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ENSURING ACCESS TO HIGH QUALITY MOLECULAR ONCOLOGY LABORATORY TESTING AND CLINICAL CANCER GENETIC SERVICES IN ONTARIO

Report of the Molecular Oncology Task Force | December 2008

EXECUTIVE SUMMARY

Science today allows us to examine the genetic makeup of individuals and use the information to predict cancer risk, diagnose cancer, predict response to treatment, and better target therapies to individual patients. This exciting breakthrough field, called molecular oncology, has evolved rapidly. Ontario has built an impressive foundation in basic science in the field, and established 20 laboratory testing sites and 22 clinical services sites that offer risk assessment and genetic counselling. Test volumes grew 52% from 2003 to 2007. Despite this growth, the system in Ontario is not keeping pace with the demand for testing or the availability of tests offered[1]. As a key initiative of the *2008–2011 Ontario Cancer Plan*, Cancer Care Ontario's Molecular Oncology Task Force (the Task Force) was convened to provide recommendations aimed at ensuring the Ontario system can meet the demands for these services and ensure quality and safety for patients, and is prepared to capitalize on this rapidly advancing field of knowledge.

THE CASE FOR CHANGE

The growth of genetic studies is leading to the increased pace of discovery of new predictive predisposition tests. In recent news, the quality of laboratory services offered in Canada has been brought into question. Reports from Newfoundland and New Brunswick of misdiagnosis of cancer and patients receiving inappropriate drug therapy have placed a spotlight on this issue. Compared with these jurisdictions, Ontario has a strong licensing and quality assurance program in place for most types of testing; however, the system has not kept pace with rapid advances in genetics and molecular testing. Accountability to monitor and evaluate molecular oncology activities is unclear, although Molecular Genetics is a new class of test at the Ministry of Health and Long-Term Care (MOHLTC), and, therefore, now part of the mandate of Quality Management Program – Laboratory Services (QMP-LS).

In addition to gaps in regulation and quality assurance, there is currently no effective mechanism to evaluate new tests for clinical utility, clinical and analytical validity, and cost-effectiveness, or to manage their introduction into clinical service. There is no standardized process for determining which tests should be offered as part of clinical oncology services in Ontario. Most tests have been added to service based on specific interests of local clinicians or researchers, and their ability to secure a budget allocation within a specific hospital. There is a need to enhance links to translational research to facilitate bringing new knowledge more quickly to patient care. Ontario lags behind other jurisdictions in terms of molecular test availability. For those services that are offered, geographic variation persists and patients are being under-referred. Part of the cause is the lack of a comprehensive, up-to-date resource of information about the services that are offered, and when and how to refer patients.

[1] For a comparison of tests offered in Ontario v. North America please refer to Figure 7.

Immediate action is required on the part of all stakeholders in the system to ensure access, quality, accountability and sustainability, to strengthen quality and safety, and to prepare the system for the future. The recommendations put forth by the Task Force are intended for testing in public hospital labs being considered for public funding.

TASK FORCE RECOMMENDATIONS

1) Immediately establish a provincial oversight body for molecular oncology services to oversee system planning for these services in Ontario; and to advise key stakeholders on test approval, delisting of obsolete tests, funding, licensing, accreditation, credentialing, quality assurance, location of services, and to ensure alignment of oncology services with all other genetic services.

2) Implement a mandatory approval process for each genetic test performed by laboratories in Ontario and administered by the appropriate regulatory agencies to ensure that only appropriately accredited and licensed laboratories with credentialed personnel are reporting and interpreting laboratory results that impact patient care.

3) Ensure that each genetic test performed by a laboratory meets rigourous quality assurance criteria and is regularly subjected to proficiency testing (external validation).

4) Establish and fund an existing or new information-sharing mechanism to ensure that critical information is readily available to referring physicians and the public regarding availability of tests, how to refer, what data the test will yield, its limitations, patient eligibility criteria, specimen handling guidelines, and clinical management.

5) A comprehensive and competitive approach to funding should be established that addresses dynamic volumes and variation in complexity of testing and clinical care, as well as the costs associated with risk assessment and genetic counselling. Funding should capture province-wide utilization of testing and clinical services and be linked to quality and utilization data.

6) Promote translational research and establish an “advance notice” process to ensure the system is prepared to implement new tests and technologies when evidence warrants.

By working together to facilitate the above recommendations, government, Quality Management Program – Laboratory Services (QMP-LS), researchers, Cancer Care Ontario, training organizations and the clinicians/scientists providing service will ensure a stronger, sustainable, safe and cost-effective system of molecular oncology services for Ontario. Not addressing these issues will result in insufficient infrastructure to meet growing demands and an inability to implement and fund new tests. In the absence of a coordinated system with proper oversight and quality assurance mechanisms in place, the potential for a breakdown of the system that affects patient safety and treatment (like the Newfoundland experience) is a genuine risk.

An Example of the Current Challenge: K-RAS Testing

At the American Society of Clinical Oncology Conference in June 2008, clinical trials data were presented showing that a biologic therapeutic used in patients with metastatic colorectal carcinoma was not beneficial for those with a mutation in the K-RAS gene. These findings were based on multi-centre trials, and involved labs that did molecular genetic testing to determine K-RAS status.

Following the release of these data there was demand from clinicians for local genetics labs to offer this test in Ontario instead of having the testing done in the United States.

As of November 2008, the anti-EGFR Antibody used to treat metastatic colorectal cancer had been approved for funding in Ontario provided that K-RAS testing is done first to ensure efficacy of the treatment. Despite this requirement, testing remains unfunded and unlicensed. In the absence of a clear oversight mechanism, and in an effort to implement the test expeditiously, arrangements were made by the manufacturer for testing in a single laboratory. Some patients being considered for the drug are having their testing paid for by the drug manufacturer while others are paying out-of-pocket, or are having the testing paid for by individual insurance companies, or the MOHLTC's Out of Province Testing Program. In addition, there are research labs offering to do the test on a fee for service basis.

Individual clinicians try to make the best decisions around treatment of their patients based on the information available to them. Once there is compelling evidence that a biomarker can stratify responders and non-responders or tailor/improve therapy there needs to be a mechanism by which drug programs, labs, MOHLTC, and Cancer Care Ontario can work together to get these tests and the genetic services associated with them quickly available to health care providers.

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INTRODUCTION

Background

The explosion of information regarding human genetics and its role in cancer has had a profound impact on genetic testing and related clinical cancer genetic services in Ontario. The issue is becoming less a question of whether biomarkers are known and tests have been developed and increasingly a question of how quickly and effectively individuals can be counselled, tested, and clinically managed. New molecular tests permit better patient management and more efficient use of targeted cancer therapies; however, effective testing requires adequate licensing, personnel, oversight of quality, and financial support.

The quality of laboratory tests offered in Canada has recently been brought into question. Reports from Newfoundland and New Brunswick of inaccurate laboratory testing and of patients subsequently receiving inappropriate drug therapy have placed a spotlight on this issue. The current regulatory environment for molecular oncology testing is insufficient to ensure such problems will be avoided here. Other countries have far more sophisticated oversight and regulation of molecular oncology testing and clinical cancer genetic services than Ontario does. In the United States, tests are funded based on evidence of clinical utility and several oversight and regulatory bodies (CLIA, CAP, CDC, FDA) are in place. Similarly, the United Kingdom Genetic System Network has a good system of oversight[2]. Australia and New Zealand also have organizations for oversight[3].

According to results from a survey sent to physicians, referring laboratories and testing laboratories, the importance of molecular oncology will increase in all areas of diagnosis, prognosis and treatment over the next 5 years[4]. Input from Regional Cancer Program leaders and Cancer Care Ontario's (CCO) Provincial Pathology and Laboratory Medicine Program led to the inclusion of the issue of access to these services as one of four key initiatives in the *Ontario Cancer Plan*[5]. This resulted in CCO striking the Molecular Oncology Task Force to provide recommendations aimed at ensuring access to high-quality molecular oncology laboratory testing and clinical cancer genetic services, and the development of a sustainable system for quality assurance processes and funding of molecular oncology services[6].

What is Molecular Oncology?

Molecular oncology is the application of genetic knowledge to predict a patient's predisposition to cancer, to diagnose and monitor cancer or predict prognosis, or to improve cancer treatments with personalized therapies[7].

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[2] More information available at http://www.ukgtn.nhs.uk/gtn/Information/The+UKGTN/Organisation+Structure

[3] Australia and New Zealand Health Policy, 2006. 3:13.

[4] Miller, Fiona; Krueger, Paul; Christensen, Robert; Ahern, Catherine; Carter, Ronald; and Kamel-Reid, Suzanne. Postal Survey (2006) of physicians and laboratories: Practices and perceptions of molecular oncology testing (Unpublished, August 18th, 2008 version submitted to *CMAJ*)

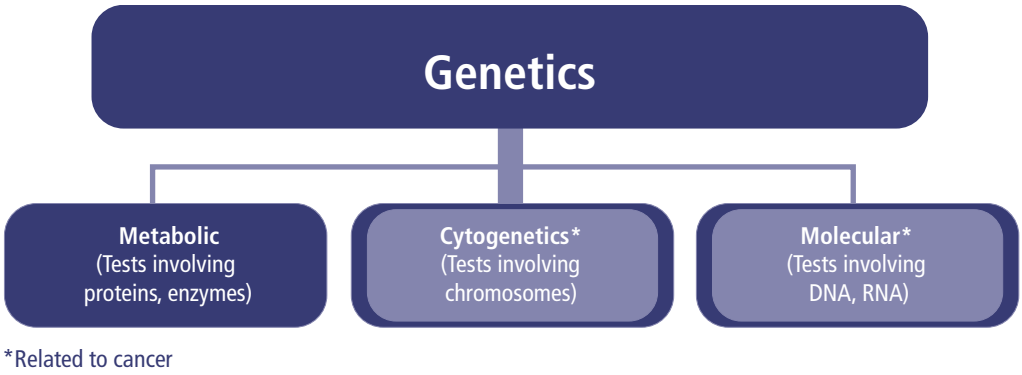
[5] Ontario Cancer Plan 2008–2011, CCO, available at http://www.ontariocancerplan.on.ca

[6] See Appendix 2 for a list of Task Force members, and Appendix 3 for an overview of methods used in preparing this report.

[7] See Appendix 1: Glossary for definitions of terms used throughout this report.

Genetic testing comprises three distinct types of laboratory testing: metabolic (tests involving proteins and enzymes), cytogenetics (tests involving chromosomes using techniques like FISH and karyotyping), and molecular (tests involving DNA and RNA). See Figure 1. The methods, personnel and equipment can be different for each type of testing. There are currently no metabolic genetic tests for cancer; therefore, molecular oncology currently comprises cytogenetics and molecular genetics services only. They can test for either "inherited" or "acquired" genetic changes that cause or predispose to cancer.

Figure 1: Types of Genetic Laboratory Testing



Acquired disease, or **acquired cancer**, refers to disease that *cannot* be passed onto offspring, whereas inherited disease, or **inherited cancer**, *can* be passed down through generations to other family members. While the vast majority of cancers are considered to be acquired there are several common cancers, including breast, ovarian and colorectal, with small, but well-described hereditary subsets, and evaluation of these patients and families consumes considerable resources.

Molecular oncology includes both laboratory testing and clinical cancer genetic services. **Clinical cancer genetic services** include the study of an individual's family and clinical history in conjunction with genetic testing to assess his/her risk of getting a disease, genetic counselling for individuals who may choose to have testing, and the use of molecular oncology test results in surveillance and treatment planning. It involves professionals who provide related clinical services such as medical geneticists, genetic counselors, oncologists and nurses.

CURRENT STATE OF MOLECULAR ONCOLOGY IN ONTARIO

Maria, a 43 year old mother of two started feeling unwell with a two-month history of increasing fatigue, weight loss, night sweats and dizziness. She went to her doctor, who took a blood sample and found her white blood cell count to be very high. Maria was then seen by an oncologist who suspected Chronic Myeloid Leukemia (CML), based on cell morphology and flow analysis. A molecular genetics test was ordered to confirm this diagnosis. The genetics test identified a fusion of two genes causing a gene mutation, consistent with a diagnosis of CML. Chemotherapy was started using a drug that specifically targets this mutation and subsequently kills the cancer cells. Initially, Maria had a good response to treatment and was monitored routinely using a genetics test that can quantify the presence of the gene mutation. Cells with the gene mutation were undetectable. After 18 months, however, this genetics test indicated that once again there were cells present with this mutation and they were increasing in number. After confirming her genetics test result, her oncologist increased the chemotherapy dose and requested a different genetics test to determine if an additional mutation had occurred, one which now makes her less responsive to her chemotherapy drug. The genetics test revealed that indeed, she did have such a mutation, and should therefore be switched to a different drug. Her therapy was changed, she responded well, and she remains disease free 12 months later. Genetic testing allowed treatment to be specifically tailored to Maria's cancer.

Laboratory Testing

Between 2003 and 2007, molecular oncology (cytogenetics and molecular) testing volumes grew by 52% from 18,771 to 28,517 tests in Ontario in those labs for which volumes are tracked[8]. The pace of growth is likely to continue or increase, since both cancer incidence and the pace of relevant scientific discoveries continue to grow. See Figure 2 for the growth of molecular genetic testing volumes for acquired and inherited cancer tests, and, Figure 3 for the growth of cancer cytogenetics testing volumes.

[8] Provincial volumes collected from individual Ontario laboratories by Ontario Genetics Secretariat, 2008. See Appendix 8.

Figure 2: Molecular Genetic Volumes for Acquired and Inherited Cancer in Provincially Recognized Ontario Labs, 2003–2007

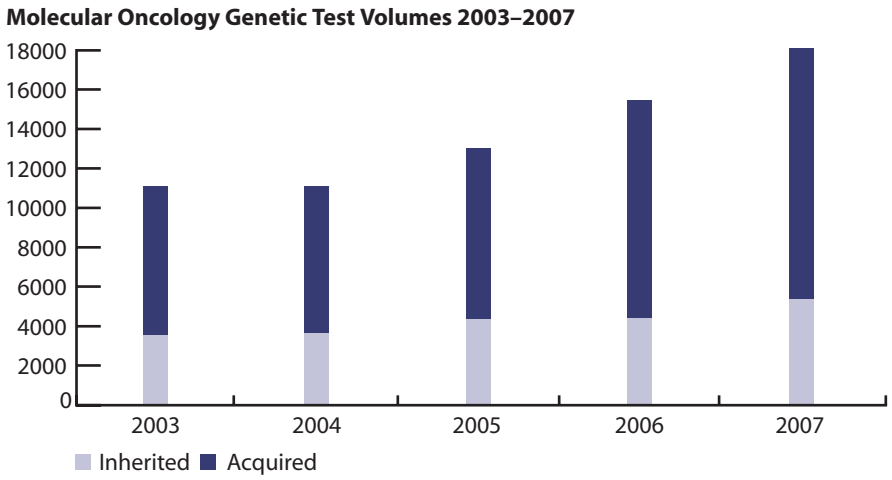
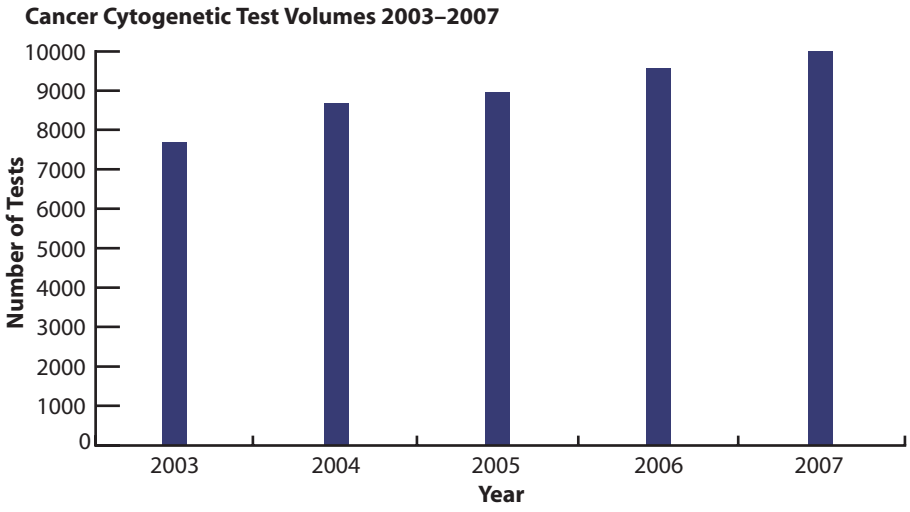


Figure 3: Cancer Cytogenetics Test Volumes in Provincially Recognized Ontario Labs, 2003–2007



Data includes both inherited and acquired volumes together.

There is no standardized process for determining which tests should be offered as part of clinical oncology services in Ontario. Most have been added to service based on specific interests of local clinicians or researchers, and their ability to secure a budget allocation within a specific hospital. There is also no process for delisting obsolete tests.

There are nine molecular genetics and eleven cytogenetics labs in Ontario formally recognized by the Laboratory Licensing Branch of the Ministry of Health and Long-Term Care (Ministry) who provide yearly volume data to the MOHLTC and who also provide budget and volume details to the Ontario Genetics Secretariat (OGS). Budget and volume figures used in this report are based on data submitted to OGS. There are an additional four molecular labs that submit volumes to Ministry but whose data were not available and were therefore not included in this report. All 24 labs are housed in hospitals. See Appendix 4 for a complete list of labs.

Molecular genetics labs are referred to as "provincial" resources. For higher volume molecular tests, there may be several labs offering the test. The decision about which tests to offer rests largely with individual lab directors and is often based on Institutional demand. For rarer tests, there was an effort amongst the labs in the past to centralize testing in fewer labs for quality assurance and cost-effectiveness purposes. In recent years, there has been a trend toward more duplication of services, with less regard for volume and cost considerations.

Cytogenetics labs are considered regional resources. These labs tend to offer similar services and serve a smaller catchment area. Their catchments are historically determined and are not aligned with LHIN boundaries.

The provincially recognized labs are not the only labs in Ontario offering molecular oncology testing services. Task Force members are aware of testing being done for patient care in haematology, pathology and research labs of hospitals other than those listed in Appendix 4. The Task Force was not able to quantify this testing within the timeframe of its mandate, but members agree that the amount of testing performed in such labs is not insignificant.

Susan is 36 and has recently been diagnosed with breast cancer. Her mother had ovarian cancer at age 58. Her maternal aunt had breast cancer at 49. Susan is referred for genetics counselling. She is counselled about inherited breast and ovarian cancer, the two causative genes, and the impact of genetic testing. She learns she is eligible for mutation testing of BRCA 1 and 2. She is keen to pursue this in order to learn more about her own health, her risks for future cancer, optimal surveillance, and future risks that her sister, brother and young daughter might have.

Clinical Cancer Genetic Services

Genetic counselling is the process of helping people understand and adapt to the medical, psychological and familial influences of genetic contributions to disease. Clinical Cancer Genetic Services use family and medical histories to assess the possibility of predisposition to occurrence, or recurrence, of disease; provide education about inheritance, testing, management, prevention, resources and research; and, includes genetic counselling to promote informed choices and adaptation to potential disease risk[9].

There are 13 regional centres and nine Northern or satellite clinics throughout Ontario offering cancer genetic services. A regional centre has a full complement of skilled clinical and laboratory staff and provides a wide range of services to the catchment area. A Northern or satellite clinic has a limited complement of staff on-site, chiefly genetic nurses/counsellors, augmented by a formal relationship with a clinical geneticist in a regional centre. Such services may serve a large catchment area, usually with lower population density. See Appendix 5 for a list of these centres. There is variable consistency among all service sites in terms of using a standard service delivery model (i.e., types of referrals seen at each site, types of health care professionals providing services, and wait times). Although there are standard criteria for inherited cancer for counselling, testing and clinical management, there is a need to ensure they are up to date and used consistently, and to have the ability to track utilization of counselling services. This would facilitate the monitoring of access to services, ensure a quality standard for the services delivered across the province, and highlight gaps in services related to wait times and availability of services in various regions, as well as assist in resource planning (personnel, funding, service locations).

According to a survey of 22 of the centres/clinics conducted by the Task Force in June 2008, referrals for cancer-related genetic counselling have increased by 61% since 2002 (3,966 referrals reported in 2002, compared with 6,378 referrals reported in 2007) with no evidence of a plateau to date[10]. See Figure 4. It is estimated that 5% to 10% of cancers are currently believed to be related to an inherited predisposition[11]. Based on cancer incidence projections, this would equate to an anticipated demand of 6,300 primary referrals for counselling, plus eligible family members[12]. There was consensus within the Task Force that clinical services are not able to meet current need. Also, the survey revealed that hereditary breast and ovarian cancer referrals dominate current service use and account for about 80% of all referrals. In the opinion of both the survey respondents and representatives of the Ontario Familial Colon Cancer Registry[13], colorectal cancer patients are currently being under-referred.

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[9] National Society of Genetic Counselors Definition Task Force; Resta R, Biesecker BB, Bennett RL, Blum S, Hahn SE, Strecker MN, Williams JL. A New Definition of Genetic Counselling: National Society of Genetic Counsellors Task Force Report. J Genet Couns. 2006; 15(2):77-83.

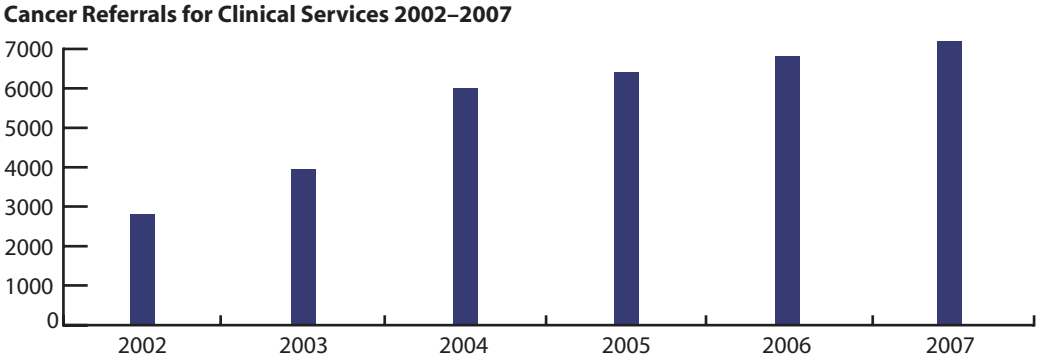
[10] CCO Molecular Oncology Task Force Clinical Services Survey, June 2008.

[11] Brose MS et al. Genetic Predisposition to Cancer. In: Bast RC et al, ed. Cancer Medicine e5. Hamilton, ON: B.C. Decker; 2000: 168-184

[12] CCO iPort, accessed October 2008. 2007 projected cancer incidence is 62,545

[13] August 2008 correspondence from S. Gallinger and M. Aronson to S. Kamel-Reid.

Figure 4: Cancer Referrals for Clinical Services 2002–2007



Human Resources

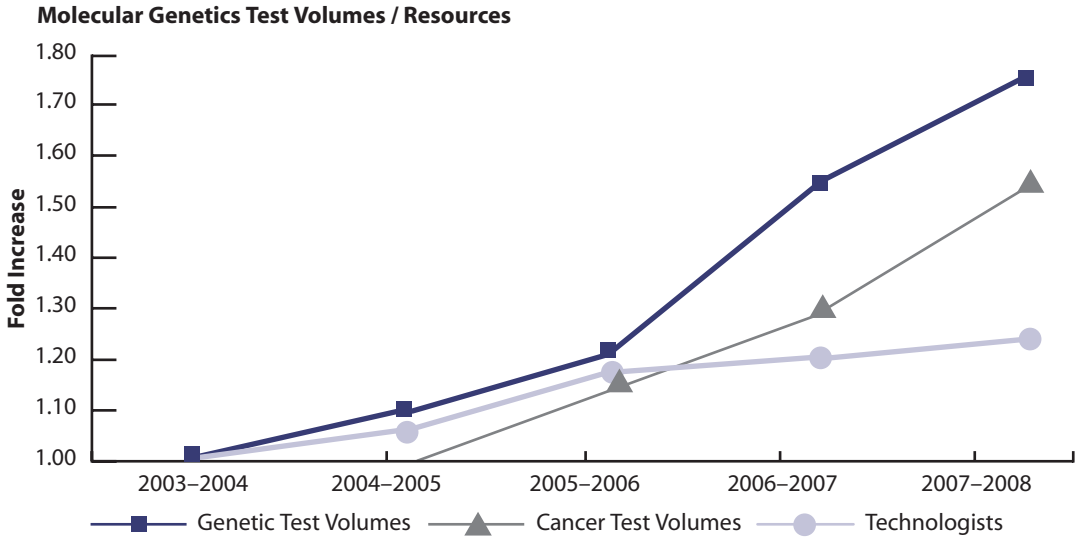
According to statistics tracked by the Ontario Genetics Secretariat, there are 260 full-time equivalent staff members working in the provincially recognized genetics labs as of 2007. Eighty-three percent of these are technical staff performing testing services[14]. Staffing numbers have grown 9% in the five years ending in 2007, with technical staff growing at the fastest rate (11%). These personnel perform all cancer and non-cancer genetic testing services within the molecular and cytogenetic labs. There are insufficient data available to distinguish the specific number of personnel who provide cancer-related services only. See Appendix 6 for staffing levels for each type of lab, by year, by category.

The growth in knowledge of the genome is the most significant factor influencing test growth and therefore human resource needs. The inability to quantify the gap in service demand means that the Task Force was unable to accurately quantify the need for additional human resources. Variable test complexity and the availability of technology to automate components of analysis also make it difficult to project human resource requirements.

What is known is that in contrast to the increase in testing volumes and the increased demand for molecular genetic testing, resources have remained relatively stable. See Figure 5. This has resulted in increased efficiencies of testing, but sub-optimal service delivery as evidenced by unavailability of tests in Ontario that are routinely offered in the U.S. See Figure 7.

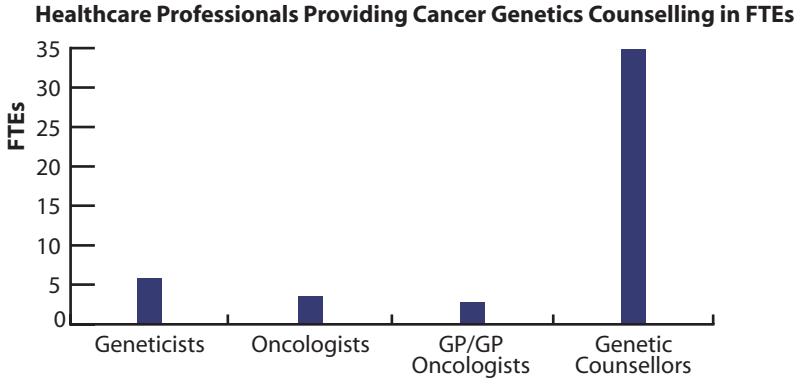
[14] Ontario Genetics Secretariat data, 2008, provided by P. Ray. Includes molecular and cytogenetic labs. Excludes metabolic labs, since they do not perform cancer services.

Figure 5: Growth Rate of Genetic Testing and Number of Technologists in Ontario, 2003–2008



Based on the results of the Clinical Survey, there are 45.49 FTEs that are providing cancer genetics counselling in Ontario[15]. For a breakdown of the healthcare professionals providing these services see Figure 6.

Figure 6: Healthcare Professionals Providing Cancer Genetics Counselling in FTEs



[15] CCO Molecular Oncology Task Force Clinical Services Survey, June 2008.

Funding, Expenditures and Volumes

The volume-based "Priority Program" funding for genetics put in place by government in the early 1990's was discontinued in 2004/05. A test-based funding program for HER2/Neu testing for breast cancer, administered by Cancer Care Ontario, was put in place by the Ministry in 2005/06 to address the pressures on labs when new evidence led to the need for a rapid increase in test volume. Now that volumes have stabilized, responsibility for this testing and associated counselling is expected to be covered by global budgets of hospitals.

Annual 2007/08 expenditures reported by provincially recognized genetic labs were $32.3 million, representing testing and personnel costs. What the Task Force was not able to ascertain was a comparison of what is currently funded v. incremental growth and more data is needed to do this analysis. The majority of the $32.3 million is used in cytogenetic labs (48%) and molecular genetic labs (42%), with only 10% being ascribed to metabolic genetic labs[16]. This is an under-representation of total costs of genetic testing currently being done in Ontario because it excludes:

- The testing being done outside of the formally recognized centres whose data were captured by OGS,
- Expenditures by the Ministry for out-of-province services,
- The costs of testing paid for by patients, though the extent of this is unknown and not thought to be significant.

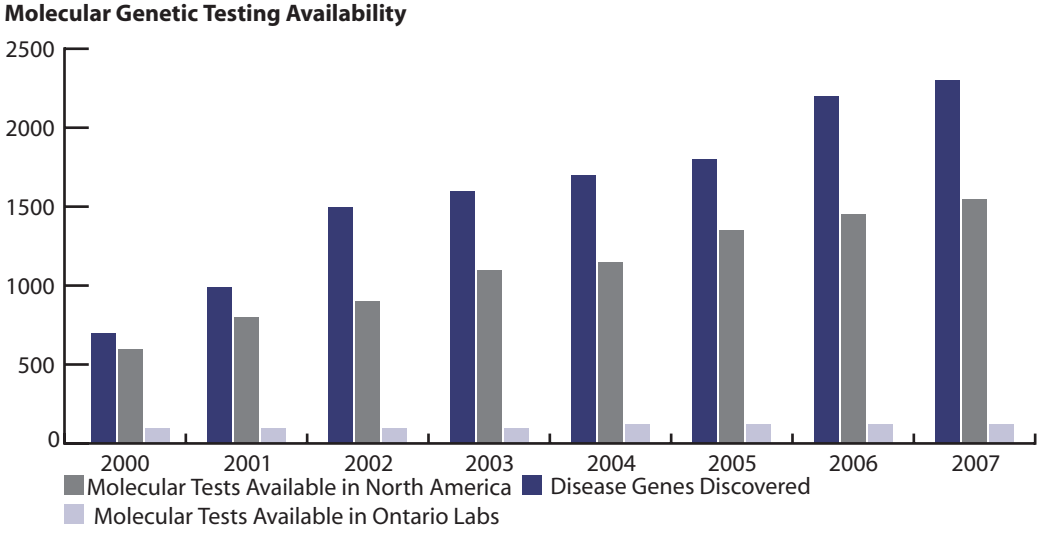
There are insufficient data to delineate the costs of the cancer-related testing from this overall budget. However, in terms of volume, cancer-related testing represents about 17% of the province's total overall genetic testing volume (29,000 out of 167,000 total genetic tests reported in 2007/08)[17]. Currently, cancer represents 39% of all cytogenetics testing and 23% of molecular genetics testing with volumes increasing by an average of 6% per year for cytogenetics and nearly 20% per year for molecular genetics. See Appendix 7 and Appendix 8 for budget and volume details.

The growth rate in test volumes is striking, with cytogenetics test volumes growing 11% over the five years ending in 2007, and molecular genetic testing growing by 70%. While a portion of this growth is related to increasing disease incidence, particularly in cancer, most of this growth is driven by the growing knowledge base in genomics and the subsequent demand for new tests. The numbers of total tests available in Ontario grew 65% from 2000 to 2007 (from 115 to 190). However, the availability of tests in Ontario is low when compared with North America as a whole. See Figure 7 below. **It is unclear how many tests should be offered in Ontario, since there is currently no formal process in Ontario for new tests to be reviewed and added to clinical service**.

[16] Ontario Genetics Secretariat survey, 2008. Included are salaries, benefits and laboratory operating costs. Excludes capital and overhead.

[17] Ontario Genetics Secretariat survey, 2008

Figure 7: Molecular Genetic Testing Availability, Ontario and North America, 2000–2007



Source: Ontario statistics are from Ontario Genetics Secretariat, 2008. Genes discovered from genetests.org and molecular test availability in North America from ncbi.nlm.nih.gov, accessed 2008.

Licensing and Regulation

Licensing and regulation have not kept pace with the growth in new genetic knowledge. As a result, well-meaning clinicians have found mechanisms to work around the regulatory barriers in order to continue to provide access to services. For example, out-of-province testing is arranged for patients, and, some testing done under a research umbrella is being used to guide clinical decision making. In both of these instances the quality of the testing and interpretation is not subject to provincial quality assurance standards.

The regulatory environment for molecular oncology services involves both provincial and federal jurisdictions. The Ministry's Laboratories Branch is accountable for licensing labs. Products sold as kits and used in clinical testing must be approved by Health Canada. In practice, neither of these regulatory processes comes to bear on the vast majority of oncology testing that is currently offered in Ontario.

In terms of licensing, the Ministry provides each lab with an institutional license with the requirement that each type of test is approved individually for each lab. At the time of the review, very few of the molecular oncology tests offered in Ontario had been approved through this process. The process is time-consuming and there is no clear incentive for labs to participate. Referring physicians do not check on license status before referring a specimen for testing; the Ministry has no mechanism to find out what tests are being offered outside of the provincially recognized labs; funding for the tests is through hospital global budgets and is not linked to licensing; hospital leadership may be under the mistaken impression that genetic testing has the same rigourous licensing and quality assurance protocols of more established labs services.

Furthermore, molecular genetic tests are not licensed or under the same strict regulation as other disciplines that must submit applications to verify evidence of clinical utility and validity[18].

Health Canada's regulatory processes for Medical Devices and In Vitro Devices apply to reagents and equipment used for molecular oncology testing done for clinical care[19]. In practice, manufacturers of the reagents and equipment used in molecular genetic testing routinely attach labels specifying "For Research Purposes Only Not for Use in Diagnostic Procedures" thereby avoiding the application of the regulation. There is no process for assessing the quality of "research only" materials used in clinical services testing.

Testing can be done using what is referred to as a testing "kit," which is a combination of reagents, enzymes and other inputs. In circumstances where there is no Health Canada approved kit for a specific test (there may not be a kit available commercially, or the kit may be awaiting approval from Health Canada), labs create what is referred to as a "home-brew" test. A home-brew test is one that is developed within a lab using commercially available materials. This is the mechanism by which most testing is done, since many tests do not have a commercially available kit, and those that are available are often prohibitively expensive to use. The development of home brew tests is a highly common practice in labs across the world as well as in Ontario. There is little regulatory oversight in place for such tests, although in theory all labs are required to show evidence of quality assurance procedures and participation in proficiency testing for every clinical test they offer[20].

While outside of the scope of this review, another issue on the horizon that may affect quality and access to testing is intellectual property rights related to gene patents. Current efforts to patent some genetic tests are creating a complex operating environment raising questions around where these tests can be legally performed and under what quality standards.

Quality Assurance

Oversight for quality of lab services in Ontario is within the mandate of the Quality Management Program – Laboratory Services (QMP-LS), which, as an Agent of the Ministry, is operated as a department within the Ontario Medical Association. QMP-LS has two operating divisions: 1) External Quality Assessment (EQA); and 2) Ontario Laboratory Accreditation (OLA). EQA for molecular oncology is not currently within the mandate of QMP-LS, as it has not been directed to address these services by government.

[18] QMPLS Genetics Committee Report to Health Canada OECD, September 2007

[19] QMP-LS Genetics Committee Report to Health Canada, OECD 2007.

[20] As of July 2008, with the release of OLA 4.1, this is now a requirement of Ontario Laboratory Accreditation.

Earlier this decade, Cancer Care Ontario, in conjunction with the lab community, instituted minimum volume standards and an EQA process for HER2/Neu testing for breast cancer. Part of the HER2/Neu testing algorithm, the FISH test, is a cytogenetic test. In this program, testing laboratories are linked to one of two reference centres. Labs are required to meet minimum volume standards and to provide samples of both positive and negative results from their lab for review by their reference centre on a regular basis. HER2/Neu reference labs subscribe to out-of-province EQA programs, and as of this year, will begin exchanging samples with each other for testing. For the past two years, CCO has administered a test-based funding mechanism for HER2/Neu testing that provided a potential lever to ensure concordance with standards. While the reference centre model has provided a successful model for at least one molecular oncology test, it is not without its drawbacks. As of this fiscal year, test funding will be returned to hospital global budgets, thus ending funding as a quality assurance lever. Another drawback is the lack of a clear process and authority on the part of the reference centres to act in the presence of poor quality assurance results or insufficient testing volumes. To date, any quality problems identified by an individual lab or its reference lab have been addressed successfully through mutual collaboration. There is a risk inherent in this system based largely on goodwill, which must be acknowledged.

A second mechanism for EQA currently in place in some labs is subscription to an out-of-country EQA program, for example, the College of American Pathologists (CAP). These are fee-based programs and, at the moment, not all molecular oncology tests are covered by such programs.

In addition to external proficiency testing, QMP-LS operates the Ontario Lab Accreditation Program (OLA). All labs in Ontario performing molecular genetics and cytogenetics testing are required to follow the processes, procedures and requirements outlined in the OLA molecular or cytogenetics checklists, respectively. Research labs that offer clinical testing are currently not inspected by OLA. This practice may place patients at risk.

There are currently no standardized mechanisms in place to measure turn around times for lab tests, or wait times for counselling. CAP has set a benchmark for cytogenetic labs requiring that 90% of test results must be delivered within 21 days[21]; however, there is no such benchmark for molecular tests. According to the Task Force survey, wait times to see a genetic counsellor, in those centres that track this statistic, are at a median of 16 weeks for non-urgent cases in the regional centres and 10 weeks at the Northern/satellite centres. Urgent cases are generally seen within two weeks. Only 62% of familial cancer programs currently track wait times[22]. A provincial mechanism is needed to facilitate tracking of wait times for clinical services in all regions of the province. One way to achieve this would be by linking familial cancer program wait times to funding as is currently done with surgical procedures and waits. This would enable a complete assessment of service gaps in Ontario, planning for services in light of anticipated increasing demand for genetic testing, and the linking of funding to service delivery.

[21] Commission on Laboratory Accreditation *Cytogenetics Checklist*, College of American Pathologists, 2007.

[22] CCO Molecular Oncology Task Force Clinical Services Survey, June 2008

Coordination and Advice

There has been little organization provincially within the genetics community over the past several years. The Ontario Advisory Committee on Genetics struck by the Ministry in the late 1990s was disbanded several years later, ostensibly due to a misalignment of the advice required and the nature of the advice provided.

In 2006, CCO established a provincial Pathology and Laboratory Medicine Program to advise on a quality agenda for cancer services in this domain. Access to and quality of genetic testing were identified as key priorities by this group.

In 2007, the community focusing on inherited genetics voluntarily came together with the support of the Hospital for Sick Children to form the Ontario Genetics Secretariat (OGS). The mandate of the OGS is to strengthen collaborations among the labs and clinical genetic service centres, and work towards improving genetic services across the province to ensure timely and leading edge genetic services to the people of Ontario. The presence of the OGS and its active work in building a community of practice for providers and in data tracking has filled a significant gap. With the focus of OGS being predominantly on adult and paediatric inherited disease, there continues to be a need for an oversight body focused on cancer, which is largely an acquired disease.

Access and Awareness

The referral base for cancer genetic testing is broad. Referrals for acquired disease are likely to come from an oncologist, often on the advice of pathologists. For inherited disease, referrals for genetic counselling and possible genetic testing may come from geneticists, surgeons, oncologists or primary care providers. Currently, there is no comprehensive resource of information for referring physicians to turn to in order to find out what cancer genetic tests are available in Ontario, where they are located, which patients are eligible, and how to refer patients for testing. Though tracking is difficult, the Task Force believes that access to service varies widely according to geography. There is currently a web-based tool available, ONGENE, operated by QMP-LS, that could fill this gap, provided its expansion is funded.

Research

Ontario is well positioned in the cancer biomarker sector due to the internationally recognized strengths of its basic oncology research community. There is also some initial effort underway to link Ontario-based bio-repositories to clinical/administrative data to provide a rich information source for researchers.

There is a weakness in translational research despite the additional infrastructure and support provided by the Ontario Institute for Cancer Research (OICR). The poor understanding and perceptions of the value of translational cancer research often inhibit active participation of internationally regarded cancer researchers in this area.

There is also a lack of interest on the part of research funding organizations to address certain types of questions related to test development that are in need of attention. For instance, there is a need to study appropriate methods for preparation, handling and analysis of specimens, and a need to develop technologies to allow more information to be gleaned from individual specimens (i.e., multiple marker testing).

On the clinical trials side, trials of therapeutic agents often do not address biomarker questions or they lack sufficient sample sizes to allow for proper evaluation of markers, and there are few trials focused directly on testing the predictive value of biomarkers.

There is no communication mechanism between researchers, clinicians and those who are planning for and funding clinical services. Without an advance notice process to alert system funders, planners and managers to what is coming, the system can be faced with a new marker, a strong evidence-base, and pressure from the public and providers to provide the test right away. In the face of this pressure, and due to a lack of process, the system must scramble to organize licensing and quality assurance, and to find funds and capacity to provide the service. The current shortfalls in availability of K-RAS testing for metastatic colorectal cancer is a prime example of a system that is not currently set up to respond quickly to the growing demands for genetic testing.

Education and Credentialing

Currently there is variable credentialing and education required for those conducting genetic testing and interpreting results. PhD lab directors and/or physicians signing out cases that impact patient care should have the appropriate competency in Laboratory Genetics. Some, but not all, lab directors are credentialed through the Canadian College of Medical Geneticists (CCMG) or the American Board of Medical Genetics (ABMG), both of which require specific post-graduate training in Clinical Laboratory Genetics and which provide formal training in interpreting clinical genetics laboratory results. Medical lab technologists, who perform the tests, are licensed by the College of Medical Lab Technologists of Ontario. There are specific training programs in molecular genetics and cytogenetics available for technologists, but there are no standards in place to require such training outside provincially recognized labs. Currently some clinical testing is being done in labs, such as research labs, where individuals performing and interpreting the test results have no formal training in genetics. While this testing may be a small fraction of overall genetics testing, any testing being done that impacts clinical management of patients should be done in licensed labs with appropriately credentialed personnel.

George, a previously healthy 77 year old grandfather, went to see his doctor due to increasing fatigue, bruising and spontaneous bleeding from the mouth and nose. Blood work revealed low blood cell counts. He was referred to a specialist, where a bone marrow test was performed that revealed acute leukemia. A sample of the bone marrow was then sent to the genetics lab, where a specific test was done to look for the presence of a gene abnormality. This abnormal gene was found in George, which lead to a diagnosis of acute promyelocytic leukemia. This strain of leukemia is highly responsive to treatment with all trans-retinoic acid (ATRA). During the course of treatment George received ATRA and chemotherapy and achieved complete remission. This was followed up with further chemotherapy and ATRA for a period of seven months. For two years after remission, monitoring of the bone marrow was done to look for the return of the gene abnormality. The bone marrows remained negative for the presence of this disease marker and George is now healthy and has been in remission for three years, with an excellent long-term prognosis. Prior to identification of this gene abnormality and the specific treatment associated with it, patients >70 years of age had only a 15% chance of surviving five years. Now nearly 80% of patients will live longer than five years.

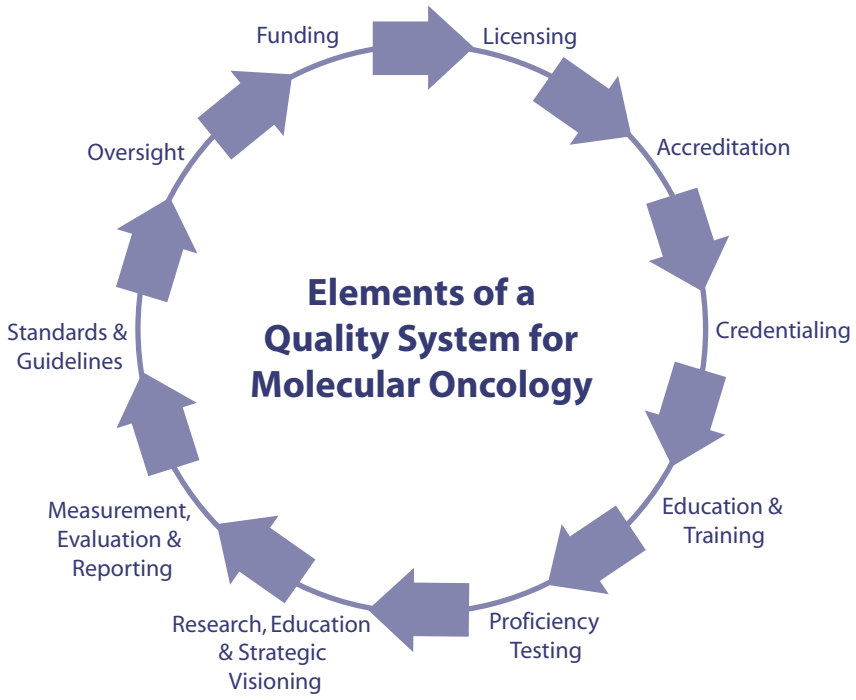
RECOMMENDATIONS FOR ONTARIO

The following recommendations build on several highly successful elements of the Ontario system, including:

- The current structure of molecular genetic laboratories as provincial resources to foster efficient provision of test services with sufficient volumes to ensure quality
- The presence of existing infrastructure within QMP-LS for accreditation and proficiency testing of lab services
- The presence and use of OLA to ensure that labs providing genetic testing are meeting quality standards and following proper processes and procedures
- The presence of a licensing infrastructure for laboratory services
- The presence of an emerging community of practice for genetics services overall, the Ontario Genetics Secretariat
- Successful programs at CCO for development of evidence-based guidelines, planning, and performance management that can be leveraged
- A strong cadre of qualified individuals performing current services

However, there are actions that need to be taken to further enhance patient access, and improve quality, accountability and oversight for the attainment of a high-performing molecular oncology system. See Figure 8.

Figure 8: Elements of a Quality System for Molecular Oncology



The following recommendations are tied to testing occurring within public hospital labs that are being considered for public payment.

Recommendation 1: Establish Provincial Oversight

Immediately establish a provincial oversight body for molecular oncology services to oversee system planning for these services in Ontario; and to advise key stakeholders on test approval, delisting of obsolete tests, funding, licensing, accreditation, credentialing, quality assurance, location of services, and to ensure alignment of oncology services with all other genetic services.

Better regulation and oversight of genetic services is needed to ensure Ontarians have access to high-quality services and to meet the needs of government and the healthcare system. Other countries, such as the United States, United Kingdom, Australia and New Zealand, have introduced oversight and regulation of molecular oncology services, and Ontario should review their models to help shape the system here.

The oversight body should:

I. Oversee planning related to:

- System capacity assessment and projections for cancer genetic testing and clinical cancer genetic services
  - Identifying human resource requirements and providing advice to educational institutions on future needs
  - Monitoring and reporting on key performance indicators related to access and quality
- Establishment of a rapid evidence-based test approval/delisting process
- Overall system monitoring including:
  - Working with CCO's Program in Evidence-Based Care (PEBC) to develop and disseminate clinical and organizational guidelines for service delivery
  - Establishing a molecular oncology testing minimum dataset that can be linked to existing oncology datasets to enable evaluation and management of services
  - Assessing and making recommendations about testing volumes and funding linked to quality criteria

II. Liaise with:

- Quality Management Program - Laboratory Services (QMP-LS) and the Ministry of Health and Long-Term Care (MOHLTC) to expand licensing, accreditation and quality assurance requirements for molecular oncology testing

- Research community to strengthen links to translational research to aid in bringing new knowledge more quickly to patient care
- Stakeholders to ensure alignment between the oncology component and all other genetic services
- Stakeholders to promote specialization within clinical genetics training programs and expand relevant curricula to include clinical and laboratory aspects of acquired and inherited cancer

III. Advise government on a sustainable funding mechanism for these services

Recommendation 2: Strengthen Licensing of Labs and Tests and Credentialing of Personnel

Implement a mandatory approval process for each genetic test performed by laboratories in Ontario and administered by the appropriate regulatory agencies to ensure that only appropriately accredited and licensed laboratories with credentialed personnel are reporting and interpreting laboratory results that impact patient care.

The Ministry's lab licensing process should ensure molecular genetic and cytogenetic tests are licensed in the same manner as other tests, and that they meet provincial requirements (OLA). Sufficient resources must be in place to ensure licensing requests can be processed in a timely fashion.

All labs providing genetic testing for patient care should be accredited by OLA as a genetic centre. Enforcement of this requirement will be facilitated by tying funding to accreditation, and also by introducing the information service that will provide a reference for patients and physicians about the licensed and accredited services available in Ontario and where to access them.

The following steps outline the Task Force's proposed process for bringing new tests into clinical service. These steps should be rapid and some processes can take place concurrently. It incorporates a similar rigorous review process such as that currently used for cancer drug review.

Steps:

I. An oversight body of clinical and laboratory experts and health economists monitors new knowledge and advises on the need for consideration of a new test and the need to de-list existing tests.

II. CCO's Program in Evidence-Based Care conducts a systematic review of the literature, environmental scan and expert consensus process, and makes recommendations about test acceptance, the organization of services (clinical and laboratory), and key quality criteria.

III. A cost-effectiveness analysis is completed, where applicable.

IV. CCO's Planning Unit provides an impact assessment outlining system requirements in terms of costs and human resources.

V. Based on the recommendations from the oversight body, the Ministry makes funding and licensing decisions. Funding and licensing are tied directly to the quality criteria.

VI. The Ministry sets a reimbursement rate for the test and related clinical services.

VII. Service providers submit applications for licensing.

VIII. QMP-LS expands the proficiency testing program and quality indicators.

IX. The information service notifying patients and referring physicians about test availability is updated as new information/tests become available.

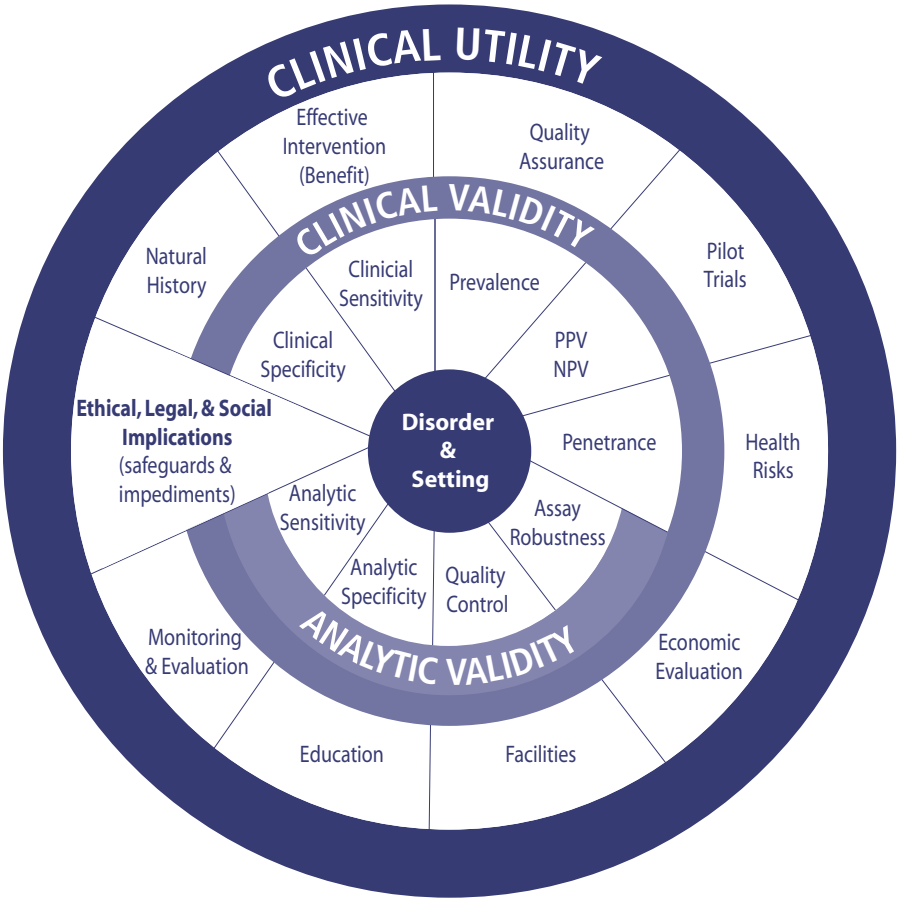
X. CCO to provide operational support and make funding recommendations based on performance management on behalf of MOHLTC.

Lab directors that are interpreting data and signing out results that impact patient care should have the competency and appropriate training in genetics to do so. Credentialing through the Canadian College of Medical Geneticists (CCMG) or the American Board of Medical Genetics (ABMG) or equivalent, should be considered. This ensures that individuals responsible for releasing genetic results have specific training in clinical laboratory genetics. Technologists should be specifically trained in molecular genetics or cytogenetics through an accredited training program such as the Michener Institute Program and licensed through the College of Medical Lab Technologists of Ontario (CMLTO). The complexity of genetic testing, and often difficult interpretation of test results necessitates the need for personnel with specialized training to maintain patient safety.

In addition, the oversight body should work to promote specialization within clinical genetics training programs to increase the number of medical geneticists with specific expertise in cancer genetics. It should encourage the relevant bodies of genetics to enhance and expand the curricula of geneticist, genetic counselling and oncologist training programs to include clinical and laboratory aspects of acquired and inherited cancer. The body's planning work should advise on the need to expand the number of training positions for medical geneticists, laboratory geneticists, technologists, oncologists, and genetic counselors.

The oversight body should consider adopting a framework to ensure comprehensiveness for test evaluation such as the ACCE framework developed by the U.S. Centers for Disease Control. ACCE stands for "Analytical validity, Clinical validity, Clinical utility and Ethical, legal and social implications of genetic testing." Analysis should be focused on a particular disease state in a particular population, for example, K-RAS testing for drug therapy decision making in metastatic colorectal patients. The framework is based on the principle that the evaluation of genetic tests should be an integrated process including all of these domains, as applicable. See Figure 9.

Figure 9: The ACCE Evaluation Process for Genetic Testing[23]



Recommendation 3: Mandate External Proficiency Testing

Ensure that each genetic test performed by a laboratory meets rigourous quality assurance criteria and is regularly subjected to proficiency testing (external validation).

The oversight body should identify the need for and oversee development of evidence-based standards by relevant bodies (CCO and QMP-LS) for all of the ACCE domains. This includes developing minimum volumes for labs, turnaround times, and wait times for clinical services.

[23] http://www.cdc.gov/genomics/gtesting/ACCE.htm, accessed October 2008.

The oversight body should work in conjunction with QMP-LS to ensure the frequency and scope of cytogenetics test challenges is sufficient.

Proficiency testing programs should be established by QMP-LS for all molecular oncology tests. The programs need to be developed on a test-specific basis, taking into account costs and volumes. Different tests may benefit from different models. There may be circumstances for which it is necessary for Ontario to support EQA elsewhere, such as the case when a proficiency testing program is not available through QMP-LS. Some tests may have sufficient volumes to allow them to benefit from a reference laboratory structure such as that which is in place for HER2/Neu. For others, a QMP-LS led program may be the best approach.

Recommendation 4: Inform Providers and Patients about Services

Establish and fund an existing or new information-sharing mechanism to ensure that critical information is readily available to referring physicians and the public regarding availability of tests, how to refer, what data the test will yield, its limitations, patient eligibility criteria, specimen handling guidelines, and clinical management.

For example, a web-based tool such as QMP-LS's ONGENE may be an option.

Recommendation 5: Link Funding to Quality and Access Goals

A comprehensive and competitive approach to funding should be established that addresses dynamic volumes and variation in complexity of testing and clinical care, as well as the costs associated with risk assessment and genetic counselling. Funding should capture province-wide utilization of testing and clinical services and be linked to quality and utilization data.

The current system of funding a therapeutic such as a new drug, but expecting the related testing and genetic counselling services to be absorbed into hospital global budgets is not sustainable. Where a test is linked to a therapeutic, the approval and funding of the related testing and clinical services must be addressed concurrently with consideration of the therapeutic. A new funding mechanism should be established for all molecular oncology services, regardless of whether or not they are tied to a therapeutic.

The funding mechanism needs to:

- Be tied to quality criteria.
  - Hospitals should be funded only if minimum testing volume criteria are met, the lab participates in a high-quality external proficiency testing program, the lab is accredited, turnaround times for testing are within guidelines, and appropriately trained and credentialed staff provide the laboratory and clinical services.

  - Evidence-based eligibility criteria should be developed for referral to hospitals/health units with appropriately credentialed and sufficient genetic counselling service providers and accompanying support staff to meet the demand for cancer risk assessment of Ontario residents.

- Allow flexibility for temporary movement of testing services, if required, for quality assurance purposes.
  - Regular laboratory quality assurance processes will uncover problems that need to be addressed. When new products are introduced into the test process (e.g., a new reagent or platform), testing is conducted to ensure continued reliability of clinical results. If problems arise, a lab needs to suspend clinical service while such issues are resolved. Within the HER2/Neu program, labs temporarily shifted testing to their reference lab in order to prevent an interruption in patient care. The funding mechanism needs to allow this kind of flexibility to ensure that quality criteria can still be met and turnaround times do not suffer as a result.
- Address all of the relevant costs, including:
  - Laboratory testing costs (equipment, materials, personnel) and related clinical services (professional and support personnel) to ensure patients and their physicians have appropriate information to support decision making along the continuum of care;
  - Proficiency testing;
  - Education/information for patients and referring physicians.
- Address the varying complexity of testing.
  - Each test is unique in terms of the complexity of testing, the size and nature of the eligible patient population and the need for related clinical services (genetic counselling and ongoing clinical management).
  - Allow the system to respond to rapid changes in knowledge and technology.

Recommendation 6: Get Discoveries to Patients More Quickly

Promote translational research and establish an "advance notice" process to ensure the system is prepared to implement new tests and technologies when evidence warrants.

Ontario needs to increase capacity for translational research in molecular oncology and strengthen the ability to bring new knowledge more quickly to patient care. There are several ways in which this can be accomplished without the requirement for significant investment in the short-term.

For example, the oversight body can work with clinical trials groups such as the National Cancer Institute of Canada – Clinical Trials Group and the Ontario Clinical Oncology Group to design trials that include assessment of the clinical utility of biomarkers. The oversight body can also encourage the ongoing development of links between tumour data repositories and clinical/administrative datasets.

The oversight body should develop a mechanism that brings basic science and health services researchers to the table with system planners and managers. The same body of experts that reviews the scientific literature and makes recommendations for which tests to add to clinical service and who should be eligible to have them, should also be tasked with providing alerts to the system about promising research. Planners and managers should act on that information to avoid a last minute scramble to organize services when an appropriate threshold of evidence is reached.

There is no easy answer to the lack of research activity in addressing issues such as optimal specimen handling and assessment of new technologies to facilitate multiple marker testing. Once it is operational, the oversight body should begin to explore opportunities to influence this gap.

Finally, existing research funders, such as CCO and the Ontario Institute for Cancer Research, should foster translational research in molecular oncology through creation of research chair positions.

FUNDING IMPLICATIONS

Current spending on provincial genetic laboratory services is estimated to be just over $32 million, and this is probably an underestimate. As noted elsewhere in this report, Ontario's test availability lags behind other jurisdictions. Additional detailed analysis is required to better understand this gap and, subsequently, to estimate the related funding implications for laboratory and clinical services. Perhaps even more importantly, the door to discovery within molecular oncology testing is just beginning to open and the pace of discovery of new genes is likely to eclipse cancer incidence as a driver of service demand. There is a need for a body to complete this analysis in order to ensure quality and safety for patients, access to services, and sustainable services and testing for the future.

Immediate investment is recommended to initiate the oversight functions at CCO. In addition there is a need to immediately mandate and fund QMP-LS to develop or co-ordinate an EQA program for current molecular tests. The size of this investment requires detailed work-up by QMP-LS. As a starting point, all provincially recognized labs should show evidence of participation in EQA either by subscription to available programs or by participating in inter-lab or intra-lab challenges.

Work of the oversight body would allow development of estimates of the cost of filling the existing service gap in Ontario and preparing for the future.

CONCLUSION

Ontario is not alone in facing the challenge of addressing the rapid advancements in knowledge in this field. Many jurisdictions are grappling with significant funding, educational and logistical gaps between discovery research and service delivery[24].

The medical and research communities have made significant strides in the area of molecular oncology. The dramatic increase in the level of understanding of human genetics has had a tremendous impact on the way patients are diagnosed and treated. New molecular tests have been developed that have greatly enhanced our ability to predict, diagnose, manage and monitor cancer, as well as to determine the most appropriate therapy for patients with this disease. It is expected that these advances will continue to improve our ability to screen, prevent and treat cancer patients, especially as more targeted and personalized therapy becomes the standard of care.

In order to maximize the benefits of these developments, oversight is required that applies a performance management strategy which addresses the issues of access and quality of services, and funds these elements appropriately. The Task Force has concluded that there are tremendous opportunities available to ensure Ontarians have access to high-quality molecular oncology laboratory testing and clinical cancer genetics services. It is important that these opportunities be seized in the short-term to ensure that the health and confidence of Ontarians is maintained.

[24] SACGS Oversight Document. UKGTN URL, Australia Oversight URL

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- Task Force Co-Chairs
- Task Force Members
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APPENDICES

Appendix 1 Glossary

For the purposes of this report the term "**molecular oncology**" refers to the application of nucleic acid (RNA, DNA) or "molecular" and chromosome based or "cytogenetic" knowledge by clinicians and laboratory staff across the cancer care continuum, including prevention; risk reduction and stratification; diagnosis; prediction; and disease monitoring. It includes both laboratory testing and genetic counselling for cancer patients.

Key Abbreviations and Definitions:

Analytic Validity: the ability of a test to accurately and reliably measure the genotype of interest.

Biomarker: a gene or allele or genetic marker that is associated with a disease or can be used to predict outcome.

Clinical Utility: the probability that a genetic test will lead to an improved clinical outcome.

Clinical Validity: the ability of a genetic test to predict the presence or absence of clinical disease or a phenotype.

Cytogenetics: the branch of genetics that analyzes chromosomes using techniques such as FISH (fluorescence in situ hybridization) and karyotyping.

Home Brew Testing: a test that is developed within a lab using commercially available reagents; most molecular tests are developed in-house as manufactured kits are often not available or prohibitively expensive to use.

Karyotyping: a test to examine chromosomes in the nuclei of dividing cells, which can help identify structural and/or numerical chromosomal changes as the cause of, or associated with a disorder or disease or cancer.

Fluorescent in situ hybridization (FISH): use of fluorescently labeled DNA segments to specifically identify structural and numerical changes/large genetic changes in chromosomes

Molecular Testing: the analysis of specific regions of the genome using DNA or RNA based technology

Translational Research: A) research that is directed at answering a clinical question as related to patient care and health; B) relevance of basic research to clinical problems; C) integrative research between clinicians and basic scientists; and D) research focused on rapid application of basic science to patient care.

Appendix 2 Task Force Membership

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Appendix 3 Process for Developing this Report

Convening a Panel

CCO convened a task force of stakeholders with a mandate to formulate recommendations about Ontario's ability to meet the demand for molecular oncology testing, provide advice on action required to ensure that Ontarians receive equitable access to high-quality molecular oncology testing and related clinical cancer genetic services, and recommend a process for the rapid introduction of new tests into clinical practice. Terms of Reference were provided for the Task Force. Dr. Suzanne Kamel-Reid (PhD) was appointed to Chair the Task Force. Dr. Kamel-Reid is Head of Laboratory Genetics and Director of Molecular Diagnostics at the University Health Network and a Professor at the University of Toronto. She is also boarded in Clinical Molecular Genetics by The American Board of Medical Genetics and is a Fellow of the American College of Medical Genetics. Dr. Kamel-Reid and CCO leadership appointed the remaining Task Force members with input from regional cancer programs. The Task Force included representation from system leaders and managers at the laboratory level, MOHLTC, OMA Section on Labs and Genetics, Canadian College of Medical Genetics, QMP-LS, Laboratory Directors, Medical Oncologists, Genetic Counsellors, Researchers, an Ethicist and an Epidemiologist. A complete list of task force members is attached as Appendix 2. A LHIN representative was desired, but could not be arranged during the short timeframe of the review. Although pediatrics is not specifically covered by the mandate of the Task Force, during the course of the task force activities, committee membership expanded to include a representative from SickKids (Dr. Peter Ray) due to his experience and membership in previous Genetics advisory boards.

Survey of Laboratories in Ontario

The Ontario Genetics Secretariat surveyed nine Molecular and 11 Cytogenetics Labs in Ontario to create a picture of the testing landscape in Ontario. See Appendix 4 for a list of labs included in the survey. See Appendix 7 and Appendix 8 for a summary of testing volumes and costing data for laboratories. The budget data covers all salaries and benefits, and operating costs, and excludes costs related to capital equipment and infrastructure for those labs surveyed. The testing volumes and overall budgets are the actual numbers provided by the individual labs and the cancer budget was calculated as the total genetics budget multiplied by the percentage of tests that are for cancer.

Survey of Clinical Cancer Genetic Services

The Task Force formulated a survey that was administered in June 2008 and completed by geneticists and counsellors who represent all 22 regional cancer centres, regional genetics centres and Northern/satellite centres in order to identify access and quality issues related to genetic counselling across Ontario. Excluded from this survey was the Hospital for Sick Children since they deal with very rare cancers involving children and were unable to fully complete the survey. This survey is referred to as the Clinical Survey, 2008, throughout this report.

Environmental Scan

The Task Force conducted a limited scope internet-based environmental scan to acquire information from relevant literature and organizations including the Quality Management Program-Laboratory Services (QMP-LS), United Kingdom Genetic Testing Network (UKGTN), United States Secretary's Advisory Committee on Genetics, Health and Society (SACGHS), Ontario Health Technology Advisory Committee (OHTAC), Organization for Economic Co-operation and Development (OECD), European Society of Human Genetics, British Society for Human Genetics, National Genetics Reference Laboratory and National Comprehensive Cancer Network (NCCN). The Task Force also reviewed reports and recommendations from the Report to Health Canada by QMP-LS (September 2007) regarding their response and recommendations for the implementation of the OECD report and the SACGHS Oversight Report 2008, as well as other clinical practice guidelines. References from these reports and additional information including survey results and data are used throughout this report.

Acquiring Available Data

Complete laboratory tracking and volume data were difficult to obtain due to outdated test lists and an inability to abstract data from databases since laboratory tests are not all specifically coded, especially cancer tests. The MOHLTC provided provincial service volumes for only those laboratory tests that are approved and were assigned a "U" code in 2006 and 2007. Provincial laboratory testing and volumes data used in this report were obtained from the Ontario Genetics Secretariat based on the nine molecular genetics and 11 cytogenetics labs listed in Appendix 4. Cancer incidence data were supplied by the Canadian Cancer Society/Canadian Cancer Statistics 2008 and projections developed by CCO's informatics and planning unit. Detailed access and quality data related to clinical cancer genetic services were obtained through a survey administered in June 2008.

Costing was based on the total amount paid out per period and not the cost per test. Budget numbers included laboratory and operational costs (supplies and technology) and salaries and benefits (professionals, administrative and technologists), while exclusions were related to capital equipment and infrastructure costs.

Formulation of Recommendations

The Task Force held three well-attended, face-to-face meetings in April, May and June of 2008. Initially the Task Force was divided into three working groups representing laboratory services, clinical cancer genetic services and research to contemplate expertise specific information. Task Force members reviewed the information provided from the environmental scan, survey results and available volume data to formulate recommendations in the areas of oversight, access, quality and funding that are outlined within this Report.

Review of Recommendations

Comments on draft recommendations were invited from CCO's Provincial Leadership Council and the Clinical Standards, Guidelines and Quality Committee of the Board of Directors. It was deemed that review and discussion with LHIN representatives is desirable and should be solicited in the near future. The Task Force is collaborating with the Ontario Genetics Secretariat to ensure the recommendations for cancer genetics are well integrated into recommendations for all genetic services.

Appendix 4: List of Provincially Recognized Molecular and Cytogenetic Labs

Hospital Name	Molecular Genetics	Cytogenetics
1. Children's Hospital of Eastern Ontario (Ottawa)	X	X
2. Credit Valley Hospital (Toronto)	X	X
3. Hamilton Health Sciences Centre	X	X
4. Hospital for Sick Children (Toronto)	X	X
5. Kingston General Hospital	X	X
6. London Health Sciences Centre	X	X
7. Mount Sinai Hospital (Toronto)	X	X
8. North York General Hospital (Toronto)	X	X
9. University Health Network (Toronto)	X	X
10. Lakeridge Hospital (Durham)		X
11. Sudbury General Hospital		X
Total Number of Labs	**9**	**11**

Other molecular labs submitting volumes to the MOHLTC include Sudbury General Hospital, Ottawa General Hospital, Sunnybrook Health Sciences Centre, Women's College Hospital. Please note that the volume and budget numbers from these labs have not been included in this report.

Appendix 5: Location of Clinical Cancer Genetics Services in Ontario

Regional Centres	Northern/Satellite Centres
1. Credit Valley Hospital (Mississauga)	1. Algoma Health Unit (Sault Ste. Marie)
2. Grand River Hospital (Kitchener)	2. North Bay Parry Sound District Health Unit
3. Hamilton Health Sciences Centre	3. Orillia Soldier's Memorial Hospital (Orillia)
4. Kingston General Hospital	4. Peterborough County City Health Unit
5. Lakeridge Health Sciences Centre(Oshawa)	5. Porcupine Health Unit (Timmins)
6. London Health Sciences Centre	6. Sudbury Regional Hospital
7. Mount Sinai Hospital (Toronto)	7. Thunder Bay District Health Unit
8. North York General Hospital (Toronto)	8. Windsor Regional Hospital
9. Sunnybrook Health Sciences Centre (Toronto)	9. York Central Hospital (Richmond Hill)
10. University Health Network (Princess Margaret, Toronto)	
11. Women's College Hospital (Toronto)	
12. Children's Hospital of Eastern Ontario (Ottawa)*	
13. Hospital for Sick Children (Toronto)*	

*Paediatric services only

Appendix 6: Staffing (FTE) of Provincially Recognized Molecular and Cytogenetic Labs 2003–2007

FTE STAFF IN PROVINCIALLY RECOGNIZED GENETICS LABS					
Year	**2003**	**2004**	**2005**	**2006**	**2007**
Molecular Genetics					
Techs(total)	56	59	65	67	68
Senior Staff	13	14	15	15	14
Admin	8	8	8	8	9
Cytogenetics					
Techs(total)	140	144	145	149	149
Senior Staff	12	13	13	13	12
Admin	9	9	9	9	9
Total (Molecular + Cytogenetics Combined)					
Techs(total)	**196**	**203**	**210**	**216**	**217**
Senior Staff	**25**	**26**	**28**	**28**	**26**
Admin	**17**	**17**	**17**	**17**	**18**

Source: Ontario Genetics Secretariat data collection, 2008. Source data from recognized provincial molecular and cytogenetic labs only. This does not represent all genetic testing in the province.

Appendix 7: Provincial Lab Budget

ONTARIO LICENSED GENETIC LAB BUDGETS					
	03/04	**04/05**	**05/06**	**06/07**	**07/08**
Molecular Genetics	$9,978,977	$11,081,853	$11,975,444	$12,569,951	$13,494,503
Cytogenetics	$8,129,054	$10,516,812	$13,822,820	$16,318,651	$15,632,817
Metabolic Genetics (no cancer)	$1,019,575	$1,153,965	$2,152,078	$2,141,846	$3,129,927
Total Budget	$19,127,605	$22,752,630	$27,950,341	$31,030,448	$32,257,247

Source: Ontario Genetics Secretariat data collection, 2008. Source data from recognized provincial molecular and cytogenetic labs only. This does not represent all genetic testing in the province.

Appendix 8: Molecular and Cytogenetic Testing Volumes in Ontario, 2003–2007

Year	2003	2004	2005	2006	2007
Molecular Genetics					
Non-cancer	37,257	41,486	45,315	57,110	64,221
Inherited cancer	3,416	3,309	4,395	4,288	5,317
acquired cancer	7,676	7,487	8,640	11,196	13,029
All specimens	48,349	52,282	58,350	72,493	82,427
% that is cancer-related	23%	21%	22%	21%	22%
Cytogenetics					
Non-cancer	24,628	24,067	24,996	26,362	25,762
Cancer	7,679	8,798	9,002	9,577	10,171
All specimens	32,307	32,865	33,998	35,939	35,933
% that is cancer-related	*31%*	*37%*	*36%*	*36%*	*39%*
Metabolic Genetics					
Non-cancer	30,331	37,765	38,794	46,816	47,913
Cancer	–	–	–	–	–
Total (Molecular and Cytogenetics Combined)					
Total tests	110,987	122,912	131,142	155,248	166,273
Total Cancer	18,771	19,594	22,037	25,061	28,517
% that is cancer-related	17%	16%	17%	16%	17%

Source: Ontario Genetics Secretariat data collection, 2008. Source data from recognized provincial molecular and cytogenetic labs only. This does not represent all genetic testing in the province.