INTRODUCTION

Upon receiving news that results of a chromosome analysis are abnormal (and even sometimes that they are normal), a patient will frequently ask, “How do I know that the lab didn’t make a mistake? How do I know that the sample they reported on was really mine? How can I be certain that this is all correct?” Most would be surprised to learn of the myriad of checks and balances that exist. Practice standards (American College of Medical Genetics [ACMG], 2003) based on the consensus of professionals and common sense are the basis for oversight by regulatory agencies, to prevent clinical and clerical errors. These comprise the area of laboratory medicine known as quality assurance and quality control (QA/QC). These are supplemented by both total quality management (TQM) and complete quality improvement (CQI) programs that seek to minimize errors where the laboratory interfaces to referring physicians and their patients.

The nature of clinical cytogenetics is such that it includes both quantitative and qualitative components of tests. Some aspects are generic to practices in laboratories of any kind, and others are specific to cytogenetic laboratory tests.

A proper QA/QC program requires that policies for validation of protocols and reagents, training and credentials of individuals performing chromosome analysis, sample identification, safety for laboratory staff, and other compliance issues must all be in place. Laboratories are inspected periodically by various state and national entities, and most have institutional and internal regulations and guidelines as well.

There are many steps that occur between obtaining a specimen for chromosome analysis and the generation of a final clinical report. After collection of the specimen itself, accessioning, culturing, harvesting, slide preparation and staining, microscopic analysis, photography or electronic imaging, karyotype production, creation of a final report, and actual reporting of results are the path that specimens follow as they progress into and out of the cytogenetics laboratory. During this process, many variables can subject a specimen or data to a variety of conditions that must be managed in order to reach a proper diagnosis.

Central to any QA/QC program is the laboratory’s Standard Operating Procedure (SOP) Manual. This often formidable document contains the policies and procedures that must be followed in order for the laboratory to perform chromosome analysis: physical space and mechanical requirements, sample amount and collection, transport requirements, personnel experience and credential requirements, and safety and protection requirements for those personnel. It includes sections on training and compliance with the various regulatory agencies that monitor and inspect laboratories, and, finally, it might contain a section pertaining to quality assurance and quality control. The majority of these issues pertain to the analytic component of testing. The format of the SOP manual is specified by the National Accrediting Agency for Clinical Laboratory Sciences (NAACLS), which requires
that, in addition to containing a detailed protocol for every procedure the laboratory performs, the manual also includes the clinical and technical rationale behind each one.

With the rapid growth of knowledge and expansion of genetic testing, the laboratory has become increasingly involved in ensuring that the preanalytic and postanalytic aspects of testing also are designed to ensure the appropriate use of tests and their results. These commonly include issues of analytical test validation, documentation of clinical validity, interpretation of test results, and educational materials that allow the laboratory’s clients to interface with it. These aspects are commonly encompassed in a complete quality improvement program.

Books could be written that address each of these issues in detail; entire chapters could be devoted to labels alone! Such detail is beyond the scope of this book, however; this chapter will provide an overview of the ways in which laboratories deal with many of these steps in order to ensure proper patient care.

PREANALYTICAL TESTING COMPONENTS

Before a test specimen arrives in the laboratory, there are a number of steps that must be done correctly to ensure that an accurate and useful test result is provided. Laboratories often develop and provide to their clients materials to guide them in understanding when to test, what to test, and how to order tests. Often considered outside of the day-to-day functioning of the laboratory, these are important to ensuring safe and effective testing.

Test Validation

Prior to initiating testing, there should be evidence of clinical validation of the test. This can be done by the laboratory developing the test or be apparent from the scientific literature and merely documented. With the advent of the 1992 modifications to the 1988 Clinical Laboratory Improvement Amendments (CLIA ’88) regulations, laboratories are required to validate all tests being introduced into service whether they were newly developed or long used in other laboratories. Furthermore, all new tests must be revalidated every 6 months. Approaches to validation vary for quantitative versus qualitative tests. Classical concepts such as sensitivity (the ability to detect a target when it is present) and specificity (the ability to not detect a target when it is not present) are common measures of analytical validity for quantitative tests (ACMG, 2003). These are most often applied to fluorescence in situ hybridization (FISH) tests (see Chapter 17), particularly when interphase-based, but also are important when mosaicism is considered. Requirements for validation can vary with the regulatory status of a product. When a test is Food and Drug Administration (FDA) approved, the laboratory is expected to demonstrate that the test operates within the performance characteristics described by the manufacturer. When tests are not FDA approved or have been modified, the laboratory is expected to demonstrate their validity independently. For the more qualitative classical chromosome analysis, laboratories commonly validate their ability to process particular specimen types, perform particular tests, or to detect a particular abnormality by testing samples from individuals with those abnormalities.

Submitting a Specimen

Specimens are almost always collected by individuals who rely upon the laboratory to provide a requisition form and instructions for specimen collection and transport. Considering this, QA/QC begin through an interaction with the health care providers who collect and submit specimens for chromosome analysis.

Collection Protocol

A collection protocol from the cytogenetics laboratory is of critical importance, as it establishes the collection guidelines for individuals who are not intimately familiar with the operating procedures of the laboratory. A collection protocol should include the following: