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The Polymerase Chain Reaction (PCR): The Second Generation of DNA Analysis Methods Takes the Stand

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INTRODUCTION

The goal of this Comment is to discuss and describe for the non-scientist attorney: (1) the technologies involved in the three major methods of DNA testing; (2) potential uses for the polymerase chain reaction (PCR), and issues surrounding its use in the forensic setting, including the cases to date; and (3) proposed regulations and legislative action. Also, this comment refutes some of the criticisms levelled against DNA testing in general and attempts to correct some of the errors in previously published legal papers regarding DNA technology and cases. Prosecutors, commercial laboratories, and the media are not the only ones who are pushing DNA profiling evidence into court. It is hoped that the "stunned defense bar"[1] will realize the tremendous exculpatory potential of DNA analysis.

While the technique utilizing restriction fragment length polymorphisms (RFLP) has been accepted by many more appellate level and higher courts,[2] PCR has also been accepted by some ap-

1. Janet C. Hoeffel, Note, *The Dark Side of DNA Profiling: Unreliable Scientific Evidence Meets the Criminal Defendant*, 42 STAN. L. REV. 465 (1990); Rorie Sherman, *DNA Unraveling*, 15 NAT'L L.J. 1 (1993).

2. United States v. Jakobetz, 955 F.2d 786 (2d Cir. 1992); People v. Axell, 81 Cal. Rptr. 2d 411 (Cal. Ct. App. 1991); State v. Pennington, 393 S.E.2d 847 (N.C. 1990); Kelly v. State, 792 S.W.2d 579 (Tex. Ct. App. 1990); Glover v. State, 787 S.W.2d 544 (Tex. Ct. App. 1990); State v. Woodall, 385 S.E.2d 253 (W. Va. 1989); Caldwell v. State, 393 S.E.2d 436 (Ga. 1990); People v. Wesley, 533 N.Y.S.2d 643 (N.Y. Co.Ct. 1988); Martinez v. State, 549 So.2d 694 (Fla. Dist. Ct. App. 1989); State v. Pennell, 584 A.2d 513 (Del. Super. Ct. 1989) [DNA test results admitted, but not probability evidence]; Cobey v. State, 559 A.2d 391 (Md. Ct. Spec. App. 1989); Andrews v. State, 533 So.2d 841 (Fla. Dist. Ct. App. 1988).

pellate courts[3] and by the Virginia Supreme Court.[4] However, as recently demonstrated by the California First District Court of Appeal,[5] acceptance of RFLP is not uniform. Given the overwhelming acceptance and adoption of PCR in the scientific community, it is likely that such acceptance by the judicial system will come with time.[6]

Probably because of the quantity of attention given RFLP, commonly referred to as "DNA Fingerprinting," it is a little known or appreciated fact that PCR was successfully used to the benefit of the defense in the very first criminal case involving DNA analysis in the country.[7] However, PCR is useful for both the prosecution and defense, as was shown in a recent San Mateo County, California case.[8] This case dramatically illustrated the usefulness of PCR in both exonerating and implicating suspects of such crimes as sexual assault.

BASIC GENETICS AND DNA REPLICATION

In recognition of the fact that many attorneys do not have easy access to genetics texts[9] recent enough to describe PCR, and the

3. Fuller v. Texas, 827 S.W.2d 919 (Tex. Crim. App. 1992); Trimboli v. Texas, 817 S.W.2d 785 (Tex. Ct. App. 1991).

4. Spencer v. Commonwealth, 393 S.E.2d 609 (Va. 1990); Spencer v. Commonwealth, 385 S.E.2d 850 (Va. 1989); Spencer v. Commonwealth, 384 S.E.2d 775 (Va. 1989); Spencer v. Commonwealth, 384 S.E.2d 785 (Va. 1989).

In another case, the Massachusetts Supreme Court agreed with an indigent defendant that PCR might help exonerate him, but refused to require the state to fund post-conviction investigations that might reveal exculpatory evidence. Commonwealth v. Davis, 574 N.E.2d 1007 (Mass. 1991).

5. People v. Barney, 10 Cal. Rptr.2d 731 (Cal. Ct. App. 1992).

6. The wide and enthusiastic support and acceptance of PCR in the scientific community is illustrated by the inclusion of over 12,000 PCR references in the Medline database accessed through LEXIS. A LEXIS (MEDIS, MEDLNE Library, 86-91 File) search ("polymerase w/1 chain w/1 reaction") conducted on 14 Jan. 1993 retrieved 12,016 references. A narrower, modified search ("and forens!") retrieved 94 references.

7. Pennsylvania v. Pestinakis, *cited in DNA Typing Draws First Blood in Pennsylvania*, SCI. SLEUTHING NEWSL., Summer 1987, at 1, 1.

8. People v. Quintanilla, No. C-23691 (San Mateo Super. Ct., Aug. 16, 1991). In this case, the DNA typing requested by the initial suspect excluded him. Based on this and other evidence, the prosecution dismissed the charges against the suspect. Approximately one year later, a second suspect, already under investigation in several rape cases, was implicated. This suspect was included through PCR typing. Although various samples had been submitted to Cellmark Diagnostics (Germantown, MD) for RFLP analysis, Cellmark was unable to obtain banding patterns. Nonetheless, PCR results implicated him, he matched the original victim's physical description, his wife possessed jewelry stolen from the victim, and his fingerprints matched those lifted from her car. Following a *Kelly-Frye* hearing, the PCR evidence was admitted in his trial, and he was convicted. *Id.*

9. For exhaustive coverage of genetics, the reader is referred to such texts as BENJAMIN LEWIN, GENES (2d ed. 1985); BRUCE ALBERTS ET AL., MOLECULAR BIOLOGY OF THE

observation that accurate and sufficiently simple (yet detailed enough to be useful) descriptions of DNA technology are few and far between in the legal literature, a relatively large portion of this comment is devoted to the science involved in DNA analysis.

Deoxyribonucleic acid (DNA) is the "genetic blueprint" or "code" which makes each living organism, with the exception of identical twins, unique from all others. DNA is contained within every nucleated cell in the human body.[10] With the exception of the reproductive cells, human DNA is arranged in 23 pairs of distinct and separate chromosomes.[11] Each chromosome is composed of many "genes"[12] and the entire DNA complement is called the "genome."[13] Thus, the human genome is composed of 46 total chromosomes which are paired such that homologous chromosomes are bound together within the nucleus.

Chromosomes are divided into two general groups—the autosomes and sex (X and Y) chromosomes. Autosomes are all chromosomes other than the sex chromosomes. Somatic human cells (body cells that are non-reproductive) have 22 pairs of autosomes and 1 pair of sex chromosomes. The total number of paired chromosomes in somatic cells is called "diploid" (2n). Reproductive cells (egg and sperm) are called "gametes" or "germ cells." Gametes contain the "haploid" chromosome number (n). This means

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CELL (1983); MAXINE SINGER & PAUL BERG, GENES AND GENOMES (1991), and virtually any recent biology or molecular biology textbook.

10. The major portion of DNA in each cell is located within a "nucleus." Thus, cells without nuclei do not contain DNA. While most cells are nucleated, such cells as the mature red blood cells of mammals do not have nuclei and thus do not contain DNA. *See* LUIS C. JUNQUEIRA & JOSE CARNEIRO, BASIC HISTOLOGY 261 (4th ed. 1983).

Animals and plants also contain a minor amount of extrachromosomal DNA. This DNA is contained within organelles responsible for energy production. Thus, in animal cells this DNA is located within mitochondria; in plants, it is located within chloroplasts.

11. Humans have 22 matched pairs of autosomes and one pair of sex chromosomes. LORNE T. KIRBY, DNA FINGERPRINTING 8 (1990).

12. Although the term "gene" was coined by Johanssen in the early 1900's, Gregor Mendel advanced the concept of the "gene" as early as 1865. *Id.* at 7.

13. The human genome is composed of approximately 3 billion base pairs. Chromosomes range in size from about 80 to 300 million base pairs. It has been estimated that only a minor fraction of DNA (perhaps less than 10%) represents coding DNA and regulatory sequences. The remainder consists of repetitive and other sequences, the function and importance of which are not presently understood. Eric D. Green & Robert H. Waterston, *The Human Genome Project; Prospects and Implications for Clinical Medicine*, 266 JAMA 1966, 1967 (1991).

Of the estimated 50,000 to 100,000 genes present in the human genome, approximately 5000 have been catalogued, 1900 have been assigned to particular chromosomes and 600 have been isolated (in cloned form). Less than 0.1% of the DNA sequences in the human genome have been determined. *Id.*

that they contain one copy of each autosome and one sex chromosome.

Basically, one chromosome in each pair is inherited from the individual's mother, and the other chromosome is inherited from the father. Thus, during normal embryonic development, a particular gene from the father will be paired with the homologous gene from the mother.[14] Each homologous chromosome pair contains genes situated in pairs at certain places ("loci"). Paired genes which code for certain characteristics are called "alleles."[15]

As organisms must be able to replenish dead cells as well as produce gametes, DNA replication is an important facet of cell growth and development. Each time somatic cells divide,[16] DNA replication must occur in order to ensure that each of the two daughter cells will contain a diploid chromosomal number.[17] In the first step of this complicated process, the rungs of the "ladder" are separated between the paired bases to produce two "complementary" strands of DNA.[18] Each strand becomes a "template" to

14. This is made possible by the process known as "meiosis," which occurs during the development of eggs and sperm (gametes). LEWIN, *supra* note 9, at 688. In the process of meiosis, after chromosomal replication occurs, the nucleus and cell divide twice to produce four cells, each with one-half the original chromosome number. Thus, each gamete will contain only one of the two homologues of the parent chromosomes (it is "haploid"). Somatic cells contain two copies of each chromosome and are called "diploid." *Id.* at 27-33.

15. Alleles are alternate forms of the genes that determine the expression of some particular characteristic. KIRBY, *supra* note 11, at 7-8.

While a person may inherit the allele for blue eyes from one parent and the allele for brown eyes from the other, only one eye color is normally expressed. In this example, the brown eye gene is "dominant" and the blue eye gene is "recessive;" this brown-eyed person would be "heterozygous" for the eye color gene. If the person had inherited brown eye genes from both parents, he would be "homozygous" for the gene which codes for eye color. *Id.* at 8.

16. The process whereby a somatic cell divides after chromosomal replication is called "mitosis." LEWIN, *supra* note 9, at 688.

17. For example, when skin is injured, new skin cells must be produced in order to replace the dead ones. The skin cells surrounding the damaged area are stimulated to begin dividing. The DNA of these cells is replicated and the cells undergo "mitosis," or cell division. This ensures that normal skin cells containing the proper diploid number of chromosomes will replace those killed as a result of the injury.

18. DNA is commonly described as a "twisted helix," "twisted ladder," or "spiral staircase." The ladder rungs (or steps in the staircase) are composed of pairs of "nucleotide" bases. Within DNA, there are four bases—adenine (A), thymine (T), cytosine (C) and guanine (G). Normally, each base is paired with another through hydrogen bonds, with adenine paired with thymine and cytosine paired with guanine. The ladder's handrails are composed of sugar (deoxyribose) and phosphate molecules. Strictly speaking, a nucleotide is a base connected to a sugar and a phosphate. The paired bases are often referred to as "base pairs." It is the particular base sequence which determines the characteristics of the individual animal.

The other nucleic acid, ribonucleic acid or "RNA," is composed of the same nucleotides, with the exception that thymine is replaced by uracil (U) (which like thymine, pairs with

which new nucleotides are added. To accomplish this, an enzyme called "DNA polymerase" travels along each of these separated "template" strands, binding complementary bases in their appropriate places thereby building new ladders from each of the two strands and producing two identical DNA molecules from one original parent DNA. This process allows each daughter cell to contain one DNA strand from the parent cell and maintains the genetic integrity of the organism.

Although DNA polymerase is not entirely mistake-proof, it is quite reliable and will faithfully reproduce the parent DNA molecule. As DNA replication is a very important function in cell division, DNA polymerases are not limited to complex animals.[19] While there are many other enzymes involved in DNA replication,[20] DNA polymerase is the enzyme of primary interest in the polymerase chain reaction.

FORENSIC DNA ANALYSIS

The genes of greatest interest in genetic analysis are those for which there are many variations and are thus termed "polymorphic."[21] Usually, for a locus to be considered polymorphic, the most common allele must occur at a frequency of less than 99% and according to the Hardy-Weinberg law,[22] at least 2% of the population must be heterozygous at that locus.[23] At the molecular level, polymorphism may result from a single nucleotide base change, or from a change in the number of tandem repeats in a

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adenine). RNA is copied from the DNA and is involved in protein production. Some viruses (e.g., the retroviruses, such as the human immunodeficiency viruses, and feline leukemia virus) have RNA as their genetic material instead of DNA.

19. Lower organisms such as bacteria, fungi and parasites have their own DNA polymerases which carry out the same replication functions. As discussed below, DNA polymerases and other enzymes from bacteria and other organisms are useful tools in molecular biology and genetic engineering.

20. For descriptions of the structures and functions of the various enzymes involved in eukaryotic (e.g., human) and prokaryotic (e.g., bacteria) DNA replication, see the appropriate chapters in ARTHUR KORNBERG, DNA REPLICATION (1980).

21. "Polymorphism" refers to different forms of the same basic structure. There are many examples of polymorphism in human genetics, such as ABO blood types and eye color.

22. According to the Hardy-Weinberg law, in a large randomly mating population, where no disturbances by outside influences such as mutation, migration, or selection exist, the relative proportions of the different genotypes remain constant between generations. KIRBY, *supra* note 11, at 168. *See also* Victor Weedn, *DNA Profiling*, 1 EXPERT EVIDENCE REP. 61, 66 (1989), for a simple explanation of the Hardy-Weinberg principles.

The "genotype" is the genetic make-up of an organism. The "phenotype" is the appearance or other characteristic of the organism which results from the interaction of its genetic constitution with the environment. LEWIN, *supra* note 9, at 25, 689.

23. KIRBY, *supra* note 11, at 25.

repetitive DNA sequence. The changes may be neutral, with no detectable phenotypic effect, or they may result in the production of different forms of the same protein or enzyme ("isozymes")[24] or they may be lethal.

There are three basic DNA analysis methods commonly used to determine identity and relatedness between individuals: (1) direct gene sequencing or "mapping," (2) RFLP, and (3) PCR. Prior to testing by any of these methods, electrophoresis or spectrophotometry is often used to determine the amount and size characteristics of the DNA present in the sample, if any.

Direct Sequencing

The goal of direct sequencing is to determine the exact nucleotide sequence present in the DNA molecule of interest.[25] Because DNA is ultimately responsible for the uniqueness of each individual, direct DNA sequencing is the only method which can determine identity with 100% accuracy.[26]

Understandably, mapping the large numbers of genes present on each individual chromosome by direct sequencing requires Herculean efforts.[27] Nonetheless, due to advances in equipment and

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24. *Id.*

25. ALBERTS ET AL., *supra* note 9, at 185.

26. George Sensabaugh, *Use of DNA Fingerprinting in Forensics*, Paper presented at the American Society for Microbiology, Northern California Branch and Northern California Association of Public Health Microbiologists, 8th Annual Combined Fall Conference (October, 1991).

27. Sequencing the human genome is the goal of the "Human Genome Project," an ambitious, international, 15-year (minimum) cooperative venture. Anthony V. Carrano, *Human Genome Project—A Global and Local Perspective*, Paper presented at the American Society for Northern California Branch and Northern California Association of Public Health Microbiologists, 9th Annual Combined Fall Conference (Oct. 1992). PCR is largely responsible for making a project of this magnitude feasible. As stated previously, in order to analyze each genomic sequence, many copies of DNA are necessary. Thus, the researchers must make thousands, if not millions, of copies of each gene. This would take much longer if traditional methods of molecular cloning such as those described in R.W. OLD & S.B. PRIMROSE, PRINCIPLES OF GENE MANIPULATION (4th ed. 1989) and J. SAMBROOK ET AL., MOLECULAR CLONING (2d ed. 1989) were necessary.

The implications of sequencing the human genome are staggering. The recent discoveries of the genes associated with muscular dystrophy, manic depression, cystic fibrosis, and Alzheimer's disease are merely illustrative aspects of the tremendous potential presented by this project. Hereditary defects may also be diagnosed more efficiently and earlier in pregnancies. Eventually, such defects may be eliminated through sophisticated genetic techniques. *See* Green & Waterston, *supra* note 13.

Concerns have arisen in association with the Human Genome Project, including privacy issues related to the database which will be generated. *See* Deborah Jackson, *Hacking the Genome*, SCI. AM., Apr. 1992, 128, 128, for a description of the problems involved in establishing the database. Other issues include patenting of the DNA involved in this project. While some scientists within the National Institutes of Health desire to patent DNA of un-

knowledge, the combination of either direct sequencing or RFLP and PCR will probably become the third generation of DNA testing.[28]

Restriction Fragment Length Polymorphism (RFLP)

A. Introduction

RFLP is the DNA testing technique commonly referred to within the legal profession as "DNA fingerprinting," due to the barcode-like results observed in the ultimate product of the analysis.[29] RFLP, the first generation in DNA analysis for casework, was developed by Alec Jeffreys and his colleagues in Britain.[30] It has been used extensively in the United States, the United Kingdom,[31] Canada[32] and China.[33] RFLP was used in the first sensa-

known coding specificities, many others are opposed to patenting these gene sequences. In fact, this controversy over patenting contributed to the resignation of James Watson as the head of the Human Genome Project. *See* Leslie Roberts, *Two Strikes Against CDNA Patents*, 257 SCI. 1620 (1992).

28. *See* Carolyn S. Harrington et al., *HLA DQα Typing of Forensic Specimens by Amplification Restriction Fragment Length Polymorphism (RFLP) Analysis*, 51 FORENSIC SCI. INT'L 147 (1991); Kentaro Kasai et al., *Amplification of a Variable Number of Tandem Repeats (VNTR) Locus (pMCT118) by the Polymerase Chain Reaction (PCR) and Its Application to Forensic Science*, 35 J. FORENSIC SCI. 1196 (1990); Ulf B. Gyllensten & Henry A. Erlich, *Generation of Single-Stranded DNA by the Polymerase Chain Reaction and its Application to Direct Sequencing of the HLA-DQA Locus*, 85 PROC. NAT'L ACAD. SCI. 7652 (1988).

29. Because DNA typing is based on very different principles than traditional fingerprinting, it is somewhat unfortunate that the term "Fingerprinting" has been associated with DNA testing. While this term has traditionally only referred to RFLP, some commentators unfamiliar with the science and technology group all DNA testing methods, including PCR applied to specific genetic loci within the term. Also, contrary to some accounts, "DNA Fingerprinting" was not "discovered" by Jeffreys, it was invented by him. *See* Ricardo Fontg, Comment, *DNA Fingerprinting: A Guide to Admissibility and Use*, 57 MO. L. REV. 501, 502-503 (1992).

30. Jeffreys' work developed from fundamental research done by E.M. Southern on the technique of "Southern blotting" DNA from electrophoresis gels onto membranes (E.M. Southern, *Detection of Specific Sequences Among DNA Fragments Separated by Gel Electrophoresis*, 98 J. MOLECULAR BIOLOGY 503 (1975)) and the work of Wyman and White on a polymorphic DNA locus which was characterized by a number of "variable number tandem repeats," better known as VNTR's (A.R. Wyman & R. White, *A Highly Polymorphic Locus in Human DNA*, 77 PROC. NATL. ACAD. SCI. USA 6754 (1980)).

Publication of Jeffrey's work heralded the present era of exploration into the study of DNA in many disciplines. Alec J. Jeffreys et al., *Hypervariable 'Minisatellite' Regions in Human DNA*, 314 NATURE 67 (1985).

31. *See* David J. Werrett et al., *The Introduction of DNA Analysis Into Home Office Forensic Science Laboratories in England and Wales*, BANBURY REP. 32: DNA TECH. AND FORENSIC SCI. 233 (1989).

32. *See* Barry D. Gaudette, *Forensic DNA Analysis in the Royal Canadian Mounted Police*, BANBURY REP. 32: DNA TECH. AND FORENSIC SCI. 229 (1989).

33. *See* Xiao-Wei Zhang et al., *Restriction Fragment Length Polymorphism Analysis of Forensic Science Casework in the People's Republic of China*, 36 J. FORENSIC SCI. 531 (1991).

tionalized DNA criminal case, which catapulted DNA analysis into the public and legal spotlight.[34]

However, this case was not the first use of DNA profiling in the forensic setting. Alec Jeffreys was also involved in a 1983 immigration case involving the son of a Ghanian woman who was a legal resident of the United Kingdom. When authorities refused to allow the boy to immigrate to the U.K., Jeffreys was able to show that there was only a one in 6×10^{-6} probability that the boy was not the woman's son. Conceding that as the world's population was only about 4 billion, authorities eventually allowed the boy to immigrate.[35] Thus, RFLP has found an important niche in paternity (or maternity) testing, as it correlates well with traditional methods and may be very informative in cases where traditional methods yield inconclusive or insufficient results.[36]

Because of the tedious, time-consuming, labor-intensive and subjective procedures which require specific training in the techniques of molecular biology, RFLP is perhaps best done in research labs. Presently, there are relatively few forensic labs which use RFLP (such as Lifecodes, Cellmark, GeneScreen, the Department of Justice, and the FBI).

While someone sufficiently trained in the methodology may consistently obtain meaningful results, it is an inherently complex test system. This is probably one of the reasons why the large private labs (e.g., Cellmark and Lifecodes) are primarily molecular biology laboratories. Their forensic work is simply an offshoot of their primary efforts related to genetic testing.

Given the technical challenges[37] involved in the development

34. This highly celebrated British case was the subject of Joseph Wambaugh's book, THE BLOODING (1989). The case involved three quiet villages in Leicester, two murdered 15-year old girls, a baker named Colin Pitchfork, a colleague named Ian Kelly who passed himself off as Pitchfork in the massive DNA sample collection efforts which led to the submission of samples from 5,512 males between the ages of 13 and 30 residing in the villages, and a geneticist named Alec Jeffreys. In this case, reports indicated that the odds against two unrelated persons having the same banding pattern as the suspect and Pitchfork was about 30 billion to one. Anthony Schmitz, *Murder on Black Pad*, HIPPOCRATES, Jan-Feb. 1988, at 49.

35. For an account of this case, see Alec J. Jeffreys et al., *Positive Identification of an Immigration Test-Case Using Human DNA Fingerprints*, 317 NATURE 818 (1985); William G. Hill, *DNA Fingerprint Analysis in Immigration Test-Cases*, 322 NATURE 290 (1986); John I. Thornton, *DNA Profiling*, CHEMICAL ENGINEERING NEWS, Nov. 20, 1989, at 18.

36. Lois A. Tonelli et al., *Use of Deoxyribonucleic Acid (DNA) Fingerprints for Identity Determination: Comparison with Traditional Paternity Testing Methods—Part I*, 35 J. FORENSIC SCI. 1265 (1990); Karen R. Markowicz et al., *Use of Deoxyribonucleic Acid (DNA) Fingerprints for Identity Determination: Comparison with Traditional Paternity Testing Methods—Part II*, 35 J. FORENSIC SCI. 1270 (1990).

37. These challenges include: (1) preliminary sequencing of the DNA of interest; (2) production of oligonucleotide probes (strings of single-stranded nucleotide bases complemen-

of useful RFLP systems, it is easy to understand why molecular biologists have been involved in this type of research. While some criminalists are molecular biologists, many must return to school to learn the language and methods of molecular biology in order to become proficient. Forensic scientists, such as criminalists who conduct DNA analyses, must truly have a hybrid education—they must apply their knowledge and understanding of the forensic science world in the realm of molecular biology. They must have a good working knowledge of the legal system, particularly in areas related to the evidentiary system and testifying in court. Unlike the molecular biologist working in the research setting, criminalists must put their reputations on the line every time they testify as to their laboratory results; their techniques and methods are continuously under close scrutiny. Thus, while research molecular biologists play important and necessary roles in the development of forensic DNA tests, the members of the forensic community are in the best position to determine and designate the optimal routes to take in the ongoing collaboration of forensics and molecular biology.

B. Technology

Basically, RFLP involves (1) using restriction enzymes to chop up the DNA of interest into segments of differing sizes and molecular weights;[38] (2) running these DNA segments on an electrophore-

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tary to the DNA of interest); (3) dealing with the vagaries of electrophoresis and "Southern" blots; (4) subjective analysis of differences in band migration through the electrophoresis gel; and (5) the infamous "band shift" frequently mentioned in RFLP court cases such as People v. Castro, 545 N.Y.S.2d 985 (N.Y. Sup. Ct. 1989). *See also* Colin Norman, *Maine Case Deals Blow to DNA Fingerprinting* 246 SCI. 1556, 1557-1558 (1989).

38. As indicated above, *see supra* note 13, most of the human genome is composed of "non-coding" DNA (DNA that does not contain the code for a protein). Within these non-coding regions, there are repetitive segments of varying lengths. These repetitive segments are called VNTRs (variable number tandem repeats) because they are composed of sequences of nucleotide bases which are repeated in tandem, any number of times. Thus, VNTRs are polymorphic—different individuals will have a different number of repeated sequences at a particular spot in the genome.

Restriction enzymes recognize specific base pair sequences and will cleave the DNA only at these particular sites. Thus, if a specific recognition base sequence is present, a restriction enzyme which recognizes that site will cleave the DNA molecule to produce fragments of a certain length. If the site is absent, a fragment of different length will be produced.

Polymorphism often results from neutral changes (changes in which mutations create or abolish recognition sites for restriction enzymes in noncoding DNA). KIRBY, *supra* note 11, at 26. Obviously, if changes occur within controlling sequences or structural genes (e.g., those which code for proteins), there may be serious phenotypic consequences (such as cystic fibrosis). *Id.*

sis gel[39] to separate them into "bands" based on their size and weight; (3) denaturing the DNA to make it single-stranded; (4) "blotting" the DNA onto a membrane; (5) adding radioactively-labelled DNA oligonucleotide probes complementary to a particular sequence of interest; (6) exposing the membrane to X-ray film to produce an autoradiogram; (7) observing the banding patterns produced by the radioactive probes on the autoradiogram (or "autorad"); and (8) comparing the banding patterns produced by the different test samples.

Because many DNA samples are run in different lanes on the electrophoresis gel at the same time,[40] the scientist is able to compare the migration distances of the bands in each lane separated in the gel during electrophoresis. If the banding patterns in two samples are identical, this indicates the samples may have originated from the same source.

By using various restriction enzymes, the scientist can produce different DNA segments with correspondingly different base sequences and lengths. Through sample comparisons, the use of multiple restriction enzymes, and statistical methods, the analyst determines whether the "evidence" sample was from the suspect, victim or someone else. "Direct sexing" of DNA may be used as an internal control and/or for sex determination in cases where the sex of the person is unknown.[41]

One major problem with RFLP that is commonly dealt with in the forensic setting is the minute amount of sample which is often the only evidence available. Current RFLP technology requires 1 to 10 g of DNA for a single analysis.

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39. Electrophoresis is a technique commonly used to separate component parts of proteins, nucleic acid fragments or other molecules. In RFLP, the restriction enzyme-treated sample DNA is placed in a lane on an agarose gel (or other gel material). When an electric current is applied to the gel, the DNA fragments move through the gel at rates dependent upon such factors as their electrical charges, size and weight.

For a detailed description of the technical aspects involved in RLFP, see KIRBY, *supra* note 11, at 91-131, 135-145.

40. In addition to the samples from each person involved and any evidence samples available, a size-marker DNA cocktail is also run in one lane. This sample, containing DNA fragments of known molecular weight and size, is used as a reference to determine the number of base pairs which correspond to each band in the test sample patterns.

The "blotting" of DNA fragments from an agarose gel to a more solid support, such as a nylon membrane or cellulose acetate filter paper, for subsequent detection is called "Southern blotting," named for the researcher who originally developed the technique. *See* Southern, *supra* note 30, at 29.

41. Lilya V. Verbovaya & Pavel L. Ivanov, *"Sexing" Deoxyribonucleic Acid (DNA) on DNA Fingerprint Gel: An Internal Control for DNA Fingerprint Evidence*, 36 J. FORENSIC SCI. 991 (1991).

> Blood contains 5000 to 10,000 nucleated cells per microlitre; this corresponds to 25 to 50 μg of DNA/mL. Thus bloodstains would have to contain at least 50 μL of blood to be amenable to analysis. The corresponding limit value for semen is about 10 μL. To put this latter value in context, a vaginal swab holds about 100 μL of fluid; thus semen collected on swabs cannot be diluted more than about 1:10.[42]

This is also a problem when multiple test procedures are necessary. The decision must then be made whether to use the entire sample for RFLP anaylsis, or forego RFLP in favor of other analytic methods. Another consideration is that there may be an insufficient quantity of high molecular weight DNA available due to sample degradation by bacterial action, sunlight or other DNA-destroying forces. The relative stability of dried DNA has been studied in controlled experimental studies,[43] as well as from teeth,[44] mummy tissue and 140-year-old dried muscle.[45] In some cases, RFLP is possible.[46] However, this is not always the case, and other methods such as PCR are sometimes required.

In addition to requiring relatively large samples, RFLP has a major drawback in that it commonly involves the use of radioactive reagents, a distinct disadvantage for crime labs. Unlike most

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42. George F. Sensabaugh, *Forensic Biology—Is Recombinant DNA Technology in its Future?*, 31 J. FORENSIC SCI. 393, 395 (1986).

43. Peter Gill et al., *Forensic Application of DNA Fingerprints*, 318 NATURE 577 (1985); Dwight E. Adams et al., *Deoxyribonucleic Acid (DNA) Analysis by Restriction Fragment Length Polymorphisms of Blood and Other Body Fluid Stains Subjected to Contamination and Environmental Insults*, 36 J. FORENSIC SCI. 1284 (1991); David J. Walsh et al., *Isolation of Deoxyribonucleic Acid (DNA) From Saliva and Forensic Science Samples Containing Saliva*, 37 J. FORENSIC SCI. 387 (1992); Terry L. Laber et al., *Evaluation of Four Deoxyribonucleic Acid (DNA) Extraction Protocols for DNA Yield and Variation in Restriction Fragment Length Polymorphism (RFLP) Sizes Under Varying Gel Conditions*, 37 J. FORENSIC SCI. 404 (1992); C.T. Comey & Bruce Budowle, *Validation Studies on the Analysis of the HLA-DQα Locus Using the Polymerase Chain Reaction*, 36 J. FORENSIC SCI. 1633 (1991)

44. Ted R. Schwartz et al., *Characterization of Deoxyribonucleic Acid (DNA) Obtained from Teeth Subjected to Various Environmental Conditions*, 36 J. FORENSIC SCI. 979 (1991); John S. Waye et al., *Sensitive and Specific Quantitation of Human Genomic Deoxyribonucleic Acid (DNA) in Forensic Science Specimens: Casework Examples*, 36 J. FORENSIC SCI. 1198 (1991).

45. R. Higuchi et al., *DNA Sequences From the Quagga, an Extinct Member of the Horse Family*, 312 NATURE 282 (1984).

46. J.E. Allard, *Murder in South London: A Novel Use of DNA Profiling*, 32 J. FORENSIC SCI. SOC'Y 49 (1991); William D. Haglund et al., *Identification of Decomposed Human Remains by Deoxyribonucleic Acid (DNA) Profiling*, 35 J. FORENSIC SCI. 724 (1990); Evan Kanter et al., *Analysis of Restriction Fragment Length Polymorphisms in Deoxyribonucleic Acid (DNA) Recovered From Dried Bloodstains*, 31 J. FORENSIC SCI. 403 (1986); Alan Giusti et al., *Application of Deoxyribonucleic Acid (DNA) Polymorphisms to the Analysis of DNA Recovered From Sperm*, 31 J. FORENSIC SCI. 409 (1986); S. Pääbo, *Molecular Cloning of Ancient Egyptian Mummy DNA*, 314 NATURE 644 (1985); Higuchi *supra* note 45.

clinical laboratories, many forensic labs do not have the facilities required for isotope work.[47] Major concerns associated with the use of radioactive reagents include their cost, relatively short half-lives (while some of the radioactivity may remain for a long time, the reagent will degrade to the point where it is no longer sensitive enough for use in the test system), hazardous waste disposal considerations, the need to monitor personnel and lab space for radiation dose and contamination, and licensing regulations. If a spill occurs, it is possible that at least a portion of the laboratory will become unusable because no one will be allowed to enter the contaminated area. Due to these factors, many laboratorians are unwilling to accept the risks and disadvantages of using radioactive test methods. These concerns have helped stimulate the development of much simpler and less dangerous test methods (e.g., PCR) which utilize enzyme-based detection systems, rather than radioactive labels.

One strong advantage of RFLP is that it is possible to derive phenomenonal probability statistics relating to the determination of whether a particular person is responsible for the crime under investigation. The greater the probability that the RFLP patterns observed in the evidence samples and the subject match, the greater the likelihood that the person is the one responsible for the crime.[48] There are even methods which may be used to determine the identity of a suspect who claims that another family member was responsible for the crime.[49] Thus, RFLP's "power of discrimination" is potentially very high.

Because population genetics form the basis for these determinations, there has been much research into the genetic makeup of various human subpopulations.[50] The methods used to estimate the probabilities are relatively complex. In the forensic setting, most

47. Sensabaugh, *supra*, note 42, at 396.

48. "In any case, using a single probe, . . . [t]he probability that another, unrelated individual would share exactly the same pattern is 3×10^{-11}. Add the products of a second probe, and the probability shrinks further, to 5×10^{-19}." Roger Lewin, *DNA Fingerprints in Health and Disease*, 233 SCI. 521, 522 (1986).

In a recent appellate case, the frequency of the defendant's genotype in the Caucasian population was determined to be one in 300 million. United States v. Jakobetz, 955 F.2d 786, 789 (2d Cir. 1992).

49. I.W. Evett, *Evaluating DNA Profiles in a Case Where the Defence is "It was my brother,"* 32 J. FORENSIC SCI. SOC'Y 5 (1992).

50. M. Baird et al., *Allele Frequency Distribution of Two Highly Polymorphic DNA Sequences in Three Ethnic Groups and Its Application to the Determination of Paternity*, 39 AM. J. HUM. GENETICS 489 (1986); Balazs et al., *Human Population Genetic Studies of Five Hypervariable DNA Loci*, 44 AM. J. HUM. GENETICS 182 (1989). *See also*, Robert Gaensslen, *When Blood is Their Argument: Use and Interpretation of Genetic Marker Frequency Data in Forensic Serology*, 12 CRIME LABORATORY DIG. 75 (1985).

discussion has centered around two statistical methods. For example, the FBI uses a "fixed bin method" to establish this probability.[51] The National Research Council's (NRC) Committee on DNA Technology in Forensic Science recommend the "ceiling principle" as a method which is even more conservative than the FBI's fixed bin method.[52] As discussed below, population genetics and the statistics used to produce impressive probabilities are a subject of concern to many commentators and expert witnesses.[53]

Perhaps, in their rush to gain court acceptance of RFLP, its advocates have been overzealous in promoting its discriminatory capabilities. It is one thing to say that there is a 1 chance in a million that this test has identified the person responsible for the crime. It may be too much for many people to comprehend that there is a 1 chance in 1,000,000,000,000. Its extraordinary claims make it somewhat suspicious, much like the promises made by the patent medicine salesman from an earlier time in our history. The claims simply seem too good to be true. Thus, association of such claims with the test method may make it much easier for the judge or jury to disregard the evidence as untrustworthy.

Although some of the distrust associated with RFLP has overflowed into the PCR arena, the concerns with PCR are much different than those associated with RFLP. Also because its power of discrimination is not as great as that of RFLP, such claims of unreliability based on skewed population genetics and statistics are not as applicable to PCR.

The Polymerase Chain Reaction (PCR)

A. History

While at Cetus, biochemist and researcher Kary Mullis conceived and began developing methods to use polymerase to produce

51. For a detailed explanation of this statistical method, see Bruce Budowle & Keith L. Monson, *A Statistical Approach For VNTR Analysis*, 1989 PROC. INT'L SYMP. FORENSIC ASPECTS DNA ANALYSIS, 121 (1989). *See also, The FBI's Response to Recommendations by the Committee on DNA Technology in Forensic Science of the National Research Council, National Academy of Science*, 19 CRIME LABORATORY DIG. 57-59 (1992).

52. NATIONAL RESEARCH COUNCIL, DNA TECHNOLOGY IN FORENSIC SCIENCE 90-93 (1992).

53. Bruce Budowle & John Stafford, *Response to Expert Report by D.L. Hartl Submitted in the Case of United States v. Yee*, 18 CRIME LABORATORY DIG. 101 (1991); Bruce Budowle & John Stafford, *Response to "Population Genetic Problems in the Forensic Use of DNA Profiles" by R.C. Lewontin Submitted in the Case of United States v. Yee*, 18 CRIME LABORATORY DIG. 109 (1991); Eric S. Lander, *Population Genetic Considerations in the Forensic Use of DNA Typing*, BANBURY REP. 32: DNA TECH. AND FORENSIC SCI. 143 (1989). *See also* Eric Lander, *Expert's Report in People v. Castro* (undated).

multiple DNA copies.[54] The elegant simplicity and tremendous theoretical potential of this DNA multiplication scheme has revolutionized molecular biology. Indeed, it rapidly became the method of choice of molecular biologists and others who study DNA. "While the field of forensic serology was being revolutionized by the prospect of DNA analysis, the field of molecular biology was being revolutionized by the invention of the polymerase chain reaction (PCR), which ultimately has had an impact on every area of biological science."[55] Given its utility, it is perhaps not surprising that PCR represents a significant intellectual property concern with immense economic potential.[56]

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54. *See* K. Mullis & F. Faloona, *Specific Synthesis of DNA In Vitro Via a Polymerase Catalysed Chain Reaction*, 155 METHODS ENZYMOLOGY 335 (1987); K. Mullis et al., *Specific Enzymatic Amplification of DNA in Vitro: The Polymerase Chain Reaction*, 51 COLD SPRING HARBOR SYMP ON QUANTITATIVE BIOLOGY 263 (1986); Randall K. Saiki et al., *Enzymatic Amplification of β-Globin Genomic Sequences and Restriction Site Analysis For Diagnosis of Sickle Cell Anemia*, 230 SCI. 1350 (1985); Randall K. Saiki et al., *Analysis of Enzymatically Amplified β-Globin and HLA-DQα DNA With Allele-Specific Oligonucleotide Probes* 324 NATURE 163 (1986).

55. Rebecca Reynolds et al., *Analysis of Genetic Markers in Forensic DNA Samples Using the Polymerase Chain Reaction*, 63 ANALYTICAL CHEMISTRY 1,1 (1991).

56. Cetus successfully defended two very important PCR patents (U.S. Patent Nos. 4,683,195 and 4,683,202) against Du Pont in 1991. Du Pont De Nemours & Co. v. Cetus Corp., 19 U.S.P.Q. 2d (BNA) 1174 (N.D. Cal. 1990); Du Pont De Nemours & Co. v. Cetus Corp. No. 89-2860, 1990 U.S. Dist. LEXIS 18382 (N.D. Cal. Dec. 11, 1991).

Until Cetus sold its entire GeneAmp PCR technology business to Hoffman-La Roche for an aggregate cash price of $300 million plus royalties on future Roche PCR sales, Cetus sold PCR equipment through a joint venture with Perkin-Elmer. *Cetus To Sell PCR Business to Hoffman-La Roche for $300 Million Plus Royalties*, BUS. WIRE, July 22, 1991, *available in* LEXIS/Nexis Library Bus. Wire File. PCR sales through the joint venture amounted to $26 million for the fiscal year ending June, 1991 and were expected to grow 40-50% in 1992. Sabin Russell, *Cetus Wins Patent Case Over Du Pont: Crucial Victory For Biotech Firm*, S.F. CHRON., Feb. 28, 1991, at C1.

Cetus and Chiron Corporation recently merged to form the second largest independent biotechnology firm. The new company, worth about $600 million in cash assets, focuses on diagnostics, vaccines, cancer therapeutics and ophthalmics. *Chiron and Cetus to Form "Second Largest" Biotech Firm*, BIOTECHNOLOGY NEWSWATCH, August 5, 1991, at 1. Almost simultaneously with the Chiron merger, Cetus sold the PCR rights to Roche. Emma Chynoweth, *Cetus Sells Diagnostics to Roche, Merges With Chiron*, CHEMICAL WK., July 31, 1991, at 12. Prior to the sale, Roche agreed to abide by the decision in a lawsuit brought against Cetus by Eastman Kodak Company to seek injunctive relief in regard to technology co-developed during the terms of an agreement between Cetus and Kodak. *Stockholders Make it Official: Chiron, Cetus to Merge, Roche Acquires PCR*, BIOTECHNOLOGY NEWSWATCH, December 16, 1991, at 1; Eastman Kodak Co. v. Cetus Corp., 1991 Del. Ch. LEXIS 151 (Del. Ch. Oct. 4, 1991); *See also*, Eastman Kodak Co. v. Cetus Corp., 1991 Del. Ch. LEXIS 197 (Del. Ch. Dec. 11, 1991).

Hoffman LaRoche is aggressively enforcing its rights to the large *Taq* market (in Europe, it was valued at $26 million in 1991), as demonstrated by the recent suit filed against Promega. *See* Peter Aldhous, *Roche Gets Tough on Illicit Sales of PCR Reagent*, 258 SCI. 1572 (1992).

While much attention has been focused on the somewhat controversial Human Genome Project, PCR is also becoming increasingly important in many other areas. Development of PCR methods led to the subsequent development of the DQα test used in the forensic setting,[57] human immunodeficiency virus (HIV) detection and diagnostic techniques,[58] methods for the identification and detection of other microorganisms in various settings, including the aquatic environment, food, dairy, soil and clinical samples,[59] neonatal screening[60] (e.g., detection of genes associated with cystic fibrosis,[61] and sickle cell anemia[62]), identification methods for chro-

57. Henry A. Erlich et al., *The Use of the Polymerase Chain Reaction for Genetic Typing in Forensic Samples*, 1989 PROC. INT'L SYMP. FORENSIC ASPECTS DNA ANALYSIS 93; George F. Sensabaugh, *Forensic Application of the Polymerase Chain Reaction*, 31 J. FORENSIC SCI. SOC'Y 201 (1991); Rebecca Reynolds et al., *supra* note 55; Atsushi Akane et al., *Sex Identification of Forensic Specimens By Polymerase Chain Reaction (PCR): Two Alternative Methods*, 49 FORENSIC SCI. INT'L 81 (1991); Cetus Corporation, *Forensic Analysis By the Polymerase Chain Reaction (PCR)*, CETUS BACKGROUNDER, Feb. 1990; James J. Harrington, An Evaluation of the Forensic Application of the Polymerase Chain Reaction Technique for Use in New Jersey: Legal and Scientific Considerations, (unpublished manuscript).

58. Chin-Yih Ou, *DNA Amplification For Direct Detection of HIV-1 in DNA of Peripheral Blood Mononuclear Cells*, 239 SCI. 295 (1988); M.F. Rogers et al., *Use of the Polymerase Chain Reaction For Early Detection of the Proviral Sequences of Human Immunodeficiency Virus in Infants Born to Seropositive Mothers*, 320 NEW ENG. J. MED. 1649 (1989); M. Rayfield et al., *Mixed Human Immunodeficiency Virus (HIV) Infection in an Individual: Demonstration of Both HIV Type I and Type 2 Proviral Sequences By Using Polymerase Chain Reaction*, 158 J. INFECTIOUS DISEASES 1170 (1988).

59. E.J. Thomas et al., *Sensitive and Specific Detection of Listeria Monocytogenes in Milk and Ground Beef with the Polymerase Chain Reaction*, 57 APPL. ENVIRON. MICROBIOL. 2576 (1991); Henry A. Erlich et al., *Recent Advances in the Polymerase Chain Reaction*, 252 SCI. 1643, 1649 (1991); David H. Persing, *Polymerase Chain Reaction: Trenches to Benches*, 29 J. CLINICAL MICROBIOL. 1281 (1991); Richard A. Gibbs, *DNA Amplification by the Polymerase Chain Reaction*, 62 ANALYTICAL CHEM. 1202 (1990); Deborah Y. Kwoh & T. Jesse Kwoh, *Target Amplification Systems in Nucleic Acid-Based Diagnostic Approaches*, AM. BIOSCIENCES LABORATORY 14 (Oct. 1990); *Polymerase Chain Reaction Project Exploring Potential Clinical Applications*, AIDS RES. EXCHANGE, July/Aug. 1989, at 1; Ichiro Saito et al., *Detection of Epstein-Barr Virus DNA by Polymerase Chain Reaction in Blood and Tissue Biopsies From Patients with Sjogren's Syndrome*, 169 J. EXPERIMENTAL MED. 2191 (1989); Shuichi Kaneko et al., *Detection of Serum Hepatitis B Virus DNA in Patients with Chronic Hepatitis Using the Polymerase Chain Reaction Assay*, 86 PROC. NAT'L ACAD. SCI. 312 (1989).

60. Edward R.B. McCabe et al., *DNA Microextraction From Dried Blood Spots on Filter Paper Blotters: Potential Applications to Newborn Screening*, 75 HUM. GENETICS 213 (1987); Edward M. Rubin et al., *Newborn Screening by DNA Analysis of Dried Blood Spots*, 82 HUM. GENETICS 134 (1989).

61. C. Williams et al., *Same Day, First-Trimester Antenatal Diagnosis For Cystic Fibrosis By Gene Amplification*, 2 LANCET 102 (1988); A. Handyside et al., *Birth of a normal girl after in vitro fertilization and preimplantation diagnostic testing for cystic fibrosis*, 327 NEW ENG. J. MED. 905.

62. R.K. Saiki et al., *Enzymatic Amplification of β-globin Genomic Sequences and Restriction Site Analysis For Diagnosis of Sickle Cell Anemia*, 230 SCI. 1350 (1985); S.H. Embury et al., *Rapid Prenatal Diagnosis of Sickle Cell Anaemia By a New Method of DNA Analysis*,

mosomal abnormalities and specific mutations,[63] gene replacement therapy[64] and the development of other tests too numerous to mention.[65] PCR can even be used to determine ABO genotypes and sex.[66] The ability of PCR to amplify DNA from both a single human sperm and a diploid cell represents a major breakthrough in human pedigree analysis.[67] PCR is also useful in cases where the person is dead, but some of their tissues have been preserved in paraffin.[68] Use of these preserved samples precludes the necessity of exhumation and allows DNA analysis on those who have been cremated. PCR methods such as the AmpliType™ DQα kit may also be used in cases where bones are available for analysis.[69] PCR has also been used to study the epidemiology of Lyme disease, a recently recognized, yet ancient disease.[70]

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316 NEW ENG. J. MED. 656 (1987). PCR can also be used to diagnose many other genetic diseases, such as Huntington's disease (I. McIntosh et al., *Prenatal Exclusion Testing for Huntington Disease Using the Polymerase Chain Reaction*, 32 AM. J. MED. GENETICS 274 (1989)), and phenylketonuria (Cynthia Bottema et al., *Direct Carrier Testing for Phenylketonuria by PCR Amplification of Specific Alleles*, AMPLIFICATIONS, Mar. 1990, at 27).

63. PCR made the identification of chronic myeloid leukemia as the first cancer in which a specific genetic abnormality was identified. Ernest S. Kawasaki et al., *Diagnosis of Chronic Myeloid and Acute Lymphocytic Leukemias by Detection of Leukemia-Specific mRNA Sequences Amplified In Vitro*, 85 PROC. NAT'L ACAD. SCI. USA 5698 (1988).

64. Mark R. Hughes & C. Thomas Caskey, *Medical Genetics*, 265 JAMA 3132 (1991).

65. For an excellent review of the applications of PCR in medical diagnostics for genetic diseases, see Barry I. Eisenstein, *The Polymerase Chain Reaction, New Method of Using Molecular Genetics for Medical Diagnosis*, 322 NEW ENG. J. MED. 178 (1990). *See also*, Shirley Kwok & John Sninsky, *Application of PCR to the Detection of Human Infectious Diseases*, *in* PCR TECHNOLOGY 235 (Henry A. Ehrlich ed., 1989).

For an excellent recent overview of PCR and its multitude of applications, *see* Henry A. Erlich et al., *supra* note 57.

66. James Chun-I Lee & Jan-Gowth Chang, *ABO Genotyping by Polymerase Chain Reaction*, 37 J. FORENSIC SCI. 1269 (1992); Rebecca Reynolds, *Rapid Determination of Gender Using the Polymerase Chain Reaction*, Paper presented at the 77th Semi-Annual Seminar of the California Association of Criminalists (May, 1991).

67. Honghua Li et al., *Amplification and Analysis of DNA Sequences in Single Human Sperm and Diploid Cells*, 335 NATURE 414 (1988).

68. Darryl Shibata et al., *Fixed Human Tissues: A Resource for the Identification of Individuals*, 36 J. FORENSIC SCI. 1204 (1991); Darryl Shibata et al., *Human Immunodeficiency Viral DNA Is Readily Found in Lymph Node Biopsies from Seropositive Individuals*, 135 AM. J. PATHOL. 697 (1989); and Eric C.J. Claas et al., *Human Papillomavirus Detection in Paraffin-Embedded Cervical Carcinomas and Metastases of the Carcinomas by the Polymerase Chain Reaction*, 135 AM. J. PATHOL. 703 (1989).

69. M.N. Hochmeister et al. *Typing of Deoxyribonucleic Acid (DNA) Extracted From Compact Bone From Human Remains*, 36 J. FORENSIC SCI. 1649 (1991).

70. David H. Persing et al., *Detection of Borrelia burgdorferi DNA in Museum Specimens of Ixodes dammini Ticks*, 249 SCI. 1420 (1990); and David H. Persing, *Borrelia, Babesia, Yersinia: Emerging Blood-Borne Pathogens*, Paper Presented at the American Society for Microbiology, Northern California Branch and Northern California Association of Public Health Microbiologists, 8th Annual Combined Fall Conference (Oct. 1992).

PCR has been a major factor in the development of the newly-formed fields of molecular anthropology[71] and molecular paleontology,[72] in which evolutionary relationships between species and the development of modern organisms are investigated.[73] PCR is even being used to monitor environmental contamination,[74] establish the new medical field of diagnostic molecular pathology,[75] and to help identify those killed in the recent conflict in the Persian Gulf.[76] The tremendous contributions which PCR has made in so many areas related to molecular biology led to its designation as "Molecule of the Year" in 1989 by Science, a leading scientific journal.[77]

B. Technology

PCR is based on a very simple idea. Perhaps the most appropriate analogy for PCR is as a genetic photocopy machine.[78] The PCR amplification system simply takes advantage of the natural DNA replication system and manipulates it to the advantage of the analyst to produce many millions of DNA copies.

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71. David A. Lawlor et al., *Ancient HLA Genes From 7,500 Year-Old Archaeological Remains*, 349 NATURE 785 (1991); S. Pääbo et al., *Mitochondrial DNA Sequences From a 7000-Year Old Brain*, 16 NUCLEIC ACIDS RES. 9775 (1988); S. Pääbo, *Ancient DNA: Extraction, Characterization, Molecular Cloning, and Enzymatic Amplification*, 86 PROC. NAT'L ACAD. SCI. USA 1939 (1989); Erika Hagelberg et al., *Ancient Bone DNA Amplified*, 342 NATURE 485 (1989); Ulf B. Gyllensten & Henry A. Erlich, *Ancient Roots for Polymorphism at the HLA-DQα Locus in Primates*, 86 PROC. NAT'L ACAD. SCI. USA, 9986 (1989); and Philip E. Ross, *Eloquent Remains*, SCI. AM., May, 1992, at 115. *See also*, Thomas J. White et al., *The Polymerase Chain Reaction*, 5 TRENDS IN GENETICS 185 (1989); Leslie Roberts, *How to Sample the World's Genetic Diversity*, 257 SCI. 1204 (1992)..

72. Jared M. Diamond, *Old Dead Rats Are Valuable*, 347 NATURE 334 (1991); Svant Pääbo & Allan C. Wilson, *Polymerase Chain Reaction Reveals Cloning Artefacts*, 334 NATURE 387 (1988); and D. Janczewski et al., *Molecular Phylogenetic Inference From Saber-Toothed Cat Fossils of Rancho La Brea*, 89 PROC. NAT'L ACAD. SCI. USA 9769 (1992).

73. Bryan Sykes, *The Past Comes Alive*, 352 NATURE 381, 382 (1991).

74. Asim K. Bej et al., *Detection of Coliform Bacteria in Water By Polymerase Chain Reaction and Gene Probes*, 56 APPLIED ENVTL. MICROBIOL. 307 (1990); Asim K. Bej et al., *Detection of Escherichia coli and Shigella spp. in Water Using the Polymerase Chain Reaction and Gene Probes*, 57 APPLIED ENVTL. MICROBIOL. 1013 (1991); Asim K. Bej et al., *Detection of Viable Legionella pneumophila in Water By Polymerase Chain Reaction and Gene Probe Methods*, 57 APPLIED ENVTL. MICROBIOL. 597 (1991).

75. W.W. Grody et al., *Diagnostic Molecular Pathology*, 2 MOD. PATHOLOGY 553 (1989).

76. George W. Clarke, *'Genetic Fingerprinting' Grows as Important Forensic Tool*, L. ENFORCEMENT Q., May-June-July 1991, at 5, 28.

77. Daniel E. Koshland, *The Molecule of the Year*, 246 SCI. 1541 (1989); Ruth L. Guyer & Daniel E. Koshland, *The Molecule of the Year*, 246 SCI. 1543 (1989).

"Like the radio telescope and electron microscope, it represents an advance of a fundamental nature." J. Madeleine Nash, *Ultimate Gene Machine*, TIME, August 12, 1991, at 54, 56.

78. Robert Keeler, *Uses for PCR Are Multiplying in Gene-Related Research*, 30 RES. DEV., Aug. 1991, at 30.

To accomplish this, DNA is extracted from the test sample and combined with a mixture of the heat-stable DNA polymerase (*Taq*) originally obtained from a hot springs bacterium (*Thermus aquaticus*) and all of the building blocks necessary for DNA replication, including nucleotides and primers.[79]

A machine, such as the Perkin-Elmer thermal cycler,[80] is used to heat the sample DNA. Heating causes the bonds between the bases to break, separating the molecule into two strands (the DNA is "denatured"). This allows the primers to bind ("anneal") to the complementary sequences on the single-stranded template DNA strands. DNA polymerase then works from the site of the annealed primer-template and catalyzes the synthesis of new DNA strands by linking nucleotides together in the precise order specified by the template DNA strands. This is termed "extension." The cycle of denaturation, annealing and extension is then repeated as many times as necessary to produce the desired number of DNA copies.[81] Under highly "stringent" conditions, the *Taq* polymerase is able to very faithfully reproduce the DNA molecule.[82] Thus, the amplifi-

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79. Primers are segments of DNA with known sequences, designed and produced by the researcher so that they will bind ("anneal") to the DNA sequences which flank the section of DNA of interest in the sample to be amplified. When they are bound to the DNA, the primers serve as signals for the DNA polymerase to attach to the DNA and begin forming the complementary strands.

80. The Perkin-Elmer DNA Thermal Cycler is a microprocessor-controlled, thermal cycling instrument which automates the rapid and precise temperature changes needed in the PCR process. User-programmable files and preprogrammed protocols can be used. The sample holding block will accommodate 48 0.5 L microcentrifuge reaction tubes. The temperature range is -50C to 1000C. PERKIN-ELMER CETUS, DNA THERMAL CYCLER 480 SALES BROCHURE 8-9 (1990).

81. In the DQα test kit, the program of denaturation, annealing and extension is repeated for 30 cycles. CETUS AMPLITYPE® HLA DQα FORENSIC DNA AMPLIFICATION & TYPING KIT, PACKAGE INSERT 13 (undated) [hereinafter AMPLITYPE® PACKAGE INSERT].

82. This works because the hydrogen bonds between incorrectly paired bases (such as adenine and cytosine, for example) are too weak to withstand the heat. Thus, if the DNA polymerase made a mistake and tried to pair the wrong base to the parent DNA strand, the base would "fall off" and either DNA replication would be halted at this point or the correct base would be added before the DNA polymerase moved on down the molecule.

The rate at which the AmpliTaq® DNA polymerase (the *Taq* polymerase included with the DQα test kit) misincorporates nucleotides (inserts an incorrect base while it is extending a DNA chain) is estimated to be from 1 per 10,000 to 1 per 200,000 incorporated nucleotides per replication cycle.

> Using a "worst case" (mutation rate assumptions of 1 in 10,000, 32 doublings at 100% efficiency and the fewest number of replicates which can be detected in the AmpliType® Kit), no more than 1 product molecule in 50 could have a replication error in the region of an allele specific oligonucleotide probe. (A more reasonable estimate is 1 molecule in 500, and even this low probability is based on "worst case" assumptions). The probability of such an error converting one allele to another in a probe region is even lower: even if such an

cation products truly reflect the content of the original DNA sample. Prior to the detection steps described below, the amplified DNA is again denatured. This allows the "oligonucleotide-specific DNA probes" to bind to complementary sequences which may be present in the sample of amplified DNA.

Detection of the DNA of interest in the test sample is accomplished with these oligonucleotide-specific probes which are composed of DNA strands complementary to those of the DNA of interest.[83] In most common test systems, including the AmpliType™ DQα test kit, a "dot" of each probe correlating to the DNA sequence of each allele under investigation is attached to a nylon membrane at a distinct location.[84] Under suitably stringent conditions, the probe captures complementary amplified DNA; the probe will not bind to any non-complementary DNA sequences. This characteristic greatly contributes to the test's high degree of specificity.

In the DQα test kit and many other test systems, the detection component is comprised of three molecules—biotin, streptavidin, and horseradish peroxidase.[85] Biotin is bound to the primers while the streptavidin and horseradish peroxidase are used together as an "enzyme conjugate." This conjugate is added during the final steps of the test procedure. Biotin has an extremely strong affinity and is highly specific for streptavidin.[86] Thus, if the DNA in the sample and its attached primer is bound to the probe, the horseradish per-

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error were to occur in the first amplification cycle, it would not generate a detectable signal using this amplification and typing procedure.

CETUS CORPORATION, AMPLITYPE™ USER GUIDE 6-30 (version 2, 1990) [hereinafter USER GUIDE].

83. Thus, if the sequence in the amplified DNA is ATTCG, the probe sequence will be TAAGC.

84. This is called a "reverse dot-blot." R.K. Saiki et al., *Genetic Analysis of Amplified DNA With Immobilized Sequence-Specific Oligonucleotide Probes*, 86 PROC. NATL. ACAD. SCI. USA 6230 (1989). In the original DQα test kit, the sample DNA was dotted onto nylon membrane strips held within individual wells; different solutions, each containing a different probe was added to each strip. This is called a "dot blot." R.K. Saiki et al., *Analysis of Enzymatically Amplified β-Globin and HLA-DQα With Allele-Specific Oligonucleotide Probes*, 324 NATURE 163 (1986); Catherine T. Comey, *The Use of DNA Amplification in the Analysis of Forensic Evidence*, 15 CRIME LABORATORY DIG. 99 (1988).

There is an inherently much greater chance of human error involved in the dot blot procedure. Care must be used to properly and thoroughly label each well and add the correct probe solutions. In the DQα test kit reverse dot-blot format, the kit is supplied with each of the probe DNAs bound to membrane strips. Thus, the analyst just needs to add the test DNA to the strip. While labelling and care should be used with this test also, there are fewer steps involved, thereby decreasing the amount of manipulation required.

85. Radioactive probes, such as those used for RFLP, are used by some researchers.

86. Meir Wilchek & Edward A. Bayer, *The Avidin-Biotin Complex in Immunology*, 5 IMMUNOLOGY TODAY 39 (1984). *See also*, Pennina R. Langer et al., *Enzymatic Synthesis of*

oxidase reacts with a soluble, colorless compound tetramethylbenzidine (TMB), to produce an insoluble blue product. The allelic composition of the sample DNA is indicated by the presence of blue spots on the nylon membrane. In addition to the "test" spots used to identify the discrete alleles, there is also a "control" spot which will turn blue if the DQα genes have been amplified. The intensity of each test dot is compared with that of the control spot; if the control dot is not present, the test is deemed unreadable.[87]

There are several important considerations which must be kept in mind while developing PCR technology for use in genetic marker detection in the forensic setting. As listed below, various criteria have been expounded:

> In order to be of maximum benefit to the forensic scientist, a genetic marker system for forensic PCR analysis should satisfy the following criteria:
>
> 1. The marker should be highly polymorphic and have a high level of genetic heterozygosity.
> 2. The target sequence should be easily and specifically amplified.
> 3. Methods for detecting allelic variation should be uncomplicated and thoroughly reliable.
> 4. Population data on genotype frequencies must be available in order to assign estimates of the marker's power of discrimination and the probability of false inclusion.
> 5. The marker systems should be inherited independently so that frequencies derived from one marker system can be multiplied with those from others, thereby increasing the power of discrimination. Independent inheritance occurs when the markers are on separated chromosomes or are in linkage equilibrium when present on the same chromosome.[88]

Presently, there are very few test systems which have been sufficiently developed for forensic use. The most well-known is the AmpliType™ DQα test kit.[89] While AmpliTaq™ (the *Taq*

Biotin-Labeled Polynucleotides: Novel Nucleic Acid Affinity Probes, 78 PROC. NATL. ACAD. SCI. USA 6633 (1981).

87. *See* USER GUIDE, *supra* note 82, at 4-1. Dots with signals less than the "C" dot should be interpreted with caution.

88. Cecilia H. von Beroldingen et al., *Applications of PCR to the Analysis of Biological Evidence*, *in* PCR TECHNOLOGY: PRINCIPLES & APPLICATIONS FOR DNA AMPLIFICATION 209, 210 (Henry A. Erlich ed., 1989).

89. Another test system used by some companies detects polymorphisms within a related locus, DQβ. This test system takes advantage of many of the same reagents as the DQα

polymerase) is the subject of patents,[90] the primer and probe sequences are not proprietary.[91] Thus, unlike the proprietary probes used in RFLP (e.g., the probes developed by Jeffreys), the sequences of these molecules are available for any scientist to produce and test.

In the AmpliType™ test kit, a specific portion of the human genome which is known to code for particular structures on white blood cells ("leukocytes") is amplified and used to "type" the person being studied.[92] The human leukocyte antigen system (HLA) is the area of interest in the AmpliType™ kit. This kit has been developed and refined to the point where a trained person can use the necessary equipment and the reagents provided in the kit, easily follow the established protocol and obtain useful results. Importantly, this area of the human genome has been extensively studied due to its role in immune system function.

C. The Human Leukocyte Antigen System (HLA)

The HLA system is composed of proteins (or "antigens") which are coded for by a large number of genetic loci present on

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kit, such as the *Taq* polymerase and the thermal cycler. Different probes and primers are used to detect allelic variations within the β subunit of the DQ molecule, instead of the α subunit which is the basis of the Cetus DQα test kit.

GeneScreen of Dallas, Texas was the major company utilizing DQβ. Linda Carrico, *Texas' First Forensic Lab Set to Open in Dallas*, 4 TEX. LAW. 1 (1989). However, they have recently switched to the more well-known DQα test kit. Telephone Interview with Robert Giles, Scientific Director, *Gene Screen* (Dec. 1991).

90. *Taq* DNA polymerase and AmpliTaq™ DNA polymerase are covered by U.S. Patent No. 4,889,818, assigned to Cetus Corporation. Cetus is also the assignee of the GeneAmp™ PCR Process covered by U.S. Patent Nos. 4,683,202; 4,683,195; 4,800,159; and 4,965,188.

91. The probe sequences of the Cetus DQα test kit are published in USER GUIDE, *supra* note 82, at Figure 1-4.

92. These structures are called "antigens." Antigens are recognized by antibodies, the small proteins produced by a sub-group of white blood cells known as B lymphocytes or B-cells. Antibodies are extremely important in the proper functioning of the immune system and help the body recognize "foreign" antigens, such as those contained on viruses and bacteria. They also help in the recognition and potential elimination of abnormal tissue cells, including malignant and senescent cells.

Tissue typing is used to determine which array of antigens are present in the tissue; this is of utmost importance in transplantation and other medical procedures. If someone receives an organ from a donor of a different type, it is very likely that the recipient will reject the transplanted organ, often leading to other complications and death. Therefore, it is very important that the tissue type of both the donor and recipient be determined before any transplantation attempts are made. Tissue typing is also often used in paternity investigations.

Thus, PCR DQα typing can be considered tissue typing on a genetic level, instead of at the antigenic level. PCR simply goes straight to the source of the code.

chromosome #6.[93] Due to the large number of allelic variations in these proteins, there is a large degree of polymorphism.[94] The HLA proteins are divided into two structurally and functionally distinct groups—Class I and Class II.[95] Within Class II, there are three families of proteins—DP, DQ and DR.[96] Each of these Class II proteins is composed of two subunits, "α" and "β," which are separately encoded in the DNA of each gene cluster.[97] HLA DQA1 is the gene which codes for the α subunit.[98]

Within DQα, there are eight different alleles and one "pseudogene."[99] The "major" alleles, DQA 1, 2, 3 and 4, differ from one another at many nucleotide positions; they are easily dif-

93. Karen A. Sullivan & Bernard Amos, *The HLA System and Its Detection, in* MANUAL OF CLINICAL LABORATORY IMMUNOLOGY 835, 835 (Noel R. Rose et al. eds., 1986).

94. *Id.*

95. *Id.* at 835-837. The Class I antigens are present on the membranes of most nucleated cells and are recognized as the classical tissue transplantation antigens ("histocompatibility antigens"). Benjamin D. Schwartz, *The Human Major Histocompatibility HLA Complex, in* BASIC & CLINICAL IMMUNOLOGY 55, 59 (Daniel P. Stites et al. eds., 5th ed. 1984). The Class II proteins are found on the immune system cells. These proteins are very important in bone marrow transplantation and autoimmune diseases.

Autoimmune diseases are diseases which are caused by the attack of the body's immune system on the body itself. Examples of these very destructive diseases include systemic lupus erythromatosus (SLE), pernicious anemia, rheumatoid arthritis, juvenile diabetes, and others. JOHN W. KIMBALL, INTRODUCTION TO IMMUNOLOGY 494 (2d ed., 1986); and Henry A. Erlich & Teodorica L. Bugawan, *HLA Class II Gene Polymorphism: DNA Typing, Evolution, and Relationship to Disease Susceptibility, in* PCR TECHNOLOGY: PRINCIPLES & APPLICATIONS FOR DNA AMPLIFICATION 201 (Henry A. Erlich ed., 1989).

96. Sullivan & Amos, *supra* note 93, at 836.

97. *Id.*

98. The World Health Organization developed a new nomenclature system for these antigens. This comment uses the old nomenclature simply to avoid confusion with much of the literature which also uses the old nomenclature.

The new nomenclature, shown in the table below for the protein, gene and various alleles associated with the locus, was adapted from WHO, *Nomenclature for Factors of the HLA System*, 1989, 31 IMMUNOGENETICS 131 (1990).

	Nomenclature used in this review	WHO revised nomenclature
Protein	DQα	DQα
Gene	DQα	DQA1
Allele	DQA 1.1	DQA1*0101
	DQA 1.2	DQA1*0102
	DQA 1.3	DQA1*0103
	DQA 2	DQA1*0201
	DQA 3	DQA1*0301
	DQA 4.1	DQA1*0501
	DQA 4.2	DQA*0401
	DQA 4.3	QA*0601
Pseudogene	DXα	DQA2

99. Pseudogenes are nonfunctional gene copies which remain in the genome, although

ferentiated by one probe sequence.[100] There are also subtypes within 1 (1.1, 1.2, 1.3) and 4 (4.1, 4.2, 4.3). Although these subtypes differ from each other by only one or a few nucleotides, they will all bind with the probe for the major type (i.e., 1.1, 1.2, and 1.3 will all bind with the probe for 1); the 1 subtypes are distinguished by using additional probes specific to the correspondingly different sections for each allele.[101] While 4.1, the most common type 4 allele, can be distinguished from 4.2 and 4.3, these other alleles are relatively rare and are identical to each other in the sequence detected by the AmpliType™ HLA DQα test system.[102] Therefore, because 4.2 and 4.3 are not included, the test system only makes use of the six most important alleles.

Following PCR amplification of the evidence samples, the DQα types are compared. If the DQα genotype of the suspect is different from that of the evidence sample, the suspect is "excluded" and cannot be the donor of the evidence. Unlike matches or inclusions, exclusions are independent of the frequencies of the genotype in the population.[103]

If the suspect and evidence have the same genotype, then the suspect is "included" as a possible source of the evidence sample. The probability that another, unrelated individual would also match the evidence is equal to the frequency of that genotype in the relevant population. Multiple studies have been conducted to determine the genotype frequencies in various ethnic and geographically-defined population groups; significant differences were observed between the ethnic groups examined.[104]

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they may have recently lost their function in evolution. *See*, USER GUIDE,*supra* note 82, at 1-3.

100. R. Saiki et al., *Genetic Analysis of Amplified DNA With Immobilized Sequence-Specific Oligonucleotide Probes*, 86 PROC. NAT'L ACAD. SCI. USA 6230 (1989).

101. USER GUIDE, *supra* note 82, at 1-3.

102. *Id.*

103. *Id.* at 5-1.

104. In a recent study, over 1400 individuals were typed using both the dot-blot and reverse dot-blot methods to determine the DQα genotypes for 11 population groups. The observed frequencies of DQα genotypes did not significantly deviate from those expected on the assumption of Hardy-Weinberg equilibrium. There was a slight excess of homozygotes in one Hispanic (denoted by "Spanish surname") and one Southeast Asian group which was found to be consistent with the heterogeneity of these groups. These data indicate that the HLA-DQα marker system is useful in individual identification because genotype frequencies can be reliably estimated from allele frequency data. Rhea Helmuth et al., *HLA-DQα Allele and Genotype Frequencies in Various Human Populations, Determined Using Enzymatic Amplification and Oligonucleotide Probes*, 47 AM. J. HUM. GENETICS 515 (1990).

D. Population Genetics and the DQα Level of Discrimination

As stated above, in order to develop PCR kits, (e.g., AmpliType™), it is necessary to identify all of the possible alleles which could be present at the locus of interest, determine their DNA sequences and then study large populations to determine the frequencies of each allele and genotype for various ethnic groups.[105] These population genetics data are used to determine the statistical probabilities that a certain person within a particular racial group will have a particular combination of HLA DQα alleles. As discussed in more detail below, the DQα system is more discriminating than any of the traditional genetic markers used in forensics.[106]

For example, each person has two DQA alleles (one contributed from each parent) and there are a total of six alleles detected in the AmpliType™ system. Thus, there are 21 potential genotypes which may be detected. The frequencies of these genotypes range from less than 0.0005 to 0.15.[107] The discriminating power (DP) of the DQα typing system is 0.93.[108] This compares favorably with the discriminating power of the ABO red cell typing system (DP = 0.60), and analysis of the isozyme PGM (phosphoglucomutase) (DP = 0.76).[109] From these numbers, it is evident that, by itself, PCR DQα typing can neither provide individual identification nor achieve the phenomenally high numbers generated by RFLP methods. However, it has proved useful in conclusively including or excluding criminal suspects in circumstances where conventional typing has failed or insufficient DNA was available for RFLP.[110]

There are some distinct advantages to PCR over RFLP. Unlike presently used RFLP systems, it is an allele-specific system which identifies a discrete trait inherited in a clear Mendelian fashion. The distinctness and permanence of the DQα allelic variants is clearly demonstrated by their maintenance over millions of years.[111] Comparison of the observed genotype frequencies with the Hardy-

105. *Id.*; *See also*, Sara A. Westwood & David J. Werrett, *An Evaluation of the Polymerase Chain Reaction Method for Forensic Applications*, 45 FORENSIC SCI. INT'L 201 (1990).

106. George F. Sensabaugh & Cecilia von Beroldingen, *The Polymerase Chain Reaction: Application to the Analysis of Biological Evidence*, *in* FORENSIC DNA TECHNOLOGY 63, 72 (Mark A. Farley & James J. Harrington eds., 1991).

107. von Beroldingen et al., *supra* note 88, at 212.

108. Discriminating power is the probability of distinguishing between two randomly selected individuals from all of the populations studied.

109. Sensabaugh & von Beroldingen, *supra* note 106 at 212.

110. *See, e.g.*, People v. Quintanilla, No. C-23691 (San Mateo Superior Ct., Aug. 16, 1991). For a discussion of this case, *see supra* note 8.

111. Gyllensten & Erlich, *supra* note 71.

Weinberg expected frequencies can help validate typing methods—an excess of homozygosity would reveal a population substructure.[112] The close fit between the observed and expected DQα genotype frequencies affirms the typing methodology and genetic model.

Thus, although the discrimination power for the DQα marker system is less than that for most RFLP systems, it is a simple and rapid method which is capable of analyzing minute and degraded samples. As more PCR-based markers are researched and become readily available, a panel of tests will likely be developed which, in addition to the exclusionary value already provided by the DQα system, will provide valuable information for individual inclusions.

Alone, the AmpliType™ system for DQα provides a power of discrimination of approximately 83 to 94%.[113] However, because the DQα alleles are inherited independently from the conventional marker systems, results can be combined to increase the overall power of discrimination. Thus, combining the individualization potentials for DQα, ABO, PGM and secretor status in a typical sexual assault case increases this power of discrimination to 99%.[114]

The following table is from an informational flyer provided by Cetus, which illustrates how DQα test results can be presented in court in conjunction with results from conventional genetic marker typing in a typical sexual assault case.

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112. Helmuth et al., *supra* note 104, at 521.

The assumption of Hardy-Weinberg equilibrium allows estimation of genotype frequencies from observed allele frequencies and makes high levels of individual discrimination possible from relatively limited population data. For many VNTR (variable number tandem repeat) or RFLP systems, the discrimination of alleles is limited by gel electrophoresis resolution. A great excess of homozygotes may be found in VNTR population samples. Eric Lander, *DNA Fingerprinting on Trial*, 339 NATURE 501 (1989). The inability to fully discriminate classes due to limitations of the typing methodology and potential subpopulation structure may contribute to an excess of homozygotes. High mutation rates in some VNTR systems also creates the expectation of homozygote excess (up to 5%). Alec Jeffreys et al., *Spontaneous Mutation Rates to New Length Alleles at Tandem Repetitive Hypervariable Loci in Human DNA*, 332 NATURE 278 (1988).

113. Helmuth et al., *supra* note 104, at 520.

114. *See* Sensabaugh, *Biochemical Markers of Individuality*, *in* FORENSIC SCIENCE HANDBOOK 338-415 (Richard Saferstein ed., 1982).

Sample	ABO/Secretor Status	PGM	HLA DQα
Victim Reference Blood	O Secretor	1+	1.2,1.2
Vaginal Swab	A & H Activity	1+1−	1.3,2 (Sperm) 1.2,1.2 (Epithelial cells)
Questioned Hair From Victim's Pubic Combing	Not Done	Not Done	1.3,2
Suspect Reference Blood	A Secretor	1+1−	1.3,2

The results in the above hypothetical case indicate that the suspect cannot be excluded because the semen contributor is an ABO Type A Secretor with PGM type 1+1− or 1− activity and DQα type 1.3,2. Without including DQα gene frequency information, this combination of types occurs in approximately 7% of the white population.[115] But, if DQα gene frequency information is included, the combination of types occurs in approximately 0.09% of the white population.[116] Furthermore, the suspect is also not excluded as the source of the questioned pubic hair. DNA extracted from the hair root was 1.3,2, which is consistent with the DQα type of the suspect. This DQα genotype occurs in approximately 1.9% of the white population, a genotype frequency less common than that of the conventional ABO, PGM and secretor systems combined.

Recognizing the great potential in combining PCR with RFLP or direct sequencing, many researchers are studying the possibilities.[117] The combination of PCR and RFLP affords a greater detection sensitivity than can be achieved by the RFLP method alone and greater discrimination than can be achieved by PCR alone.[118] This is a very powerful combination of methods which could result

115. B.W. Grunbaum et al., *Distribution of Genetic Frequencies and Discrimination Probabilities for 22 Human Blood Genetic Systems in Four Racial Groups*, 25 J. FORENSIC SCI. 428 (1980).

116. *Id.*

117. K. Kasai et al., *Amplification of VNTR Locus (pMCT118) by the Polymerase Chain Reaction (PCR)*, 1989 PROC. INT'L SYMP. FORENSIC ASPECTS DNA ANALYSIS 279 (1989); Bruce Budowle et al., *Analysis of the VNTR Locus D1S80 by PCR Followed by High-Resolution PAGE*, 48 AM. J. HUM. GENETICS 137 (1991); David R. Engelke et al., *Direct Sequencing of Enzymatically Amplified Human Genomic DNA*, 85 PROC. NAT'L ACAD. SCI. USA 544 (1988).

118. *See*, Bruce Budowle et al., *Review Article: An Introduction to the Methods of DNA Analysis Under Investigation in the FBI Laboratory*, 15 CRIME LABORATORY DIG. 8,18 (1988). *Also see, Proceedings of the International Seminar on the Forensic Application of PCR*

in another generation of DNA typing methods.[119]

E. Perceived Problems Associated with PCR

In addition to the low level of discrimination, as discussed above, there are several perceived problems with PCR. However, while some of these problems are of valid concern, others appear to be make-weight legal arguments against the use of the technology. Concerns voiced in the literature and cases include:

(1) "allelic drop-out";
(2) the sensitivity of the test and the potential for contamination;
(3) the small number of laboratories conducting the test; and
(4) interpretation problems.

1. "Allelic Drop-Out"

This is a term which has been used to describe differential or preferential amplification, the situation in which the procedure greatly favors one of the two alleles present in a heterozygous individual such that the results would lead one to wrongly conclude that the individual was homozygous at the locus examined.[120] However, there is no scientific basis for the belief that differential amplification occurs in the AmpliType™ system.

First, there is no evidence that selective priming for some alleles relative to other alleles occurs in the AmpliType™ system.[121] However, an alternative explanation is that there is selective denaturation of some alleles relative to others. An experiment was conducted on DNA from a DQα 1.1,4 heterozygote to determine whether selective denaturation occurs.[122] At 90°C or above, there

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Technology, 18 CRIME LABORATORY DIG. (1991), and Bruce Budowle, *AMP-FLPs: Genetic Markers for Forensic Identification* 18 CRIME LABORATORY DIG. 134 (1991).

119. Amplified restriction fragment length polymorphisms (AmpFLPs) are recently developed test systems in which a DNA sample too small for conventional RFLP analysis is first amplified and then tested by RFLP. G.T. Horn et al., *Amplification of a Highly Polymorphic VNTR Segment by the Polymerase Chain Reaction*, 17 NUCLEIC ACIDS RES. 2140 (1989); E. Boerwinkle et al., *Rapid Typing of Tandemly-Repeated Hypervariable Loci by the Polymerase Chain Reaction: Application to the Apolipoprotein B 3' Hypervariable Region*, PROC. NAT'L ACAD. SCI. 212 (1989). A test kit for D1S80 is currently available. This kit may become the first AMP-FLP kit used for forensic purposes. *See* Kasai et al., *supra* note 28, and Y. Nakamura et al., *Isolation and mapping of a polymorphic DNA (pMCT118) on chromosome 1p (Dis80)*, 16 NUCLEIC ACIDS RES. 9364 (1988). This method not only takes advantage of the exquisite sensitivity of PCR, but it also minimizes the problems of bacterial DNA contamination, and increases the quantity of sample DNA so that RFLP is possible.

120. USER GUIDE, *supra* note 82, at 6-24.

121. *Id. See also* Gyllensten & Erlich, *supra* note 71.

122. The sequences of DAQ 1.1, 1.2 and 1.3 alleles significantly differ from the DQA 2,3,

was consistent typing of DQα 1.1 and 4. Below 88°C, neither allele amplified nor typed. However, at 88°C, the results reflected preferential amplification of DQA 4 as compared to DQA 1.1 (DQA 4 allele could be amplified, but not DQA 1.1). These results are based on the ability of the DQA 4 allele to be denatured and serve as a template at this low temperature.

Therefore, preferential amplification and hence, allelic drop-out is a possibility if the temperature of the reaction is substantially below the specified temperature of 94°C. If the temperature of the thermal cycler wells is close to 94°C during denaturation, preferential amplification and "allelic dropout" should not occur.[123] Thus, this important study indicated that the phenomenon is possible, but improbable, as long as the equipment is properly calibrated and maintained. Therefore, as an additional control, the kit presently on the market contains a heterozygous human genomic DNA control of DQα type 1.1,4.

Also, the population genetics data do not reveal an excess of homozygotes which would be attributable to some hypothetical "blank" or "null" allele that might fail to amplify.[124] In addition, as the oligonucleotide primers are capable of amplifying a specific DQα fragment from many different primate species, the sequences to which the primers are complementary are highly conserved in evolution.[125] Thus, allelic drop-out is a "non-problem" which a proponent of PCR evidence should be able to discuss if the opponent of the evidence brings it up.

2. Sensitivity and Contamination

The exquisite sensitivity of PCR is both its blessing and its curse. PCR has the capability to amplify the DNA present in a single hair root,[126] including several-month-old fallen hairs in

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and 4 alleles in that they have a higher GC to AT base pair ratio. USER GUIDE, *supra* note 82, at 6-24. This is significant in denaturation because there are three hydrogen bonds between GC pairs and only two bonds between AT pairs. *See* LEWIN, *supra* note 9, at 17-24. Thus, higher temperatures (more energy) are required to break GC bonds than AT bonds. The experiment was designed to determine whether, under non-standard conditions, preferential amplification occurs due to the selective denaturation of some alleles.

123. USER GUIDE, *supra* note 82, at 6-24.

124. Helmuth et al., *supra* note 104, at 520.

125. Gyllensten & Erlich, *supra* note 71.

126. Russell Higuchi et al., *DNA Typing From Single Hairs*, 332 NATURE 543 (1988). In this publication, the authors indicate that the DNA in hair is often limited and/or degraded. *Id.* at 544. This does not appear to be a major problem for PCR, but would preclude the use of RFLP.

The use of hair samples has various advantages over the use of blood. Some suspects may be unwilling to provide blood for testing due to their religious beliefs or customs. In

which DNA was not detectable by the usual chemical methods (representing less than 1 ng DNA).[127] This is of particular significance because hair is one of the most frequently found forms of biological evidence at crime scenes.[128]

Given this extreme sensitivity, one major concern is that "contaminating" DNA present in the sample will be amplified and completely mask the true DNA of interest.[129] However, there are many routes by which such contaminating DNA may be avoided, detected and/or eliminated. Nonetheless, a justifiable concern is that forensic samples are relatively rarely pure (with the exception of blood collected by venipuncture).

There are many potential sources of contaminating DNA, including DNA contributed by the victim, bystanders, the analyst, or even other organisms. There is also the concern that previously amplified DNA will contaminate the test DNA sample as it is being processed within the lab.[130]

Contaminating DNA From Species Other Than Humans. The DQα test system is designed with very specific primers and probes. In numerous tests, it was established that only primate DNA is amplified in this test system.[131] DNA from dogs, cats, bacteria, viruses and other organisms will not be amplified nor even detected.[132] Thus, unless a chimpanzee or gorilla is involved in a crime scene,

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some situations, transport of blood is impractical. In the veterinary setting, hair samples may be much easier to get than blood. This could be very important in endangered species programs where the risk of stress and/or anesthesia used during blood collection may be too great. Collection of hair samples makes it much easier to get the information desired, but with the least impact upon the animal. Also, if the animal is dead, blood may not be available, making hair the sample of choice.

See also, Rieko Uchihi et al., *Deoxyribonucleic Acid (DNA) Typing of Human Leukocyte Antigen (HLA)-DQA1 From Single Hairs in Japanese*, 37 J. FORENSIC SCI. 853 (1992).

127. Higuchi et al., *supra* note 126, at 545.

128. RICHARD E. BISBING, THE FORENSIC IDENTIFICATION AND ASSOCIATION OF HUMAN HAIR 185 (Richard Saferstein ed., 1982).

129. *See*, Russell Higuchi & Edward T. Blake, *Applications of the Polymerase Chain Reaction in Forensic Science*, BANBURY REP. 32: DNA TECH. AND FORENSIC SCI. 265, 273 (1990)

130. S. Kwok & R. Higuchi, *Avoiding False Positives with PCR*, 339 NATURE 237, 237 (1989); Eden Fisher & David R. Lincoln, 7 RECOMBINANT DNA TECH. BULL. 1 (1984); J. Fenton Williams, 7 BIOTECHNIQUES 762, 767 (1989); and Richard A. Gibbs & Jeffrey S. Chamberlain, *The Polymerase Chain Reaction: A Meeting Report*, 3 GENES & DEVELOPMENT 1095, 1097 (1989).

131. USER GUIDE, *supra* note 82, at 6-27; Cetus Corporation, *Background Information: Polymerase Chain Reaction—PCR Technology*, Nov. 1987; and Cetus Corporation, *Forensic Analysis By the Polymerase Chain Reaction (PCR)*, CETUS BACKGROUNDER, Feb. 1990.

132. USER GUIDE, *supra* note 82, at 6-27. Also, while amplified DNA from chimps and gorillas will hybridize to the probes, amplified DNA from more distantly related primates does not hybridize. *See also* Gyllensten & Erlich, *supra* note 71.

there is no danger that non-human DNA will be amplified or detected by this test.

Contaminating DNA From "Extraneous" Humans. One concern voiced by some commentators is that, unlike the "pristine" medical setting in which pure samples are supposedly ensured, forensic samples often contain DNA from more than one person.[133]

However, while mixed samples are probably the norm for forensic samples, anyone who has worked in a hospital can attest that the medical environment is anything but pristine, and pure samples are sometimes impossible to obtain. A prime example of this is amniocentesis, in which samples contain cells contributed by the mother as well as by the fetus. Another example involves the detection of cancerous[134] or HIV-infected cells,[135] where the entire point of the test is to identify the few malignant or infected cells hidden within a large population of normal cells. A third example is the detection of HIV-1 in discarded needles.[136] It would seem very difficult to argue that these three situations reflect the "large," and "clean" samples many commentators associate with the use of PCR and other DNA techniques in medical and research labs.[137] Contrary to the depiction by one commentator that "scientists analyze fresh, hygienic and relatively unlimited amounts of DNA,"[138] clinical and research laboratories often must work with small quantities of contaminated samples which are not necessarily "fresh" nor

133. Peter J. Neufeld & Neville Colman, *When Science Takes the Witness Stand*, SCI. AM. May 1990, at 46; Simon Ford & William C. Thompson, *A Question of Identity*, 4 CAL. DEFENDER No. 3 42, 43 (undated); Anthony Pearsall, Comment, *DNA Printing: The Unexamined "Witness" in Criminal Trials*, 77 CAL. L. REV. 665 (1989); Stephen C. Petrovich, *DNA Typing: A Rush to Judgment*, 24 GA. L. REV. 669 (1990); William C. Thompson & Simon Ford, *DNA Typing: Acceptance and Weight of the New Genetic Identification Tests*, 75 VA. L. REV. 45 (1989) [hereinafter *DNA Typing*]; William C. Thompson & Simon Ford, *Is DNA Fingerprinting Ready for Trial? (An Update)*, 4 CAL. DEFENDER No. 3, 36 (undated); C. Thomas Blair, Comment, *Spencer v. Commonwealth and Recent Developments in the Admissibility of DNA Fingerprint Evidence*, 76 VA. L. REV. 853 (1990); Hoeffel, *supra* note 1; Michael Damore, *What Every Criminal Lawyer Should Know*, 27 CRIM. L. BULL. 114, 116-117 (1991).

134. This includes detection of human papillomavirus infection, a risk factor for development of squamous and glandular neoplasia of the genital tract. Marion T. Cornelissen et al., *Localization of Human Papillomavirus Type 16 DNA Using the Polymerase Chain Reaction in the Cervix Uteri of Women with Intraepithelial Neoplasia*, 70 J. GEN. VIROLOGY 2555 (1989).

135. Winand Lange et al., *Detection by Enzymatic Amplification of ber-abl mRNA in Peripheral Blood and Bone Marrow Cells of Patients with Chronic Myelogenous Leukemia*, 73 BLOOD 1735 (1989); *PCR Profiles: Polymerase Chain Reaction in Situ*, AMPLIFICATIONS Mar. 1990 at 20. *See also*, Ou, *supra* note 58.

136. Stephen Raffanti et al., *Determination of HIV-1 Status of Discarded Sharps: Polymerase Chain Reaction Using Minute Quantities of Blood*, 264 JAMA 2501 (1990).

137. Thompson & Ford, *supra* note 133, at 36, 38; Pearsall, *supra* note 133, at 671.

138. Pearsall, *supra* note 133, at 671.

"hygienic." It is also very difficult to argue that some settings in which PCR has found widespread use provide large and clean samples (e.g., molecular anthropology and paleontology).

If medical science can cope with potentially significant "contamination" problems, it is reasonable to believe that contamination problems may be just as effectively dealt with in the forensic setting. Indeed, this has been recently and conclusively established in two cases, one involving the rather gruesome disappearance of a child,[139] and the other involving identification of a murder victim from 8-year old skeletal remains.[140] The tidbits of human tissue mixed among corn silage and the skeletal remains exposed to the elements for eight years were amenable to the PCR analysis which answered the questions asked in these two cases. Thus, it is highly likely that PCR will continue to be used in similar cases where vanishingly small quantities of sample are available, as well as in cases where the species of the sample source must be determined.[141] PCR may also prove useful in cases in which there may be a question of whether the blood present in an evidence sample was contributed by a human or some other animal.

The FBI conducted an extensive validation study on the effects of induced contamination and sample handling on the ability to perform PCR analysis.[142] The study included dried or moist stains put together, blood mixed with perspiration stains on a shirt, bloodstains which were physically handled, contaminated by exposure to aerosols created by coughing, mixed with shed scalp tissue, and placed in contact with contaminated scissors, and blood that was

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139. The 2-year old daughter of two farm laborers was reported as missing during the corn harvest. Unidentifiable tissues were subsequently found among the silage. Samples from the parents and the recovered tissues were tested with both RFLP and the DQα test system. The DNA results indicated that the tissue recovered from the silage was human and confirmed the probable parentage of the two farm workers. P. Mulhare et al., *An Unusual Case Using DNA Polymorphisms to Determine Parentage of Human Remains*, 12 AM. J. FORENSIC MED. PATHOLOGY 157 (1991).

140. Enka Hagelberg et al., *Identification of the Skeletal Remains of a Murder Victim by DNA Analysis*, 352 NATURE 427 (1991).

141. For example, this could be of great importance in the prosecution of wildlife poachers and importers of endangered species. PCR methods (not HLA DQα) may be developed to identify which species or subspecies a particular confiscated steak, pelt or mounted trophy belongs. For a discussion of how RFLP is already in use for such purposes, see KIRBY, *supra* note 11, at 233-259. For a brief description of the laboratory most likely to use DNA typing in such circumstances, the National Fish and Wildlife Forensics Laboratory in Ashland, Oregon, see Thomas Brom, *All God's Creatures*, CAL. L., Dec. 1991, at 44-45. A recent article describes the development of probes suitable for use in wildlife forensic science. R.S. Blackett & P. Keim, *Big Game Species Identification by Deoxyribonucleic Probes*, J. FORENSIC SCI. 590 (1992).

142. C.T. Comey & B. Budowle, *supra* note 43.

mixed with other substances such as saliva.[143] No detectable contamination was found to be introduced by handling, coughing, or the presence of perspiration. Likewise, the two moist stains placed in contact with each other and allowed to dry did not cross-contaminate. However, the mixture of saliva and blood equal amounts apeared to result in a combined HLA-DQα phenotype; the salivary phenotype appeared to be stronger, probably due to the presence of a large number of epithelial cells.[144]

3. Small Number of Forensic Laboratories Using the Test

The small number of forensics laboratories using the test has been a factor for some courts which have excluded PCR evidence.[145] As of March 1991, Cetus reported that over 30 forensic labs were performing DQα typing.[146] Given the capital outlay required to begin PCR analysis, it is not too surprising that more labs have not started using the technology.[147] In addition, there are costs of training personnel in the proper use of the methods.[148] Sending samples to an outside laboratory is also expensive.[149] Although there are probably many labs who would like to have the capability of using PCR, most of them are unlikely to have the necessary resources available in these lean economic times.[150]

In view of the advantages presented by PCR as compared with

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143. *Id.*

144. *Id.*

145. People v. Mack, No. 861116 (Sacramento Super. Ct. 1991).

146. *Cetus Corporation, Attorney/Investigator Slide Presentation of Forensic DNA Analysis Methods* (unpublished manuscript) [hereinafter Slide Presentation]. In comparison, over 50 forensic labs were "capable" of performing RFLP as of the same date. *Id.*

147. In March 1991, Cetus estimated the total purchase price for all the new capital equipment necessary for PCR analysis to be $15,000 to $20,000 for a typical crime lab. However, this is comparatively inexpensive, as RFLP capital equipment costs are estimated at approximately $150,000 to 200,000. *Id.*

148. In 1991, the cost of a one week training course at Cetus was $1000. *Id.*

149. In June 1989, DNA testing ranged from $325/sample at Lifecodes to $490/sample at Cellmark to $1500/case at Forensic Science Associates. The expert witness fees (daily rate plus expenses) ranged from $1,000/day for a Ph.D. or $750/day for a non-Ph.D. from Cellmark, $100-$125/hour for Forensic Science Associates and $750/day for Lifecodes. OFFICE OF TECHNOLOGY ASSESSMENT, U.S. CONGRESS, OFFICE OF TECHNOLOGY ASSESSMENT, GENETIC WITNESS: FORENSIC USES OF DNA TESTS 25 (1990) [hereinafter GENETIC WITNESS].

150. The FBI's report on forensic DNA testing indicates that many labs would be interested in conducting DNA analysis, but lack of necessary personnel, insufficient space or equipment, insufficient budget resources, and insufficient caseload or local demand for DNA testing fail to justify establishing a DNA laboratory. The lack of or difficulty in obtaining a Nuclear Regulatory Commission (NRC) license for handling radioactive materials, the length of time required to become operational and the unavailability of DNA testing training

RFLP, it would be very useful if this analysis was available in every crime lab. Most cases do not require the sophisticated techniques, sometimes difficult interpretations and astronomical numbers generated by RFLP. In most cases, it would seem likely that PCR in combination with other serological markers would provide a quick, relatively inexpensive and very reliable yes/no (inclusion/exclusion) answer.[151]

4. Interpretation Problems

Some witnesses have testified to discrepancies in the reading of the dot blots. However, these concerns have largely been negated by the inclusion of a "control" dot on the probe strips. This is because in order for the test to be deemed "readable," the intensity of color at a test dot must be at least as intense as that of the "All Control."[152] Thus, if the "all control" (C) dot is more intense than the other dot, it is an indication that the results need careful analysis.

Sexual Assault Evidence Samples. In forensic DNA PCR analysis, sexual assault evidence samples are often involved. Usually, these are the archetypal mixed samples, typically containing a sperm cell component contributed by the male rapist and vaginal epithelial cells contributed by the female victim. Techniques such as "differential lysis" have been developed, which allow good separation between the sperm and epithelial cell fractions.[153]

Differential lysis takes advantage of the physical and biochemical characteristics and differences between the relatively resistant sperm cells and the relatively fragile epithelial cells. Epithelial cells will lyse (burst) under conditions which are much less harsh than those required to lyse sperm. Thus, by lysing the epithelial cells and centrifuging the sample to physically separate the sperm from the epithelial DNA now present in suspension on the top of the sperm

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were other concerns. Jay V. Miller, *The Outlook for Forensic DNA Testing in the United States*, 17 CRIME LABORATORY DIG. 1 (Supp. 1) (1990).

151. PCR analysis can be completed within a few days, while RFLP often requires weeks of work. Slide Presentation, *supra* note 146, at 15.

152. The "C" dot is the weakest on the strip. If it is absent, an accurate determination of the type cannot be made. This is because there may be other probe signals below the threshold of detection. The "C" dot provides assurance that the appropriate typing and sub-typing dots should be clearly visible. If visible dots with signal intensities less than the "C" dot are present, this is an indicator of possible procedural error, mixed samples, DNA contamination or the presence of DXα, DQα type 1.3,4, or subtypes of the DQA 4 allele. USER GUIDE, *supra* note 82, at 4-1. The package insert also contains a useful section on troubleshooting. *Id.* at 29-34.

153. Giusti et al., *supra* note 46; and USER GUIDE, *supra* note 82, at 3.18 to 3.19.

fraction, the DNA from the victim may be harvested from the evidence sample. In subsequent steps, the sperm are lysed and the rapist's DNA is harvested.

In a typical sexual assault case, many samples are tested simultaneously. "Mixed" evidence samples, such as those from vaginal swabs or semen stains on the victim's clothes, are tested along with "pure" DNA collected from both the suspect and the victim, and the sperm cell and epithelial cell fractions are isolated from a portion of the "mixed" evidence sample. By testing all of the various combinations of the above samples, along with samples from any other person who may have contributed DNA to the evidence (e.g., sperm contributed by the victim's boyfriend if he had intercourse with the victim prior to the sexual assault) will allow determination of the allelic composition of each sample. Because each person only has two alleles, a maximum of two alleles should be identified in each sample. However, if the sample is mixed, it is very likely that three or more alleles will be detected. Of course, if the two people share the same DQα type, there will still only be two alleles identified, even if the sample is "mixed." However, they will also be found to have the same type in their "pure" samples. Thus, there are internal controls within the test methodology which help ensure that the results obtained by the laboratory are correct and reliable. Nonetheless, these results simply mean that the suspect can neither be included nor excluded from the pool of potential suspects based on PCR DQα typing. Other means of identification and other types of evidence will probably be required for conviction.[154]

Other Sample Types. Mixed samples may also be found in bloodstains and other biological evidence. In this case, it becomes even more important to test "pure" samples from both the victim and the suspect. Differential lysis will not work in this situation, as there is no significant difference in the resistance to harsh environmental conditions of blood cells obtained from different people.

While mixed samples are very common, there are numerous legal circumstances in which "pure" DNA samples are available. These include paternity determinations[155] and cases involving the identification of murder victims.[156] The expense of DNA testing is

154. USER GUIDE, *supra* note 82, at 4-6 to 4-8.

155. *See* B.P. Ludes et al., *Parentage Determination on Aborted Fetal Material Through Deoxyribonucleic Acid (DNA) Profiling*, 36 J. FORENSIC SCI. 1219 (1991).

156. Akane et al., *supra* note 57; Yvonne Baskin, *DNA Unlimited*, DISCOVER, July 1990, at 77; Cetus Corporation, *supra* note 57; Jeremy Cherfas, *Genes Unlimited*, NEW SCIENTIST, April 1990, at 29; *Forensics Experts Tackle Task of Identifying Thousands of 'Disappeared' Victims*, 261 JAMA 1388 (1989); Hagelberg et al., *supra* note 140; Lawrence Kobilinsky &

particularly justified when corroborating evidence in difficult cases is needed to help convince the jury of the suspect's guilt or innocence. However, it is unlikely to supplant the other major identification test systems such as fingerprint analysis, red cell typing (e.g., ABO), and other methods commonly used to identify a suspect as the perpetrator of a crime. It is most probable that PCR will be used as an adjunct test in combination with other evidence and analyses to help bolster a case and ensure either a conviction or an acquittal.

F. Laboratory Design and Test Protocols

This section highlights additional aspects of DNA testing which attorneys must keep in mind. While attorneys involved in DNA cases must understand the technology to a certain extent, they also must have an awareness of laboratory set-up and procedures. It is important for the legal community to realize that laboratory design and test protocols are potentially significant aspects of the tests which may need to be addressed in court.

It is highly advisable for attorneys to be extremely familiar with the laboratory and the person who conducted the tests on the evidence. Thus, if the opponent to the test procedure raises issues regarding contamination, the well-prepared proponent of the evidence should be able to counter the arguments with specific descriptions, photographs or other documentation of the care and diligence with which samples are handled and tested in the laboratory. On the other side of the fence, if the opponent of the evidence is aware of sloppy technique, the lack of controls and/or unsuitable laboratory design which could foreseeably lead to contamination, this would be an important argument against the evidence.

Because laboratory design and test protocols play potentially very significant roles in the success of DNA testing conducted in a particular facility, the laboratory and test protocols should be established with the potential contamination problems in mind. Envi-

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Louis Levine, *Recent Application of DNA Analysis to Issues of Paternity*, 33 J. FORENSIC SCI. 1107 (1988); Henry C. Lee et al., *Genetic Markers in Human Bone: I. Deoxyribonucleic Acid (DNA) Analysis*, 36 J. FORENSIC SCI. 320 (1991); Henry C. Lee et al., *DNA Analysis in Human Bone and Other Specimens of Forensic Interest: PCR Typing and Testing*, 31 J. FORENSIC SCI. SOC'Y 213 (1991); Roger Lewin, *A Matter of Maternity*, 233 SCI. 522 (1986); B.P. Ludes et al., *Parentage Determination on Aborted Fetal Material Through Deoxyribonucleic Acid (DNA) Profiling*, 36 J. FORENSIC SCI. 1219 (1991); J. Madeleine Nash, *Ultimate Gene Machine*, TIME, August 12, 1991, at 54; Schwartz et al., *supra* note 44; and Darryl Shibata et al., *Fixed Human Tissues: A Resource for the Identification of Individuals*, 36 J. FORENSIC SCI. 1204 (1991).

ronmental contamination from within the laboratory may result from the introduction of DNA from the analyst, another unamplified sample or a previously amplified sample. Although these present important considerations, good laboratory practice will overcome them.[157] Gloves should be worn at all times, masks should be worn by laboratorians working with samples, aerosols should be minimized, and sample tubes should be tightly closed when not in use.[158]

To prevent the transfer of DNA from one sample to another, extra precautions should be taken during the DNA extraction and PCR setup steps. Simple precautions such as using a fresh pipette tip for each sample, carefully opening reaction tubes, and keeping the tubes closed when they are not being used will prevent this type of contamination.[159] The DNA extraction and PCR setup of evidence samples should be done at a separate time from the DNA extraction and PCR setup of reference samples to prevent cross-contamination.[160] It is also recommended that DNA extraction of samples containing high levels of DNA (e.g., whole blood) be conducted separately from samples with low DNA levels (e.g., single hairs, small bloodstains, etc.).[161]

Laboratory design features and strict adherence to recommended methods will avoid the problem of "carry-over" (contamination of a sample with amplified DNA from a previous PCR reaction). Carryover contamination is a major concern because amplification product is an ideal substrate for subsequent amplifications.

> A single PCR reaction produces an enormous number of copies (as many as 10^{13}) that can potentially contaminate samples yet to be amplified. Since the number of copies of amplified DNA in a completed PCR reaction is so high, inadvertent transfer of even a minute volume to a yet to be amplified sample by splashing or aerosol may result in the amplification and typing of the "contaminating" DQα sequence. For example, if reusing a pipette tip transfers 0.1 μL, this can be as many as 10^{10} copies of amplifiable sequence. By comparison, a microgram of human genomic DNA contains only about 10^5 copies of a single-copy gene like

157. "Tidiness and adherence to a strict set of protocols can avoid disaster." B. Furrer et al., *Improving PCR Efficiency*, 346 NATURE 324 (1990); *see also*, S. Kwok & R. Higuchi, *Avoiding False Positives With PCR*, 339 NATURE 237 (1989).

158. USER GUIDE, *supra* note 82, at 2-1. Also, as a general rule, it is good practice to wear lab coats to protect street clothes from splashed chemicals.

159. *Id.*

160. *Id.* at 2-3.

161. *Id.*

DQα.[162]

Thus, nothing should move "upstream" in the flow of analysis. The laboratory should be organized into three designated work areas so that the area in which amplified DNA is handled is physically isolated from the DNA extraction and PCR setup work areas (e.g., separate rooms). While they may be located in the same room, the evidence handling and DNA extraction area should be a separate, distinct work area from the PCR set up area.[163] Microscopy, photography and any other evidence handling activities should be conducted in the DNA extraction work area.[164] If the work area where amplified DNA is handled is a separate but contiguous room, the laboratory design should be such that air flows toward the amplified DNA area. Dedicated equipment should be clearly labelled for use in each specific work area and not be used elsewhere.

Various researchers concerned with the problems of carryover contamination and the expenses involved in completely segregated laboratory designs have developed internal methods within the PCR reaction tubes to control such contamination.[165] In these methods, amplified DNA is rendered incapable of re-amplification in a subsequent test should it contaminate another sample. While these methods provide additional protection against contamination, they still must be used in conjunction with good laboratory technique.

Regardless of the contamination prevention methods used, no equipment, large or small, expendable or not, should be allowed to move from one designated section of the lab to another.[166] The

162. *Id.* at 2-1.

163. USER GUIDE, *supra* note 82, at 2-2.

164. For detailed special precaution guidelines regarding this area, *see Id.* at 2-3 to 2-4.

165. Stephen Isaacs et al., *Post-PCR Sterilization: Development and Application to an HIV-1 Diagnostic Assay*; 19 NUCLEIC ACIDS RES. 109 (1991); George D. Cimino et al., *Post-PCR Sterilization: A Method to Control Carryover Contamination for the Polymerase Chain Reaction*, 19 NUCLEIC ACIDS RES. 99 (1991); Chin-Yih Ou et al., *Use of UV Irradiation to Reduce False Positivity in Polymerase Chain Reaction*, BIOTECHNIQUES 442 (1991); Yu Sheng Zhu et al., *The Use of Exonuclease III for Polymerase Chain Reaction Sterilization*, 19 NUCLEIC ACIDS RES. 2511 (1991); Mary C. Longo, *Use of Uracil DNA Glycosylase to Control Carry-over Contamination in Polymerase Chain Reactions*, GENE 125 (1990); Gobinda Sarkar & Steve Sommer, *Shedding Light on PCR Contamination*, 7 NATURE 343 (1990); Gobinda Sarkar & Steve Sommer, *More Light on PCR Contamination*, 347 NATURE 340 (1990); Y. Jinno et al., *Use of Psoralen as Extinguisher of Contaminated DNA in PCR*, 18 NUCLEIC ACIDS RES. 6739 (1990); and PERKIN-ELMER CETUS, GENEAMP PCR CARRY-OVER PREVENTION KIT, PART NO. N808-0068 PRODUCT LITERATURE (undated).

166. For example, the thermal cycler should not be placed in the area in which samples are prepared.

work flow should always be directed one way. This represents significant protection for the incoming samples as they are processed. As the concerns are no less acute in the forensic setting than they are in the medical and diagnostic arena, preventing carry-over contamination by previously amplified samples through sectioning of the work area, and preventing the upstream movement of samples, equipment and supplies represents good laboratory technique which should be appreciated by everyone who works with PCR. Prior to sending samples to a lab, the attorney would do well to visit the lab and determine whether these precautions are in place.

ADMISSIBILITY AND OTHER ISSUES INVOLVING DNA ANALYSIS IN CRIMINAL TRIALS

With the increasing acceptance of DNA tests in courts throughout the United States, it appears that the admissibility questions regarding these testing methods will eventually be moot. However, the battles are not yet over. PCR cases have been held in Pennsylvania, Kansas, Texas, California, Florida, Virginia, New York, Colorado, Ohio, and Oregon.[167] Overall, as of October, 1991, PCR-based DQα typing methods were used in biological evidence analysis in over 250 cases.[168] PCR has also been admitted in Italy.[169] The evidence has been excluded in only a few cases.[170] However, the skirmishes are not likely to be over permanently until more appellate level or higher courts have heard PCR cases.

Controversy has long surrounded the admissibility of scientific techniques, especially in the criminal trial setting. Since the 1923 decision in *United States v. Frye*,[171] new scientific evidence has been scrutinized by various legal tests throughout the different jurisdictions within the United States.

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167. Forensic Science Associates, PCR DNA COURT CASES, HLA DQα FORENSIC DNA AMPLIFICATION AND TYPING INFORMATIONAL HANDOUT (3/29/91). In one of the latest cases, People v. Groves, No. 90CA1049, 1992 Colo. App. LEXIS 369 (Colo. Ct. App. October 8, 1992), the court ruled that the erroneous inclusion of PCR test results related solely to transactional evidence was harmless error even though the trial court did not conduct a preliminary *Frye* test on the PCR evidence.

168. Edward Blake et al., *Polymerase Chain Reaction (PCR) Amplification and Human Leukocyte Antigen (HLA)-DQα Oligonucleotide Typing on Biological Evidence Samples: Casework Experience*, 37 J. FORENSIC SCI. 700 (1992).

169. *See* Bruno Dallapiccola et al., *PCR DNA Typing for Forensics*, 354 NATURE 179 (1991). A subsequent paper challenged the methods used in the PCR tests admitted in the case referred to in the Dallapiccola paper. Angelo Fiori & Vincenzo L. Pascali, *Forensic Use of PCR in Italy*, 356 NATURE 471 (1992).

170. People v. Martinez, No. C 82183 (Los Angeles Super. Ct. 1989); and People v. Mack, No. 861116 (Sacramento Super. Ct. 1990).

171. 293 F. 1013 (D.C. Cir. 1923).

> Just when a scientific principle or discovery crosses the line between the experimental and demonstrable stages is difficult to define. Somewhere in this twilight zone the evidential force of the principle must be recognized, and while courts will go a long way in admitting expert testimony deduced from a well-recognized scientific principle or discovery, the thing from which the deduction is made must be sufficiently established to have gained general acceptance in the particular field in which it belongs.[172]

As with many other scientific methods, there has been a long history of attacks on the scientific analysis of blood and other body fluids. As recently as 1988, there were court challenges to the reliability of ABO typing of blood and other stain evidence.[173]

In the case of DNA analyses, most of the arguments go back to the traditional claim that forensic evidence is different from clinical samples obtained in the "pristine" medical setting. These same arguments occurred in the 1970s-1980s regarding electrophoretic typing of proteins such as PGM in bloodstains and other bodily fluid evidence.[174] It was not until the relatively recent case of *People v. Reilly*,[175] that the electrophoresis debate was settled for good in California.

The DNA debate is still very active, as evidenced by the approximately twenty appellate and state supreme court decisions discussing the admissibility of DNA typing.[176]

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172. *Id.* at 1014.

173. C. Holden, *Science in Court*, 243 SCI. 1658 (1987); and W.F. Rylaarasdam, *Farewell to Hired Guns, Judges Should Pick Their Own Experts to Testify on Technical Issues*, S.F. DAILY J., August 26, 1992, at 4. *See also*, Sheila Jasanoff, *Science on the Witness Stand*, ISSUES SCI. TECHN., Fall 1989, at 80.

174. David D. Dixon, *The Admissibility of Electrophoretic Methods of Genetic Marker Bloodstain Typing Under the Frye Standard*, 11 OKLA. CITY U. L. REV. 773 (1986); R.E. GAENSSLEN, SOURCEBOOK IN FORENSIC SEROLOGY, IMMUNOLOGY, AND BIOCHEMISTRY (1983); R.E. GAENSSLEN (ED.), SOURCEBOOK IN FORENSIC SEROLOGY, IMMUNOLOGY, AND BIOCHEMISTRY UNIT IX: TRANSLATIONS OF SELECTED CONTRIBUTIONS THE ORIGINAL LITERATURE OF MEDICOLEGAL EXAMINATIONS OF BLOOD AND BODY FLUIDS (1983); Joseph R. Melvin et al., *Paternity Testing*, *in* 2 FORENSIC SCIENCE HANDBOOK 273 (Richard Saferstein ed., 1988); F. Samuel Baechtel, *The Identification and Individualization of Semen Stains*, *in* 2 FORENSIC SCIENCE HANDBOOK 348 (Richard Saferstein ed., 1988); Henry C. Lee, *Identification and Grouping of Bloodstains*, *in* FORENSIC SCIENCE HANDBOOK 267 (Richard Saferstein ed., 1988); and Sensabaugh, *supra* note 114.

175. 242 Cal. Rptr. 496 (Cal. Ct. App. 1987).

176. George W. Clarke, *supra* note 76, at 5,7. For a sample of a *Kelly-Frye* motion in opposition to the introduction of RFLP evidence, *see* Walter F. Krstulja, *Sample Kelly-Frye Motion Opposing the Introduction of DNA (RFLP) Evidence*, 5 CAL. DEFENDER, No. 1, 1992, at 40.

A. *California's Kelly-Frye Test*

In assessing whether scientific evidence should be admitted, California uses the test set forth in *People v. Kelly*,[177] a case which expands the basic legal prerequisites for admissibility previously established by *Frye*.

> [The] admissibility of expert testimony based upon the application of a new scientific technique traditionally involves a two-step process: (1) the *reliability of the method* must be established, usually by expert testimony, and (2) the witness furnishing such testimony must be properly qualified as *an expert to give an opinion* on the subject. Additionally, the proponent of the evidence must demonstrate that correct scientific procedures were done in the particular case.[178]

The function of the *Kelly-Frye* rule is to safeguard against the presentation of either unfounded or prematurely developed scientific methods, or unfounded evidence to juries.[179] The reasoning is that "[l]ay jurors tend to give considerable weight to 'scientific' evidence when presented by 'experts' with impressive credentials."[180]

Kelly-Frye hearings are preliminary hearings in which the judge determines whether or not to permit particular scientific evidence to be presented to the jury during trial. In a typical *Kelly-Frye* hearing, both the proponent and the opponent of the scientific technique bring in a parade of scientific experts and present their best arguments for or against the admissibility of the particular scientific evidence involved. Thus, the proponent's witnesses will testify to the usefulness, reliability and overwhelming acceptance of the technology within the appropriate scientific community, while the opponent's witnesses will testify to its absolute worthlessness.

It is important to remember that the issue to be decided in a *Kelly-Frye* hearing is the admissibility, not the weight of the evidence.[181] In California, the decisions in *People v. Smith*[182] and *People v. Farmer*[183] have more clearly defined the narrow scope of the legal admissibility inquiry. As stated in *Smith*, "the *Frye* test dictates that *criticism of the specific methodology employed goes to the*

177. 549 P.2d 1240 (Cal. 1976).

178. *Id.* at 1244 (citations omitted)(emphasis in original); *See also*, People v. Shirley, 641 P.2d 775, 795 (Cal. 1982); and People v. Brown, 709 P.2d 440, 447-448 (Cal. 1985).

179. People's Points and Authorities Defining the Parameters of the *Kelly-Frye* Hearing at 2, People v. Lewis, No. C-27037 (San Mateo Super. Ct. Oct. 15, 1991).

180. *Kelly*, 549 P.2d at 1245 (1976).

181. People v. Marx, 126 Cal. Rptr. 350, 356 (Cal. Ct. App. 1975).

182. 263 Cal. Rptr. 678 (Cal. Ct. App. 1989).

183. 765 P.2d 940 (Cal. 1989).

credibility of the testimony, not admissibility."[184]

As there is no requirement that the court must understand the technology in question, the judge's role in *Kelly-Frye* is relatively limited. In a case involving hypnosis, the California Supreme Court stated, "our duty is not to decide whether hypnotically induced recall of witnesses is reliable as a matter of 'scientific fact,' but simply whether it is generally accepted as such by the relevant scientific community."[185] Nonetheless, because most people probably prefer to know what is going on around them, it would be advisable to present the evidence in such a way that the judge is able to grasp the concepts and understand the technology and vocabulary, at least on a rudimentary level.

Also importantly, there is no requirement for absolute unanimity of views within the scientific community prior to the determination that a new scientific method is reliable.

> The *Frye* test does not demand the impossible—proof of an absolute unanimity of views in the scientific community before a new technique will be deemed reliable; any such unanimity would be highly unusual, ... Rather, *the test is met if the use of the technique is supported by a clear majority of the members of that community.*[186]

> Kelly/Frye does not demand judicial absorption of all the relevant literature, nor does it require a decision once and for all whether a particular kind of scientific evidence is reliable. The court need only conduct a 'fair overview' of the subject, sufficient to disclose whether 'scientists significant either in number or expertise publicly oppose [a technique] as unreliable' [citation].[187]

Quite simply, the only determination to be made during a *Kelly-Frye* hearing is whether or not the scientific technology is generally regarded as reliable within the relevant scientific community. This itself has fueled some debate concerning the scope of the relevant scientific community and the degree of acceptance which can be considered "general." In terms of the "relevant scientific community," it appears that most courts are willing to adopt a broad view with regard to PCR testing.[188]

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184. *Smith*, 263 Cal. Rptr. at 682-83 n.4 (citing State v. Adams, 418 N.W.2d 618 (S.D. 1988))(emphasis in original).

185. People v. Shirley, 641 P.2d 775, 797 (Cal. 1982).

186. People v. Reilly, 242 Cal. Rptr. 496, 509 (Cal. Ct. App. 1987)(quoting People v. Guerra, 690 P.2d 635, 656 (Cal. 1984))(emphasis added).

187. *Reilly*, 242 Cal. Rptr. at 509 (quoting People v. Brown, 709 P.2d 440, 450 (Cal. 1985)).

188. The judges in some cases have indicated that the relevant scientific community is

At the hearing, the proponent of the evidence has the burden of bringing in suitable expert witnesses willing to testify to the acceptance of the technology in the scientific community. In order to testify, the witness(es) must be properly qualified by the court as expert(s) in the field. With the help of the attorney, the proponent's expert witnesses must establish, by a preponderance of the evidence, that the method is reliable and accepted within the scientific community. Thus, the proponent of the evidence has the burden of making the necessary showing of compliance with *Frye*, (i.e., of demonstrating by means of qualified and disinterested experts that the new technique is generally accepted as reliable in the relevant scientific community).[189]

In addition to the reliability of the evidence and the qualification requirements for expert witnesses, there is a "correct procedure" prong in the *Kelly-Frye* standard.[190] Thus, it must be determined that the technique was performed reliably in the case at issue, before the evidence may be presented to the trier of fact.[191] If the test procedure was not reliably performed, then the evidence should not be admitted. This requirement highlights the necessity for the attorneys to be familiar with the lab and personnel who conducted the DNA analysis.

In addition to correct laboratory procedures, attorneys must be familiar with the statistical methods used to calculate the probabilities that the person on trial is the one responsible for the crime. This is largely due to the large amount of discussion regarding the admissibility status of statistical evidence.

For example, in *People v. Collins*,[192] the prosecution's use of statistical approximation was criticized on two levels: (1) the prosecution failed to introduce proof of the probability of individual events; and (2) the prosecution failed to present any proof of the mutual independence of those individual frequencies. However, this decision does not stand for the proposition that in the face of

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not limited to forensics, but encompasses the entire scientific community which uses PCR. People v. Moffett, No. 103094 (San Diego County Super. Ct. May, 1991); People v. Quintanilla, No. C-23691 (San Mateo County Super. Ct. Aug. 16, 1991). However, there have been other *Kelly-Frye* hearings in which the PCR evidence was excluded as not being accepted in the relevant scientific community. People v. Mack, No. 86116 (Sacramento Super. Ct. Sept. 1990).

189. *Shirley*, 641 P.2d at 796. *See also, Brown*, 709 P.2d at 447-448, and *Kelly*, 549 P.2d at 1244.

190. *Kelly*, 549 P.2d at 1244.

191. *Reilly*, 242 Cal. Rptr. at 513-14; *People v. Dellinger*, 209 Cal. Rptr. 503, 509-10 (Cal. Ct. App. 1984).

192. 438 P.2d 33 (Cal. 1968).

disagreement regarding the quality of proof on either of these points, a trial judge has the authority to preclude their presentation to the jury.

In *People v. Yorba*,[193] the court followed well established California precedent in finding that statistical estimations based on biological evidence is a weight and not an admissibility issue, particularly when the estimations are based on the application of long-standing scientific principles.[194] It would certainly seem that the Mendelian inheritance exhibited by HLA DQα would fall into the category of "long-standing scientific principle." Even test procedures which have the potential for statistical estimation, but which yield only equivocal results, have been deemed admissible.[195] The simple fact that a defendant is not excluded by test results has been found relevant for the jury to learn.[196] Thus, the population genetics and frequencies associated with PCR and RFLP should go to the weight of the evidence, not its admissibility.

Nonetheless, many commentators have argued that DNA evidence should be regarded as unreliable unless and until detailed evidence on population structures is available.[197] However, probabilities have been used for many years. Thus, there is no reason to summarily disregard them simply because they are applied to DNA analyses. A "statement of a probability is, by its nature, a statement of partial knowledge, so it is paradoxical to imply that in principle we cannot calculate the probability of an event without further empirical knowledge."[198] Much is already known about the population substructures for various loci, including DQα. Also, when is enough, enough? When would the opponents to the use of DNA in court cases be satisfied that the population studies were sufficient and the statistical methods appropriate?[199]

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193. 257 Cal. Rptr. 641 (Cal. Ct. App. 1989).

194. *Id.* at 645-646.

195. In People v. Cooper, 809 P.2d 865 (Cal. 1991), two cigarette butts found at a crime scene were analyzed in an attempt to determine whether the defendant might have smoked them.

This endeavor would have been much easier if PCR had been used to analyze saliva on the cigarette butts. M.N. Hochmeister et al., *PCR-Based Typing of DNA Extracted From Cigarette Butts*, 104 INT'L J. L. MED. 229 (1991).

196. *Cooper*, 809 P.2d at 888.

197. *See, e.g.*, R.C. Lewontin & D.L. Hartl, *Population Genetics in Forensic DNA Typing*, 254 SCI. 1745 (1991).

198. John Brookfield, *Law and Probabilities*, 355 NATURE 207 (1992).

199. See D.A. Stoney, *Reporting of Highly Individual Genetic Typing Results: A Practical Approach*, 37 J. FORENSIC SCI. 373 (1992) for a detailed discussion of the interpretation of serologic typing data, population genetics, statistics, and the peculiarities of DNA testing in the forensic arena.

B. *The Bar's Response to DNA Testing*

It is somewhat surprising that defense associations are so adamantly opposed to DNA tests when they can absolutely exclude a person on trial from being the perpetrator of the crime.[200] A good example is the first suspect arrested in the *Quintanilla* case, but exonerated based on PCR typing.[201] Of 250 PCR cases, 70% of the PCR analyses were requested by the prosecution and 30% by the defense.[202] In 198 cases, 35% resulted in the exclusion of the suspect and 65% in inclusion; the same percentage of inclusions was obtained for cases done at the request of the prosecution as those done at the request of the defense.[203]

The power of exclusion represents much of the benefit provided by PCR. If a suspect is excluded, that's it. If a suspect is included, that's all it means. Other evidence will be needed in order to conclusively establish that the person is indeed the true culprit. The defense should consider the possibility that without DNA evidence, an innocent person may be convicted.

The high rate of exclusions (including inconclusive results) may be due to various factors, including the irrelevance of the evidence to the crime, or, in sexual assault cases, the failure of the rapist to ejaculate, or recent sexual activity of the victim.[204] Until additional systems are developed which will enhance the discrimination power of the tests, other testing methods and/or evidence will be required in order to result in conviction. Because DNA testing is so useful to the innocent defendant, one would think that defense attorneys would be more circumspect in their evaluation of the methods. Post-conviction reversals due to PCR test results have been obtained in at least five cases.[205] It is rather hypocritical to oppose the admission of DNA tests when the prosecution is the proponent of the evidence, but vigorously work for its admission when

200. Edward T. Blake et al., *Polymerase Chain Reaction (PCR) Amplification and Human Leukocyte Antigen (HLA)-DQα Oligonucleotide Typing on Biological Evidence Samples: Casework Experience*, 37 J. FORENSIC SCI. 700 (1992). *See also*, Sherman, *supra* note 1.

201. *See supra* note 8.

202. Blake et al., *supra* note 200, at 721.

203. *Id.*

204. *Id.*

205. Telephone Interview with Edward Blake, Forensic Science Associates (Nov. 5 1992). These defendants include Gary Dotson (Illinois), Woodall (West Virginia), Joe Jones (Kansas), Steve Linscott (the "dream slayer") (Illinois), and Cary Cotler (New York).

In the Woodall case, the defendant recently settled with West Virginia for $1 million, the maximum sum which he could have received had there been a trial. This settlement was apparently arranged by the state in order to avoid revealing the full extent of prosecutorial misconduct which occurred during Mr. Woodall's trial. *Id.*

the defense is the proponent.[206] Indeed, this appears to be the case in an on-going attempt by Peter Neufeld, a prominent New York attorney, to reverse the New York conviction of a man serving time for rape.[207] Mr. Neufeld has been against the admission of DNA results.[208] However, as it now appears that PCR will be able to exonerate a client, he has become a proponent of the test.

To date, there have been no cases in which an innocent defendant has been convicted solely on the basis of DNA analysis. Such a circumstance is likely to never occur. Indeed, in a recent Connecticut case, the jury completely disregarded the exonerating DNA evidence.[209] "At times, testing fails to produce results, but it has never created false positives."[210]

One author argues that the rights involved in criminal trials are so overwhelmingly important that such a new technology should not be used.[211] However, these arguments are greatly diminished by the fact that PCR is used in many life and death settings, many of which involve no "suspect."[212] For example, PCR is used in genetic counselling[213] and may contribute to the decision of a couple to terminate a pregnancy should the fetus be severely de-

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206. Judge Mudd noted that in different cases, both the prosecution and the defense have opposed PCR. Reporter's transcript, at 1010, People v. Moffett, No. 103094 (San Diego Super. Ct. 1991). Judge Mudd views this as indication that PCR is ready for the courtroom; it isn't any different from any other evidence—"if it's for you, you're willing to support it; if it's agin you, you're willing to challenge it." *Id.* at 1010. He found it an interesting and telling factor that in a number of cases, the defense had found it necessary to support PCR. *Id.* at 1010-1011.

207. As relayed by Edward Blake, *supra* note 205. *See also*, Sherman, *supra* note 1.

208. *See* Peter J. Neufeld and Nelville Colman, *When Science takes the Witness Stand*, SCI. AM. May, 1990, at 46.

209. In March 1990, a six-person jury ignored the exculpating DNA evidence analyzed for the defense by the FBI laboratory and convicted Ricky Hammond of a 1987 kidnapping and rape. *See Connecticut's Doubtful Claim to Fame: DNA Results Rejected by Jury*, SCI. SLEUTHING NEWSL., Winter 1990, at 6; Jack Ewing, *Connecticut Jury Disregards DNA Test*, NAT'L L.J., Apr. 23, 1990, at 9.

In *Moffett*, Judge Mudd noted that, "I don't think trial lawyers give jurors enough credit for being intelligent, because my personal experience with RFLP was that in jury questionnaires they were able to put that particular evidence in the context of the entire trial and give it the weight to which they felt it to be entitled." Kelly/Frye Hearing Transcript at 1014, People v. Moffett, CR-103094 (San Diego Super. Ct. 1991).

210. L. Koblinsky, *Recovery and Stability of DNA in Samples of Forensic Science Significance*, 4 FORENSIC SCI REV. 67, 79 (1992).

211. *See* Hoeffel, *supra* note 1, at 495.

212. The fact that life and death decisions are being made daily based on PCR made such a significant impression on Judge Mudd, that he commented on Judge Tochterman's finding that in criminal law, the standard must go beyond that acceptable in the medical, scientific and research communities. Reporter's Transcript at 1007, People v. Moffett, No. 103094 (San Diego Super. Ct. 1991).

213. This also includes determining the sex of a fetus. Michal Witt & Robert P. Erick-

formed or genetically "defective." The couple is able to make the tough, yet informed decision concerning whether to terminate the pregnancy or be prepared for a child with special requirements and needs should they choose to continue the pregnancy. The use of PCR in the genetic assessment of fetuses is most certainly of life and death importance and magnitude.

The use of PCR in genetic counselling may impact the choice of prospective parents to even conceive.[214] If they know that they are extremely likely to have an infant with serious mental and/or physical impairments, a couple may be more likely to adopt a healthy child rather than take the risk of having their own.

With the overwhelming acceptance of PCR in a wide variety of scientific disciplines and its increasing court acceptance, admissibility should soon be an issue of the past. The fight can then be shifted to the weight of the evidence, as it is with most other types of physical evidence presented at trial. Whether the laboratory is reputable, conducts "good" science, and follows established protocols will become the primary focus. If the laboratories conducting the tests meet the strictest of controls, then the evidence should be allowed to speak for itself in either implicating or exonerating the involved person. Expert witnesses should help, rather than hinder the court in understanding the technologies and their limitations.

C. *Expert Witnesses*

In view of its widespread use and overwhelming adoption by a great number of scientists working in numerous disciplines worldwide, it is very difficult to imagine that a molecular biologist with any practical experience would agree to testify that PCR is unreliable and not useful in the appropriate scientific community.[215] Perhaps the availability of generous expert witness fees and the perceived ego-boost associated with legal recognition as an "expert" has led some scientists, traditionally short of funding for their research projects to make statements in court which are not only misleading, but are actually false.

Great care must be used in the selection of expert witnesses.

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son, *A Rapid Method for Detection of Y-Chromosomal DNA From Dried Blood Specimens by the Polymerase Chain Reaction*, 82 HUM. GENETICS 271 (1989).

214. *See* Scott C. Kogan et al., *An Improved Method for Prenatal Diagnosis of Genetic Diseases By Analysis of Amplified DNA Sequences*, 317 NEW ENG. J. MED. 985 (1987).

215. It is even included as an important part of the most recent genetics textbooks such as SINGER & BERG, *supra* note 9, at 420-25.

One author suggests that qualified experts should exhibit the following:

> (1) undergraduate and graduate degrees in the relevant field of expertise, (2) specialized training in the subject area as it relates to forensics, (3) some training in forensics, (4) those professional licenses or certifications universally required by recognized professional groups in the expert's discipline, (5) evidence of experimentation, teaching, publication within the specialty area, or some combination of these, (6) prior disciplinary evidence that is direct and relevant to the issues or issues being considered. Also desirable would be (1) postgraduate (or postdoctoral) training, (2) publications which appear in (reviewed) sceintific journals, (3) the development of scientifically acceptable tests or procedures, (4) association with, and leadership in, appropriate scientific societies, and (5) experiences as an expert witness.[216]

Not only must expert witnesses in DNA trials be well-informed and current on the most up-to-date technologies, they should also have practical experience in the methods used to analyze DNA. Those "experts" whose only experience has been gained tangentially or solely through the literature should be viewed with great skepticism.

The Court in *People v. Brown*,[217] included an additional caveat—that the witness "must also be 'impartial,' that is, not so personally invested in establishing the acceptance of the technique that he might not be objective about disagreements within the relevant scientific community."[218] Common warning signs that an expert witness is biased include, that he/she (1) is exclusively or almost exclusively, a witness for one side (prosecution or defense), (2) makes statements that he/she "could not be wrong," (3) does not describe the evaluation procedures used in his/her laboratory ("they are classified" or "too complex to understand"), (4) does not bring data, materials or the relevant examination results to the courtroom, and/or (5) makes unwarranted (oftentimes vague) personal attacks on opposing witnesses.[219]

Financial ties and potential biases of any expert witnesses should be disclosed in the trial before the jury, not at the admissibility preliminary hearing stage. The court in *New Jersey v. Wil-*

216. H. Hollien, *Expert Witness: Ethics and Responsibilities*, 35 J. FORENSIC SCI. 1414, 1417 (1990).

217. People v. Brown, 709 P.2d 440 (Cal. 1985).

218. *Id.* at 448.

219. Hollien, *supra* note 216, at 1416.

liams[220] stated that, "evidence of the financial rewards that a witness or a corporation with whom he is associated will gain from the use of the new scientific technique will surely be presented to the jury which can determine what weight, if any, to give to the testimony of each expert."[221] As the State in the same case contended, "simply because learned experts earn a living with their expertise should not prohibit the admissibility of their opinions."[222] Impartiality concerns have lead to many discussions regarding the testimony of scientists who are very involved in the development and use of new technology, usually within the industry setting. However, there are those within the academic research community who could be viewed as biased one way or another regarding the technology.[223] Perhaps the ties of all experts should be disclosed to the jury. It is possible that jurors would be shocked at the very generous fees collected by expert witnesses, some of whom seem to be on the "circuit" so to speak, ready and willing to testify for a fee.

One product of the litigation involving DNA typing has been the development of a "cottage industry" or "welfare state" of defense experts (including some attorneys) who travel around the country to testify against the admissibility of DNA testing. For many of these experts, most of their yearly income is derived from in-court testimony.[224] Various authors have expressed concern about the ethics or advocacy displayed by some experts.[225] Perhaps, as some authors have suggested, the court should appoint and pay for expert witnesses, as courts do in other countries.[226]

Regardless of their source of payment, it is possible that personal vendettas and a desire to continue a controversy long after it has been resolved (quite possibly in order to continue collecting expert witness fees) will continue to greatly disserve the legal and scientific communities and justice system. Instead of directly addressing the issues in the case, the attorneys, judges and juries are forced to witness the in-fighting and personality conflicts between scientists who sometimes have egos as large as their counterparts in

220. No. 1991 WL 276327, at *7 (N.J. Super. L. Aug. 5, 1991).

221. *Id.*

222. *Id.*

223. Perhaps this is fostered by the highly competitive "publish or perish" mentality within academia. It is undoubtedly a resume enhancer if a scientist can include testifying in court regarding science.

224. Clarke, *supra* note 76, at 27-28.

225. *See* Hollien, *supra* note 216, at 1415 for a list of references which express this view.

226. Holden, *supra* note 173; and Rylaarsdam, *supra* note 173.

the legal profession.[227]

Some scientists, by succumbing to the seductive aspects of testifying in court, have done much to discredit themselves in the eyes of the scientific community at large. Many of these people are simply ill-informed. Although they may not intentionally misrepresent the technology, many are unfamiliar with courtroom procedures, cross-examination, and/or forensics and are made to look like fools through their own testimony.[228]

Expert witnesses must be familiar with the techniques used in the particular case in which they are testifying. Many principal researchers within the academic community are professors who do very little actual laboratory research; they are often forced to leave the "bench work" to their post-doctoral fellows, graduate students, undergraduates and technicians. The reality of the academic situation is that professors must devote time to acquiring and administering grants, serving on school committees, advising graduate, undergraduate and potential students, preparing and presenting papers at professional meetings and for publication, participating in school events, as well as teach. It is easy to see why many academics simply do not have the time to conduct much hands-on research themselves. However, it is only through the practical application of these techniques that a scientist will become sufficiently familiar with the methods to testify fairly and accurately.

One embarrassing example is the testimony of Dr. Mary-Claire King, an expert witness who testified in the *People v. Mack*[229] and *People v. Mello*[230] *Kelly-Frye* hearings regarding the AmpliType™ DQα test kit. In the *Mack* hearing, Dr. King stated that she was not aware of the results of the test kit blind trials conducted by the California Association of Crime Laboratory Directors and that these results had not been published.[231] However, the results of the first round were published in 1988. She also admitted that she was in error when she stated in the *Mello* hearing that Alan Wilson developed PCR technology.[232] Furthermore, she admitted that she had not even read the protocol manual used in conjunction with the

227. *See* Reporter's Transcript, at 53-54, People v. Williams, No. 110047 (San Francisco Super. Ct. 1983); People v. Brown, 709 P.2d 440 (Cal. 1985).

228. *See, e.g.*, Reporter's Transcript, at 2248-2252, People v. Mack, No. 86116 (Sac. Super. Ct. 1990) [hereinafter, Mack Transcripts]. *See also*, Hollien, *supra* note 216 at 1416-1417.

229. Mack Transcripts, *supra* note 228.

230. Reporter's Transcript at 3480, People v. Mello, No. 27819 (Riverside Super. Ct. 1989) [hereinafter Mello Transcripts].

231. Mack Transcripts, *supra* note 228, at 2244-2247.

232. Mello Transcripts, *supra* note 230, at 2248-2250.

AmpliType™ DQα test kit ("AmpliType™ User Guide")[233], although she testified that she had used the kit. She also testified that she learned about PCR from a paper on the extinct quagga;[234] the "quagga paper" did not even involve the use of PCR.[235]

This type of testimony is a shining example of why the academic community is not necessarily the best source for expert witnesses, contrary to the admonitions of Thompson and Ford, two commentators on the use of DNA testing who stated that "[t]o find experts who are "disinterested and impartial," courts will need to look to the academic community."[236] It would seem highly probable that an expert in PCR and molecular biology would at least know who originally developed PCR technology. An indignant contingent of scientists very knowledgeable in PCR and molecular biology were sufficiently outraged by the *Mello* admissibility hearings to publish a response to the inaccurate interpretation of the DQα evidence.[237]

Justification for the use of academicians as expert witnesses has also included such statements as "[m]ost studies evaluating DNA typing are published by employees of these companies, or university researchers who have a financial relationship with these companies."[238] However, with the literally thousands of articles on PCR and DNA typing published in the scientific literature, this statement is very difficult to defend.

It is also important for the legal community to realize that one of the major goals of the scientific literature is to present materials, methods and results of particular experiments and investigations, especially in peer-reviewed journals.[239] Scientific articles must be published in a manner such that the experiments may be repeated by others. Results from these repeated experiments are published which either confirm or dispute the procedures and/or results of the original experimenters. It is through this continual interaction between researchers, that scientific principles develop and gain acceptance.

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233. *Id.* at 2234-2236, 2281-2282.

234. *Id.* at 3480.

235. Higuchi et al., *supra* note 45.

236. *DNA Typing, supra* note 133, at 59. *See also,* Ricardo Fontg, *supra* note 29, at 530.

237. Henry A. Erlich et al., *Reliability of the HLA-DQα PCR-based Oligonucleotide Typing System*, 35 J. FORENSIC SCI. 1017 (1990).

238. *DNA Typing, supra* note 133, at 59.

239. Given the large number of comments and articles in the legal literature which contain erroneous material regarding DNA testing and methods, perhaps the legal profession should consider adopting a peer-review process for law reviews.

It is very unlikely that there is a paper published in the scientific literature which refutes the statements and results of the Higuchi et al. paper,[240] called into question by Thompson and Ford[241] because two of the authors, Higuchi and Erlich are Cetus researchers. Also, not mentioned in the Thompson and Ford article, the other two researchers involved, Celia von Beroldingen and George Sensabaugh, were associated with the University of California, not Cetus. Regardless of their affiliation, just because a scientist works for a particular company does not mean that he or she will be unethical on the witness stand or in the scientific press. To do so is professional suicide. Such persons are eventually discovered and made to pay the price, a good example being the recent investigations into Gallo's laboratories regarding the discovery of HIV.[242] Whether a scientist works in the biotechnology industry or at an university, it does not necessarily mean that they leave their ethics at home when they come to testify in court.

D. *The Impact of People v. Castro*[243]

Easily the most discussed DNA case, *Castro* has become the signal case used by those opposed to the use of DNA evidence, as it represents the first successful challenge to DNA typing evidence. However, despite the outburst of criticism and dire predictions in the legal and lay literature, *Castro* has not been repeated.

Although others may disagree, and although the case did not even involve a "crime lab" per se, the fiasco of *Castro* has had both positive and negative effects on forensic science. Notwithstanding the outcry regarding the case, the impact of *Castro* in New York courts appears to be minimal, as demonstrated by subsequent cases.[244] In many respects, the entire *Castro* incident was really nothing more than a tempest in a teapot.

> What has been lost in the excitement generated by the case is the fact that the opinion is merely the trial court's assessment of a legal issue which the prosecution had rendered moot by conceding in its brief that the evidence of a match in DNA patterns was inadmissible. Mr. Castro later pled guilty, thus the soundness of the trial court's legal opinion will never be reviewed on

240. Higuchi et al., *supra* note 126.

241. *See DNA Typing, supra* note 133, at 59.

242. Malcolm Gladwell, *At NIH, An Unprecedented Ethics Investigation: New Questions Involving Scientist Robert Gallo and Discovery of HIV Being Probed*, WASH. POST, Aug. 17, 1990, at A8.

243. 545 N.Y.S.2d 985 (N.Y. Sup. Ct. 1989).

244. *See, e.g.*, People v. Shi Fu Huang, N.Y.S.2d 920 (N.Y. Co. Ct. 1989).

appeal.[245]

On the positive side, *Castro* put the laboratories conducting DNA testing on notice that the judicial system is not willing to accept evidence based on sloppy and questionable test methods. While the *Castro* court declined to state that evidence gained through proper procedures would be inadmissible, it did exclude the evidence in this case because Lifecodes, the lab hired to conduct the DNA (RFLP) tests, did not even follow its own guidelines.[246] *Castro* also points out some areas in which attorneys can deal with this type of data and possibly find sources of error.[247]

On the negative side, *Castro* provided much fodder for the opponents of DNA testing who sensationalize the issues and claim to consider DNA testing as either unreliable, unverifiable, too invasive of privacy and/or simply too difficult and complex to understand.[248]

One bit of science that the *Castro* court seized upon was the "mixing" experiment. While in its judicial activism mode, the court made several suggestions to the scientific community regarding certain procedures, one of which was the mixing experiment proposed by Lander, a prominent population geneticist. Lander insisted that if one mixed a known sample with an unknown sample which was thought to be from the same source prior to performing RFLP, then if the bands moved to the same place on the gel, they could be from the same source.[249] While this type of solution to bandshifting in RFLP may be appropriate for paternity cases, it has been shown to be unworkable in forensic cases.[250] Unfortunately, the *Castro* court gave great weight to this advice.

Other aspects deserving of mention include: (1) all of the evidence was consumed in the testing; (2) the trial court ruled that the forensic DNA identification test met the *Frye* standard; (3) the court ruled that population frequency data should be related to the

245. Rockne Harmon, *DNA Fingerprinting Critics Titillate Rather Than Inform*, L.A. DAILY J., March 14, 1990, at 6.

246. *Castro*, 545 N.Y.S.2d at 997.

247. Roger Parloff, *How Barry Scheck and Peter Neufeld Tripped Up the DNA Experts*, AM. L., Dec. 1989, at 50.

248. *See* Petrovich, *supra* note 133; Pearsall, *supra* note 133; Lander, *supra* note 112; Hoeffel, *supra* note 1. These are but a few of the multitude of review articles covering *Castro* and the problems encountered.

249. Lander, *supra* note 112.

250. McNally et al., *Increased Migration Rate Observed in DNA From Evidentiary Material Precludes the Use of Sample Mixing to Resolve Forensic Cases of Identity*, 1 APPLIED THEORETICAL ELECTROPHORESIS 267 (1990), discussed in Amicus Curiae's Brief at 29, People v. Barney, No. A048789 (Cal. Ct. App. 1 Dist. 1991).

weight of the evidence, not the admissibility; (4) the court rendered an opinion in spite of the prosecution's concession that the match between the samples was unreliable and therefore inadmissible; (5) the results conceded by the prosecution to have been unreliable and deemed by the court to have been deficient were later demonstrated to have given the correct result; when Mr. Castro later pled guilty, he admitted that the blood on his watch spattered there when he stabbed the victim; (6) private labs such as Cellmark and Lifecodes are not crime labs per se, and their analysts are molecular biologists who generally have no appreciation for the characteristics of forensic samples, nor the considerations involved in testing them; and (7) because there was a guilty plea, the legal soundness of the trial court's decision will never be examined on appeal. One development, due largely to the debacle of *Castro*, has been the call for state and/or federal regulations pertaining to the use of DNA evidence.

PROPOSED REGULATIONS

A. *History*

In the forensic science world, regulations have long been controversial. Unlike clinical laboratories,[251] crime laboratories are not subject to regulation.[252] Many criminalists have long felt that there is no need for outside regulation because, in contrast to the clinical setting, crime laboratories are subject to rigorous review by courts and juries.[253] While this is true, there has been much concern voiced in the legal and forensic literature regarding the need for regulation through some other mechanism.[254]

A recent report by the Committee on DNA Technology in Forensic Science, as approved by the National Research Council

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251. Clinical laboratories are subject to various regulatory programs and agencies, including the Health Care Financing Administration (HCFA) of the U.S. Department of Health and Human Services and the Joint Commission for the Accreditation of Hospitals and Health Care Organizations (JCAHO). The most recent major legislation concerning clinical laboratories was the Clinical Laboratory Improvement Amendments of 1988 (CLIA), Pub. L. No. 100-578, 102 Stat. 2901 (1988) which addresses the need for uniform federal proficiency testing standards. *See also*, 55 Fed. Reg. 20,896 (1990); 42 C.F.R. Parts 405, 416, 440, 482, 483, 488 and 493.

252. The exception to this is blood alcohol analysis, which in California is administered by the Department of Health Services under Cal. Admin. Code Title 17.

253. Interview with Gordon Deeg, Senior Criminalist, San Mateo Police Department, in San Mateo, CA (Oct. 5 1992).

254. David Helvarg, *Crime Labs Under the Microscope*, CAL. L., Dec. 1991, at 43; Simon J. Young, *DNA Evidence—Beyond a Reasonable Doubt?*, 1991 CRIM. L.R., 264. *See also*, Mark Thompson, *DNA's Troubled Debut*, CAL. L., June 1988, at 36.

(NRC),[255] and the FBI's Response to that Report stress the necessity for national standards.[256] The call for standards is primarily related to a desire to instill public confidence in the accuracy and reliability of DNA test results.[257] Contrary to the disinformation published in the lay press upon the release of the Report by the Committee on DNA Technology in Forensic Science,[258] the Committee did not conclude that "courts should cease to admit DNA evidence until laboratory standards have been tightened and the technique has been established on a stronger scientific basis."[259] The Committee does however emphasize the need for a high level of quality control in the collection, analysis and interpretation of data. It also recommends standardization of laboratory procedures, and establishment of a mandatory accreditation program.[260] While most of the concern is related to proficiency testing for RFLP methods, PCR is also included.

While there are problems associated with allowing the court system to determine the quality of DNA testing, there is no need for courts to stop admitting evidence obtained through properly conducted and analyzed DNA test procedures. Concerns regarding the courts' ability to determine the quality of DNA testing include the fact that courts only see a fraction of a forensic scientist's analyses.[261] Also, if the charges are dropped against a suspect, the court will never see the evidence, regardless of the analytical result. As they do not have the expertise, resources or mechanisms to control or supervise scientific quality control programs, courts should not be expected to do so. Although the court is not the ideal forum for ensuring quality science, the adversary process is a means by which those who practice "bad" science may be discredited, while those who practice "good" science may enjoy the credibility they deserve.

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255. COMMITTEE ON DNA TECHNOLOGY IN FORENSIC SCIENCE, DNA TECHNOLOGY IN FORENSIC SCIENCE (1992) [hereinafter DNA TECHNOLOGY].

256. FEDERAL BUREAU OF INVESTIGATION, U.S. DEPARTMENT OF JUSTICE, RESPONSE TO THE REPORT BY THE COMMITTEE ON DNA TECHNOLOGY IN FORENSIC SCIENCE (1992) [hereinafter FBI RESPONSE].

257. John W. Hicks, *Message From the Assistant Director in Charge of the FBI Laboratory*, 19 CRIME LABORATORY DIG. 41, 41 (1992).

258. Gina Kolata, *U.S. Panel Seeking Restriction on Use of DNA in Courts*, N.Y. TIMES, Apr. 14, 1992, at A1, A1.

259. *Id.*

260. DNA TECHNOLOGY, *supra* note 255, at 97-110; Victor A. McKusick, *Opening Statement*, April 14, 1992 (unpublished).

261. *See* Randolph N. Jonakait, *Forensic Science: The Need for Regulation*, 4 HARV. J. L. TECH. 109, 166-172 (1991), for a discussion of the courts and the quality of forensic science.

Quality control/quality assurance[262] is the responsibility of those working in the laboratories. As with all professions, there are no doubt individuals within forensics who do not act responsibly nor even ethically. However, there are also many individuals within the field who take professional pride in their work, act responsibly, and treat their duty to the court with respect and honesty.

It is unfortunate that both the lay and legal literature on crime labs has stressed the problems in such a way that it would appear that every lab within the U.S. is inept and incompetent.[263] This may be at least partially fostered by the fact that while many criminalists are scientists who work in the law enforcement setting, some technicians working in crime labs have law enforcement backgrounds, but no science education.[264] This is an area of concern, as sometimes unqualified individuals attempt to undertake responsibility that is beyond their capabilities. However, just because a technician is involved in a case does not mean that their work is shoddy. Technicians perform tasks according to strict protocols and their work is overseen by a supervisor. They have no authority to make procedural changes nor the latitude to exercise judgment. In contrast, the forensic scientist or analyst is foremost a scientist who conducts the preliminary assessments of evidence as it is received, identifies the legal and/or investigative questions which must be answered in the case, and develops the analytical strategies to answer those questions.[265] The analyst either assigns the project to someone or conducts the analysis himself/herself, and then must interpret the results. If there are any discrepancies or questions regarding the test accuracy, the approach is to re-analyze the evidence.

The ultimate results must then be explained in an impartial, non-technical way to law enforcement personnel, attorneys, judges

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262. Or, as it is now often termed, "continuous quality improvement."

263. Helvarg, *supra* note 254; George J. Annas, *DNA Fingerprinting in the Twilight Zone*, HASTINGS CENTER REP., March/April 1990, at 35; Randolph N. Jonakait, *supra* note 261; Edward J. Imwinkelried, *The Debate in the DNA Cases Over the Foundation for the Admission of Scientific Evidence: The Importance of Human Error as a Cause of Forensic Misanalysis*, 69 WASH. U. L.Q. 19 (1991).

264. Helvarg, *supra* note 254, at 44.

265. George Sensabaugh, *Genetic Typing of Biological Evidence, Comments for the Cooper Amicus Brief*, CAL. ASSOC. CRIMINALISTS NEWSL., July 1987, at 11, 16.

As exemplified by the court in People v. Young, 381 N.W.2d 270 (Mich. 1986), some courts and experts have a misguided belief that a higher degree (e.g., Ph.D.) is a prerequisite for status as a scientist, or perhaps without a higher degree, one can't be anything more than a technician. A scientist is a person who does science, regardless of the initials after their name. The better assessment criteria are the responsibilities and expectations associated with the person's position in employment and in the scientific community to which they belong.

and juries. Thus, the forensic analyst bears a substantial burden of responsibility for knowing what to do, how to do it and how to explain it in terms understandable to the layperson. Regardless of its importance, forensics training is often not readily available to many experts.[266] This is a great disservice to the legal system, as the expertise of many scientists goes unappreciated and misunderstood by juries and judges.

B. *Validation Studies, Standards and Proficiency Testing*

As with any new technology, validation studies and proficiency testing have been facets in the development of the AmpliType™ HLA DQα test kit. Concurrently, the growth of DNA analysis stimulated much discussion and study into the regulation of laboratories conducting DNA testing. "Setting standards for forensic applications of DNA testing is the most controversial and unsettled issue. Standards are necessary if high-quality DNA forensic analysis is to be ensured, and the situation demands immediate attention."[267] In a recent case, *People v. Schwartz*,[268] the Minnesota Supreme Court denied the admissibility of DNA test results on the grounds that the lab performing the test did not meet TWGDAM Guidelines or provide proper discovery.[269] TWGDAM is the FBI's Technical Working Group on DNA Analysis Methods which is charged with examining quality assurance, population statistics and databanking. TWGDAM held its first meeting in November 1988, and its members include representatives from crime labs which are implementing or close to implementing DNA analysis, and commercial laboratories.[270] It is somewhat ironic that at the time the evidence was analyzed in *Schwartz*, there were no TWGDAM guidelines available to follow.

Various professional organizations, such as the American Society of Human Genetics, the California Association of Crime Laboratory Directors (CACLD) and The Society for Forensic Haemogenetics, have published official statements or position papers regarding DNA analysis.[271] The interest in establishing a na-

266. Hollien, *supra* note 216, at 1416-1417.

267. GENETIC WITNESS, *supra* note 149, at 10.

268. 447 N.W.2d 422 (Minn. 1989).

269. *Id.* at 427-428.

270. GENETIC WITNESS, *supra* note 149, at 13; TWGDAM, *Guidelines for a Quality Assurance Program for DNA Restriction Fragment Length Polymorphism Analysis*, 16 CRIME LABORATORY DIG. 40 (1989).

271. Ad Hoc Committee on Individual Identification by DNA Analysis, The American Society of Human Genetics, *Individual Identification by DNA Analysis: Points to Consider*, 46

tionwide DNA database will help foster standardization and conformity; consistency is required if an efficient and useful computerized system is to be established.[272] Setting the necessary standards will require much thought and research.

As must be done with all new test systems, extensive validation studies have already been conducted on PCR. These studies have shown that DQα typing can be accomplished without producing false positive or false negative results.[273]

C. *AmpliType™ Kit Development*

Validation and proficiency testing have been important aspects of the AmpliType™ kit since its inception. In 1986, the FBI approached Cetus about PCR-based forensic DNA typing. In 1989, a prototype DQα typing system was sent to the FBI and beta testing of the Cetus AmpliType™ kit began. From 1989-1990, over 3,000 samples were analyzed by the FBI, including fresh samples, dried stains, and samples for population studies. Research on the effects of sample exposure to light, chemical and biological agents was also performed. The AmpliType™ kit did not become available for sale in the U.S. until February, 1990. In March, 1990, it became available in Europe, Australia and Asia. From late 1990 to May 1991, the FBI analyzed over 750 casework samples.[274]

There are also other mechanisms for proficiency testing in place.[275] For example, CACLD conducted two rounds of blind

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AM. J. HUM. GENETICS 631 (1990); *California Association of Crime Laboratory Directors, Position on DNA Typing of Forensic Samples*, CAL. ASSOC. CRIMINALISTS NEWSL., April 1988, at 4; *AABB Parentage Committee: Proposed Standards for Tests Involving DNA Polymorphisms—November 1987, reprinted in* CAL. ASSOC. CRIMINALISTS NEWSL., April 1988, at 5; *Statement of the Society for Forensic Haemogenetics Concerning DNA Polymorphisms, reprinted in* CAL. ASSOC. CRIMINALISTS NEWSL., April 1988, at 5. On Mar. 30, 1990, a resolution was adopted by the CACLD membership to endorse the TWGDAM guidelines for DNA analysis and support establishment of a national forensic data base system based on the FBI's RFLP analysis.

272. Stanley D. Rose & Tim P. Keith, *Standardization of Systems: Essential or Desirable?*, BANBURY REP 32: DNA TECH AND FORENSIC SCI. 319, 319 (1989); and Henry C. Lee & Robert E. Gaensslen, *The Need for Standardization of DNA Analysis Methods*, BANBURY REP 32: DNA TECH AND FORENSIC SCI. 217 (1989).

273. Catherine T. Comey et al., *Validation Studies on the Analysis of the HLA DQα Locus Using the Polymerase Chain Reaction*, 36 J. FORENSIC SCI. 1633 (1991).

274. Sharon Reid, U.S. and International Use of the AmpliType™ Kit, presented at a PCR Workshop Presented by Cetus for the California Association of Criminalists (May 18, 1991).

275. Proficiency testing is currently offered through programs such as the Collaborative Testing Service (CTS), in association with the Forensic Science Foundation (FSF). Participation in this program is voluntary and anonymous. It includes physiological fluids and samples for DNA testing. GENETIC WITNESS, *supra* note 149, at 79-80.

proficiency tests with Cellmark, Lifecodes and Forensic Science Associates/Cetus (FSA/Cetus).

D. *California Association of Crime Laboratory Directors (CACLD) Tests*

In the first round of 51 samples, Lifecodes obtained DNA results from 37 samples and made no errors. In its set of 50 samples, Cellmark obtained DNA results from 44 samples and made 1 incorrect match. This was a human error which was subsequently remedied by purchasing a large capacity centrifuge, thereby reducing sample manipulation. FSA/Cetus obtained results for all 50 of the samples provided. There was one incorrect match reported. Again, this was due to a human error (failure to introduce a sample into the appropriate chamber or a bubble in the vacuum apparatus), which was subsequently remedied by the routine testing of all samples in duplicate.[276]

In the second round of testing, all three laboratories received 50 samples. Lifecodes obtained results for 48 samples, while FSA/Cetus obtained results for all 50 samples. Neither Lifecodes nor FSA/Cetus reported any incorrect matches. Cellmark obtained results for 45 samples, reported that two samples gave inconclusive results and made one incorrect match.[277]

The errors made in the blind trials were all human errors, not errors that decreased the reliability of the procedure itself. In determining the admissibility of a technology, it is important to distinguish between the validity of the technology and the possibility that human error may lead to an incorrect result in the application of that technology. The statistical probabilities obtained with DNA testing (e.g., RFLP) have nothing to do with the possibility of human error in the performance of the test. While the possibility of human error is unfortunate, it can never be totally eliminated.[278]

Apparently, unlike most people (including attorneys, who may also be involved in a case involving life and death), criminalists are subject to a requirement of 100% accuracy. Not only is this unfair to the scientists who are conducting the work, it is impossible. While some commentators decry the errors made in the crime lab as

276. If significantly different results are observed for these duplicate tests, the scientist is on notice that there is a problem and the test should be repeated.

277. Report of CACLD Blind Trial #2, March 29, 1990.

278. Frederick R. Millar, Jr., *DNA: Facts and Myths*, CAL. L., July 1989 at 12 (letter to the editor).

unacceptable,[279] it is important for those within the legal profession to recognize that crime labs are not infallible. As with all professionals, including attorneys, forensic scientists should be held to a reasonable standard of care.

The technology is ready and able to do what it was designed to do; the potential for human error(s) must be recognized and fail-safe protocols must be followed in order to avoid erroneous results. Testing samples in duplicate, saving aliquots of samples for later testing, careful labelling of samples and meticulous record-keeping all help reduce the potential for human error. Thus, there are methods by which forensic scientists may reduce the possiblity of such error. These factors should be taken into consideration when the court addresses the weight, not the admissibility of the evidence.

Critics of proficiency programs argue that the results serve to emphasize the need for tighter control, including mandatory regulation through legislation.[280] In a rather contentious debate, played out in the editorial section of "California Lawyer," it was claimed that in a recent hearing in Ventura, "the president of the California Laboratory Directors and two other association members covered up errors made by a commercial DNA laboratory in a "blind" test of its accuracy."[281] Another author, Mark Thompson also stated,

> [F]or that matter, it turns out the proficiency test wasn't exactly blind. One of the genetic fingerprinting labs, Cellmark Diagnostics, initially turned in its result in a form that was "unintelligible," admitted Margaret Quo head of the Orange County Sheriff's Department crime lab, in recent testimony in a Ventura County hearing. She contacted Cellmark officials, met with them to review the problems, and allowed them to submit cleaned up conclusions three months later. That laundered report is what was released as the results of a "blind" proficiency test.[282]

In a response letter, CACLD DNA Committee members Jan Bashinski, Linda Hartstrom and Margaret Kuo (not "Quo") stated:

> [T]he CACLD DNA Committee conducted the blind trials fairly and honestly. Neither the organization nor the individual committee members and the agencies they represent benefit financially or personally from administering the test irrespective of the outcome. To suggest that we would jeopardize our reputation to help cover up Cellmark's error is ridiculous.[283]

279. Jonakait, *supra* note 261.
280. GENETIC WITNESS, *supra* note 149, at 149.
281. William C. Thompson, *Letter to the Editor*, CAL. L., July 1989, at 16.
282. Mark Thompson, *Letter to the Editor*, CAL. L., July 1989, at 16.
283. Jan Bashinski et al., *More on DNA*, CAL. L., Sept. 1989, at 17.

Mr. William Thompson's statement that there was a cover up regarding the CACLD DNA proficiency study is completely false. The hearing he refers to was in *People v. Axell*,[284] at which, on May 8, 1989, Margaret Kuo testified regarding the CACLD study.

In a responsive "Letter to the Editor," Carol J. Nelson, the prosecutor in *People v. Axell*,[285] stated that claims made in Dr. Thompson's letter were "patently untrue." She suggests reading the transcripts of the *Kelly-Frye* hearing to determine the amount of weight Ms. Kuo's and Mr. Thompson's testimony on both direct and cross-examination should be given. For example, "he is currently earning a significant percentage of his income attacking DNA identification in courts throughout the country. As such, he is hardly an unbiased observer of what is happening in the courtroom or in the field of DNA identification."[286]

This whole sequence of letter exchanges has another layer of involvement. The letter from Mr. William Thompson was printed despite an appeal to the editor by the author to remove the inaccurate reference to a cover-up. Also, the editor was initially unwilling to publish Ms. Nelson's response letter. This led the CACLD DNA Committee to consult an attorney and send a response letter. The editor printed a portion of the letter, not including a reference to the request Dr. Thompson made to alter his original letter to the editor. Thus, in addition to the expert witnesses who travel around the country and testify against DNA testing admissibility in court, the legal press is also distorting the facts regarding cases and testimony.

> As of mid-February 1990, DNA typing evidence has prevailed in virtually every legal skirmish. In spite of this overwhelming success, media portrayals, such as a January New York Times article, "Some Scientists Doubt the Value of Genetic Fingerprint Evidence," continue in their attempts to polarize and sensationalize the issues, often taking quotations out of context. If DNA's legal successes were covered as thoroughly as its few setbacks, the readership would be bored to tears. . . . Opponents of the technology point to their few limited successes, ignoring the reality of the entire legal experience to date.[287]

For the benefit of all who have read the various opinions, the facts were that the blind aspect of the testing was never compromised, there never was a "cover-up," nor has Margaret Kuo given

284. Ventura Sup. Ct. CR-23911, May, 1989.

285. Carol J. Nelson, *Letter to the Editor*, CAL. L., Sept. 1989, at 17-18.

286. *Id.*

287. Rockne Harmon, *supra* note 245, at 6.

any testimony to support this claim.[288]

E. *Federal Legislation*

There have been two bills introduced into Congress which deal with DNA testing. The first bill, H.R. 3371, known as the "DNA Identification Act of 1991" (Edwards bill) was introduced by Representative Don Edwards in 1991 and incorporated into the 1991 Crime Control Act passed by the House of Representatives.[289] This bill was drafted in consultation with the FBI and the forensic community; the FBI has registered its support of the bill.[290] The bill would authorize a DNA advisory board with the responsibility of recommending standards for quality assurance and proficiency testing to the FBI Director, who after consideration, would issue standards to serve as the basis for proficiency testing programs administered by laboratory testing organizations.[291]

The other bill, H.R. 339, known as the "DNA Proficiency Testing Act of 1991" (Horton Bill), was introduced by Representative Frank Horton in January, 1991. This bill requires that states desiring to acquire equipment through federal funds, agree that their labs will meet standard guidelines and participate in proficiency testing at least every six months.[292] This bill proposes that the FBI publish DNA testing standards based on TWGDAM guidelines and that the FBI certify forensic DNA laboratory proficiency testing programs. The bill also provides that the DNA database program under development by the FBI in conjunction with state and local forensic laboratories be tied to the requirements of the Act.[293] The FBI does not support the Horton Bill and opposes a direct regulatory role for itself.[294] Thus, it remains to be determined who will regulate forensic labs who conduct DNA tests.

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288. For accounts of the blind trials, *see Statement of the DNA Committee Regarding the Cellmark Blind Trial Report*, DNA COMMITTEE REPORT (1989).

289. DNA Identification Act of 1991 (H.R. 3371) Title X, Omnibus Crime Control Act of 1991, §§ 1002, 1003, 1004.

290. *The FBI's Responses to Recommendations by the NRC's Committee on DNA Technology in Forensic Science*, 19 CRIME LABORATORY DIG. 55-56 (1992) [hereinafter *The FBI's Response*].

291. *Id.*

292. H.R. 339 (1991).

293. This program, designated CODIS (Combined DNA Index System) is the FBI's national DNA identification system which is being designed to allow the storage and exchange of DNA records submitted by state and local forensic DNA laboratories. FEDERAL BUREAU OF INVESTIGATION, U.S. DEPARTMENT OF JUSTICE, LEGISLATIVE GUIDELINES FOR DNA DATABASES (1991).

294. *The FBI's Response*, *supra* note 290, at 56.

If not the U.S. Department of Health Services, it is likely that the responsibility will fall on the states.

F. *State Regulation*

In addition to the federal government, states have the authority to regulate forensic DNA typing by both private labs and public crime laboratories. At first blush, it would appear that the State Department of Health Services (Health Services) would be the appropriate regulatory branch to oversee forensic DNA labs, as this department is responsible for clinical and public health labs.[295] However, regardless of the source of the regulations, it is important to remember that regulation in itself will not solve all of the problems.

For example, the experience in California crime labs in the context of blood alcohol regulation is very disturbing. The Department of Health Services oversees blood alcohol testing in the state and has set forth very exacting requirements for labs conducting these tests.[296] There are some very real problems in the relationship between the state's labs and Health Services, which could make efficient regulation of DNA labs very troublesome.[297]

In order to avoid the regulatory problems caused by Health Services, the CACLD Professional Practices Committee prepared a legislative proposal in 1989 which would have organized a Board of Forensic Science Practices administered under the auspices of the Department of Consumer Affairs.[298] The Board of Forensic Science Practice was not accepted by the Attorney General's Advisory Board; the Attorney General declined to sponsor legislation to create the bodies recommended by CACLD, and the Governor dropped funding for all of the proposed regional DNA labs with the exception of the Department of Justice lab in Berkeley. Thus, state regulation, at least in California, is on questionable footing.

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295. With the implementation of CLIA *see supra* note 251, public health and other departments may not have the personnel nor funds to initiate involved regulatory programs for forensic laboratories.

296. For example, there are a number of pages of complex regulations governing breathalyzer tests within the CAL. REGS., tit. 17, §§ 1215-1222.2.

297. For example, while there is a mechanism for input to the Health Services Director concerning regulations regarding forensic alcohol analysis provided for in CAL. HEALTH & SAFETY CODE § 436.50 (West 1990)(amended 1992), and an "Advisory Committee" was formed, this committee has not met since 1985. Also, although procedural changes must be submitted to Health Services, it may take three years to gain approval. Telephone Interview with Kathryn Holmes, Contra Costa Crime Laboratory (Jan. 10, 1992).

298. PROFESSIONAL PRACTICES COMMITTEE OF THE CALIFORNIA ASSOCIATION OF CRIME LABORATORY DIRECTORS, REPORT TO THE BOARD (1989).

G. *Self-Regulation*

Self-regulation is another avenue by which the goals of regulation may be achieved without the intervention of a regulatory agency.[299] The California Association of Criminalists has instituted a voluntary written examination for Certificates of Professional Competency in Criminalistics. The test and certification program recognize the variety inherent in criminalistics and are designed to demonstrate that the criminalist has a basic understanding of the underlying concepts, principles and other aspects of the profession.[300] While it is a completely voluntary program, it does represent a step toward responsible self-regulation of the criminalistics profession at the local level.

Because of the diverse subject areas within forensics, a uniform, federal regulatory or proficiency testing program for all of these areas would require a large commitment of manpower, money, effort and time. For example, criminalists may be required to gain expertise in such diverse areas as protein, organic and inorganic chemistry, molecular biology, biology, firearms, arson, explosives, fingerprint comparisons, photography, computers and other electronic equipment, analysis of drugs, soil, fiber, glass, animal and human hair, human and animal sperm, bloodstains, blood spatters, paint, gunshot residue, alcohol, inks and handwriting, questioned documents, and various other disciplines.

Again, the major considerations are economic. Who will pay for all of this? Is the public willing to foot the bill for a system that in most instances already works quite well? There is a fair probability that the cost of regulating all of the subdisciplines within crime labs would be too exorbitant, especially considering all

299. GENETIC WITNESS, *supra* note 149, at 73-75. Self-regulation is also described in Jan S. Bashinski, *Laboratory Standards: Accreditation, Training and Certification of Staff in the Forensic Context*, BANBURY REPORT 32: DNA TECHNOLOGY AND FORENSIC SCI. 159 (1989). The American Society of Crime Laboratory Directors (ASCLD) is another professional forensic science organization which has established voluntary quality assurance programs through a nationwide crime lab accreditation program.

300. *An Open Letter to the Association Membership*, CAL. ASSOC. CRIMINALISTS NEWSL., Jan. 1990, at 10.

The American Board of Criminalistics (ABC) will administer the first ABC General Examination in 1993. ABC Diplomate certificates will be available for those who received the California Association of Criminalists Certificate of Professional Competency in Criminalistics. The ABC certificates will expire five years after their dates of issuance. For Diplomate status, applicants must possess a minimum of an earned baccalaureate degree or its equivalent in a natural science or an appropriately related field from an accredited institution. A minimum of two years full-time experience of active work in criminalistics is also required. "Fellow" status has additional experience and testing requirements. American Board of Criminalistics, Inc., *Certification Process*, Sept. 1992.

of the effort that would be expended to oversee such a comparatively small number of laboratories. The cost-benefit ratio would likely tilt toward non-regulation.

Regardless, the self-regulation route would require much cooperation between crime labs and law enforcement agencies nationwide, if a nationwide DNA database program is to be effective. In some aspects, it also comes back to the legal profession. While the prosecution often has no choice in the laboratory facility used, the defense may utilize any laboratory it wishes. If an attorney uses a laboratory with a questionable reputation, the work product will also seem questionable. It is very prudent to know the strengths and weaknesses of each lab available; the networks within the legal community should make this type of information readily available. With the importance of the issues involved in criminal trials, the choice of crime laboratory (and, perhaps, analytical method) would seem to warrant at least the same amount of consideration as one puts into choosing a family physician.

H. *Who Will Be Regulated, and By Whom*

Regardless of the method, proficiency testing of DNA analysis methods is on its way. It remains to be seen how standards will be implemented. Another unknown is the identity of the agency responsible for implementing these standards. For example, will federal and/or state regulatory agencies (such as Health Services) have roles to play? Hopefully, the regulations will be fair, meaningful, reasonable and practical.

While it appears likely that forensics regulations will be modelled after those for clinical laboratories, the rule-makers must remember that crime labs and clinical labs are very different entities. While they will be able to draw from the experience gained from clinical laboratory regulation in order to keep from reinventing the wheel, crime labs serve very different functions and clientele. Unlike clinical laboratories, crime labs do not have patients who pay for their services. Thus, crime labs cannot pass costs along to consumers. It is highly unlikely that defendants will be made to pay for the evidentiary analyses associated with the alleged crime. Also, who will be regulated—all crime labs, only those associated with police departments, only private labs, etc.? Thus, while regulation and proficiency testing requirements are inevitable, many questions remain, such as:

(1) Who will pay for the proficiency testing?
(2) Who will prepare and distribute the necessary samples?

(3) Will it be mandatory or voluntary?
(4) Will it apply to all laboratories or just those associated with law enforcement agencies (i.e., prosecution)?[301]
(5) What role will state agencies, such as Health Services play?
(6) Will professional societies and organizations have a voice in regulation implementation?
(7) Will regulation extend to other areas of criminalists (e.g., questioned documents, firearms, drug analysis, microscopy, fingerprinting etc.)? and
(8) Will certification of criminalistics be required and if so, how will this be administered?

CONCLUSIONS AND PROGNOSTICATIONS FOR THE FUTURE

While RFLP will undoubtedly continue to be an important test method in DNA analysis both within and beyond the forensic community, it is almost inevitable that PCR will supplant it. The ease of use, the very minimal requirement of a single nucleated cell, and the elegant simplicity of the entire methodology make it particularly attractive for use in the crime lab setting. Although contamination is a potential problem, care in laboratory design and protocols will help ensure that it will not be a factor in genetic analyses of forensic samples. It is quite possible that combination systems like the "AmpFLP's" now available or direct sequencing in combination with PCR will supplant both PCR alone and RFLP.[302]

The development of alternative test systems, including the mitochondrial[303] DNA test procedures used to identify "missing" per-

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301. For example, in California, the prosecution must use an accredited laboratory for its alcohol analyses, while the defense can go anywhere, no matter how incompetent the lab is.

302. *See supra* notes 118-119 for various references other advances have also proven to be significant improvements in PCR analysis. A modified DNA extraction process using Chelex® 100 has been developed, which appears to provide better results and facilitates the combination of PCR and RFLP. Sean Walsh et al., *Chelex 100 as a Medium for Simple Extraction of DNA for PCR-Based Typing From Forensic Material*, 10 BIOTECHNIQUES 506 (1991). Chelex® 100, followed by PCR of DQα and D1S80 were recently used to genetically characterize saliva from cigarette butts. This study included three cigarette butts recovered from two crime scenes (adjudicated cases) and indicated that PCR-based DNA typing is a potential method for analyzing traces of saliva left on such seemingly innocuous pieces of evidence as cigarette butts. Hochmeister, *supra* note 195.

303. Mitochondria are "organelles" contained within cells which serve as the cell's energy factory. Any energy the cell needs to survive or divide is obtained through the intensively biochemically active mitochondria. ALBERTS ET AL., *supra* note 9, at 484-500.

Unlike the other organelles within the cell's cytoplasm (with the exception of the nucleus, the cytoplasm comprises the entire area within the cell), mitochondria contain their own complement of DNA. It is hypothesized that mitochondria represent the evolutionary "remains" of bacteria which infected cells long ago and were commandeered by the cells as

sons in Argentina,[304] also have additional potential for the forensic setting and parentage determinations.[305] As mitochondrial DNA is inherited only through the maternal lineage, the maternal history of a person may be determined by analyzing their mitochondrial DNA.[306] This is also of great potential value in the study of genetic diseases, especially those which have a sex-linked component.

Modified PCR methods designed to analyze RNA have proven to be extremely valuable, especially in the development of medical diagnostic tests. It is also possible that RNA analysis could be utilized in the forensic setting.

The future of DNA analysis as applied to forensics as well as the traditional areas of medical research appears quite bright. Perhaps the best advice to the legal community is to be prepared.[307] Before deciding whether or not to use DNA analysis in court, the attorney will need to obtain many items and much information from the laboratory doing the analysis, and should if at all possible, visit the site in order to get a first-hand feel for the facility and the people doing the work.[308]

As additional techniques and refinements are developed, it is likely that the technology will continue to improve as well. As additional PCR systems are developed, they must be thoroughly characterized and proven to be reliable. During the time the kits are developed and marketed, it would be to the profession's ultimate benefit if they were subjected to the same rigorous standards as are applied to clinical diagnostic test kits. Although this would delay

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energy factories. This is supported by the fact that mitochondria contain DNA which is completely independent of the DNA contained within the nucleus. *Id.* at 541-542.

304. Chris Raymond, *Forensics Experts Tackle Task of Identifying Thousands of 'Disappeared' Victims*, 261 JAMA 1388 (1989).

305. Denise S. Rath & Carl R. Merril, *Mitochondrial DNA and Its Forensic Potential*, PROC. INT'L SYMP. FORENSIC ASPECTS DNA ANALYSIS 113 (1989).

306. Allan C. Wilson & Rebecca L. Cann, *The Recent African Genesis of Humans*, SCI. AM., April, 1992, at 68; and R. Cann et al., *Polymorphic Sites and the Mechanisms of Evolution in Human Mitochondrial DNA*, 106 GENETICS 479 (1984).

307. As legend has it, Pasteur once said, "Chance favors the prepared mind."

308. The decision whether or not to use DNA will require much thought. Be sure to get a copy of the complete lab file for the case, a list of the standard operating procedures (especially those used in your case), a curriculum vitae of the person who performed the test (it might be advisable to also get a copy of their supervisor's curriculum vitae as well), peer-reviewed articles characterizing the probes used in your case, if RFLP was done, a description of the database used in your case (including allele frequencies, sample sources, database size and any ethnic characterizations of the samples) and a description of the method to calculate frequencies and the confidence intervals applicable to the case. Be sure to also get copies of the curriculum vitae for all the expert witnesses you might use. Finally, be sure to determine if there are any relationships between the testing laboratory and the expert witnesses.

the introduction of new methods and/or genetic markers, it would help decrease the amount of court time and written criticism dedicated to the use of genetic markers in the legal system. However, regardless of its future development, a firm foundation of reliability and tremendous usefulness is in place.

OTHER SELECTED ARTICLES:

Allen B. Wagner, *Human Tissue Research: Who Owns the Results?*, 3 SANTA CLARA COMPUTER & HIGH TECH. L.J. 231 (1987).

This article examines ownership issues in relation to human tissue research. The author provides an overview of the research process, the nature of property interest in human tissue research, and methods of accessing human tissue for research. In addition, public policy issues are addressed.

Patricia A. Martin & Martin L. Lagod, *Biotechnology and the Commercial Use of Human Cells: Toward an Organic View of Life and Technology*, 5 SANTA CLARA COMPUTER & HIGH TECH. L.J. 211 (1989).

This article deals with the legal and policy issues concerning the commercial use of human cells raised by *Moore v. Regents of the University of California.*

Adrienne M. Grover, *A New Twist in the Double Helix: Admissibility of DNA "Fingerprinting" in California,* 5 SANTA CLARA COMPUTER & HIGH TECH. L.J. 469 (1989).

This comment provides a description of DNA "fingerprinting" and an in-depth analysis of the admissibility of DNA evidence in California under the *Kelly/Frye* standard.

Naomi Obinata, *Genetic Screening and Insurance: Too Valuable an Underwriting Tool to be Banned from the System,* 8 SANTA CLARA COMPUTER & HIGH TECH. L.J. 145 (1992).

This comment examines the moral and practical implications of allowing insurance companies to utilize genetic screening with respect to underwriting. The author provides background on genetic screening and risk classification by insurance companies. The comment advocates use of genetic screening in the underwriting process and discusses the benefits of genetic screening.

Daniel L. McKay, *Patent Law and Human Genome Research at the Crossroads: The Need for Congressional Action*, 10 SANTA CLARA COMPUTER & HIGH TECH. L.J. 465 (1994).

This comment discusses the need for patent protection of gene fragments. It is the author's position that Congress should take affirmative steps in affording gene fragments patent protection in order to encourage further research in the area. The author provides background on human genome research and examines whether gene fragments are patentable under the then current law.

Shaoyi Alex Liao, *Resolving the Dilemmas between the Patent Law and Biotechnology: An Analysis of Three Recent Biotechnology Patent Cases*, 11 SANTA CLARA COMPUTER & HIGH TECH. L.J. 229 (1995).

The author provides a basic overview of recombinant DNA technology and patent law with respect to biotechnology and, in particular, the doctrine of equivalents. The article analyzes several relevant cases: *Hormone Research Foundation v. Genentech, Inc.*, 708 F.Supp. 1096 (N.D.Cal. 1988); *Scripps Clinic & Research Foundation v. Genentech*, 666 F.Supp. 1379 (N.D.Cal. 1987); and *Genentech, Inc. v. Wellcome Foundation, Ltd.*, 14 U.S.P.Q.2d 1363 (D.Del. Mar. 8, 1990).

Philippe Ducor, *Recombinant Products and Nonobviousness: A Typology*, 13 SANTA CLARA COMPUTER & HIGH TECH. L. J. 1 (1997).

This article discusses the application of obviousness case law to recombinant technology. It provides an overview of recombinant technology and a detailed analysis of obviousness in the field of recombinant technology.

Meena Lal, *The Role of the Federal Government in Assisted Reproductive Technologies*, 13 SANTA CLARA COMPUTER & HIGH TECH. L. J. 517 (1997).

This comment discusses the public policy and governmental interests in in-vitro fertilization and the constitutional basis for its regulation. The author makes a legislative proposal based on the Warnock Committee Report.

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