Chapter 5

Quality Assurance

Contents

Boxes

Figure

Chapter 5
Quality Assurance

Quality assurance for cystic fibrosis (CF) carrier screening is multifaceted. In particular, three aspects of quality assurance are important to ensuring the safety, efficacy, and accurate interpretation of DNA-based CF assays:

- the quality of clinical laboratory services;
- the quality of genetic diagnostic kits, reagents, assays, and instrumentation; and
- the quality of professional services, including diagnostic and counseling services.

Oversight of quality assurance extends to Federal, State, and local governments. It includes the judiciary, professional societies, and clinical laboratories as well. All have a stake in ensuring high-quality diagnostic services, although the extent of involvement varies. For example, all play apart in oversight of laboratory performance, but the Federal Government has primary responsibility for ensuring the safety and efficacy of clinical laboratory devices (e.g., DNA test kits). Professional societies and courts, on the other hand, have a large impact on the quality of professional services.

This chapter concentrates on the roles of all interested parties in ensuring that both private and public facilities provide high-quality DNA-based genetic analysis, especially CF mutation screening. It discusses voluntary versus mandatory standards, and how both regulatory and nonregulatory mechanisms can facilitate efforts to guarantee high quality.

QUALITY ASSURANCE FOR CLINICAL LABORATORIES

Laboratories use quality control to ensure that a laboratory's results meet predetermined criteria. It includes the steps taken by a laboratory to produce valid, reproducible, and reliable results each time the test is performed. Quality assurance programs document the satisfactory performance of quality control, and can include proficiency testing and external inspections (83,84,85). Quality control and quality assurance are essential components of good laboratory practice.

In 1991, Congress reviewed progress toward overcoming longstanding difficulties with ensuring the accuracy of diagnostic laboratory tests performed by facilities across the Nation. Congressional concern persists that quality problems could remain unresolved, despite recent changes in Federal law (167). Questions about laboratory quality are important to CF mutation analysis.

First, the quality of a laboratory's performance affects the quality of counseling services. Accurate reporting and interpretation of the mutations used by a laboratory are necessary if used by genetics and other health professionals are to convey accurate results to their clients. Failure to assay a less common mutation (or to properly interpret the results of the battery of mutations used) could result in clients mistakenly believing themselves to be at negligible risk of conceiving a child with CF. Conversely, misinterpreting test results could also mislead individuals to think they are at increased risk and to decide against conception. Second, the technical skills of both the technician and laboratory are essential for maintaining an acceptable standard of practice to allow a laboratory to conduct DNA analysis of CF mutations. Today's assays, for example, use the polymerase chain reaction (PCR), and some observers have concerns about the proper controls to ensure against potential mishaps—chiefly contamination—using PCR-based techniques (54,74,169).

Because the intensity of Federal interest in clinical laboratory performance is new and evolving, and because Congress has expressly involved itself by taking action in this area, this section focuses on recent congressional action, chiefly the Clinical Laboratory Improvement Amendments of 1988 (CLIA) (Public Law 100-578). States and professional organizations, however, also play key roles in certain aspects of laboratory quality assurance. Thus, this section also examines how each has been involved in specific debates surrounding quality assurance for clinical facilities performing DNA-based diagnostic procedures, which include carrier screening and testing for CF.

The Clinical Laboratory Improvement Amendments of 1988

To remedy problems of inadequate and inconsistent clinical diagnostic testing, the 100th Con-

Photo credit: Vivigen, Inc.

Facilities that perform DNA-based diagnostic tests are subject to the Clinical Laboratory Improvements Amendments of 1988.

gress passed legislation that subjects most clinical laboratories to a number of requirements, including qualifications for the laboratory director, standards for the supervision of laboratory testing, qualifications for technical personnel, management requirements, and an acceptable quality control program. Many of these same standards were already in place prior to 1988 with regard to laboratories doing testing for Medicare or accepting samples across State lines, but CLIA represents the congressional response to national concern over shortcomings in the stringency and coverage of the original 1967 law. Designed to strengthen Federal oversight of laboratories to ensure that test results are accurate and reliable, CLIA creates a national, unified mechanism that regulates virtually every laboratory in the country-not just those involved in interstate commerce or participating in Medicare. Another impact of CLIA, beyond its extension to all laboratories, is the integration of the previously separate inspection and enforcement systems.

Prior to enactment of CLLA, Federal regulations covered the approximately 12,000 laboratories that either transported samples between States or performed tests billed to Medicare. In 1990, however, the Health Care Financing Administration (HCFA) of the U.S. Department of Health and Human Services (DHHS) began exercising sweeping regulatory authority over clinical laboratories. HCFA's mandate is to set standards for staffing and maintaining all medical laboratories, including physician office testing. HCFA is also directed to manage a comprehensive program to police the facilities, and it can impose sanctions.

Under CLIA, the Secretary of DHHS (hereinafter the Secretary) shall establish national standards for quality assurance in clinical laboratory services. The Secretary must implement recordkeeping, inspection, and proficiency testing programs, and report to Congress on a range of issues gauging the impact of various quality assurance mechanisms. Regulatory requirements will vary according to whether the facility performs tests considered "simple," "moderately complex,' or "highly complex" (42 CFR 493). For example, cytogenetic testing-examining chromosome profiles—is likely to be considered "highly complex" (108). DNA-based genetic tests are not yet covered by the cytogenetics category, but unless specifically categorized, a test is considered "highly complex" (57 FR 7245). Tests similar to DNA-based genetic assays—i.e., DNA analysis to detect viruses-have been classified "highly complex" (57 FR 7288).

CLIA and the Omnibus Budget Reconciliation Act of 1989 (Public Law 101-239) grant HCFA the power to suspend or revoke a lab's certificate for violation of the rules. Further, fines up to $10,000 for

each violation or each day of noncompliance can be levied, and jail sentences of 3 years can be imposed, The law continues to permit, subject to approval by the Secretary, States or private associations to substitute for the Federal accreditation process. Currently, these include at least the College of American Pathologists (CAP), the American Association of Bioanalysts, accrediting agencies in three States, the Joint Commission on Accreditation of Healthcare Organizations, and the American Osteopathic Association.

Monitoring Laboratory Performance

HCFA will continue using State agencies for onsite monitoring because those agencies have the most experience in inspection activities, have the ongoing responsibilities for assessing laboratory compliance, inspect an entire facility (HCFA agents inspect only specific areas), and make periodic recertification (56 FR 13430).

Beyond onsite monitoring and inspection, proposed HCFA regulations aim to help physicians and patients avoid laboratories that perform poorly by issuing an annual laboratory registry (42 CFR 493.1850). The registry will include, for example, those facilities that have had their CLIA certificates suspended and those that have had their accreditation withdrawn or revoked. The registry is designed to create a national enforcement mechanism that affects virtually every clinical laboratory in the country.

For the first time, CLIA regulates the estimated 98,000 physician office laboratories. In total, HCFA estimates that from 300,000 to 600,000 physician, hospital, and freestanding laboratories in the Nation could potentially come under these provisions, and that the registry will likely change the practice patterns of laboratories across the country. Some laboratories might close because they cannot meet the requirements. Others, out of fear of being sanctioned, might choose not to perform certain tests. Some laboratories will increase their fees to private patients to cover the costs of upgrading facilities to meet CLIA standards and to pay the user fee (57 FR 7188) being imposed to fund the survey and other CLIA requirements. Some laboratories, however, are exempt, including certain State facilities and some performing drug abuse tests (57 FR 7190). Facilities limited to some types of insurance testing could also be exempt (108).

State Authority Under CLIA

States will be substantially affected by CLIA. On one level, they will probably experience some additional administrative burden if they identify an increased number of noncompliant laboratories. The principal impact, however, will be on the relationship between the Federal Government and the States in the area of direct laboratory regulation. Prior to CLIA's enactment, the Federal Government had no regulatory authority over the numerous intrastate laboratories, including those located in physicians' offices. These were, in many cases, though not all, regulated by the States; such facilities are now subject to CLIA requirements.

As mentioned earlier, however, CLIA does not preclude continued State regulation and licensure (57 FR 7188), although the thrust of States' role is changed. Primary emphasis focuses on licensing personnel and providing information, inspection, and some proficiency testing services. (A later section in this chapter describes specific State initiatives in overseeing clinical laboratories.)

Proficiency Testing

One issue of critical concern to Congress in passing CLIA was proficiency testing programs. Until CLIA, such programs varied broadly in testing criteria and in grading of test results. Moreover, uniform or minimally acceptable Federal standards did not exist. Now, except under certain circumstances, proficiency testing shall be conducted every 4 months, with uniform criteria for all examinations and procedures. The Secretary shall also establish a system for grading proficiency testing performance. HCFA expects to propose rules on proficiency testing before the end of 1992. None of these rules is expected to apply to DNA-based CF tests (65,185).

Sanctions

HCFA has moved more quickly on the issue of sanctions against laboratories not meeting Federal requirements (57 FR 7218). Such sanctions can be imposed instead of, or before, suspending, limiting, or revoking the laboratory's certificate and canceling the laboratory's approval to receive Medicare payment for its services.

Prior to CLIA and the Omnibus Budget Reconciliation Act of 1987, the only recourse HCFA had against a noncomplying laboratory was cancellation of its approval to receive Medicare payment for its

services. In developing a range of new sanctions, HCFA has attempted to establish consistency between the enforcement approach for Medicare laboratories and for laboratories that do not participate in Medicare. At the direction of Congress, the sanctions include directed plans of correction, civil money penalties, payment for the costs of onsite monitoring by the agency responsible for conducting certification inspections, and suspension of all or part of Federal payments to which the laboratory would otherwise be entitled for services furnished after the effective date of sanction.

HCFA proposes three levels of noncompliance, with graduated severity according to levels of deficiencies: those posing immediate jeopardy to patients, those not posing immediate jeopardy, and those that are minor. HCFA can also impose sanctions in specific categories or subcategories, and thus discourage laboratories from performing tests in which they do not comply with CLIA without discouraging testing in categories in which no deficiencies are identified. CLIA also provides for incarceration and fines for any person convicted of intentionally violating any CLIA requirement. It specifies administrative and judicial review procedures available to a laboratory when HCFA imposes a sanction or suspends, revokes, or limits the facility's CLIA certificate.

Impact of CLIA on DNA Tests

As with other clinical diagnostic tests, CLIA will affect DNA analysis performed by clinical facilities. Currently HCFA can limit CLIA certificates at the specialty or subspecialty level. No special category exists for DNA tests, but facilities performing such assays clearly fall within CLIA's regulatory rubric. Furthermore, HCFA theoretically could limit CLIA certificates at the level of individual tests rather than at the specialty or subspecialty level. For example, a laboratory could lose its authority to perform CF mutation analyses, while retaining authority to continue performing, and receiving payment for, sickle cell tests. Such detailed oversight, however, would probably strain HCFA's administrative capacities (34).

One aspect of CLIA important to carrier testing and screening for CF will be the development of proficiency testing standards. The legislation is quite detailed in addressing proficiency testing for other clinical tests, but is silent for DNA analyses. Nonetheless, HCFA expects voluntary participation of DNA laboratories in a proficiency testing program (148). As described later, professional societies and nonprofit associations are likely to play the major role in this aspect of quality assurance, although their involvement is neither required nor approved by HCFA.

State Authorities

Since CLIA, the principal State role in quality assurance for clinical facilities is licensure and certification of personnel. All licensing of medical and clinical personnel is based on State law. State and Federal tort actions to remedy issues related to personnel and service quality are discussed separately in this chapter.

As mentioned earlier, however, CLIA does not prevent States from regulating and licensing facilities within certain guidelines (55 FR 33936). At least one State views CLIA as too broad-based to appropriately address issues raised by DNA tests, California established an expert advisory committee to develop standards and to hire qualified consultants to conduct onsite inspections. After a pilot study using voluntary approvals, the California Department of Health Services (CDHS) intends to ask for specific licensing laws and regulations for DNA and cytogenetic laboratories. CDHS will use any acceptable national proficiency testing program, but will develop its own if those being developed by professional organizations (described in a following section) are not satisfactory (34).

Another State, New York, has regulated clinical laboratories since 1964, prior to enactment of the original Federal legislation in 1967 (184), More important to the issue of quality assurance for CF carrier screening, New York State has established a genetics quality assurance program that includes requirements for licensing personnel, licensing facilities, laboratory performance standards, and DNA-based proficiency testing (box 5-A).

The Role of Professional Societies

While CLIA clearly expanded the Federal role in clinical laboratory oversight, the law continues to permit, subject to approval by the Secretary, the involvement of other parties in regulating laboratory practices. In particular, private nonprofit associations and professional societies could have the greatest impact in proficiency testing. Of those associations with standing under the past Federal

Box 5-A—The New York State Genetics Quality Assurance Program

Responding to the development of DNA-based tests for genetic conditions, New York State has created a permit category for genetic tests. Since January 1, 1991, all facilities within the State, or that handle samples from the State, have had to be State licensed. Included among the types of technologies for which a permit is required is DNA analysis for carrier or disease status. To date, 40 facilities—15 within New York and 25 out-of-State-have been accredited.

In the area of personnel qualifications, the New York State regulations detail specific minimum requirements for training and education of the laboratory director, including experience with molecular biology and genetic linkage analysis. To receive a laboratory license, applying facilities must undergo an onsite inspection by the New York State Department of Health, The laboratory also must meet several other requirements, including documenting that it: periodically tests equipment; monitors and performs proper quality control of its reagents and standards; adheres to appropriate confidentiality of records; participates in some form of external quality assurance program (where available); and demonstrates that it has a clear, appropriate, interpretive report format that explains findings for nongeneticist physicians. These reports must also caution the provider about possible inaccuracies and suggest alternative or additional testing if necessary. Finally, to maintain its license, the facility must undergo interlaboratory proficiency testing for DNA analytical methods.

Beginning in August 1992, New York State will administer a quarterly proficiency testing program. Under the program, a single sample will be sent to accredited laboratories. Using five systems of their choosing, the laboratories will analyze and interpret results for the unknown sample and report the findings to the State Department of Health, Clinical Laboratory Evaluation Unit.

SOURCE: Office of Techology Assessment, 1992, based on P.D. Murphy, "New York State Genetics Quality Assurance program,' meeting abstract Biotechnology and the Diagnosis of Genetic Disease: Forum on the Technical, Regulatory, and Societal Issues, Arlington VA, Apr. 18-20, 1991.

regulatory structure, CAP is likely to be most important to quality assurance of laboratories doing DNA analysis.

In 1989, CAP established the Molecular Pathology Resource Committee to develop appropriate guidelines for all clinical tests involving DNA probes or other molecular biological techniques. Its scope includes not only DNA genetic diagnostics, but also the use of DNA assays to detect infectious diseases and neoplasms, and for forensic identification. The Committee has administered two DNA-based proficiency testing pilot programs, although their focus was not genetic disorders (66).

Besides CAP, several organizations are poised to facilitate the development of monitoring laboratories through proficiency testing for DNA-based assays. The Council of Regional Networks for Genetic Services (CORN), which receives Federal support, has been active in an array of quality assurance issues for genetic service facilities, including proficiency testing since 1985 (38). The CORN Proficiency Testing Committee sponsored a DNA-based genetic test pilot of 20 laboratories in 1990. The Southeastern region has a regional proficiency testing program, and will be enlarging its planned second survey into a national test, to be completed in 1992; this effort includes CF mutation analysis (100).

The American Society of Human Genetics (ASHG) has recently become active in the area. A joint ASHG/CAP DNA pilot proficiency testing program commenced in 1992. Full proficiency testing is planned by 1994 (5,66,99). ASHG and CORN also have designated liaisons with each other's efforts.

Proficiency testing is widely viewed as an important component of quality assurance. It provides a reliable and identifiable benchmark to assess quality performance; in the past, professional societies' involvements have predominated. Today, each of three principal organizations clearly fills a niche in the evolving area of proficiency testing programs for genetic DNA assays: Historically, CAP has led and administered an array of proficiency testing programs; CORN, with its extensive regional structure and practitioner community emphasis, has long been active in improving education, training, and laboratory quality to improve genetic services delivery; and ASHG has served as the leading national professional society for genetics researchers and service providers. Cooperation among these groups

will be essential for the timely development of proficiency testing programs for DNA-based genetic diagnostics. Such cooperation will become increasingly important, since professional programs could affect proficiency testing for CF mutations (and other DNA tests) well before HCFA proposes proficiency testing rules under CLIA (100).

U.S. FOOD AND DRUG ADMINISTRATION AND MEDICAL DEVICE REGULATION

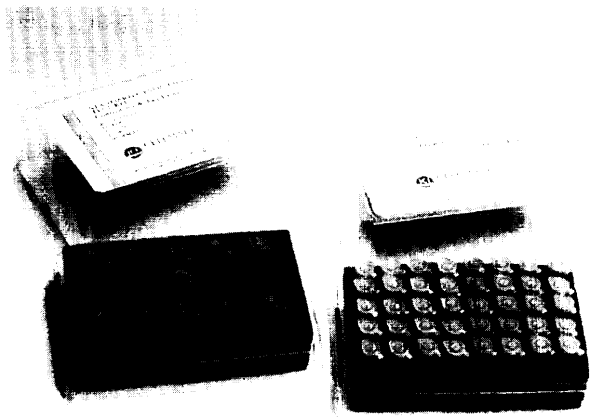
Today, DNA-based CF tests are done at research laboratories, commercial facilities, public health laboratories, and hospitals. Most attention on ensuring high quality focuses on the institution or individual performing the assay, At some future date, however, DNA-based genetic tests-e. g., for CF mutation analysis—will be marketed widely in the form of kits such as those that exist for pregnancy testing, infectious disease analysis, or forensic DNA identification. At least one U.S. company has begun evaluating a prototype CF mutation test kit in pilot studies (47,48). Cellmark Diagnostics, U. K., is also testing a kit that detects DF508 plus three additional mutations (figure 5-1; ch. 10),

The U.S. Food and Drug Administration (FDA) has authority to ensure the safety and efficacy of diagnostic test kits. ' This section briefly analyzes FDA approval procedures that might apply to new genetic diagnostic kits. A comprehensive analysis of Federal policies and the medical devices industry appears in a 1984 OTA report (168).

FDA Authority to Regulate Test Kits

FDA regulates drugs, devices, and biologics during all phases of their development, testing, production, distribution, and use, Genetic diagnostic kits fall within the definition of a device—i.e., a medical device is a health care product that does not achieve its primary, intended purposes through chemical action in or on the body, or by being metabolized. Thus, the extent to which physicians, genetic counselors, and their clients come to rely on CF mutation analysis kits--or other DNA-based genetic test kits—will depend on FDA regulation of devices.

Figure 5-I—DNA-Based Test Kit for Cystic Fibrosis Mutations



SOURCE: Cellmark Diagnostics (Imperial Chemical Industries PLC), United Kingdom, 1992.

FDA's regulatory options range from registering an item's presence and periodically inspecting facilities to ensure good manufacturing practices, to setting performance and labeling requirements, to premarket review of a device. In addition, the agency may engage in postmarketing surveillance to identify ineffective or dangerous devices; it may ban devices it deems unacceptable.

The Federal Food, Drug, and Cosmetic Act of 1938

Products such as in vitro DNA diagnostics are regulated under section 351 of the Public Health Service Act (42 U.S.C. 262), but are also subject to the adulteration, misbranding, and registration provisions of the Federal Food, Drug, and Cosmetic Act of 1938 (FFDCA) (21 U.S.C. 301 et seq.). Additionally, ''good manufacturing practices" are currently applied to licensed in vitro diagnostics.

The Medical Device Amendments of 1976 and Safe Medical Devices Act of 1990

The Medical Device Amendments of 1976 (MDA) (Public Law 94-295) and the Safe Medical Devices Act of 1990 (SMDA) (Public Law 101-629) clarfied and enlarged the 1938 FFDCA definition of ''device' to include items used in diagnosing conditions other than disease (e.g., pregnancy, in vitro diagnostic products), and specific products previously

1 Though FDA also could have regulated reagents currently used in CF mutation assays, it does not and likely will not. FDA does not regulate reagents unless they are submitted by manufacturers for clearance or approval. Manufacturers of reagents offer them labeled "for investigational use only. Facilities may develop such reagents into analytical procedures, and then offer tests such as CF mutation analysis-and other DNA-based genetic diagnostics-as clinical services. The practices, but not reagents, are regulated under CLIA.

Box 5-B—FDA Regulation of In Vitro Diagnostic Devices

Under section 5 IO(k) of the Federal Food, Drug, and Cosmetic Act of 1938, manufacturers must notify the U.S. Food and Drug Administration (FDA) 90 days prior to marketing any medical device thought to be substantially equivalent to one legally on the U.S. market. On the basis of this submission, FDA evaluates how similar the new device is to the existing device. (Devices manufactured before passage of the Medical Device Amendments of 1976 (Public Law 94-295) may be exempt from certain regulatory controls.) If FDA finds the proposed device is substantially equivalent, FDA notifies the manufacturer that it can be marketed. Since 1976, 6 percent of new devices underwent stringent premarket review (clinical trials and other demonstrations of safety and effectiveness); 94 percent were reviewed and entered the market on data provided by manufacturers that indicated they were substantially equivalent to existing devices (162).

At present, the majority of biotechnology-based medical devices represent clinical laboratory or in vitro diagnostic applications. In vitro diagnostic devices include reagents, instruments, and systems intended for use in the diagnosis of disease or other conditions-including a determination of the state of health-in order to cure, mitigate, treat, or prevent disease or its sequelae. Manufacturers submit about 1,200 new in vitro diagnostic applications each year to FDA, of which a significant percentage are biotechnology-based.

Although most biotechnology in vitro diagnostic devices submitted are monoclinal antibody-based reagent systems, a number employ DNA technologies, particularly those that detect and identify infectious agents in clinical specimens. The majority of these applications are processed through FDA's 5 IO(k) premarket notification program. Under the 510(k) process, a proposed device maybe marketed if it is demonstrated to be substantially equivalent to a legally marketed U.S. product, In many cases, a biotechnology-based in vitro diagnostic device can be shown to be equivalent if the sponsor demonstrates that the new item has essentially equivalent intended use, performance characteristics, and patient risk to an existing product. For example, the first DNA tests for infectious agents were compared to previously cleared 510(k) monoclinal antibody reagents for the same intended uses.

In some instances, comparison to an existing conventional product is not possible and, therefore, introduction raises new types of risk questions that require scientific evaluation of safety and effectiveness through the premarket approval process. In this case, the new product would be classified as Class III, and subject to the regulatory scheme described elsewhere in this chapter. Such was the case for the review of a DNA test for gene rearrangements to assess certain leukemias.

With enactment of the Safe Medical Devices Act of 1990 (Public Law 101-629), manufacturers now introducing a permanently implantable device, a life supporting or life sustaining device, or a device that potentially presents a serious risk to health must conduct postmarked surveillance of the device. FDA may also require any other manufacturer of a device, such as a CF mutation test kit, to conduct postmarked surveillance.

SOURCE: Office of Technology Assessment, 1992, based on K.B Hellman and J.L Hackett, U.S. Food and Drug Administration, Rockville, MD, personal communication December 1991.

regulated as new drugs (e.g., bone cement, sutures, or soft contact lenses). Based on the 1976 amendments, DNA-based genetic tests would be considered "devices.' Box 5-B describes the general regulatory process FDA employs for in vitro diagnostic devices, similar to those under development for CF mutations.

FDA formed the Center for Devices and Radiological Health in 1982 to centralize both the implementation of MDA (and now SMDA) and the development of programs to ensure that unsafe and ineffective medical devices are not sold in the United States. With SMDA, Congress intended that perceived shortcomings in MDA would be addressed. SMDA expands FDA authority to require postmarketing surveillance and to order a temporary or permanent halt to sales of a device in light of postmarketing surveillance results. (FDA's new authority was demonstrated in early 1992 with its consideration of silicone breast implants (73).) SMDA also expands the category of facilities and users required to communicate problems to FDA. MDA/SMDA directs FDA to classfiy devices into one of three categories, with different levels of regulation applying to each.

Class I Devices. Class I contains devices for which general controls authorized by MDA/SMDA are sufficient to provide a reasonable assurance of

safety and effectiveness. Before they can be marketed in the United States, new Class I devices that have not been exempted require premarket notification to FDA demonstrating their substantial equivalence to legally marketed devices. Manufacturers of Class I devices are subject to general controls, meaning they must register their establishments, List the devices with FDA, conform to good manufacturing practices, and submit to periodic inspections (21 U.S.C. 360).

Theoretically, genetic test kits could fall within this frost of three classifications. Included in Class I are: chlarnydia serological reagents, dye and chemical solution stains, tissue processing equipment, blood bank supplies, and examination gowns. One current Class I product used for genetic diagnosis is the chromosome culture kit, defined as "a device containing the necessary ingredients . . . used to culture tissues for diagnosis of congenital chromosomal abnormalities" (21 CFR 864.2260).

Class II Devices. Class II is a regulatory class of devices for which general controls are insufficient to provide a reasonable assurance of safety and effectiveness and for which scientific information is sufficient to establish ''special controls' to provide such assurances. The' general control provisions of Class I devices also apply to Class II devices, as does the premarket notification requirement. In addition, Class II devices must meet special controls, which can include adherence to performance standards, postmarketing surveillance, establishment of patient registries, and clinical data submission. Older, established genetic test kits not involving DNA methods (e.g., abnormal hemoglobins and alpha-l-antitrypsin assays) have been designated as Class II (21 CFR 862,864, 868).

In theory, DNA-based genetic diagnostic kits could be classified at this level if FDA determined that general controls, such as good manufacturing practices, are insufficient to give the kits the reliability already exhibited by similar kits classified in Class I. If, for example, FDA considered a DNA-based CF mutation analysis kit similar to abnormal hemoglobin assays, it might classify it as Class II. On the other hand, if FDA finds the reliability of the technologies used in DNA-based diagnostic tests differs substantially, or if the tests raise new issues of safety and effectiveness, FDA could define it as Class III. In fact, concern about the reliability of a DNA-based kit that employs essentially the same methods-PCR and DNA probes—as those that might be developed for CF tests has been raised in criminal court (74).

Class ***III Devices.*** Devices purported to be "life supporting, life sustaining, or for a use which is of substantial importance in preventing impairment of human health," or "devices which present an unreasonable risk of illness or injury" comprise Class III. In addition to general controls, these products require premarket approval by FDA based on data demonstrating that a device is safe and effective for its intended use. Manufacturers introducing Class III devices since January 1991 have been required to conduct postmarked surveillance. (SMDA additionally empowered FDA to require any other manufacturer of an existing device to conduct postmarked surveillance.)

Examples of Class III devices include a DNA probe to detect the "Philadelphia chromosome" in patients with myelogenous leukemia, tests to detect chromosomal rearrangements in certain immune cells, and maternal serum alpha-fetoprotein (MSAFP) assays for neural tube defects. Class III is an automatic classification level for new devices not yet shown to be substantially equivalent to an existing device on the market-about 2 percent per year. About 5 percent of all medical testing devices are ultimately subject to Class III regulation (51 FR 26342), and it is likely that DNA-based test kits will be categorized as Class III (185,189,190).

Investigational Device Exemption. Under the Investigational Device Exemption, FDA may exempt investigational devices from regulatory requirements that might hinder developing scientific data demonstrating safety and effectiveness. In most cases, these clinical studies of medical devices are performed to gather data or to support a premarket notification submission or a premarketing approval application.

Regulatory Future of Cystic Fibrosis Mutation Test Kits

Experience with other test kits, such as that for MSAFP (box 5-C), could shed light on **the** regulatory future of CF mutation test kits. On the other hand, congressional concerns about medical device regulation and SMDA have occurred since the debate about MSAFP test kits (152-160,164-166,168), although questions persist about the adequacy of medical device regulation (163). Further,

Box 5-C—Maternal Serum Alpha-Fetoprotein Test Kits and the FDA

In many respects, questions raised in the 1970s and 1980s about screening the serum of pregnant women to determine the concentration of alpha-fetoprotein parallel today's debate about routine carrier screening for cystic fibrosis (CF). (See also ch. 6.) One controversy surrounding maternal serum alpha-fetoprotein (MSAFP) screening involved FDA approval of test kits.

In the 1970s, British medicine had taken the lead in assessing MSAFP screening to detect neural tube defects. Based on a study of 5,800 patients screened for MSAFP in the United Kingdom, the Immunological Panel of the Bureau of Medical Devices, U.S. Food and Drug Administration (FDA), recommended in June 1977 that MSAFP test kits be classified as Class 11 devices. The panel further recommended that FDA require kits be labeled to indicate that a single positive test did not constitute an accurate diagnosis in and of itself and was insufficient to warrant pregnancy termination, although some panel members (and outside experts) viewed this recommendation as an overextension of FDA authority and an inappropriate attempt to regulate medical practice.

Historically, reagents used in MSAFP screening either qualified under the Investigational Device Exemption (IDE) (21 CFR, part 812) or were not directly regulated because the components were produced within a laboratory for its own diagnostic use. MSAFP test kits, however, were not commercially marketed in the United States prior to the enactment of the Medical Device Amendments of 1976 (MDA) (Public Law 94-295), and thus were subject to MDA. In October 1978, FDA appeared to be on the verge of releasing MSAFP test kits on an unrestricted basis.

Concern about the kits quickly mounted from laboratories, physicians, consumers, and professional societies such as the American College of Obstetricians and Gynecologists and the American Academy of Pediatrics. As with CF carrier screening, objections about the accuracy of the test, the difficulty in interpreting results, and the potential burden from increased caseloads for genetic counselors were raised. Concern was also voiced that anti-abortion groups were influencing FDA to slow approval. Others complained, by contrast, that commercial influences were rushing the move to approve MSAFP kits, which had 1979 sales of $250 million outside the United States. Some contended that FDA's decision to send the device to the Immunological Advisory Group (rather than to a panel of obstetricians and geneticists) resulted in inadequate attention to some of the clinical and programmatic aspects of widespread use of the kits (34).

In February 1979, FDA held a public hearing on MSAFP test kits before two of its advisory committees (the Obstetrics-Gynecologic Device Section and the Immunology Device Section); in August 1979, FDA announced it intended to restrict the sale, distribution, and use of MSAFP test kits. FDA classified MSAFP test kits as Class III, which required premarket approval. Further, premarketing approval applications (PMAs) would not be approved until FDA determnined what restrictions, if any, were necessary to ensure the reliability, safety, and efficacy of the kits, Manufacturers were not permitted to distribute MSAFP kits in the United States for investigational use under the IDE. In November 1980, FDA published 13 proposed restrictions for MSAFP test kits (45 FR 74158), and announced public comment would be received at hearings in January 1981.

Despite support for the restrictions—based on concerns about accuracy and efficacy as just described-several objections were raised to FDA's proposed rules. Testimony was offered that 90 percent of hospitals offered MSAFP screening and were using materials not regulated (because they were not kits); that FDA's lack of action on pending PMAs violated due process under MDA; that the proposed regulations extended beyond medical device regulation under MDA into the realm of clinical laboratory regulation (generally the domain of the Health Care Financing Administration and the Centers for Disease Control); and that the proposed regulations thrust FDA into an inappropriate role of regulating private medical practice.

FDA issued revised regulations in 1983, and MSAFP test kits have been widely employed in the United States since that time. Today, the debate is less a matter of the approval of the test kit per se, but on ancillary issues that include the role of State health agencies (35) and whether results generated by small, decentralized laboratories are of lower quality (98, 144).

SOURCE: Office of Technology Assessment, 1992.

because each device is evaluated on a case-by-case basis, the regulatory future of a PCR-based CF (or comparable) test kit remains speculative until one wends its way through the FDA process.

The 1984 medical devices reporting (MDR) regulation and SMDA require a report to FDA of any association between a device and serious injury or death of a patient and could be one level of quality

assurance of CF test kits. The regulation, however, is limited to instances of patient death or serious injury. Because use of test kits like those under development for CF is unlikely to result in injury or death to a patient, problems are not likely to be reported on this basis. Kits with poor reliability could, however, lead to unnecessary pregnancy terminations, as well as cause significant emotional harm to patients. The prospect of such pregnancy terminations might prompt FDA to order post-marketing surveillance of CF test kits.

If the MDR regulation and SMDA were to apply to genetic diagnostic kits, they might serve as an early warning system of problems with accuracy and reliability. The congressional General Accounting Office (GAO) found that the MDR regulation generally increased the flow of information about device defects by a factor of 7. Nonetheless, GAO estimated that, prior to SMDA, only one-fourth of manufacturers were in compliance and that FDA was ill-equipped to handle the data flow, data management, and data analysis required (161,162).

In the absence of an actual product, what is the regulatory outlook for test kits like those under development for CF carrier screening? Enhanced postmarketing surveillance under SMDA, coupled with a shift within FDA toward increased regulatory attention to medical devices, might indicate CF mutation analysis kits will be subject to more stringent review than previous non-DNA genetic test kits. FDA recently embarked on a series of measures directed at tightening up regulation and postmarketing surveillance of devices, as well as other items regulated by FDA (73,78). One target of increased regulatory attention, for example, has been monoclinal antibody kits, which are being subjected to increased scrutiny (53). The general change in tone at FDA and accompanying personnel changes have led to consternation among some industry spokespersons (81). Thus, it is difficult to predict how MDA and SMDA will ultimately apply to DNA-based diagnostic test kits.

GENETIC SERVICES DELIVERY

Delivering high-quality genetic services to clients depends on ensuring a su.fflcient number of skilled professionals, which in turn demands adequate education and training. Developing and ensuring that high standards are maintained, providing mechanisms to evaluate professional performance, and affording methods for client redress when lapses occur are the subjects of the following section of this chapter. In particular, this section addresses:

- whether primary care physicians (e.g., obstetricians/gynecologists, internists, or family practice specialists) are now expected to discuss CF mutation tests or to provide genetic services related to them as an aspect of routine medical care;
- what all genetic professionals-physicians, genetic counselors, nurses, social workers, or Ph.D. clinical geneticists—are expected to do when counseling individuals about the assays; and
- what remedies exist for consumers harmed by inadequate care.

Licensing and Certification

For genetic tests and information-as for other medical procedures-the quality of care is largely determined by the expertise of the health professionals and the quality of the laboratory services. The expertise and reliability of the providers, in turn, depends on the quality of medical and genetics education (ch. 6) and the quality of State certification, licensure, and discipline of such professionals within its jurisdiction.

Genetics professionals who are physicians are formally licensed by States. The process of medical licensure, making the practice of medicine without a license a criminal offense, both permits individuals to practice medicine and forbids those without a license born competing. As well as providing minimum standards, licensing of physicians provides States with the right to review an individual's practice and to discipline the person. Sanctions range from simple censure to license revocation for failure to follow proper standards in delivering services. As such, licensing can have an impact on the quality of services. A State license is the only one required to practice medicine or any of its specialties. Neither failure to obtain specialty board certification nor failure to maintain membership in a professional medical specialty society in any way limits a physician's legal ability to practice a medical specialty.

Nonetheless, economic and intellectual incentives in the 1930s and 1940s led to the development of certification procedures for specialties, to hospital-based specialty training programs, and finally to the

growth of voluntary professional medical specialty societies (143). Genetic counselors and Ph.D. geneticists are not licensed by States, but until 1992 were certified by the American Board of Medical Genetics (ABMG) (as are M.D. geneticists). Beginning in 1993, Ph.D. and M.D. geneticists will be certified by ABMG, but future certification of master' s-level counselors is uncertain.

Factors Affecting Physician Decisions About Cystic Fibrosis Carrier Screening

No definitive mechanism exists for determining when physicians should routinely inform people about the availability of tests that could reveal their propensity to have a child with a genetic disorder, such as CF (70). Physician practice maybe driven by judgment of what is in a patient's best interest, consumer demand, patient autonomy, liability fears, economic self-interest, or a combination of these factors. CF carrier screening presents a classic instance of the perennial problem of appropriately controlling the evolution of practice standards as a new technology becomes available,

Physicians can now offer individuals with no family history of CF a test that can determine, with 85 to 95 percent sensitivity, whether they are CF carriers. With professional opinion in a state of flux and knowledge of the test's existence continuing to spread among patients, physicians might wonder whether they are obligated to inform patients of its availability, even before patients ask about it. Determining when to routinely inform people about the availability of tests that reveal their propensity for having a child with CF is a contentious issue.

OTA's survey of genetic counselors and nurses in genetics revealed that some consumers are interested in CF carrier screening: about 19 percent of respondents said they were "frequently' or ''very frequently' asked by clients about DNA carrier testing or screening for CF (170). On the other hand, some physicians report that consumer willingness to undertake CF carrier screening is modest at present (1 1,13). This reticence could stem from, in part, resistance to the tests' costs, which patients must generally self-pay.[2] It might also arise from a barrier common to many types of medical screening: lack of interest and reluctance to uncover what might be perceived as potentially unpleasant news (145).

Generally, physicians are obligated to inform patients of the risks and benefits of proposed tests and procedures, so that patients themselves may decide whether to proceed. This obligation extends to diagnostic techniques (150). Where a patient specifically asks about a test, physicians would seem to be obligated to discuss the test, even if they do not recommend that it be taken. Preliminary results from one survey, for example, indicate that up to 90 percent of physicians responding would order a CF carrier test if asked to by a patient (76). Physicians do not appear, however, to be obligated to ask patients about their potential interest in a test or procedure that the physician does not view as warranted by individuals' circumstances (box 5-D) (104), although they are under an obligation to elicit family histories that reveal whether a person is at a particular risk for conceiving a child with a genetic disorder.

A 1989 California appellate court held that a couple, whose family did not appear to have members of an ethnic group at elevated risk for Tay-Sachs disease, had no basis to complain of malpractice when a physician failed to inform them that Tay-Sachs carrier screening is available (104). Expert witnesses advised that the 1 in 167 carrier frequency for Tay-Sachs in the general population was sufficiently low that customary medical practice does not recommend carrier screening for those not at elevated risk-i. e., those who are neither Ashkenazic Jews nor descended from a few other groups with elevated carrier incidence.

For CF, however, the incidence of carriers is more common in the general Caucasian population (1 in 25) than is Tay-Sachs for Ashkenazic Jews (1 in 31) (134). Physicians might ponder whether the 1 in 25 carrier frequency, which results in a 1 in 2,500 incidence of CF among live births in the general population, is sufficiently high that they should inform patients that CF carrier mutation analysis

[2] Physicians seeing patients who rely on health insurance to cover part of their costs usually inform them that their coverage generally precludes reimbursement for CF mutation analysis without a family history of the condition (i.e., for screening purposes). OTA recognizes that in the present health care system, and with current reimbursement policies by insurers (ch. 7), the reality is that choosing to be screened usually depends on the ability to self-pay. As mentioned earlier, however, the issue of economic access to CF carrier screening is no different-and inextricably linked--to the broad issue of health care access in the United States (172), a topic beyond the scope of this report. In this report, OTA analyzes the issue in the context of today's health care system, but points out that in the view of some opponents of widespread CF carrier screening, nonuniversal access is an a priori reason for why CF carrier screening should not proceed.

Box 5-D—Medical Malpractice and Standards of Care

Tort law permits individuals to sue those who have negligently caused them harm, achieving financial and emotional compensation for some victims and providing one means of quality assurance in medical practice. Theoretically, making providers responsible for their actions provides an incentive for them to act reasonably and prevent patient harm. In practice, medical malpractice litigation sometimes suffers the shortcoming of juries and judges second guessing past physician practice as a means of stimulating future improvements. In general, tort suits do a better job of enforcing standards after they have been developed. Nevertheless, medical malpractice litigation allows a jury to review the acts of a treating physician, remedy individual grievances, and force development of a good practice standard.

A physician whose treatment complied with the standard of care in the field, i.e., conformed with that offered by the "reasonable prudent physician" (or specialist, if the defendant is a specialist) under the same or similar circumstances, can rarely be found liable for medical malpractice. Statements issued by a relevant professional society are viewed as evidence of what a reasonably prudent physician might have done; so is expert witness testimony (43,51,58,173). Thus, current customs of practice protect physicians. The law assumes, however, that customary medical practice adequately reflects scientific learning and otherwise represents appropriate public policy to be enforced by the courts against individual practitioners (70).

Yet a court can devalue a standard of care by asserting that limited adoption of a practice by some professionals is sufficient to call into question the reasonableness of the defendant's practice-regardless of the extent to which that practice was accepted generally by the profession (40). The plaintiff no longer needs to show a deviation form what the average practitioner would have done. Instead, he or she can establish negligence based only on the defendant's failure to do what some cohort of the same profession was doing (40,188). Even with uniform practice within an industry (147) or profession (75,82,95), conformity with guidelines and customary practice is not an absolute defense beeause "there are precautions so imperative that even their universal disregard will not excuse their omission" (147).

In the context of medical care, however, only a few courts have followed this reasoning (52,71,96,149). Instead, most courts have deferred to the usual and customay practice of the majority of similarly skilled physicians—sometimes limiting review to local practice standards—when evaluating the actions of a particular physician (37,101,115).

No empirical data exists on current customs of practice about generally informing individuals about CF carrier tests. Physicians are somewhat protected, however, by professional society statements that advise against CF carrier screening for all individuals. On the other hand, because the content of some professional statements are in flux and because the technology changes quickly, a provider might worry that failure to offer the test or at least to inform couples of the assay's existence-will fall below rapidly evolving customs of care.

Since a variety of professionals provide genetic counseling, another question is whether the same standard of care should apply to all. Generally, each class of health care professionals is held to a separate standard of care (24). But this rule is premised, in part, on the notion that each group performs distinct types of services. Where the service is identical+. g., CF carrier screening and subsequent counseling about risks by a genetic counselor, nurse, social worker, fertility specialist, obstetrician/gynecologist, internist, or family practitioner-anyone performing the service would be expected to meet at least a common minimum standard of care (24). Where the professional in contact with the patient does not possess the requisite skill, that professional will be under a duty to recognize his or her limitations and refer to the appropriate specialist (90).

SOURCE: Office of Technology Assessment, 1992.

exists. Whether physicians are *obligated* **to** do so depends, however, on the customary practice of similarly skilled and situated physicians.

With respect to CF carrier screening, customary physician practice might evolve faster than that recommended by physicians' own professional societies (box 5-E), by managed health care facilities or insurance companies, or by government programs. This raises the question of how customary practices develop during a time of diverse opinion. The policy statements of professional societies (6,44,49) and participants at a Government-sponsored workshop (107) all state that CF mutation tests are not recommended for individuals without a family history of CF.

In addition to taking their cues from professional society and government guidelines, physicians might oppose informing patients of the availability of CF

Box 5-E—Professional Societies and Standards of Care

Professional societies can set voluntary, informal standards for professional behavior, require members to participate in continuing professional education to maintain active membership status, or require periodic examination. They can have codes of ethics governing general behavior, as do the American Medical Association (AMA) and the National Society of Genetic Counselors. A professional organization, such as the new American College of Medical Genetics, can also survey its members and gather data on new techniques. Membership in professional societies is voluntary, as is members' adherence to an organization's code of conduct and standards and participation in membership surveys.

When faced with a complaint about malpractice, courts will generally hold that the customary practice of similarly skilled physicians will be deemed ''reasonable" care. To determine what is customary and appropriate, courts often look to guidelines established by the relevant professional societies. Conversely, to protect their members, customary practices are often incorporated in professional statements and guidelines.

Identification of DF508 in 1989 resulted in intense speculation about the appropriate standard of care for general population CF carrier screening—speculation that heightens as the assay's capability to detect prevalent mutations improves. At the center of the discussions, professional societies faced the question: Should offering CF carrier screening become the standard of care in medical practice?

While acknowledging that a spectrum of individual opinions exists, the American Society of Human Genetics (ASHG), the largest professional society comprised of members of the human genetics research and clinical communities, issued a statement in 1990 about the timing of widespread carrier screening for CF. ASHG's leadership, based on its own analysis and not a poll of the membership, took the position that routine CF carrier screening is "*NOT* yet the standard of care" (25). The Committee on Obstetrics: Maternal and Fetal Medicine of the American College of Obstetricians and Gynecologists endorsed the ASHG position statement soon thereafter (44), and the AMA has also issued a similar position statement on CF carrier screening (49).

In mid-1992, after extended discussion, ASHG's leadership approval a revised statement that CF mutation analysis ''is not recommended at this time' for those without family histories of CF (6). Some argue that the subtle change in language of the 1992 statement retreats from the absoluteness of the 1990 statement. This view holds that the new statement reflects an evolution of debate within the society—that some believe CF carrier screening may now *be offered to* individuals without a family history of CF, although it might not be the 'standard of care. Others argue that ASHG's position is unchanged-that the new statement is tantamount to restating that CF carrier screening *should not be offered* to individuals without a family history of CF. In either case, the statement cannot be interpreted to mean that CF carrier screening *should be offered* to all individuals.

Professional statements can exert significant influence beyond helping courts and juries to evaluate malpractice claims. On the basis of the first ASHG statement, at least one commercial facility initially did not promote its CF tests for population screening purposes (56,61), although it appears to do so now. Additionally, OTA's survey of genetic counselors and nurses revealed that 53 percent felt in June 1991 that it was inappropriate to provide CF carrier screening compared to 20.6 percent who believed CF carrier tests for cases of negative family history was appropriate (20.6 percent uncertain); 74 percent of respondents knew of the ASHG statement (versus 31 percent who knew of the NE-I statement), and many specifically cited the ASHG statement as influencing their or their institutions' policies.

SOURCE: Office of Technology Assessment, 1992.

carrier screening because they judge that the test is too psychologically risky to be worth any potential benefits to those without a family history of CF. The very existence of prenatal diagnoses can produce stress in potential parents (89). For some patients, tests' availability sharpens otherwise low-level, diffuse concerns that surface only "on bad days, " and turns them into real and dreaded possibilities (89). Even with accurate delivery of statistical information concerning the incidence of CF, people can become worried about their carrier status--even if they never worried about it when the test was unavailable. The effects of this concern can be significant, ranging from sleepless nights to hesitation about conceiving or bearing a child (131). Physicians might also decline to screen patients because a third-party payor or managed care provider judges the test to be too expensive for expected benefits.

Opponents of CF carrier screening also argue that inappropriate financial incentives drive the practice—

that physicians paid on a fee-for-service basis find CF mutation tests profitable, as has been the case for other diagnostic procedures (72), or contend that physicians' recommendations might be influenced by laboratories marketing their tests in the same way that pharmaceutical companies currently market drugs to doctors (32,64). Some opponents also express concern that increased CF carrier screening will pressure third-party payers and managed care facilities to provide reimbursement for the test's cost, thereby necessitating a rise in premiums or discontinuation of coverage for other tests that these opponents view as more important.

Some physicians, however, have already chosen to incorporate (CF carrier screening into their practices because they disagree with the existing guidelines. They believe the assays are sufficiently sensitive for general use, and that even patients with unknown risk of conceiving a child with CF should now have the information to exercise choice in managing their health care. Still other physicians might be offering the assay out of concern that failing to could subject them to charges of medical malpractice if a couple has a child with CF and a court subsequently finds that CF carrier screening had indeed become the standard of care, despite professional statements to the contrary (19). They may worry and practice "defensive medicine" (171), afraid that the growing practice of offering the test to self-paying patients—those who have specifically asked about and those who have not—sets a de facto (and therefore de jure) standard of care for all individuals (box 5-F).

Concerns about defensive medicine are especially important because, although courts look to professional society statements for evidence of practice standards, in the end it is the actual practice of similarly skilled professionals that tends to set the minimum threshold for reasonable care. Defensive medicine has been blamed for the proliferation of many other medical tests and procedures of limited value to certain populations. The problem is particularly acute with regard to procedures performed in the context of reproductive medicine, since the birth of a baby with severe medical problems can result in substantial damage awards to cover medical expenses of the child's projected lifespan (79). CF carrier screening seems to fall squarely within this concern (57).

As of mid-1992, customary medical practice has not evolved to routine CF carrier screening. Nor has any court had occasion to consider whether the standard of care for good medicine requires CF carrier screening. To date, the statements of professional societies have slowed the adoption of such a standard of care by signaling to physicians, third-party payers, and courts that CF carrier screening is not necessary to meet definitions of reasonable care. On the other hand, while no empirical data exist on current customs of practice about informing individuals in a clinical setting about the availability CF carrier tests, trends in the number of assays performed suggest increasing numbers of providers are informing individuals about their availability (ch. 2). Whether such practices will be sustained-and hence become the standard of care-is unclear. But if doubts about the appropriateness of CF carrier assays fade, an obligation to offer them to all individuals is likely to heighten (128).

Clearly, a balance among professional guidelines, physician views, and patient demand must be struck with regard to CF carrier screening. Overall, physicians acting on behalf of individuals will establish customs of care. Nevertheless, standard setting in the area of medical practice is diffuse and generally unregulated. In the end it might be up to courts and juries to determine, on a case-by-case basis through retrospective review in the context of medical malpractice litigation, what level of care is owed to patients.

Duties of Care for Genetic Counseling

Genetic counseling requires professionals to educate patients about the availability of genetic services, to elicit enough information to determine whether patients are in particular need of genetic tests, to help patients decide whether genetic information would be useful to them, especially in light of their personal and religious values, and to assist patients in obtaining quality genetic analysis if desired.

A decision to offer information about tests for CF carrier screeninger to provide the assay itself—raises questions: What constitutes quality genetic counseling? What about confidentiality of information obtained in the course of counseling?

Box 5-F—The Maine Medical Liability Demonstration Project: An Alternative Approach to Set Practice Standards?

In response to concerns about defensive medicine, Maine enacted legislation in 1990 that creates a demonstration project designed to ensure high quality medical care, to reduce costs associated with medical malpractice litigation, and to decrease incentives to practice defensive medicine. The project hopes to accomplish these goals by having groups of physicians work with representatives of patients and insurers to form consensus opinions on practice standards in defined areas of medical care. These practice standards are then available to participating physians in the form of professional education. If a participating physician complies with the practice standards, then he or she is largely protected from claims of medical malpractice.

Advisory committees in a particular area of practice will be composed of experts relevant to the area as well as public members. For example, the Medical Specialty Advisory Committee on Obstetrics and Gynecology consists of nine members, including six physicians representing diverse interests (e.g., a tertiary hospital, mid-sized hospital, and rural practice) and three public members (one representing the interests of payers of medical costs, one representing consumers, and a representative of allied health professionals).

Each medical specialty advisory committee shall develop practice parameters and risk management protocols in the area relating to that committee. Practice parameters must define appropriate clinical indications and methods of treatment within that specialty. Risk management protocols must establish standards of practice designed to avoid malpractice claims and increase the defensibility of those that are pursued. Once the medical specialty advisory committee recommends a set of actions, the Board of Registration in Medicine and the Board of Osteopathic Examination and Registration shall review and approve the parameters and protocols for each medical specialty area, and adopt them as rules under the Maine Administrative Procedure Act. Each medical specialty advisory committee shall also provide a report to the Legislature setting forth the parameters and protocols that have been adopted, and describe the extent to which the risk management protocols reduce the practice of defensive medicine.

For claims of professional negligence against a participating physician (or the employer of a participating physician) that allege a violation of the standard of care, only the participating physician (or the physician's employer) may introduce into evidence, as an affirmative defense, the existence of the practice parameters and risk management protocols developed and adopted for that medical specialty area. Unless independently developed from a source other than the demonstration project, the practice parameters and risk management protocols are not admissible in evidence in a lawsuit against any physician who is not a participant in the demonstration project.

For malpractice policies beginning on or after July 1, 1990, the State superintendent of insurance shall determine the amount of the savings in professional liability insurance claims and claim settlement costs to insurers anticipated in each 12-month period as a result of the project. A portion of the savings could be subject to an assessment that would be used to address other health care needs of the State.

The Maine project represents an innovative approach to questions raised about appropriate medical practice standards. It formalizes the role of professional societies in establishing standards of care, giving them statutory authority and protection. It also expands the decisionmaking process to explicitly include members of the public. As the project progresses, it could provide interesting perspectives and results in the area of standards of care and medical liability to policymakers.

SOURCE: Office of Technology Assessrnent, 1992, based on Title 24. Insumnce, Chapter 21. Maine Health Security Act, **Subchapter IX.** Medical Liability Demonstration Project, 24 M.R.S. **2971** (1990).

Pretesting

To meet standards of responsible care, a genetics professional must understand enough about the patient's health and his or her reproductive plans. The provider must also be aware of what technologies are available to take an appropriate family history and proceed with necessary analyses. For a nonspecialist, it might be enough to recognize the need for a referral (24,106). These tasks have become more difficult as the timing for genetic affected child to prior to a patient's frost conception. Thus, the usual signal of a patient at risk (i.e., the birth of an affected child) would not be present.

Today, providers might elicit information concerning a patient's plans with regard to children and family history for a wide variety of detectable disorders, some of which are quite rare, during general checkups and annual gynecological visits. This would then be followed by client education to

help individuals decide whether they wish to pursue further counseling or tests. Less than that could give patients grounds to complain of a false assurance of safety.

Counseling

Having elicited information and obtained test results, the professional's next task is to communicate the results in a meaningful way. An important aspect of this task involves explaining the reproductive risks clients face. Because statistical information can be difficult to understand, this responsibility is more complex than merely stating the odds that a child will be born with a genetic condition.

All professionals who do genetic counseling—genetic counselors, nurses, doctors, social workers, and clinical geneticists—realize that translating technically accurate information into understandable information is essential and difficult (63,91, 114,124,130,137,179). Making information meaningful to nonprofessionals includes :

- supplying an accurate, or at least tentative, diagnosis;
- explaining the pattern of inheritance along with known uncertainties;
- recognizing and understanding psychosocial and ethnocultural issues;
- presenting the range of therapeutic options for treatment and management of the disorder;
- offering options for further diagnostic tests, if available; and
- counseling on medical options for preventing the birth of affected children, if desired by the patient (1,7,24,1 11,123,178).

Judging whether information has been delivered in a sufficiently comprehensible way is not simple. People interpret information about genetic risk in a highly personal manner (93,183), and a counselee can misperceive, misunderstand, or distort information. Such an effect could have significant emotional impact that affects the individual's decisionmaking or adjustment to the circumstance (131,176,179). Some consumers could perceive that a negative result from the use of "cutting edge' DNA technology means no risk, thus mistakenly interpreting the assay's resolution. Still others might believe that administration of the test itself conveys protection from risk.

In one study on risk communication and patient interpretation, over one-quarter of women surveyed

Photo credit: Beth Fine

A genetic counselor discusses results with clients. Genetic counseling can help individuals and families understand the implications of positive and negative test outcomes.

could not correctly explain the meaning of 1 out of 1,000. Of those who gave the correct answer, 16 percent said the defect occurred "often or occasionally," versus "rarely or very rarely. ' Thirty-one percent of those who incorrectly answered the question judged the defect occurred "often or occasionally' (26). Another study of clients showed that those perceiving their numerical risk as higher than others who were at the same risk were more likely to ask the genetic counselor about having another child. At the same time, patients tend to interpret a given mathematical risk as ''low' more often than do the counselors describing it (183). Finally, leaving the mathematical ability of patients aside, parents' perceptions of uncertainty in genetic counseling significantly affects qualitative decisions they make (94).

Given the nuances of information delivery and reception, and differences in situations encountered, is there a standard for genetic counseling? One commentator argues in favor of a standard for genetic counseling based on what patients would want to know (modeled after informed consent requirements) because there is no freed professional norm as an alternative, and because adequacy of the information conveyed turns more on the values of the patient being counseled than on professional norms: "It seems proper for a counselor to aim at informin g the counselees about everything the latter would find material to the decision they have to make as determined on the basis of a lay, not expert,

standard' (24). The more prevalent standard, however, appears to be based on a review of what most professionals do, rather than what an individual patient wants (29,87), The problem with relying solely on professional custom is that standards are still evolving, and there are distinctive schools of thought about methods of counseling (78,137,142).

In light of the 1991 Supreme Court decision in *Rust v. Sullivan (132),* it is unlikely that patients at a clinic receiving Federal funds from Title X of the Public Health Service Act could easily receive information about the option of choosing to terminate a pregnancy that is at risk of resulting in the birth of a child with a genetic disorder. This judicial decision runs counter to beliefs of many in the genetics community: ASHG members overwhelmingly assert that genetic counseling about all reproductive options is imperative (4). *Rust* upheld Federal regulation requiring clinics receiving these monies to respond to all inquiries concerning abortion by stating that abortion is not an appropriate family planning option. In the context of genetic counseling, many argued that the rule is inconsistent with the standards of medical care required by State malpractice statutes and cases—i, e., that abortion is within the range of options that physicians and health care providers are expected to disclose to their patients (23). In March 1992, the rule was reinterpreted to permit physicians to discuss abortion, but it does not permit them to counsel where it can be obtained. Nurses and counselors may not discuss abortion. As the vast majority of interactions at clinics receiving Title X funds are between patients and nurses, the reinterpretation will have limited effect on counseling practices.

Depending on the condition, pregnancy termination is chosen by 57 to 97 percent of parents who learn that a fetus will be born with a genetic disorder (16,41,50,62). A 1990 general survey of the American public found 32 percent of respondents would undergo an abortion if a genetic test proved positive; an additional 18 percent reported that having an abortion would depend on the nature of the defect (140). With respect to CF specifically, a recent sampling in New England of parents who had a child with CF found 80 percent would continue a pregnancy even if prenatal testing determined that the fetus was affected, although the majority said abortion should be a legally available option for those who utilize such testing (181,182). Another study of families who had children with CF in the Rochester, NY area found 56 percent approved that a woman should have the option of terminating CF-affected pregnancies, but the question did not ask whether they, themselves, would (102). No data on general population attitudes (no family history) toward CF carrier screening, prenatal diagnosis, and abortion exist, but data are accumulating from a limited number of experiences in CF carrier screening pilots. Indications are that, compared to couples with family histories of CF, fewer individuals from the general population would continue an affected pregnancy (14,21).

The 1992 U.S. Supreme Court decision in *Planned Parenthood of Southeastern Pennsylvania v. Casey*[3] means abortion now turns largely on State law, although it also appears that absolute obstacles to such a choice will be held unconstitutional. At issue was the 1973 decision in *Roe v. Wade (129),* which held a woman's liberty of conscience and bodily integrity may not be sacrificed to State interests in protecting fetal life. The 1992 decision announced such liberty remains protected from State efforts to prohibit abortion, but States now may make a woman's choice to terminate a pregnancy following prenatal diagnosis more financially, medically, or emotionally difficult unless the restriction is a substantial obstacle to choosing abortion. This new standard, the ''undue burden' test, represents a retreat from the standard in *Roe,* which held that abortion was a fundamental right. As a fundamental right, abortion was protected horn all State impediments except those based on a compelling need and implemented in the least restrictive manner possible—the "strict scrutiny" test. The new standard requires empirical data as to the effect of State regulations on women's ability to choose *pregnancy* terminations, Thus, State regulations restricting or shaping genetic counseling might be evaluated to determine if they pose a ''substantial' obstacle to a woman's choice of pregnancy termination. The 1992 opinion appears to tolerate a potentially wide range of State laws **that** might be enacted to discourage women from using prenatal testing or aborting affected fetuses. The decision explicitly upholds the constitutionality of State preferences for childbirth over abortion throughout pregnancy, and not merely following viability.

[3] *Planned Parenthood of Southeastern Pennsylvania* v. *Casey,* __S.Ct.__ (1992), 60 U. S.L.W. 4795.

Keeping Genetic Information Confidential

Both ethics and law obligate professionals with information on the carrier or affected status of a patient to keep that information confidential absent a few, specific exceptions (3,8,60,88,187). Professional codes of ethics guide practitioners (3,109), as do State statutes or case law in States with no specific statutory authority (27,67,68,77,110,139). Not all genetic information must remain confidential, however.

A patient is presumed to have consented to disclosure to his or her partner, for example, if the individual comes in for genetic counseling as part of a couple and the initial history is performed on both partners. Similarly, consent to disclosure is generally assumed when test results are raised as an issue in a malpractice suit or in an appeal for benefits denied by a govemment agency (126). State statutes also require that certain medical findings be reported, such as certain birth defects or communicable diseases, sexual and physical abuse of children, gunshot wounds, and drug abuse (8,60). At least 12 States require that birth defects be reported to a registry (Florida, Indiana, Iowa, Louisiana, Maryland, Michigan, Minnesota, New Jersey, Virginia, Washington, West Virginia, and Wisconsin).A

The closest analogy to a situation in which a provider might wish to reveal genetic information to third parties without a patient's permission appears to be the case of disclosure of communicable diseases. As with disclosing a risk of infection, the motivation would be to spare third parties the ill effects of the disorder. In the case of CF, this would entail a wish to help relatives of the patient be aware that they, too, could beat higher than average risk of conceiving a child with CF. If, after a patient has been advised to inform relatives that they could carry a CF mutation, the provider is persuaded that the relatives will not be notified, he or she may want to breach confidentiality. The impulse to breach confidentiality could be legal as well as humanitarian. Genetics providers might be concerned that they have a legal duty to protect third parties from intentional, foreseeable harm when they know that one of their patients poses a threat (146), although courts still narrowly construe such a duty.

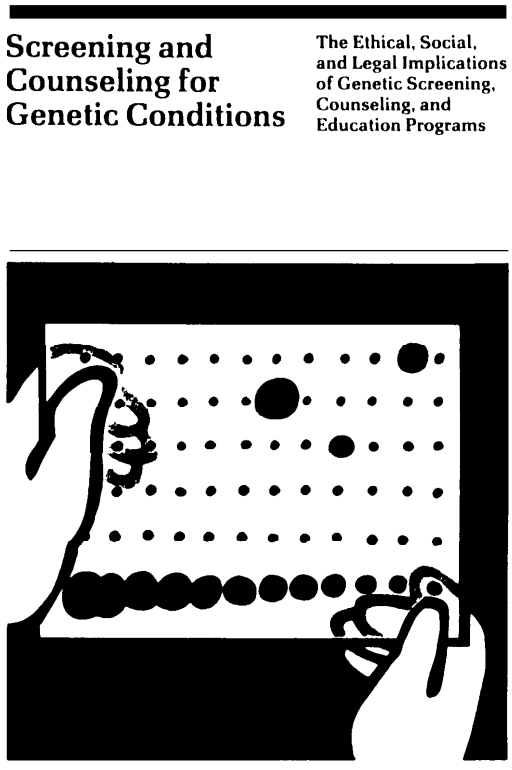


Photo credit: office of Thehnology Assessment

A 1983 report of the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research.

From an ethical perspective, the 1983 President's Commission delineated four conditions that should be satisfied before overriding confidentiality with regards to genetic information. First, reasonable efforts to elicit voluntary consent for disclosure have failed. Second, a high probability exists that harm will occur if the information is withheld and that the disclosed information will actually be used to avert harm. Third, the harm that identifiable individuals would suffer would be serious. Fourth, appropriate precautions are taken to ensure that only the genetic

[4] **Florida** Stat. Ann. Sec. 41 1.203(9)(b) **(West** 1986); **Florida Admin.** Code. Ann. R. 1OJ-8.OO7 (1990) and Guideline **VII(b)** (1981); Indiana Stat. Ann. See. **16-4-10-1(Michie 1990); Iowa Code Ann. Sec. 136A.6 (West 1989); Louisiana** Department of Health and Human Services, Guidelines: Neonatal **Screening,** Sec. **III(F)** (1988); **Maryland Regs.** Code Tit. 10, Sec. 10.38.11 (1975); Michigan **Comp. Laws** 333.5721 (1990); Minnesota Reg. 7.1.172(c)(2)(b) (1979); New Jersey Stat. Sec. **26:8-40.22** (1989); Virginia Code Ann. 32.1 -69.1 (1990); Wash. Rev. Code Sec. 70,58.320 (1990); West Virginia Code Sec. 16-5-12a (**Michie** 1990); Wisconsin Stat. Sec. 146.028 (1987-88).

information needed for diagnosis or treatment of the condition in question is disclosed (119).

Evaluating CF carrier screening in light of the President's Commission's criteria reveals that:

- The patient is not the source of the danger to the third party, as is the case with communicable disease. Rather, the patient's carrier status is merely an indication that the mutation is present in the family and that each blood relative is at increased risk of being a carrier.
- Even if the relative is a carrier, it poses no threat to his or her person because only those carrying two copies of the mutation exhibit any ill effects. Being a carrier carries no personal threat of illness.
- Being a carrier does not pose a problem in reproductive planning unless the relative's partner is also a carrier.

Overall, then, the risk to the third party from nondisclosure must be balanced against the benefit of maintaining the expected confidentiality of the provider-patient setting. A provider contemplating breach of confidentiality and disclosure to a patient's spouse must weigh the patient's own confidentiality against the spouse's interest in sharing decisions concerning conception, abortion, or preparation for the birth of a child with extraordinary medical needs. For CF, the chances of harm also must be evaluated: The spouse must also be a CF carrier for the probability of having a child with CF to rise to 25 percent.

In actual practice, a recent international survey of M.D. and Ph.D. geneticists revealed that 60 percent of respondents in the United States (and 66 percent from 17 other countries) said they would disclose a child's diagnosis of hemophilia A to interested maternal relatives who might be at risk for conceiving children with hemophilia A—against the wishes of the client. Twenty-four percent of respondents would seek out relatives and tell them even if they did not ask for the information (180), (Hemophilia A is an X-linked, recessive disorder, and hence carriers are only female. For CF, both paternal and maternal relatives could be carriers. Hence, the situation is not strictly equivalent, but is illustrative for CF carrier screening.)

Finally, as important as maintaining confidentiality of CF carrier status within families, is confidentiality with respect to third parties. At least one life insurance group acknowledges that existing mechanisms to maintain confidentiality of genetic test information might not be appropriate, and that special protection might be necessary (2). Recent evidence indicates that the Cystic Fibrosis Foundation (CFF), as part of its annual survey of CF centers, has begun to request information on mutation status (31,174). CFF releases only aggregate information for research purposes, but because data are delivered by centers to CFF without express consent in a fashion that is identifiable to individuals and their families, questions about the advisability of this practice have arisen. A sampling of institutions reveals that institutional review boards have not reviewed such practices nor been consulted about releasing such information (31).

Compensation for Inadequate Genetic Counseling

Practitioners who provide inadequate genetic counseling, including failing to prescribe needed tests or failing to keep results confidential, might be subject to sanctions by a regulatory body or a professional society. As with other areas of civil law enforcement, sanctions can range from a mild reprimand to revocation of applicable licenses to practice. Courts also can issue an injunction to prevent a practitioner from disclosing certain information, on pain of being found in contempt of court. Finally, courts (and juries) can award monetary compensation for out-of-pocket expenses and mental or physical suffering to those harmed by poor counseling. In particularly outrageous cases, punitive damages may be assessed against a defendant.

Failure to Adequately Test or Counsel

People are human and mistakes are made. But what happens when the birth of an affected child occurs because a health professional breaches a duty to adequately test or counsel a client? Increasingly, courts have become arbiters of whether a health care provider has met his or her professional obligations to a patient, which has increased the impact of judicial decisionmaking on quality assurance of professional services.

Inadequate counseling for genetic tests can result in a number of outcomes. First, patients might forego conception or terminate a pregnancy when correct information would have reassured them. Second, people might choose to conceive children when they otherwise would have practiced contra-

ception, they might fail to investigate using donor gametes that are free of the genetic trait they wish to avoid, or they might lose the opportunity to choose to terminate a pregnancy. The latter situations could result in the unwanted birth of an affected child.

Medical personnel have a duty to provide information to expectant parents so that they can be fully informed about any reproductive decision they choose to make (17,20,24,39,86,105,125, 127). Courts have also occasionally recognized a duty for health care providers (and even parents) to prevent persons not yet conceived from being conceived in a manner that would result in their birth under conditions where they would suffer serious genetic or congenital disorders (36,69).

Wrongful Birth and Wrongful Life. Wrongful birth and wrongful life are the terms used to describe the forms of malpractice claims that arise from the birth of an affected child. In a wrongful birth claim, parents assert that failure to receive timely, accurate information robbed them of the opportunity to avoid conception or birth of an affected child. Wrongful birth claims can result in special danages (usually medical expenses and other special costs associated with the care of an affected child) and general damages (those encompassing all the ordinary costs of raising the child). Since the 1973 Roe v. *Wade* decision (129), courts tend to award special danages when a case has merit.[5] Most courts remain reluctant to award general damages.

Although some courts have rejected the wrongful birth claim altogether (10,86), most jurisdictions allow compensation to parents for the negligent failure to inform or to provide correct information in time for them to either prevent conception or to decide whether to terminate a pregnancy if a fetus shows evidence of a genetic disorder. Rarely have State legislatures acted to categorically deny parents access to wrongful birth claims,[6] except to forbid claims based on allegations that the parents would have terminated the pregnancy had they been adequately counseled and tested.[7] Such State statutes limit parental claims for wrongful birth to cases of preconception counseling and testing that result in parental loss of opportunity to forego conception in favor of adoption or the use of donor gametes.

With regard to CF, at least one court has ruled that parents might collect the extra medical costs associated with managing the condition. In this case, the couple complained that they would have avoided conceiving a second child had their physicians accurately diagnosed CF in their first child and thus realized both parents were carriers (136).

In wrongful life claims, the child asserts he or she was harmed by the failure to give the parents an opportunity to avoid conception or birth, because never having existed would be better than to exist with severe disabilities. U.S. courts, however, have been reluctant to allow damages because most have been uncomfortable with any decision that hints nonexistence might be preferable to life, even when that life includes pain and suffering.

As of 1991, courts in only three States recognized a cause of action for wrongful life: California (15 1), New Jersey (120), and Washington (69). The status of the cause of action is unclear in Louisiana and Indiana, whose courts have held that physicians do have a duty to advise parents prior to conception that they have an elevated risk of giving birth to a severely afflicted child and that a wrongful life action might be an appropriate remedy for the child (33,1 18).[8] In contrast, 21 States have judicially rejected a common law cause of action for wrongful

[5] Should *Roe v. Wude* ultimately be overturned, wrongful birth and wrongful life cases would again tum largely on State abortion law. Where abortion becomes illegal, State courts could conclude that failure to inform a woman of significant fetal abnormalities does not deprive her of the choice to terminate the pregnancy, as that choice is foreclosed by State law. Since it is unlikely, however, that all States would outlaw abortion, the ability to travel to a jurisdiction where abortion remained legal could lead courts to conclude that an opportunity nonetheless had been lost due to a faulty diagnosis of genetic impairment. Thus, while wrongful life and wrongful birth claims might be weakened by overturning *Roe v. Wade, they* would not be eliminated. The ASHG recently endorsed model statutory language designed to protect the reproductive options of women at risk for bearing children with serious genetic or congenital disorders (5).

[6] Colorado Stat. Sec. 13-64-502.

[7] Mimesota Stat. Ann. Sec. 145; Missouri Am. Stat. Sec. 188.130; South Dakota Stat. Sec. 21-55-2; Utah Stat. Sec. 78-11-24 (30).

[8] In the Indiana case, the court held that the State statute prohibiting wrongful life suits applied only when the child asserted he or she should have been aborted. By its terms, the statute did not prohibit suits that claim the child should never have been conceived (33).

[9] Alabama (45); Arizona (177); Colorado (92); Delaware (59); Florida (103); Georgia (9,55); Idaho (18); Illinois (1 38); Kansas (22); Kentucky (135); Massachusetts (175); Michigan (121); Missouri (186); New Hampshire (141); New York (15); North Carolina (10); Pennsylvania (46); South Carolina (1 17); Texas (1 12); West Virginia (80); Wisconsin (42)

life.[9] At least eight State statutes prohibit a cause of action against a physician for wrongful life.[10]

Overall, then, parents can sue successfully for extraordinary medical costs associated with the birth of a child with a disability whom they would not have conceived or carried to term if they had received timely, accurate information about the risks the pregnancy posed to the affected child and to their own emotional and financial stability. Ordinary costs of raising the infant, however, usually are not reimbursed. Children suing on their own behalf for wrongful life are far less successful; most courts are unable to conclude that they have been harmed by living with severe disabilities when the only alternative is never to have lived.

Breach of Confidentiality

At least 21 State statutes explicitly protect patient "formation regarding medical conditions and treatment.[11] Offending physicians can have their licenses revoked or be subject to other disciplinary action. Four of these States—Illinois, New Mexico, North Dakota, and Oregon-punish both negligent and willful disclosures, Idaho and Michigan do not differentiate between the two types of disclosure, and the remainder punish only willful breaches of confidentiality (8).

Patients whose confidential records have been revealed can also bring civil suit against the physician or facility for tortious public disclosure of private facts (122). This is not the same as a suit for defamation, which requires that the information divulged be false; it merely requires that the disclosure offend community standards of decency or expectations of privacy (12,68). Like defamation, however, the plaintiff must demonstrate an actual harm before compensation can be awarded.

Other civil suits a patient could bring for breach of confidentiality include a breach of contract action. While not common, such suits have been recognized as legitimate by State courts (68,77,97). They are premised on the notion that the provider-patient relationship is contractual, and that breach of contract litigation may be used to enforce the implied contract of confidentiality-for example through an injunction or, alternatively, to obtain financial redress following an unauthorized disclosure (8,1 13). Actions brought under breach of contract would also be possible against employees and nonphysician health care workers, either because these individuals are party to the contractual relationship (e.g., clerks at a medical facility) or under a theory of respondent superior (24).

Some suits for unauthorized disclosure could be premised on Federal and State guarantees of a right to privacy, thus limiting the ability of government agencies, such as health departments, to obtain medical records (116,133). In addition, several States have statutes that protect the confidentiality of medical records, independent from State licensure and discipline legislation.[12]

Health care professionals who release genetic or other medical information about a patient, however, would not be legally liable to that patient or subject to disciplinary action if there were a valid defense to the action. Such defenses would include the consent of the patient, waiver of the right to object to disclosure, the need to comply with a valid State or Federal law, or, at times, the need to prevent physical harm to a third party, as discussed earlier.

SUMMARY AND CONCLUSIONS

Quality assurance for CF carrier screening means ensuring the safety and efficacy of the tests themselves, whether they are performed de novo in

10 Indiana Code Ann. Sec. 34-1.1.11 (Burns Supp. 1989); Maine Rev. Stat. Ann. Tit. 24, Sec. 2931 (Supp. 1989); Minnesota Stat. Ann. Sec. 145.42 (West 1990); Missouri Ann. Stat. Sec. 188.1301 (Vernon Supp. 1990); North Dakota Cent. Code Sec. 32-03-43 (Supp. 1989); Pennsylvania 42 C.S. Sec. 8305 (Supp. 1991); South Dakota Codified Laws Sec. 21-55-1 (1987); Utah Code Ann. Sec. 78-11-24 (Supp. 1989).

11 Arizona, Rev. Stat. Ann. Secs. 32-1401(20)(b), -1451 (Supp. 1990); Arkansas, Stat. Ann. Sec. 17-93-44)9(15) (1987); California, Bus. and Prof. Code Sees. 2227, 2228 (West Supp. 1991) and 2263 (West Supp. 1990); Delaware, Code AM. Tit. 24, Sec. 173(a), (b)(12) (1987); Idaho, Code Sec. 54-1814(13) (1988); Illinois, Ann. Stat. ch. 111, pa-m. 4400-22(A)(30) (Smith-Hurd Supp. 1990); Kansas, Stat. Ann. Sec. 65.2386(c) (Supp. 1989); Kentucky, Rev. Stat. Ann. Sec. 311-595 (Baldwin Supp. 1990); Maine, Rev. Stat. Ann. Tit. 32, Sec. 3282-A(2) (Supp. 1990); Michigan, Comp. Laws Ann. Sec. 333.16221 (e)(ii) (West Supp. 1990); Minnesota, Stat. Ann. Sec. 147-091(l)(m) (West 1989); Nebraska, Rev. Stat. Sees. 71-147(10), 71-148(9) (1990); Nevada, Rev. Stat. AM. Sec. 6303065(1) (1989); New Mexico, Stat. Ann. Sec. 61-6-15@)(5) (1989); North Dakota, Cent. Code Sec. 43-17 -3](13) (Supp. 1990); Ohio, Rev. Code Ann. Sec. 4731.22 (B)(4) (Baldwin 1987); Oklahoma, Stat. Ann. Tit. 59, Secs. 503, 5@(4) (West 1989); Oregon, Rev. Stat. Sec. 677.190(5) (1989); South Dakota, Codified Laws Arm. Sees. 36-4-29 (1986) and 36-4-30(4) (Supp. 1990); Tennessee, Code Ann. Sec. 63-1-120(15) (1990); Utah, Code Ann. Sees. 58-12-35(l)(a), 56-12-36(3) (1990).

12 California Civil Code Sec. 56,10 (West 1988); Montana Code Ann. Sec. 50-15-525 (1987); Rhode Island Gen'l Laws Sees. 5-37.3-1to.3-11 (1987); Wisconsin Stat. Ann. Sec. 146.82 (West 1987).

clinical diagnostic laboratories or via test kits. It also encompasses guarantees for accurate interpretation of the test results by health care professionals. Ensuring that consumers receive high-quality technical and professional service for DNA-based CF carrier tests is the responsibility of providers, under the shared oversight of the Federal Government, State and local governments, private entities, including professional societies, and the courts.

Quality assurance to assess clinical laboratory performance is still in flux, in large measure because the 1967 legislation governing regulation of clinical testing facilities was overhauled by Congress in 1988. Rulemaking by the executive branch is under way for some aspects of clinical laboratory regulation, but not others. The Health Care Finance Administration hopes to propose rules, for example, on proficiency testing, a key quality assurance component, by the end of 1992.

The Clinical Laboratory Improvement Amendments of 1988 clearly encompass facilities performing DNA-based genetic analyses. But, while CLIA details particular performance standards for several types of clinical diagnostic procedures, it does not specifically address DNA-based tests. This lack of detailed directives for DNA-based diagnostics could be a strength in the short-term, since the field is rapidly changing. Whereas a predominant Federal role appears the likely result for certain clinical laboratory protocols, multiple stakeholders might ultimately share oversight of DNA-based genetic assays (e.g., CF carrier tests). For example, the efforts of New York State in the area of genetic test laboratory certification and proficiency testing could influence the Federal approach to regulating genetic analyses. Similarly, the impact of professional organizations (e.g., the College of American Pathologists, the Council of Regional Networks for Genetic Services, and the American Society of Human Genetics) on proficiency testing will be important.

To a certain extent, truly broad dissemination of CF carrier screening depends on the availability of test kits now under development. Such kits will be subject to regulation by the U.S. Food and Drug Administration. Since no DNA-based genetic diagnostic test kit comparable to that being developed for CF carrier assays exists, it is difficult to predict what regulatory status will evolve for such kits. Two events could, however, serve as a gauge: The enactment of the Safe Medical Devices Act of 1990, which reflected congressional response to concern about FDA's oversight of medical devices, and indications that FDA is increasing medical device regulation and postmarketing surveillance. If congressional intent is served and increased FDA scrutiny is extended to DNA-based diagnostic test kits, developers can expect more stringent regulation of their products than previous non-DNA genetic tests (e.g., assays for abnormal hemoglobinopathies). Increased regulation could, in turn, slow the implementation of widespread CF carrier screening, since the availability of an easy, quick kit-similar to what exists for maternal serum alpha-fetoprotein screening-would otherwise facilitate screening individuals in primary care settings.

Finally, quality assurance for CF carrier screening ultimately depends on the interaction of the health care professional with the client. Customs of care are still evolving regarding the obligation of physicians, genetic counselors, and other health professionals to inform individuals about the availability of CF carrier screening. Although professional societies and government advisory bodies currently state that CF mutation assays are too imperfect to be used in the general population, physicians are nonetheless free to offer information and screening. Absent consistent resistance on the part of insurers to reimburse for the assays, it would appear that practitioner interest, patient demand, and the perceived threat of medical malpractice litigation will encourage some physicians and genetic counselors to offer information about CF carrier screening to a larger population than that recommended by their own professional societies. The increase in information concerning patients' genetic backgrounds can be expected to increase the number of situations in which health professionals will need to balance confidentiality of patient information against demand from relatives and other third parties for access to that information.

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