TESTIMONY FROM OTHER EXPERTS

Other molecular biologists from the academic community and the clinical community have expressed similar objections to the concerns voiced by Drs. Lewontin, Roberts, and Mullis. For instance, Dr. Ashok Bhagwat, a professor in the Chemistry Department at Wayne State University, had extensive experience studying molecular biology at Cold Spring Harbor where he received his post doctoral training working under Dr. Richard Roberts. In Washington v. Gentry, Dr. Bhagwat offered these succinct views:

> Q: Dr. Bhagwat, is PCR technology generally accepted in the scientific community for use on crime scene evidence?
>
> A: No, it's not.
>
> Q: And could you describe to the Court some of the general reasons why you have that opinion?
>
> A: There are several problems with the material that you are likely to obtain at a crime scene. It is most likely to be contaminated. And let me just slightly digress and say, PCR is so powerful that a single cell contamination could be devastating to the result, and hence, contamination is a big potential problem and it is unlikely that it is easily solvable for evidence arising from crime scenes.

Gentry, 28 RP 2238-2239.

Dr. John Gerdes is clinical director at Immunological

> enough doubt about it in the scientific community that the legal community should take notice that the scientific community is not even using that much any more. They're starting to sequence. We're doing it easily.

McIntosh, 2451 line 22 - 2452 line 13.

Associates of Denver, a reference laboratory that uses the same PCR technology involved in this case in conjunction with transplants (matching organ donors and recipients) and screening for AIDS and other infectious diseases. He has testified over twelve times expressing, from the hands-on perspective of one who runs a clinical laboratory, the same objections raised by Drs. Lewontin, Roberts and Mullis. Dr. Gerdes testified most recently in the McIntosh case, in tandem with Dr. Mullis, and the defense submits this transcript for the Court's edification.

(a) Contamination from PCR carryover.

Most of the discussion so far has focused on cross-contamination of forensic samples in their collection, preservation, handling, and processing. Before leaving the subject of contamination, however, special mention must be made of the phenomenon of PCR product contamination: contamination of samples by PCR product from previously run reactions in a laboratory. This is sometimes called "carryover contamination."

One of the developers of the Cetus/Roche kit, Dr. Russell Higuchi, describes the phenomenon:

> More unique to PCR is the possibility of carryover contamination from a completed PCR to another sample yet to be amplified. Because by the nature of PCR, PCR product will seed production of more PCR product, the sheer number of copies of PCR product after amplification can make the consequences of such contamination more dramatic. A typical PCR could have 10^{12} copies of an amplified gene. If a preparer inadvertently transfers, as before, 0.1 μl[82] of PCR sample A into sample B, even though sample B has a relatively high concentration of human DNA, the number

[82] A μl is a microliter (one millionth of a liter).

of copies of the target, single-locus gene that derive from sample A far outnumber the copies that actually stem from sample B. Thus, the DNA type obtained will be that of A and not B, and the relative amount of the B type is so small that it would not even show up in the test, eliminating the possibility that the presence of more than two alleles would flag the occurrence of the contamination.[83]

The NRC highlighted the problem of PCR carryover contamination as a key area of vulnerability, declaring "it has become clear that carryover products from one PCR reaction to another must also be eliminated." NRC Report, at 67. Accordingly, the NRC commented that "[m]ethods of detecting and preventing contamination from one PCR reaction to another in forensic laboratories are generally still in their early stages, and additional development should be encouraged."

It is plain, however, that forensic PCR laboratories, including those involved in the instant case, have not responded appropriately. For example, the NRC pointedly suggested that it would be a good idea to treat all evidence samples with uracil N-glycose (UNG) before amplification to destroy any PCR carryover from previous PCR reactions. Id. Clinical laboratories have followed up on this idea. Dr. Gerdes reports that his and other clinical laboratories "don't do anything without UNG anymore," McIntosh, Gerdes, 1915 line 6, and that the UNG control was featured in a PCR chlamydia kit which won recent FDA approval. Id., 1914 line 19. Forensic PCR laboratories, including the ones

---

[83] R. Higuchi and E.T. Blake, "PCR in Forensic Science, DNA Technology and Forensic Science," 32 Banbury Report, Cold Spring Harbor Laboratory Press (1989), at page 275.

which did testing in this case, do not use UNG to protect against carryover contamination.

Most importantly, since PCR carryover contamination can be a systemic, cumulative problem in a laboratory, the NRC demanded that controls must be in place to monitor "general contamination" in forensic PCR laboratories:

> In view of the problem of contamination due to handling and carryover, laboratories must incorporate contamination control into their standard operating procedures. And outbreaks of contamination and the steps taken to correct the problem should be documented.

NRC Report, at 67 [emphasis added].

Yet, at every turn, the prosecution and the laboratories have attempted to thwart discovery of laboratory contamination problems. Other than some systematic review of hybridization strips, there is no way to ascertain the extent of contamination in a forensic PCR laboratory, especially when the laboratory does not make a comprehensive effort to monitor or document the occurrence of contamination. Cellmark and the prosecution has opposed, along with Cellmark, the defense's request to view hybridization records from ten cases before and after the analysis performed in the instant matter. The prosecution has opposed the same request with respect to DOJ. Despite evidence that the LAPD laboratory has experienced "outbreaks" of contamination, and has not taken adequate steps to document or correct the problem, the prosecution and the laboratory continue to resist defense efforts to review hybridization strips. Indeed, despite specific reference in the NRC to "outbreaks of

contamination," the prosecution and the laboratories claim they don't understand what is meant by that phrase in defense discovery requests. See Letter of Dr. Robin Cotton, September 27, 1994, at 2 ("Note: Please ask for a clarification on what is meant by 'an outbreak of contamination'"...), attached to People's Response to Discovery Sanction Motion of September 28, 1994.

Given the crucial importance of demonstrating the absence of contamination in PCR laboratories to general acceptance in the scientific community, a strong inference should be drawn against the proponents of forensic PCR evidence for their refusal to permit adequate discovery of their contamination controls and their abject failure to monitor contamination.

2. Misincorporation, Differences in Qualitative and Quantitative Fidelity, and Differential Amplification.

PCR amplification products do not always faithfully represent the starting material in the sample, either qualitatively or quantitatively.

During PCR amplification nucleotides are known to be "misincorporated" at the rate of one per 10,000 nucleotides per cycle. If amplification is performed on a sample that has a large number of molecules, and if the misincorporation is random ("stochastic fluctuation"), then the low frequency of random errors will not skew typing results. The NRC warns, however, that "for systems in which misincorporation is not random," difficulties will arise. NRC Report, at 64. In particular, in DNA systems that contain tandem repeat sequences, "the DNA

polymerase can slip during amplification, introduce or delete copies of the repeat, and produce a heterogeneous collection of fragments, often making interpretation difficult." Id. D1S80 is a VNTR with tandem repeat sequences, thereby requiring, in the NRC's view, that its properties be "thoroughly characterized" before it goes on line.

Differential amplification is also a potential problem:

> In some cases, PCR can be qualitatively faithful but quantitatively unfaithful, because some alleles amplify more efficiently than others. A sample might contain a 50:50 mixture of two alleles and yield an amplified product with a 90:10 ratio. Differential amplification can arise through several mechanisms. It has been observed in the amplification of allelic products of different sizes (larger products tend to amplify less efficiently than shorter products) and in the amplification of sequences that differ significantly in GC content (because of differing denaturation efficiencies). In some cases, faithful amplification occurs at some temperatures and differential amplification at other temperatures. The possibility of differential amplification needs to be addressed in the design and development of amplification protocols for each genetic marker system. The safeguards to ensure that differential amplification does not occur should be defined and documented.

NRC Report, at 64-65.

When dealing with mixed forensic samples, especially small degraded samples, quantitative analysis with current forensic PCR methods can be, in the NRC's words, "problematic." Id.

It should be noted that Dr. Mullis believes that PCR based sequencing methods, such as those being developed now on mitochondrial DNA, can avoid the problems of quantitative and qualitative amplification:

> But the sequencing -- the reason I was so strong on sequencing is that it doesn't rely -- sequencing

doesn't rely on the quantitative accuracy in the amplification of different bands. The quantitative aspect is not as important. Just as long as you've got enough to sequence, it won't matter if you were sort of inefficient in your amplification if you have enough to sequence. If you don't, you can just amplify some more until you do...

If you're sequencing -- if you're sequencing with PCR amplification, [inefficient amplifications] won't change the results. It will say well, you didn't get enough to even get a sequence, so go back and amplify some more. It won't change the sequence. The data that you come out with will be the same, regardless of whether any of those things are wrong.

McIntosh, Mullis, 2377 line 13 to 2378 line 13.

3. The Absence of External Blind Trials Precludes Validation, and General Acceptance, of the PCR Methods Used In This Case.

The importance of external blind proficiency testing on samples that replicate case work has already been discussed in the context of developing a reliable method to determine the error rate of a laboratory. External blind trials, however, also serve a critical role in establishing the reliability of a new method, or validating that a laboratory can reliably apply a generally accepted method. The NRC was unequivocal on this point:

> Most important, there is no substitute for rigorous external proficiency testing via blind trials. Such proficiency testing constitutes scientific confirmation that a laboratory's implementation of a method is valid not only in theory, but in practice. No laboratory should let its results with a new DNA typing method be used in court, unless it has undergone such proficiency testing via blind trials.

NRC Report, at 55 (emphasis added).

None of the laboratories in this case have undergone external proficiency testing via blind trials with any of the PCR

based methods. Given the controversy about the reliability of forensic PCR methods among the leading scientists in the field, the NRC's bright line injunction has particular force: None of the PCR testing should be used in this case because the testing laboratories have not demonstrated its reliability through external blind proficiency testing.

CONCLUSION

The NRC warned that forensic PCR testing "poses even more serious issues of proficiency, control, and technology transfer than RFLP typing." NRC Report, at 70. It decried reliance upon the commercially distributed PCR "kits" that are being used in this case and observed that "[i]nformation on the extent of the contamination problem in PCR analysis and the differential amplification of mixed samples needs to be further developed and published." Id.

Basic methodological issues in the forensic PCR testing remain unexplored or in controversy.[84] Despite the admonitions of the NRC and leading scientists, forensic laboratories have not responded to the fact that techniques for the collection, preservation, and handling of crime scene samples is an essential part of forensic PCR testing methodology because of the special problem of sample contamination. Unlike the American Society for

---

[84] For example, a recent paper by molecular biologists and mathematicians at USC who are independent of the forensic laboratories, demonstrates that a multiple control tube method (they recommend 10) "is superior to the standard one-tube procedure, either when the sample is small or when laboratory contamination is a potential problem." Navidi, Arnheim, and Waterman, "A Multiple-Tubes Approach for Accurate Genotyping of Very Small DNA Samples by Using PCR: Statistical Considerations," 50 Am. J. Hum. Genet. 347-359, 347 (1992).

Similarly, scientists from the FBI have recommended the use of formamide to improve HLA DQ Alpha amplification based on research that shows eight mistypings of bloodstain evidence without using formamide. Comey, Jung, and Budowle, "Use of Formamide to Improve Amplification of HLA DQ Alpha Sequences," 10 Biotechniques No. 1 (1990).

Histocompatibility and Immunogenetics, which has, for PCR techniques, detailed "Standards for Histocompatibility Testing," there is no comparable set of guidelines for forensic PCR testing.

POINT IV

THE DNA EVIDENCE SHOULD BE EXCLUDED PURSUANT TO EVIDENCE CODE §352 BECAUSE IT CREATES SUBSTANTIAL DANGERS OF UNDUE PREJUDICE, OF CONFUSING THE ISSUES, AND OF MISLEADING THE JURY THAT OUTWEIGH ITS PROBATIVE VALUE.

The substantial dangers of undue prejudice, misleading the jury, and confusion of issues that arise from the statistical estimates offered by the prosecution about the value of DNA evidence are self-evident, and emanate from the core of the statistical controversy that continues to rage within the scientific community.

A. Prejudice and Confusion From the Coincidental Match Controversy.

One danger of undue prejudice arises, of course, from the controversial methods used to determine the probability of a coincidental match. Many courts have recognized this danger and found it, in conjunction with the general acceptance issue, to be a compelling basis to exclude DNA statistical evidence. After reviewing many Frye hearing transcripts and taking testimony at his own, Judge Henry Kennedy of the District of Columbia put the problem bluntly:

> [This] court intends no disrespect to the citizens from whom jury panels are drawn when it states, unequivocally, that jurors are not competent to evaluate and resolve these extraordinarily complex and subtle issues...It is almost certain that jurors would simply "jump" to the bottom line numbers without giving any meaningful consideration to any dispute over the principles which underlie the methodology used to generate those numbers. To permit the fancy of jurors to operate in this manner is the antithesis of "due process."

United States v. Porter, FO6277-89, Sup. Ct. Dist. of Colum., Crim Div., Slp. Opn., at 88.

The Supreme Court of Arizona engaged in the same line of reasoning in Arizona v. Bible, 858 P.2d 1152, 1181-83 (Ariz. Sup. Ct. 1993). Significantly, the Bible Court was considering not only the admissibility of DNA evidence, but whether it should abandon the Frye rule and adopt Daubert. It concluded, after reviewing undue prejudice and jury confusion factors, that "the field of DNA testing is probably the worst subject to use to decide whether or how to refine, replace, or abolish Frye":

> ...even were we to use Daubert's reliability/scientific validity analysis, we should still be left with the problem posed by Frye: precisely when "in [the] twilight zone the evidential force of the [scientific] principle must be recognized." Whether the Frye or Daubert standard is used, that line is hard to draw for DNA testing, a subject that fuels even greater scientific ferment and controversy than the legal controversy engendered by Frye.
>
> The science in question makes line-drawing in this case particularly difficult. Not only are we in a complex scientific field, but the technology is still evolving. Furthermore, this is not an area in which the jury can easily penetrate the aura of infallibility, nor one in which the principles are easily demonstrable in the courtroom.

Bible, at 1183.

The Bible court also relied on some trenchant observations from McCormick on Evidence suggesting that courts should ratchet up the standard for admissibility when evidence is potentially dispositive and difficult for the jury to evaluate:

> Where methods involve principles and procedures that are comprehensible to a jury, the concerns over the evidence exerting undue influence and inducing a battle of the experts have less force. On the other hand, when the nature of the technique is more esoteric, as with some types of statistical analyses and serologic tests or when the inferences from the scientific evidence sweep broadly or cut deeply into sensitive areas, a

> stronger showing of probative value should be required....By attending to such considerations, the rigor of the requisite foundation can be adjusted to suit the nature of the evidence and the context in which it is offered.

1 McCormick on Evidence §203, at 873-76 (footnotes omitted), cited in Bible, at 1182."

B. Prejudice And Confusion From the Effect of False Positive Error Rates on DNA Statistical Estimates.

Since the publication of the NRC Report scientific and legal commentators have justifiably expressed alarm about a second, more drastic danger of undue prejudice and confusion than the controversy over coincidental match probabilities -- the effect false positive error rates have on the value of DNA statistical estimates.

Everyone agrees that the false positive error rates for informative DNA tests (RFLP, polymarkers, D1S80) must be substantially higher than the probability of a coincidental match. Therefore, many, if not a clear majority of commentators, believe "the incriminatory value of a DNA "match" can never be greater than the false positive error probability." Lempert, Comment: Theory and Practice of DNA Fingerprinting, in DNA Fingerprinting: A Review of the Controversy, 9 Stat. Science 255, 257 (1994) [no emphasis added]. If this is the case, then there is enormous prejudice in permitting DNA evidence to go before the jury with just an astronomical statistic about the probability of a coincidental match, and only fuzzy, non-quantified statements about the probability of a false positive error. Professor Lawrence Tribe identified this problem twenty-three years ago in

his seminal article, Trial By Mathematics: Precision and Ritual in the Legal Process:

> The syndrome is a familiar one: If you can't count it, it doesn't exist...Readily quantifiable factors are easy to process -- and hence more likely to be recognized and then reflected in the outcome -- than are factors that resist ready quantification. The result, despite what turns out to be a spurious appearance of accuracy and completeness, is likely to be significantly warped and highly suspect.

84 Harv. L. Rev. 1329, 1361-62 (1971).[85]

Presenting a questionable or "soft" estimate of false positive error rate based on insufficiently rigorous proficiency tests that fall below generally accepted scientific standards, or offering a hopelessly open-ended statistic (it could be zero, it could be 30%, the laboratory does not know because it has taken so few proficiency tests), does not mitigate the undue prejudice. In fact, permitting such "soft" estimates on a "crucial variable" that could severely alter the statistical value of the evidence being offered exacerbates unfair prejudice. It invites the jury to weigh probabilities based on admittedly problematic data upon which no one could draw sound conclusions. "If mathematical probabilities are to be of any use in the courtroom setting, all crucial variables must be quantified exactly." People v. Cella, 139 Cal. App.3d 404 (4th Dist. 1983) (Probability estimate of

---

[85] California courts have long recognized that interjecting sophisticated theories of mathematical probability in criminal trials raises especially serious concerns about misleading the jury. See, People v. Collins, 68 Cal.2d 319, 320 ("Mathematics, a veritable sorcerer in our computerized society, while assisting the trier of fact in the search for truth, must not cast a spell over him.").

expert excluded under §352). Dr. Eric Lander's succinct comment on this point bears repetition: "...it is simply crazy and scientifically unacceptable to agonize over the exact population frequencies, which might be one in a million, or one in a thousand, or one in ten thousand for the frequency of a genotype in a population, and yet not have actual data for the accuracy, the proficiency of a laboratory's handling of samples." Prof. Eric Lander, Testimony as a Court's Witness in U.S. v. Porter, District of Columbia Criminal Docket # F-6277-89, p. 46, July 28, 1994.

Even if one assumes away the controversies in the scientific community about the reliability of the methods used by forensic laboratories to calculate coincidental match probabilities and false positive error rates, a very substantial prejudice issue remains: Should the value of the DNA evidence be expressed as one statistic (just the false positive error rate or a likelihood ratio combining the false positive error rate and the probability of coincidental match), or should it be presented as two statistics (e.g., the probability of a coincidental match is 1 in a million and the laboratory's false positive error rate is 1 in 200)?

The NRC suggested that two statistics be presented to the jury. But before, and particularly since the publication of the NRC Report, many scientists and statisticians have disagreed with that approach. A substantial number of scientists, including Bruce Weir, an expert frequently called by the prosecutors to

testify about the probability of a coincidental match, have proposed using a likelihood ratio that combines the probability of a coincidental match and the false positive error rate. But, when the false positive rate is high (1 in 200) and the coincidental match probability is low (1 in a million), the likelihood ratio offered by Dr. Weir and others will invariably produce a result (approximately 1 in 200) that is about the same as the false positive error rate.

As Dr. Donald Berry observes, when presented with the tiny coincidental match probability and the high false positive error rate, "the common practice among scientists is to ignore events of low probability," i.e., the coincidental match statistic. Berry, "Comment," in "DNA Fingerprinting: A Review of the Controversy," 9 Stat. Science 252, 253 (1994). Lay jurors, however, are not scientists or statisticians and it is extremely unlikely they will be able to ignore an astronomical statistic like 1 in a million. On the contrary, there is a substantial danger jurors will give the coincidental match probability undue weight (more weight than most scientists!).[86]

There is an abundant body of research produced by

---

[86] This problem has sometimes been characterized as "selection effect" dangers. Professor Tribe has warned that the selective use of characteristics for probabilistic analysis can greatly distort the apparent mathematical odds that events occurred by chance. This "selection effect" may arise from a party's power to choose matching features for quantification (here the probability of a coincidental match) while ignoring non-matching features (false positive error rate), thereby producing a grossly exaggerated estimate of the improbability that the observed matching would have occurred by chance. Tribe, supra, at 1342, fn. 40.

psychologists and statisticians dealing with the cognitive difficulties people experience reasoning about probabilities and statistics. The defense intends to present evidence from experts in this field that will substantiate its claims about the substantial dangers of undue prejudice and of misleading the jury if an astronomical coincidental match probability is presented to the jury.

C. Prejudice and Confusion From the Introduction of Multiple Probabilities of Different DNA and Conventional Serology Tests Absent Compelling Proof of Independence.

If the court permits the prosecution to offer coincidental match probabilities and/or separate false positive error rates for all the DNA and genetic marker tests performed in this case the dangers of prejudice and issue confusion are nearly overwhelming.

1. People v. Collins Requires Compelling Proof of Independence When Offering Multiple Probabilities At A Criminal Trial.

In People v. Collins, the prosecution sought to compute the probability of a series of characteristics through application of the product rule. This rule holds that the probability of a series of independent events is found by multiplying each of the individual probabilities together. Thus, as the prosecutor suggested in Collins, if the individual probabilities of events A, B, C, and D are 1/10, 1/100, 1/1000, and 1/1000, their combined probability is 1/10 x 1/100 x 1/1000 x 1/1000 = 1/1,000,000,000 (i.e., 1 in 1 billion).

The theory underlying this rule is mathematically sound and

uncontroversial. But as the Collins Court points out, this is not enough. Meaningful application of the product rule cannot be obtained absent "information as to the degree of interdependence among the ... individual factors." Collins, at 329, fn. 15.

Now assume the frequencies for events A, B, C, and D are the frequencies from the four DNA tests the prosecution seeks to introduce -- DQ Alpha, Polymarkers, D1S80, and RFLP. If compelling proof of independence between the frequencies of these four tests is not provided, then we know only that the combined probability of the four tests lies between 1/1,000,000,000 (complete independence) and 1/1,000 (complete dependence). In all likelihood, neither endpoint value is correct and the true combined probability lies somewhere between these two values. But this is an extraordinarily broad range indeed. Whereas a jury might find a 1 in a billion probability compelling proof of identity, it may not find a 1 in 1 thousand probability compelling proof of anything. Indeed, common sense requires the conclusion that people will view these two probability values quite differently.

While the prosecution will attempt to put on proof of independence between the different DNA markers used in each DNA test, the defense knows of no study demonstrating independence between Cellmark's RFLP markers, DQ Alpha, polymarkers, and D1S80. Independence between the frequencies of these tests simply cannot be assumed.

This raises a series of critical questions. First, what is

the appropriate joint probability of this series of probabilities that cannot be shown to be independent? Can the scientific community agree on the appropriate estimate? If they cannot, what should be done with the numbers? Does it make sense to provide them to jurors and tell them, in essence, "Here, do what you will with this technical information that members of the scientific and statistical communities do not fully understand or agree upon." What, then, will jurors faced with multiple probabilities do with these numbers once they are presented? How are they to make sense of them? Will they attempt to combine them? If so, what techniques will they use? In all likelihood, a large majority of people will multiply the numbers together. This, of course, would presuppose independence without compelling proof of it. Some, perhaps, will add them. This would make no sense at all. Many other, idiosyncratic and equally inappropriate techniques for combining these numbers will surely be used.

Our position is simple. Until the scientific community provides a method for making sense of the multiple coincidental match probabilities, it is extremely prejudicial to throw these numbers at the jury in the hopes they will make sense out of them.

Similarly, the jury might assume that the false positive error rates are independent of each other even though there is clear evidence that the error rates of all the laboratories are conditioned on the error rate of the LAPD with respect to mishandling and cross-contaminating samples. A series of tests,

derived from an initial testing process of questionable reliability, does not necessarily make any subsequent test any more reliable than the first.

Faced with such a welter of statistics, there is danger the jury will be distracted from considering adequately the serious issues surrounding the reliability of DNA statistical estimates and the problems of PCR contamination. Scientists, lawyers, and judges have considerable trouble engaging and following these debates, how can a jury in this kind of circumstantial case be expected to do so given the current level of controversy?

The new NRC panel is reconsidering the coincidental match probability and error rate problems and will no doubt be wrestling with ways to simplify the presentation of multiple DNA statistics to juries. Combining error rates and coincidental match probabilities through likelihood ratios, or placing bounds on statistical estimates from multiple genetic tests where independence has not been established, are obviously suggestions being offered in the scientific literature that will merit serious review and could alleviate jury confusion. It would be a sound exercise of discretion under Evidence Code §352 to exclude the DNA evidence in this case until the new NRC panel finishes its work and the statistical controversies are closer to resolution.

CONCLUSION

For the aforementioned reasons, the DNA evidence should be excluded.

Dated: New York, New York
October 4, 1994

Respectfully submitted,

BARRY C. SCHECK

PETER J. NEUFELD

WILLIAM C. THOMPSON by PJN.