Chapter 3

Validity, Reliability, and Quality Assurance

''Science is one of the very few human activities in which errors are systematically criticized and fairly often, in time, corrected. ''

Sir Karl R. Popper
1902-

"In most cases, reasonable prudence is in fact common prudence; but strictly it is never its measure; a whole calling may have unduly lagged in the adoption of new and available devices. It never may set its own tests, however persuasive be its usages. Courts must in the end say what is required; there are precautions so imperative that even their universal disregard will not excuse their omission. "

Justice Holmes
The T.J. Hooper, 60 F.3d 737 (2d Cir. 1932)

"The right to search for truth implies also a duty; one must not conceal any part of what one has recognized to be true. '

Albert Einstein
1879-1955

CONTENTS

Boxes

Figures

Validity, Reliability, and Quality Assurance

Given the variation in DNA sequence among individuals (see ch. 2), no scientific doubt exists that technologies available today accurately detect genetic differences. Properly performed and interpreted, a sufficiently detailed examination of two samples of DNA can determine if DNA patterns match, and, if they do, the likelihood that a single source is responsible for both samples (except in the case of identical twins).

Nevertheless, it is generally agreed that applying DNA tests to forensic samples, especially criminal evidence, potentially presents more difficulties than analyzing samples in basic research or clinical diagnosis. Samples from crime scenes are frequently small and might be of poor quality because of exposure to a spectrum of environmental onslaughts. And unlike paternity samples, where each sample is from an identified source, the contributor to evidence taken from a crime scene is often unknown. To date, several studies have elucidated ways to overcome some of the demands of using DNA typing on forensic samples. Other efforts are under way to further refine and develop strategies that adhere to generally accepted practices in the scientific community.

What, then, constitutes a sufficient examination of a forensic sample? When does "sufficiently detailed" become unduly burdensome? What criteria are necessary for valid and reliable DNA typing of forensic samples? Does consensus exist for some scientific issues and not others? If so, what can be resolved? Is resolution necessary for all scientific issues? If not, what areas can and should be covered, and what areas are best left to the discretion of the forensic analyst? What are the best mechanisms for settling differences of opinion? And finally, who decides? As the U.S. criminal justice system increasingly turns to DNA tests, these questions, some of them pressing, must be addressed.

This chapter identifies and analyzes several key issues that bear on the validity and reliability of DNA tests for forensic uses, including:

- technical advantages and limitations of the restriction figment length polymorphism (RFLP) technique,
- technical advantages and limitations of the polymerase chain reaction (PCR) technology,

- standards-laboratory and personnel-for ensuring accurate DNA typing in the forensic context, and
- mechanisms for quality assurance.

For some issues, agreement or near agreement has been reached; the chapter describes these areas. It also examines how consensus has been achieved in other applications of DNA techniques or in new medical technologies, and analyzes how such processes could pertain to forensic applications of DNA technologies. Finally, the chapter discusses congressional, Federal, and State interest in quality assurance.

VALIDITY AND RELIABILITY OF DNA TECHNOLOGIES

An important matter in the use of DNA as evidence (see ch. 4) is whether the detection methods are scientifically valid. Validity centers on whether a test will correctly identify true matches and true nonmatches. For RFLP analysis, a valid test or set of tests would not falsely classify or exclude a subject by yielding a profile not true to type, i.e., a spurious pattern would not randomly arise. The Office of Technology Assessment (OTA) finds that molecular and genetic principles underlying DNA techniques are solid and can be successfully applied to forensic casework. Forensic uses of DNA tests are valid.

Initial concerns about the validity of DNA typing for forensic applications focused on the nature of the samples. Casework samples are obtained from a variety of less-than-sterile materials (e.g., glass, wood, dirt, and fabric) that are often subjected to sunlight, moisture, or desiccation. Samples can also be contaminated with unknown genetic material such as bacteria, plant, or animal secretions. Validation studies, however, have established that general DNA techniques are applicable for the breadth of conditions likely to be encountered in forensic casework, and have dispelled notions that RFLP analysis is invalid because of such conditions. For RFLP analysis, these studies confirmed that forensic samples in and of themselves are not barriers to applying DNA technologies that use single-locus and multilocus probes (2,19,32,34,35,50,52,66,67).

Similar validation studies for PCR are being performed (18,25,82).

A second aspect of DNA testing of forensic samples is reliability. Any test must be reliable i.e., it must measure reproducibly that which it is capable of measuring under routine conditions of use. Reliable tests must perform reproducibly within a laboratory, across many laboratories, and in the hands of different practitioners. Thus, reliability involves several factors, including the procedures used, laboratory performance, laboratory recordkeeping, quality control, and quality assurance. OTA finds that, properly performed, DNA technologies per se are reliable.

A reliable procedure, used carelessly, does not render the *test* unreliable-the particular *test result* would be in question. For forensic DNA analysis, questions exist about the appropriateness of using certain procedures over others, how data are interpreted, or about the extent or type of quality control and quality assurance necessary to minimize human factors and ensure that a particular **test result is** reliable (62,70,86). As described later in this chapter, some argue that because greater experience exists for RFLP analysis, it is currently more reliable than PCR.

Finally, although forensic uses of DNA tests are valid and reliable when performed properly, many harbor the misconception that DNA typing applied to forensic samples always yields a ''yes' or "no" answer. A test that does not give a ''yes' or ''no' each time is not incorrect, nor unreliable. An important and often overlooked result of an analysis could be "inconclusive"—a result that should not be misconstrued as either a match or exclusion.

Single-locus Probe Analysis

Several acceptable protocols exist to determine whether two samples yield similar or different DNA patterns at various loci. In forensic applications, the method most commonly employed in the United States involves using DNA probes that detect size dissimilarities among individuals at certain loci. By using several probes in combination or sequentially, an exam]nier can determine whether DNA patterns from questioned samples are consistent with a suspect's pattern (figure 3-1) or, in paternity cases, whether an alleged father's pattern is consistent with a child's (figure 3-2).

Figure 3-l—Example of One DNA Pattern in a Rape Case
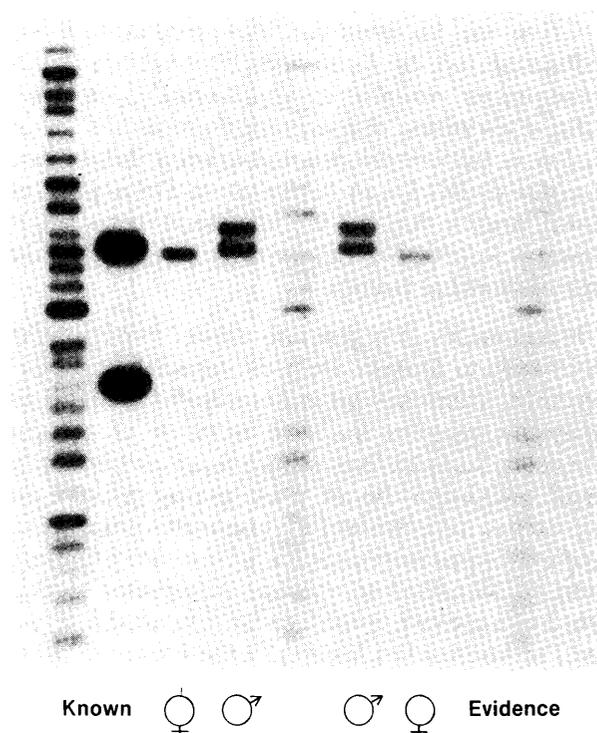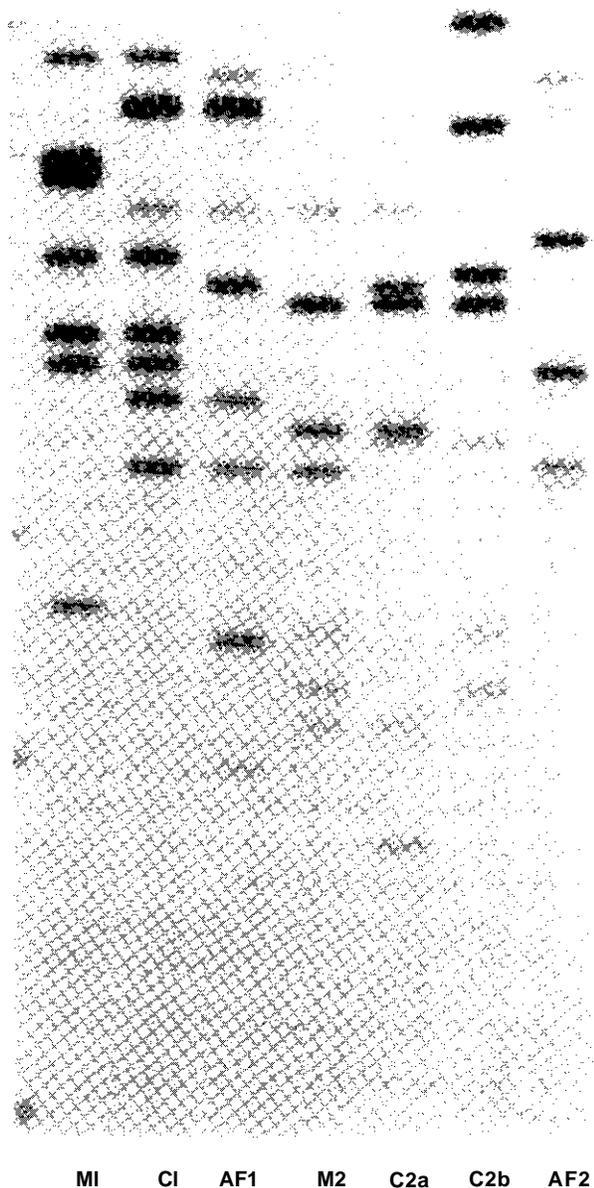

Known ♀ ♂   ♂ ♀ **Evidence**

Biological evidence from this rape case was separated by laboratory techniques into separate male and female fractions. After single-locus RFLP analysis of these fractions and known samples obtained from the victim and suspect, the results reveal that—for this particular probe~the DNA pattern of the male fraction matches the pattern of the suspect.
SOURCE: Federal Bureau of Investigation, 1989.

The basic tool used in single-locus and multilocus probe analysis is called Southern blotting, or Southern transfer (84) (see ch. 2). One of the workhorses of molecular biology, the process has been in daily use in thousands of laboratories for over a decade. Thus, extensive experience with Southern blotting in research and clinical testing supports the consensus that the technology itself is both a valid and reliable method to examine DNA.

The widespread use of Southern blotting has demonstrated that accurate and reliable single-locus analysis can be obtained across a broad spectrum of conditions. It has also defined the range of artifacts and errors that can occur, and led to solutions to avoid or minimize problems. For example, although partial digestion, differential electrophoresis, cross-hybridization, background hybridization, loading errors, probe contamination, incomplete stripping of membrane before rehybridization, and loss of small

Figure 3-2—DNA Typing in Two Paternity Cases

| MI | CI | AF1 | M2 | C2a | C2b | AF2 |

"Southern blotting"—DNA is being transferred from gels to nylon membranes. The gel is placed on a sponge, which sits in a salt solution. The nylon membrane is placed on the gel, and a stack of filter papers on top serves as a wick that draws the salt solution up through the sponge, gel, and membrane~a process that results in the transfer of DNA from the gel to the membrane. (The glass plate serves as a weight.)

DNA typing in two different paternity disputes revealed that the alleged father (AF) is the biological father in case 1, but not in case 2. Note that all bands present in the child in case 1 (CI) can be accounted for in either the mother (MI) or alleged father (AF1), In case 2, however, no bands from the alleged father (AF2) appear in either child (C2a and C2b), nor do bands that the children share with their mother (M2) match any present in the alleged father (A2). This analysis involved a "cocktail" of four single-locus probes.

SOURCE: Cellmark Diagnostics, 1989.

fragments during electrophoresis are all problems that have occurred atone time or another in laboratories, a variety of scientific controls make it possible to recognize, or account for, such situations. Further, most artifacts generally will lead to false non-matches, or exclusions (although false inclusions could occur, e.g., by incorrectly placing DNA samples on a gel or by loss of bands due to sample degradation) (63).

Nevertheless, forensic applications of single-locus analysis make somewhat different demands on the method than research and clinical applications. Whereas diagnostic testing usually consumes only a fraction of a typical sample, from which a test can be repeated, forensic case samples can be degraded, contaminated, or in limited supply. DNA diagnostics generally involves determining which RFLP a child has inherited from each parent. Since a total of at most four possibilities exists for the child (two alternatives from the mother multiplied by two alternatives from the father), the system has built-in consistency checks that alert scientists to errors, such as extra or missing bands; because choices at diagnostic loci are discrete, the results can typically be scored by visual examination alone. In contrast, a continuum of possible fragment sizes exists at loci screened in forensic DNA testing; precise measurements of the fragment lengths and objective standards for deciding whether DNA patterns match are

essential. Finally, detailed population genetics analyses are not required in diagnostic DNA testing because conclusions depend only on the samples tested. Forensic analysis, however, requires information about the frequency of DNA patterns in the general population if conclusions are to be drawn about the probability that matched patterns arose from one contributor, or whether many people in a community could have been the source.

Thus, it is important to identify potential sources of errors that could lead to false nonmatches and matches when DNA technologies are used on forensic samples. Most would agree that avoiding false matches in criminal cases is paramount, because decisions regarding liberty, and sometimes life, are at stake. Broadly speaking, three central issues must be considered in evaluating single-locus probe analysis:

- the artifacts that might appear, which might lead to a false interpretation, match or nonmatch, of the samples;
- the accuracy involved in declaring that bands are a match or nonmatch between two RFLP patterns; and
- the population characteristics of RFLP patterns. (Although the validity of forensic DNA tests per se does not involve population genet-

ics, when DNA typing results do not exclude an individual, population genetics becomes essential to the interpretation.)

Controls to Avoid Artifacts

Forensic DNA tests generally involve limited quantities of samples that could have been exposed to centaminants or environmental insults. In some instances, forensic samples might have marginally sufficient DNA to analyze; if too little DNA is obtained, less intense bands might not be detected, misleading the analyst. Some forensic DNA samples might be partially degraded, resulting in the isolation of an insufficient quantity of high molecular weight DNA; depending on the probe used, large fragments might not be detected. Finally, forensic samples can contain chemicals, or DNA from additional sources (a second person or bacteria), that interfere with complete DNA digestion by the restriction enzyme or normal gel electrophoresis.

In different ways, each of these situations could create problems that might interfere with analysis or interpretation of forensic DNA test results. Several factors to minimize potential problems are important, including: quality control of reagents; choice of enzyme and probe (box 3-A); and built-in scientific flags, or controls. Controls are especially critical.

Box 3-A-Considerations for Choosing Forensic Single-locus Probes

Over 3,000 RFLP loci have been identified to date, including more than 100 highly polymorphic loci at which many alleles exist in the population. With such a wide range available, DNA probes that minimize possible ambiguities can be used. Most agree that, ideally, a DNA probe for forensic use should:

- contain DNA sequences that detect only one chromosomal locus under a reasonable range of hybridization conditions;
- produce well-characterized patterns (such as defined size range, number of bands, and relative band intensities) so that unexpected patterns can be recognized; and
- detect a single polymorphic fragment per allele so that each person's test yields either one or two fragments, depending on whether an individual is homozygous or heterozygous, respectively.

Avoiding probes that detect fragments of varying number or intensity minimizes the problem of identifying the true bands that comprise the RFLP pattern. Otherwise, the potential exists for uncertainty about whether weak-intensity bands are part of the pattern. Furthermore, using a probe that identifies patterns with bands of variable number and intensity could make it difficult to identify bands on a dirty background.

Other considerations related to the use of a DNA probe for forensic casework include:

- using a series of probes from different chromosomes, or reasonably distant on the same chromosome, to ensure that the regions sampled are independently segregating;
- availability of the probe for research purposes, which allows other scientists to confirm its properties; and
- having the chromosomal position of the locus detected by the probe filed with the Human Gene Mapping Workshop.

SOURCE: Office of Technology Assessment 1990.

To prevent or minimize unexpected or uninterpretable results, often referred to as artifacts or anomalies, scientists have developed several precautions based both on experience in basic research and on validation studies on simulated and actual forensic samples. Controls are steps built into any scientific analysis. They tell the scientist that the assay as a whole proceeded as expected, and that results from unknown specimens are accurate and reliable. For despite vigilant quality control and rigorous adherence to an acceptable protocol, analyses can and do fail. Thus, controls tell a forensic examiner whether the overall analysis worked—i.e., whether expected results were obtained from standard samples (box 3-B).

At present, scientists agree on the necessity for some controls, but not others. Different levels of safeguards can be used in a scientific experiment in different laboratories and yield identical, accurate results. Determining the type of controls necessary to ensure confidence in the results of any single DNA typing of a forensic specimen is of the highest priority (see section on setting standards).

Match or Nonmatch?

As mentioned previously, clinical DNA analysis generally benefits from consistency checks provided by family relationships. Additionally, the types of probes usually used detect only a limited number of well-separated alleles, so that visual comparison suffices. In contrast, forensic uses of DNA tests involve determining whether one or more unknown samples match samples collected from known individuals, e.g., a suspect or victim. Probes that detect highly polymorphic loci are used in forensic testing because they provide more information about identity. In particular, because the trend in forensic cases has been to use probes that involve as many as 50 to 100 alleles that often involve fragments of similar lengths, comparing samples requires both visual comparison and precise, quantitative measurements of fragment position. What considerations are necessary in declaring that two or more DNA patterns match?

Controlling for Potential Problems—To demonstrate that two bands appearing to be the same length in a gel are in fact the same length, most molecular biologists would perform a mixing experiment. That is, they would confirm that a 50-50 mixture of the two samples yields precisely the same RFLP pattern as either sample alone. Mixing tests can often reveal even small differences between samples, since co-electrophoresis allows a perfectly controlled comparison.

Mixing assays are generally not performed by crime laboratories in any type of comparative casework (e.g., drug analysis or protein electrophoresis) (59). And, at present, it appears that most laboratories do not routinely perform mixing tests on nonpaternity DNA samples. One important concern is the limited amount of DNA often obtained from evidence. The difficulty of precisely measuring the quantity and quality of human DNA from forensic samples so as to achieve an uniform mixture is also a consideration, as is the perceived difficulty in explaining to a jury why an examiner would deliberately mix two samples. While the latter two issues seem surmountable, most agree that the question of requiring mixing assays as a matter of routine should remain open on a case-by-case basis because, in some instances, not enough DNA will be available. These voices strongly argue that a failure to perform them is not grounds for *a priori* invalidating results. Nevertheless, many consider mixing tests as the "gold standard" for DNA typing of forensic specimens—a test that should always be performed in accordance with standards linked to DNA quantity, not strictly case-by-case.

When a mixing test is not performed, identity is inferred by comparing the positions of bands, and hence their size, in two separate lanes. Because lane-to-lane differences in electrophoresis can occur within a gel, resulting in ''band shifts, '' the most accurate way to ascertain the size of a fragment is to measure its position relative to a set of internal lane controls, called monomorphic markers. That is, the unknown band should ideally be measured against one or more bands of known size in the lane itself. Although monomorphic markers were not employed initially, their use in forensic DNA analysis now seems to be generally accepted.

In forensic casework, it might be necessary to measure the sizes of bands on different gels. Forensic laboratories performing DNA analysis currently run evidence and suspect samples on the same gel whenever possible. But occasions can arise when, for example, an evidence sample is exhausted on gel A during an analysis that excludes a suspect. Following a period of time, DNA from a new suspect might need to be tested. Again, using proper controls— monomorphic probes and known size markers—

Box 3-B—Scientific Controls for RFLP Analysis

Despite vigilant quality control and rigorous adherence to protocol, analyses can fail. Every valid and reliable scientific test, therefore, includes an appropriate set of scientific controls designed to demonstrate that the procedure worked correctly. When the test works properly, these controls yield certain expected results. If the observed results for the controls deviate from what is expected, then the results for the case samples cannot be considered reliable. A variety of simple and widely accepted scientific procedures are available to detect errors and artifacts that can arise in forensic applications of RFLP tests. Such controls include, but are not limited to the following:

Control human DNA. Together with actual case samples on a gel, one lane should include a known human control DNA that yields a known pattern. If the expected pattern is obtained, it verifies that the hybridization proceeded as expected. Failure to obtain the expected pattern indicates that the hybridization went awry and should be repeated. If a Y-chromosome specific probe is used to recognize male DNA, the blot should contain both control male and control female DNA samples. (The former is a "positive control" to prove that the hybridization would detect male DNA—if present—in the forensic case sample, while the latter is a "negative control" to demonstrate that the hybridization would not yield a spurious positive even if male DNA was not present.)

Molecular size markers. To provide a "molecular ruler" against which fragments sizes can be measured, several lanes should contain discrete DNA fragments of known size. Such ladders of standard molecular size markers provide an initial test of whether the electrophoresis was uniform. By comparing the positions of fragments in the forensic samples to the markers' positions, the approximate molecular size of the unknown fragments can be calculated.

Internal lane controls. Even if the size markers appear to be distributed evenly, the analytical lanes might not have run uniformly; differences in DNA concentration (figure 3-3) or other conditions within a sample (e.g., salt concentration) can contribute to electrophoretic differences between lanes. Therefore, to account for such "band-shifting," monomorphic DNA probe controls—i.e., probes to detect bands that are not polymorphic, but of fixed size in the human population—should be used. If, in fact, lanes ran at different speeds, fragment sizes in each lane can then be more accurately computed by using the internal controls as lane-specific molecular rulers. More than one internal standard, or monomorphic probe, should be used so that there are enough reference points to allow an accurate measurement.

Internal controls can also verify the presence of adequate quantities of high molecular weight DNA. If a DNA sample is partially degraded, the quantity of DNA above a certain size might be insufficient for detection; an important consideration if the probe used detects alleles that are of high molecular weight. In this case, degraded DNA could lead to the conclusion that an individual is an apparent homozygote, rather than a heterozygote whose upper band goes undetected due to DNA degradation. Such situations could give rise either to a false match or nonmatch. A monomorphic probe that detects a high molecular weight band could be used as a control.

Test for incomplete stripping. If a membrane is not stripped completely between sequential applications of probes, radioactively labelled probe can remain attached and produce a signal in a subsequent test. Performing autoradiography on the stripped membrane can demonstrate if a signal results from residual probe. If a pattern is seen, the membrane should be re-stipped. Even if autoradiography is not performed after stripping, extra bands can be accounted for by superimposing consecutive x-ray films,

Control probing with plasmid DNA. Since plasmid vector DNA is a potential contaminant in samples and probes, a band observed on an x-ray film might not be human DNA, but plasmid DNA in the sample that is being recognized by plasmid DNA in the probe. To rule this out, some forensic labs probe the Southern blots with plasrnid DNA to identify the location of any such bands, or use synthesized DNA probes lacking plasrnid sequences.

SOURCE: OffIce of Technology Assessment 1990.

DNA from the new suspect can be tested on gel B and accurately compared with results from gel A.

In any case, unless discrete allele systems are used or mixing tests performed, determining whether two samples in different lanes match (on the same or different gels) can require fine discrimination. In addition to visual comparison, an objective match- ing rule is thus required, reflecting empirical measurement variation observed to occur when known samples are repeatedly analyzed.

Reporting a Match—The systems currently used to report a match vary. While some consensus exists on what broad steps constitute an appropriate method for determining whether two samples match when

Figure 3-3—DNA Typing and Murder: A Less Than Ideal First Analysis and a Solution

A. M K562 K1 Q1 M Q2 Q3 Q4 M Q5 Q6 M   B. M K562 K1 K1 M Q3   M
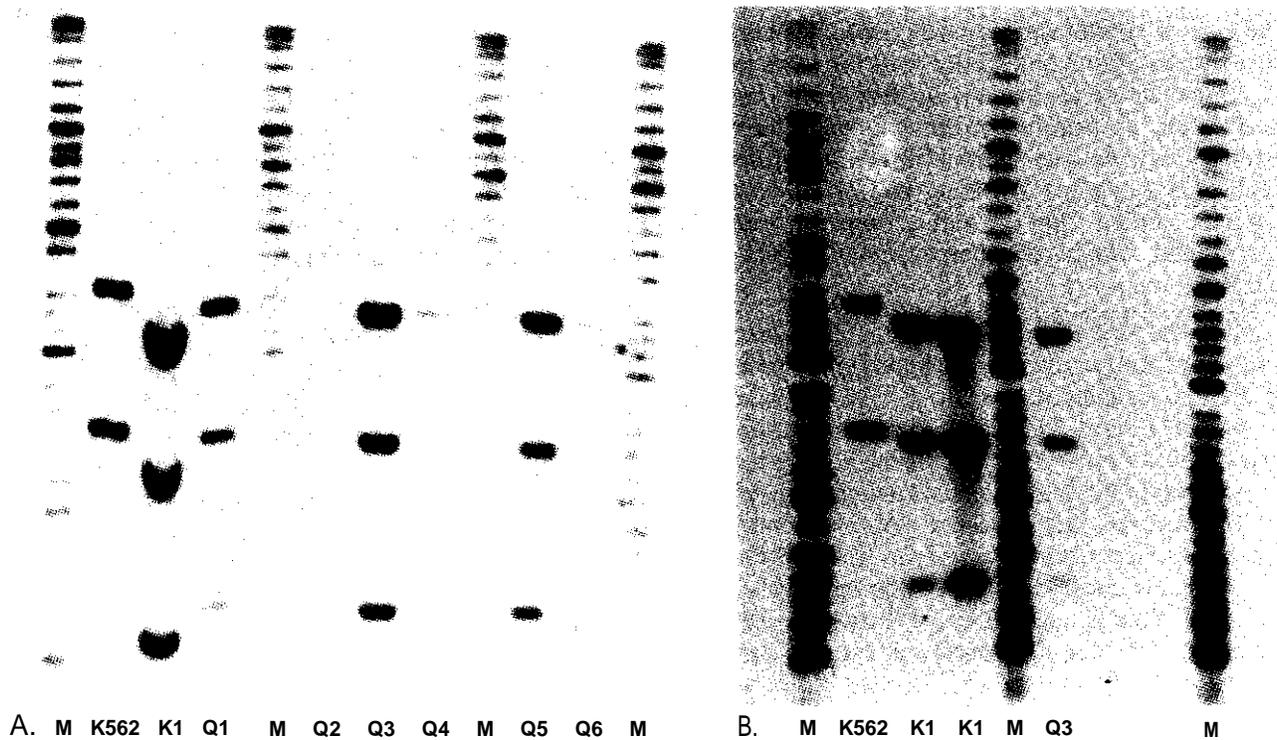
In this murder case, six separate pieces of evidence were obtained from the crime scene and a suspect identified. RFLP analysis was performed (M=markers; K1 =suspect; Q1 -6=evidence; K562=standard), but the results revealed that too much of the suspect sample (KI) had been placed on the gel, which led to distortion in the K1 lane, as well as the lanes next to it (K562 and QI) (panel A).

Even though the suspect's pattern for this probe is an extremely rare and unusual three-band pattern that is similar to the six questioned samples, the forensic analyst cannot call a "match," but must report the test "inconclusive" because the alignment is unacceptable. This, despite knowing from experience that if less suspect sample had been used, the patterns likely would have aligned and been called a match.

Fortunately, not all of evidence sample Q3 had been used in the test in panel A (although QI ,2,4-6 had been exhausted). The case was **repeated (panel B) with diluted amounts of the suspect sample (KI), which now clearly align with the evidence pattern (Q3). Had no evidence sample been available for an additional try, however, DNA analysis would have reported "inconclusive," and could not have been used as evidence to prove guilt or innocence.**

SOURCE: Federal Bureau of Investigation, 1989.

highly polymorphic loci are analyzed, scientists disagree to a certain extent on the details. This section describes the general sense of how a match should be reported when radioactive DNA probes are used, which is generally the case for criminal casework.

The initial step in examining the results of hybridizing with a single-locus probe involves identifying the bands in each lane. In all cases, each lane must be evaluated independently-the presence of a band in one lane must not influence whether a questionable signal in another lane should be identified as a band. Ideally, the x-ray film would show only RFLP bands from the test, and would show them distinctly. However, even if there is some

degree of background hybridization or the bands are faint, an exami ner can often reliably identify the pattern. For a probe that identifies a single polymorphic band per allele, the task should be relatively easy: the lane should contain one (homozygote) or two (heterozygote) bands that are much more intense than anything else in the lane. On the other hand, evidence samples might be an unequal mixture from two or more contributors, so an additional faint band (or bands) should not just be discounted.

After the bands have been identified, the examiner must then determine whether they are in matching positions. Accurate identification of a band's position depends on a properly exposed piece of x-ray film-one that yields thin, sharp bands. Overexpo-

sure (or too much DNA on a gel) results in broad bands that cover a significant size range-creating the risk of spuriously suggesting matches between distinct alleles and potentially masking other bands. A consensus exists that visual inspection must be performed, as well as objective measurement of band position with an appropriate measuring device, such as a computer digitizing pad or a computer-coupled camera. Opinion varies, however, over the extent and weight of operator involvement (see ch. 5).

Once the size of the fragments is calculated (by comparing the positions of the bands to the positions of the size standards), how close must two bands be to declare a match? Identical measurements are not to be expected, nor are they achievable. Determining an acceptable threshold of measurement imprecision is the key. In fact, because gel electrophoresis conditions vary from laboratory to laboratory, what is acceptable for one might not be appropriate for another. What is agreed on is that an objective matching rule should be used and adhered to (e.g., fragment lengths within "x" percent based on the variability observed empirically when known forensic samples are repeatedly tested).

Population Genetics

Finding that two samples have the same DNA patterns does not necessarily mean they came from the same individual, just as finding two specimens with the same blood type does not mean they came from the same person. RFLP patterns represent only a snapshot of the unique DNA sequence of each individual. Thus, in the absence of a result that excludes an individual, population genetics is an essential element in forensic uses of all genetic techniques, including DNA technologies.

The validity of forensic DNA tests does not hinge on population genetics. Interpreting test results, however, depends on population frequencies of the various DNA markers (1,9,10) (for RFLP analysis, the size of the band in a particular test). In other words, population genetics provides meaning—numerical weight—to DNA patterns obtained by molecular genetics techniques.

Once a set of patterns (or just two patterns) match, population frequencies are used to report the frequency that such an event could arise randomly; they are key to establishing confidence in associating an unknown evidence pattern with the pattern from a suspect or victim. For example, whether 1 in 30 billion, 1 in 2 million, 1 in 50, or 1 in 10 random individuals could be expected to be contributors to a specific piece of biological evidence. That basic scientific principles of population genetics can be applied to forensic DNA analysis is not in question, but how best to apply which principles to single-locus RFLP analysis is under debate. Disagreement exists as to the extent such a debate can or should be resolved.

Debate over population frequencies and RFLP analysis takes several forms (16,17,29,57,69). General agreement exists that any potential bias that could result from calculating population frequencies be conservative, i.e., favor a defendant. Nevertheless, questions are raised about whether existing population databases are properly applied, and whether they adequately support calculations of inclusion, as currently practiced. Some argue that the magnitude of the number is not the issue, just that the analyst assigns it with confidence that genetics principles have been adhered to. Others argue that because of the pivotal role population frequencies can play in reporting results of forensic DNA tests, agreement is necessary.

Calculating Population Frequencies of RFLP Patterns—After a laboratory has determined that DNA patterns from forensic sample A match forensic sample B, an analyst needs to estimate how frequently such a match might arise by chance in the relevant population. Calculating the population frequency of a DNA pattern consists of two steps. The first step involves ascertaining the frequency of individual bands by examining random population samples. The second step requires estimating the population frequency of the overall DNA pattern (box 3-c).

Determining population frequencies of DNA fragments in a pattern, represented by bands on the autoradiograms, is a fundamentally empirical exercise. The size of the band in a pattern is compared to a database containing the distribution of fragment sizes found in a previously studied group of individuals. In contrast, calculating the population frequency of the overall pattern is a fundamentally theoretical exercise. Starting with the frequencies of the individual bands, an assumption must be made that each represents statistically independent events. Using certain basic formulas from populations genetics, the probability that each of these independent

---

Box 3-C—Statistics and RFLP Analysis

Only **a** small fraction of DNA sequence differs between random individuals, except identical twins. Using DNA probes allows scientists to detect some of those differences. For forensic analysis with the single-locus RFLP technique, using several single-locus probes in combination or serially allows a forensic examiner to conclude whether two different DNA samples came from the same person (or in paternity analysis, whether a man could have fathered a child) and report remarkable statistics that the event is more than a chance occurrence-sometimes more than the number of people living on Earth.

Yet, one RFLP analysis can be thought of as only a snapshot of any given DNA sample. Thus, how many pictures need to be taken before scientists can be sure two unknown samples come from the same individual? How do they arrive at such a conclusion-expressed as a probability of the same event occurring in a random population? What is important: the number of snapshots taken? what information the snapshot reveals? or how often a certain picture can be found in a population? In other words: How many probes? How many bands? How frequently do different bands occur in the population?

Although actual calculations to assign a numerical value to RFLP analyses are far more complicated (and somewhat controversial), the following exercise is designed to provide a sense of statistics and RFLP analysis. The scenario assumes ideal genetic conditions, and eliminates one step in calculating statistics for RFLP tests by arbitrarily assigning frequencies to *patterns,* rather than *bands.*

Probe	Detects
A	3 patterns; equally distributed in the population (33.3 percent each)
B	2 patterns; equally distributed in the population (50 percent each)
c	2 patterns; Cl is found in 90 percent of the population and C2 in 10 percent of the population
D	10 patterns; equally distributed in the population (10 percent each)
E	20 patterns; equally distributed in the population (5 percent each)
F	50 patterns; equally distributed in the population (2 percent each)

Suppose in case 1, probes A, B, C, and D were used, and pattern Cl was revealed in both a suspect and evidence sample. The frequency of this event—a suspect having the same composite profile as the evidence sample-would be 0.333x 0.50x 0.90x 0.10= 0.014985, or about 1.5 percent, or every 3 in 200 people. On the other hand, if 3 probes were used in case 2—D, E, and F—the frequency of a suspect matching this overall pattern would be 0.10 x 0.05 x 0.02 = 0.000100, or 0.01 percent, or 1 in 10,000 persons. Even though fewer probes were used in case 2, a forensic analyst could declare a greater likelihood of inclusion. In fact, the absolute number of probes used in single-locus RFLP analysis is less important than what information each probe reveals.

Similarly, suppose probes C and D were used in case 3, and patterns Cl and D revealed. The frequency that the same pattern would occur in a random sample of the population would be 0.90 x 0.10= 0.09, or 9 in 100 people. Yet, if the same two probes were used in case 4, but patterns C2 and D were revealed, the frequency of this combination would be 0.10 x 0.10 = 0.01, or 1 in 100 people. Even though identical probes were used, a forensic analyst can report a lower chance that a random match had occurred in case 4 because the information provided by the C probe for case 4 was more revealing—i.e., the analyst can declare that DNA testing in case 4 narrowed the number of individuals who could have contributed the sample more significantly than in case 3.

SOURCE: OffIce of Technology Assessment **1990.**

---

events would be observed is then computed to yield the frequency with which that particular pattern (genotype) occurs at that locus in the population. Finally, assuming that different single-locus probes have been chosen because they are not correlated, the frequencies of the genotypes can be multiplied to achieve an estimate of how often that particular composite DNA profile could be expected in the population.

One critical factor: These basic calculations are only valid when applied to populations in which the DNA fragments are statistically independent. Otherwise, the value calculated might greatly underestimate the true occurrence of the pattern in the general population—making a match seem rarer than it actually is. Essentially, the population must be one where individuals randomly marry and reproduce, so that distinct subgroups are absent. In such freely mixed populations, there will be no correlation between the alleles on the maternal and paternal chromosomes (Hardy-Weinberg equilibrium) and no correlation between alleles at different loci (no linkage disequilibrium).

If the population is not freely mixed, then correlations between alleles at two loci can exist, even if they lie on different chromosomes. In fact, alleles are not randomly distributed among individuals. Certain alleles clearly concentrate within specific ethnic groups, but where do the types of genetic markers used in forensic analysis fall? Consensus exists that genetic departures as extreme as those for rare disease alleles do not exist for alleles detected by forensic DNA probes (63). The best forensic DNA probes would detect loci where the pattern of inheritance most closely resembles that expected in a freely mixed population.

However, no detailed population studies exist yet. Thus, individual population databases used to calculate probabilities of inclusion for DNA forensic analysis should be examined for departures from genetic models. Even if significant departures are found, some estimate of match probabilities is possible. Precisely how statistical tests should be applied to verify that significant deviations from random expectation do not occur is under debate, as is what mathematical compensation can be made to account for any deviation.

Population Substructures-Because the United States is multiracial, with many ethnic subgroups, special care must be taken when determining t h e likelihood of obtaining a certain pattern within distinct population subgroups. What effect does this population substructuring have on the ability to calculate genotype frequencies within racial subgroups?

For example, several population genetics databases (see ch. 5) collect and classify information as '' Hispanic,' based on self-identification or surname. Hispanic as an ethnic subgroup, however, is extraordinarily broad in the United States. In particular, it is possible that frequencies of certain RFLP patterns in Mexican-Americans differ from citizens of Puerto Rican descent, which both could differ from individuals of Cuban or El Salvadoran heritage. The Native American population in the Southwestern United States differs significantly from Native Americans in Alaska or Hawaii. Similarly, race distinction as a division of population genetics could be insufficient. RFLP patterns from persons of Japanese, Chinese, Vietnamese, and Korean ancestry all might differ, yet be classified under the designation Asian or Oriental.

Yet how important are such subdivisions in calculating the probability that a match is real or random? Most observers agree that, while a danger exists in overplaying the "numbers game," population frequencies based on existing databases can be obtained—although any reported identification frequency represents an estimate to be used in conjunction with other evidence linking a defendant to a crime. Furthermore, the numerical significance of a match that is expressed needs to take into account the frequently unknown ethnic association of the forensic specimen and details of the ethnic variation for the population database used. On the other hand, many argue that while estimates can be made, a more rigorous and formal system for determiningg association probabilities is necessary-both because many aspects of the genetics of RFLPs have yet to be elucidated, and because juries often place great store on statistics (see ch. 4) (30).

Finally, what populations should be studied? Ideally, a random sample of the U.S. population should be tested. Since true random sampling is impractical, as is sampling all ethnic subgroups in the United States, human geneticists must determine standards and criteria that will account for the strengths and weaknesses of population genetics databases. Although it might seem academic to some to know whether the frequency of random match is 1 in 10 million or 1 in 10,000, others express concern about population frequencies-especially in the context of any single individual on trial. Population studies and analyses of statistical reporting for single-locus RFLP tests are also relevant and critical to the design and potential use of national databases of DNA types (see ch. 5).

Multilocus Probe Analysis

As described in chapter 2, multilocus probes simultaneously detect a wide range of restriction fragment length polymorphisms, thus yielding a pattern of 30 or more bands per individual (33,48,49). Multilocus probes were the first probes used for DNA identification-an immigration case in the United Kingdom in 1985 (49). Initially, great excitement was generated about the use of multilocus probes in forensic cases, since they could allow unique identification from a single hybridization.

Properly performed, multilocus probe analysis is reliable and valid, using the same basic techniques as single-locus probe analysis. However, many be-

ing the issue of population genetics are the Genetics Society of America and the Society of Heredity and Evolution.

Lastly, since the technique of electrophoresis is the basis in RFLP analysis for discriminating band sizes among individuals, the expertise of members of the Electrophoresis Society also could be brought to bear on issues surrounding forensic applications of this technique. In particular, efforts of this professional society to evaluate state-of-the-art and quality control considerations for electrophoretic methods could be useful. Joint efforts involving scientists from this society and forensic practitioners would then be able to evaluate whether certain electrophoretic methods were better suited to forensic work, or if new developments in electrophoresis would be adaptable to widespread use in forensic laboratories.

Thus, several scientific professional societies that represent stakeholders in forensic applications of DNA identification exist. In addition, professional organizations devoted to interests of the legal community, including the American Bar Association, the American Association of Trial Lawyers, the National Association of Criminal Defense Lawyers, the National College of District Attorneys and the American Civil Liberties Union, have an interest in resolving issues in DNA typing of forensic samples. Cooperation among professional organizations could be a powerful mechanism to ensure quality; in the area of forensic DNA analysis, no single professional society can claim sole, or even greatest, expertise. Although each group has specific strengths and weaknesses, the collective wisdom and influence of professional groups on quality assurance should not be underestimated or discounted. Nevertheless, professional society membership or claims of adherence to different *voluntary* professional guidelines can confuse the general public, and should not be viewed as the ultimate imprimatur of quality.

Nonregulatory Mechanisms

Short of regulating crime laboratories and other facilities that perform DNA typing for nonmedical uses, States and the Federal Government could promote quality assurance through nonregulatory means. Federal efforts, in particular, could facilitate
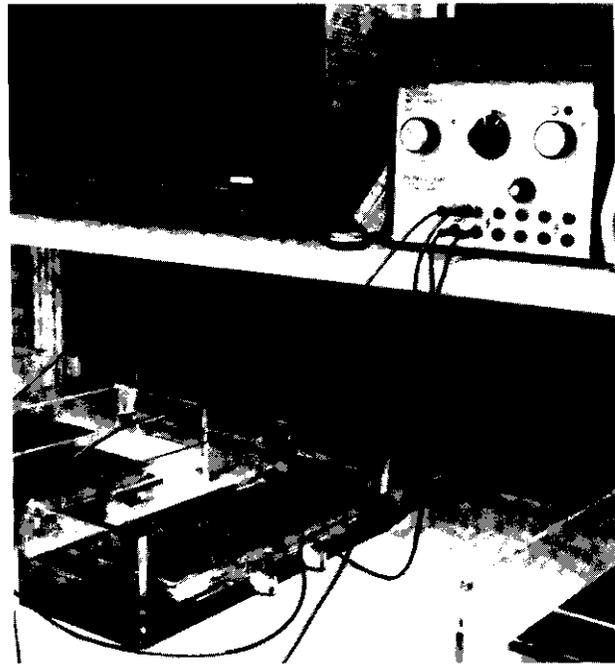

Photo credit: Robyn Nishimi

Gel electrophoresis of DNA samples.

self-regulation. Nonregulatory action could also take the form of authorizing additional Federal research in forensic sciences—particularly cross-disciplinary projects that apply emerging basic research tools to real-world casework, or enhanced population data collection for forensic DNA probes. Additional nonregulatory Federal efforts can encourage the use of governmental, professional society, and industry resources to review forensic uses of DNA tests,[1] or to hold consensus conferences that make recommendations for quality assurance of forensic DNA analysis.

A Federal role in a consensus conference process is not novel. For example, concern over costly and possibly premature applications of medical innovations led to the 1977 Consensus Development Program (71,90,97). Part of the U.S. Department of Health and Human Services (DHHS), National Institutes of Health (NIH), its purpose is to develop consensus on the clinical significance of new findings and the financial, ethical, and social impacts of a procedure's development and use. To that end, an Office of Medical Applications of Research coordinates consensus conferences and other activities

---

[1] In late 1989. at the request of several parties. including the FBI and the National Institute of Justice (NIJ), a committee of the National Research Council, National Academy of Sciences, began a study of forensic DNA analysis.

In forensic analysis, the problem of cross-contamination could be particularly serious: Should a suspect's sample accidentally contaminate a questioned sample containing degraded (or no) DNA, subsequent PCR amplification of the questioned sample would show that it perfectly matched the suspect. Thus, whereas cross-contamination in RFLP analysis might more likely arise from mislabeling of tubes than physical cross-contamination of samples, forensic uses of PCR must stringently guard against both. Proper controls, including "no DNA controls,' ' are critical to interpretation of PCR-based results.

Proper controls and precautions for forensic uses of PCR have been proposed (4,61). Laboratories must be forewarned, however, that extraordinary care is needed in sample handling-greater than the level required in RFLP analysis. Some even argue that it might be desirable if evidentiary and suspect samples were not stored or amplified in the same room. In any case, even with carefully controlled tests, some argue that results in forensic casework should probably be reconfined by an independent repetition from the original sample. (Fortunately, the minimal sample requirements of PCR and the ease of the procedure make it practical, for the most part, to repeat the test multiple times.)

Misincorporation

Rarely-about once or twice every 20,000 to 1 million bases—in the molecular copying process of PCR is a nucleotide misincorporated (28,78). Can this amount of misincorporation affect the validity of PCR for forensic uses? Theoretical modeling indicates that although a proportion of PCR products can contain some misincorporation, such events occur at random. Within an amplified sample, the chances of having a group of DNA molecules with the exact same single base substitution would then be minuscule (80), unless the substitution occurs early in the reaction, when the effect could be significant (63).

In fact, misincorporation does not create problems in DNA sequencing analysis or probe typing of PCR-amplified DNA (28), because the entire population of molecules is being examined, not a single molecule. Thus, misincorporation of nucleotides might not affect the ability of PCR to distinguish among different DNA profiles in forensic samples. On the other hand, misincorporation of nucleotides could be an issue if the initial amount of DNA is minute, which is often the situation in a forensic case. One component of standards for forensic use of PCR might include the threshold quantity of DNA that would be acceptable for valid and reliable examination (25).

Differential Amplification

Differential amplification, i.e., preferential copying of one allele over the other, is a concern in PCR testing. During the course of an amplification, differential amplification of one or the other of the two alleles can occur due to variation in length (47), sequence difference, or contamination with non-DNA material in an evidence sample (63). As mentioned previously, individuals are often heterozygous—i.e., have one band larger than the second band in an RFLP pattern. Thus, if one allele is preferentially amplified, one of the bands might not be detected and the person mistakenly typed as a homozygote.

Differential amplification can be addressed, in part, by carefully characterizing the regions to be examined and establishing standards of practice to avoid contamination. Thus, despite concerns about this matter and the previously mentioned issues, few doubt that ongoing research will overcome questions raised about PCR, with full technology transfer of PCR in criminal investigations occurring in the next few years.

Population Genetics

Population genetics considerations for PCR depend on the genetic locus amplified. At present, the only genetic system generally employed in forensic casework using PCR is the HLA *DQx-* 1 system—a human white blood cell antigen system. Results in this system are scored through the "yes' '/''no" assay described in chapter 2. HLA DQx-1 is a valid and well-defined system (78), but it is not as discriminating as RFLP analysis. It can distinguish between two random individuals 93 percent of the time (98). Such discriminating power has proved useful in excluding or including suspects in criminal cases where conventional serological genetic analysis has failed, or where insufficient DNA was available for single-locus analysis. And, although few population studies involving PCR-based detection systems have been defined to date, such information can be expected to accumulate rapidly as experience in research laboratories increases. One population genetics issue that might need address-

ing: accounting for differential amplification of alleles in a PCR-based analysis that reveals an apparent homozygote (63).

QUALITY CONTROL AND QUALITY ASSURANCE

Laboratories use quality control to ensure that an assay's quality achieves specified criteria. Quality control includes the steps taken by a laboratory to produce consistent, interpretable results each time the test is performed. A quality assurance program provides evidence that quality control is being satisfactorily performed. Such documentation can include proficiency testing and external inspections (5,54-56,85). Quality control and quality assurance are essential components of good laboratory practice.

Congress has long had an interest in quality assurance issues. Through its charge to protect the public welfare, Congress and the Federal Government have implemented an array of quality assurance programs-ranging from specific legislative action to encouraging voluntary mechanisms—in a variety of fields. In particular, quality assurance for both drug testing (box 3-D) and clinical diagnostic laboratories has been the focus of recent congressional and executive attention (53 FR 11970; Public Law 100-71; Public Law 100-578; 88,89,96).

The issue of quality assurance for the Nation's crime laboratories is not novel. Scrutiny of crime laboratories has been an issue since their proliferation in the 1970s (68,73). Publicity surrounding DNA typing in criminal casework, coupled with the fact that DNA technologies often capture government and public interest (91,93-95), has simply renewed interest in the performance of forensic facilities. Thus, while DNA testing served as the catalyst for today's debate about quality assurance for crime laboratories, other tests previously sparked attention about this subject (38,39,68).

In one respect, however, concern about forensic DNA analysis differs from previous attention to quality assurance of forensic services: Both public and commercial private providers are involved. While some mechanisms to attain uniform, high-quality service can be the same for both sectors, other approaches might apply to only one.

This section concentrates on the role that can be played by professional societies, State and local

---

governments, and the Federal Government to ensure that both private and public laboratories provide high-quality forensic DNA typing. It discusses the structure of professional societies and their potential for providing practitioner education, setting standards, assuring adequate staffing and laboratory facilities, and developing a consensus among all parties who have an interest in high-quality forensic DNA analysis.

Further, Congress has declared that crime is essentially a local problem that must be dealt with by State and local governments (with Federal financial and technical support) if it is to be effectively controlled (42 U.S.C. 3701). Crime laboratories are, in fact, public agencies, and State and local governments play a key role in determining quality of

forensic services. Thus, this section examines the role of State and local governments in quality assurance of DNA profiling.

In addition, the Federal role in quality assurance can operate at both nonregulatory and regulatory levels. The Federal Government can facilitate nonregulatory efforts to guarantee high quality. It can also actively regulate standards of practice, protocols, and commerce in forensic services (especially those paid for by government programs). In particular, this section describes quality assurance protocols implemented by the Federal Government in other laboratory testing areas, such as clinical diagnostics laboratories and drug testing facilities. Finally, the Federal Government has, over the last 15 years, formed commissions that have recommended action on topics related to applications of the new DNA technologies. Federal powers to implement the suggestions of these advisory groups also are explored.

The Role of Professional Societies

Membership in professional societies is purely voluntary, as is members' adherence to an organization's code of conduct and standards. Professional organizations can set informal standards, make members undergo continuing professional education to maintain active membership status, and require periodic examination. A professional organization can also survey its members and gather data on new techniques. Again, taking part in such studies is voluntary on the part of the membership.

In the forensic sciences, one of the many influential societies is the American Academy of Forensic Sciences (AAFS). A nonprofit professional society organized in 1948, AAFS is devoted to the improvement, administration, and achievement of justice through the application of science to the processes of law. The organization draws members from the 50 States, all U.S. territories, and over 30 countries, and is the largest professional society devoted to forensic practices. An ad hoc committee has been established to examine forensic applications of DNA tests and, as quality assurance mechanisms develop, AAFS members will play a key role in developing standards and disseminating information.

Another group of forensic professionals is the American Society of Crime Laboratory Directors (ASCLD). ASCLD guidelines do not bind a society's members to a particular practice, but do serve to develop some consensus among practitioners. For example, a DNA implementation committee has been established (see ch. 6). ASCLD also encourages proficiency testing before an analyst is assigned casework (6). In particular, ASCLD provides professional advice to a proficiency testing program, and offers a voluntary accreditation program (described in following sections).

In addition to national organizations, forensic practitioners in regional jurisdictions have pioneered efforts to establish guidelines for quality assurance. For example, in 1987, the California Association of Criminalists (CAC) and the California Department of Justice held a statewide symposium of serologists to examine standards in quality assurance, training, record collection and evidence preservation, method validation, and data interpretation. As a result of the symposium, a document articulating the professional consensus of serology practices within California was published (22). In addition, the California Association of Crime Laboratory Directors (CACLD) endorsed a series of guidelines to evaluate DNA testing by commercial services (21), which could provide criteria for measuring performance of public crime laboratories.

Other professional organizations, such as the Council on Forensic Science Education, the American Association of Blood Banks (AABB), the American Society for Histocompatibility and Immunogenetics (ASHI), and the International Society for Forensic Haemogenetics (ISFH), are likely to play an important role in debates surrounding quality assurance for DNA analysis by crime laboratories. For example, AABB and ASHI have standards for using DNA polymorphisms in parentage testing (3,4). ASHI standards address both RFLP analysis and PCR/HLA typing (4). ISFH recommendations encompass RFLP analysis for parentage and criminal samples (45).

Another important professional society, although not directly involved in forensic sciences per se, is the American Society of Human Genetics (ASHG). A society principally composed of scientific experts in human genetics, ASHG could be useful in evaluating the utility, validity, and reliability of newly emerging DNA technologies, as well as analyzing population genetics data. A recent statement raises several points that ASHG believes should be considered in forensic DNA testing (7). Other professional societies that could contribute to debates surround-

ing the issue of population genetics are the Genetics Society of America and the Society of Heredity and Evolution.

Lastly, since the technique of electrophoresis is the basis in RFLP analysis for discriminating band sizes among individuals, the expertise of members of the Electrophoresis Society also could be brought to bear on issues surrounding forensic applications of this technique. In particular, efforts of this professional society to evaluate state-of-the-art and quality control considerations for electrophoretic methods could be useful. Joint efforts involving scientists from this society and forensic practitioners would then be able to evaluate whether certain electrophoretic methods were better suited to forensic work, or if new developments in electrophoresis would be adaptable to widespread use in forensic laboratories.

Thus, several scientific professional societies that represent stakeholders in forensic applications of DNA identification exist. In addition, professional organizations devoted to interests of the legal community, including the American Bar Association, the American Association of Trial Lawyers, the National Association of Criminal Defense Lawyers, the National College of District Attorneys and the American Civil Liberties Union, have an interest in resolving issues in DNA typing of forensic samples. Cooperation among professional organizations could be a powerful mechanism to ensure quality; in the area of forensic DNA analysis, no single professional society can claim sole, or even greatest, expertise. Although each group has specific strengths and weaknesses, the collective wisdom and influence of professional groups on quality assurance should not be underestimated or discounted. Nevertheless, professional society membership or claims of adherence to different *voluntary* professional guidelines can confuse the general public, and should not be viewed as the ultimate imprimatur of quality.

Nonregulatory Mechanisms

Short of regulating crime laboratories and other facilities that perform DNA typing for nonmedical uses, States and the Federal Government could promote quality assurance through nonregulatory means. Federal efforts, in particular, could facilitate
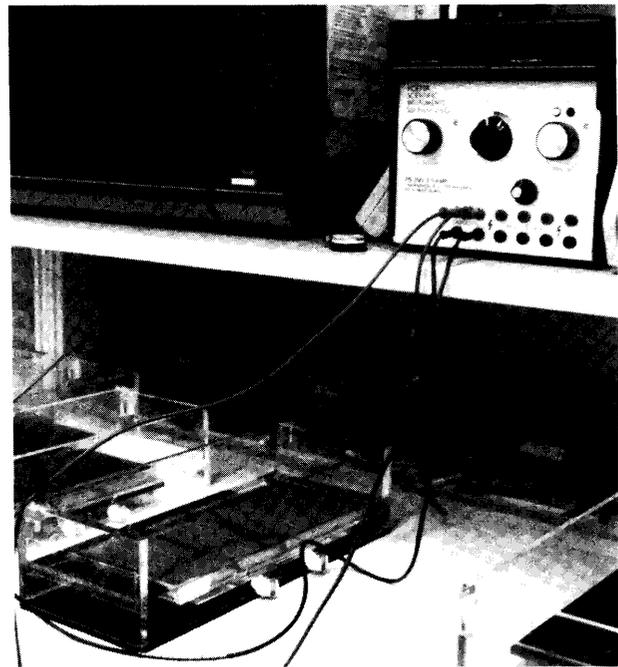

Photo credit: Robyn Nishimi

Gel electrophoresis of DNA samples.

self-regulation. Nonregulatory action could also take the form of authorizing additional Federal research in forensic sciences—particularly cross-disciplinary projects that apply emerging basic research tools to real-world casework, or enhanced population data collection for forensic DNA probes. Additional nonregulatory Federal efforts can encourage the use of governmental, professional society, and industry resources to review forensic uses of DNA tests,[1] or to hold consensus conferences that make recommendations for quality assurance of forensic DNA analysis.

A Federal role in a consensus conference process is not novel. For example, concern over costly and possibly premature applications of medical innovations led to the 1977 Consensus Development Program (71,90,97). Part of the U.S. Department of Health and Human Services (DHHS), National Institutes of Health (NIH), its purpose is to develop consensus on the clinical significance of new findings and the financial, ethical, and social impacts of a procedure's development and use. To that end, an Office of Medical Applications of Research coordinates consensus conferences and other activities

---

[1]In late 1989. at the request of several parties. including the FBI and the National Institute of Justice (NIJ), a committee of the National Research Council, National Academy of Sciences, began a study of forensic DNA analysis.

with the NIH Bureaus, Institutes, and Divisions, and guides the appointment of expert advisory panels to review and make recommendations on medical innovations and their applications.

NIH consensus conferences are open to the public and generally involve interdisciplinary panels drawn from a range of interests. Over 60 consensus conferences have been convened in the last decade, with noticeable effects on the practice of medicine in some areas (44,71). The NIH process has served as a general model for consensus development and group judgment programs in the United States and abroad (8,44).

Consensus conferences on forensic DNA analysis, for example, could evaluate data on DNA probes, including studies of the population genetics of probes, and recommend protocols that list the best methods. Conferences and reports could also help define a "successful" program, or distinguish experimental from standard investigative techniques.

One important consideration in whether an NIH-like consensus process would be appropriate to forensic DNA testing is whether the questions are primarily scientific, or primarily ethical or economic. The conferences are more effective when they are the former (58,92), although a recent external review of the program made recommendations that could strengthen its economic, social, and ethical evaluations (44). Thus, the consensus confer-

ence process might be most amenable to resolving debates about appropriate probes, electrophoresis conditions, criteria for declaring a match, or calculating population frequencies, but be less successful in addressing a topic such as privacy of DNA databases. Nevertheless, an NIH-like consensus conference process could be effective and lead to greater quality assurance in forensic practices using DNA tests.

One nonregulatory Federal initiative to examine quality control and quality assurance issues is being spearheaded by the Federal Bureau of Investigation's (FBI) Technical Working Group on DNA Analysis Methods (TWGDAM) (see ch. 6). Consisting of individuals representing forensic facilities at or near implementation of DNA profiling techniques, one TWGDAM document outlines a multifaceted program to ensure quality RFLP analysis (box 3-E) (85).

Although some predict the TWGDAM guidelines are likely to be the nucleus around which national consensus on standards for quality assurance will evolve, others are less sanguine. Some critics object to the closed nature of the initial decisionmaking or lack of representation in the group of certain interested parties. A few argue that the FBI-largely an investigative and enforcement body—is an inappropriate lead player, and thus they oppose any role for the FBI in quality assurance mechanisms and standards. On the other hand, the TWGDAM guidelines

---

Box 3-E--Quality Assurance and the FBI Technical Working Group on DNA Analysis Methods

From the outset, one goal of the FBI's TWGDAM (see ch. 6) was to suggest guidelines that would assist a crime laboratory in developing a quality assurance program for forensic RFLP analysis. Following review and revision of proposed guidelines, the policies were published in 1989.

The TWGDAM guidelines are designed to encompass 'all significant aspects of the laboratory process." The program includes considerations for personnel education and training, proper documentation of pertinent records, evidence handling, validation of analytical procedures, technical controls and standards, data analysis and reporting, proficiency testing, and independent auditing.

For proficiency testing, the TWGDAM guidelines state that open and blind proficiency tests must be performed, and recommend that an analyst be subject to both types of proficiency testing annually. Yearly independent audits should be conducted, and it is "highly desirable" that the inspection include at least one person from outside the agency.

Policies detailed in the TWGDAM program "represent the minimum quality assurance requirements for DNA RFLP analysis. " Although the guidelines are strictly voluntary, they could become the de facto standard for quality assurance. For example, the Minnesota Supreme Court cited the TWGDAM guidelines in ruling on the admissibility of DNA tests (see ch. 4).

SOURCE: Office of Techmology Assessment 1990, based on Technical Working Group on DNA Analysis Methods (TWGDAM), "Guidelines for a Quality Assurance Program for DNA Restriction Fragment Length Polymorphism Analysis," *Crime Laboratory Digest* 16(2):40-59, 1989.
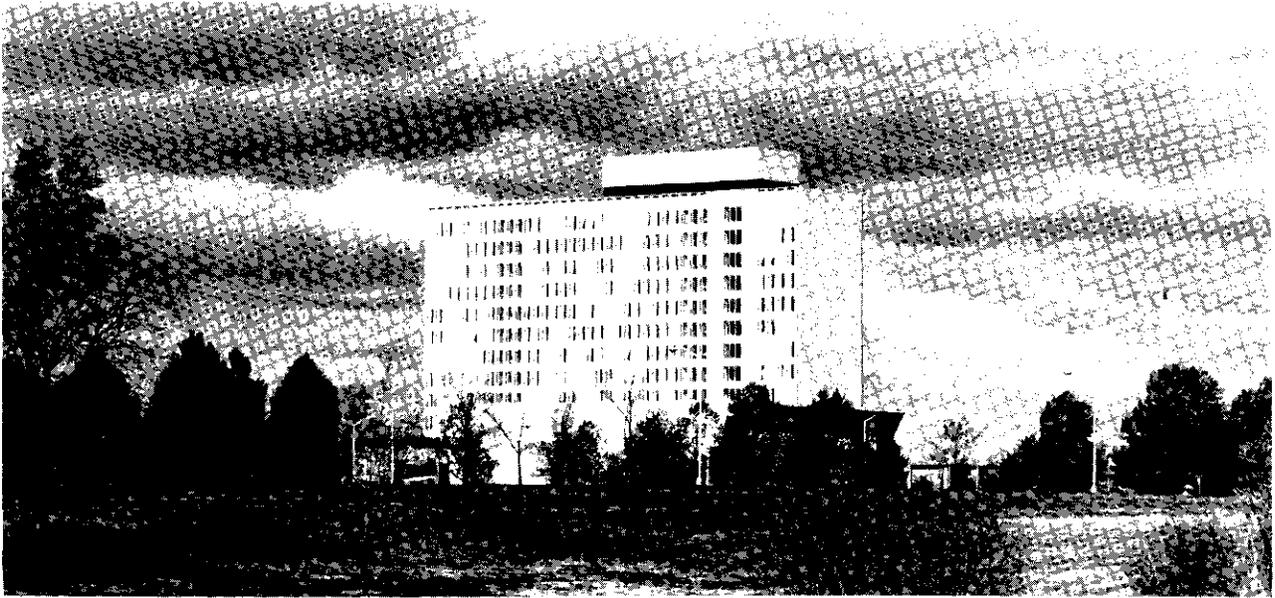
U.S. Department of Commerce, National Institute of Standards and Technology, Gaithersburg, MD.

represent a first-step in a probable multistage process to achieve consensus on quality assurance programs. In particular, because its members are forensic practitioners, TWGDAM proposals are likely to address the concerns and solutions of this stakeholder.

Finally, a significant part of quality assurance involves confidence in measurement standards. The U.S. Department of Commerce, National Institute of Standards and Technology (NIST) (formerly known as the National Bureau of Standards), established in 1901 (15 U.S.C. 271), is a neutral, nonregulatory agency that conducts research providing groundwork for the Nation's measurement systems. At present, NIST activities include evaluating size markers, reagent quality, and electrophoresis conditions, so that DNA fragment sizes can be more accurately determined (76). Additionally, NIJ, through its Law Enforcement Standards Laboratory at NIST, has initiated a program to examine standards for DNA processing (75). As the only Federal laboratory with the explicit goal of researching and providing reference standards, NIST proposals, as they become available, will likely play an important role in quality assurance of forensic uses of DNA identification.

State Authority To Regulate Crime Laboratories

States individually make and enforce most criminal laws. Inherent in this authority is the ability to marshal the evidence required for conviction. Thus, each State controls how DNA evidence is analyzed—including setting standards for performance-and presented in court (see ch. 4). Accordingly, States have the authority to regulate forensic DNA typing by both private laboratories and public crime laboratories. All State jurisdiction is limited by the provisions of the U.S. Constitution regarding the rights of individual citizens, but a State's inherent powers to protect victims and suspects are broad and provide many potential avenues for regulation, even if parallel areas of Federal authority have developed.

Regulation of medical facilities might provide guidance to the States. All licensing of medical personnel and facilities is based on State law, and almost all tort law is State-based, despite Federal activity in all these areas (92). State authorities most relevant to forensic uses of DNA tests are licensing of laboratory personnel and monitoring facilities. At least one State, Maryland, maintains regulatory authority over one private forensic labo-

ratory through the issuance of a clinical laboratory license in the area of molecular biology (31).

To date, no State has enacted general licensing requirements for crime laboratories. Several have requirements in restricted areas such as forensic alcohol analysis, but no State has licensing requirements for DNA typing in forensic casework. Nor does any State have forensic licensing requirements regulating DNA typing by private companies. One nonregulatory means to regulate forensic uses of DNA tests could be negligence litigation (box 3-F).

Crime Laboratory Personnel

Two general mechanisms to assure quality of laboratory personnel exist: certification and licensure. Certification is a voluntary process, while licensing is government mandated. Licensing of personnel is generally the domain of State governments. It is a formal mechanism intended to protect both the public and the profession, as well as provide guidance to the judicial system. For forensic DNA testing, a State could specify particular qualifications necessary for either public or private facilities. States could require their licensees to follow certain nationally recognized standards.

As well as requiring minimum standards, licensing provides States with the right to review an individual's practice, and to discipline the person with sanctions ranging from simple censure to license revocation for failure to follow proper standards in delivering services. On the other hand, without licensing, enforcement of honest practice might be stronger, not weaker, because general antifraud provisions might apply (36). In some instances, possession of a license can provide a practitioner with a misleading imprimatur of expertise (36).

At present, no State requires licensing of crime laboratory personnel or private practitioners performing DNA analysis on forensic samples. In contrast, a majority of States regulate the qualifications of clinical laboratory personnel (79). Although no State licenses criminalists or serologists, voluntary certification programs are in place for some forensic fields, but not in criminalistics. As early as 1979, proposals surfaced for certifying criminalists (26). At the time, a majority of professionals in criminalistics withheld support, and no national certification program yet exists. In 1988, certification efforts for criminalistics were revived, and an American Board of Criminalistics was incorporated in August 1989 (27). At the State level, CAC began a certification test in May 1989 (11).

To set and implement licensing or certification guidelines, however, the forensic science professional community must define the body of special-

---

Box 3-F—Negligence Litigation

Tort law is a nonregulatory means for social control of risks to health and safety. Permitting individuals to sue those who have wronged them through negligence serves as a mechanism for financial and emotional compensation, and for quality control. Theoretically, by making people responsible for their actions, individuals have an incentive to act responsibly. In practice, negligence litigation involving DNA typing would probably suffer from the same shortcoming found in medical malpractice litigation-a focus on past errors rather than future improvements. Nevertheless, as with medical malpractice, negligence litigation could have an effect on private entities that provide DNA typing for forensic purposes, particularly parentage testing.

To prove negligence, an individual would need to prove the commercial forensic practitioner breached a duty through neglect or lack of due care. Most likely, the plaintiff would have to show that the defendant did not adhere to "good accepted practice," or that the industry-wide definition of such practice is so flawed that failure to go beyond it constitutes negligence.

In the absence of a good-practice standard for forensic DNA testing, each party in a suit must look to other fields to judge the defendant's conduct. This problem complicates the presentation and evaluation of evidence. If one judge tries more than one case involving DNA testing, a de facto standard could develop for that courtroom, but would have little value as precedent outside that jurisdiction. Most courts also are not in a position to promulgate such standards outside the confines of a trial. Thus, while tort suits may remedy individual grievances, they do little to force development of a nationwide, good-practice standard. Tort suits do a better job of enforcing standards after they have been developed. Without standards, the importance of negligence litigation on quality assurance for forensic DNA typing would appear to be minimal at present, and its future impact uncertain.

SOURCE: Office of Technology Assessment 1990,

ized knowledge required, establish a system to identify qualified persons who meet minimum standards of practice, and agree to guidelines against which courts can measure scientific evidence and performance (12). In particular, minimum curricular requirements, training, and continuing education need delineation. At present, professional training is largely through on-the-job apprenticeships, seminars, and workshops, including training by the FBI's Forensic Science Research and Training Center (FSRTC) in an array of forensic specialties for about 300 State and local crime laboratory personnel annually (51). Formal academic coursework in forensic science at the undergraduate and graduate levels is available in only a few institutions, with internships not widely available.

Recently, however, progress in defining training and educational requirements has been made. For example, the TWGDAM quality assurance guidelines address education and training of forensic personnel (85). The Council of Forensic Science Educators has been formed with the goal of developing standards for forensic science education (12)$_0$ In the field of serology, that area where DNA typing expertise is likely to fall, the Southern Association of Forensic Scientists has drawn up a training outline (83). Serologists in California have proposed basic educational requirements and training needs for professionals in their State (22).

While some predict national consensus for training and education requirements will be achieved, implementation of such a program does not seem imminent. Clearly, one of the best mechanisms to guarantee quality is providing adequate resources for educating and training forensic laboratory personnel. At present, such resources are woefully inadequate, and most agree that increased State and Federal attention in this area is necessary.

In addition to adequate education and training of forensic laboratory personnel, quality control and quality assurance before evidence samples reach the laboratory door has been underemphasized to date. Providing education for field personnel on how best to gather and preserve evidence so that DNA identification can be performed will aid and enhance the efforts of the forensic examiner.
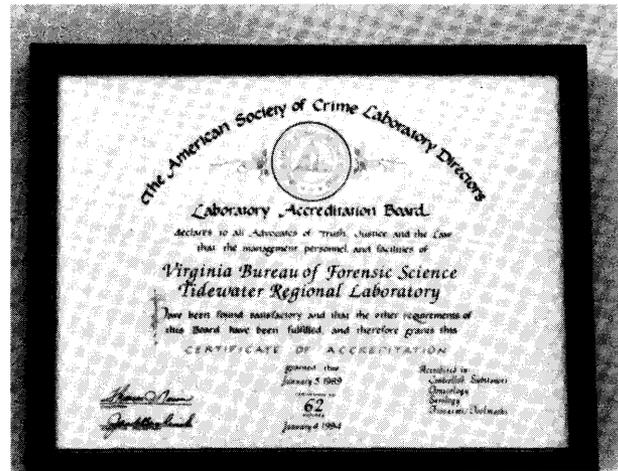

Photo credit: Robyn Nishimi

Certificate of accreditation for voluntary program offered to forensic laboratories by the American Society of Crime Laboratory Directors.

Crime Laboratory Facilities

As well as requiring licensing of personnel, States can mandate licensing of facilities or specific services within facilities. States could, for example, adopt laboratory licensing regulations aimed specifically at DNA typing programs, and not other forensic technologies, in private and public laboratories. Supplemental to or in place of licensing can be an accreditation process offered by a neutral, external body, such as the College of American Pathologists for medical genetics or the Joint Commission on Accreditation of Healthcare Organizations for various medical facilities. Accreditation can be strictly voluntary, and traditionally has been. But increasingly, as a condition of receipt of certain privileges or in exchange for funding, State or Federal officials require accreditation by a specific group or groups.

Licensing—As mentioned, no State currently regulates forensic service facilities in general, although States do have clear authority to oversee such services. In contrast, all 50 States and the District of Columbia require that public and private hospitals be licensed, although the scope of the laws varies considerably (101). In 1988, in an effort to ensure quality services, Congress passed sweeping legislation that subjects all clinical testing laboratories to a uniform standard of regulations (Public Law 100-578) (box 3-G).

Accreditation-Although not subject to mandatory oversight, one voluntary accreditation program

---

Box 3-G-Quality Assurance and Clinical Laboratories

In October 1988, Congress passed sweeping legislation that subjects clinical laboratories to a number of requirements, including qualifications for the laboratory director, standards for the supervision of lab testing, qualifications for technical personnel, management requirements, and an acceptable quality control program. Prior to enacting the Clinical Laboratory Improvement Amendments of 1988 (CLIA) (Public Law 100-578), Federal regulations covered the approximately 13,000 labs that either transported samples between States or performed tests billed to Medicaid and Medicare. Beginning in 1990, however, the Health Care Financing Administration (HCFA) of the U.S. Department of Health and Human Services (DHHS) will exercise sweeping regulatory authority over clinical laboratories. HCFA will set standards for staffing and maintaining all medical laboratories, including physician office testing. HCFA will also manage a comprehensive program to police the facilities and can impose sanctions.

CLIA is at once broad, encompassing the estimated 98,000 physician labs, and specific. For example, the Secretary of DHHS is to establish national standards for quality assurance in cytology services, including the maximum number of cytology slides that any individual may screen in a 24-hour period. The Secretary is also required to determine and implement recordkeeping, inspection, and proficiency testing programs, and to study and report to Congress on a range of issues gauging the impact of various quality assurance mechanisms.

CLIA expands DHKS's regulatory authority over clinical laboratories, and grants 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, the involvement of State or private nonprofit associations (which at present include the College of American Pathologists, the American Association of Bioanalysts, agencies in 3 States, the Joint Committee on Accreditation of Healthcare Organizations, and the American Osteopathic Association) to substitute for the Federal regulatory process.

Prior to CLIA's enactment, one issue of critical concern to Congress 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 on a quarterly basis, with uniform criteria for all examinations and procedures. The Secretary shall also establish a system for grading proficiency testing performance.

SOURCE: Office of Technology Assessment 1990.

---

for crime laboratories does exist. Established in 1981 by ASCLD, the program includes a self-evaluation, an inspection process, and required proficiency testing. As of December 1988, 58 laboratories representing 15 Federal, State, and local agencies—about 20 percent of the Nation's crime laboratories-have been accredited during the program's 7 years of operation. (An additional seven laboratories were accredited as of May 1989.) In comparison, a 5-year-old AABB program to evaluate parentage testing laboratories had accredited 48 labs representing about 39 percent of potential facilities as of December 1988 (1 1,12).

Many criticize current optional accreditation efforts as inadequate, and assert that mandatory accreditation by an external, neutral body is essential.[2]

Others strongly argue that current voluntary programs improve quality and are sufficient. Many feel that action should focus on increasing participation in voluntary programs, rather than mandating accreditation.

Nevertheless, while simultaneously contributing to quality assurance, mandatory accreditation of laboratories by independent, impartial organizations —in consultation with forensic practitioners and academic forensic scientists-could be effective in dispelling the notion of some that crime laboratories are not neutral bodies. Such programs could remove the perception of many defense attorneys and their clients that crime laboratories are biased-working principally toward conviction for prosecutors and police departments, and secondarily in defendants'

---

[2]Arguments have been made that mandatory accreditation (and licensing), in general, needs to be evaluated for anticompetitiveness considerations (36,37). It is unlikely, however, that the Antitrust Division of the U.S. Department of Justice (or private individuals or corporations) will find any occasion to attack concerted action in forensic services per se, since these are largely public facilities, or generally run as small business. Additionally, it is difficult to imagine Federal Trade Commission scrutiny for potential ''unfair practices'' related to information disclosure: Individuals involved in commercial services have routinely communicated their findings and procedures, in part to satisfy legal requirements of introducing DNA tests in court.

interest. On the other hand, accredi. tation, licensing, and certification are costly and time-cons uming endeavors that would likely place an additional personnel and financial burden on public facilities already overwhelmed with criminal casework and generally underfunded (74).

Proficiency Testing-Proficiency testing in crime laboratories is currently offered through a program administered by Collaborative Testing Services (CTS) in association with the Forensic Science Foundation (FSF) (the research arm of the AAFS). Participation is voluntary and anonymous, and more than half the crime laboratories subscribed to the physiological fluids program in 1985 (65), which now includes samples for DNA testing. In place since the mid-1970s, the CTS-FSF program has supporters and critics. Proponents point out that although not compulsory, the program provides a crime laboratory an opportunity to monitor the technical performance of its employees and compare results with other laboratories. Critics argue that results from the program merely underscore the need for tighter control, even mandatory regulation through legislation.

A 1978 study (73) found that an 'appalling' (68) number of participating laboratories reported erroneous results in testing blind samples, with as many as 94 out of 132 laboratories participating obtained ''unacceptable' blood typing results. Another critic reports that from 1978 through June 1988, the number of errors for bloodstain or physiological stain proficiency tests varied from 7 percent for one test to 77.7 percent for another, and that overall, an average of 25 percent of crime laboratories returning results made errors (38). In one human blood test to evaluate genetic markers, 15 of 69 participating laboratories (21.7 percent) made at least 1 error (38). None of these tests involved DNA typing.

In contrast, another review of the CTS-FSF serology testing program reported strikingly different findings for 7,827 tests performed during 1978 to mid-1986 (81): an error rate of 2.4 percent (189 errors). Further analysis revealed that 88 of these errors arose in laboratories that made three or more errors in the particular trial; which was acknowledged as an amount signifying serious problems. Subtracting the errors made by these laboratories reduced the rate to 1.3 percent. The study, which included all but one proficiency trial during that period, concluded that, on average, 79.1 percent of reporting laboratories were error-free; 4.2 percent of

DNA samples for RFLP analysis.

laboratories reported three or more errors (81). The author of this report, as well as many others, attribute the different findings to how ''error' was defined in each study. The analysis reporting the greater error rate counted ''inconclusive' results as errors, a practice with which the vast majority of scientists disagree. Similarly, "unacceptable" in the 1978 study is attributed to laboratories lagging behind in employing certain state-of-the-art tests, not to actual performance (82).

In addition to the CTS-FSF program, some crime laboratories subscribe to the voluntary proficiency program sponsored by the AABB parentage testing committee, which also includes DNA typing. Both the CTS-FSF and AABB voluntary programs, however, are less rigorous than the comparable program in the United Kingdom. Not only is DNA proficiency testing already in place in the United Kingdom, but the program includes blind tests slipped into the flow of actual casework (100). Interspersing blind tests with case samples clearly yields the most accurate measure of a laboratory's performance on a test.

With respect to blind trials of forensic DNA testing in the United States, CACLD organized trials using case-simulated samples in 1987 and 1988. The three major commercial facilities then performing forensic DNA analysis participated in each trial. In

the first trial, out of 50 samples, 2 firms each declared 1 false match (60) that could have resulted in the conviction of an innocent person. The errors apparently arose from sample handling problems (11). The third company declared no false matches (60). In the second trial, one company again reported an incorrect match (13).

To date, the FBI has not provided blind trials to commercial laboratories, nor does it have plans to do so in the future. However, the FBI's FSRTC will provide initial open proficiency tests to those State and local laboratories that participate in the FBI's training program. FSRTC also prepares proficiency samples to monitor the performance of the FBI DNA Analysis Unit. In addition, the FBI plans to administer a program that offers seed money to encourage commercial ventures to develop proficiency samples and testing (14,41). The FBI will not analyze DNA work performed by State and local laboratories, however, having a longstanding policy not to reexamine evidentiary materials previously examined by another crime laboratory.

Some observers, generally not forensic analysts, suggest that a mandatory, independent process of proficiency testing for public and private forensic laboratories engaged in DNA testing should be established. Others, usually from crime laboratories, support open and blind proficiency tests per se, but categorically oppose an independent, mandated program. What is clear is that proficiency testing has long been recognized to be a key component of quality assurance. Clinical laboratories, for example, are required by Federal law to meet acceptable performance criteria under a proficiency testing program on a quarterly basis (Public Law 100-578). One administrator of a clinical laboratory proficiency testing program argues that such a program is the best, economically feasible, external source for determining lab quality (53). In fact, the TWGDAM quality assurance guidelines-whose authors include crime laboratory personnel-include requirements for proficiency testing (85).

Although consensus exists that some sort of DNA proficiency testing program is desirable, disagreement arises over who shall administer it, who shall judge what constitutes acceptable performance, and the role of proficiency test results in court proceedings. Some argue that forensic practitioners alone are best able to make such decisions, while others maintain that involvement of molecular biologists

and human geneticists is necessary. And, while many feel the present CTS-FSF program is well-placed to administer DNA proficiency testing, others believe a new system is necessary.

Finally, disagreement exists about the general availability of proficiency testing results for trial examination. Some maintain that such testing is designed for internal quality assessment and feedback, and should not be applied punitively against all work performed by a particular examiner or laboratory. Others strongly disagree, arguing that proficiency testing data-especially in the absence of standards-is the only way to determine whether reliable findings were obtained for any case. And, as demonstrated by the studies of the CTS-FSF program, how ''inconclusive' results are classified is important when error rates are reported.

Federal Authority To Regulate Crime Laboratories

In theory, the Federal Government can only exercise those powers specifically granted to it in the Constitution. None of those powers relate directly to forensic practices in general, or to DNA typing by crime laboratories in specific, Yet the Federal Government is not powerless in this area. With respect to setting standards of practice for other types of laboratories-most notably clinical diagnostics and drug testing-Congress and the executive branch have separately and together imposed requirements designed to ensure consistently high quality. The following sections examine congressional authority to regulate forensic uses of DNA technologies, and analyze present Federal regulation of clinical and drug testing laboratories.

Taxing and Spending Authority

Article I, Section 8 of the Constitution states that Congress may spend money "for the common Defense and general Welfare of the United States.' It is through the use of conditional appropriations—i.e., attaching strings to grants of money—that Congress derives its power to regulate through spending (87). The Supreme Court has upheld congressional authority to impose conditions on the use of funds directly distributed to States by the Federal Government. States, to the extent they wish to avail themselves of such monies, must comply with those conditions (40).

Direct finding of crime laboratories would give the Federal Government the authority to determine a wide variety of requirements for the delivery of high-quality service. For example, the government could attach certain conditions to funds earmarked for crime laboratories for DNA analysis, or attach conditions for general quality assurance to appropriations such as recent finding for drug analysis. Several models of this type exist, for example reimbursement criteria under Medicare for an array of circumstances. One section of DHHS's 1987 ''Medicare Program Criteria for Medicare Coverage of Heart Transplants'' (52 FR 10935) requires that eligibility for Medicare reimbursement for heart transplants depends on a facility's demonstrated experience and survival rate. For DNA analysis of forensic samples, tying funding to actual performance on proficiency tests could have a powerful influence on the quality of services.

In addition to stipulations for direct funding to crime laboratories, the Federal Government also has the power to condition the receipt of Federal monies by a State (instead of by a single laboratory) on the State's taking a specific regulatory action. Examples of these types of stipulations include recent policies that tie State highway improvement grants to maximum speed limits or the minimum drinking age. Thus, the Federal Government could link funds provided to State commissions or agencies to the adoption of certain quality assurance procedures or regulations that effect both State and local crime laboratories. The power to apply such conditions is likely true even when the connection between the State program and DNA analysis is quite attenuated (92). Congress could mandate, for example, certain quality monitoring protocols for States accepting funds for prison construction or other non-DNA-related criminal justice uses.

Authority Over Interstate Commerce

The second major area over which Congress has wide authority to regulate forensic uses of DNA techniques is through the commerce clause of Article I, Section 8, which provides the authority "To regulate Commerce . . . among the several States. . . ." Congressional authority to pass laws relating in any reasonable manner to interstate commerce is such a broad power that judicial review affirming the right is largely a formality (87). Most judicial review focuses instead on the intent of
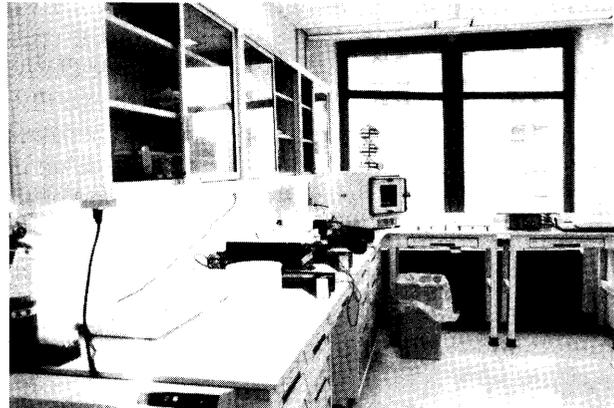

Photo credit: Federal Bureau of Investigation

A laboratory of the FBI DNA Analysis Unit, Washington, DC.

Congress to interpret the reach and scope of the legislation.

Regulation of Products—The commerce power provides Congress the specific authority to regulate articles of commerce that pass between two or more States. The Federal Government clearly could use the commerce authority to require licensing of forensic facilities that solicit or provide forensic DNA typing services to out-of-State clients, as it has for medical laboratories engaged in interstate commerce (42 U.S.C. 263). At the moment, only a handful of facilities would be subject to regulation by Congress under this authority. Extremely broad, this authority also could be used to establish a mechanism to regulate products used in DNA typing for forensic applications.

Monitoring the Use of DNA Technologies-Con-gressional and executive interest and oversight of DNA technologies is not unprecedented. Recombinant DNA technologies have been subject to Federal scrutiny since the early 1970s. The NIH Recombinant DNA Advisory Committee, its Working Group on Human Gene Therapy, and more recently the Biotechnology Science Coordinating Committee have all been established to monitor or regulate various uses arising from the new genetic technologies. Thus, the Federal Government could establish a committee or commission to monitor or regulate forensic applications of DNA tests.

As mentioned, the FBI is the principal investigative arm of the Department of Justice, with no direct authority to regulate individual crime laboratories. The FBI is under the authority of the Attorney General and acts under the Attorney General's

general statutory authority. Some suggest that the FBI should use its authority to issue official standards for DNA analysis of forensic casework. On the other hand, others oppose an official role for the FBI, believing its laboratories and research facilities should be subject to an independent commission or authority established to provide guidance and oversight of all private and public entities that do forensic DNA identification.

SETTING STANDARDS

Setting standards for forensic applications of DNA testing is the most controversial and unsettled issue, yet standards are the cornerstone of quality assurance. Technical and operational standards for DNA typing in forensic casework are needed, and needed soon. The FBI (23), industry, molecular biologists, biochemists, population geneticists, and forensic scientists all agree that standards are desirable. Agreement on what standards are appropriate, who should decide, how implementation of standards is best achieved, and whether they should be mandatory has not yet been reached.

Technical standards are needed to specify proper gel controls, electrophoresis conditions, the extent that computer-assisted matching should be permitted, population data to compute probabilities of matches, and many other parameters. It appears that setting technical standards-allowing flexibility for the vagaries of forensic casework and emerging scientific developments—is within reach. A majority agree that such efforts should include balanced input from all relevant scientific disciplines.

In contrast, operational standards, such as recordkeeping and proficiency testing, are likely to be more controversial, for attempts to regulate any sector have historically been met with resistance. Nevertheless, such standards are necessary if full quality assurance is to be achieved. Forensic scientists—practitioners and educators—argue that they are most knowledgeable about how best to set operational standards that achieve quality and meet the needs of crime laboratories without being unduly burdensome. Some in the forensic community are prepared to meet this challenge.

Yet while many forensic scientists acknowledge the need for standards in DNA typing, they resent the imposition of such standards by another scientific community unfamiliar with the vagaries of forensic

casework—i.e., molecular geneticists. Some molecular geneticists, on the other hand, believe their experience over the past two decades with recombinant DNA technologies places them in a position to define how DNA tests should be applied to forensic casework. In fact, both communities can and should contribute to standard setting. Forensic practitioners are most familiar with the practical problems and unique situations that can arise in the course of an investigation, which are situations not encountered by molecular geneticists in laboratories. Likewise, research molecular biologists have knowledge about DNA tests on which forensic examiners can draw. Forensic academicians, who often are involved in early stages of evaluating basic research tools before a technology transfers into crime laboratories, are perhaps well placed to bridge the gap between crime laboratory personnel and genetics researchers.

Many have expressed the opinion that an independent commission is the best mechanism to handle both technical and operational standards. Others call for a lead role for the FBI, which some reject as a conflict of interest. Still others seek Federal or State legislative solutions. In any case, crime laboratories and forensic research have generally been underfunded, and new requirements will only increase financial difficulties. In addition, various Federal grant assistance mechanisms have been severely reduced or eliminated in the past decade. Thus, while development of standards for recordkeeping and proficiency testing should be encouraged to move forward, their costs should be recognized. Nevertheless, formalizing quality assurance mechanisms, including standards, should proceed without delay. Such efforts will assist crime laboratories making decisions about using DNA profiling onsite (see ch. 6), private laboratories, the Federal Government, and the courts.

Some commentators contend that ultimately the judicial process can provide a stringent test of scientific evidence and the quality of work in a particular case. Others strongly disagree, maintaining that it seldom does. The vast majority of scientific evidence introduced in criminal cases goes unchallenged by the opposition, usually the defense (72), which generally lacks sufficient resources to dispute such evidence. Many argue that reliance on judicial review for quality assurance has been an unfulfilled promise.

STANDARDIZATION

Setting standards to ensure quality is distinct from developing a uniform, national system—i.e., standardization-of DNA typing within the forensic science community. Some contend that standardizing the process is institutional insurance-an additional layer of quality assurance. Others maintain that while this step is a necessary component of usable investigative DNA databanks, its role in ensuring quality is minimal. Still others believe standardization could stifle rapid integration of future innovations.

No amount of standardization, especially of procedures, however, can be substituted for appropriate scientific analysis during the progress of an individual case. By nature, nothing is routine in forensic casework. The discretion of a qualified investigator to evaluate a situation and implement appropriate measures-within standards that need to be established—is a fundamental component of quality assurance.

Is standardization desirable, or even possible? Chapter 5 discusses standardization in greater detail. Nevertheless, achieving some modicum of standardization (e.g., for restriction enzyme-probe combinations used and data interpretation), appears necessary for an effective, national database.

FINDINGS AND SUMMARY

Prior to the DNA era, the genetic analysis of forensic samples was based strictly on a paradigm of exclusion. Each genetic marker provided limited information that eliminated a fraction of the general population as the originator of a sample (e.g., excluding 30 percent, 67 percent, or 1.2 percent of persons as potential contributors), depending on the marker detected and the test result. Combining results for several different markers reduced the pool of persons who could have contributed to the biological sample. The objective, of course, was to exclude as many individuals as possible—i.e., to reduce the number of potential sources to the smallest possible value.

DNA tests operate no differently. Yet their potential power to discriminate has altered the perception that genetics can be used only for positive exclusion, not positive identification. Among all humans except identical twins, no two share the same DNA sequence. Using single-locus probe analysis, foren-

sic examiners can accurately detect some of these differences to the extent that examination of several DNA markers can lead to a report that is, in effect, perceived to be a statistically positive association between an individual and a piece of biological evidence. This change in perception, however, does not alter the fact that forensic uses of DNA tests—like traditional genetic marker analysis—are valid.

Are DNA tests reliable? Under routine conditions of use, do they perform reproducibly within a laboratory, across many laboratories, and in the hands of different practitioners? OTA finds that, properly performed, DNA *tests* per se are reliable. Serious questions are raised, however, about how best to ensure that any particular *test result* is reliable. These questions focus on data interpretation, how to minimize realistic human error, and the appropriate level of monitoring to ensure quality. Such questions, which stem from actual court cases, underscore the need to develop both technical and operational standards now.

Standards alone should not be construed as making evidence analysis absolutely reliable. Standards would, however, provide a benchmark against which all interested parties can judge a particular analysis. Undoubtedly some queries will still arise on a case-by-case basis. At such times, specific details can and should be evaluated in court. But, with time and implementation of standards, such questions should decrease.

What standards are needed for private and public facilities doing forensic DNA testing, and who decides? At present, only a vague consensus exists for the first question, and none for the second. Nor does consensus exist on how standards should be administered. Professional societies are making efforts toward regularization of forensic uses of DNA tests, as is the Federal Government, especially the FBI and NIST. Some contend that such efforts are insufficient because compliance is, or will be, entirely voluntary. These voices argue that quality assurance lapses in both private and public facilities will persist with voluntary guidelines. Balanced against this is the belief of many that voluntary standards are sufficient. Implicit in this point of view is the conviction that consensus and implementation of technical guidelines and standards is imminent.

Yet while consensus has been achieved for some issues, other areas remain contentious. One area

THE RIGHT TO SEARCH FOR TRUTH

IMPLIES ALSO A DUTY.

ONE MUST NOT CONCEAL

ANY PART

OF WHAT ONE HAS RECOGNIZED

TO BE TRUE

Photo credit: Gary Ellis

needing particular attention is the population genetics of RFLP analysis. Controversy centers on the size of the databases used and the precise approach that should be used to calculate population frequencies. Some argue that the magnitude of the number is not the issue, just that the analyst assigns it with confidence that genetics principles have been adhered to. Others argue that because of the pivotal role population frequencies can play in reporting results of forensic DNA tests, agreement is necessary. Nevertheless, using certain conservative assumptions probably allows an analyst to assert a likelihood that matched samples came from the same person. General agreement does exist that any potential bias that could result from calculating population frequencies favor a defendant.

One area of population genetics of forensic DNA typing might have an impact on both data analysis and privacy considerations (see ch. 5). The dynamic and diverse nature of the U.S. population calls for special attention to collection and classification of genetic differences based on ethnic and racial subgroups. For example, genetic data classified as ''Hispanic' on the basis of self-identification or surname could skew reported population frequencies, since DNA profiles for Mexican-Americans v. other Hispanic individuals, including those of Puerto Rican, Cuban, or El Salvadoran descent, could differ. Increased population data for RFLP analysis would benefit both questions of population substructuring, as well as calculating population frequencies in general.

Quality assurance mechanisms in forensic DNA profiling encompass a range of options, including certification, licensure, accreditation, and proficiency testing. Methods to implement these options exist,

such as efforts by professional societies, and formal, nonregulatory methods such as consensus building among all interested stakeholders. States have authority to regulate DNA typing for forensic purposes by both private and public facilities, but to date no State has enacted general licensing requirements for private laboratories, crime laboratories, or personnel. Likewise, the Federal Government has the authority to direct that solutions be found for quality assurance of forensic services.

Federal efforts toward quality assurance for laboratories doing forensic DNA profiling need not develop in a vacuum. Congress and the executive branch have a longstanding interest in quality assurance for other laboratory services, most notably clinical diagnostics and employee drug testing. As such, solutions for these sectors could prove useful in evaluating quality assurance for laboratories performing DNA analysis in forensic casework.

Setting standards for quality assurance should proceed without delay. Such efforts will assist private laboratories, the Federal Government, the courts, and public crime laboratories making decisions about implementing DNA profiling onsite. Such endeavors must also acknowledge that introducing and maintaining formal quality assurance mechanisms can be costly and time-consuming, and will place additional personnel and financial burdens on public facilities already overwhelmed with casework and traditionally underfunded.

Finally, many questions surrounding forensic uses of DNA technologies are really questions of public policy, as much as technical and operational issues of forensic practice. As such, the influence and input of attorneys, businesses, government officials, and others in settling quality assurance issues is appropriate and important.

CHAPTER 3 REFERENCES

1. Acton, R. T., "Comparison of VNTR Allele Frequencies in White and Black Populations," proceedings, The International Symposium on Human Identification 1989: Data Acquisition and Statistical Analysis for DNA Typing Laboratories, Madison, WI, 1990.
2. Adams, D.E., Baechtel, F. S., and Budowle, B., "DNA Analysis of Body Fluid Stains Subjected to Environmental, Chemical and Biological Insults," abstract, American Academy of Forensic Sciences, 41st Annual Meeting, Las Vegas, NV, February 1989.
3. American Association of Blood Banks, AABB Standards Committee, "P.7000 DNA Polymorphism Testing," *Standards for Parentage Testing Laboratories, 1989.*
4. American Society for Histocompatibility and Immunogenetics, *ASHI Quarterly 14(1), 1990.*
5. American Society for Quality Control, "Quality Systems Terminology," *American National Standard ANSI/ASQC A3-1978, 1978.*
6. American Society of Crime Laboratory Directors—Laboratory Accreditation Board, *Accreditation Manual* (Lansing, MI: T.J. Nasser, Michigan State Police, 1985).
7. American Society of Human Genetics, Ad Hoc Committee on Individual Identification by DNA Analysis, "Individual Identification by DNA Analysis: Points to Consider," *American Journal of Human Genetics 46:631-634, 1990.*
8. Andreasen, P. B., "Consensus Conferences in Different Countries: Aims and Perspectives,' *International Journal of Technology Assessment in Health Care 4:305-308, 1988.*
9. Baird, M., Balazs, I., Giusti, A., et al., "Allele Frequency Distribution of Two Highly Polymorphic DNA Sequences in Three Ethnic Groups and Its Application to the Determination of Paternity, *American Journal of Human Genetics 39:489-501, 1986.*
10. Balazs, I., Baird, M., Clyne, M., et al., "Human Population Genetic Studies of Five Hypervariable DNA Loci,' *American Journal of Human Genetics 44:182-190, 1989.*
11. Bashinski, J. S., California DNA Lab, California Department of Justice, Berkeley, CA, personal communication, August 1989.
12. Bashinski, J. S., ''Laboratory Standards: Accreditation, Training and Certification of Staff in the Forensic Context," *DNA Technology and Forensic Science,* J. Ballantine, G. Sensabaugh, J. Witkowski (eds.) (Cold Spring Harbor, NY: Cold Spring Harbor Laboratory Press, 1989).
13. Bashinski, J.S. (chair), "California Association of Crime Laboratory Directors: DNA Committee Report of CACLD Blind Trial #2," California DNA Lab, California Department of Justice, Berkeley, CA, March 1990.
14. Biotechnology Newswatch, "FBI To Offer Seed Money for Probing Forensic DNA Proficiency," *Biotechnology Newswatch 9(18):5, 1989.*
15. Blake, E. T., ''DNA Amplification and Typing From Aged Biological Evidence," abstract, An International Symposium on the Forensic Aspects of DNA Analysis: U.S. Department of Justice, Federal Bureau of Investigation, Quantico, VA, June 1989.
16. Brenner, C., and Morns, J., "Paternity Index Calculations in Single Locus Hypervariable DNA Probes:

Validation and Other Studies," proceedings, The International Symposium on Human Identification 1989: Data Acquisition and Statistical Analysis for DNA Typing Laboratories, Madison, WI, 1990.

17. Budowle, B., ''Data for Forensic Matching Criteria for VNTR Profiles,' proceedings, The International Symposium on Human Identification 1989: Data Acquisition and Statistical Analysis for DNA Typing Laboratories, Madison, WI, 1990.

18. Budowle, B., Federal Bureau of Investigation, Quantico, VA, personal communication, April 1989.

19. Budowle, B., Shutler, G., Waye, J., et al., ''Selection of Restriction Endonuclease and Interprobe Comparison for RFLP Technology,' abstract, American Academy of Forensic Sciences, 41 st Annual Meeting, Las Vegas, NV, February 1989.

20. Buoncristiani, M., von Beroldingen, C., and Sensabaugh, G. F., "Effects of *W* Damage on DNA Amplification by the Polymerase Chain Reaction, ' abstract, An International Symposium on the Forensic Aspects of DNA Analysis: U.S. Department of Justice, Federal Bureau of Investigation, Quantico, VA, June 1989.

21. California Association of Crime Laboratory Directors, "Position on DNA Typing of Forensic Samples" (Oakland, CA: J. Bashinski, Oakland Crime Laboratory, November 1987).

22. California Association of Crirninalists, Bureau of Forensic Science and Unysis Corp., *Report of a Symposium on the Practice of Forensic Serology, 1987* (Sacramento, CA: F. Springer, Bureau of Forensic Services, 1987).

23. Castonguay, R. T., Federal Bureau of Investigation, Washington, DC, personal communication, April 1989.

24. Cohen, J. E., "DNA Fingerprinting for Forensic Identification: Potential Effects on Data Interpretation of Subpopulation Heterogeneity and Band Number Variability, ' *American Journal of Human Genetics 46:358-368, 1990.*

25. Comey, C. T., Federal Bureau of Investigation, Quantico, VA, personal communication, April 1989.

26. Criminalistics Certification Study Committee, *Certification in Criminalistics: A Find Report to the Profession (Los* Angeles, CA: W.J. Cadman, California State University, Los Angeles, 1979).

27. Criminalistics Certification Study Committee, **Certification of Criminalists: A Report to the Criminalistics Profession (Los** Angeles, CA: W.J. Cadman, California State University, Los Angeles, 1988).

28. Erlich, H. A., Cetus Corp., Emeryville, CA, personal communications, May, August 1989.

29. Evett, I. W., and Werrett, D. J., "Bayesian Analysis of Single Locus DNA Profiles, ' proceedings, The International Symposium on Human Identification 1989: Data Acquisition and Statistical Analysis for DNA Typing Laboratories, Madison, WI, 1990.

30. Fienberg, S.E. (cd.), Panel on Statistical Assessments as Evidence in the Courts, National Research Council, *The Evolving Role of Statistical Assessments as Evidence in the Courts (New* York, NY: Springer-Verlag, 1989).

31. Garner, D. D., Cellmark Diagnostics, Germantown, MD, personal communication, July 1989.

32. Garner, D. D., Green, D. J., Herrin, G. L., et al., "Validation Studies Utilizing the Jeffreys DNA Probes,' abstract, American Academy of Forensic Sciences, 40th Annual Meeting, Philadelphia, PA, February 1988.

33. Gill, P., Jeffreys, A.J., and Werrett, D.J., "Forensic Application of DNA 'Fingerprints','' *Nature* 318:577-579, 1985.

34. Gill, P., Lygo, J.E., Fowler, S.J., et al., "An Evaluation of DNA Fingerprinting for Forensic Purposes,' *Electrophoresis 8:38-44, 1986.*

35. Giusti, A., Baird, M., Shaler, R., et al., 'Application of Deoxyribonucleic Acid (DNA) Polymorphisms to the Analysis of DNA Recovered From Sperm, '' *Journal of Forensic Sciences 31;409-417, 1986.*

36. Givens, R. A., Botein, Hays & Sklar, New York, NY, personal communication, July 1989.

37. Goldenberg, M., "Standards, Public Welfare Defenses, and the Antitrust Laws,' *Business Lawyer 42(3):629-674, 1987.*

38. Grunbaum, B. W., Moraga, CA, personal communication, June 1989.

39. Grunbaum, B. W., "Physiological State Evidence: Guidelines to Assure Quality Analysis," *The California Defender 1:20-26, 1984.*

40. *Harrisburg Hospital v. Thornburgh, 616* F. Supp. 699 (D.C. Pa. 1985).

41. Hicks, J. W., Federal Bureau of Investigation, Washington, DC, personal communication, February 1990.

42. Higuchi, R., and Blake, E, T., "Applications of the Polymerase Chain Reaction in Forensic Science," *DNA Technology and Forensic Science,* J. Ballantine, G. Sensabaugh, J. Witkowski (eds.) (Cold Spring Harbor, NY: Cold Spring Harbor Laboratory Press, 1989).

43. Higuchi, R., von Beroldingen, C. H., Sensabaugh, G. F., et al., "DNA Typing From Single Hairs," *Nature 332:543-546, 1988.*

44. Institute of Medicine, Council on Health Care Technology, Committee to Improve the National Institutes of Health Consensus Development Program, *Consensus Development at the NIH: Improving the Program* (Washington, DC: National Academy Press, 1990).

45. International Society for Forensic Haemogenetics, "DNA Recommendation," *Vox Sang* 57:276-277, 1989.

46. Jeffreys, A. J., University of Leicester, Leicester, England, remarks at An International Symposium on the Forensic Aspects of DNA Analysis: U.S. Department of Justice, Federal Bureau of Investigation, Quantico, VA, June 1989.

47. Jeffreys, A. J., Wilson, V., Neumann, R., et al., "Amplification of Human Minisatellites by the Polymerase Chain Reaction: Towards DNA Fingerprinting of Single Cells," *Nucleic Acids Research 16:10953-10971, 1988.*

48. Jeffreys, A. J., Wilson, V., and Thein, S.L., "Hypervariable Minisatellite Regions in Human DNA, " *Nature 314:67-73, 1985.*

49. Jeffreys, A. J., Wilson, V., and Thein, S. L., "Individual Specific 'Fingerprints' of Human DNA, " *Nature 316:76-79, 1985.*

50. Kanter, E., Baird, M., Shaler, R., et al., 'Analysis of Restriction Length Polymorphisms in Deoxyribonucleic Acid (DNA) Recovered From Dried Bloodstains," *Journal of Forensic Sciences 31:403408, 1986.*

51. Kearney, J. J., Federal Bureau of Investigation, Quantico, VA, personal communication, August 1989.

52. Kearney, J. J., Federal Bureau of Investigation, Quantico, VA, presentation before the U.S. Congress, Office of Technology Assessment, Advisory Panel on *Forensic Uses of DNA Tests,* April 1989.

53. Kiely, T., "Making Medical Labs Measure Up," *Technology Review,* pp. 14-15, July 1989.

54. Kilshaw, D., "Quality Assurance. 1. Philosophy and Basic Principles, ' *Medical Laboratory Sciences 43:377-381, 1986.*

55. Kilshaw, D., "Quality Assurance. 2. Internal Quality Control," *Medical Laboratory Sciences 44:73-83, 1987.*

56. Kilshaw, D., "Quality Assurance. 3. External Quality Assessment" *Medical Laboratory Sciences 44: 178-186, 1987.*

57. *Kirby, L. T., DNA Fingerprinting: An Introduction (New* York NY: Stockton Press, 1990).

58. Kosecoff, J., Kanouse, D.E., Rogers, W.H., et al., "Effects of the National Institutes of Health Consensus Development Program on Physician Practice,' *Journal of the American Medical Association 258:2708-2713, 1987.*

59. Kuo, M., Orange County Sheriff-Coroner's Crime Laboratory, Santa Ana, CA, personal communication, July 1989.

60. Kuo, M. (chair), "California Association of Crime Laboratory Directors: DNA Committee Report to the Board of Directors, Report #6,' Orange County Sheriff-Coroner's Crime Laboratory, Santa Ana, CA, 1988.

61. Kwok S., and Higuchi, R., "Avoiding False Positives With PCR," *Nature 339:237-238, 1989.*

62. Lander, E. S., "DNA Fingerprinting On Trial," *Nature 339:501-505, 1989.*

63. Lander, E. S., "Reliability and Validity of DNA Typing for Forensics," contract paper prepared for the Office of Technology Assessment, U.S. Congress, October 1989.

64. Li, H., Gyllensten, U. B., Cui, X., et al., ' 'Amplification and Analysis of DNA Sequences in Single Human Sperm and Diploid Cells,' *Nature 355:414-417, 1988.*

65. Lucas, D., Leete, C., and Field, K., "An American Proficiency Testing Program," *Forensic Sciences International 27:71, 1985.*

66. McNally, L., Shaler, R. C., Giusti, A., et al., "Evaluation of Deoxyribonucleic Acid (DNA) Isolated From Human Bloodstains Exposed to Ultraviolet Light, Heat, Humidity, and Soil Contamination," *Journal of Forensic Sciences 34(5):1059-1069, 1989.*

67. McNally, L., Shaler, R. C., Giusti, A., et al., "The Effects of Environment and Substrata on Deoxyribonucleic Acid (DNA): The Use of Casework Samples From New York City," *Journal of Forensic Sciences 34(5):1070-1077.*

68. Moenssens, A.A., Inbau, F.E., and Starrs, J.E., *Scientific Evidence in Criminal Cases,* 3rd ed. (Mineola, NY: The Foundation Press, Inc., 1986).

69. Mueller, L. D., University of California, Irvine, Irvine, CA, personal communication, August 1989.

70. Neufeld, P. J., and Colman, N., "When Science Takes the Witness Stand," *Scientific American 262:46-53, 1990.*

71. Perry, S., "The NIH Consensus Development Program: A Decade Later," New *England Journal of Medicine 317:485-488, 1987.*

72. Peterson, J.L., Department of Criminal Justice, The University of Illinois at Chicago, Chicago, IL, personal communication, August 1989.

73. Peterson, J. L., Field, K., Fabricant, E., et al., *Crime Laboratory Proficiency Testing Research Program* (Washington, DC: U.S. Government Printing Office, 1978).

74. Peterson, J. L., Mihajlovic, S., and Bedrosian, J. L., ''The Capabilities, Uses and Effects of the Nation's Criminalistics Laboratories," *Journal of Forensic Sciences 30(1):10-23, 1985.*

75. Rau, R. M., National Institute of Justice, Washington, DC, personal communication, July 1989.

76. Reeder, D. J., National Institute of Standards and Technology, Gaithersburg, MD, personal communication, April 1989.

77. Reynolds, R., von Beroldingen, C., and Sensabaugh, G. F., "Effects of DNA Degradation on Amplification by the Polymerase Chain Reaction,' abstract, An International Symposium on the Forensic Aspects of DNA Analysis: U.S. Department of

Justice, Federal Bureau of Investigation, Quantico, VA, June 1989.

78. Saiki, R.K., Gelfand, D.H., Stoffel, S., et al., "Primer-directed Enzymatic Amplification of DNA With a Thermostable DNA Polymerase,' *Science 239:487-494, 1988.*

79. Schaeffer, M. (cd.), *Federal Legislation and the Clinical Laboratory* (Boston, MA: G.K. Hall Medical Publishers, 1981).

80. Sensabaugh, G.F., "Consequences of Nucleotide Misincorporation During the Polymerase Chain Reaction, abstract, An International Symposium on the Forensic Aspects of DNA Analysis: U.S. Department of Justice, Federal Bureau of Investigation, Quantico, VA, June 1989.

81. Sensabaugh, G. F., "Genetic Typing of Biological Evidence: Comments for the Cooper Amicus Brief," *California Association of Criminalists Newsletter, pp. 11-19,* July 1987.

82. Sensabaugh, G. F., University of California, Berkeley, CA, personal communication, August 1989.

83. Southern Association of Forensic Scientists, *Forensic Serology Training Program,* E. Quarles (cd.) (Decatur, GA: Bureau of Forensic Science, 1988).

84. Southern, E., "Detection of Specific Sequences Among DNA Fragments Separated by Gel Electrophoresis," *Journal of Molecular Biology 98:503-517, 1975.*

85. Technical Working Group on DNA Analysis Methods (TWGDAM), ''Guidelines for a Quality Assurance Program for DNA Restriction Fragment Length Polymorphism Analysis," *Crime Laboratory Digest 16(2):40-59,* April-July 1989.

86. Thompson, W. C., and Ford, S., "DNA Typing Acceptance and Weight of the New Genetic Identification Tests," *Virginia Law Review 75:45-108, 1989.*

87. Tribe, L., *American Constitutional Law* (Mineola, NY: Foundation Press, 1978).

88. U.S. Congress, General Accounting Office, *Employee Drug Testing: Regulation of Drug Testing Laboratories, GAO/GGD-88-127FS,* Washington, DC, 1988.

89. U.S. Congress, House of Representatives, Committee on Energy and Commerce, *Clinical Laboratory Improvement Amendments of 1988,* Rpt. 100-899 to accompany H.R. 5150 (Washington, DC: U.S. Government Printing Office, 1988),

90. U.S. Congress, Office of Technology Assessment, *Development of Medical Technology: Opportunities for Assessment, OTA-H-34* (Springfield, VA: National Technical Information Service, 1976).

91. U.S. Congress, Office of Technology Assessment, *Genetic Testing in the Workplace* (Washington, DC: U.S. Government Printing Office, forthcoming, 1990).

92. U.S. Congress, Office of Technology Assessment, *Infertility: Medical and Social Choices,* OTA-BA-358 (Washington, DC: U.S. Government Printing Office, 1988).

93. U.S. Congress, Office of Technology Assessment, *Mapping Our Genes-Genome Projects: How Big, How Fast?, OTA-BA-373* (Washington, DC: U.S. Government Printing Office, 1988).

94. U.S. Congress, Office of Technology Assessment, New *Developments in Biotechnology: Public Perceptions of Biotechnology, OTA-BP-BA-45* (Washington, DC: U.S. Government Printing Office, 1987).

95. U.S. Congress, Office of Technology Assessment, *Technologies for Detecting Heritable Mutations in Human Beings, OTA-H-298* (Washington, DC: U.S. Government Printing Office, 1986).

96. U.S. Congress, Senate, Committee on Governmental Affairs, Subcommittee on Oversight of Government Management, *Health Care Financing Administration's Management of Medical Laboratories,* hearings Mar. 23-24, 1988, S. Hrg. 100-765 (Washington, DC: U.S. Government Printing Office, 1988).

97. U.S. Department of Health, Education, and Welfare, Ethics Advisory Board, *Report and Conclusions: HEW Support of Research Involving Human In Vitro Fertilization and Embryo Transfer* (Washington, DC: U.S. Government Printing Office, 1979).

98. von Beroldingen, C. H., Blake, E. T., Higuchi, R., et al., "Applications of PCR to the Analysis of Biological Evidence," *PCR Technology: Principles and Applications for DNA Amplification,* H.A. Erlich (cd.) (New York NY: Stockton Press, 1989).

99. Walsh, S., Blake, E., and Higuchi, R., ''PCR Inhibition and Bloodstains, " abstract, An International Symposium on the Forensic Aspects of DNA Analysis: U.S. Department of Justice, Federal Bureau of Investigation, Quantico, VA, June 1989.

100. Werrett, D. J., remarks at Banbury Conference on "DNA Technology and Forensic Science," Cold Spring Harbor, NY, November 1988.

101. Wing, K. R., *The Law and the Public's Health,* 2d ed. (Ann Arbor, MI: Health Administration Press, 1985).