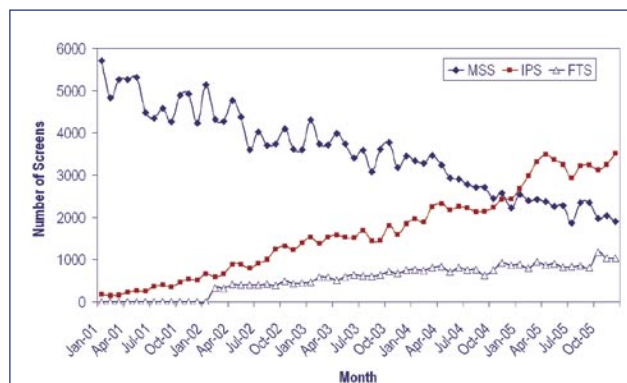


Figure 23. Ontario changes in screening practice, January 2001–December 2005

Table 20. Ontario Screening Modality Summary 2005

Screening Modality	Markers	Number of Screens	% of Screens	Positive Rate (%)
5-Marker Integrated Prenatal Screen	AFP, uE ₃ , hCG, PAPP-A, NT	35 429	47	2.4
3-Marker Maternal Serum Screen	AFP, uE ₃ , hCG	17 297	23	8.1
3-Marker First Trimester Screen	PAPP-A, NT, fBhCG	9719	13	3.9
4-Marker Maternal Serum Screen	AFP, uE ₃ , hCG, DIA	9500	13	6.4
5-Marker Serum Integrated Prenatal Screen	AFP, uE ₃ , hCG, DIA, PAPP-A	1982	3	4.3
Total		74 916	99	

POINT-OF-CARE TESTING

GLUCOSE METERS

Testing Model

Two surveys were planned for 2005 to test the performance of glucose meters. The surveys were distributed in April (POCT-0504-GL) and September (POCT-0509-GL) and consisted of three vials of a commercially prepared suspension of stabilized human red blood cells and known levels of glucose in a buffered medium containing preservatives. Sufficient material was sent to evaluate all of the glucose meters within an institution. The September survey contained one set of duplicate vials for a precision study at a normal concentration of glucose.

Participation in the surveys remains voluntary at this time with 191 institutions reporting results. Ten participants are institutions without laboratories. The users of the glucose meters are expected to perform the testing.

Survey Assessment

The computer flagging rules for bias are as follows:

Bias

- Glucose ≤ 5.0 : results >1.0 mmol/L from specific glucose meter model mean
- Glucose >5.0 : results $>20\%$ from the glucose meter model mean

If a result is $>15\%$ from the mean of results reported from within an institution for a specific glucose meter model (or >1.0 mmol/L for glucose ≤ 5.0), it will be flagged.

The following flagging rules apply for imprecision:

Imprecision

- Glucose ≤ 5.0 : results >1.0 mmol/L difference in results reported on duplicate vials
- Glucose >5.0 : results $>20\%$ difference in results reported on duplicate vials

Results are compared to the glucose meter model mean rather than the all-methods' mean (AMM), due to matrix effects with the survey material.

Glucose Meter Performance

Eighteen different models of glucose meters are currently in use across the province. Precision PCx, continues to support the highest volume of participants followed, in order, by the Accu-Chek Inform, Surestep Flexx, Glucometer Elite and the Precision QID.

Survey POCT-0504-GL

A total of 3186 glucometer results were received for each of the three survey vials. The range of instrument means for vial 1 was 6.0–11.3 mmol/L, for vial 2 was 1.4–4.6 mmol/L and for vial 3 was 16.2–23.5 mmol/L. The range of instrument CVs was slightly less than noted in previous surveys ranging from 2.8%–9.4% for vial 1, 3.6%–18.0% for vial 2 and 3.1%–8.2% for vial 3. The number of results flagged for bias is shown in Table 21. As has been the case in previous surveys, the majority of flags were for bias at elevated levels of glucose. Memoranda were sent to 12 institutions for flagged results that were considered to be clinically relevant.

Table 21. Number of Results Flagged for Bias and Imprecision for Survey POCT-0504-GL

POCT-0504-GL n=3186	Number of Results >20% from Glucometer Mean	Number of Results >15% from Site Mean
Vial 1 (elevated glucose)	12	16
Vial 2 (low glucose)	8	1
Vial 3 (high glucose)	19	11

Table 22. Number of Results Flagged for Bias and Imprecision for Survey POCT-0509-GL

POCT-0509-GL n=3298	No. of Results >20% from Glucometer Mean	No. of Results >15% from Site Mean	No. of Precision Flags on Duplicate Vials 1 and 2
Vial 1 (normal glucose)	12	16	19
Vial 2 (normal glucose)	8	1	
Vial 3 (high glucose)	19	11	

Survey POCT-0509-GL

A total of 3298 glucometer results were received for each of the three survey vials. Vials 1 and 2 were duplicates with glucometer means ranging between 3.69–8.41 mmol/L. The range of instrument means for vial 3 was 15.96–23.76 mmol/L. The range of instrument CVs was 3.5%–7.5% for vial 1, 3.9%–7.2% for vial 2 and 3.5%–6.5% for vial 3. The number of results that were flagged for bias and imprecision is shown in Table 22. Memoranda were sent to 13 institutions for results flagged for bias and imprecision and were considered to be clinically relevant.

The number of results flagged for bias has decreased since the beginning of the program in 2001 (Table 23).

FUTURE ACTIVITIES

The Hematology and Chemistry Committees have recommended expansion of the QMP–LS program for point-of-care testing (POCT) to include coagulation testing (INR). QMP–LS will conduct a survey in 2006 to assess the current practice in POCT and will convene a committee of POCT stakeholders to review and recommend on quality requirements for POCT in Ontario health care institutions.

Table 23. Number of Flagged Results (>20% or ± 1 mmol/L From Glucometer Mean) for 2001–2005

Sample	Target Value (mmol/L) High Glucose	Flagged Results	Per cent
U-0105 Vial 2	20.2	22	0.9%
U-0108 Vial 3	18.6	14	0.6%
POCT-0205 Vial 2	22.9	15	0.6%
POCT-0209 Vial 1	22.4	5	0.2%
POCT-0209 Vial 2	13.9	8	0.3%
POCT-0309 Vial 2	15.7	4	0.1%
POCT-0404 Vial 2	17.2	6	0.2%
POCT-0404 Vial 3	17.2	1	0.03%
POCT-0409 Vial 1	12.6	4	0.1%
POCT-0409 Vial 3	17.5	6	0.2%
POCT-0504 Vial 3	18.3	19	0.6%
POCT-0509 Vial 3	18.5	8	0.2%
Elevated Glucose			
U-0105 Vial 1	7.3	16	0.6%
U-0105 Vial 3	7.3	23	0.9%
U-0108 Vial 1	8.9	10	0.4%
POCT-0504 Vial 1	7.4	12	0.4%
Normal Glucose			
POCT-0205 Vial 1	4.7	11	0.4%
POCT-0205 Vial 3	4.7	7	0.3%
POCT-0209 Vial 3	6.7	5	0.2%
POCT-0404 Vial 1	5.8	6	0.2%
POCT-0509 Vial 1	5.5	8	0.2%
POCT-0509 Vial 2	5.4	9	0.3%
Low Glucose			
U-0108 Vial 2	2.8	6	0.2%
POCT-0309 Vial 1	2.7	1	0.03%
POCT-0309 Vial 3	2.7	2	0.07%
POCT-0409 Vial 2	2.6	0	0%
POCT-0504 Vial 2	3.0	8	0.3%

ROUTINE HEMATOLOGY

TESTING MODEL

Testing material for routine complete blood count (CBC) and automated leukocyte differential counts, representing clinical samples, was obtained from R&D Systems, Inc., Minneapolis, Minnesota. Survey material included realistic clinical low, normal and high values. The material consisted of human erythrocytes with mammalian leukocytes and thrombocytes in a plasma-like fluid. The variety of blood cell analyzers used in Ontario continues to

pose a challenge for this survey since there is no single material that is compatible with all instruments. Depending on the instrument, the CBC and automated leukocyte differential may vary; specifically the hematocrit (Hct), mean cell volume (MCV), thrombocyte and automated leukocyte differential. Participants were divided into eight groups and each received material compatible with their reported blood cell analyzer (Table 24). With the release of new instruments, it is likely that a ninth group will need to be added for 2006.

The committee continues to experience difficulty assessing results from laboratories where there are only a few users of a specific instrument, or in some cases, where the laboratory is the only user of an instrument.

A fresh K₃EDTA human whole blood survey for CBC and automated leukocyte differential was also distributed in May 2005. Unlike the previous whole blood surveys, which were targeted to selected laboratories, this survey was distributed to all laboratories licensed to perform CBCs. The survey material was obtained from the Hamilton Regional Laboratory Medicine Program, which also supplied the fresh K₃EDTA whole blood for the two reticulocyte surveys.

New in 2005 was a Body Fluid pilot survey conducted in May. Two vials of simulated cerebral spinal fluid (CSF) were distributed to laboratories licensed to perform code L391. These samples were obtained from R&D Systems, Inc. and consisted of mammalian erythrocytes and leukocytes suspended in a plasma-like fluid.

Table 24. Instrument Groups for Automated Differential Survey Material

Group	No. of Labs
No differential/1-, 3-part differential	26
Beckman Coulter 5-part differential	93
Abbott 5-part differential	59
Sysmex 5-part differential	3
Bayer 5-part differential	11
Abbott/Sysmex 3-part differential	10
Beckman Coulter (A ^c T) 5-part differential	5

Hematology (Routine, Red Cell Disorders, G6PD, Fetal Maternal Hemorrhage, Bone Marrow)	
No. of Participants (Dec. 2005)	209
No. of Participants (Dec. 2004)	209
No. of Surveys Conducted in 2005	15

Hematology-Flow Cytometry

No. of Participants (Dec. 2005)	23
No. of Participants (Dec. 2004)	22
No. of Surveys Conducted in 2005	7

Coagulation

No. of Participants (Dec. 2005)	195
No. of Participants (Dec. 2004)	198
No. of Surveys Conducted in 2005	3

Morphology

No. of Participants (Dec. 2005)	200
No. of Participants (Dec. 2004)	201
No. of Surveys Conducted in 2005	3

Transfusion Medicine (Set A and Set B)

No. of Participants (Dec. 2005)	168
No. of Participants (Dec. 2004)	170
No. of Surveys Conducted in 2005	5

As in 2004, the peer method group mean serves as the reference against which the laboratories' results are assessed provided that there are ten or more participants. Where there are less than ten participants, the all-methods' mean (AMM) serves as the reference mean.

Flagging limits, used to alert the committee to values outside the group mean, to unexpected results and/or clinically misleading results were maintained without change throughout 2005. The flagging criteria are shown in Table 25.

Table 25. Hematology Flagging Limits

Parameters	Deviation Allowed From Mean
Leukocyte count	15
Erythrocyte count	6
Hemoglobin	7
Hematocrit	6
Mean cell volume	5
Thrombocyte count	25
Leukocyte differential	3 SD or ± 0.5

LABORATORY PERFORMANCE

At the end of 2005, 205 laboratories participated in the routine survey, just one less than the previous year. For reticulocyte counting, 153 laboratories participated in 2005, the same number as the previous year. It appears that, after several consecutive years where the number of participating laboratories has shown a slow but persistent decline, this trend has halted, at least temporarily.

Challenges were conducted in May and October. Each challenge consisted of 4 vials for routine CBC parameters, 2 vials for CBC and automated leukocyte differential counts and 2 vials for reticulocyte counts. In each survey, two of the CBC vials were from the same lot number and precision studies were conducted.

In addition, the May survey included two vials of fresh whole blood and two vials of simulated body fluid.

CBC and Automated Leukocyte Differentials

Participants were expected to report leukocyte count, erythrocyte count, hemoglobin (Hb), Hct, MCV, and thrombocyte count for each vial. Laboratories with a 5-part differential instrument were expected to report absolute numbers of lymphocytes, monocytes, granulocytes, eosinophils and basophils. Participants using a 3-part differential instrument were expected to report absolute numbers of lymphocytes, monocytes and granulocytes. Those using a 1-part differential instrument were expected to report only absolute numbers of lymphocytes.

For both surveys, a total of 18 826 results were analyzed. Overall performance was, once again, excellent. Survey error rates for combined CBC and automated leukocyte differential were 0.30% and 0.12% in May and October 2005, respectively.

Whole Blood Survey

Two vials of fresh K₃EDTA human whole blood were distributed to laboratories licensed to perform CBCs. Although the survey results could not be analyzed statistically, the survey was a valuable exercise in confirming that the consistent instrument group differences observed in the MCV and Hct using simulated material are related to the use of "fixed" cells since differences in these parameters are not observed with whole blood. Because these samples can deteriorate in a fairly short timeframe, they are not suitable for widespread use and QMP-LS does not plan to conduct further surveys of this type.

Reticulocyte Counting

Two whole blood reticulocyte count challenge surveys were distributed in 2005. Participants were requested to perform erythrocyte and per cent reticulocyte counts on receipt of the sample, and from these results, calculate the absolute reticulocyte count. Results were assessed based on all three results for each sample.

The two samples included in the May survey, sample A was from an individual with an increased reticulocyte count and sample B was from a normal healthy individual. However, upon analysis of the results submitted, it became apparent that there were problems with these fresh whole blood samples related to both lack of homogeneity and sample deterioration. Consequently, the results could not be analyzed satisfactorily and errors were not assessed.

For the second survey in October, a similar approach was employed. Sample A was from an individual with an increased reticulocyte count and laboratories were expected to report a result greater than their reference interval. Sample B was from a normal healthy individual and participants were expected to report a result within their reference interval.

Of 153 laboratories expected to participate, 150 submitted results on time. A total of 450 results were analyzed for each sample and ten laboratories were assessed errors for a survey error rate of 1.6%. This is similar to that seen in other recent surveys. Flagging limits are shown in Table 26.

Table 26. Reticulocyte Count Flagging Limits

Parameter	Deviation Allowed From Mean
Erythrocyte	±6%
Absolute Reticulocyte Count	2 SD from Instrumentation/Method Mean

The breakdown of methods has not changed significantly from the previous year. As noted earlier, automated methods consistently demonstrate better precision than manual methods. Although there has been improvement, the committee continues to have concerns with respect to reported reference intervals. There is wider variation than expected in both the lower limit ($10\text{--}40 \times 10^9/\text{L}$) and the upper limit ($72\text{--}135 \times 10^9/\text{L}$) that is not method dependent. Participants are encouraged to carefully validate that their reference ranges are current and appropriate. Two further reticulocyte count challenge surveys will be conducted in 2006.

A comprehensive patterns-of-practice survey was conducted mid-year to determine different laboratories approaches to establishing reference intervals for a broad range of hematological parameters. Results of this survey will be published in 2006.

Body Fluid Pilot Survey

In May 2005, QMP-LS conducted a body fluid pilot survey designed to assess proficiency in the performance of manual body fluid cells counts. Accurate body fluid analyses are important for the diagnosis and subsequent treatment of certain diseases but performance had not previously been assessed.

Two samples, similar in appearance to cerebral spinal fluid (CSF), were distributed to laboratories licensed to perform code L391. These samples were supplied by R&D Systems, Inc. and consisted of mammalian erythrocytes and leukocytes suspended in a plasma-like fluid with preservatives. Participants were requested to perform manual leukocyte and erythrocyte counts using a hemocytometer and to provide reference interval and method information for CSF analysis.

Of 153 laboratories, 147 submitted results on time. Of these, approximately two-thirds utilized stains to assist in identifying and counting cells while the remainder counted unstained cells. While there were no significant differences in overall performance between these two groups, the type of stain utilized may have had an impact. Around 90% of participants indicated that they used a Neubauer counting chamber with the remainder using the larger volume Fuchs-Rosental hemocytometer.

Overall performance was satisfactory with more than 80% of participants achieving acceptable results for both vials. There were a variety of errors but the most common problem appeared to be difficulty in differentiating leukocytes from erythrocytes.

BROADSHEET: INTERNAL QUALITY CONTROL PRACTICE UPDATE

A Broadsheet on internal quality control practice was published in November 2005. The core information was subsequently presented at a joint meeting hosted by the Ontario Society of Clinical Chemists (OSCC) and QMP-LS held at White Oaks Conference Resort, Niagara-on-the-Lake. This Broadsheet is available on the secure, password-protected Document Server through the QMP-LS Web site.

DISCORDANT FINDINGS CAUSE ANALYSIS

The contributing causes of discordant findings for routine hematology surveys in 2005 are shown in Figure 24.

Table 27 contains information relating to the number of discordant results. It does not indicate the actual number of assigned errors.

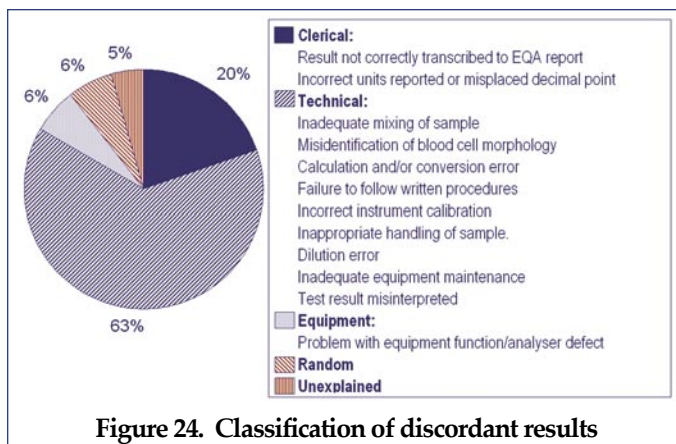


Table 27. Summary of Discordant Findings for Routine Hematology

No. of Potential Discordant Findings	Type of Discordant Finding	No. of Discordant Findings	%
19276	Clerical	13	0.07
19276	Technical	42	0.22
19276	Equipment	4	0.02
19276	Random	4	0.02
19276	Unexplained	3	0.02
Total		66	0.35

RED CELL DISORDERS

TESTING MODEL

In 2005, two survey challenges composed of fresh whole blood and one educational paper-based dry challenge were distributed to participants licensed for L452 sickle cell preparation, L453 sickle cell solubility test (screen), L419 hemoglobin electrophoresis or chromatography to include Hb A₂ fraction.

Seventy-seven laboratories in Ontario participated in the Hb S screening survey and 23 laboratories (including one out-of-province) submitted results for the Hb fraction quantitation challenges.

LABORATORY PERFORMANCE

Hemoglobin (Hb) S Screen

The Hb S screening survey focused on the ability of Ontario laboratories to differentiate a patient positive for Sickle Cell Solubility testing from a patient negative for the same screening procedure.

The survey included two samples. Vial A was obtained from a 24-year-old female—patient A—presenting with a low mean cell volume (MCV) detected in the prenatal screening. Vial B was from patient A's 26-year-old male partner.

The various sickle screen methods used are illustrated in Table 28. All laboratories follow the QMP–LS recommendation of performing a sickle cell solubility screen test as opposed to a slide-sickling test as their primary screen.

In general, this survey was very well performed. All participants reported vial A as positive for Sickle Cell Solubility Screen. Seventy-six laboratories reported vial B as negative. One laboratory was assigned a significant error for reporting both vials A and B as positive. Lesser errors were assigned to two laboratories that reported vial A as positive for Sickle Cell Solubility Screen but reported they would not recommend or perform further testing.

The presence of a low MCV detected in a prenatal screen should prompt further investigation to distinguish iron deficiency from thalassemia.

Hemoglobin Fraction Quantitation Wet Challenge Survey

This survey consisted of two fresh whole blood samples. Vial A was obtained from a 29-year-old asymptomatic female. All laboratories reported the acceptable interpretation of “Sickle cell trait.” Vial B was obtained from a 52-year-old asymptomatic male. All laboratories reported the expected interpretation “No hemoglobinopathy detected.”

The various hemoglobinopathy screening methods used in Ontario are noted in Table 29.

Table 28. Hb S Screening Methods in Use in 2005

No. of Labs	Method
51	Ortho Sickledex
13	In-house sodium dithionite solubility
0	In-house sodium metabisulfite slide sickling
1	Mich Colone Sickle Heme/Sickle Cell Reagent Test Kit
1	Dade Behring Sickle-Sol
2	Nova Century Scientific Sickle Heme
11	Nova Century Scientific Sickle Cell/Hemo S
2	Sickle-Chex Solubility Test – Streck Laboratories

Table 29. Hemoglobinopathy Screening Methods in Use in 2005

Method	Kit	Manufacturer	No. of Labs
Electrophoresis	Cellulose Acetate	Gelman	2
Electrophoresis	Cellulose Acetate	Helena	1
Electrophoresis	Agarose Gel	Beckman Coulter	1
Electrophoresis	Agarose Gel	Sebia	4
HPLC	Cation Exchange (β Thalassemia Short kit)	BioRad	10
HPLC	Cation Exchange (Variant II HbA ₂ /HbA _{1c} Dual kit)	BioRad	4
Isoelectric Focusing, densitometry scanning		BioRad	1

Fourteen (61%) laboratories now use the BioRad Variant or Variant II HPLC method rather than Hb electrophoresis for hemoglobinopathy screening. HPLC is the method of hemoglobinopathy investigation recommended in the *Good Practice Guidelines for Laboratory Investigation of Hemoglobinopathies* published by QMP–LS in *Laboratory Hematology* in December 2003.

The survey was well performed, with all laboratories arriving at the correct diagnosis for both samples.

One laboratory reported the correct diagnosis of sickle cell trait but was assigned a lesser error for reporting Hb S as 0.003 and “Other hemoglobin” as 0.349.

Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency Detection

One survey was conducted in September 2005. Each participant received two test vials containing 2 mL of K₃EDTA anticoagulated whole blood. Vial A contained blood from a deficient donor and vial B contained blood from a normal donor. Samples were stored and shipped frozen in cryovials creating a hemolysate. Participants were instructed to handle the hemolysate as if it were whole blood.

No errors were assessed for this survey. All 23 laboratories reporting a G6PD screen obtained deficient results on vial A. Laboratories in this group that performed a G6PD assay all reported results markedly below their lower limit reference interval. The results ranged from 0.1 to 1.6 U/g Hb. All 23 laboratories reported a normal G6PD screen on vial B. Laboratories in this group that performed a G6PD assay all reported results within their reference interval. The results ranged from 6.1 to 12.4 U/g Hb.

There continues to be a wide range of reference intervals reported by laboratories that perform the assay. Lower interval limits ranged from 4.6 to 7.0 U/g Hb with a mode of 4.6 U/g Hb and upper interval limits ranged from 11.0 to 20.5 U/g Hb with a mode of 13.5 U/g Hb.

Educational Paper-based Fetal Maternal Hemorrhage Dry Challenge Survey

Fetal Maternal Hemorrhage Educational Survey was a dry laboratory challenge designed to introduce participants to current limitations of fetal maternal hemorrhage (FMH) testing and its clinical implications. Previous QMP-LS surveys (RCD-0204-FH and RCD-0404-FH) and publications (Lafferty J, Raby A, Crawford L, Linkins L, Richardson H, Crowther M. Fetal maternal hemorrhage detection in Ontario: *Am J Clin Pathol*, 2003;119: 72–77) have highlighted many of the current limitations in testing for fetal maternal hemorrhage and issues of inadequate Rh immune globulin prophylaxis.

There were four objectives of this educational dry challenge survey. The first was to familiarize participants with limitations of current testing for fetal maternal hemorrhage. The second was to give laboratories the opportunity to demonstrate proficiency in ability to calculate volume of FMH when given a fixed percentage of fetal red cells. The third was for participants to apply their understanding of the American Association of Blood Bank (AABB) Rh immunoglobulin (Rhlg) dosing recommendations. The fourth was to highlight the clinical importance of Rh immune globulin prophylaxis in the prevention of Rh disease of the newborn.

Forty-three laboratories participated in this survey. The majority of laboratories correctly identified the importance of testing for fetal maternal hemorrhage in all D negative women at risk of Rh immunization.

This educational survey was helpful in identifying areas that require improvement in the management of fetal maternal hemorrhage. Specifically, previous challenges primarily focused on the inaccuracy of testing by demonstrating wide CVs in all current quantitative tests for fetal maternal hemorrhage. This educational survey removed the inaccuracies of the fetal bleed quantitation and focused on the limitations of testing, calculation of fetal maternal hemorrhage based on known percentage bleeds and Rh immune globulin dosing. A little more than half (56%) of the participants recognized the need for testing all D negative women at risk of immunization. An OLA requirement states that if an Rh-negative woman delivers an Rh-positive fetus, the maternal blood shall be tested for fetal-maternal hemorrhage to ensure that the standard dose of Rh immunoglobulin will provide effective prophylaxis.

A minority (33%) of participants recognized that the rosette test and acid elution test are highly sensitive screening tests and 44% recognized that all quantitative assays, acid elution and flow cytometry, are inherently inaccurate with high coefficients of variation.

All participants correctly estimated the volume of fetal hemorrhage in both cases when provided with a known percentage of fetal cells. This represents an improvement over previous surveys (RCD-0304-FH and RCD-0404-FH) where calculation errors were a concern and demonstrates the improvement of laboratory practice through proficiency testing. Despite accurate assessment of the fetal bleed, approximately 30% of the participants did not provide the appropriate dosing of Rh immune globulin to cover this bleed adequately according to the AABB standards. The survey highlights the need for further education and dissemination of guidelines regarding the appropriate treatment for fetal maternal hemorrhage.

Educational Paper-based Hemoglobinopathy Dry Challenge Survey

The September hemoglobinopathy educational dry laboratory challenge introduced participants to a patient with combined β thalassemia and the structural hemoglobin variant—Hb D. Participants were asked questions regarding the diagnosis, limitations of specific diagnostic tests and clinical implications.

Twenty-three Ontario laboratories participated in the survey. Clinical and laboratory data were provided and participants were asked a series of six multiple-choice questions. No errors are assessed on educational surveys.

Performance on this survey was very good overall with the majority of laboratories identifying the compound heterozygote of β thalassemia and abnormal hemoglobin variant—Hb D. The majority of laboratories recognized the clinical relevance, the potential for the patient's offspring to inherit a sickling syndrome Hb S/D or Hb S/ β^0 thalassemia. Concerns were raised regarding a few laboratories (3/24) that had greater than four erroneous answers in the survey suggesting the need to review *Good Practice Guidelines for Laboratory Investigation of Hemoglobinopathies*.

The case demonstrated the importance of presenting complex hemoglobinopathy problems in this format as an educational tool.

DISCORDANT FINDINGS CAUSE ANALYSIS FOR RCD SURVEYS

The contributing causes of discordant findings for red cell disorder surveys in 2005 are shown in Figure 25.

Table 30 relates to the number of discordant results. It does not indicate the actual number of assigned errors.

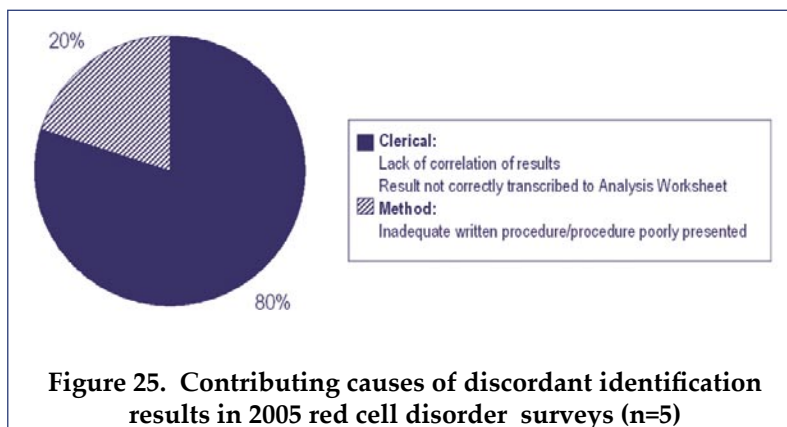


Table 30. Summary of Discordant Findings for Red Cell Disorders

Results Reported	Type of Discordant Finding	No. of Discordant Findings	%
418	Clerical	4	0.96
418	Method	1	0.24
Total	Total	5	1.2

BONE MARROW EXAMINATION

TESTING MODEL

Two rotational slide-based bone marrow surveys were distributed in March and July. These surveys consisted of a peripheral blood film, bone marrow aspirate or biopsy and relevant clinical and laboratory data. The case distributed in March was previously distributed in March 2002 (HEMA-0203-BM) while the July case had not been previously circulated. The March survey material was obtained from a patient diagnosed with lymphoma. Fifty-nine participants returned their Analysis Worksheet on time, six participants declined to participate. The July survey material was obtained from a patient diagnosed with acute myelomonocytic leukemia with eosinophilic differentiation (M4Eo). Sixty-one laboratories returned their Analysis Worksheet and four declined to participate. In addition to the July slide-based survey, a Web-based survey was conducted utilizing digital images of a case of sideroblastic anemia. It was distributed to assess response to reporting a standardized set of images. Sixty-one participants returned their Analysis Worksheets on time and four declined to participate. The photomicrographs and multiple-choice questions were posted on the secure, password-protected QMP-LS Document Server through the QMP-LS Web site. Bone marrow surveys were considered educational, participation was voluntary and performance was not assessed. QMP-LS did not communicate with laboratories in the event of a discordant finding.

LABORATORY PERFORMANCE

Lymphoma

In the March survey (HEMA-0503-BM), the bone marrow biopsy was from a 65-year-old female presenting with fever, weight loss, and a mass in the groin.

Participants were provided with the CBC reference results (Table 31).

The flow cytometry reference results showed a clonal B-cell process expressing IgMD Kappa (Brightly), CD19, CD20, CD22 and HLA-DR, indicative of a B-cell lymphoproliferative disorder. Examination of the peripheral blood film showed the presence of numerous small, cleaved lymphocytes representing the leukemic phase of a malignant lymphoma. The biopsy contained several, irregular paratrabecular lymphocytic infiltrates which are characteristic of marrow involvement by a follicular lymphoma.

Of 59 laboratories, 57 (97%) reported the reference diagnosis of lymphoma (Table 32). Two laboratories reported the diagnosis of both leukemia and lymphoma, which is semantically correct given the presence of circulating lymphoma cells.

This case was chosen as a point for discussion of lymphoid infiltrates of the bone marrow, benign and malignant, which is commonly seen in clinical practice and often provide diagnostic difficulties especially when immunohistochemistry is unavailable.

Table 31. Reference Results

Leukocyte count	58.0 × 10 ⁹ /L
Hemoglobin	128 g/L
Hematocrit	0.392 L/L
Mean cell volume (MCV)	83.4 fL
Thrombocyte count	271 × 10 ⁹ /L
Red cell distribution width (RDW)	14.5%
Erythrocyte count	4.70 × 10 ¹² /L
No automated differential	

Table 32. Frequency of Reporting

Diagnosis	No. of Labs	% of Labs
Acute leukemia	2	3
Lymphoma	57	97
Would not report, but would refer to an outside laboratory	1	2

Further studies, comments or tests for diagnosis and followup:

	No. of Labs	% of Labs
Further studies required	56	95
Cytogenetic studies	18	31
Molecular studies	6	10
Immunohistochemistry	10	17
Immunostains	4	7
Immunocytochemistry	11	19
Immunophenotyping by flow cytometry	52	88
Biopsy on mass in groin	4	24
Ultrasound and CT scan of abdomen	1	2

The distinction between benign lymphoid aggregates and malignant infiltrates may require a number of special investigations including molecular studies and may co-exist in the same patient. Many malignant lymphomas show characteristic patterns of marrow involvement and these should be correlated with the findings of ancillary investigations including flow cytometry and molecular studies (if available) to arrive at the correct diagnosis. Specifying the exact type of lymphoma may not be necessary as the histological classification of lymphomas is usually performed on a lymph node biopsy but occasionally the primary site may be inaccessible for biopsy and therapy decisions are based on the marrow and or peripheral blood film findings.

The majority of respondents reported the correct diagnosis as well as identified the ancillary investigations that would be helpful in diagnosis and follow up.

Acute Myeloid Leukemia (M4Eo)

In the July survey (HEMA-0507-BM) the bone marrow aspirate was obtained from a 62-year-old male presenting with diffuse petechiae, headache and increasing tiredness.

Participants were provided with the CBC reference results (Table 33).

The flow cytometry reference results showed varying positivity for CD34 and CD33, CD13 and myeloperoxidase. Markers associated with monocytic differentiation, CD4, CD14 and CD64 were positive in a population of cells associated with light scatter of monocytes. Additionally, CD2, a marker associated with lymphocytes, was present on a population of the monocytic cells, consistent with the diagnosis of an acute myeloid leukemia (AML) French-American-British (FAB) type M4 (myelomonocytic).

Of 61 laboratories, 50 (82%) reported the reference diagnosis of acute leukemia (Table 34).

This was a challenging case of acute leukemia and the majority of respondents reported the expected diagnosis with many correctly subtyping the leukemia as acute myelomonocytic leukemia or acute monocytic leukemia with abnormal eosinophils. This is a rare form of adult acute leukemia (3%–5% of cases) with distinct morphological and molecular features. The large abnormal granules may impart a basophilic appearance to these blasts and peripheral eosinophilia is very rare. The blasts may simulate promyelocytes with sheets of basophilic granules obscuring the nucleus of the cell. However, these cases do not have the typical number of Auer rods in the cytoplasm, which would lead to the diagnosis of acute promyelocytic leukemia (APL “typical” or hypergranular type).

In addition, the flow cytometry findings would differ, in that CD34 is rarely, if ever seen in cases of APL. This diagnosis imparts therapeutic importance in that cases of APL are treated with different induction chemotherapy agents. Generally, cases of acute leukemia are investigated using cytogenetic and molecular studies for both diagnostic and prognostic purposes. The characteristic cytogenetic translocations specific to both APL and monocytic leukemia with abnormal eosinophils would be detected before therapy is commenced or completed.

Table 33. Reference Results

Leukocyte count	16.0 × 10 ⁹ /L
Hemoglobin	80 g/L
Hct	0.23 L/L
MCV	99.1 fL
Thrombocyte count	<10 × 10 ⁹ /L
RDW	17.7%
Erythrocyte count	2.27 × 10 ¹² /L

Automated Differential:

Neutrophils	14.1 × 10 ⁹ /L
Lymphocytes	1.4 × 10 ⁹ /L
Monocytes	0.5 × 10 ⁹ /L
Eosinophils	0.0 × 10 ⁹ /L
Basophils	0.0 × 10 ⁹ /L
Flagged differential	Yes

Table 34. Frequency of Reporting

Diagnosis	No. of Labs	% of Labs
Acute leukemia	50	82
Acute promyelocytic leukemia	10	16
Metastatic carcinoma	1	2
Myelodysplastic syndrome	2	3
Other, specify	19	31
Other responses included:		
Chronic myelomonocytic leukemia	2	3
Acute promyelocytic leukemia	4	7
Acute myelomonocytic leukemia M4Eo	4	7
Acute myelocytic leukemia M4Eo	8	13
Evolving monocytic leukemia	1	2

Sideroblastic Anemia

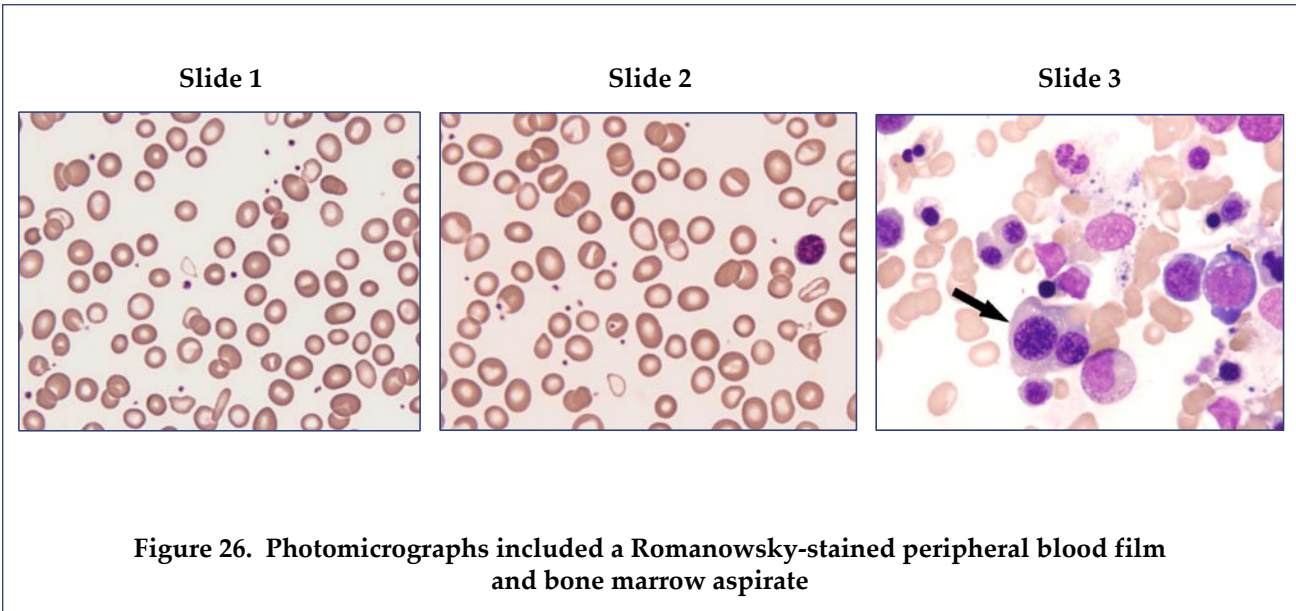
The Web-based survey (HEMA-0507-BW) included photomicrographs from a 79-year-old male presenting with a macrocytic anemia, evidence of iron overload and liver cirrhosis.

Participants were provided with the CBC reference results (Table 35). Photomicrographs included a Romanowsky-stained peripheral blood film and bone marrow aspirate (Figure 26).

These images represented a case of Sideroblastic Anemia (SA). This disorder may be inherited or acquired, the former being rarely seen in clinical practice, while the latter may be associated with a known underlying etiology such as alcoholic liver disease or may have no known identifiable cause. SAs represent a heterogeneous group of complex disorders that require a bone marrow examination to diagnose by the presence of a complete or partial perinuclear ring of abnormally coarse siderotic granules in a substantial proportion of erythroblasts (usually >15%). The formation of ringed sideroblasts is most often due to insufficient heme formation, due to defective protoporphyrin production, which in turn is attributable to decreased d-aminolevulinic acid synthase activity.

Twenty-three per cent of the participants reported the most likely diagnosis as megaloblastic anemia. Both sideroblastic anemia and megaloblastic anemia are associated with ineffective erythropoiesis and similar but not identical morphological findings. The co-existence of liver disease, as in this case, may lead to a number of overlapping hematological features that may dilute or confound the classical features of possible iron deficiency, iron overload, hypersplenism and vitamin B₁₂ or folate deficiencies that are often seen in these patients.

Table 35. Reference Results	
Leukocyte count	3.3 × 10 ⁹ /L
Hemoglobin	99 g/L
Mean cell volume	106 fL
Thrombocyte count	211 × 10 ⁹ /L
FREQUENCY OF REPORTING	
SLIDE 1	
Best morphology description of blood film:	
	No. of Labs % of Labs
Dimorphic erythrocytes	61 100
SLIDE 2	
Most likely diagnosis:	
	No. of Labs % of Labs
Sideroblastic anemia	47 77
Megaloblastic anemia	14 23
SLIDE 3	
Erythroid precursor indicated by the arrow shows:	
	No. of Labs % of Labs
Normoblastic maturation	1 2
Megaloblastic maturation	43 71
Cytoplasmic vacuolation	16 26
Features of dysplasia	55 90



SUBMISSION OF NEW CASES

Participants are requested to submit interesting bone marrow cases to QMP-LS. Please contact the QMP-LS office to ascertain whether the case would be suitable for distribution. At least 24 well made, stained and coverslipped peripheral blood and bone marrow aspirate and/or biopsy preparations are required.

FLOW CYTOMETRY

TESTING MODEL

Two wet surveys were conducted in 2005, 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 service 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. In November 2005, a dry challenge survey provided on CD-ROM for hematological malignancies was conducted. This allowed participants to review listmode data using their own computer analysis programs and also to review a case history and digital slides from the case.

LABORATORY PERFORMANCE

Lymphocyte Immunophenotyping for HIV

Samples from HIV positive donors were distributed to 18 participants—16 Ontario and two out-of-province. All laboratories utilized CD45 as gating agent. The majority of laboratories used dual platform analysis, but the per cent of laboratories that used single platform analysis has gradually increased from 10% in March 1999 to 39% in the September 2005 survey. All laboratories now use 3- or 4-colour combinations. The majority used 4-colour combinations. Surveys for HIV testing have been conducted since 1995 and the performance is summarized in Table 36. There were no errors assessed in the 2005 surveys.

Table 36. Performance on 1995–2005 Surveys, Lymphocyte Phenotyping for HIV Investigation

Survey Vial	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	5	0	26.3
H-0108-FC-A	HIV	1	0	4.8
FLOW-0203-HV	HIV	0	0	0
FLOW-0208-HV	Normal	0	0	0
FLOW-0303-HV	HIV	0	0	0
FLOW-0309-HV	HIV	1	0	4.8
FLOW-0403-HV	HIV	1	0	4.8
FLOW-0409-HV	HIV	0	0	1
FLOW-0503-HV	HIV	0	0	0
FLOW-0509-HV	HIV	0	0	0

* Error Rate % = # errors × 100/ # laboratories

Leukocyte Phenotyping for Neoplastic Hematological Disorders

Two clinical cases were distributed (between March and September) to 18 participants (13 Ontario and five out-of-province). Participants were expected to include the following in their submissions:

- blood film morphology;
- flow cytometry analysis results and histograms;
- interpretation of results and;
- laboratory-generated reports showing interpretation of results.

The first sample was from a patient with hairy cell leukemia. Overall, this was a successful survey. All participants included hairy cell leukemia in the differential diagnosis. Three laboratories also included splenic marginal zone lymphoma in the diagnosis. No errors were assessed on this survey. The second sample was from a patient with large granular lymphocyte leukemia, NK-cell type. One participant reported the presence of an NK-cell population expressing kappa light chains. This is not a credible result and probably reflects selective reactivity of the NK-cell population with the specific reagent used by this laboratory.

CD-ROM Dry Challenge

This was a case of adult T-cell leukemia/lymphoma, possibly Sezary syndrome. All participants correctly identified the case as a mature T-cell neoplasm. Qualitative results were generally performed well, however there is an issue with how participants are reporting them. For example, while all participants reported the malignant cell as CD7 negative, the results in the quantitative section would suggest otherwise. This is because of the presence of normal T cells intermixed with the malignant population. Further surveys will be designed to specifically ask for marker intensity only on the population of interest.

Performance on this survey was excellent. The diagnosis of T-cell neoplasms is always challenging and the participants reached the correct diagnosis.

CD 34 Analysis

Two surveys were conducted in 2005, each consisting of commercial-fixed whole blood and diluted apheresis samples. There were 16 participants (12 Ontario and four out-of-province). Over two-thirds of laboratories are performing single platform analysis and almost all are using the ISHAGE gating strategy. Overall, the September survey showed higher than expected %CV on both samples. There is no evident explanation for sample FLOW-0509-SC-1. However, sample FLOW-0509-SC-2 had a low CD34 count and was from a patient who failed to mobilize significantly after treatment with cytokine therapy. This is not an unusual finding in a large transplant program and this sample, therefore, evaluated an important level of CD34+ cells in apheresis products (approximately 0.1%). Future surveys will require results of viability testing to be submitted by participating laboratories.

SUMMARY

For 2006, the testing model will remain essentially the same, with increased attention paid to those laboratories using inappropriate gating strategies in the analysis of leukemia and lymphoma samples. This will be supported by the Web-based case study format, which allows a significant educational opportunity in this area. As noted above future surveys will require results of viability testing on CD34 analysis to be submitted by participating laboratories.

COAGULATION

TESTING MODEL

Two coagulation challenge surveys were conducted in 2005. Testing materials were chosen to represent a variable, but clinically meaningful, range of results. Prothrombin Time/International Normalized Ratio (PT/INR) testing was monitored using lyophilized coumadinized plasmas supplied by South Manchester University Hospital NHS Trust, Manchester, UK. The activated partial thromboplastin time (APTT) lyophilized survey material consisted of normal control plasma and heparinized control plasma supplied by bioMerieux Canada, Inc., Saint Laurent, Quebec. Affinity Biologicals Inc., Hamilton, Ontario provided lyophilized plasma for APTT testing that was spiked with unfractionated heparin giving an anti-Xa activity of 0.68 U/mL. In addition, Affinity Biologicals, Inc. supplied QMP-LS with lyophilized immuno-depleted factor VIII and factor IX samples for factor assay testing. A thrombophilia challenge survey was conducted in September 2005. In this survey, two patients' derived samples were distributed to centres identified as performing thrombophilia investigations. The plasma samples were obtained from individuals diagnosed with a factor V Leiden (in one case homozygous receiving warfarin, in the other heterozygous not receiving warfarin). Performance in routine and specialized testing was generally good.

Flagging rules, utilized to bring laboratory results to the attention of the committee for review, are noted in Table 37.

Table 37. Coagulation Flagging Limits

INR	20% of all method's mean (AMM)
APTT	20% of reagent mean
Factor Assay	20% of AMM

LABORATORY PERFORMANCE

PT/INR

Routine surveys were distributed in February (COAG-0502) and September (COAG-0509). The previously identified survey material matrix effect, reported by participants using IL Test PT/Fibrinogen Recombinant reagent and an ACL coagulation instrument, was apparent throughout the year; thus, users of this reagent/instrumentation combination were evaluated against their reagent group peers, rather than the AMM.

Laboratories that performed PT/INR testing using lyophilized coumadinized plasmas were assessed two significant errors and three lesser errors on the two surveys. The committee is very pleased with INR testing—the number of errors continues to be exceptionally low considering the number of contributing laboratories (Table 38).

Table 38. INR Target Values, All-Methods' Mean and Minimum and Maximum Results

Vial	Material	Target INR	All-Methods' Mean	Min. and Max. Result
Survey COAG-0502				
A	Coumadinized plasma	6.6	7.0	5.1–11.0
B	Coumadinized plasma	6.6	7.0	5.0–10.7
Survey COAG-0509				
A	Coumadinized plasma	1.6	1.6	1.4–2.0
B	Coumadinized plasma	4.4	4.0	3.1–6.1

APTT

APTT testing was included in the February (COAG-0502) and September (COAG-0509) surveys. A total of three significant errors and 13 lesser errors were assessed on the two surveys. Three vials, in two surveys, contained heparinized lyophilized samples to assess the quality of heparin monitoring in the province. The other vial consisted of normal reference control plasma. Two of the heparin samples were identical and precision studies were performed. APTT testing remains good, and the committee has no specific comments concerning routine APTT monitoring.

The APTT sample containing unfractionated heparin giving an anti-Xa activity of 0.68 U/mL produced high APTT results. The committee noted a marked variability in the maximum cut-off of APTTs. On similar reagent-instrument combinations, the cut-off values ranged from 120 to 212 seconds. Although difficult to mandate in the absence of any scientific information, the committee would suggest laboratories use an APTT cut-off value that is likely to be within a clinically useful range; an APTT maximum cut-off value of >150 seconds would likely satisfy most clinical needs.

Factor VIII and IX

In the February survey (COAG-0502-FA), coagulation factor assay analysis was carried out on immuno-depleted factor VIII and IX samples. The factor VIII and factor IX samples represented a “marked” deficiency state. One significant error and one lesser error were assessed to participants reporting factor VIII and factor IX, respectively. The significant error was assigned for reporting a factor VIII assay of 0.05, which would have altered the patient's clinical treatment. A total of 20 laboratories are licensed to perform factor assays. In addition, one voluntary laboratory participated in this survey. Coagulation factor assays were routinely well performed and the committee does not have any systematic concerns with coagulation factor testing in the province. Proficiency of coagulation factor assays will be assessed with similar assays in 2006.

D-dimer

D-dimer testing remains problematic due to difficulties in procuring suitable EQA survey material. QMP-LS staff presented the results of the 2004 international collaboration with UK NEQAS proficiency testing program at the International Society of Thrombosis and Haemostasis (ISTH). As a result of the deliberations at this conference QMP-LS will distribute two D-dimer surveys using purified, laboratory derived D-dimer in 2006.

Thrombophilia

The September (COAG-0509-TH) survey included two samples for thrombophilia testing. Samples were sent to 12 laboratories licensed to perform one or more of the following tests: antithrombin, protein C, protein S, activated protein C resistance, Russell's viper venom (test and confirm) and DNA analysis for factor V Leiden and prothrombin gene mutation. In addition, one voluntary laboratory participated in this survey. Sample A was obtained from a patient with prior history of deep vein thrombosis (DVT) who was receiving warfarin and known to be homozygous for factor V Leiden, while the second patient had no known prior DVT, was not receiving warfarin and was heterozygous for factor V Leiden.

Thrombophilia testing in Ontario was uniformly performed perhaps due to the fact that this type of testing is confined to referral laboratories. Three lesser errors were assessed; one error for an inappropriate low protein S result in the patient not receiving warfarin and two errors as a result of inappropriately high protein C levels in the patient receiving warfarin. Reporting of thrombophilia testing has improved, however selected laboratories continued to report unclear free text comments causing confusion regarding interpretation; these difficulties were discussed with the specific laboratories. In the future, QMP-LS will carefully examine both the results and the comments for accuracy and clarity, and will reserve the right to assign errors to laboratories reporting ambiguous thrombophilia comments.

Two thrombophilia surveys are planned for 2006. These surveys will be conducted in collaboration with the QMP-LS Genetics Committee to reflect that factor V Leiden and prothrombin gene mutation testing is oftentimes carried out in molecular genetic laboratories. From a molecular genetic perspective the committee is interested in the content of the hard copy report and whether laboratories are conforming to the OLA requirements.

Heparin Assay

There has been a rapid increase in the use of low molecular weight heparin (LMWH) in Ontario. Therefore, in 2006, the committee will be performing two surveys, one using LMWH spiked into pooled plasma and one using unfractionated heparin spiked into pooled plasma to assess anti-Xa heparin levels.

REFERENCE INTERVALS

The committee will continue to request that laboratories determine the effect of new reagent lot numbers, reagent suppliers or new instrumentation will have on their reference intervals. An error will be assessed if laboratories report clearly erroneous reference intervals or reference intervals that cannot be validated.

DISCORDANT FINDINGS CAUSE ANALYSIS

The contributing causes of discordant findings for coagulation surveys in 2005 are shown in Figure 27.

Table 39 contains information relating to the number of discordant results. It does not indicate the actual number of assigned errors.

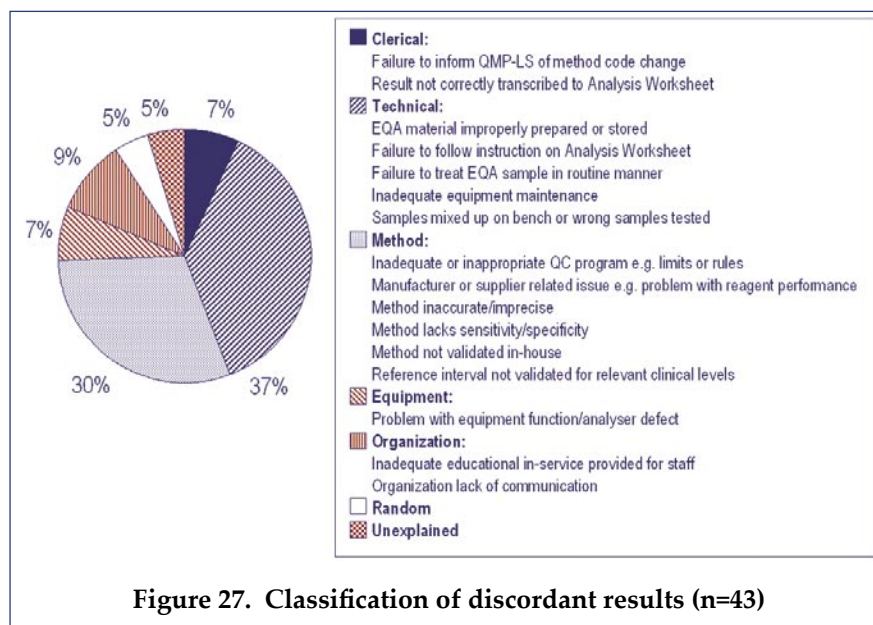


Table 39. Summary of Discordant Findings for Coagulation

Results Reported	Type	No. of Discordant Findings	%
1727	Clerical	3	0.17
1727	Technical	16	0.93
1727	Method	13	0.75
1727	Equipment	3	0.17
1727	Organization	2	0.12
1727	Random	4	0.23
1727	Unexplained	2	0.12
Total		43	2.49

MORPHOLOGY

TESTING MODEL

Three peripheral blood slide-based surveys were performed in 2005. All participants were able to retain their slides, which then form part of the laboratory's slide teaching/reference collection, a valuable resource for laboratory staff.

In February the participants received a slide obtained from a patient with infectious mononucleosis. This was part of a Canadian Coalition for Quality in Laboratory Medicine (CCQLM) survey. A total of 822 laboratories from across Canada participated in this survey. In Ontario, 201 laboratories were expected to participate. Three laboratories were late in submitting their Analysis Worksheet and one laboratory did not return its Analysis Worksheet. The July survey material was obtained from a patient diagnosed with megaloblastic anemia. A total of 200 laboratories were expected to participate in this survey. Four laboratories did not return their Analysis Worksheet. The November survey material was obtained from a patient with a diagnosis of *Plasmodium vivax* infection. Two hundred laboratories were expected to participate in this survey. One laboratory did not return its Analysis Worksheet. In July, in addition to the morphology survey, a questionnaire was circulated addressing laboratory practices for the preparation of peripheral blood films, with 198 laboratories responding. The survey was informative and may be used as a foundation for examining the technical workflow path associated with peripheral blood film preparation.

The peripheral blood morphology surveys were considered educational, participation was voluntary, and the surveys were not assessed.

LABORATORY PERFORMANCE

Infectious Mononucleosis

In the February survey (MORP-0502) the peripheral blood film was from a 20-year-old female with infectious mononucleosis, presenting with sore throat, mild fever, malaise, and lymphadenopathy.

Participants were provided with the CBC results (Table 40). Although the white blood cell count was not elevated, the differential showed the presence of reactive lymphocytes, with the reference laboratory result of $1.4 \times 10^9/L$ reactive lymphocytes. The infectious mononucleosis was due to an acute infection with Epstein-Barr virus infection, with the patient having a positive Monospot test and serological evidence of recent infection, with the presence of IgM and IgG antibodies against the viral capsid antigen (VCA).

Table 40. Reference Results

Leukocyte count	$4.9 \times 10^9/L$
Erythrocyte count	$4.48 \times 10^{12}/L$
Hemoglobin	137 g/L
Hematocrit	0.41 L/L
Mean cell volume	91 fL
Red cell distribution width	11.9%
Thrombocyte count	$133 \times 10^9/L$

This survey was very well done, with all but one laboratory correctly identifying the presence of reactive or atypical lymphocytes, with reactive lymphocyte being the preferred terminology. The results from the participating laboratories showed a mean number of reactive lymphocytes of $1.9 \times 10^9/L$ with a CV of 41.4%. The results of this across Canada survey are reported in an upcoming issue of the Canadian Journal of Medical Laboratory Science.

Megaloblastic Anemia

The July survey (MORP-0507) was a peripheral blood film from a 59-year-old female with weakness, shortness of breath, and chest pain.

Participants were provided with the CBC results (Table 41). The major morphologic findings on the peripheral blood film were hypersegmented neutrophils, oval macrocytes, teardrop forms, polychromasia, fragments, nucleated red blood cells, and mild thrombocytopenia. Further investigations, not available to participants at the time of the survey, disclosed low serum Vitamin B₁₂, normal serum folate, and normal serum ferritin, consistent with a diagnosis of megaloblastic anemia due to Vitamin B₁₂ deficiency.

This survey was well done, with greater than 95% of laboratories identifying the key morphological features of oval macrocytes and hypersegmented neutrophils, and the appropriate diagnostic conclusion of megaloblastic state. Several laboratories provided other diagnostic statements in addition to megaloblastic state, a reasonable approach, not knowing the Vitamin B₁₂ or folate status of the patient. It is worrisome that five laboratories did not include megaloblastic state in their diagnostic statement. Megaloblastic anemia due to Vitamin B₁₂ deficiency is a serious, but very treatable disorder. Overlooking this diagnosis could have significant clinical consequences (Table 42).

Plasmodium Vivax Infection

In the November survey (MORP-0511) the participants were provided with a peripheral blood film obtained from a 50-year-old male with a two-day history of fever, chills, nausea, periumbilical pain and hematuria.

The main features in this case were the presence of intra-cellular and extra-cellular organisms and slightly decreased thrombocytes. Participants were expected to recognize the difference between *falciparum* and non-*falciparum* malarial species. The reference parasitemial level was 0.005 (SI units), which is a parasitemia level of 0.5%.

The majority of the laboratories (91%) correctly identified non-*falciparum* malarial species (Table 43). Of concern are the results from 12 laboratories, which diagnosed *Plasmodium falciparum*, including several laboratories licensed for malarial speciation. Correspondence with these laboratories directed their attention to this issue. Distinguishing between *falciparum* and non-*falciparum* species is important. *P. falciparum* may be resistant to many medications and may be rapidly fatal if not recognized and treated. The non-*falciparum* malaria species, *P. vivax* and *P. ovale*, need to be identified as additional treatment is required to clear the hepatic forms to prevent relapse.

There was marked variation in the reported parasitemia levels, most likely due to participants confusing SI units with per cent parasitemia (Table 44). The reporting form has been updated to enable the participants to report in either SI units or percentage parasitemia level.

The 2006 testing model will remain essentially the same except the differential and descriptive morphological observations will be scored and the diagnostic statement will remain voluntary and will not be assessed.

Table 41. Reference Results

Leukocyte count	4.8 x 10 ⁹ /L
Erythrocyte count	1.11 x 10 ¹² /L
Hemoglobin	48 g/L
Hematocrit	0.141 L/L
Mean cell volume	127 fL
Red cell distribution width	23.2%
Thrombocyte count	128 x 10 ⁹ /L

Table 42. Frequency of Reporting

Diagnosis	No. of Labs
Megaloblastic state	191
Myelodysplastic syndrome	34
Myelofibrosis	23
Immune hemolysis	10
Sideroblastic state	9
Microangiopathic hemolytic anemia	8
Drug/chemical toxicity	7
Macroangiopathic hemolytic anemia	5
Myeloproliferative disorder	5
Anemia of chronic disease	4
Peripheralizing lymphoma	3
Alcohol toxicity	2
Hepatic dysfunction	2
Iron deficiency	2
Anemia under treatment	1
Bacterial infection	1
Other hemoglobinopathy	1
Post-splenectomy/hyposplenism	1

Table 43. Frequency of Reporting

Diagnosis	No. of Labs
Plasmodium other than falciparum	181
Plasmodium falciparum	12
Other parasite/organism	6
No clinical statements	6
Malaria	1
Leukemoid reaction	1

Table 44. Frequency of Reporting

Parasitemia Level, SI Units	No. of Labs
Parasitemia level not reported	11
0.001 to 0.01	134
0.011 to 0.1	20
0.2 to >1.2	34

TRANSFUSION MEDICINE

TESTING MODEL

Four wet surveys were conducted in 2005 (Table 45). As in previous years, challenges were based on the laboratory license, using two sets of material from different sources:

- Set A is procured mostly from a U.S. supplier and is distributed to laboratories with licenses that include antibody identification. The number of participants in this category ranged from 85–86.
- Set B is procured from a Canadian supplier and is distributed to laboratories with licenses that include antibody detection, but not identification. The number of participants in this category was 83.

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.

Table 45. Samples Distributed in 2005

Set A		Set B	
TMED-0502-1	O Rh Positive, R1R1, anti-c	TMED-0502-7	A Rh Positive, antibody present
TMED-0502-2	B Rh Positive, R1r, anti-D	TMED-0502-8	A Rh Positive
TMED-0502-3	O Rh Positive, R1R2	TMED-0502-9	A,B Rh Negative, antibody present
TMED-0502-4	O Rh Negative, rr	TMED-0502-10	AB Rh Positive
TMED-0505-1	O Rh Unknown, anti-K + Fy ^a	TMED-0505-7	AB Rh Unknown, antibody present
TMED-0505-2	B Rh Negative, anti-D	TMED-0505-8	B Rh Negative, antibody present
TMED-0505-3	O Rh Positive, K–, Fy(a–)	TMED-0505-9	B Rh Positive
TMED-0505-4	O Rh Negative, K–, Fy(a+)	TMED-0505-10	B Rh Negative
TMED-0509-1	A Rh Positive,	TMED-0509-7	O Rh Positive, DAT pos (IgG)
TMED-0509-2	AB Rh Positive, DAT pos (IgG)	TMED-0509-8	AB Rh Positive, DAT pos (IgG)
TMED-0509-3	O Rh Positive, anti-E	TMED-0509-9	B Rh Negative
TMED-0509-4	B Rh Negative, anti-K	TMED-0509-10	A Rh Negative
TMED-0511-1	AB Rh Negative, anti-D	TMED-0511-7	A Rh Unknown
TMED-0511-2	A Rh Unknown	TMED-0511-8	A Rh Negative, anti-D
TMED-0511-3	A Rh Positive	TMED-0511-9	O Rh Positive
TMED-0511-4	AB Rh Positive	TMED-0511-10	A Rh Positive
TMED-0511-5	O Rh Positive	TMED-0511-11	O Rh Positive
Automation			
TMED-0509-1A	O Rh Positive		
TMED-0509-2A	AB Rh Negative		
TMED-0509-3A	A Rh Negative		
TMED-0509-4A	O Rh Negative		

Set A

Participants were challenged with:

- a variety of ABO and Rh groups for typing and interpretation;
- prenatal testing samples/antibody titration;
- detection and identification of single and multiple antibodies;
- Rh phenotyping;
- detection of mixed-field agglutination in both the ABO and Rh groups;
- performance of direct antiglobulin test (DAT) on samples coated with IgG and;
- crossmatching to detect incompatibility.

Participants were surveyed about:

- procedures for performance of antibody titration.

Set B

Participants were challenged with:

- a variety of ABO and Rh groups for typing and interpretation;
- detection of mixed-field agglutination in both the ABO and Rh groups;
- detection of antibodies;
- performance of direct antiglobulin test (DAT) on samples coated with IgG and;
- crossmatching to detect incompatibility.

Automation

- Twenty-one laboratories using automated instrumentation participated in the Automation Survey.

Educational Survey

- A Web-based educational survey was provided to all participants as an opportunity to view ABO and Rh mixed-field agglutination in the various testing platforms.

ASSESSMENT OF RESULTS

Scenarios were representative of those commonly encountered in transfusion medicine laboratories, but were designed to be challenging. Clinical information and testing directions were provided for each survey.

The committee's assessment of errors for 2005 is displayed in Tables 46 and 47, and the five-year review of errors is displayed in Table 48.

Table 46. Committee Assessment of Errors for 2005 Surveys, Set A Only

Error Type	TMED-0502		TMED-0505		TMED-0509		TMED-0511		Total 2005	
	Significant	Lesser	Significant	Lesser	Significant	Lesser	Significant	Lesser	Significant	Lesser
ABO	1	0	0	9	0	0	1	3	2	12
Rh	0	0	0	29	0	3	0	19	0	51
DAT	0	0	0	1	0	6	0	1	0	8
Ab Detection	0	0	0	1	0	0	0	0	0	1
Ab Identification	0	0	1	0	0	0	0	0	1	0
Phenotype	0	1	0	0	0	0	0	1	0	2
Crossmatch	0	0	0	2	0	0	0	3	0	5
Total	1	1	1	42	0	9	1	27	3	79

Table 47. Committee Assessment of Errors for 2005 Surveys, Set B Only

Error Type	TMED-0502		TMED-0505		TMED-0509		TMED-0511		Total 2005	
	Significant	Lesser	Significant	Lesser	Significant	Lesser	Significant	Lesser	Significant	Lesser
ABO	0	1	0	11	0	0	0	0	0	12
Rh	0	0	1	23	0	0	1	19	2	42
DAT	0	0	0	0	0	1	0	0	0	1
Ab Detection	0	0	0	0	0	2	0	0	0	2
Phenotype	0	0	0	0	0	0	0	0	0	0
Crossmatch	0	0	0	6	0	0	1	9	1	15
Total	0	1	1	0	0	3	2	28	3	72

Table 48. Committee Assessment of Errors, 2001–2005

Error Type	2001		2002		2003		2004		2005	
	Significant	Lesser	Significant	Lesser	Significant	Lesser	Significant	Lesser	Significant	Lesser
ABO	1	43	7	14	2	121	1	19	2	24
Rh	0	57	2	18	2	93	3	5	2	93
DAT	4	11	0	6	1	14	0	10	0	9
Ab Detection	4	21	6	13	0	1	5	3	0	3
Ab Identification	1	3	1	2	2	0	1	0	1	0
Phenotype	0	17	0	12	0	6	0	0	0	2
Crossmatch	4	2	9	1	2	5	2	7	1	19
Total	14	154	25	66	9	240	12	44	6	151

The total number of significant errors decreased last year (six in 2005, compared to 12 in 2004). However, there was a marked increase in lesser errors for both Set A and Set B participants (78 for Set A and 72 for Set B in 2005, for a total of 151 lesser errors compared to 44 in 2004). This is almost entirely due to the inclusion of ABO and Rh mixed-field agglutination samples in 2005—none was provided in 2004 and this type of survey in the past has typically resulted in a large number of lesser errors due to failure to detect a mixed-field reaction.

ABO and Rh

ABO and Rh errors (four significant and 117 lesser) make up the majority of errors in 2005. Contributing causes of discordant results are shown in Figure 28. All significant errors were the result of errors in transcription. The majority of lesser errors were due to failure to recognize mixed-field agglutination. Despite the large number, this represents a significant improvement in performance compared to the previous survey in 2003 when samples demonstrating mixed-field agglutination were included. Table 49 provides a summary of mixed-field detection from 2003 to 2005.

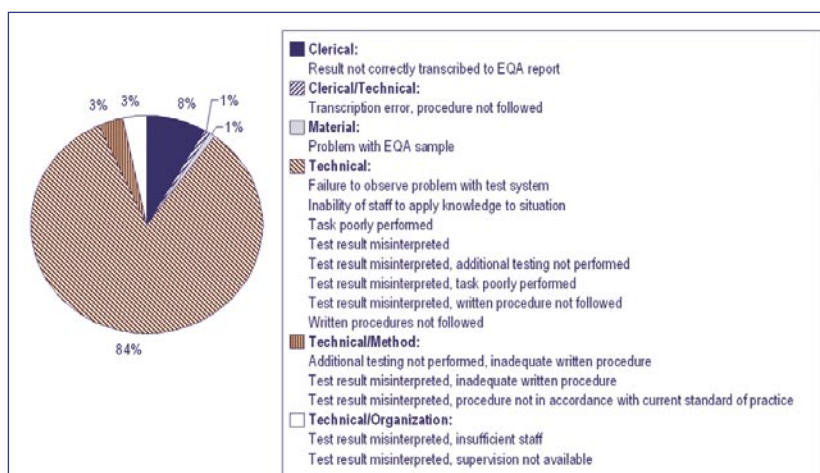


Figure 28. Contributing causes of ABO/Rh errors (n=121)

Table 49. Detection of Mixed-Field Reaction, 2003-2005

	Rh Mixed-Field Agglutination			ABO Mixed-Field Agglutination	
	Survey Samples	TMED-0303-1	TMED-0505-1	TMED-0511-1	TMED-0303-2
		TMED-0303-10	TMED-0505-7	TMED-0511-7	TMED-0303-9
Sample Composition		60% O Negative	50% O Negative	50% A Negative	50% AB Positive
		40% O Positive	50% O Positive	50% A Positive	50% B Positive
Set A Participants		66 (70%) n=94	58 (67%) n=86	64 (77%) n=83	82 (87%) n=94
Set B Participants		44 (54%) n=82	59 (71%) n=83	64 (77%) n=83	74 (89%) n=83

Direct Antiglobulin Testing

Nine lesser errors were assigned in 2005 (eight for Set A participants and one for Set B) compared to ten lesser errors in 2004. The committee's expectations for differential DAT testing (anti-IgG and anti-C3) have increased in recent years and will continue to be strictly applied.

Antibody Detection and Identification

There were no significant and three lesser errors in antibody detection and one significant error in antibody identification in 2005 compared to five significant and three lesser errors in antibody detection and three lesser errors in antibody identification in 2004. The significant error was due to an error in transcription.

Phenotyping

There were two lesser errors assigned for phenotyping in 2005 compared to none in 2004. These were errors in transcription.

Crossmatching

One significant and 19 lesser crossmatch errors were assigned in 2005 compared to 2004 (two significant and seven lesser errors). The committee's expectations for crossmatch testing have increased in recent years and will continue to be strictly applied.

Automation

An increasing number of participants have requested involvement with the automated survey, as they introduce instrumentation to their facilities. These tend to be large and medium sized facilities with considerable testing volume, indicating that a large percentage of transfusion testing is now being routinely tested by automated means. In light of this trend, automated surveys will be expanded to two per year.

Educational Survey

The first transfusion medicine Web-based educational challenge was used to address ongoing concerns regarding detection of mixed field agglutination using the three routine testing platforms for ABO and Rh testing. This venue enabled participants to make result interpretations based on their routine testing platform and determine the most likely cause of the identified results. They were also able to review reactions using the other platforms in order to make comparisons.

Facilities were encourage to use the Web-based survey to provide opportunities for review and competency of all staff involved in transfusion testing. Technical challenges were identified from the feedback provided by participants and will be used to enhance future Web-based surveys.

The success of this educational survey was demonstrated in the marked improvement in detection of mixed-field agglutination in subsequent routine challenges.

CHARACTERIZATION OF ERRORS

Contributing causes of discordant results were characterized as technical (attributable to actions of staff), methodological (problem in test system or procedure), clerical (transcription errors) and material (problem with EQA samples). The contributing causes of errors in transfusion medicine testing, as assessed by the laboratories, are shown in Figure 29.

CORRECTIVE ACTIONS

Extensive analysis and discussion appeared in Committee Comments during 2005 for the following:

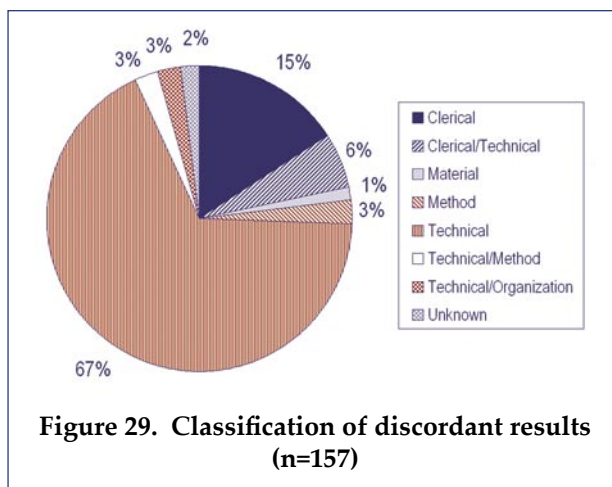
- procedures for prenatal antibody testing and titrations;
- recognition and causes of ABO and Rh mixed-field agglutination;
- policies and procedures for DAT investigation and;
- consequences of transcription errors.

PUBLICATIONS

The broadsheet on Rh Typing was updated and revised in 2005.

FUTURE ACTIVITIES

A scoring system is under development and will be used in parallel to the current assessment model during 2006. The Web-based survey format will be used to provide a “dry” educational challenge in 2006.



BACTERIOLOGY

TESTING MODEL

Table 50 shows an overview of the 2005 testing model. Four challenge surveys consisting of 16 samples for isolation and identification of 17 clinically significant microorganisms were distributed. Antimicrobial susceptibility testing was appropriate for ten of these organisms. Ten samples were lyophilized and six were simulated “fresh” specimens. The simulated “fresh” specimens included two wound swabs, a vaginal/rectal swab and one each of faeces, urine and blood. Four vials contained a mixture of organisms, as either representative commensal flora or multiple clinically significant organisms.

Four unstained smears for detection of acid-fast bacilli (AFB) were sent to those laboratories licensed to perform this testing.

Two questionnaire-based patterns-of-practice surveys were conducted. One questionnaire (BACT-0504-PP) accompanied the “fresh” simulated vaginal/rectal swab for prenatal Group B Streptococcus (GBS) screening and the second questionnaire (BACT-0506-PP) was sent to determine laboratory practices for specimens for anaerobic culture.

SURVEY ASSESSMENT

Participants’ results for identification, antimicrobial susceptibility testing and AFB detection were assessed against the consensus results of seven 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 putative site in the clinical scenario provided

Table 50. 2005 Bacteriology Surveys

BACT-0502	3 lyophilized cultures 1 “fresh” simulated wound swab
BACT-0504	2 lyophilized cultures 1 “fresh” simulated faecal specimen 1 “fresh” simulated vaginal/rectal swab
BACT-0504-AF	2 smears for acid-fast bacilli (AFB) staining
BACT-0504-PP	Patterns-of-practice survey: prenatal Group B Streptococcus screening
BACT-0506-PP	Patterns-of-practice survey: anaerobes
BACT-0509	2 lyophilized cultures 1 “fresh” simulated urine specimen 1 “fresh” simulated wound swab
BACT-0511	3 lyophilized cultures 1 “fresh” simulated blood culture specimen
BACT-0511-AF	2 smears for acid-fast bacilli (AFB) staining

Bacteriology

No. of Participants (Dec. 2005)	107*
No. of Participants (Dec. 2004)	113†
No. of Surveys Conducted in 2005	6

Mycology

No. of Participants (Dec. 2005)	22
No. of Participants (Dec. 2004)	22
No. of Surveys Conducted in 2005	2

* Includes laboratories licensed for Gram stain only

† Includes laboratories licensed for Gram stain and/or blood cultures only

Parasitology

No. of Participants (Dec. 2005)	19
No. of Participants (Dec. 2004)	22
No. of Surveys Conducted in 2005	2

Virology

No. of Participants (Dec. 2005)	75
No. of Participants (Dec. 2004)	72
No. of Surveys Conducted in 2005	10

and for not reporting the antibiotic of choice. Errors were assessed according to the potential impact a similar error would have on patient care. A significant error was assigned for results that were considered potentially clinically misleading and a lesser error was assigned for results outside of acceptable limits but considered not to have a negative impact on patient management. Errors were not assessed for some samples sent for educational purposes only.

LABORATORY PERFORMANCE

Isolation and Identification

Table 51 summarizes performance in organism isolation and identification. Noteworthy observations include:

- Methicillin-resistant *Staphylococcus aureus* (MRSA) (nasal swab, MRSA surveillance screen [BACT-0502-2]): Only 3/91 (3.3%) laboratories failed to report MRSA from this specimen. Two of these laboratories actually isolated the organism on their selective MRSA culture media but were unable to confirm oxacillin resistance for the isolate using the Mueller-Hinton agar + oxacillin (6 mg/L) screen plate (MHOX). This was excellent performance given that this was a heteroresistant MRSA strain known to grow poorly on MHOX. This challenge provided the opportunity to highlight the use of the cefoxitin disk test as a surrogate test to the MHOX for determining oxacillin results for both *S. aureus* and coagulase-negative staphylococci.
- Group B Streptococcus ("fresh" simulated vaginal/rectal swab, prenatal GBS screen, penicillin allergic patient (36 weeks gestation) [BACT-0504-4]): The specimen consisted of GBS mixed in equal proportions with *Escherichia coli* and *Enterococcus faecalis*. The presence of enterococci made this a difficult challenge but only 1/89 (1.1%) laboratories failed to isolate the GBS from this specimen.

Table 51. Organisms Distributed in 2005 and Performance in Identification

Survey	No. of Laboratories Reporting	Organism	%Correct * Identification (Excellent)	% Partial † Identification (Acceptable)	% Incorrect ‡ Identification (Unacceptable)
BACT-0502-1	91	<i>Salmonella</i> Enteritidis	1.1	98.9	0.0
BACT-0502-2§	91	Methicillin-resistant <i>Staphylococcus aureus</i>	96.7	0.0	3.3
BACT-0502-3	91	<i>Staphylococcus aureus</i>	100.0	0.0	0.0
BACT-0502-4	91	<i>Aeromonas hydrophila</i>	78.0	20.9	1.1
BACT-0504-1¶	98	<i>Campylobacter jejuni</i>	74.5	22.4	3.1
		No <i>Salmonella</i> , <i>Shigella</i> , <i>Campylobacter</i> , <i>Yersinia enterocolitica</i> or <i>E. coli</i> O157:			
BACT-0504-2#	98	H7 isolated	89.8	10.2	0.0
BACT-0504-3	89	<i>Stenotrophomonas maltophilia</i>	97.8	2.2	0.0
BACT-0504-4**	89	Group B Streptococcus	98.9	0.0	1.1
BACT-0509-1	90	<i>Streptococcus pneumoniae</i>	100.0	0.0	0.0
BACT-0509-2††	90	<i>Corynebacterium urealyticum</i>	31.3	38.9	29.8
BACT-0509-3	90	<i>Fusobacterium necrophorum</i>	31.1	63.3	5.6
BACT-0509-4	90	<i>Klebsiella pneumoniae</i>	98.9	0.0	1.1
BACT-0511-1‡‡	89	<i>Haemophilus influenzae</i>	85.4	3.4	11.2
BACT-0511-2	89	<i>Enterobacter sakazakii</i>	97.8	2.2	0.0
BACT-0511-3§§	96	<i>Saccharomyces cerevisiae</i>	18.8	72.9	8.3
BACT-0511-4A	89	<i>Bacteroides fragilis</i>	60.7	18.0	21.3
BACT-0511-4B	89	<i>Clostridium perfringens</i>	70.8	28.1	1.1
BACT-0511-4C	89	<i>Enterococcus faecalis</i>	78.7	16.9	4.5

* 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

§ Simulated lyophilized nasal swab specimen for MRSA surveillance screening

|| "Fresh" simulated wound swab

¶ "Fresh" simulated faecal specimen (mixture of *Campylobacter jejuni*, *Escherichia coli*, *Enterobacter cloacae* and *Enterococcus faecalis*)

Simulated lyophilized faecal specimen (pure culture of *Pseudomonas aeruginosa*)

** "Fresh" simulated vaginal/rectal swab for prenatal Group B Streptococcus screening (mixture of *Streptococcus agalactiae*, *Escherichia coli* and *Enterococcus faecalis*)

†† "Fresh" simulated urine specimen, educational challenge

‡‡ Simulated lyophilized sputum specimen [mixture of *Haemophilus influenzae* (predominant organism), *Haemophilus parainfluenzae*, non-pathogenic *Neisseria* species and viridans streptococcus]

§§ "Fresh" simulated blood culture specimen

|||| Mixed culture (simulated lyophilized bone biopsy from foot of diabetic patient)

- *Corynebacterium urealyticum* (“fresh” simulated urine, patient with history of kidney stones and ongoing urinary symptoms [BACT-0509-2]): This was an educational challenge and errors were not assessed. Sixteen laboratories reported ‘no growth obtained,’ which was not unexpected since this organism presented as very tiny colonies after 24 hours incubation on blood agar and grew even more poorly on CLED (Cystine-Lactose-Electrolyte-Deficient) agar. Only 28/90 (31%) laboratories isolated and correctly identified this organism to species level. While not difficult to identify, the key issue in this survey was recognizing the need to do so, since diphtheroid-like organisms are considered to be contaminants in urine cultures. However, *C. urealyticum* is associated with struvite stone formation and also alkaline encrusted cystitis. It was recommended that laboratories consider incubating urine culture plates longer than the traditional 18 to 24 hours for patients who are identified as having recurrent symptoms, especially those with a history of renal stones and in whom repeat urine cultures are negative and to screen Gram-positive, catalase-positive isolates present in significant numbers with a urease test.
- *Haemophilus influenzae* (good quality sputum specimen, patient with chronic obstructive pulmonary disease [BACT-0511-1]): This sample contained predominant numbers of *H. influenzae* mixed with *Haemophilus parainfluenzae*, non-pathogenic *Neisseria* species and viridans streptococcus. Of concern, 10/89 (11%) laboratories failed to report *H. influenzae*. Failure to do so was most often attributed to not recognizing that two types of *Haemophilus* species were present, not streaking the primary culture plates to achieve adequate isolated colonies so that *H. influenzae* could be recognized as predominant compared to the other organisms present or to the use of a blood agar plate with a ‘staph’ streak rather than chocolate agar to culture the specimen.
- *Bacteroides fragilis* (bone biopsy from foot of diabetic patient [BACT-0511-4]): Of 89 participating laboratories, 17 (19%) failed to report this organism, which was present in a mixed culture with *Clostridium perfringens* and *Enterococcus faecalis*. The common factor that led to this failure was not including a selective culture medium for anaerobic Gram-negative bacilli in the specimen set-up protocol. One of the “best-practice” recommendations made as a result of the patterns-of-practice survey on anaerobes (BACT-0506-PP) addressed the need to use a combination of selective media for primary culture of specimens expected to be polymicrobial.

The error rate for isolation and identification (3.4%) (Table 52) was lower than in 2004 (4.9%) and identical to that in 2003 (3.4%). Many of the significant errors (27/44) occurred for survey BACT-0511 for failing to report *H. influenzae* in vial 1 and *B. fragilis* in vial 4 as discussed above.

Table 52. Errors Assessed for Organism Isolation and Identification in 2005

Survey	No. of Laboratories	Opportunities for Error*	No. of Significant Errors	%	No. of Lesser Errors	%	No. of Total Errors	%
BACT-0502	91	364	3	0.8	5	1.4	8	2.2
BACT-0504	98	379	4	1.1	0	0.0	4	1.1
BACT-0509	90	360	5	1.4	4	1.1	9	2.5
BACT-0511	89	534	32	6.0	2	0.4	34	6.4
Total	...	1637	44	2.7	11	0.7	55	3.4

* Number of participating laboratories × number of organisms for isolation/identification

Antimicrobial Susceptibility Testing

A reference result was available for 2742 antimicrobial susceptibility testing results reported by laboratories and 97 (3.5%) results were flagged as being incorrect (Table 53). The majority of the flagged results were due to two antibiotic/organism combinations:

- Ampicillin for *Klebsiella pneumoniae* (BACT-0509-4): This isolate of *K. pneumoniae* was specifically selected as a challenge because of its unusual *in vitro* susceptibility to ampicillin. Fifteen laboratories reported an ampicillin-susceptible result but five commented that ampicillin would be reported resistant regardless of the *in vitro* result, which was also the practice for the 64 laboratories that reported ampicillin as resistant. This

practice was endorsed by the Microbiology Committee, which specifically recommended that laboratories report all *Klebsiella* species as ampicillin-resistant regardless of the *in vitro* testing results. Errors were not assessed to laboratories that reported an ampicillin-susceptible result.

- Quinolones for *Salmonella enterica* subsp. *enterica* serovar Enteritidis, blood culture, veterinary student (BACT-0502-1): This strain of *Salmonella* had reduced susceptibility to fluoroquinolones but tested susceptible *in vitro* to ciprofloxacin and levofloxacin using 2005 Clinical and Laboratory Standards Institute (CLSI) interpretive criteria. The reduced susceptibility to fluoroquinolones was detected by *in vitro* resistance to nalidixic acid as recommended in the CLSI standards. Forty-one laboratories reported a ciprofloxacin-susceptible result and three reported levofloxacin-susceptible. Of these, 22 laboratories added a comment to their report that the strain was nalidixic acid-resistant and therefore may not be eradicated by fluoroquinolone treatment as recommended by CLSI or indicated that the isolate would be referred for nalidixic acid testing. However, 20 (22%) laboratories reported a fluoroquinolone-susceptible result for this isolate without any cautionary comment, in spite of the fact that QMP-LS endorsed the CLSI recommendation in 2003 for testing extraintestinal isolates of fluoroquinolone-susceptible *Salmonella* against nalidixic acid. These laboratories were assessed a lesser error.

Table 53. Antimicrobial Susceptibility Testing Interpretive Error Flags in 2005

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	%
Amoxicillin/clavulanate	6	0	0	0	0	0.0	...	...	...	...	...	...
Ampicillin	251	20§	0	2	22	8.8	66	0	0	0	0	0.0
Azithromycin	0	...	...	...	...	...	1	0	0	0	0	0.0
Cefazolin	139	3	0	4	7	5.0	0	...	...	...	...	...
Ceftazidime	11	0	2	0	2	18.0	0	...	...	...	...	...
Cefotaxime	57	0	0	0	0	0.0	0	...	...	...	...	...
Cefoxitin	8	1	0	0	1	12.5	0	...	...	...	...	...
Cefotetan	1	0	0	0	0	0.0	0	...	...	...	...	...
Ceftriaxone	68	0	0	0	0	0.0	0	...	...	...	...	...
Cefuroxime	11	0	1	0	1	9.1	0	...	...	...	...	...
Cephalothin	40	0	1	0	1	2.5	0	...	...	...	...	...
Chloramphenicol	24	0	0	0	0	0.0	0	...	...	...	...	...
Ciprofloxacin	141	41	0	0	41	29.1	4	0	0	0	0	0.0
Clindamycin	0	...	...	...	...	...	105	8	0	0	8	7.6
Erythromycin	0	...	...	...	...	...	239	0	0	2	2	0.8
Gatifloxacin	0	...	...	...	...	...	3	0	0	0	0	0.0
Gentamicin	177	0	0	0	0	0.0	13	0	0	0	0	0.0
Gentamicin (high level)	0	...	...	...	...	...	37	0	0	0	0	0.0
Imipenem	21	0	0	0	0	0.0	0	...	...	...	...	...
Levofloxacin	36	3	0	0	3	8.3	48	0	0	0	0	0.0
Linezolid	0	...	...	...	...	...	2	0	0	0	0	0.0
Meropenem	19	0	0	0	0	0.0	0	...	...	...	...	...
Ofloxacin	0	...	...	...	...	...	0	...	...	...	...	...
Oxacillin	0	...	...	...	...	...	91	0	1	0	1	1.1
Penicillin	0	...	...	...	...	...	211	0	1	0	1	0.5
Piperacillin	28	0	0	0	0	0.0	0	...	...	...	...	...
Piperacillin/tazobactam	11	0	0	0	0	0.0	0	...	...	...	...	...
Streptomycin (high level)	0	...	...	...	...	...	21	0	1	0	1	4.8
Tetracycline	0	...	...	...	...	...	15	0	0	0	0	0.0
TMP/SMX	283	0	3	0	3	1.1	143	0	1	0	1	0.7
Tobramycin	15	0	0	0	0	0.0	0	...	...	...	...	...
Vancomycin	0	...	...	...	...	...	178	0	0	0	0	0.0
β-lactamase	133	2	0	0	2	1.5	85	0	0	0	0	0.0
Total	1480	70	7	6	83	5.6	1262	8	4	2	14	1.1

* 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 I when the reference result is S or R.

§ 15 for *Klebsiella pneumoniae* (BACT-0509-4)

|| All for *Salmonella enteritidis* (BACT-0502-1)

The error rate for incorrect antimicrobial susceptibility testing results (1.9%) (Table 54) was slightly lower than in 2004 (2.6%) but slightly higher than in 2003 (1.5%). The majority of the significant errors (6/8) were for reporting ampicillin or cefazolin as susceptible for *Enterobacter sakazakii* (BACT-0511-2). As a member of the SPICE group (i.e. *Serratia*, *Providencia*, *Morganella*, *Citrobacter*, *Enterobacter*), this organism is considered intrinsically resistant to ampicillin and first-generation cephalosporins and should be reported as such, regardless of *in vitro* testing results. This practice was recommended in 2004.

The number of errors (53) for inappropriate antimicrobial reports or failure to report antibiotic of choice (Table 55) was up significantly from 2004 (38) and 2003 (35) but almost half (21/51) of the inappropriate errors were assessed for reporting antibiotic susceptibility results for *Aeromonas hydrophila* (BACT-0502-4), an organism for which there are no CLSI interpretive criteria.

Table 54. Errors Assessed for Incorrect Antimicrobial Susceptibility Results in 2005

Survey	No. of Laboratories	Opportunities for Error*	No. of Significant Errors	%	No. of Lesser Errors	%	No. of Total Errors	%
BACT-0502	91	809	0	0.0	22	2.7	22	2.7
BACT-0504	89	337	0	0.0	7	2.1	7	2.1
BACT-0509	90	799	0	0.0	3	0.4	3	0.4
BACT-0511	89	837	8	1.0	13	1.6	21	2.5
Total	...	2782	8	0.3	45	1.6	53	1.9

* Number of participating laboratories × number of antibiotic results reported (with reference result available)—includes β-lactamase errors

Table 55. Errors Assessed for Reporting Inappropriate Antimicrobial Agents (for Organism and/or Site) or Failure to Report Antibiotic of Choice in 2005

Antimicrobial Agent(s)	Organism	No. of Significant Errors	No. of Lesser Errors
Ciprofloxacin	<i>Enterobacter sakazakii</i> (neonatal ICU patient)*	0	7
	<i>Enterococcus faecalis</i> †	0	5
Erythromycin	<i>Enterococcus faecalis</i>	0	1
Gentamicin	<i>Salmonella</i> Enteritidis	0	1
Levofloxacin	<i>Streptococcus agalactiae</i> (prenatal GBS screen)	0	1
	<i>Enterococcus faecalis</i> †	0	1
Meropenem, piperacillin/tazobactam and cefpodoxime	<i>Salmonella enteritidis</i>	0	1‡
Quinolone	<i>Salmonella enteritidis</i> §	0	2
Tetracycline	<i>Stenotrophomonas maltophilia</i>	0	1
	<i>Enterococcus faecalis</i> †	0	1
Not applicable	MRSA (nasal swab, MRSA surveillance screen) ¶	0	9
	<i>Aeromonas hydrophila</i> #	0	21
β-lactamase	<i>Klebsiella pneumoniae</i>	0	2
Total		0	53

* Inappropriate for neonate

† Inappropriate for non-urine isolate

‡ Lab noted would only be reported if requested by physician

§ Failure to report antibiotic of choice

|| No NCCLS disk diffusion interpretive criteria for this antibiotic/organism combination

¶ Inappropriate to report antimicrobial results for an isolate from a surveillance specimen

No NCCLS interpretive criteria for this organism

AFB Smear Interpretation

Performance on the four prepared smears of concentrated sputa for acid-fast staining and interpretation (Table 56) was not as good as in 2004 or 2003. One of the smears was particularly challenging (BACT-0504-AF-1), as there were only 10–20 AFB per slide. However, even the smears that were negative for AFB (BACT-0511-AF-1 and BACT-0511-AF-2) proved to be problematic for some laboratories. As a result the error rate for AFB smear interpretation (14.4%) (Table 57) was higher than it has been since 2000. Committee Comments for survey BACT-0504-AF provided guidance on potential sources of error for both fluorescent and carbol fuchsin staining methods.

Table 56. Performance in Microscopic Identification of AFB for Smears Distributed in 2005

Survey	No. of Laboratories Reporting	Quantity of Acid Fast Bacilli	%Correct* Identification (Excellent)	%Partial† Identification (Acceptable)	% Incorrect‡ Identification (Unacceptable)
BACT-0504-AF-1	37	Low moderate AFB present	64.9	0.0	35.1
BACT-0504-AF-2	37	Moderate AFB present	67.6	24.3	8.1
BACT-0511-AF-1§	36	No acid-fast bacilli present	86.1	0.0	13.9
BACT-0511-AF-2§	36	No acid-fast bacilli present	91.7	0.0	8.3

* 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

§ Same material used for both slides

Table 57. Errors Assessed for Incorrect AFB Interpretation in 2005

Survey	No. of Laboratories	Opportunities for Error*	No. of Significant Errors	%	No. of Lesser Errors	(%)	Total No. of Errors	(%)
BACT-0504-AF	37	74	10	13.5	3	4.1	13	17.6
BACT-0511-AF	36	72	2	2.8	6	8.3	8	11.1
Total	...	146	12	8.2	9	6.2	21	14.4

* Number of participating laboratories × number of slides

Patterns-of-Practice Surveys

Significant findings from the patterns-of-practice survey on prenatal genital specimens for GBS screening (BACT-0504-PP) were as follows:

- 96% (85/89) of Ontario laboratories licensed for bacteriology performed prenatal GBS screening on genital specimens.
- 96% (82/85) processed combined vaginal/anorectal swabs, 75% (64/85) processed vaginal swabs and 10% (9/85) processed endocervical swabs for GBS.
- 6% (5/85) required that the number of weeks gestation be provided with screening requests and 87% (74/85) accepted all specimens regardless of the number of weeks gestation.
- 31% (26/85) used selective enrichment broth only on initial processing, 42% (35/85) used a combination of selective broth and agar media and 28% (24/85) used culture protocols not in keeping with current guidelines.
- 30 laboratories subcultured the selective broth to blood agar (BA), 23 to colistin-nalidixic acid (CNA) agar, 4 to BA and CNA, 2 to BA and phenylethyl alcohol (PEA) agar, 1 to PEA and 1 to BA with neomycin.
- Protocols for GBS bacteriuria during pregnancy were as follows: 35 laboratories reported GBS from urine when pregnancy was noted, 20 from all women of childbearing age, 5 on all urines from female patients and 21 on all urines regardless of sex or age; 46 reported any amount of GBS present in these urine specimens, 30 if the count was $\geq 10 \times 10^6$ CFU/L, 5 if $\geq 100 \times 10^6$ CFU/L, 1 if $\geq 50 \times 10^6$ CFU/L and 1 if 'significant growth.'
- 60% (51/85) routinely performed antibiotic susceptibility testing on all GBS isolates from prenatal screening specimens and 19 (22%) did so only on request; all tested erythromycin, 68 tested clindamycin and 32 tested vancomycin; 31 laboratories automatically reported clindamycin as resistant if macrolide-resistant and 36 performed the disk approximation test to screen for inducible clindamycin resistance.

Results of this survey were compared to the 2002 recommendations of the Centers for Disease Control and Prevention (CDC), Atlanta and the 2004 guidelines published by the Society of Obstetricians and Gynaecologists of Canada (SOGC). Findings and a summary of the current guidelines encouraging laboratories to update their protocols were distributed as Committee Comments.

Significant findings from the patterns-of-practice survey on specimens for anaerobic culture (BACT-0506-PP) were as follows:

- 97% (87/90) of Ontario laboratories licensed for bacteriology processed specimens for anaerobes.
- 74% (64/87) had rejection criteria for specimens for which anaerobic culture was requested.
- 53% (46/87) had a time restriction for specimen collection to receipt in the laboratory.
- 98% (85/87) performed a direct Gram stain on specimens for anaerobes.
- 28% (24/87) only used a non-selective agar medium for primary culture of anaerobes and 97% (84/87) also used an enrichment broth.
- 94% (82/87) waited 42 to 48 hours before examining primary isolation plates for anaerobes and 60% (52/87) reincubated plates after initial examination even if there was growth.
- 66% (57/87) incubated anaerobic culture plates for a total of five or more days.
- 70% (61/87) used either a stereomicroscope or magnifying lens to examine primary isolation plates for anaerobes.
- 30% (26/87) were able to identify most anaerobes to species level, 52% (45/87) to genus level and 18% (16/87) to Gram stain morphotype.
- 7% (6/87) performed AST on anaerobes; all used the Etest® method.

Findings and “best-practice” recommendations were distributed as Committee Comments. Feedback on the recommendations was invited from participating laboratories and guidelines were published in January 2006.

CAUSE ANALYSIS OF DISCORDANT RESULTS

For the third consecutive year, laboratories were asked to complete an investigation form to assist them in performing cause analysis for their discordant results on QMP-LS surveys. This information was assessed and collated to determine the factors that contributed to reporting of discordant results on bacteriology surveys. Contributing causes were classified as clerical, technical, method or organization-related.

Antibiotic Susceptibility Testing

There were three categories of antibiotic discordance in 2005—incorrect antibiotic results (including β -lactamase testing), reporting inappropriate antibiotics for the organism and/or site and failure to report the antibiotic of choice. Discordant antibiotic results were almost equally divided between incorrect and inappropriate results with only a small proportion due to not reporting the antibiotic of choice (Figure 30). As in the previous two years, the majority of discordant antibiotic results for all categories of antibiotic discordance were due to method-related problems (Figure 31).

The most significant contributing cause of method-related errors was antibiotic testing/reporting protocols that were not in accordance with CLSI standards (e.g. reporting antibiotic results for *A. hydrophila*, reporting ciprofloxacin on a non-urine isolate of *E. faecalis*, not testing an extra-intestinal isolate of *Salmonella* for decreased susceptibility to fluoroquinolones with the surrogate nalidixic acid test) (Figure 32). This type of error is readily preventable if laboratories put a process in place to ensure that they receive,

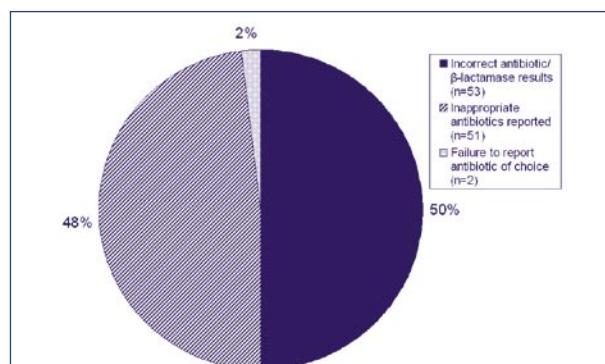


Figure 30. Categories of antibiotic discordance for 2005 bacteriology surveys (n=106)

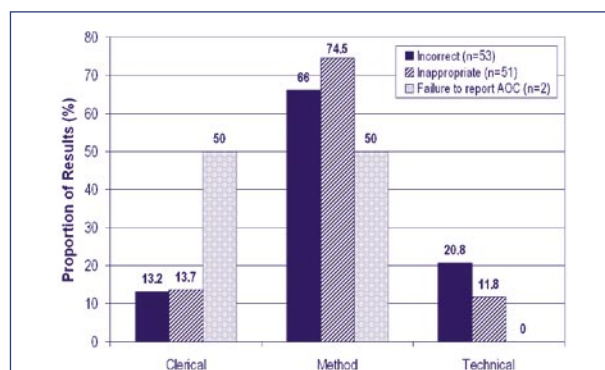


Figure 31. Contributing causes of discordant antibiotic results in 2005 bacteriology surveys (n=106)

review and implement any changes recommended in the CLSI susceptibility testing standards, which are updated annually. Other standard operating procedure (SOP)-related problems such as procedures not in accordance with current standard of practice (e.g. antibiotic reporting protocol for MRSA from surveillance specimens not specific to agents used for eradication therapy) were also important contributors to method problems. Laboratory information system (LIS) software problems (e.g. system not programmed to apply antibiotic reporting rules based on age or specific organism/antibiotic combinations or failure to validate that the rules worked properly) and failure of the automated susceptibility testing system to generate the correct result were other method-related factors.

Technical-related errors were due to failing to follow SOPs (e.g. not incubating a β -lactamase test for the full 30 minutes as specified or testing *Klebsiella pneumoniae* for β -lactamase production even though this was not part of the documented protocol), an error in the interpretation of a test result (e.g. interpretation of the trimethoprim-sulfamethoxazole disk diffusion result for *Stenotrophomonas maltophilia* where the haze of growth was interpreted as falsely resistant), use of an incorrect inoculum or because a task was poorly performed (Figure 33).

Almost half of the clerical errors (46%) were due to manual transcription of results to the QMP-LS Analysis Worksheet as opposed to issuing a computer-generated report, which is the usual practice for patient specimens (Figure 34). An example was the reporting of ciprofloxacin on a non-urine isolate for *E. faecalis* (BACT-0511-4), a result that would have been automatically suppressed by the LIS for a patient report. To prevent this type of error, laboratories should generate reports for QMP-LS samples in the same way as for patient samples and use that report to manually enter the results on the QMP-LS Analysis Worksheet. Other clerical-related problems were due to transcription of the antibiotic result, failing to add a qualifier to the report and manual labelling of QMP-LS specimens versus computer labelling of patient specimens.

Isolation and Identification

There were three categories of identification discordance—failure to isolate or report the target organism, incorrect identification and reporting an organism that was not present in the sample (i.e. over-reporting) (Figure 35). Failure to isolate the target organism was the most

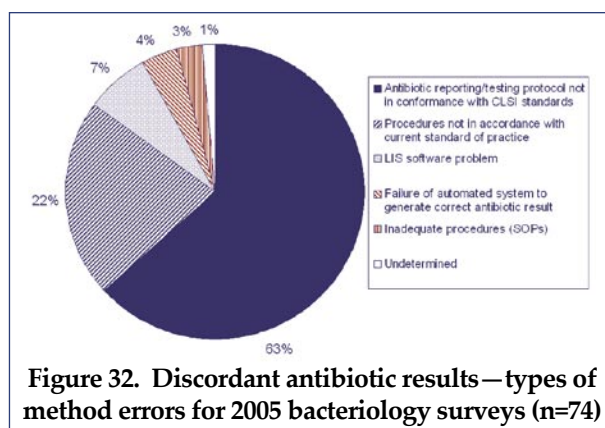


Figure 32. Discordant antibiotic results—types of method errors for 2005 bacteriology surveys (n=74)

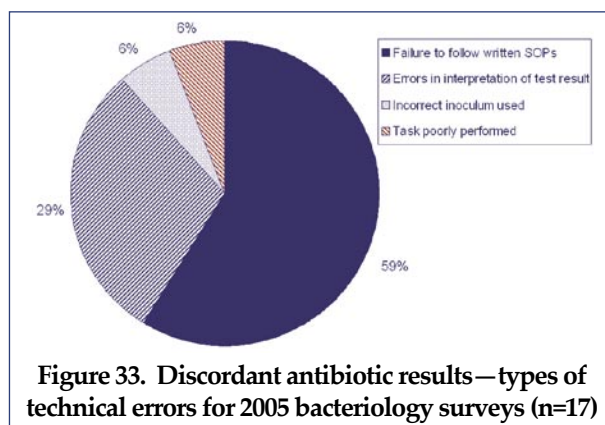


Figure 33. Discordant antibiotic results—types of technical errors for 2005 bacteriology surveys (n=17)

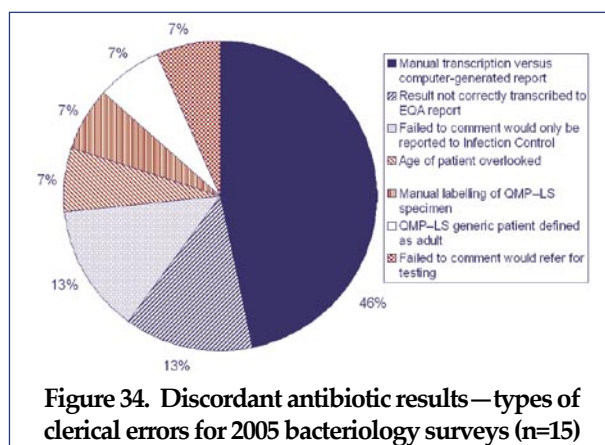


Figure 34. Discordant antibiotic results—types of clerical errors for 2005 bacteriology surveys (n=15)

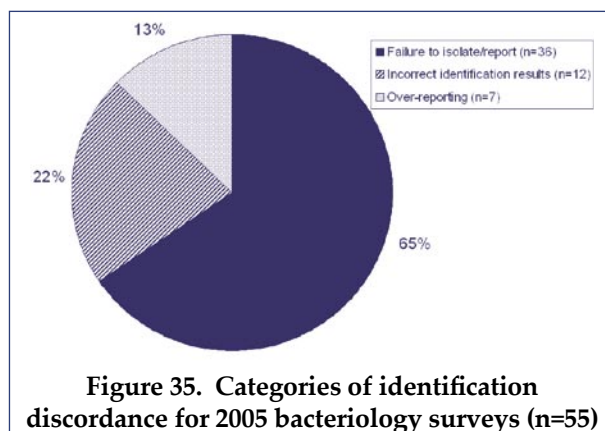


Figure 35. Categories of identification discordance for 2005 bacteriology surveys (n=55)

common type of discordant identification result in 2005 and method or technical-related problems or a combination of the two contributed fairly equally to this type of discordance (Figure 36). Incorrect identification and over-reporting were primarily due to technical factors. One laboratory indicated an incorrect identification was due to failure to ensure that situational knowledge was transferred to all rotating staff (organization-related).

Most (80%) of the method-related errors were due to inadequate SOPs (e.g. not including a selective medium for anaerobic Gram-negative bacilli on a bone biopsy specimen from a diabetic foot) (Figure 37). Other contributing factors were an inaccurate method (e.g. using mannitol salt agar with 6 mg/L of oxacillin for isolation of MRSA from a surveillance specimen), inadequate QC, a problem with equipment function or inappropriate incubation conditions (e.g. not incubating cultures for *Campylobacter jejuni/coli* at 42°C). A variety of factors contributed to technical-related errors such as failure to observe a mixed culture, contamination of the survey material during the set-up process, misinterpretation of Gram stain morphology, failure to correlate the Gram stain with culture results, an error in the interpretation of the test result, mixing up samples, failure to follow instructions on the Analysis Worksheet and using an incorrect inoculum (Figure 38). There was only one clerical error in which the result was not correctly transcribed to the QMP-LS report.

NUMBER OF PROVIDERS

The number of laboratories that provide a comprehensive testing menu in bacteriology decreased by three in 2004 (Figure 39). Three laboratories licensed for AFB smear interpretation have dropped this testing since 2004 (Figure 40).

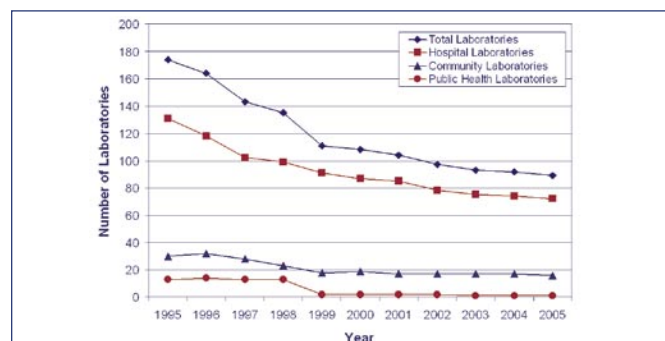


Figure 39. Number of bacteriology laboratories in Ontario by facility type

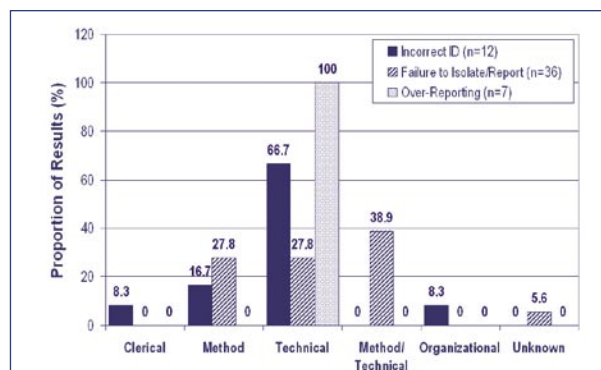


Figure 36. Contributing causes of discordant identification results in 2005 bacteriology surveys (n=55)

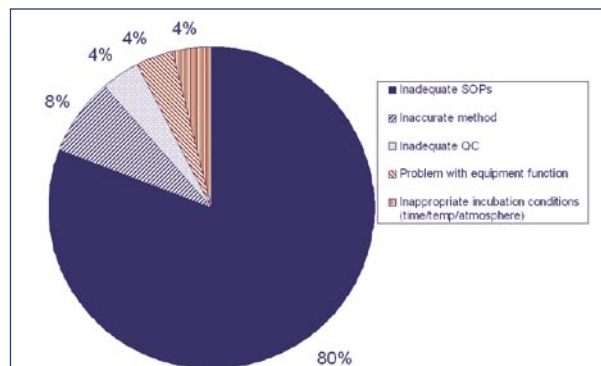


Figure 37. Discordant identification results—types of method errors for 2005 bacteriology surveys (n=26)

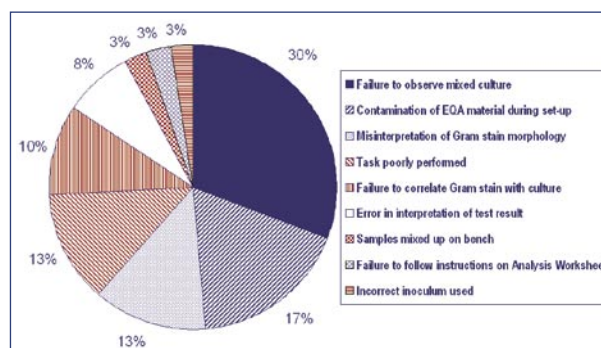


Figure 38. Discordant identification results—types of technical errors for 2005 bacteriology surveys (n=39)

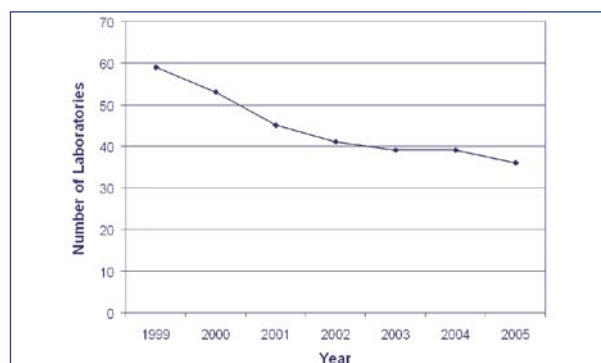


Figure 40. Number of laboratories performing AFB smear examination

MYCOLOGY

TESTING MODEL

In 2005, two surveys were conducted consisting of nine challenge samples. As in previous surveys, the challenges were selected from the three groups of medically significant fungi—dermatophytes, yeasts and moulds. For the first time since the inception of the mycology program, QMP-LS purchased testing material from a commercial supplier, Sporometrics Inc., on a cost recovery basis. Cultures are being purchased by Sporometrics from well known culture collections like:

- University of Alberta Microfungus Collection and Herbarium, Edmonton, Alberta (UAMH);
- the Centraalbureau voor Schimmelcultures, The Netherlands, (CBS) and;
- Agricultural Research Service (ARS) Culture Collection, National Center for Agricultural Utilization Research, Peoria, Illinois, U.S.A.

Sporometrics, Inc. provides a certificate of analysis for each of the specimens with detailed information fully characterizing the strain as a type culture with all quality assurance testing results. Sporometrics prepares the culture for surveys by:

- subculturing from the lyophilized culture;
- assuring consistency with the expected phenotypic features of the organism;
- preparing sufficient vials for participants;
- conducting viability, stability and homogeneity controls and;
- labelling vials and supplying the distributor according to a prescribed timeline.

Testing material was distributed to laboratories as live cultures on agar slants. The type of specimen, hypothetical microscopic information and a limited clinical history were provided to participants on the Analysis Worksheets. Laboratories were required to process the cultures as if they were patient specimens. The licence to perform mycology culture includes yeasts and/or dermatophytes and/or systemic fungi. Some laboratories may not routinely culture specimens in all categories. All challenge samples are sent to laboratories and each laboratory reports based on its level of practice. Performance assessment of submitted results is correlated with that laboratory's stated level of practice. Four reference laboratories include the Toronto Public Health Laboratory, Wadsworth Centre for Laboratories and Research, Albany, New York, Laboratoire de Santé Publique du Québec and University of Toronto, Occupational and Environmental Health Laboratory.

The identification of organisms by the OSIMIB code is the only component of the survey that is currently scored. Until now, extensive information provided by participants as a required element of the Analysis Worksheets (including isolation media, macroscopic and microscopic findings, other identification features) was captured in the survey database. However, although reviewed, it was used only occasionally to evaluate performance. This year the committee reviewed and extensively revised the format of the worksheet. The new format is consistent with the Bacteriology Analysis Worksheet, with codes provided to participants for all key features used to describe mycology organisms. Participants enter principle test results used to inform their decision for the OSIMIB code they reported. Using both new and old Analysis Worksheets, a pilot study was conducted in August (MYCO-0508) by the Microbiology Committee laboratories. No issues arose with the new Analysis Worksheet. The revised Analysis Worksheet will be implemented for all participants in 2006.

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. Laboratories received photomicrographs of distinguishing microscopic characteristics of the fungi used in the challenges as a component of Committee

Comments. The photography was generously provided on the actual cultures used in the challenge by Dr. James Scott, University of Toronto, Faculty of Medicine.

Laboratory Participation

The number of laboratories participating in Ontario at the end of 2005 was 22 (Figure 41), the same as 2004. In 2005, 21/22 laboratories handled yeasts (including yeast from systemic infections); 19/22 reported results for dermatophytic fungi from superficial skin specimens, while 21/22 licensed laboratories cultured fungi from systemic specimens. One mycology laboratory refers all specimens from systemic infections; three mycology laboratories refer all superficial samples involving dermatophytes. Specimen referral patterns for identification of organisms varied with the nature of the agent isolated.

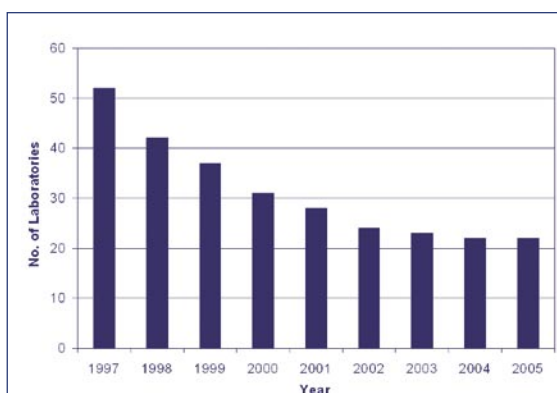


Figure 41. Laboratories participating in mycology surveys, 1997–2005

Overall Performance

Challenge Surveys

Laboratory performance on survey MYCO-0505 was good (Tables 58 and 59). Of 23 laboratories, 16 reported *Aspergillus flavus*, *Bipolaris* sp., and *Candida tropicalis* correctly to species. The majority of remaining laboratories gave an acceptable identification based on their level of practice—named to the genus level, or to a general classification, which would necessitate referral to a reference laboratory. One laboratory reported *Aspergillus flavus* as *A. fumigatus*, which resulted in a lesser error. One laboratory that was assigned a significant error failed to grow the *Bipolaris* sp. Of 21 laboratories, five correctly identified *Chrysosporium keratinophilum* with 16/21 giving an acceptable identification requiring referral.

Table 58. 2005 Organism Distribution and Survey Performance*

Survey	No. of Laboratories Reporting	Organism	Correct† Identification (%) (Excellent)	Partial‡ Identification (Acceptable)	Incorrect§ Identification (%) (Unacceptable)
MYCO-0505-1	23	<i>Aspergillus flavus</i>	16/23 (69.6)	6/23 (26.1)	1/23 (4.3)
MYCO-0505-2	23	<i>Bipolaris</i> sp	16/23 (69.6)	6/23 (26.1)	1/23 (4.3)
MYCO-0505-3	23	<i>Candida tropicalis</i>	16/23 (69.6)	7/23 (30.4)	0/23
MYCO-0505-4	21	<i>Chrysosporium keratinophilum</i>	5/21 (23.8)	16/21 (76.2)	0/21
MYCO-0508-1	22	<i>Aspergillus sydowii</i>	10/22 (45.5)	10/22 (45.5)	2/22 (9.1)
MYCO-0508-2	24	<i>Candida krusei</i>	18/24 (75.0)	6/24 (25.0)	0/24
MYCO-0508-3	24	<i>Absidia corymbifera</i>	11/24 (45.8)	13/24 (54.2)	0/24
MYCO-0508-4	24	<i>Exophiala dermatitidis</i>	13/24 (54.2)	13/24 (54.2)	0/24
MYCO-0508-5	22	<i>Microsporum canis</i>	19/22 (86.4)	3/22 (13.6)	0/22
Total	206				

* Numbers include reference laboratories

† 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

Table 59. Comparison of Performance Between Survey MYCO-0505 and Past Surveys

	MYCO-0505	Previous Survey
<i>Aspergillus flavus</i>	16/23 (69.6 %) correct; 1 SE	B-9703-W-4: 30.6 % of 49 correct; 12.3 % incorrect
<i>Bipolaris</i> sp.	First challenge: 16/23 (69.6 %) correct; 1 SE	...
<i>Candida tropicalis</i>	First challenge: 16/23 (69.6 %) correct; no errors	...
<i>Chrysosporium keratinophilum</i>	First challenge: 5/21 correct; 16/21 acceptable	...

Performance for MYCO-0508 is summarized in Tables 58 and 60. Participants were introduced to *Asperillus sydowii* and *Exophiala dermatitidis* for the first time. Approximately half correctly identified both to species. *Aspergillus sydowii* was incorrectly identified by two laboratories as *Scopulariopsis*. Five laboratories placed the organism in the *Aspergillus versicolor* group which may have resulted from copper/zinc deficient media not allowing complete pigment production. This is not considered an error but is discussed in the Committee Comments. Participants received their second challenge with *Candida krusei* since 1997. Of 24 participants, 18 (75.0 %) correctly reported *Candida krusei*, and the rest gave an acceptable identification. Previously in survey B-9703-W-3, 68.0% of 50 participants correctly identified *Candida krusei*; 26.0% provided identification to genus, or correct general classification; 6.0% were incorrect. Participants were previously introduced to *Absidia corymbifera* in 1998 (B-9803-W-2) where only 17.1% of 35 participants correctly identified the organism; 48.6% provided partial identification and 34.3% were incorrect. In MYCO-0508-3 there were no errors by participants with 11/24 (45.8 %) laboratories correctly identifying *Absidia corymbifera*. Of 24 laboratories, 5 correctly indicated the organism as *Absidia* species; 5 indicated it was a zygomycete and 3 a filamentous fungus. Participants received *Microsporum canis* in 1998 (B-9803-W-3). MYCO-0508-5 marked the second challenge. The performance was better than the 1998 survey with 19/22 (86.4%) reporting the organism as *Microsporum canis*, 1 as *Microsporum* species and 2 a filamentous fungus. In 1998, 78.4% of 37 participants provided the correct identification; 16.2% provided identification to genus or a general classification (filamentous fungus) considered acceptable for their level of service; 5.4% were incorrect.

The most desirable scenario to be projected for mycology performance would be an increase in laboratories able to identify organisms completely or, at minimum, to genus. Characterization of filamentous fungi takes days to weeks. If the primary laboratory handling the specimen identification cannot at least place the organism into the correct genus, a further delay ensues while the culture is sent to a reference laboratory. More time passes as the reference laboratory subcultures and characterizes the organism. In 2006 the committee hopes to focus on wording and clinical relevance of reports.

Table 60. Comparison of Performance Between Survey MYCO-0508 and Past Surveys

	MYCO-0508	Previous Surveys
<i>Aspergillus sydowii</i>	First challenge: 10/22 (45.5 %) correct; 2 SE	...
<i>Candida krusei</i>	18/24 (75.0 %) correct	B-9703-W-3: 68.0% of 50 correct
<i>Absidia corymbifera</i>	11/24 (45.8 %) correct; no errors	B-9803-W-2: 17.1% of 35 correct; 34.3% incorrect
<i>Exophiala dermatitidis</i>	First challenge: 13/24 (54.2 %) correct; no errors	...
<i>Microsporum canis</i>	19/22 (86.4 %) correct; no errors	B-9803-W-3: 78.4% of 37 correct; 5.4% incorrect

PARASITOLOGY

TESTING MODEL

Two surveys were conducted in 2005, each consisting of three vials of SAF-preserved faecal specimens. Laboratories were required to prepare both a concentrate and stained smear from each sample and report findings from both preparations.

SURVEY ASSESSMENT

Performance was evaluated by comparing participants' results to the consensus results of ten referee laboratories. The ten participating laboratories with the highest average score over the preceding four surveys were designated as the referee group for each survey. The collated results of these laboratories were used to determine the scoring scheme and flagging criteria. A result was scored if more than 50% of the referee laboratories reported it. Three marks were awarded for each correct stage and quantity of parasite reported and two marks were awarded if the quantity reported fell outside the expected range. Three marks were deducted for reports of parasite species not present in the sample (i.e. over-reporting).

Errors were assigned only when a parasite was not reported in both the concentrate and stained smear preparation or if a parasite not actually present in the specimen was reported in either the concentrate or stained smear. Errors for failing to report a parasite were not assessed unless there was at least 90% agreement among the referee laboratories. A significant error was assigned for either failing to report or over-reporting a pathogenic parasite and a lesser error was assigned for failing to report or over-reporting a non-pathogenic parasite.

LABORATORY PERFORMANCE

Performance on the two surveys was excellent and is summarized in Table 61. The six samples contained a total of 14 different parasite species, including 6 amoebae, 2 flagellates, 5 helminths and *Blastocystis hominis*. One of the samples was negative for parasites.

Three significant and ten lesser errors were assessed for an overall error rate of 3.9%, down from 2004 (5.8%) and 2003 (5.7%) (Table 62). The significant errors were for over-reporting *Cyclospora cayetanensis* (1) in survey PARA-0505-2 and for misidentifying *Entamoeba polecki* as *Entamoeba histolytica/dispar* (2) in survey PARA-0505-3.

CAUSE ANALYSIS OF DISCORDANT FINDINGS

For the third consecutive year, laboratories were asked to complete an investigation form to assist them in performing cause analysis for their discordant results on parasitology surveys. This information was assessed and collated to determine the factors that contributed to reporting of discordant results. Contributing causes were classified as clerical, technical, method or organization-related.

There were three categories of discordant results for 2005 parasitology surveys—failing to report a parasite that was deemed to be present by the referee laboratories, misidentifying a parasite as the wrong species and reporting a parasite that was not present in the specimen. Over-reporting accounted for almost half of the discordant results (Figure 42). The contributing cause of all of the discordant results was related to technical factors, which included misinterpretation of organism morphology and failure to follow the instructions on the Analysis Worksheet (Figure 43).

NUMBER OF PROVIDERS

The number of parasitology laboratories in Ontario decreased by four (two hospital and two community laboratories) since 2004 leaving a total of 19 testing facilities (Figure 44).

Table 61. Overall Performance of Referee and Participating Laboratories in 2005

Survey	Expected Parasite	Quantity	Referee Agreement	%	Participant Agreement	%*
PARA-0505-1C (Concentrate)	<i>Entamoeba histolytica/dispar</i> cysts	D	10/10	100	20/20	100
	<i>Entamoeba histolytica/dispar</i> cysts	D	10/10	100	20/20	100
	<i>Entamoeba histolytica/dispar</i> trophozoites	D	10/10	100	20/20	100
PARA-0505-1S (Stained slide)	Small flagellate trophozoites or <i>Enteromonas hominis</i> trophozoites	B	7/10	70	15/20	75†
PARA-0505-2C (Concentrate)	Hookworm ova	A	8/10	80	17/20	85†
	<i>Schistosoma mansoni</i> ova	A	6/10	60	13/20	65†
PARA-0505-2S (Stained slide)	Hookworm ova	A	4/10	40	9/20	45†
	<i>Schistosoma mansoni</i> ova	A	5/10	50	9/20	45†
	<i>Fasciola/Fasciolopsis</i> ova	B	10/10	100	20/20	100
	<i>Hymenolepis nana</i> ova	A	5/10	50	7/20	35†
	<i>Schistosoma mansoni</i> ova	D	10/10	100	20/20	100
PARA-0505-3C (Concentrate)	<i>Endolimax nana</i> cysts	B	10/10	100	19/20	95
	<i>Entamoeba polecki</i> cysts	C	10/10	100	15/20	75
	<i>Fasciola/Fasciolopsis</i> ova	A	10/10	100	19/20	95
	<i>Hymenolepis nana</i> ova	A	5/10	50	8/20	40†
	<i>Schistosoma mansoni</i> ova	C	10/10	100	20/20	100
	<i>Endolimax nana</i> cysts	B	10/10	100	20/20	100
	<i>Endolimax nana</i> trophozoites	C	10/10	100	20/20	100
	<i>Entamoeba polecki</i> cysts	B	10/10	100	17/20	85
	<i>Entamoeba polecki</i> trophozoites	C	10/10	100	17/20	85
PARA-0505-3S (Stained slide)	Small flagellate trophozoites or <i>Enteromonas hominis</i> trophozoites	B	7/10	70	15/20	75†
	<i>Strongyloides stercoralis</i> larvae	C	10/10	100	19/19	100
	<i>Endolimax nana</i> cysts	A/B	4/10	40	6/19	32†
	<i>Entamoeba coli</i> cysts	D	10/10	100	19/19	100
	<i>Entamoeba hartmanni</i> cysts	B	10/10	100	19/19	100
	<i>Entamoeba histolytica/dispar</i> cysts	A	5/10	50	8/19	42†
PARA-0510-1C (Concentrate)	<i>Iodamoeba buetschlii</i> cysts	D	10/10	100	19/19	100
	<i>Blastocystis hominis</i>	D	7/10	70	13/19	68
	<i>Strongyloides stercoralis</i> larvae	C	10/10	100	19/19	100
	<i>Endolimax nana</i> cysts	A	3/10	30	6/19	32†
	<i>Endolimax nana</i> trophozoites	A	4/10	40	6/19	32†
	<i>Entamoeba coli</i> cysts	C	10/10	100	19/19	100
	<i>Entamoeba coli</i> trophozoites	C	10/10	100	19/19	100
	<i>Entamoeba hartmanni</i> cysts	B	10/10	100	19/19	100
	<i>Entamoeba hartmanni</i> trophozoites	B	10/10	100	19/19	100
	<i>Entamoeba histolytica/dispar</i> cysts	A	6/10	60	8/19	42
	<i>Entamoeba histolytica/dispar</i> trophozoites	A	9/10	90	16/19	84
	<i>Iodamoeba buetschlii</i> cysts	D	10/10	100	19/19	100
PARA-0510-1S (Stained slide)	<i>Iodamoeba buetschlii</i> trophozoites	D	10/10	100	19/19	100
	<i>Blastocystis hominis</i>	D	10/10	100	16/19	84
PARA-0510-2C (Concentrate)	No parasites seen	X	10/10	100	19/19	100
PARA-0510-2S (Stained slide)	No parasites seen	X	10/10	100	19/19	100
PARA-0510-3C (Concentrate)	No parasites seen	X	5/10	50	6/19	32
	or <i>Blastocystis hominis</i>	D	5/10	50	13/19	68
PARA-0510-3S (Stained slide)	<i>Dientamoeba fragilis</i> trophozoites	D	10/10	100	19/19	100
	<i>Blastocystis hominis</i>	E	10/10	100	18/19	95

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

* All laboratories including referee laboratories

† No errors assessed due to low referee agreement

Table 62. Errors Assessed in Parasitology in 2005

Survey	No. of Laboratories	Opportunities for Error*	No. of Significant Errors	%	No. of Lesser Errors	%	No. of Total Errors	%
PARA-0505	20	180	3	1.7	3	1.7	6	3.3
PARA-0510	19	152	0	0.0	7	4.6	7	4.6
Total	...	332	3	0.9	10	3.0	13	3.9

* Number of participating laboratories x number of parasites present

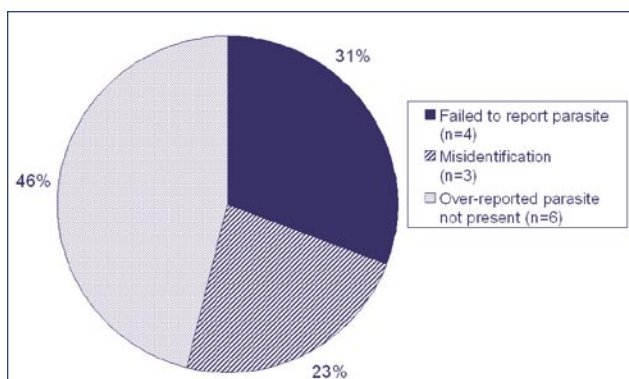


Figure 42. Categories of discordant results for 2005 parasitology surveys (n=13)

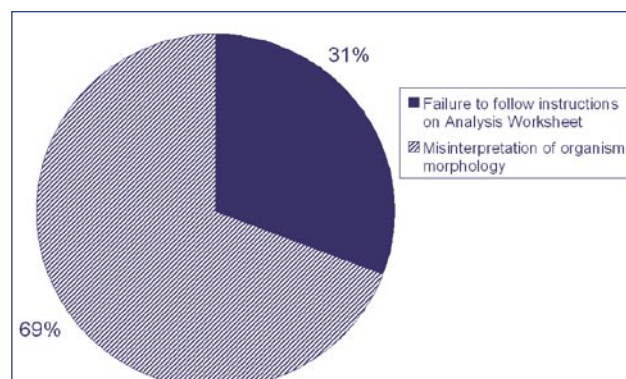


Figure 43. Discordant results—types of technical errors for 2005 parasitology survey

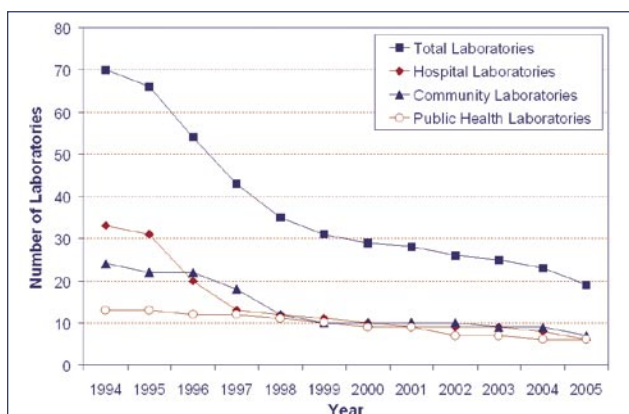


Figure 44. Number of parasitology laboratories by facility type

VIROLOGY

TESTING MODEL

Four surveys were conducted during 2005. Traditionally, the two fall surveys were conducted in October and November; however in 2005, these were scheduled earlier (September and October). The change was intended to reduce the time required to provide participants with Committee Comments and correspondence. The committee met in November to review the fall surveys, which allowed the Committee Comments to be completed in January 2006. More improvement is planned for 2006.

Tables 63 and 64 show the number of laboratories participating for each survey. Each survey contained five samples per viral agent. The Chlamydia surveys also contained five samples per survey. The VIRO-0502 and VIRO-0509 panels contained serum or plasma samples to be tested for antibody and/or antigen to hepatitis A virus (HAV), hepatitis B virus (HBV) hepatitis C virus (HCV), and samples for human immunodeficiency virus (HIV) antibody screening. VIRO-0503 and VIRO-0510 panels contained three components:

- serum or plasma samples for rubella virus, varicella-zoster virus (VZV) and cytomegalovirus (CMV);
- chlamydial antigen and;
- respiratory antigens to be tested according to individual laboratory protocol for influenza A and B virus, respiratory syncytial virus (RSV), adenovirus and parainfluenza virus 1, 2 and 3.

The challenge material for HAV, HBV, HCV, HIV and rubella/VZV/CMV surveys was either serum or plasma, not heat or otherwise inactivated. Material for chlamydia, RSV, influenza A virus challenges was obtained from a commercial source.

In addition to the Ontario laboratories participating in the surveys, four out-of-province laboratories participated in portions of the virology surveys (three for hepatitis and one for the respiratory panel).

SURVEY ASSESSMENT

For surveys VIRO-0502 and VIRO-0503 participant results were compared to those obtained by reference laboratories. Reference laboratories were the laboratories of Virology Committee members. For VIRO-0509 and VIRO-0510 the number of reference laboratories was reduced to one—the Toronto Public Health Laboratory. The reduction in the amount of reference testing followed a review of how reference results were being used and an estimate of the cost of that testing. Discordant results from the reference results were flagged. Errors were assessed as being either significant or lesser errors depending on the potential impact of the reported results on patient outcomes or risk for disease transmission. The summary of errors is shown in Table 65.

Table 63. Number of Laboratories Reporting Results for 2005 Hepatitis and HIV Panels

Virus	Marker	VIRO-0502	VIRO-0510
Hepatitis B	HBsAg	41	40
	Anti-HBs	38	36
	Anti-HBc	32	31
	Anti-HBc IgM	14	12
	HBeAg	11	10
	Anti-HBe	10	9
	Anti-HAV	21	18
	Anti-HAV IgM	23	20
Hepatitis C	HCV antibody screen test	31	30
HIV	HIV antibody screen test	17	16

Table 64. Number of Laboratories Reporting Results for 2005 Chlamydia, Direct Respiratory Viral Antigen Testing and Rubella/VZV/CMV Serology Panels

Viral Agent Reported	Number of Laboratories Reporting by Survey	
	VIRO-0509	VIRO-0503
Adenovirus	6	6
Influenza A	38	38
Influenza B	35	34
Parainfluenza 1	6	5
Parainfluenza 2	6	5
Parainfluenza 3	6	5
RSV	50	47
Chlamydia	16	17
Rubella antibody	26	28
Varicella Zoster (VZV) antibody	12	11
Cytomegalovirus (CMV)	10	10

Table 65. Error Assessment for Ontario Laboratories in 2005 Virology Surveys

Analyte	Number of Sites for Two 2005 Surveys	Opportunities for Error	Significant Error	Lesser Error	Total Errors	Error Rate (%)
Chlamydia	33	330	1	...	1	0.30
HIV	33	165	2	1	3	1.82
HCV	61	305	1	1	2	0.66
Hepatitis A and B	366	1830	7	...	7	0.38
Rubella/VZV/CMV	97	2910	3	2	5	0.14
Respiratory Antigen	290	1450	8	2	10	0.69
Total	880	6990	22	6	28	0.40

OVERALL PERFORMANCE

Chlamydia trachomatis

In 2005, the number of Ontario laboratories participating was 17 compared with 18 in 2004. The performance for chlamydia improved in 2005 as the overall error rate declined to 0.30 % from 0.57% in 2004. One sample (VIRO-0509-C2) most likely contained a low level of chlamydial antigen, which was not intended for this challenge. Only laboratories using assays based on nucleic acid amplification (NAA) reported VIRO-0509-C2 positive. Participants using non-amplified assays like DNA probe, EIA, or DFA, reported VIRO-0509-C2 negative. The results reported for this vial were not scored. This incident and other problems that occurred in 2004 and again in 2005 with respiratory antigen testing material prompted a search for an alternate supplier.

Hepatitis A, B and C

The Analysis Worksheets for survey VIRO-0510 were revised from previous surveys and participants were required:

- to record numerical values for the signal, with cut off, for the assay;
- to interpret the result by indicating if the value reported was considered positive or negative and;
- to provide the HBV and HAV immune status.

Previously the survey analysis was qualitative only. This change is consistent with the QMP-LS initiative to provide statistical analysis of quantitative test parameters and report inter-laboratory comparisons in 2006.

The performance for detection of HAV and HBV antibody was slightly reduced in 2005 with an error rate of 0.38% for hepatitis A and B compared with 0.21% reported in 2004. The error rate for HCV was 0.66 % in 2005, which is marginally higher than 0.32% noted in 2004. The error rate combines significant and lesser errors for a number of markers including HBsAg, anti-HBs, anti-HBc and anti-HCV antibody. The seven errors summarized in Table 66 were all significant errors. Three were errors for anti-HBc, two for anti-HAV and two for improperly interpreting the immune status for HBV.

Table 66. Summary of Errors for Hepatitis B Markers (VIRO-0502 and VIRO-0510)

Hepatitis Marker	Survey	Result reported	Significant Error	False Positive	False Negative
Anti HBc	VIRO-0502	HP3 positive (reference negative)	X	X	
	VIRO-0502	HP5 positive (reference negative)	X	X	
	VIRO-0510	HP3 positive (reference negative)	X	X	
Anti HAV	VIRO-0502	HP3 negative (reference positive)	X		X
	VIRO-0510	HP1 positive (reference negative)	X	X	
Hepatitis B Immune Status	VIRO-0510	● all five vials immune (all non immune sera)	X		
		● HP1 immune (reference antigen positive—not immune)	X		

HIV Antibody Detection

Seventeen laboratories participated in survey VIRO-0502 and 16 in VIRO-0510. There were no HIV errors for VIRO-0502 but three for VIRO-0510. Table 67 summarizes the error rate from 1996, when the HIV EQA program was initiated, to 2005. Two of the three errors in 2005 were errors in interpretation i.e. the laboratory reported the correct numerical value but reported a positive HIV sample negative. One laboratory was assigned a lesser error for failure to provide an interpretation of the numerical values for all vials.

VIRO-0510 included a questionnaire designed to update information regarding demographics of QMP-LS participant HIV laboratories. Participants were requested to provide the reason they perform HIV antibody screening and to indicate participation in other EQA programs (Table 68).

Table 67. Summary of HIV EQA Performance 1996–2005

Year	Number of Surveys	Tests per Survey	Survey Material	Number of Participants	Number of Errors/ Opportunities for Error	Per cent Errors
1996	2	4	...	21	0/164	0
1997	3	4	5 positive 7 negative	21	4/252	1.6
1998	3	4	7 positive 5 negative	20	1/236	0.4
1999	3	4	6 positive 6 negative	20	5/244††	2.1
2000	3	4	...	21	1/244	0.4
2001	3	4	Stopped heat inactivation	20	1/236	0.4
2002	2	4	...	15*	1/136	0.4
2003	3	4	6 positive 6 negative	20	1/232	0.4
2004	2	5	4 positive† 6 negative	18	0/180	0
2005	2	5	2 positive 8 negative	17/16	3/165§	1.8

* Participant number affected by strike by Public Health Laboratories

† HIV 1 indeterminate, HIV 2 positive included to test performance of laboratories with various systems for their ability to detect HIV 2 subtypes; early HIV testing systems were designed to detect only HIV 1 subtypes

†† Four errors due to mislabeling by one laboratory

§ Errors in interpretation

Table 68. Profile of HIV Laboratories in Ontario with Reasons for Testing and Participation in Other EQA in Addition to QMP-LS

Laboratory Profile	Diagnostic Screening	Screen Organ Donors	Insurance Immigration	Blood Screening	Employee Exposure	Prenatal Screening	Clinical Trials	Participate in Health Canada EQA	Participate in CDC NLHRS* EQA	Do not Participate in Other EQA	Participate in CAP†
PHL (n=8)	8	3	2	...	3	2	...	6	3	1	...
Community Laboratory (n=3)	...	...	2	...	...	...	2	...	...	1	2
Hospital (n=4)	...	3	...	...	3	...	...	2	1	...	...
Canadian Blood Services (n=2)	...	...	...	1	...	...	...	...	...	...	...

* Centers for Disease Control and Prevention National Laboratory for HIV Reference Services

† College of American Pathologists

Rubella Antibody Detection

The sera provided for rubella form a panel to be tested for rubella/VZV/CMV antibody. Twenty-six laboratories participated in the March survey (VIRO-0503) and 28 participated in September (VIRO-0509). Both surveys included five samples. The sera used for Rubella, VZV and CMV vials 2, 3, 4 and 5 in VIRO-0503 were identical to sera used in vials 2, 3, 4 and 5 of the 2004 survey (VIRO-0410). Figures 45 and 46 illustrate the precision attained by 25 participants for vial 5 in those two surveys.

The error rate for Rubella was 0.77% with one lesser error in VIRO-0503. The error rate was the same in 2004.

Survey VIRO-0509 marked the first time Rubella participant results were assessed based on numerical quantitative values reported (rather than only by interpretive qualitative $\pm$ values).

VZV Antibody Detection

Twelve laboratories tested for VZV in survey VIRO-0503 and 11 for VIRO-0509. No errors were assessed.

CMV Antibody Detection

Ten laboratories tested for CMV antibody for both surveys—five samples for each survey. The sera used for vials 2, 3, 4 and 5 in VIRO-0503 were identical to sera used in vials 2, 3, 4 and 5 of the 2004 survey (VIRO-0410). There were no errors in the 2004 CMV antibody survey (VIRO-0410). Table 69 summarizes two significant errors in survey VIRO-0503. One false negative error in VIRO-0503 (vial 4) did not occur in the identical sample in VIRO-0410. There was a lesser error for not including an interpretation of numerical values for one laboratory in survey VIRO-0509.

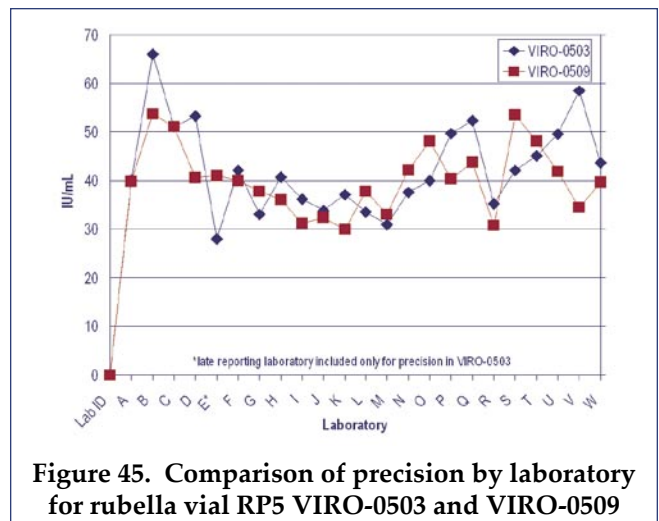


Figure 45. Comparison of precision by laboratory for rubella vial RP5 VIRO-0503 and VIRO-0509

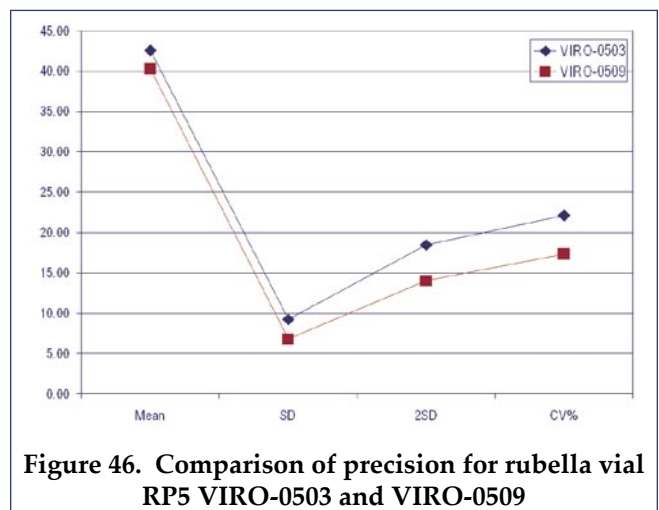


Figure 46. Comparison of precision for rubella vial RP5 VIRO-0503 and VIRO-0509

Table 69. Summary of Errors for CMV Antibody in Surveys VIRO-0503 and VIRO-0509

Survey (CMV)	Result Reported	Significant Error	False Positive	False negative
VIRO-0503	RV1 positive (reference negative)	X		
VIRO-0503	RV4 negative (reference positive)	X		
VIRO-0509	Reported correct numerical value but did not provide an interpretation			X

Respiratory Antigen Detection

Simulated Specimen Challenge

For both the February (VIRO-0502) and September surveys (VIRO-0509), there were five specimens in the panel containing two respiratory antigens—influenza A and RSV. Laboratories were asked to test all survey samples for their range of respiratory antigens. One out-of-province laboratory participated in both surveys. Table 70 shows the number of participants and the viral antigen reported in 2004 and 2005.

Table 70. Comparison of the Number of Laboratories Reporting Results of Direct Viral Antigen Testing in 2005 and 2004

Viral Agent Reported	Number of Laboratories Reporting by Survey			
	VIRO-0509	VIRO-0503	VIRO-0410	VIRO-0402
Adenovirus	6	6	6	6
Influenza A	38	38	35	36
Influenza B	35	34	29	28
Parainfluenza 1	6	5	6	5
Parainfluenza 2	6	5	6	5
Parainfluenza 3	6	5	6	5
RSV	50	47	49	49

The format of testing material was altered for survey VIRO-0509 from the previous surveys. Participants testing by DFA or IFA microscopy were provided with prepared slides rather than fluid material from which to prepare slides because the material supplier was unable to comply with our specifications for this survey. The supplier modified the production process after an incident involving another proficiency testing program, in which case they circulated live H2N2 influenza A virus to participants. The H2N2 subtype has not been isolated from clinical specimens for many years and is not currently included in the World Health Organization (WHO) Influenza vaccine. The H2N2 influenza strain used was a well-defined ATCC type culture but that incident created the potential for disseminating an infectious agent dangerous to public health. The supplier chose not to provide live virus, no matter what the subtype, as a result of the incident. That meant the material for VIRO-0509 was in two formats depending on whether participants used rapid antigen detection by EIA or microscopy (DFA/IFA)—one fluid without cellular material for EIA and one prepared slides for DFA/IFA. No live virus or cellular material was contained in the samples. That also meant EIA participants were not required to centrifuge material as previously required.

The February survey revealed ten errors out of 1450 opportunities for errors—a 0.69% error rate (see Table 65). For the first time participants were asked the following questions:

- 1) Does your laboratory perform culture also?
- 2) Does your laboratory refer specimens for confirmation?
- 3) Does your laboratory confirm results of antigen detection by culture/NA amplification?
- 4) Does your laboratory refer specimens to a reference laboratory for culture/NA amplification, if positive?
- 5) Does your laboratory refer specimens to a reference laboratory for culture/NA amplification, if negative?

The questions were included to allow the committee to assess the clinical significance of laboratory errors.

For survey VIRO-0503 only respiratory panel (RP) vial 1 contained RSV. Forty-seven laboratories reported results for RP 1–5. One laboratory reported all five vials positive when only one vial was positive by the reference result. Two other laboratories incorrectly reported three false positive results (reference negative). Survey VIRO-0503 resulted in seven significant errors. Laboratories with discrepancies were using BD EIA. All were using different lot numbers. These laboratories were encouraged to assess:

- reasons for error;
- answers to questions regarding confirmation and referral (Analysis Worksheet) and;
- potential for clinically misleading errors.

The committee is concerned when laboratories, without the experience of virus isolation, test and report EIA results to clinicians without knowing the limitations of EIA kits, especially when they report to QMP-LS no protocol for confirmation or referral of specimens to reference laboratories. The questions asked in the February survey allow analysis of reporting practices by participants.

For survey VIRO-0509 vials VIRO-0509-RP-3 and VIRO-0509-RP-5 contained RSV. Fifty laboratories reported results for VIRO-0509-RP vials 1–5. Only one significant error was assessed for RSV—one laboratory incorrectly reporting vial RP5 negative (reference positive).

Two other errors for the respiratory panels were the result of a clerical transcription by one laboratory reporting RSV as adenovirus in VIRO-0503.

CORRECTIVE ACTIONS

All errors assessed to a laboratory result in correspondence from QMP–LS. Laboratories are required to respond by completing the QMP–LS Discordant Findings Form and may provide specific information regarding the error and their own assessment of the situation. The Virology Committee reviews the response for knowledge and implementation of appropriate corrective action.

NUMBER OF PARTICIPANTS

Table 71 shows the number of laboratories participating in respective surveys by constituent. The number of laboratories testing for virology constituents/markers in 2005 was similar to that of 2004.

Table 71. Number of Ontario Participants Testing Virology by Constituent and/or Marker

Virus	Constituent/Marker	2000	2001	2002	2003	2004	2005
Hepatitis	HBsAg	50	44	42	41	40	40
	anti-HBs	43	39	35	35	37	36
	Anti-HBc	32	31	31	30	32	31
	Anti-HBc IgM	13	13	13	12	13	12
	HBeAg	11	11	11	11	11	10
	Anti-HBe	10	10	10	11	10	9
	Anti-HAV	20	20	20	20	21	18
	Anti-HAV IgM	23	22	22	21	22	20
Hepatitis C	HCV Screening Tests	26	24	31	32	31	30
Rubella	Rubella Ab	29	29	28	27	26	28
	Rubella IgM	4	4	4	3	1	1
VZV	VZV Ab	13	13	10	12	12	11
CMV	CMV Ab	...	...	...	10	9	10
HIV	HIV Ab	21	19	15	20	18	16
Chlamydia	<i>C. trachomatis</i> Ag or NA	26	26	20	16	17	16
Respiratory Panel	Influenza A	...	...	...	30	36	38
	Influenza B	...	...	...	25	29	35
	RSV	...	48	50	50	49	50
	Other viral antigens	...	...	...	5	6	6

Note: The last survey in each year was used for comparison for each of the constituents.

TESTING MODEL

Two histotechnology staining surveys were distributed in 2005.

The immunohistochemistry survey PATH-0504 was distributed to 54 laboratories licensed to perform immunohistochemistry (L731) on May 2, 2005. Each participant received a total of ten sequential unstained paraffin sections from a composite tissue block. The block contained samples of two different breast tumours, tonsil and small bowel. Participants were requested to perform stains for the estrogen receptor protein (ER), cytokeratins (wide spectrum), vimentin and CD3 (or other pan T cell antibody). Participants not performing the ER stain were requested to substitute a stain for the S-100 protein.

The routine and special stain survey PATH-0510 was distributed to 76 laboratories licensed to perform surgical pathology (L720) on October 19, 2005. Each participant received six sequential unstained paraffin sections from a composite tissue block. The block contained samples of small bowel, colon, kidney and spleen. Participants were requested to perform a routine oversight stain (H&E, HPS, etc.), a trichrome stain, a reticulin stain and a periodic acid Schiff (PAS) stain for mucosubstances.

PERFORMANCE ASSESSMENT

Survey PATH-0504

Fifty-two laboratories responded on time. One responded as non-participating due to a change of laboratory status. Two laboratories responded as not performing any of the requested immunostains. Two laboratories failed to respond on time. Four committee members each independently assessed the submitted slides, using the criteria and scoring system previously published as Committee Comments. The average score for those laboratories performing ER staining (49% of licensed laboratories) reflects only an adequate overall standard of performance for this stain. This is in contrast to the good overall standard of performance in the previous pilot study. In this survey the lower average score is entirely due to a marked increase in partial section detachment and damage produced by the heat induced epitope recovery (HIER) process. HIER is necessary in order to demonstrate ER with the monoclonal antibodies currently available. Partial section detachment and damage is a common occurrence in laboratories performing ER immunoassays, but was completely absent in the pilot survey. If only the staining function scores are considered, i.e. the ability to demonstrate ER, then the average score for this survey is identical to that of the pilot survey and also reflects a good overall standard of performance.

The average score for those laboratories performing the alternate S-100 stain (43.4% of licensed laboratories) reflects an acceptable overall standard of performance for this stain.

The average score for laboratories performing cytokeratin staining (90.6% of licensed laboratories) reflects an acceptable overall standard of performance for this stain.

The average score for laboratories performing Vimentin staining (90.6% of licensed laboratories) reflects an acceptable overall standard of performance for this stain. This is a significant improvement over the previous survey.

The average score for those laboratories performing CD3 staining (79% of

Anatomic Pathology

No. of Participants (Dec. 2005)	76
No. of Participants (Dec. 2004)	77
No. of Surveys Conducted in 2005	10

licensed laboratories) reflects only an adequate overall standard of performance for this pilot stain. The results of this survey will shortly be published as Committee Comments.

Survey PATH-0510

Seventy-five laboratories responded on time. Four laboratories responded as not performing any of the requested stains on-site. One laboratory failed to respond on time. Four committee members each independently assessed the submitted slides, using the criteria and scoring system previously published as Committee Comments. The average score for laboratories performing the H&E oversight stain (91.7% of licensed laboratories) reflects an excellent overall standard of performance. The average score for laboratories performing the HPS oversight stain (8.3% of licensed laboratories) reflects a good overall standard of performance. The average score for all laboratories combined reflects an excellent overall standard for the oversight stains. This is an improvement on the good overall standard achieved in the previous survey.

The average scores for laboratories performing the trichrome (91% of licensed laboratories) and reticulin (88% of licensed laboratories) stains reflect acceptable overall standards of performance.

The average score for laboratories performing the pilot PAS stain (91% of licensed laboratories) also reflects an acceptable overall standard of performance. Further analysis is currently underway. The results will shortly be published as Committee Comments.

REVIEW OF PERFORMANCE

Participants receive frequency charts for each stain—a histogram is also provided allowing participants to compare their final score with that of their peers. The frequency charts list the grouped scoring criteria and show the participant's individual score, the maximum score achievable and the survey average score for each criterion. A guideline for the interpretation of final scores has been published. Comparison of the participant's individual score to the maximum score achievable for each criterion provides an opportunity for cause analysis and quality improvement.

SUMMARY OF OTHER ACTIVITIES

- Extensively illustrated Committee Comments for both PATH-0402 and PATH-0409 were published in 2005.
- A bank of suitable test materials was established.
- Criteria were established for the pilot PAS stain, together with the score weightings established by paired comparison analysis.

2006 PLANS

Two histotechnology staining surveys are planned in 2006 each will include a new pilot stain. In March 2006, QMP-LS issued a call for test material, which included materials for the Anatomic Pathology test bank. New volunteer assessors will be trained to assist the Anatomic Pathology Committee members with this time consuming task. The Committee will work on establishing performance tracking over several surveys.

TESTING MODEL

An interpretive slide survey was not circulated during 2005 while the survey model was being redeveloped.

PATTERNS-OF-PRACTICE SURVEY

The purpose of this survey (CYTO-0507-PP) was to gather information about cytopathology practice in 2004 and to assess general trends in distribution of cases, screening, reporting and quality assurance of gynecologic (GYN) and non-gynecologic (non-GYN) cytology.

For the first time, data was collected pertaining to the processing and number of slides produced from a sample of fresh, unfixed, ascitic fluid (see Table 72 and Figure 47).

The most common preparatory techniques used were cytocentrifugation and direct smears from sediment, with most laboratories using two or more methods. Cytocentrifugation with a cell block was the most common combination. The maximum number of slides produced per sample was nine, with the minimum number of slides produced being one. The mode was four slides. These results show the lack of standardization across laboratories in Ontario, which may result in variation in sensitivity and test accuracy.

Data was also collected to identify the current practices in human papilloma virus (HPV) testing.

Twenty-six laboratories offered HPV testing, with the testing being performed at three locations—one hospital laboratory and two private/community laboratories.

Twenty-four laboratories reported using Digene Hybrid Capture method and two laboratories reported using PCR (PCR was carried out at the Public Health Laboratory, who have since stopped testing for cervical HPV). The majority of laboratories used LB GYN residuum and a separately collected sample for HPV testing.

Table 72. Routine Preparation Method for a 50 mL Sample of Fresh, Unfixed Ascitic Fluid in 2004

Routine Preparation Method	Total No. of Laboratories (n=64)
Direct Smears from Sediment	34 (53.1%)
Cytocentrifuge	35 (54.7%)
Cytoc ThinPrep	8 (12.5%)
Paraffin cell block (where possible)	8 (12.5%)
Other	6 (9.4%)
	3 filter imprint
	1 millipore filter
	1 nucleopore filter
	1 not specified

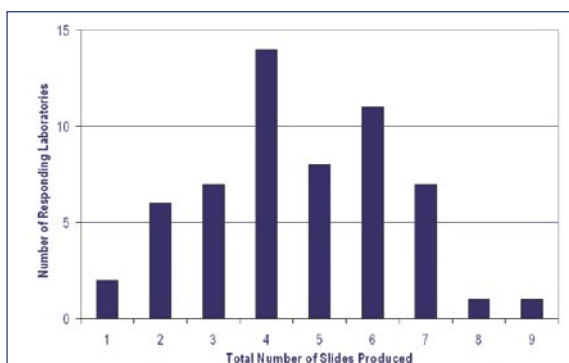


Figure 47. Total number of slides produced from a single 50 mL sample of ascitic fluid

Cytology

No. of Participants (Dec. 2005)	78
No. of Participants (Dec. 2004)	85
No. of Surveys Conducted in 2005	0

Detailed results and discussion from this survey (CYTO-0507-PP) were published as Committee Comments.

SUMMARY OF OTHER ACTIVITIES

Two slide surveys, CYTO-0504 and CYTO-0506, were conducted and reviewed for the Alberta Laboratory Quality Enhancement Program (ALQEP) of the College of Physicians and Surgeons of Alberta in 2005.

New slide survey material was submitted, assessed and added to the QMP-LS slide inventory.

PLANNED INITIATIVES FOR 2006

After final review and approval of the new slide survey model, the Cytology Committee hopes to send out two cytology interpretive slide surveys in Ontario for 2006. A wet survey to assess preparation and staining techniques will also be considered.

The Genetics Committee membership has representation from both cytogenetics and molecular genetics disciplines.

CYTOGENETICS

TESTING MODEL

The cytogenetics EQA model remains essentially unchanged. Four clinical challenge surveys were scheduled in 2005. One survey was cancelled due to material difficulties. A participating laboratory provides 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. Laboratories submitted their results using the same reporting format as patient results to physicians. Participants who 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 has been routinely assessed on the technical procedure and interpretive report. Due to issues surrounding the assessment of the interpretive component, the scoring system used in 2004 continued to be applied to surveys in 2005 and only the technical component was assessed. However, as there has been a resolution to the concerns of evaluating the interpretive component, the committee decided to resume evaluation of the interpretation in 2006. The scoring system used before 2003 will be implemented.

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

LABORATORY PERFORMANCE

The Ontario cytogenetic laboratories continue to perform well and the results were within acceptable limits.

MOLECULAR DIAGNOSTICS OF INHERITED HUMAN DISEASES

No surveys were conducted in 2005.

OTHER ACTIVITIES

QMP-LS continues to provide EQA services 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. Consideration of this possibility will be explored as the survey model is developed.

Genetics

No. of Participants (Dec. 2005)	11
(plus 12 out-of-province laboratories)	
No. of Participants (Dec. 2004)	11
(plus 13 out-of-province laboratories)	
No. of Surveys Conducted in 2005	3

INTRODUCTION

In 2003, Ontario Laboratory Accreditation (OLA) was implemented after 2 ½ years of planning and development. This new advancement made it mandatory for all licensed medical laboratories in the Province of Ontario to undergo accreditation. OLA's accreditation process includes regular peer assessment visits (every five years) and ongoing surveillance. Surveillance activities include self-assessments that occur between visits, and monitoring of external quality assessment performance. During 2005, initial assessment of Ontario's 242 licensed medical laboratories continued with 53 peer assessments, while 27 laboratories (who have not yet received a peer assessment visit) submitted reports of their second self-assessments.

OLA's principle function is to help laboratories deliver high-quality, efficient laboratory services. The purpose of accreditation is to determine if appropriate laboratory processes are in place, while ongoing EQA monitors whether those processes are effective. OLA accreditation is valid provided the laboratory demonstrates ongoing competence through satisfactory performance in EQA surveys. OLA's operating principles were reaffirmed in 2005. An OLA Advisory Panel provides advice, guidance and direction in the operation of the accreditation program. OLA staff coordinate assessments and ensure processes and procedures are documented.

OLA is a peer review program that relies on the services of volunteers from the laboratory community. OLA trains and certifies volunteers who conduct assessments and identify those accreditation requirements not met by laboratories. The current pool of certified assessors consists of 269 individuals with broad credentials and expertise. In turn, laboratories have the opportunity to submit corrective actions to resolve non-conformances and these are approved by assessors designated as assessment team leaders and nine volunteers who serve on the OLA Advisory Panel.

As of December 31, 2005, 114 of the 242 Ontario licensed laboratories were assessed against accreditation requirements—94 laboratories hold accreditation certificates. Implementation of OLA will continue into 2008.

In keeping with the quality management system principles of QMP-LS, this report is organized into five sections: customer service; management responsibility; resource management; service realization; and measurement and analysis.

CUSTOMER SERVICE

Goals that were achieved:

- Sharing program information to licensed laboratory personnel, identified stakeholders and assessors, as conformance updates and to provide clarification of operations.
- Developing new program information packages to share on request to interested parties.
- Reviewing customer feedback.
- Monitoring provincial, national and international initiatives in accreditation.

OLA's program values exist to ensure that accreditation criteria and the assessment process is fair, objective, consistent, responsible and prudent. OLA staff, advisors and assessors strive to be impartial, non-discriminatory, respectful and, when required, flexible and adaptable. In delivering accreditation services to Ontario's laboratories, it is OLA's goal to be open and transparent. To achieve this goal, QMP-LS News and the QMP-LS Web site provide our primary communication channels for laboratory personnel, identified stakeholders and certified assessors.

OLA articles appeared in the January, June, July, August and September issues of *QMP-LS News*. They dispelled myths about the accreditation program, highlighted the benefits of a quality management system, clarified the intent of accreditation certificates and their scope, provided an update on certificate issue, explained the process for self-assessments and announced the release of Version 3 of the OLA requirements, guidance information and references.

New content was added to the QMP-LS Web site—a slide show titled *Peer Assessments: What to Expect*. It

- states the purpose and value of peer assessment visits;
- clarifies the relationship between OLA and EQA;
- outlines the peer assessment process, visit arrangements and follow-up;
- explains how multi-site and single assessments differ;
- shows what information assessors are provided;
- identifies practical tips to prepare for peer assessment visits and;
- summarizes the conditions of an accreditation certificate.

The program information available on the QMP-LS Web site was revised and made available for download in the format of a manual. This 16-page manual includes information about QMP-LS, OLA, the accreditation process, the accreditation requirements, and provides links to information for assessors, educational tools, and frequently asked questions.

Any laboratory undergoing peer assessment has the right to submit an error of fact if laboratory personnel believe an identified non-conformance is in error. During 2005, only six errors of fact were received, five of which resulted in the release of a revised summary report. Additional direct feedback was received by e-mail (individuals may submit feedback via the QMP-LS Web site) and mail. The majority of this feedback seeks clarification of the intent of OLA accreditation requirements. A summary of frequently asked questions appears on the QMP-LS Web site. This information provides clarification to laboratory operators in a readily available format. In addition, OLA staff respond to direct inquiries received by mail, telephone and e-mail.

OLA staff monitor provincial, national and international initiatives in quality and accreditation in an effort to offer the citizens of Ontario the best possible accreditation service for licensed medical laboratories. Two staff participated in the writing of the new certification exam for medical laboratory assistants/technicians administered by the Ontario Society for Medical Technologists. The director attended meetings at the Standards Council of Canada (SCC) for accreditation partners and the Program for the Accreditation of Laboratories/Canada (PALCAN) accreditation program. The director chaired the Accreditation Working Group of the Canadian Coalition for Quality in Laboratory Medicine (CCQLM) and was elected to the executive committee as president-elect. She also attended one regional conference (NORONT), one provincial conference *Quality Management, From Concept to Practice* sponsored by the British Columbia Provincial Laboratory Coordinating Office and two international conferences—the international *Spotlight on Quality* conference and the conference of the International Society for Quality in Healthcare. One staff technologist completed training on the ISO 17011:2004 standard for *Conformity assessment—General requirements for accreditation bodies accrediting conformity assessment bodies*.

Interest in OLA's activities is widespread across Canada and internationally, recognizing that it is the first medical laboratory program in North America to offer accreditation based on ISO 15189:2003 *Medical laboratories—Particular requirements for quality and competence* (CAN/CSA Z15189-03). Five invited presentations and one poster were provided at regional, national and international meetings (Appendix E).

One additional stakeholder organization was officially recognized in 2005—the Canadian Society for Medical Laboratory Science. This brings the total number of stakeholder organizations recognized by OLA to 16 (Table 73).

In 2006, additional customer feedback will be sought through values-based evaluation forms and possibly a formal questionnaire.

Table 73. OLA Stakeholders

1. Canadian Council on Health Services Accreditation
2. Canadian Society for Medical Laboratory Science
3. Clinical Laboratory Management Association Trillium Chapter
4. College of Medical Radiation Technologists of Ontario
5. College of Medical Laboratory Technologists of Ontario
6. College of Physicians and Surgeons of Ontario
7. College of Respiratory Therapists of Ontario
8. College of Nurses of Ontario
9. Coroner of Ontario
10. Ontario Association of Medical Laboratories
11. Ontario Association of Pathologists
12. Ontario Hospital Association
13. Ontario Medical Association Section on Laboratory Medicine
14. Ontario Society of Clinical Chemists
15. Ontario Society of Medical Technologists
16. Standards Council of Canada

MANAGEMENT RESPONSIBILITY

Goals that were achieved:

- Aligning policies, processes and procedures with the QMP–LS quality management system, in order to document OLA's service realization.
- Performing a gap analysis against ISO 17011:2004 *Conformity assessment—General requirements for accreditation bodies accrediting conformity assessment bodies*.
- Establishing operating principles consistent with ISO 17011:2004, including the establishment of criteria for the relationship and reporting mechanisms between OLA and EQA.
- Enhancing the database capabilities to monitor conformance plus improve efficiencies.

OLA staff formalized 105 processes and procedures in 2005, and placed them under document control. In 2006, additional processes and procedures for assessor refresher training, requirement maintenance and self-assessments will be placed under document control.

In order to execute the agreement with Standards Council of Canada described under Service Realization, OLA must conform to a new operating standard ISO 17011:2004 *Conformity assessment—General requirements for accreditation bodies accrediting conformity assessment bodies*. OLA staff completed an initial gap analysis to this standard and determined that operations may comply with only 49% of its clauses. In 2006, a project plan to implement changes to comply with this standard will be put into place.

Management was successful in overseeing enhancements to the database (as reported under Measurement and Analysis) that monitor conformance and improve efficiencies of operations.

The following two goals were deferred due to a lack of resources:

- Initiating a program evaluation to validate processes for accreditation.
- Initiating a competency assessment program for staff.

RESOURCE MANAGEMENT

Goals that were achieved:

- Recertifying assessors by delivering refresher training electronically, and/or ensuring participation in peer assessments.
- Refining the assessor, visit and requirement databases to enhance assessment coordination and process evaluation.
- Certifying approximately 45 new assessors by conducting three classroom assessor training sessions.
- Securing permanent employees for all staff positions.

OLA peer assessment visits are conducted by trained and pre-certified assessors. In 2005, three training sessions were conducted with 44 attending. This brings the total number of active, certified assessors to 269. Mr. Jim Moran (The Learning Alliance, Inc.) conducted assessor training with the assistance of OLA staff. Each classroom training session was 2 ½ days in length, culminating with a one-hour examination to assess the preparedness of trainees for assessments. In 2005, training content was updated, a new

examination utilized, and a new refresher tool implemented. Each certified assessor is required to recertify annually by conducting at least one assessment or completing an on-line refresher. Refresher training is offered to each assessor on the anniversary of his or her certification. In 2005, 165 assessors were recertified.

Assessors show some interest in using electronic tools to complete their assessments, and making this a reality will be pursued in 2006.

In 2005, one staff technologist who was previously on a temporary contract became a permanent employee. This brings the full staffing complement at OLA to 2.8 full-time equivalent staff technologists and one full-time senior administrative assistant, in addition to a full-time Director, OLA.

The QMP-LS secretariat is indebted to the 11 advisors who served on its OLA Advisory Panel in 2005 (Appendix A). Two members, Ms. Sheila Woodcock and Dr. Sandip Sengupta, retired in March. The mandate of the panel is to provide advice, guidance and direction in the operation of an accreditation program in accordance with OLA operating principles, international guidelines and Ontario regulations. The panel reviews, recommends and approves accreditation policies, processes, and requirements for accreditation. It is also responsible for the review of corrective actions submitted by laboratories and for recommending either that accreditation certificates be issued or withdrawn. In 2005, the panel met on eight occasions, either in person or by conference call. Its activities are described within the Service Realization section.

SERVICE REALIZATION

Goals that were achieved:

- Conducting peer assessment visits to approximately 54 laboratories.
- Coordinating self-assessments in approximately 54 laboratories.
- Releasing Version 3 of the accreditation requirements.
- Pursuing a partnership agreement with Standards Council of Canada for the delivery of OLA.

Accreditation is a peer review assessment process by which an authoritative body ensures that laboratories meet explicit quality management criteria, in order to provide formal recognition that the laboratory is competent to carry out examinations. OLA assessments for licensed Ontario laboratories determine if laboratories conform to requirements, for all examinations performed for diagnosis, prophylaxis and treatment of humans. Regular peer assessment visits and surveillance self-assessments encompass all aspects of laboratory practice. Program requirements are comprehensive and process-based. They focus on the management of quality to reduce errors, and validate that quality management processes are in place. In 2005, the definitions of non-conformances were altered slightly, in order to clarify what constitutes a major non-conformance (Table 74).

Table 74. Non-conformance Classification

Major non-conformance

- Requirement not addressed by laboratory's quality manual or operating procedures or
- Procedures are consistently NOT followed or
- Existing protocols fail to address requirement or
- Non-conformance directly impacts patient safety or
- Consistent/persistent incidence of non-conformance or
- Repeated incidence of non-conformance in the majority of sections of the laboratory.

Minor non-conformance

- Isolated incident of non-conformance or
- Adherence to procedures is inconsistent (usually followed but sometimes not) or
- Existing protocols address requirement but are not necessarily followed.

The mandatory peer review accreditation program was fully operational in 2005. As of December 31, 2005, 114 of the 242 Ontario licensed laboratories were assessed against accreditation requirements, and 94 accreditation certificates issued. In 2005, 53 peer assessment visits were conducted and accreditation certificates were issued following assessments (one two-year certificate and 52 five-year certificates). One additional laboratory

scheduled for peer assessment relinquished its laboratory licence. One laboratory was referred to the Ministry of Health and Long-Term Care (MOHLTC) because it initially failed to meet the criteria for issue of a certificate. However, following its referral to and mediation by the MOHLTC, this laboratory was successful in achieving two-year accreditation.

Peer assessment visits conducted in 2005 spanned the province geographically, and included Ontario public hospital laboratories, community laboratories, Public Health Laboratories and Canadian Blood Service laboratories. Thirty-four assessments were conducted for single laboratories and seven multi-site visits encompassing 19 laboratories were conducted.

Commencing April 1, 2005, second self-assessments were initiated in 60 laboratories, and 27 laboratories submitted their completed self-assessment reports prior to December 31, 2005. These surveillance self-assessments serve to:

- ensure that laboratories continue to meet accreditation requirements
- identify the degree to which laboratories meet accreditation requirements and;
- determine accreditation requirements that may be difficult to achieve.

Standards for accreditation are identified in advance of assessment. OLA accreditation requirements translate the standards into explicit criteria for accreditation. Program requirements are based on the Canadian national (ISO) standard CAN/CSA Z15189-03 *Medical laboratories—Particular Requirements for Quality and Competence*. Their development was aided by cross-referencing this standard to generally accepted principles of good practice in Ontario:

- Canadian Statutes and Regulations,
- Ontario Statutes and Regulations (Ontario laboratories only),
- Health Canada Guidelines,
- Standards and guidelines achieved through consensus by international, North American, Canadian and provincial associations, federations, organizations and regulatory bodies.

Each requirement has an accompanying reference source. Additional good practice recommendations are included with the requirements. QMP-LS committed to reviewing the requirements, in detail, once every two years in order to ensure continued suitability in light of changes to the reference sources and current laboratory practice. In 2005, participant and stakeholder feedback was solicited for the review of requirements, and this feedback added to the multitude of comments collated since the introduction of Version 2 in May 2003. An extensive review by staff and advisors culminated in the release of Version 3 of the requirements in September 2005. It contains 506 requirements and 40 good practice recommendations with guidance information and individual reference sources—45 fewer requirements and 21 fewer good practice recommendations than the previous version. The pertinent changes are outlined in (Table 75).

On average, conformance during 2005 peer assessments (n=53) was 94.4% against an average of 450 applicable requirements. The number of major non-conformances assessed per laboratory was between 0 and 104, and the

Table 75. Changes Encompassed in Version 3 of the OLA Accreditation Requirements

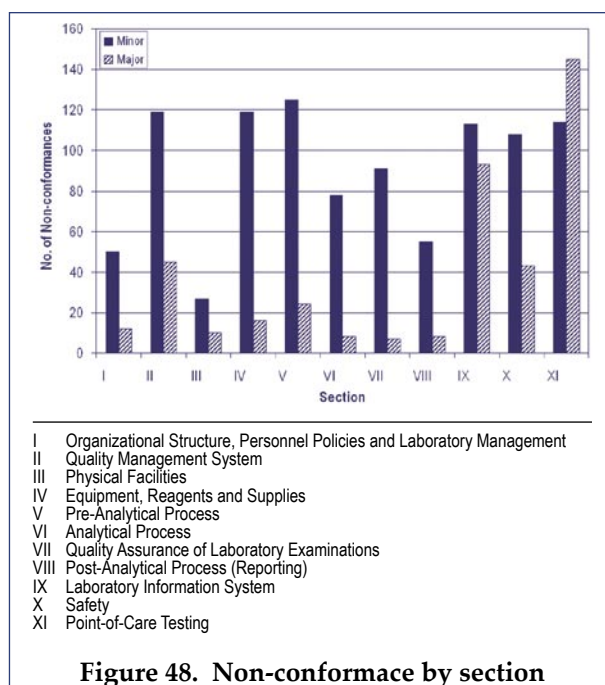
Type of Change	Amount/Reason/Impact
Updated references	Reflect new documents and revised versions
Removal of duplications	60 requirements removed 6 good practice recommendations removed
Clarification of intent or minor modifications	152 changes to clarify intent or correct typographical errors
Modifications that may affect laboratory practice	64 changes including 15 good practice recommendations upgraded to requirements and 8 discipline-specific pieces of guidance information

number of minor non-conformances between 0 and 79. The most frequently cited non-conformances are for point-of-care testing followed by laboratory information system, quality management system, safety and the pre-analytical process (Figure 48). In all 114 assessments concluded by the end of 2005, the average conformance was 93.7%. Comparative performance statistics are shown in Table 76.

The OLA Advisory Panel considered reassessment criteria when:

- changes occur in laboratory ownership, location, or the menu of tests;
- self assessments reveal concerns about patient safety;
- results on consecutive EQA results are unsatisfactory and question the competency of a laboratory;
- the expiry of two year certificate is imminent.

The Panel also approved the process to initiate accreditation in a newly licensed laboratory.



Further operational changes that might be necessitated will be considered in 2006.

In August, a partnership agreement was signed with the Standards Council of Canada for the delivery of joint accreditation of medical laboratories to ISO 15189:2003 *Medical laboratories—Particular requirements for quality and competence* (CAN/CSA Z15189-03). This national program will be voluntary for any licensed Ontario laboratories and other laboratories seeking recognition of competence in meeting this international standard. Expected to be available in 2006, this voluntary program will mirror the existing, mandatory accreditation program operated by QMP–LS but SCC will formally recognize compliance with ISO 15189:2003 *Medical laboratories—Particular requirements for quality and competence* (CAN/CSA Z15189-03).

The following goal will continue in 2006:

- Rationalizing activity with EQA division.

Certificates of accreditation are valid for the stated time frames and scopes of testing provided that laboratories continue to meet accreditation requirements and demonstrate competence in external quality assessment. Because accreditation assessment ensures that quality management processes are in place but external quality assessment ensures ongoing competence, in 2005, QMP–LS began exploring necessary changes in operations to establish a link between OLA and EQA activities. Exploration will continue in 2006.

Table 76. OLA Peer Assessment Conformance Statistics, 2004 and 2005

Category	2003 (n=6)	2004 (n=55)	2005 (n=53)	Inclusive (n=114)
Minimum	79.5%	82.0%	74.8%	74.8%
Maximum	97.6%	100%	100%	100%
Average	86.5%	93.8%	94.4%	93.7%
Number of Major non-conformances	0–24	0–49	0–104	0–104
Number of Minor Non-conformances	0–89	0–69	0–79	0–89

MEASUREMENT AND ANALYSIS

Goals that were achieved:

- Making the assessor, visit and requirement databases fully operational by defining and implementing reports to assist with assessment coordination and conformance summary reports for reporting to committees.
- Initiating performance measurement and operational process control.
- Reviewing peer assessment feedback to identify potential process improvements.
- Completing the internal review of the effectiveness of assessor training.

A few enhancements were made to the SQL database that assists in the management of assessor records and assessment coordination. These enhancements help to ensure that peer assessment visits are coordinated with efficiency. Additional information on the expertise of assessors in safety, laboratory information systems (LIS) and French language proficiency was added. Additional data capture and reporting capabilities were made available in 2005 that allow better capture of key information regarding assessments, monitoring our ability to meet target turnaround times for the issue of accreditation certificates, and identifying conformance levels for peer assessments. In addition to expanded data entry fields that electronically maintain historical information about peer assessment visits, assessors and requirements, expanded reporting capability for administrative management reports was added.

Table 77 is an example of the conformance information available through the database. It shows the OLA requirements most frequently assessed non-conformances during 2005. This information is tallied by capturing

Table 77. Top Ten Non-conformances 2005, by Number of Actual Non-conformances

No.	Requirement	Text	Number and Frequency
1	V.B.3 Pre-analytical	<i>There shall be instructions describing the necessary specimen preservatives to ensure integrity, and the acceptable temperature range for transit. Systems used to transport specimens to the laboratory shall be evaluated to ensure the designated temperature range requirements can be met during transit and that the preservatives used are an effective means to ensure stability during transit.</i>	24 non-conformances (50%) 4 major and 20 minor
2	VI.3 * Analytical	<i>All laboratory procedures, including manufacturer's instructions used as procedures and electronic instructions, shall be documented and available at the workstation for relevant staff.</i>	23 non-conformances (47%) All minors
3	VI.1 * Analytical	<i>All laboratory examinations shall be based on methods cited in published peer reviewed texts or journals, or be recommended by international, national, or regional guidelines. If in house developed procedures are used, they shall be validated for their intended use and fully documented.</i>	20 non-conformances (41%) 1 major and 19 minors
4	XI.J.3 POCT	<i>The patient record shall include the point of care test result in clearly defined units, the date and time the test was performed, and the reference interval for the test.</i>	18 non-conformances (42%) 4 majors and 14 minors
5	III.8 Physical Facilities	<i>The laboratory shall monitor and record environmental conditions (as appropriate) to ensure they do not adversely affect the quality of examination results (e.g. dust, humidity, temperature, sound levels, vibration levels, ventilation).</i>	14 non-conformances (29%) All minors
6	XI.A.4.1 POCT	<i>The laboratory director and/or designated responsible person(s) shall implement a quality management system for point of care testing.</i>	14 non-conformances (30%) 5 majors and 9 minors
7	VI.6 Analytical	<i>If any abridged instructions and information are used at workstations, they shall correspond and refer to a complete manual or procedure. Any such abridged procedures shall be part of the document control system.</i>	14 non-conformances (30%) 4 majors and 10 minors
8	I.B.10 Personnel	<i>The facility shall evaluate staff skills to perform assigned tasks following training and periodically thereafter.</i>	14 non-conformances (29%) all minors
9	IV.2 * Equipment, Reagents, Supplies	<i>Laboratory management or the facility shall define a process and/or procedure for inspection, acceptance/rejection and storage of consumable materials. The inventory control system shall ensure continuity of supply and minimize shortages. Records of actions taken shall be maintained.</i>	13 non-conformances (27%) All minors
10	VIII.7 Reporting	<i>Laboratory management, in consultation with the requesters, shall establish clinically appropriate turnaround times for each of its examinations.</i>	13 non-conformances (27%) 3 majors and 10 minors

* On Top Ten list in 2004

the number of non-conformances per requirement, based on the number of assessments in which the requirement was applicable (i.e. frequency). They include requirements for personnel, physical facilities, consumable supplies, pre-analytical processes, analytical processes, reporting, and point-of-care testing. Not surprisingly, the top three non-conformances are for requirements with discipline-specific “what to look for items.” Three of the 2005 top ten non-conformances appeared on the list of top ten non-conformances in 2004.

Three options may result following each peer accreditation assessment visit—issue of a five-year certificate; issue of a two-year certificate; or referral of the file because it does not meet the criteria for issue of an accreditation certificate. As of December 31, 2005, 94 of the 242 licensed Ontario laboratories held accreditation certificates. In 2005, one two-year certificate and 52 five-year certificates were issued. As noted above, one laboratory was referred to the MOHLTC because it initially failed to meet the criteria for issue of a certificate. Commencing April 1, 2005, second self-assessments were initiated in 60 laboratories, and 27 laboratories submitted their completed self-assessment reports prior to December 31, 2005.

In 2005, OLA staff designed and implemented a performance measurement mechanism for service realization. The objective of this performance measurement is to ensure that certificates are issued in a timely fashion following peer assessment visits. The process monitored is the time elapsed between the conclusion of a peer assessment visit and:

- issue of the written conformance report (target within 30 days);
- receipt of a laboratory’s corrective action (target within 90 days);
- issue of an accreditation certificate (target 150 days).

The method employed is for the director to obtain the elapsed time on certificates issued in each quarter (three month’s time), utilizing a report available from the SQL database that contains assessment information. Elapsed time in days is compared against arbitrary targets established in consultation with other accreditation programs and participating laboratory personnel. The elapsed range, mean, median and mode are calculated. The number and percentage of assessments that exceed target time lines are tabulated in a textual report, corrective action is identified, approved by the Managing Director and implemented. Trends are noted in subsequent quarters. Timely turnaround time for the issue of accreditation certificates is considered a measure of the quality of the accreditation program, because it impacts on participants’ perception of the assessment process efficiency. The limitations of this performance measure include the fact that some steps in the process are not within the control of OLA staff—namely the submission of laboratories’ corrective action and further information when requested. In addition, corrective action must be reviewed and approved by the team leader and the OLA Advisory Panel, whose schedules are not under our control. This first year of performance data will be used to establish a baseline and to validate the targets.

Throughout 2005, all reports were issued on time and corrective actions were received from laboratories on time. In the fourth quarter of 2005, 18% of certificates issued took longer than targeted, which was an improvement over previous quarters (29%, 37.5% and 42%). In all cases where certificates were delayed, the cause was attributed to the reviewing of corrective actions. The main factor contributing to delays was heavy schedules of team leaders and OLA Advisory Panel representatives. As a result, procedures were altered to identify alternate reviewers when the team leader and OLA Advisory Panel member are not readily available and to ensure these individuals understand their role in the corrective action review process. Measurement in 2005 proves that QMP-LS can issue assessment reports within 30 days of the peer assessment visit and laboratories can submit corrective actions within 90 days of the visit. Monitoring in 2006 will continue, in order to determine if the review of corrective actions can be concluded in a timely fashion, and to identify where targets may be shortened to reduce the overall turnaround time for issue of accreditation certificates.

During the peer assessment process, laboratory personnel, assessors and team leaders were asked to evaluate and offer feedback on the accreditation process, visit coordination and arrangements. Evaluation forms are collated

by staff and reviewed by the OLA Advisory Panel at its quarterly meetings. Generally, feedback is that processes are effective and the comments are complimentary. Constructive feedback allowed us to improve on the process in 2005, by clarifying the roles and responsibilities of assessors and laboratory staff during visit opening and closing meetings. Information gathered also allows staff coordinators to identify potential team leaders for future visits. In 2006, a goal is to redesign the evaluation form and align it with OLA's operating values. Alternatively, QMP-LS will consider surveying all laboratories assessed to date, in order to identify opportunities for improvement.

An internal review of the effectiveness of assessor training was conducted by reviewing evaluations received following peer assessment visits. The performance of assessors was evaluated by laboratory staff, coordinators and team leaders to assess the effectiveness of assessor training. The following skills and attributes are evaluated: attendance, punctuality, communication skills, interpersonal skills, knowledge of assessment process, knowledge of requirements, ability to gather objective evidence, ability to answer questions or direct questions appropriately, professionalism, and the quality/thoroughness of work. Feedback indicates that certified assessors are prepared and well-qualified to carry out assessments fairly and objectively, with consistency, impartiality and respect for laboratory personnel. These findings validate the assessment training, and assessors themselves comment that the training and certification process adequately prepares them for assessments. However, because the current evaluation is subjective, in 2006 it will be revised to align it with core competencies of assessors, and allow for a more objective response.

In 2006, an additional performance measurement indicator will be designed and utilized to monitor the efficiency of the self-assessment process.

SUMMARY

The OLA division had a very active year, and the implementation of Ontario's mandatory accreditation for all licensed medical laboratories is on schedule. Nearly one-half of the 242 laboratories have been assessed. The conformance rate achieved by Ontario's laboratories is remarkable, with the average conformance in 2005 being 94.4% and the conformance rate on all assessments concluded by the end of 2005 was 93.7%. Surveillance activities included self-assessments by 27 laboratories. Integration with external quality assessment was initiated to monitor ongoing performance.

The first biennial review of OLA accreditation requirements was completed in 2005 and Version 3 released in September. By responding to participant and stakeholder feedback and removing duplications and redundancies, the number of requirements was reduced by 45 in Version 3, which contains 506 requirements. Furthermore, the guidance information was revamped to provide more information and greater clarity of the intent of requirements, especially at the discipline level. The majority of changes were suggested by laboratory professionals within Ontario, and their incorporation into improved requirements demonstrates OLA's commitment to being responsive, flexible and adaptable.

In the pursuit of openness and transparency, OLA staff maintain open lines of communication with participants and stakeholders. In addition to one-on-one communication, *QMP-LS News*, QMP-LS Web site and conferences were utilized to convey information. The OLA Advisory Panel provided sound advice and guidance for operations. Communication efforts will continue in 2006.

Participant feedback verifies that assessments are fair, objective and consistent and that assessors are responsible, prudent, impartial, non-discriminatory and respectful. In 2006, additional customer feedback will be sought through values-based evaluation forms and possibly a formal questionnaire. Assessor competencies will be formalized and utilized for evaluation purposes.

In 2006, implementation of the mandatory accreditation for Ontario's licensed medical laboratories will continue. OLA expects that further laboratory restructuring within regional delivery areas will necessitate that its Ontario

operations continue to be flexible and adaptable. Additional indicators will enhance performance measurement and monitoring. Processes will be refined with a view to enhancing efficiency, such as exploring electronic assessment tools. Further processes and procedures will be placed under document control. It is anticipated that operations with the EQA division will be integrated to facilitate ongoing surveillance and that will prompt some changes to QMP-LS processes.

QMP-LS will continue to be active on the national and international scene. It is hoped that an option for voluntary accreditation against ISO 15189:2003 Medical laboratories—*Particular requirements for quality and competence* (CAN/CSA Z15189-03) will be available in 2006, in conjunction with Standards Council of Canada. This will necessitate that OLA meet ISO 17011:2004 *Conformity assessment—General requirements for accreditation bodies accrediting conformity assessment bodies*.

TEST REVIEW COMMITTEE

The Test Review Committee continued to advise Laboratories Branch, MOHLTC, throughout 2005 on quality requirements for tests that are not currently listed in the Schedule of Benefits for laboratory services. With the reappointment of the Chair and two members effective April 1, 2005 for a three-year term, membership remained unchanged until the resignation of two members in May 2005 (Appendix A). The committee met once on April 7, 2005 to review and revise its process for reviewing tests. Electronic communications have proved efficient and effective.

During the year, MOHLTC submitted lists of tests for consideration by the Test Review Committee. With the exception of one report for Indicans that is under review, by the end of 2005 reports for all tests were provided to MOHLTC.

Elements included in the report are:

- Quality requirements
- Patient preparation
- Collection and handling of specimen
- Quality assurance process, quality control procedures and quality indicators
- External quality assessment through interlaboratory comparisons.
- Analytical policy and technical procedures
- Practice guidelines
- Clinical utility
- Health cost implications.

Tests submitted by the Laboratories Branch to the Test Review Committee in 2005 are shown in Table 78. For the “well-established” category, preliminary comments with the relevant characteristics of note (clinical utility, external quality assessment, health cost implications, etc.) were provided to the Laboratories Branch.

The existing processes concerning appeals, unmet quality criteria and tests not requiring quality criteria (as outlined in the 2002 review) have continued to allow prompt communication between Laboratory Licensing and Inspection Services (LLIS) and the Test Review Committee. Minor modifications have been made to a few reports in response to queries received from laboratories.

The function of the Test Review Committee is greatly enhanced by the services of external advisors and current or former scientific committee members (Appendices A and B) who have willingly assisted in sharing specific knowledge and expertise in the preparation of expert opinion reports. Their contributions are acknowledged with thanks and appreciation.

Table 78. Tests Investigated and Submitted to Laboratories Branch in 2005

Mycophenolic Acid	Heparin CoFactor II	Platelet IgG Measurement	Oxycodone
7-Dehydrocholesterol	Hex LA (Hexagonal Phospholipid)	Porphobilinogen deaminase (PBG deaminase)	Haloperidol (Haldol)
Troponin (Revised)	Fibrin Monomer	Propafenone (Rythmol)	Thiopental
Myoglobin (Revised)	Protein C	Quinine	Trazodone (Desyrel)
Insulin-Like Growth Factor Binding Protein-3 (IGFBP-3)	Protein S	Sertraline	Vitamin B1 (Thiamine)
Bile Acid Breath Test	Active Protein C Resistance	Tryptase	Vitamin B6 (pyridoxine)
Amiodarone (Cordarone)	von Willebrand multimer analysis	von Willebrand Factor—Antigen Assay (vWF:ag)	Risperidone
Bupivacaine	Factor V Leiden	Warfarin	11-Deoxycortisol
Chlorpromazine	Prothrombin Variant	Naproxen	TSH Receptor Antibody
Chlorpropamide	Sulfate, urine	Paroxetine (Paxil)	High Molecular Weight Kininogen
3-alpha-androstanediol glucuronide (3 alpha diolG)	Oxygen Affinity (P50)	Tocainide (Tonocard)	Pre-kallikrein (Fletcher factor)
Fluoride	Schillings Test	Tolbutamide (Orinase)	Allergen Specific Immunoglobulin E (IgE) Antibody Tests updated to include criteria information for Allergen Specific
Fluvoxamine (Luvox)	Mucin Clot (synovial fluid)	PKU and MCAD	Immunoglobulin G (IgG) Antibody tests
Glutethimide	Ristocetin Induced Platelet Aggregation (RIPA) Studies	Methylmalonate, Serum (MMA)	Whole Blood Viscosity
Meprobamate	von Willebrand factor (vWf)—cleaving metalloprotease	Avian precipitins	Tests currently under review:
Methsuximide	Mexiletine	Reverse T ₃	Indicans
Alpha 1 Acid Glycoprotein	Paraldehyde	Tissue Thromboplastin Inhibition Test	
Hemopexin		Diphenhydramine (Benadryl)	

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Mrs. Patricia Anderson

Ms. Leela Prasaud

OMA Representatives:

Dr. Harold Richardson

Dr. Gregory J. Flynn

Dr. Michael Thoburn

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Note: Names in italics identify Chairs

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Dr. Wendy Lau	Ms. Lai Ling Wat
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Trengrove	Ms. Heather McMullen
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Jane Gun-Munro	Director, EQA
Bryan Hewlett	Consultant Technologist, EQA—Anatomic Pathology
Carol Julian	Consultant Technologist, EQA—Cytology
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Janine Marmulak	Senior Administrative Assistant, EQA
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Matt O'Connor	Corporate Administrative Assistant
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Maureen Singh	Senior Administrative Assistant, EQA
Miralla Suares	Senior Administrative Assistant, OLA
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Betty Waltenberry	Data Officer
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Margaret Hall Yousefi	Web site Officer
Manny Zamora	Expeditor

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TOPIC/EVENT	DATE	LOCATION	QMP-LS REPRESENTATIVE
<i>Coming Out and Speaking Up: Empowerment Tips for Laboratory Professionals</i> 27th NORONT Conference	March	Timmins, ON	Mrs. Linda Crawford
<i>Prenatal Screening for Down Syndrome—First Trimester, Second Trimester, or Integrated. What is the best program for my population?</i> American Association of Clinical Chemistry (AACC) Edutrak Symposium	July	Orlando, Florida	Dr. Anne M. Summers
<i>Prenatal Screening for Down Syndrome: New Developments for Biochemical and Ultrasound Markers</i> American Association of Clinical Chemistry (AACC) Edutrak Symposium	July	Orlando, Florida	Ms. Joanne Miyazaki
<i>Quality Management of Multiple Marker Prenatal Screening in Ontario, Canada</i> American Association of Clinical Chemistry (AACC) Edutrak Symposium	July	Orlando, Florida	Ms. Joanne Miyazaki
Antimicrobial Resistance—It's in the Genes Kenora Rainy River Regional Laboratory Program Annual Fall Symposium	September	Fort Frances, ON	Ms. Christine Fleming
<i>Coming Out and Speaking Up: Empowerment Tips for Laboratory Professionals</i> Kenora Rainy River Regional Laboratory Program Annual Fall Symposium	September	Fort Frances, ON	Mrs. Linda Crawford
<i>Changes to the OLA Requirements in 2005, Version 3</i> Kenora Rainy River Regional Laboratory Program Annual Fall Symposium	September	Fort Frances, ON	Mrs. Linda Crawford
<i>Investigation of Discordant Findings and Root Cause Analysis of Microbiology EQA Surveys</i> Kenora Rainy River Regional Laboratory Program Annual Fall Symposium	September	Fort Frances, ON	Ms. Christine Fleming
<i>The Path to Excellence: Ontario Experience Quality Management: From Concept to Practice—Innovation, Integration, Implementation</i> British Columbia Provincial Laboratory Coordinating Office	November	Vancouver, BC	Mrs. Linda Crawford

SYMPOSIUM	DATE	LOCATION	PLANNERS/ PRESENTERS/ MODERATORS
Joint Ontario Society of Clinical Chemists (OSCC)/Quality Management Program—Laboratory Services (QMP-LS)	November	Niagara-on-the-Lake, Ontario	
<i>Quality Matters: The Hematology Perspective on QC</i>			Mr. Jeffrey Sumner
<i>Quality Matters: Quality in Quantities</i>			Dr. Sheila Boss
<i>Quality Matters: Using ISO Statistical Procedures to Evaluate QMP-LS EQA Results</i>			Mr. Dan Tholen
WORKSHOP			
Joint QMP-LS/College of Medical Laboratory Technologists/Ontario Society of Medical Technologists <i>Case Studies & Quality Assurance/Quality Control</i>	October	Michener Institute of Applied Health Sciences Toronto, Ontario	Ms. Kim Hartill-Dadson, Ms. Aruna Kolhatkar, Ms. Peggy Kiely

APPENDIX G PARAMETERS MONITORED BY QMP-LS IN 2005, BY DISCIPLINE

CHEMISTRY

Chemistry-General

Albumin
Albumin Excretion Rate (AER)
Bicarbonate
Bilirubin, Total
Blood Gases (pH, pCO₂, pO₂, Na⁺, K⁺, Glucose, Ionized Calcium)
Hb A_{1c}
Calcium, Total
Chloride
Creatinine
Glucose
Magnesium
Phosphate
Potassium
Protein, Total
Sodium
Total Iron, TIBC, UIBC, Transferrin Saturation
Urate
Urea
Urine Chemistry (Quantitative Protein, Sodium, Potassium, Creatinine, Osmolality)

Drug Monitoring

Acetaminophen
Carbamazepine
Digoxin
Drugs of Abuse
Ethanol
Gentamicin
Lithium
Phenobarbital
Phenytoin
Salicylate
Theophylline
Tobramycin
Valproic Acid
Vancomycin

Endocrinology

Thyrotropin (TSH)
Free Thyroxine (FT₄)
Free Triiodothyronine (FT₃)
Vitamin B₁₂
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
Dehydroepiandrosterone sulphate (DHEA-S)
Alkaline Phosphatase (ALP)

Enzymes, Cardiac Markers & Lipids

Alanine Aminotransferase (ALT)
Amylase
Aspartate Aminotransferase (AST)
Gamma Glutamyl Transferase (GGT)
Lactate Dehydrogenase, Total (LD)
Lipase
Total Creatine Kinase (Total CK)
CK-2
Serum Myoglobin
Serum Troponin I
Serum Troponin T
Cholesterol
Triglycerides
HDL-cholesterol (HDL-C)
LDL-cholesterol (LDL-C)

Immunology

Antinuclear Antibody (ANA)
Rheumatoid Factor (RF)
Antimicrosomal Antibody (MAH)
Anti-TPO
C-reactive Protein (CRP)
High Sensitivity CRP
Anti ds-DNA
Specific Proteins: IgG, IgA, IgM, IgE
C3
C4
Protein Electrophoresis

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 18
Trisomy 21
Open Neural Tube Defect (ONTD)

HEMATOLOGY

Bone Marrow

Aspirate and/or Biopsy preparation
Descriptive Morphology
Diagnosis

Coagulation

International Normalized Ratio (INR)
Activated Partial Thromboplastin Time (APTT)
Heparin Assay
Factor VIII
Factor IX
D-dimer
Thrombophilia Investigation:
Activated Protein C (APC) Resistance
Antithrombin
Protein C
Protein S
Factor V Leiden
Prothrombin Gene Mutation
Russell Viper Venom (test and confirm)

Flow Cytometry

Lymphocyte Immunophenotyping (HIV)
Leukocyte Immunophenotyping (Hematological Investigation)
CD34⁺ Stem Cell Enumeration

Red Cell Disorders

Hemoglobin S Screen
Hemoglobin Fraction Quantitation
Fetal Maternal Hemorrhage
Glucose-6-phosphate Dehydrogenase (G6PD)

Morphology

Peripheral Blood Film:
Differential Leukocyte Count
Descriptive Morphology
Diagnosis

Routine Hematology

Leukocyte Count
Erythrocyte Count
Hemoglobin
Hematocrit
Mean Corpuscular Volume
Thrombocyte Count
Automated Leukocyte Differential
Reticulocyte Count
Body Fluid Cell Count

Transfusion Medicine

ABO and Rh Grouping and Interpretation
Antibody Detection
Antibody Identification
Direct Antiglobulin Testing (DAT)
Crossmatching
Phenotyping
Titrations

MICROBIOLOGY**Bacteriology**

Aerobic and anaerobic isolation and identification of organisms from:
Blood
Genital specimens
Throat swabs
Urine
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
Antigen Detection:
Chlamydia trachomatis
Respiratory Syncytial Virus
Influenza A virus
Influenza B virus
Parainfluenza virus

GENETICS**Cytogenetics**

Blood
Bone Marrow
Tumour
Tissue
Amnion Cells

**Molecular Diagnostics of Inherited Diseases
(Suspended for 2005)****ANATOMIC PATHOLOGY****Histopathology****Histotechnology**

Routine stains
Special stains
Immuno-histochemistry stains

Cytopathology (Suspended for 2005)

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 H TESTING MATERIAL SUPPLIERS AND REFERENCE LABORATORIES

TESTING MATERIAL SUPPLIERS

CHEMISTRY DISCIPLINES

Chemistry

Bio-Rad Laboratories (Canada) Ltd.
Hamilton Regional Laboratory Medicine Program,
Hamilton, Ontario
The Credit Valley Hospital, Mississauga, Ontario

Drug Monitoring

Centre for Addiction and Mental Health, Toronto, Ontario
The Credit Valley Hospital, Mississauga, Ontario

Endocrinology

Consolidated Technologies, Inc, Austin, Texas
Toronto General Hospital, University Health Network,
Toronto, Ontario

Enzymes, Cardiac Markers and Lipids

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

Maternal Serum Screening

United Kingdom National External Quality
Assessment Service (UK NEQAS)

Point-of-Care Testing (Glucose Meters)

Bio-Rad Laboratories, Benicia, California

HEMATOLOGY DISCIPLINES

Hematology-Routine

Hamilton Regional Laboratory Medicine Program,
Hamilton, Ontario
R&D Systems, Inc., Minneapolis, Minnesota

Hematology-Red Cell Disorders

Hamilton Regional Laboratory Medicine Program,
Hamilton, Ontario

Hematology-Flow Cytometry

London Health Sciences Centre, London, Ontario
R&D Systems, Inc., Minneapolis, Minnesota

Coagulation

Affinity Biochemicals Inc., Ancaster, Ontario
Hamilton Regional Laboratory Medicine Program,
Hamilton, Ontario
bioMerieux Canada, Inc., Saint-Laurent, Quebec
South Manchester University Hospital NHS Trust,
Manchester, U.K.

REFERENCE LABORATORIES

Reference Laboratory, Ortho Clinical Diagnostics Inc.,
Rochester, New York
Diabetes Diagnostic Laboratory, University of
Missouri-Columbia, Columbia, Missouri

Centre for Addiction and Mental Health,
Toronto, Ontario

Wadsworth Center for Laboratories and Research, New
York State Department of Health, Albany, New York
Reference Laboratory, Ortho Clinical Diagnostics Inc.,
Rochester, New York
Northwest Lipid Research Core Laboratory, University
of Washington, Seattle
Canadian External Quality Assessment Laboratory Inc.
(CEQAL), Vancouver, British Columbia

Hamilton Regional Laboratory Medicine Program,
Hamilton, Ontario

Hamilton Regional Laboratory Medicine Program,
Hamilton, Ontario

Hamilton Regional Laboratory Medicine Program,
Hamilton, Ontario

APPENDIX H TESTING MATERIAL SUPPLIERS AND REFERENCE LABORATORIES

TESTING MATERIAL SUPPLIERS

Morphology and Hematology-Bone Marrow

Various laboratories throughout the province

Transfusion Medicine

Immucor/Gamma, Houston, Texas

London Health Sciences Centre/

Canadian Blood Services, London, Ontario

MICROBIOLOGY DISCIPLINES

Bacteriology

London Health Sciences Centre, London, Ontario

AFB Smears

Central Public Health Laboratory, Toronto, Ontario

Mycology

Sporometrics Inc.—Purchased from culture collections

University of Alberta Microfungus Collection and
Herbarium, Edmonton, Alberta

the Centraalbureau voor Schimmelcultures, The
Netherlands

Agricultural Research Service Culture Collection,
National Center for Agricultural Utilization
Research, Peoria, Illinois, U.S.A.

Parasitology

Hamilton Regional Laboratory Medicine Program—

St. Joseph's Site, Hamilton, Ontario

Centre for Travel and Tropical Medicine Toronto

General Hospital, Toronto, Ontario

The Credit Valley Hospital, Mississauga, Ontario

Virology

London Health Sciences Centre, London, Ontario

Meridian Bioscience Inc., Cincinnati, Ohio

ANATOMIC PATHOLOGY

Various participating laboratories

CYTOLOGY

Various participating laboratories

GENETICS

Various participating laboratories

REFERENCE LABORATORIES

Saskatchewan Laboratory Quality Assurance Program

Northumberland Hills Hospital

Sunnybrook and Women's College Health Sciences Centre

The Credit Valley Hospital, Mississauga, Ontario

Royal Victoria Hospital, Barrie, Ontario

Central Public Health Laboratory, Toronto, Ontario

London Health Sciences Centre, London, Ontario

Mount Sinai Hospital, Toronto, Ontario

The Credit Valley Hospital, Mississauga, Ontario

The Ottawa Hospital, Ottawa, Ontario

Hamilton Regional Laboratory Medicine Program,
Hamilton, Ontario

MDS Laboratories, Etobicoke, Ontario

Central Public Health Laboratory, Toronto, Ontario

Wadsworth Centre for Laboratories and Research,
Albany, New York

Laboratoire de santé publique du Québec, Ste-Anne-
de-Bellevue, Quebec

Central Public Health Laboratory, Toronto, Ontario

National HIV Reference Laboratory, Health Canada,
Ottawa, Ontario