**Introduction:** These learning guides have been developed by the ABMGG to assist training program directors and trainees as they design, implement, monitor and evaluate the educational content of their ABMGG accredited training programs. The format of these learning guides reflects the common areas of knowledge and training that have been developed by the medical profession across the training spectra and that are often referred to as the “Six Competencies.” The ABMGG has taken these areas of knowledge and experience and translated them into more specific content areas for ABMGG accredited programs.

These learning guides are not presumed to be inclusive or exclusive. Thus you will find that they mirror many other guiding principle documents from within the genetics community. Similarly, while they attempt to cover as many specific areas of training as possible, they cannot be viewed as the only areas of knowledge and expertise that are required to become a successful medical genetics professional. They are, as indicated, learning guides, and are not rules or testing outlines. These guides are offered to the medical genetics educational community as one source of information concerning knowledge areas that may be useful in developing and evaluating the educational content of training programs.

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<tr>
<td><strong>1. Patient Care</strong></td>
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| Pre-analytic laboratory skills | Identify appropriate specimens for study, and methods of collection, preservation, and transport | • Select appropriate containers, anticoagulants, collection media, antibiotics, and preservatives for validated specimen type.  
• Identify factors important for the transport of specimens, such as overnight delivery, transport media and containers, recommended temperatures.  
• Transport/ship specimens off-site using packaging which meets OSHA safety guidelines.  
• Be aware of appropriate specimen and handling requirements. |
| Assess acceptability of specimen for study |                                                                             | • Check for appropriate labeling of specimen and requisition.  
• Evaluate suitability of specimen for requested study, both for type and amount obtained.  
• Judge quality of specimen.  
• Assess for presence of interfering substances.  
• Describe methods for possible recovery of poor samples.  
• Notify appropriate individuals of any unsatisfactory samples and document such notification. |
| Accession specimen           |                                                                             | • Assign unique laboratory accession number to specimen.  
• Record related data including patient's name, date of birth, sex, clinical history, ethnicity/race, family history and indication for study as appropriate.  
• Record accurate and complete information concerning specimen including amount, anticoagulant, appearance.  
• Record collection date and time.  
• Record special test requests, particularly those requiring transport of samples to other laboratories. |
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| **Continued...**<br>Pre-analytic laboratory skills | Track specimens | • Follow protocols to ensure proper identification and location of patient materials from accession to final report.  
• Be able to track specimen location through all aspects of the testing process. |
| | Appropriate documentation | Maintain necessary records and laboratory database, in log books or computers, as appropriate. |
| **Appropriate techniques for nucleic acid isolation from submitted specimens** | Use of aseptic techniques | • Use measures (such as Universal Precautions) that protect employees from real or potential exposure to infectious agents (e.g., protective clothing, gloves and masks, containers for sample delivery and waste disposal, biological safety cabinets).  
• Use and document methods to detect, identify, control and eliminate microbial or chemical contamination.  
• Practice measures that prevent cross-contamination between samples. |
| | Choose appropriate method for DNA/RNA isolation | • Isolate DNA/RNA expediently, with consideration to specimen type and test requested.  
• Practice measures that prevent cross-contamination between samples.  
• Monitor automated extraction instruments for carry-over. |
| | Employ proper dilution technique for isolated DNA/RNA | • Choose appropriate type of solution (e.g., TE, water, etc.) for reconstitution of DNA/RNA.  
• Choose appropriate amount of reconstitution solution for test being performed. |
| | Determine concentration of DNA/RNA, as appropriate | Options to estimate concentration and determine quality of DNA/RNA include:  
o spectrophotometry (determine optical density and nucleic acid/protein ratio of reconstituted DNA/RNA)  
o fluorometry (estimate DNA concentration)  
o direct visualization by gel electrophoresis |
| | Understand probable causes of poor or failed DNA/RNA isolation | • Identify, evaluate, and document probable causes of poor or failed DNA/RNA isolation, such as inadequate specimen or reagent failure.  
• Document corrective actions taken. |
| | Storage of DNA/RNA samples appropriately | Employ proper techniques for storage of DNA/RNA samples. |
| **Principles and techniques for polymerase chain reaction (PCR)** | Know and understand principles and techniques associated with PCR analysis | • Understand the principle of PCR.  
• Determine components and concentrations for particular reaction.  
• Assemble reagents for master mix.  
• Calculate primer dilutions.  
• Optimize conditions for amplification.  
• Troubleshoot failed or non-specific reactions.  
• Utilize appropriate controls. |
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<td><strong>Continued...</strong></td>
<td>Know which primers are appropriate for disease/area of concern</td>
<td>Perform or be familiar with the development and design of new primers.</td>
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| **Principles and techniques for polymerase chain reaction (PCR)** | Perform PCR to minimize carry over (false positive results) | • Utilize unidirectional workflow.  
• Utilize adequate physical separation of pre- and post-amplification samples to avoid amplicon contamination.  
• Change gloves frequently during processing.  
• Use dedicated pipettes (positive displacement type or with aerosol barrier tips).  
• Manipulations must minimize aerosolization.  
• “No template” controls in which target DNA is omitted (no product is expected) should be included in each run.  
• Monitor liquid handlers to eliminate carry over. |
| **Southern analysis** | Know and understand principles and techniques associated with Southern blot | Understand the Southern blot procedure including:  
  o digestion of DNA with appropriate restriction enzymes  
  o electrophoresis  
  o denaturation in alkali and transfer DNA to membrane  
  o preparation of probe (radioactive or chemiluminiscent label)  
  o denaturation of probe and hybridization of membrane  
  o exposure to X-ray film and development of the autoradiograph |
| **Targeted mutation analysis** | Know and understand principles and techniques associated with direct mutation detection | Understand a variety of methods for direct mutation detection, e.g.:  
  o restriction fragment length polymorphism analysis  
  o FRET analysis (Invader)  
  o allele-specific oligonucleotide dot blot hybridization  
  o allele-specific PCR amplification (ARMS)  
  o Pyrosequencing  
  o Exon-focused array CGH  
  o Molecular inversion probe  
  o Multiplex ligation-dependent probe amplification (MLPA) |
| **Gene scanning** | Know and understand principles and techniques associated with gene scanning | Observe, perform, or be familiar with methods for gene scanning, e.g.:  
  o heteroduplex analysis  
  o melting curve analysis  
  o MLPA |
| **Sanger (dideoxy) sequencing** | Know and understand principles and techniques associated with dideoxy sequencing of single genes or exons | • Be familiar with Sanger dideoxy sequencing  
• Perform direct DNA sequencing |
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| Next-generation sequencing  | Know and understand principles and techniques associated with sequencing of gene panels, exomes, or genomes | • Understand the technical details of next-generation sequencing – limitations and advantages of different methods of library preparation and sequencing  
• Understand the challenges, limitations, and advantages between gene panels, exome, whole genome sequencing  
• Understand the assay design process, including selecting capture baits for hybridization or primers for micro-droplet PCR  
• Understand the refinement steps of assay design to optimize data generation at difficult genomic regions, e.g., at repetitive sequences or GC-rich sequences  
• Determine components and concentrations for library preparation and sequencing and optimize conditions  
• Troubleshoot failed or non-specific reactions  
• Utilize appropriate controls  
• Understand new test validation approaches for NGS-based tests |
|                             | Understand principles of exome or whole-genome analysis                    | • Perform singleton and trio analyses of exome sequence data  
• Apply principles of homozygosity mapping and search for recessive disease mutations  
• Apply principles of using phenotype information to isolate gene lists for analysis  
• Apply modeling inheritance modes (dominant, recessive, X-linked) based on pedigree of tested individual and create priority gene lists for analysis  
• Create and use virtual gene panels for analysis based on disease phenotype information  
• Understand limitations of sequence depth coverage and implications for diagnostic testing  
• Use workflow for analyzing and reporting incidental findings |
| Quantitative PCR            | Know and understand principles and techniques associated with quantitative PCR | Observe, perform or be familiar with the use of quantitative PCR to quantify gene expression and gene dosage and to assay for mutations and single nucleotide polymorphisms.                                                                                                                                                                                                                           |
| Array Analysis              | Know and understand principles and techniques associated with microarray analysis | • Observe, perform or be familiar with the use of microarrays in the laboratory to screen for single nucleotide variants (including SNPs), intragenic deletions and duplications, chromosomal copy number variant, or gene expression.  
• Understand principles of genotyping and its applications, including carrier screening  
• Understand concepts of array probe design and relationship to data. |
| DNA labeling of target and control samples |                                                                           | Fluorescently label DNA necessary for microarray analysis.  
Determine the specific activity and the yield.                                                                                                                                                                                                                                                                                                                  |
| Microarray hybridization and washing |                                                                           | Determine the appropriate conditions for microarray hybridization and post-hybridization washing, dependent upon platform.  
Scan and analyze the data as per platform.  
Archive the appropriate data.                                                                                                                                                                                                                                                                                                                   |
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| Identity testing | Know and understand principles and techniques associated with identity testing | Perform identity testing using the analysis of polymorphic genetic markers (NOT gene mutations associated with disease), e.g.:  
  - paternity testing  
  - forensics  
  - zygosity  
  - transplantation  
  - maternal cell contamination |
| General laboratory skills, quality control, and quality assurance | Know how to prepare reagents | Prepare reagents at the proper concentration and pH, with proper labeling, using required grades of water and chemicals. |
| | Select, operate, clean, and maintain all laboratory equipment and instruments, as appropriate |  
  - Be aware of regulatory requirements for preventative maintenance of equipment and documentation of equipment repairs.  
  - Perform temperature monitoring as required.  
  - Monitor centrifuge speed, using a tachometer as appropriate.  
  - Be aware of the need for regular instrument function checks and how this is documented in the laboratory. |
| | Understand principles of sterilization and decontamination procedures | Be aware of proper use of disinfectants, steam, dry heat, gas, ultraviolet irradiation, and membrane filtration. |
| Continued... | Understand how to stock laboratory supplies and chemicals | Maintain adequate stocks of laboratory supplies and chemicals. |
| General laboratory skills, quality control, and quality assurance | Practice established procedures for laboratory safety |  
  - Employ appropriate cleaning procedures for general laboratory safety.  
  - Use Universal Precautions as established by the Centers for Disease Control (CDC) and individual state or local governments.  
  - Use appropriate procedures for laboratory emergencies (e.g., fire, accident/injury, natural disaster, chemical spill, or power failure).  
  - Use correct procedures for storage, handling, and disposal of different kinds of materials and waste: biological and chemical, volatile or stable, radioactive, sharps and glass. |
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|                               | Understand laboratory quality control in all areas and comply with all regulatory requirements | • Maintain a system to: (1) ensure accuracy of molecular tests, including appropriate documentation, throughout all steps of laboratory procedures, (2) ensure confidentiality and security of patient records, and (3) appropriately label, store, and monitor shelf life, sterility, and quality of all media, reagents, and chemicals.  
• Maintain an easily accessible collection of current Material Safety Data Sheets for all chemicals used in the laboratory procedures.  
• Maintain a system of records for equipment and instruments (serial numbers, date of purchase, maintenance checks, gauge readings, dates and type of service repair).  
• Practice the techniques, procedures, and policies used in the laboratory, as documented in the laboratory manual.  
• Assist in reviewing and revising the laboratory manual.  
• Participate in laboratory proficiency testing, as appropriate.                                                                 |
|                               | Know principles and procedures for laboratory management, supervision, and problem solving | Apply principles and procedures for laboratory management, supervision, training of personnel, determining competency of personnel, and problem solving (trouble-shooting), as appropriate.                                                                 |
|                               | Know how to design and validate a new assay in the laboratory                | Assist in the development of a new assay including:  
  o determine clinical utility, clinical validity, analytic validity (accuracy, sensitivity and specificity)  
  o understand how reference ranges are established  
  o understand how test prices are determined  
  o understand how CPT codes are used  
  o understand reporting structure and assist in the development of standard reports including description of methods, results and interpretations                                                                 |
| Bioinformatics                | Software                                                                    | • Use and understand software packages for clinical lab processing, data analysis and storage, and for report writing.  
• Understand implications of using electronic record keeping with respect to health information.  
• Understand the informatics processes that connect sample requisition to wet lab processes, data analysis, report writing, and transmission of final reports to referring physicians.  
• Understand processes to collect information from multiple individuals in the process between sample accessioning to final report.  |
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| Variant calling | • Learn to use software for next-generation sequencing for read alignment, variant calling, and confirmations  
• Genome sequence alignment software (e.g., BWA)  
• Variant calling algorithms (e.g., GATK)  
• Identifying artifacts and trouble spots in genome sequence data  
• Visualizing single nucleotide and copy number variation  
• Basic biostatistical analysis of sequencing data (depth of coverage, read quality, Q scores, mapping quality, etc)  
• Analyzing and integrating data from orthogonal confirmation methods  
• Understand the utility of and how to use in silico prediction algorithms (e.g., Polyphen, SIFT, splice detectors) | |
| Genome analysis | • Observe and understand how to use:  
• Genome browsers (UCSC, IGV, ENSEMBL)  
• Human genome variation databases (e.g., ClinVar, 1000Genomes, ExAc, DGV, DECIPHER)  
• Variant analysis software, if available (custom software or vendor software, e.g., Alamut, Ingenuity, Agilent Cartagenia, Affymetrix CytoScan HD, etc.)  
• in silico algorithms for prediction of effects of missense changes and evolutionary conservation (PolyPhen, SIFT, GERP, PhyloP, etc.)  
Understand basic biostatistical concepts – case-control studies, odds ratios, use of different statistical measurements, outcomes of population studies | |
| Post-analytic laboratory skills | | |
| Interpretation of results | • Correctly interpret results of all laboratory assays to determine normal/affected/carrier status.  
• Correlate results with other laboratory results and/or clinical information to develop an appropriate interpretation of the laboratory results. | |
| Summarize the results and report to the appropriate authority | Recognize and avoid hazards implied in oral reporting of results.  
Draft a neat, accurate report using standard nomenclature established by the current ISCN, summarizing the findings in understandable text and incorporating the patient identification, and all relevant clinical and laboratory data; forward to the appropriate individual for review and signature.  
Document oral and preliminary reports on final written report. | |
<p>| Understand additional studies needed to make a diagnosis | Report the need for additional studies to complete the diagnosis: repeat the culture, perform additional staining techniques, analyze other tissues, request family studies, FISH, microarray, DNA extraction from a new sample, confirmation by other molecular method, biochemical studies, etc. | |</p>
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| Report                         | • Prepare and generate reports (including pre-written and de novo results and interpretations) incorporating all relevant clinical and laboratory data.  
• Understand how bioinformatics pipelines can be used to prepare primary reports and issue amended reports.  
• Use nomenclature as standardized by the Human Genome Variation Society (HGVS) to describe molecular results.  
• Assess the need to recommend additional studies needed to complete the diagnosis (e.g., perform additional testing, request family studies). |                                                                                                                                                                                                       |
| Communication                  | Communicate results verbally to ordering physician, his or her designee, or genetic counselor as appropriate, following HIPAA guidelines. |                                                                                                                                                                                                       |
| 2. Genetics Knowledge [also refer to Content Outline] |                                                                                   |                                                                                                                                                                                                       |
| General principles of biology and genetics | Understand principles of general biology and genetics that relate to molecular genetics | • Understand DNA structure (base sequence, pairing, replication and packaging into chromosomes).  
• Explain transcription, splicing, translation, and variation of gene expression between tissues.  
• Explain genomic organization and gene structure.  
• Understand core technologies for allele discrimination and mutation detection. |
| Understand principles of molecular genetics |                                                                                   | • Explain mode of inheritance at level of organism (dominant, co-dominant, recessive, autosomal, sex-linked, multifactorial, polygenic, inheritance of imprinted genes).  
• Explain action of gene at cellular level (dominant-negative, recessive).  
• Describe different classes of mutations (e.g., missense, nonsense, deletion, insertion, splice-site, triplet repeat expansion).  
• Explain gene expression at cellular level (dominant, dominant-negative, or negative).  
• Discuss basic principles of genetic counseling including pedigree analysis.  
• Perform Bayesian risk analysis.  
• Describe risk factors for mutations (advanced maternal age and nondisjunction, advanced paternal age and new autosomal dominant mutations, mutagens and carcinogens).  
• Correlate molecular genetic results with cytogenetic results for prenatal diagnosis, family studies, and cancer diagnostics or cancer risk assessment and any other preanalytic clinical information. |
| 3. Interpersonal and Communication Skills |                                                                                   |                                                                                                                                                                                                       |
| Inheritance/risk counseling | Understand concepts of heritability, inheritance patterns, variability, heterogeneity, penetrance and the epidemiology/natural history of a condition | • Transmit pertinent information in a comprehensible way.  
• Explain genetics concepts and identify family members at risk.                                                                                                                                   |
| Professional                   | Know how to communicate with colleagues                                           | • Maintain comprehensive, timely and legible medical records.  
• Communicate appropriate information to health professionals one-on-one or in groups.                                                                                                             |
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<tr>
<td>communication</td>
<td>Exhibit appropriate ethical and professional standards at all times</td>
<td>Demonstrate an attitude of responsibility and respect toward the patient, a respectful and cooperative attitude toward professional colleagues and an honest, forthright manner in carrying out professional task.</td>
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<td>Know how to teach and supervise</td>
<td>Educate, mentor, and assess progress and skills, and provide appropriate feedback and appraisal.</td>
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4. Practice-Based Learning and Improvement

| **Standards of care** | Knowledge of relevant practice guidelines or consensus statements | • Compare own laboratory practices and outcomes to accepted practice/guidelines and national or peer-reviewed data.  
• Able to reflect on areas of uncertainty to identify improvement needs. |
|----------------------|-------------------------------------------------|---------------------------------------------------------------|
| **Ongoing learning** | Knowledge of tools/methods to stay current in common clinical molecular genetics topics throughout one’s career | • Seek feedback from others.  
• Research topics when needed.  
• Critique research evidence for applicability to laboratory practice.  
• Use bioinformatics resources.  
• Be receptive to feedback.  
• Participate in ABMGG Maintenance of Certification program. |
| **Quality improvement** | Know quality metrics | • Change practice behaviors in response to feedback from others and review of own practice.  
• Apply new skills or knowledge to laboratory service.  
• Exhibit willingness to change and adapt. |

5. Professionalism

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<tr>
<th><strong>Responsibility</strong></th>
<th>Understand the responsibility to the ordering physician and patient/family</th>
<th>Complete tasks required to provide laboratory services effectively in a careful and thorough manner.</th>
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</table>
| **Practices within ability** | Recognize limits of his/her abilities | • Seek consultation when appropriate.  
• Exercise authority accorded by position and/or experience.  
• Recognize cognitive, legal and ethical limitations of credentials. |
| **Patient diversity** | Recognize differences (cultural, educational, etc) | • Recognize each patient’s unique needs and characteristics.  
• Provide equitable services regardless of patient culture or socioeconomic status.  
• Respectful and sensitive to issues related to patient culture, age, gender and disabilities. |
| **Integrity and ethical behavior** | Recognize ethical dilemmas and potential conflicts of interest | • Take responsibility for actions; admit mistakes; try to address ethical dilemmas and conflicts of interest.  
• Demonstrate a commitment to ethical principles pertaining to:  
  (1) patient privacy and autonomy,  
  (2) provision or withholding of test results |
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| Professional relationships | Knowledgeable about the elements of informed consent, privacy, confidentiality, duty to warn, and is HIPAA compliant | (3) confidentiality of patient information  
(4) informed consent  
(5) conflict of interest  
(6) business practices |
| Leadership | Maintain professional interactions with healthcare professionals | Be courteous and respectful when relating with peers and referring healthcare providers. |
| Leadership | Demonstrate teamwork and leadership skills | • Provide direction to staff.  
• Educate and mentor.  
• Assess progress and skills, provide appropriate feedback and appraisal. |
| Leadership | Demonstrate teaching and managerial skills |

### 6. Systems-Based Practice

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<th><strong>Service coordination</strong></th>
<th><strong>Objectives</strong></th>
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| Know how to provide comprehensive and integrated service | • Coordinate services with other providers.  
• Provide timely service. |

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<th><strong>Evidence-based medicine</strong></th>
<th><strong>Objectives</strong></th>
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| Knowledge of evidence-based guidelines and appropriate billing | • Determine cost and cost components of tests and understand reimbursement issues.  
• Provide cost-conscious services.  
• Consider cost and benefits of test.  
• Follow accepted laboratory guidelines.  
• Use appropriate billing codes. |

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| Understand research principles | • Critically read and interpret scientific publications.  
• Be aware of policy implications. |

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<th><strong>Health services</strong></th>
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<th><strong>Skills</strong></th>
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<tbody>
<tr>
<td>Knowledgeable about system resource utilization; understand different healthcare delivery systems and medical practices</td>
<td>Interface with laboratory information systems, electronic health records, and billing systems.</td>
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</table>
| Information access | • Conduct literature review and database searches.  
• Identify resources for the patient/family and referring healthcare provider. |