

1 (OPEN COURT, JURY NOT PRESENT, AT 12:13 A.M.:)

2 THE CLERK: PLAINTIFF'S A-180A AND A-180B MARKED FOR
3 IDENTIFICATION ONLY.

4 (PLAINTIFF'S EXHIBITS A-180A &
5 A-180B MARKED FOR IDENTIFICATION)

6 (OPEN COURT, JURY PRESENT, AT 12:14 A.M.:)

7 THE COURT: YES.

8 MR. PASAHOW: SHALL I CALL OUR NEXT WITNESS?

9 THE COURT: YOU CERTAINLY MAY, YES.

10 MR. PASAHOW: OUR NEXT WITNESS IS DR. HAMILTON SMITH,
11 YOUR HONOR.

12 THE CLERK: PLEASE RAISE YOUR RIGHT HAND.

13 HAMILTON OTHANEL SMITH, DEFENDANT'S WITNESS, SWORN

14 THE CLERK: TAKE THE STAND, PLEASE.

15 PLEASE STATE YOUR FULL NAME AND SPELL YOUR LAST NAME
16 FOR THE COURT.

17 THE WITNESS: HAMILTON OTHANEL SMITH, S-M-I-T-H.

18 THE CLERK: COULD YOU PLEASE SPELL YOUR MIDDLE NAME.

19 THE WITNESS: O-T-H-A-N-E-L.

20 DIRECT EXAMINATION

21 BY MR. PASAHOW:

22 Q. GOOD AFTERNOON, DR. SMITH.

23 A. GOOD AFTERNOON.

24 Q. DR. SMITH, YOU'RE ON THE FACULTY OF THE JOHNS HOPKINS
25 UNIVERSITY SCHOOL OF MEDICINE?

1 A. THAT'S CORRECT.

2 Q. WHAT IS YOUR POSITION THERE?

3 A. I'M A PROFESSOR OF MOLECULAR BIOLOGY AND GENETICS AT THE
4 MEDICAL SCHOOL.

5 Q. WHAT DOES THAT DEPARTMENT ENCOMPASS?

6 A. WELL, IT -- IT'S A DEPARTMENT WHICH HAS THE RESPONSIBILITY
7 OF TEACHING MICROBIOLOGY TO THE MEDICAL STUDENTS, BUT THE
8 FACULTY PRIMARILY IS ENGAGED IN RESEARCH IN MOLECULAR BIOLOGY
9 AND GENETICS.

10 Q. DO YOU HAVE POST-DOCTORAL FELLOWS --

11 A. OH, YES.

12 Q. -- IN THE DEPARTMENT?

13 A. YES.

14 Q. DO YOU TEACH OR DO YOU DO RESEARCH?

15 A. I DO BOTH. I GENERALLY PARTICIPATE IN THE TEACHING OF
16 MEDICAL STUDENTS, AND ALSO I TEACH A -- SOME LECTURES IN THE
17 GRADUATE COURSE IN MOLECULAR BIOLOGY.

18 Q. ARE YOU CURRENTLY AT THE UNIVERSITY AT JOHNS HOPKINS?

19 A. YES, I'M -- WELL, NO, THIS YEAR, I'M NOT. I'M CURRENTLY
20 SPENDING A YEAR IN VIENNA, AUSTRIA.

21 Q. WHAT ARE YOU DOING THERE?

22 A. I'M WORKING AT THE INSTITUTE OF MOLECULAR PATHOLOGY. THAT'S
23 A RATHER BIG NAME, BUT IT'S AN INSTITUTE THAT WAS JUST BUILT
24 ABOUT THREE YEARS AGO AND ITS MISSION IS CANCER RESEARCH.

25 AND I DECIDED I NEEDED A YEAR AWAY TO GET BACK TO THE

1 BENCH MYSELF WITH MY OWN HANDS AND DO SOME EXPERIMENTS, SO
2 I'M -- I'M WORKING ON SOME WORK RELATED TO THE INSTITUTE THERE.

3 Q. AND YOU'RE TECHNICALLY ON A SABBATICAL FROM JOHNS HOPKINS?

4 A. THAT'S CORRECT.

5 Q. NOW, YOU SERVED FOR SEVERAL YEARS AS A CONSULTANT TO CETUS
6 CORPORATION; IS THAT CORRECT?

7 A. THAT IS CORRECT.

8 Q. ARE YOU PAID FOR YOUR WORK AS A CONSULTANT TO CETUS?

9 A. YES. I RECEIVE \$1500 QUARTERLY.

10 Q. SO EVERY THREE MONTHS?

11 A. EVERY THREE MONTHS, YES.

12 Q. WHAT DOES YOUR WORK AS A -- AS A SCIENTIFIC ADVISOR OR
13 CONSULTANT TO CETUS CONSIST OF?

14 A. GENERALLY, I VISIT THE COMPANY AND TALK TO SCIENTISTS THERE
15 ABOUT ONCE A YEAR; I ATTEND THE -- THE ANNUAL SCIENTIFIC
16 MEETING; AND I'M AVAILABLE, OF COURSE, BY PHONE.

17 I'VE ALSO, I THINK, IN THE PAST BEEN HELPFUL ON A
18 NUMBER OF OCCASIONS IN REVIEWING MANUSCRIPTS AND HELPING TO GET
19 THOSE PUBLISHED.

20 Q. DO YOU KNOW SOME OF THE SCIENTISTS AT CETUS AS A RESULT OF
21 YOUR WORK?

22 A. I CERTAINLY DO. I HAVE A NUMBER OF FRIENDS THERE.

23 Q. NOW, IN ADDITION TO YOUR WORK AS -- AS A CONSULTANT AND YOUR
24 COMPENSATION FOR THAT, ARE YOU BEING COMPENSATED AS AN EXPERT IN
25 THIS CASE?

1 A. YES, I AM. I'M . . . I'M EXPECTING TO RECEIVE MY STANDARD
2 FEE FOR CONSULTATION WORK, FOR ALL TIME SPENT IN PREPARATION AND
3 TESTIMONY.

4 Q. HOW MUCH IS THAT?

5 A. THAT'S \$500 A DAY.

6 Q. COULD YOU SUMMARIZE FOR US, PLEASE, DR. SMITH, YOUR
7 EDUCATIONAL BACKGROUND.

8 A. YES. I BEGAN AT THE UNIVERSITY OF ILLINOIS. I SPENT TWO
9 YEARS THERE MAJORING IN MATHEMATICS, AND THEN I TRANSFERRED TO
10 THE UNIVERSITY OF CALIFORNIA IN BERKELEY, WHERE I CONTINUED
11 MATHEMATICS, RECEIVING A BACHELOR'S DEGREE.

12 ON COMPLETION OF THAT, I WENT TO JOHNS HOPKINS MEDICAL
13 SCHOOL AND COMPLETED MY M.D. IN 1956.

14 AFTER GRADUATION, I DID AN INTERNSHIP AND, AT THE END
15 OF THAT INTERNSHIP, I WAS CAUGHT IN THE DOCTOR'S DRAFT AND SPENT
16 TWO YEARS IN THE U.S. NAVY IN SAN DIEGO.

17 AND THEN AT THE COMPLETION OF THAT TWO YEARS OF
18 SERVICE, I WENT AND DID A MEDICAL RESIDENCY.

19 Q. SO YOU'VE COMPLETED THE TRAINING FOR BEING A MEDICAL DOCTOR?

20 A. COMPLETE TRAINING FOR A MEDICAL PHYSICIAN.

21 Q. ARE YOU THE AUTHOR OF ANY PAPERS THAT HAVE BEEN PUBLISHED IN
22 SCIENTIFIC JOURNALS?

23 A. YES, I AM. I'VE PUBLISHED ABOUT 80 PAPERS.

24 Q. AND THOSE ARE -- ARE INDICATED ON YOUR --

25 A. THEY'RE INDICATED IN THE CURRICULUM VITAE.

2

1 Q. LET ME SHOW YOU THAT. WE'VE MARKED IT AS EXHIBIT B-46.

2 A. YES, THAT'S IT.

3 Q. AND DOES THAT SUMMARIZE YOUR BACKGROUND?

4 A. YES, IT DOES.

5 MR. PASAHOW: YOUR HONOR, I'D OFFER EXHIBIT B-46.

6 THE COURT: ANY OBJECTIONS?

7 MR. FIGG: NO OBJECTION, YOUR HONOR.

8 THE COURT: B-46 IS ADMITTED.

9 (DEFENDANT'S EXHIBIT B-46

10 RECEIVED IN EVIDENCE)

11 Q. (BY MR. PASAHOW) NOW, DR. SMITH, DURING YOUR CAREER AS A
12 TEACHER AND RESEARCHER, HAVE YOU WON ANY SIGNIFICANT HONORS FOR
13 YOUR SCIENTIFIC ACHIEVEMENTS?

14 A. YES. I'M A MEMBER OF THE NATIONAL ACADEMY OF SCIENCES. I
15 RECEIVED THE GUGGENHEIM FELLOWSHIP FOR ANOTHER SABBATICAL IN THE
16 MID-'70'S; AND . . . I'M AN AMERICAN CANCER SOCIETY
17 DISTINGUISHED PROFESSOR; AND ALSO, IN 1978, I RECEIVED THE NOBEL
18 PRIZE IN MEDICINE FOR MY WORK ON RESTRICTION ENZYMES.

19 Q. NOW, AN EARLIER WITNESS DESCRIBED RESTRICTION ENZYMES AS ONE
20 OF THE FUNDAMENTAL TECHNIQUES THAT ARE USED IN CLONING AND
21 MOLECULAR BIOLOGY. COULD YOU GIVE US A BETTER IDEA WHAT THEY
22 ARE?

23 A. OKAY. LET ME SEE IF I CAN GET IT ACROSS:

24 WELL, I SHOULD START BY SAYING THAT THEY ARE THE
25 BACTERIAL ENZYMES FOUND IN A WIDE VARIETY OF BACTERIA. AND

2
1 THEY'RE WHAT WE CALL ENDONUCLEASES; IN OTHER WORDS, THEY CLEAVE
2 DNA.

3 BUT THE RESTRICTION ENZYMES ARE INTELLIGENT ENZYMES.
4 THEY DON'T JUST CLEAVE RANDOMLY ANYWHERE IN THE DNA.

5 LET'S SUPPOSE MY ARM IS A SECTION OF A DNA MOLECULE.
6 HERE IS A RESTRICTION ENZYME (INDICATING). IT RECOGNIZES A
7 SPECIFIC SET OF BASES IN THE DNA THAT MIGHT OCCUR, FOR EXAMPLE,
8 HERE (INDICATING), OR HERE (INDICATING), ALONG THE -- ALONG THE
9 STRETCH OF DNA.

10 THE RESTRICTION ENZYME SEARCHES OUT, MORE OR LESS HONES
11 IN ON THAT PARTICULAR SEQUENCE AND CLEAVES IT WHEREVER IT FINDS
12 IT ALONG THE MOLECULE, SO THAT ONE -- ONE FORMS DISCRETE
13 FRAGMENTS.

14 Q. HOW ARE RESTRICTION ENZYMES USED IN RECOMBINANT DNA?

15 A. WELL, THEY'RE ESSENTIAL TOOLS, ACTUALLY, FOR SPLITTING . . .
16 FOR CUTTING DNA INTO DISCRETE PIECES, WHICH CAN THEN BE . . .

17 WELL, LET'S PUT IT THIS WAY: IF YOU WERE TO TAKE TWO DIFFERENT
18 DNA'S FROM DIFFERENT SOURCES AND CLEAVE THEM BOTH WITH
19 RESTRICTION ENZYMES, YOU COULD THEN TAKE THE PIECES AND JOIN
20 THEM TOGETHER SO THAT YOU HAVE HYBRID MOLECULES. THAT'S
21 RECOMBINANT DNA.

22 (PAUSE IN PROCEEDINGS)

23 Q. (BY MR. PASAHOW) ONE OF THE EARLIER WITNESSES EXPLAINED
24 THAT PCR IS CAPABLE OF CREATING DNA PIECES WITH SPECIFIC ENDS.
25 IS THAT SOMETHING LIKE WHAT RESTRICTION ENZYMES DO?

2
1 A. YES, BUT . . . WELL, A RESTRICTION ENZYME CERTAINLY CAN MAKE
2 SPECIFIC PIECES, BUT IT DOESN'T HAVE THE ABILITY TO AMPLIFY.

3 PCR, I THINK, IN MANY WAYS IS MORE POWERFUL, BECAUSE
4 YOU CAN GO IN AND LITERALLY LIFT OUT AND AMPLIFY A PARTICULAR
5 SECTION OF A DNA MOLECULE. AND YOU DON'T EVEN HAVE TO WORRY
6 ABOUT WHETHER THERE ARE SPECIFIC RESTRICTION SITES FLANKING THAT
7 PARTICULAR PORTION OF THE MOLECULE THAT YOU WANT TO AMPLIFY. SO
8 I THINK PCR REALLY HAS MORE POWER IN SOME WAYS.

9 Q. NOW, YOU MENTIONED THE TERM "RESTRICTION SITES." WHAT'S A
10 RESTRICTION SITE?

11 A. WHAT ARE RESTRICTION SITES?

12 Q. YES, SIR.

13 A. OKAY. RESTRICTION SITES ARE USUALLY . . . WELL, THEY'RE
14 SHORT . . . STRETCHES OF USUALLY ABOUT FOUR TO SIX BASES ALONG A
15 DNA MOLECULE. AND THEY'RE THE SITES THAT ARE RECOGNIZED BY A
16 PARTICULAR -- BY PARTICULAR RESTRICTION ENZYMES AND THE . . .
17 ENZYMES BIND TIGHTLY TO THOSE SITES AND THEN MAKE A CLEAVAGE.

18 Q. SO THE RESTRICTION SITES ARE WHERE THE RESTRICTION ENZYMES
19 BIND TO CUT?

20 A. THAT'S RIGHT.

21 Q. NOW, YOU, OF COURSE, ARE FAMILIAR WITH THE PCR PROCESS.

22 A. THAT'S RIGHT.

23 Q. IS IT USED IN THE LABORATORIES AT THE JOHNS HOPKINS
24 UNIVERSITY MEDICAL SCHOOL?

25 A. YES. ACTUALLY, EXTENSIVELY.

2

1 Q. SINCE WHAT TIME HAS PCR BEEN USED THERE?

2 A. I DON'T THINK I COULD DATE IT EXACTLY, BUT I KNOW AT LEAST
3 TWO FACULTY MEMBERS THAT USED IT VERY SOON AFTER THE SAIKI
4 PUBLICATION IN LATE 1985. SO I WOULD PLACE IT PROBABLY AROUND
5 '86 OR MAYBE EARLY '87.

6 Q. WAS PCR BEING USED AT JOHNS HOPKINS DURING THE PERIOD BEFORE
7 THE TAQ POLYMERASE BECAME AVAILABLE?

8 A. THAT'S CORRECT.

9 Q. HAVE YOU EVER USED PCR IN RESEARCH WORK THAT'S DONE BY YOUR
10 GROUP?

11 A. YES, I HAVE.

12 Q. DID YOU DO THE PCR REACTION?

13 A. NO. THEY WERE -- THE . . . THEY'VE BEEN PERFORMED BY A
14 NUMBER OF THE POST-DOCS IN THE LABORATORY, BUT PERSONALLY, WITH
15 MY OWN HANDS, I HAVE NOT.

16 Q. BUT --

17 A. I GET VERY LITTLE OPPORTUNITY TO GET IN THE LABORATORY AT
18 HOPKINS.

19 Q. HAVE YOU EVER TAUGHT THE PCR PROCESS TO YOUR STUDENTS AT
20 JOHNS HOPKINS?

21 A. YES. I TEACH IT IN THE GRADUATE COURSE IN MOLECULAR
22 BIOLOGY.

23 Q. HOW MANY YEARS HAVE YOU BEEN TEACHING IT THERE?

24 A. I THINK THAT I BEGAN PROBABLY THE YEAR AFTER THE SAIKI
25 PAPER. THAT WOULD BE 1986.

3
1 Q. NOW, HAVE YOU READ THE '202 AND THE '195 PATENTS THAT ARE
2 INVOLVED IN THIS CASE?

3 A. YES, I HAVE.

4 Q. AND DID YOU READ THE ENTIRE PATENTS OR JUST THE CLAIMS?

5 A. I READ THE ENTIRE PATENTS.

6 (PAUSE IN PROCEEDINGS)

7 Q. (BY MR. PASAHOW) FOR YOUR REFERENCE AS WE GO ALONG, LET ME
8 GIVE YOU THOSE TWO PATENTS. THEY'RE EXHIBITS B-1 AND B-2.

9 (PAUSE IN PROCEEDINGS)

10 Q. (BY MR. PASAHOW) AND I'D LIKE FOR YOU FIRST TO EXPLAIN, IF
11 YOU COULD, WHAT YOU SEE AS THE KEY FEATURE OF CLAIM 1 OF THE
12 '202 PATENT.

13 AND LET ME PUT UP A POSTER WE'VE MADE OF THAT CLAIM.
14 THAT'S EXHIBIT B-160.

15 A. I NEED TO SWITCH BACK AND FORTH BETWEEN MY GLASSES AND NOT
16 HAVING THEM.

17 OKAY. I'M SORRY. WOULD YOU REPEAT THE QUESTION?

18 Q. THE QUESTION, SIR, WAS: COULD YOU EXPLAIN WHAT YOU
19 UNDERSTAND TO BE THE KEY FEATURES OF CLAIM 1 OF THE '202 PATENT.

20 A. OKAY. WELL, FIRST OF ALL, THE CLAIM 1 IS A PROCESS FOR
21 AMPLIFYING A SPECIFIC TARGET SEQUENCE IN A NUCLEIC ACID OR A
22 MIXTURE OF NUCLEIC ACIDS.

23 AND I THINK IF YOU MOVE DOWN -- ACTUALLY, IT'S MARKED
24 IN YELLOW -- THE BOTTOM OF SECTION A, THE KEY THING IS THAT A --
25 THAT THE PRODUCT OF THE FIRST CYCLE BE USED -- HAS THE ABILITY

3

1 TO BE USED AS A TEMPLATE IN SUBSEQUENT REACTIONS. IN FACT, IN
2 ALL SUBSEQUENT REACTIONS.

3 Q. WHY IS THAT IMPORTANT?

4 A. AND . . . I THINK IT'S REALLY THE KEY THING, BECAUSE THAT
5 GIVES THE UNIQUE CHARACTER OF THE CHAIN REACTION OR THE
6 EXPONENTIAL CHARACTERISTICS TO THE REACTION.

7 WITHOUT THAT, YOU WOULD NOT HAVE A . . . WOULD
8 LITERALLY NOT HAVE AN EXPONENTIAL PROCESS.

9 Q. DO YOU UNDERSTAND CLAIM 1 TO BE THE BROADEST OF THE CLAIMS
10 OF THE '202 PATENT?

11 A. I THINK IT IS, YES.

12 Q. AND DO YOU UNDERSTAND CLAIM 1 TO DESCRIBE THE PROCESS THAT'S
13 USUALLY CALLED PCR?

14 A. THAT'S RIGHT.

15 Q. NOW, COULD YOU ALSO PLEASE EXPLAIN FOR US WHAT YOU
16 UNDERSTAND TO BE THE KEY FEATURES OF CLAIM 1 OF THE OTHER
17 PATENT, THE '195 PATENT.

18 A. OKAY.

19 Q. WE'VE GOT THAT ON A POSTER, B-165.

20 A. OKAY.

21 (PAUSE IN PROCEEDINGS)

22 THE WITNESS: OKAY. AGAIN, THE -- THIS IS VERY SIMILAR
23 TO THE '202 CLAIM 1. AND, AGAIN, THE KEY FEATURE IS THE ABILITY
24 OF THE SYNTHESIZED PRODUCTS TO BE USED IN SUBSEQUENT CYCLES AS
25 TEMPLATE.

3 1 IN ADDITION, OF COURSE, THIS PARTICULAR CLAIM ADDS IN A
2 DETECTION STEP USING A LABELED OLIGONUCLEOTIDE, SO THAT THE
3 PRODUCTS OF THE REACTION CAN BE DETECTED.

4 Q. (BY MR. PASAHOW) AND HOW IS THAT DETECTION DONE?

5 A. WELL, THAT'S DONE BY TAKING A SHORT OLIGONUCLEOTIDE, PERHAPS
6 15 OR 20 BASES IN LENGTH, LABELING TYPICALLY THE FIVE-PRIMED END
7 WITH A P32 -- RADIOACTIVE P32 ATOM, AND THEN -- AND I SHOULD
8 SPECIFY THAT THIS -- THAT THIS PROBE IS COMPLEMENTARY, CAN
9 HYBRIDIZE TO THE TARGET SEQUENCE.

10 AND SO THEN YOU WOULD CARRY OUT THE HYBRIDIZATION IN
11 A -- IN A STANDARD ANNEALING REACTION, AND . . . AND . . .
12 USUALLY IT'S DONE IN A PARTICULAR BODY AND PROCEDURE.

13 Q. AND YOU LOOK TO SEE WHETHER OR NOT THE PROBE IS ATTACHED TO
14 THE TARGET?

15 A. THAT'S CORRECT. THAT'S CORRECT. TO SEE IF IT SPECIFICALLY
16 LABELS THE AMPLIFIED TARGET SEQUENCE.

17 Q. NOW, DR. SMITH, DO YOU KNOW DR. KARY MULLIS, THE INVENTOR OF
18 PCR?

19 A. YES, I CERTAINLY DO.

20 Q. HOW DID YOU MEET HIM?

21 A. I MET HIM VERY EARLY ON. I CAN'T PLACE THE EXACT TIME, BUT
22 VERY EARLY IN MY ASSOCIATION WITH CETUS. I WOULD SAY EARLY
23 '80'S.

24 Q. HOW DID YOU FIRST LEARN OF DR. MULLIS' PCR INVENTION?

25 A. I THINK IT'S -- IT'S FAIR TO SAY THAT I DIDN'T KNOW ABOUT IT

3 1 WHEN I -- I DIDN'T KNOW THAT HE WAS WORKING ON IT AT THE VERY
2 BEGINNING.

3 AS BEST I CAN REMEMBER, I WOULD PLACE IT AROUND 19 --
4 EARLY 1985, PRIMARILY IN CONVERSATIONS WITH DR. GELFAND, WHO WAS
5 MY MAIN CONTACT PERSON AT CETUS. AND THEN SUBSEQUENTLY, OF
6 COURSE, WHEN THE SAIKI PAPER WAS PUBLISHED IN DECEMBER OF 1985,
7 THEN I BECAME VERY AWARE OF EXACTLY WHAT THE PROCESS WAS.

8 Q. YOU READ THAT PAPER?

9 A. I DEFINITELY READ THAT PAPER, YES. IN FACT, I MADE A COPY
10 OF IT -- I CAN REMEMBER THIS QUITE CLEARLY. I MADE A COPY OF
11 THE PAPER, AND I -- I TOOK IT INTO THE LABORATORY AND THREW IT
12 UP ON A CONFERENCE TABLE.

13 THE LABORATORY IS ONE SUCH THAT WE HAVE TWO MAIN ROOMS,
14 AND THEN A CONFERENCE ROOM WHERE WE SIT, HAVE COFFEE, AND TALK
15 ABOUT OUR EXPERIMENTS, OR ABOUT ANYTHING INTERESTING IN SCIENCE.

16 SO I PUT THIS PAPER ON THE TABLE AND I CALLED MY GROUP
17 TOGETHER, AND I SAID, "HERE'S A VERY EXCITING PIECE OF WORK. WE
18 CAN USE THIS PROCESS IN OUR RESEARCH. I WANT YOU TO START
19 THINKING ABOUT PCR." AND THEY, OF COURSE, BECAME VERY
20 INTERESTED IN THE PROCEDURE.

21 MR. PASAHOW: EXCUSE ME A MOMENT.

22 (PAUSE IN PROCEEDINGS)

23 Q. (BY MR. PASAHOW) DR. SMITH, ARE YOU FAMILIAR WITH A BOOK BY
24 DR. ARTHUR KORNBERG, DNA REPLICATION?

25 A. YES, I AM.

4
1 Q. NOW, DR. KORNBERG TOLD US THAT HE'S WORKING ON A NEW EDITION
2 OF THIS BOOK, AND IN IT HE HAS A SECTION ON PCR IN WHICH HE
3 DESCRIBES PCR AS "AN ASTONISHING AND HIGHLY USEFUL TECHNIQUE."

4 WERE YOU ASTONISHED WHEN YOU FIRST FOUND OUT THAT A
5 TECHNIQUE LIKE PCR EXISTS?

6 A. I WAS AMAZED.

7 Q. WHY?

8 A. BECAUSE THIS IS A PROCEDURE WHICH LITERALLY ALLOWS YOU TO GO
9 INTO A VERY COMPLEX DNA OR MIXTURE OF DNA'S -- FOR EXAMPLE,
10 EXTRACTED FROM HUMAN CELLS -- AND LITERALLY LIFT OUT AND AMPLIFY
11 A MILLION-FOLD A SINGLE GENE, OR ANY SINGLE SECTION OF THE
12 CHROMOSOME.

13 I MEAN, A GOOD ANALOGY WOULD BE TO IMAGINE A LARGE
14 HAYSTACK WITH A NEEDLE BURIED SOMEWHERE IN THE HAYSTACK. AND IF
15 YOU HAD A WAY TO MAKE MANY COPIES OF THAT NEEDLE, EVENTUALLY IF
16 YOU MADE MILLIONS OF COPIES, YOU WOULD BE ABLE TO EASILY DETECT
17 THE PRESENCE OF THE NEEDLE.

18 SO IT'S AN EXTREMELY IMPORTANT PROCESS.

19 Q. ARE YOU FAMILIAR WITH THE JOURNAL SCIENCE?

20 A. YES, I AM.

21 Q. WHAT IS SCIENCE?

22 A. WELL, SCIENCE IS A JOURNAL PUT OUT BY THE AMERICAN
23 ASSOCIATION FOR ADVANCEMENT OF SCIENCE. IT NOT ONLY CONTAINS
24 RESEARCH ARTICLES AND REVIEWS BUT ALSO KEEPS YOU UP WITH THE
25 POLITICS OF SCIENCE IN THE COUNTRY.

4
1 Q. NOW, IN -- IN THIS DRAFT MANUSCRIPT, DR. KORNBERG POINTS OUT
2 THAT SCIENCE MAGAZINE "SELECTED PCR AS THE MAJOR SCIENTIFIC
3 DEVELOPMENT OF 1989."

4 WERE YOU AWARE OF THAT?

5 A. YES, I WAS. I SAW THAT. I SAW THE ARTICLE, YES.

6 Q. WHAT WAS YOUR REACTION TO THAT ARTICLE?

7 A. WELL, I WAS VERY PLEASED THAT THIS IMPORTANT PROCESS WAS SO
8 RECOGNIZED.

9 Q. NOW, THE SCIENCE ARTICLE SAYS THAT THE EDITORS OF SCIENCE --
10 IF I CAN GET THIS A LITTLE LARGER HERE -- THE EDITORS OF SCIENCE
11 "SELECTED PCR BECAUSE THEY THOUGHT THE INVENTION LIKELY TO HAVE
12 THE GREATEST INFLUENCE ON HISTORY."

13 DO YOU THINK THAT PCR IS AN INVENTION OF THAT KIND OF
14 IMPORTANCE?

15 A. I BELIEVE IT IS. I ASSUME THEY'RE TALKING ABOUT THE
16 SUBSEQUENT HISTORY OF DEVELOPMENT OF SCIENCE. I THINK IT WILL
17 DRAMATICALLY CHANGE THE WAY WE DO BUSINESS IN THE LABORATORY.
18 IN FACT, IT HAS ALREADY. AND IT'S GOING TO HAVE AN ENORMOUS
19 IMPACT. IT WILL ACCELERATE OUR ABILITY TO -- TO UNDERSTAND
20 BIOLOGICAL SYSTEMS.

21 (PAUSE IN PROCEEDINGS)

22 Q. (BY MR. PASAHOW) NOW, WE HAVE PREPARED A TIMELINE THAT I'M
23 GOING TO REFER TO IN MUCH OF THE REST OF YOUR EXAM.

24 A. UH-HUH.

25 Q. FOR YOUR CONVENIENCE, I'VE PREPARED A SMALL VERSION OF IT

4
1 THAT YOU CAN REFER TO, SINCE WE'VE HAD TO TURN THE LARGE
2 SOMEWHAT AWAY FROM YOU.

3 AND I SHOULD INDICATE THAT THAT'S BEEN MARKED AS
4 EXHIBIT B-30.

5 AND ON IT, WE'VE -- WE'VE INDICATED VARIOUS PAPERS AND
6 BOOKS THAT GOT PUBLISHED AND SOME EVENTS BETWEEN THE PERIOD 1969
7 AND 1990.

8 A. (NODDING HEAD.)

9 Q. AND THE FIRST OF THESE THAT I'D LIKE TO START WITH IS THE
10 PUBLICATION OF AN ARTICLE THAT WE'VE BEEN REFERRING TO AS
11 KLEPPE, ET AL., IN 1971.

12 A. (NODDING HEAD.)

13 Q. AND THAT ARTICLE HAS BEEN MARKED AS EXHIBIT A-18. AND LET
14 ME GIVE YOU A COPY.

15 (PAUSE IN PROCEEDINGS)

16 Q. (BY MR. PASAHOW) YOU'VE READ THAT ARTICLE BEFORE?

17 A. I HAVE READ THIS ARTICLE, YES.

18 Q. AND YOU'RE FAMILIAR WITH IT, I TAKE IT.

19 A. I AM FAMILIAR WITH IT.

20 Q. NOW, I'M NOT GOING TO ASK YOU ABOUT THE FIRST 20 PAGES, BUT
21 WE FOCUSED ON A PARAGRAPH TOWARDS THE END, AND IT'S IN -- THE
22 PARAGRAPH THAT'S IN THIS POSTER B-172.

23 WHAT IS DESCRIBED IN THAT PARAGRAPH?

24 A. WELL, LET ME PUT THE PARAGRAPH IN CONTEXT HERE A LITTLE BIT.

25 THE KLEPPE ARTICLE ITSELF IS . . . WELL, LET ME GO BACK

4
1 EVEN FURTHER.

2 KHORANA'S GROUP, WHO PUBLISHED THIS PAPER, WAS VERY
3 INTERESTED IN SYNTHESIZING A COMPLETE GENE, AND THEY CHOSE A
4 SMALL TRNA GENE. AND WHEN THIS ARTICLE WAS WRITTEN, THEY WERE
5 IN THE COURSE OF . . . OF CONSTRUCTING THIS GENE BY VERY
6 LABORIOUS ORGANIC SYNTHESIS.

7 AND THEY WERE HOPING IN ONE OR TWO OR THREE YEARS TO
8 HAVE THE COMPLETE GENE SYNTHESIZED, BUT THEY EXPECTED TO HAVE A
9 VERY SMALL QUANTITY OF IT. SO THAT THEY WERE LOOKING FOR WAYS
10 TO . . . LET'S SUPPOSE THEY END UP WITH A SMALL QUANTITY OF THIS
11 GENE AFTER TWO OR THREE YEARS OF EFFORT. THEY WOULD LIKE TO BE
12 ABLE TO MAKE MORE COPIES OF THIS GENE, AS NEEDED, FOR RESEARCH
13 WITHOUT GOING THROUGH THE VERY COMPLEX ORGANIC SYNTHESIS.

14 SO THEY WERE LOOKING FOR AN ENZYMATIC OR BIOCHEMICAL
15 WAY TO DO THIS, AND THIS ARTICLE CONCERNS THAT.

16 AND THIS LAST PARAGRAPH REALLY . . . TRIES TO DESCRIBE
17 TWO HYPOTHETICAL WAYS THAT THEY MIGHT MAKE COPIES OF THE GENE
18 ONCE THEY HAVE IT.

19 Q. WHAT WAS THE FIRST OF THOSE WAYS? IS THAT PCR?

20 A. OKAY. THE FIRST WAY -- WELL, FIRST OF ALL, I DON'T BELIEVE
21 THAT IT'S PCR. IT DESCRIBES A METHOD WHICH IN HINDSIGHT HAS A
22 VAGUE RESEMBLANCE TO PCR, BUT IT'S MISSING CERTAIN CRUCIAL
23 FEATURES.

24 FIRST OF ALL, IT DOESN'T EXPLICITLY STATE THE ESSENTIAL
25 POINT THAT WAS MADE IN THE CLAIM 1; NAMELY, THAT THE PRODUCT

5

1 STRANDS FROM ONE CYCLE MUST SERVE AS TEMPLATE IN SUBSEQUENT
2 CYCLES.

3 SO, TO ME, THERE'S NO INDICATION THAT THEY WERE
4 CONCEIVING OF AN EXPONENTIAL TYPE OF PROCESS. IN FACT, I DON'T
5 THINK THEY REALLY NEEDED THAT FOR THE KIND OF MANUFACTURING
6 PROCESS THAT THEY WERE ENVISIONING HERE.

7 SO I DON'T -- ASIDE FROM THE RATHER VAGUE RESEMBLANCE,
8 I DON'T SEE THE FULL PCR PROCESS THERE.

9 Q. WELL, THE WAY WE'VE COME TO ANALYZE IT, BECAUSE THAT'S WHAT
10 THE PATENT LAW SUGGESTS --

11 A. YEAH, RIGHT.

12 Q. -- IS, WE'D LIKE TO LOOK AT HOW THIS ARTICLE WOULD BE SEEN
13 BY AN ORDINARILY-SKILLED POST-DOCTORAL FELLOW IN BIOCHEMISTRY,
14 IN A LABORATORY SUCH AS YOURS AT JOHNS HOPKINS --

15 A. YEAH.

16 Q. -- IN MARCH 1984, ONE YEAR BEFORE THE PATENT WAS APPLIED
17 FOR.

18 MR. FIGG: YOUR HONOR, I OBJECT TO THE CHARACTERIZATION
19 OF WHAT THE PATENT LAWS REQUIRE, ESPECIALLY IN TERMS OF THE
20 DEFINITION OF A POST-DOCTORATE FELLOW.

21 THE COURT: OBJECTION SUSTAINED. I'M GOING TO ASK THAT
22 YOU REPHRASE THE QUESTION. I THINK YOU CAN DO THAT AND JUST ASK
23 THE QUESTION.

24 MR. PASAHOW: I WILL, YOUR HONOR.

25 Q. I'D LIKE FOR YOU TO ASSUME, DOCTOR, THAT WE'RE TALKING ABOUT

5

1 A -- AN ORDINARILY-SKILLED POST-DOCTORAL FELLOW DURING THE
2 PERIOD MARCH 1984, SOMEONE IN THE FIELD OF BIOCHEMISTRY OR
3 MOLECULAR BIOLOGY.

4 A. UH-HUH.

5 Q. AND LET ME BEGIN BY ASKING YOU: DID YOU HAVE CONTACT WITH
6 SUCH PEOPLE AT JOHNS HOPKINS DURING THAT PERIOD?

7 A. WELL, WE HAVE -- I HAD POST-DOCTORAL FELLOWS IN MY OWN
8 LABORATORY THAT I WOULD CONSIDER THAT FIT INTO THAT CATEGORY.

9 Q. ARE YOU FAMILIAR WITH THE REPUTATION OF DR. KORNBERG'S
10 LABORATORY AND THE OTHER LABORATORIES IN DR. KORNBERG'S
11 DEPARTMENT AT STANFORD UNIVERSITY?

12 A. YES. IT WAS CONSIDERED, I THINK BY MOST . . . BIOCHEMISTS
13 AND MOLECULAR BIOLOGISTS, TO BE ONE OF THE OUTSTANDING
14 BIOCHEMISTRY DEPARTMENTS IN THE COUNTRY, AND PERHAPS IN THE
15 WORLD.

16 Q. IN MARCH 1984, HOW MANY DEPARTMENTS OR -- RATHER, HOW MANY
17 LABORATORIES WERE THERE DOING BIOCHEMISTRY AND MOLECULAR
18 BIOLOGY?

19 A. WELL, IT'S HARD TO ENUMERATE THEM, BUT I WOULD GUESS IN THE
20 UNITED STATES ALONE THAT IT WOULD NUMBER . . . PROBABLY OVER A
21 THOUSAND, AND, OF COURSE, IF YOU GO WORLD-WIDE, YOU'RE UP INTO
22 SEVERAL THOUSANDS.

23 Q. AND OF THAT SEVERAL THOUSAND, HOW MANY WERE, IN YOUR
24 OPINION, BETTER THAN OR AS GOOD AS THE DEPARTMENTS AT STANFORD,
25 THE BIOCHEMISTRY DEPARTMENT AT STANFORD?

5

1 A. I WOULD PROBABLY BE ABLE TO PICK OUT NO MORE THAN A HANDFUL,
2 FIVE OR SIX, THAT MIGHT BE COMPARABLE, AND PERHAPS EVEN LESS
3 THAN THAT NUMBER.

4 Q. NOW, LET'S GO BACK TO THIS ORDINARILY-SKILLED PERSON, THIS
5 ORDINARILY-SKILLED POST-DOCTORAL FELLOW, IN 1984:

6 DO YOU THINK THAT THAT PERSON, THIS HYPOTHETICAL MAN OR
7 WOMAN, WOULD UNDERSTAND THE FIRST OF THE METHODS DESCRIBED IN
8 THIS -- THIS LAST PARAGRAPH OF THE KLEPPE ARTICLE TO REFER TO
9 THE SAME REACTION THAT IS DESCRIBED IN CLAIM 1 OF THE '202
10 PATENT?

11 A. I THINK THEY'D HAVE SOME DIFFICULTY IN SEEING THE
12 CONNECTION.

13 (PAUSE IN PROCEEDINGS)

14 THE WITNESS: THE -- AS I MENTIONED, THE -- SOME OF THE
15 ESSENTIAL FEATURES OF THE . . . OF THE CLAIM 1 ARE NOT
16 EXPLICITLY STATED IN THIS PARTICULAR SECTION.

17 AND IT'S A VERY VAGUELY-WORDED PARAGRAPH WITH MANY
18 WORDS SUCH AS "ONE WOULD HOPE" AND SO ON AND SO FORTH. SO
19 IT'S -- IT'S LITERALLY STATED AS A RATHER HYPOTHETICAL . . .
20 POSSIBLE PROCESS.

21 Q. (BY MR. PASAHOW) WELL, LET'S LOOK AT IT IN SOME DETAIL.

22 A. UH-HUH.

23 Q. IT STARTS OFF TALKING ABOUT THE PRINCIPLES FOR EXTENSIVE
24 SYNTHESIS OF THE DUPLEX TRNA GENES.

25 A. UH-HUH.

5
1 Q. NOW, WOULD THE ORDINARILY-SKILLED POST-DOC IN 1984 KNOW
2 ANYTHING ABOUT THE TRNA GENE?

3 A. YES, THEY WOULD BE VERY ACQUAINTED WITH THE GENE, BECAUSE
4 THE -- BY THAT TIME, THERE WERE A NUMBER OF TRNA GENES THAT HAD
5 BEEN SEQUENCED AND, IN FACT, THE STRUCTURE -- THREE-DIMENSIONAL
6 STRUCTURE OF SOME OF THESE GENES WAS KNOWN.

7 SO THEY WOULD BE FULLY AWARE, FOR EXAMPLE, AS POINTED
8 OUT IN THE ARTICLE ITSELF, THAT THIS PARTICULAR GENE -- THE TRNA
9 IS A HIGHLY-HAIRPINNED STRUCTURE CONTAINING AS MANY AS FOUR
10 DIFFERENT HAIRPINS, AND A VERY COMPACT, COLLAPSED STRUCTURE
11 RATHER THAN EXTENDED MOLECULE.

12 AND THE DNA . . . THE DNA ITSELF -- THE DNA GENING HAS,
13 OF COURSE, THE SAME SEQUENCE AS THE TRNA ITSELF AND WOULD BE
14 EXPECTED TO FORM THE SAME SORT OF HIGHLY-FOLDED STRUCTURE.

15 AND THIS, OF COURSE, IS -- AS I SAY, IS POINTED OUT IN
16 THE ARTICLE ITSELF AS A POTENTIAL PROBLEM IN THIS PROCESS.

17 Q. WOULD THE 1984 POST-DOCTORAL FELLOW WE'RE TALKING ABOUT
18 EXPECT THESE FOLDS IN THE GENE TO AFFECT AN EFFORT TO COPY THE
19 GENE?

20 A. YES. I THINK THEY WOULD BE FULLY AWARE THAT YOU WOULD HAVE
21 A GREAT DEAL OF TROUBLE MAKING A COMPLETE COPY OF SUCH A FOLDED
22 STRUCTURE.

23 IF YOU -- AS THEY SUGGEST HERE, IF YOU WERE TO
24 HYBRIDIZE A PRIMER, A SHORT OLIGONUCLEOTIDE, TO THIS FOLDED
25 STRUCTURE, YOU -- ONE WOULD EXPECT THAT YOU MIGHT ONLY BE ABLE

6
1 TO GO TO THE FIRST HAIRPIN BEFORE POSSIBLY SKIPPING OVER,
2 MISSING THE WHOLE LOOP, SKIPPING OVER THAT, IN EFFECT DELETING A
3 PORTION OF THE STRUCTURE, OR SIMPLY STOPPING AT THAT POINT.

4 SO ONE WOULD GET A VARIETY OF PRODUCTS, NONE OF WHICH
5 YOU REALLY WANT, IN THIS REACTION. THAT WOULD BE THE
6 EXPECTATION.

7 Q. NOW, THE PARAGRAPH GOES ON TO DESCRIBE DENATURING THE
8 MOLECULE, AND THEN IT SAYS:

9 "THIS DENATURATION STEP WOULD BE CARRIED OUT
10 IN THE PRESENCE OF A SUFFICIENTLY LARGE EXCESS OF THE
11 TWO APPROPRIATE PRIMERS."

12 WHAT WOULD THE ORDINARILY-SKILLED POST-DOC WE'VE BEEN
13 TALKING ABOUT UNDERSTAND BY THE PHRASE "A SUFFICIENTLY LARGE
14 EXCESS OF . . . PRIMERS"?

15 A. WELL, "EXCESS" MEANS THAT YOU'D HAVE MORE COPIES OF PRIMER
16 THAN YOU HAVE OF THE -- OF THE TEMPLATE, SO . . . AND IF YOU
17 LOOK BACK IN THE ARTICLE ITSELF, THEY'RE USING EXCESSES OF ABOUT
18 TWO-FOLD IN THESE REACTIONS. SO THE OBVIOUS THING WOULD BE TO
19 ASSUME A TWO-FOLD EXCESS.

20 BUT IF IT WAS A . . . I THINK IN 1984, ONE MIGHT ALSO
21 CONSIDER LARGER AMOUNTS THAN TWO-FOLD, PERHAPS UP TO 10-, 20-,
22 POSSIBLY EVEN 30-FOLD EXCESS.

23 Q. WAS THERE ANY PARTICULAR LEARNING IN 1984 ABOUT THE USE OF
24 LARGE EXCESSES OF PRIMERS IN PRIMER EXTENSION REACTIONS?

25 A. YES. I THINK MOST OF MY POST-DOCTORAL FELLOWS, AND I ASSUME

6

1 ANYONE OF ORDINARY SKILL, WOULD HAVE KNOWN THAT -- PARTICULARLY
2 IF THEY'VE EVER DONE SEQUENCING, THE SANGER SEQUENCING, WHICH
3 INVOLVES PRIMERS AND PRIMER EXTENSION -- THAT ONE OF THE MAJOR
4 PROBLEMS THAT ONE RUNS INTO IN THAT PROCEDURE IS MISPRIMING.

5 IN SEQUENCING, YOU WANT TO START WITH THE PRIMER BOUND
6 TO A SINGLE POINT ALONG THE DNA, AND THEN YOU CAN DEVELOP A
7 CLEAN, UNIFORM SEQUENCE.

8 OBVIOUSLY, IF THE PRIMER WERE TO BIND TO TWO DIFFERENT
9 SITES, YOU WOULD GET A MIXTURE OF TWO DIFFERENT SEQUENCES.

10 AND IT WAS NOT AN UNCOMMON PROBLEM TO HAVE A
11 PRIMER . . . WHICH . . . HAD SOME PARTIAL MATCH TO OTHER POINTS
12 ALONG THE DNA MOLECULE. SO IF YOU USED A LARGE EXCESS, ENOUGH
13 TO COMPLETELY BIND UP THE CORRECT SITE AND HAVE MUCH -- MANY
14 MOLECULES LEFT OVER, THOSE MOLECULES WOULD SEEK OUT THE OTHER
15 SITES, AND YOU THEN GET A MIXTURE.

16 SO THE TENDENCY WOULD REALLY BE TO GO DOWNWARDS, TO
17 KEEP A MINIMAL AMOUNT OF PRIMER SUFFICIENT FOR THOSE REACTIONS.

18 Q. DID YOU EVER, IN FACT, SEE THE KIND OF MISPRIMING YOU
19 DESCRIBED FROM USING LARGE EXCESSES OF PRIMERS?

20 A. YES, IN SEQUENCING IN OUR OWN LAB. IN FACT, SEQUENCING IN
21 WHICH I PERSONALLY WAS INVOLVED. THIS WAS IN SEQUENCING ONE OF
22 THE RESTRICTION GENES.

23 I SPENT ABOUT A MONTH ON TRYING TO UNRAVEL THE PROBLEMS
24 IN SEQUENCING. I HAD A MIXED BAND PATTERN, AND I WAS USING A
25 COMMERCIAL PRIMER, WHICH WAS SUPPOSED TO WORK. THEY SOLD IT TO

6 1 ME WITH THE ASSUMPTION IT WOULD WORK.

2 BUT, FINALLY, AFTER TRYING EVERY POSSIBILITY, I DECIDED
3 TO TRY ANOTHER COMMERCIAL PRIMER THAT WAS LONGER, AND
4 IMMEDIATELY THE PROBLEMS DISAPPEARED. IT WAS VERY CLEAR THAT
5 THIS SHORTER PRIMER IN THE CONCENTRATIONS I WAS USING WAS
6 MISPRIMING AT VARIOUS SITES.

7 Q. NOW, THE PARAGRAPH ALSO TALKS ABOUT USING TWO APPROPRIATE
8 PRIMERS.

9 IT SAYS: "SUFFICIENTLY LARGE EXCESS OF THE TWO
10 APPROPRIATE PRIMERS."

11 WOULD THE ORDINARILY-SKILLED POST-DOC IN 1984 KNOW HOW
12 LONG THOSE PRIMERS SHOULD BE?

13 A. NOT PRECISELY. IT'S -- I MEAN, IT'S NOT STATED HERE.

14 BUT IF THEY WENT TO THE . . . YEAH, INTO THE BODY OF
15 THE PAPER, I THINK IT WAS STATED THAT YOU COULD PRIME WITH
16 SOMETHING AS SHORT AS FIVE IN LENGTH, BUT THAT IF YOU HAD
17 HAIRPIN STRUCTURES, YOU MIGHT NEED IN SOME CASES TO GO UP TO 12
18 OR SO.

7 19 IN ADDITION, IN '84, A POST-DOCTORAL FELLOW EXPERIENCED
20 IN SEQUENCING WOULD KNOW THAT PRIMERS GENERALLY WERE IN THE
21 RANGE OF 15 TO 20, SO I THINK HE WOULD PROBABLY CHOOSE THE
22 HIGHER NUMBER.

23 Q. ANYWAY, SOMEWHERE BETWEEN FIVE AND 20?

24 A. SOMEWHERE BETWEEN FIVE AND 20, POSSIBLY LARGER.

25 Q. NOW, THE ARTICLE THEN GOES ON SAYING:

7
1 "UPON COOLING, ONE WOULD HOPE TO OBTAIN TWO
2 STRUCTURES, EACH CONTAINING THE FULL LENGTH OF THE
3 TEMPLATE STRAND, APPROPRIATELY COMPLEXED WITH THE
4 PRIMER."

5 NOW, DO YOU THINK THAT -- LET ME START THAT AGAIN:

6 WOULD THE 1984 ORDINARILY-SKILLED POST-DOC EXPECT THAT
7 THIS HOPE THAT'S EXPRESSED HERE WOULD BE FULFILLED; THAT IS,
8 WOULD THE 1984 POST-DOC EXPECT YOU'D BE ABLE TO COME UP WITH TWO
9 MOLECULES APPROPRIATELY PRIMED?

10 A. I THINK THEY WOULD KNOW THAT --

11 MR. FIGG: OBJECTION, LEADING.

12 THE WITNESS: -- IT WOULD BE VERY DIFFICULT TO DO.

13 THE COURT: HOLD ON. JUST A MOMENT.

14 THE WITNESS: YEAH.

15 THE COURT: THE OBJECTION IS LEADING?

16 MR. FIGG: THIS ONE AND MANY OTHERS, BUT I'M MAKING THE
17 OBJECTION NOW, YOUR HONOR.

18 THE COURT: WELL, GET TO IT A LITTLE BIT MORE QUICKLY.
19 IT'S ALREADY BEEN ANSWERED.

20 I'M GOING TO OVERRULE THE OBJECTION AT THIS POINT. HE
21 IS ALSO CALLED AS AN EXPERT WITNESS, IN ANY EVENT, SO THE
22 OBJECTION IS OVERRULED.

23 THE WITNESS: OKAY. WOULD YOU REPEAT THE QUESTION?

24 Q. (BY MR. PASAHOW) I WILL. LET ME SHORTEN IT:

25 THE QUESTION IS: THIS REFERENCE HERE TO HOPING TO

7
1 OBTAIN TWO STRUCTURES APPROPRIATELY COMPLEXED, WOULD THE 1984
2 POST-DOC EXPECT THAT YOU WOULD BE ABLE TO OBTAIN THE TWO
3 APPROPRIATELY COMPLEXED MOLECULES OF THE PRIMER AND THE TEMPLATE
4 STRAND?

5 (PAUSE IN PROCEEDINGS)

6 THE WITNESS: I -- I THINK THAT . . . AS I STATED
7 EARLIER, THE EXPECTATION WOULD BE THAT YOU . . . WOULD HAVE
8 SHORTER PRODUCTS, OR DELETED PRODUCTS.

9 DID I NOT ANSWER THE QUESTION?

10 Q. (BY MR. PASAHOW) WHAT DO YOU MEAN BY "SHORTER PRODUCTS"?

11 A. I MEAN THAT IF YOU SKIPPED OVER A HAIRPIN STRUCTURE IN
12 THIS . . . AS I MENTIONED -- MAYBE I SHOULD DRAW THIS. I DON'T
13 KNOW.

14 Q. SURE.

15 A. THE TRNA GENES WERE KNOWN TO FORM WHAT WE CALL CLOVERLEAF
16 STRUCTURES, LIKE THE . . .

17 Q. WE'LL GET YOU A PAD. JUST A SECOND.

18 A. ALL RIGHT.

19 (PAUSE IN PROCEEDINGS)

20 THE WITNESS: (WITNESS APPROACHES EASEL.)

21 (WITNESS DIAGRAMING ON EASEL)

22 OKAY. IN THE FULLY CLOVERLEAF-FOLDED PATTERN, WHICH
23 LOOKS SOMETHING LIKE THIS, THESE ARE ESSENTIALLY PAIRED REGIONS,
24 WHERE A'S, FOR EXAMPLE, PAIRED WITH T, A G, JUST AS AN EXAMPLE,
25 WITH C AND SO ON, AND SO I COULD JUST DRAW THESE AS PAIRED

7

1 BASES.

2 THAT'S THE KIND OF STRUCTURE THAT THE
3 ORDINARILY-SKILLED POST-DOC WOULD EXPECT FROM THIS -- THIS TRNA
4 MOLECULE.

5 NOW, IT MIGHT NOT BE FORMED PERFECTLY LIKE THAT. FOR
6 EXAMPLE, IT COULD BE PARTIAL STRUCTURES, LIKE (INDICATING),
7 MAYBE WITH THIS LOOP AND THIS LOOP, AND THEN THIS (INDICATING),
8 FOR EXAMPLE. YOU MIGHT HAVE A MIX, DEPENDING ON THE CONDITIONS.

9 NOW, WHAT I MEAN IS THAT IF YOU WERE TO PRIME ALONG
10 THIS MOLECULE, THIS IS A THREE-PRIMED END, FOR EXAMPLE, YOU HAVE
11 A PRIMER, WHICH YOU HAVE HYBRIDIZED, WHICH THEY USE THE WORD
12 "COMPLEXED," BUT I THINK THE POST-DOC MIGHT ASSUME THAT THAT
13 MEANS THE APPROPRIATE HYBRIDIZATION.

14 NOW, AS YOU SYNTHESIZE ALONG, THESE ARE RATHER STABLE
15 STRUCTURES, AND IT'S NOT NECESSARILY TRUE THAT YOU'RE GOING TO
16 BE ABLE TO SYNTHESIZE RIGHT ON THROUGH LIKE THAT. IN SOME
17 CASES, YOU MIGHT ACTUALLY JUST SKIP OVER THIS WHOLE REGION HERE
18 (INDICATING) AND THEN SKIP OVER THAT (INDICATING) AND COME UP
19 LIKE THAT (INDICATING) TO GET A MOLECULE OF THAT SORT.

20 ON THE OTHER HAND, IT'S -- IT'S EVEN MORE LIKELY THAT
21 THE EXTENSION FROM THE PRIMER WOULD SIMPLY STOP IN THIS
22 STRUCTURE HERE (INDICATING), WOULD NOT BE ABLE TO GO THROUGH
23 THAT AREA. SO YOU COULD GET SHORTENED PRODUCTS AS WELL AS . . .
24 AS . . . IF -- WELL, IF YOU STOPPED RIGHT HERE, THAT WOULD BE A
25 COMPLETE PRODUCT, WHEREAS IF YOU WERE ABLE TO GO THROUGH LIKE

7
1 THAT (INDICATING), IT WOULD BE AN ACTUALLY SHORTENED OR DELETED
2 PRODUCT.

3 THESE WOULD ALL BE SEEN PROBABLY IN THE EARLY '70'S AS
4 SIMPLY INCOMPLETE PRODUCTS.

5 Q. (BY MR. PASAHOW) OKAY. THANK YOU.

6 A. (WITNESS RESUMES WITNESS STAND.)

7 (PAUSE IN PROCEEDINGS)

8 Q. (BY MR. PASAHOW) NOW, THE . . . LET ME GET THIS OUT OF MY
9 WAY HERE.

10 (PAUSE IN PROCEEDINGS)

11 Q. (BY MR. PASAHOW) THE PARAGRAPH GOES ON TO SAY THAT:

12 "TWO MOLECULES OF THE ORIGINAL DUPLEX SHOULD
13 RESULT" FROM THIS EXTENSION REACTION.

14 A. OKAY. WELL, THAT'S WHAT THEY WERE HOPING FOR.

15 (PAUSE IN PROCEEDINGS)

16 THE WITNESS: I THINK BY 1984, THE EXPECTATION WOULD BE
17 THAT YOU WOULDN'T ACHIEVE THAT.

18 (PAUSE IN PROCEEDINGS)

19 THE WITNESS: I THINK THE ONLY -- IN A CASE WHERE IT
20 WAS TOTALLY UNFOLDED, THERE MIGHT BE A SMALL AMOUNT OF THAT
21 PRODUCT FORMED. IT'S HARD TO SAY.

22 Q. (BY MR. PASAHOW) NOW, THE NEXT SENTENCE SAYS:

23 "THE WHOLE CYCLE COULD BE REPEATED."

24 WHAT WOULD HAPPEN IF YOU REPEATED THE CYCLE AND YOU HAD
25 THESE SHORTER MOLECULES YOU'VE DESCRIBED FOR US?

8

1 A. WELL, NONE OF THOSE SHORTER PRODUCTS WOULD BE CAPABLE OF
2 SERVING AS TEMPLATES IN THE SUBSEQUENT REACTION, BECAUSE WHAT
3 WE'RE ASSUMING HERE IS THAT THE -- ALTHOUGH THEY DON'T CLEARLY
4 STATE IT, WE'RE ASSUMING THAT THE TWO PRIMERS ARE AT OPPOSITE
5 ENDS OF THE MOLECULE.

6 SO THE SHORTER PRODUCTS SIMPLY WOULDN'T REACH THROUGH
7 FAR ENOUGH TO BE APPROPRIATE FOR COMPLEXING TO THE PRIMER AT THE
8 FAR END.

9 Q. WHY WOULDN'T IT FORM A COMPLEX WITH THE PRIMER? WHY
10 WOULDN'T THE PRODUCT --

11 A. WELL, THOSE SEQUENCES WOULD BE MISSING THAT ARE
12 COMPLEMENTARY TO THE PRIMER.

13 (PAUSE IN PROCEEDINGS)

14 Q. (BY MR. PASAHOW) NOW, THE ARTICLE THEN GOES ON TO SAY THAT:

15 "IT IS, HOWEVER, POSSIBLE THAT UPON COOLING
16 AFTER DENATURATION OF THE DNA -- OF THE DNA DUPLEX,
17 RENATURATION TO FORM THE ORIGINAL DUPLEX WOULD
18 PREDOMINATE OVER THE TEMPLATE-PRIMER COMPLEX
19 FORMATION."

20 A. YEAH.

21 Q. CAN -- CAN YOU TRANSLATE THAT FOR US?

22 A. YEAH. THAT'S AN ENTIRELY DIFFERENT PROBLEM WHICH ALSO, I
23 THINK, LEADS TO SERIOUS -- POTENTIALLY SERIOUS DIFFICULTIES IN
24 THIS PROCEDURE.

25 (PAUSE IN PROCEEDINGS)

8
1 THE WITNESS: IF THE -- IN THE ARTICLE HERE, THEY WERE
2 WORKING WITH A TWO-FOLD EXCESS OF PRIMER OVER THE AMOUNT OF
3 TEMPLATE. AND THE AMOUNT OF TEMPLATE WAS AT A RATHER HIGH
4 LEVEL, SO THAT ESSENTIALLY THE PRIMER AND THE TEMPLATE ARE
5 COMPARABLE CONCENTRATIONS IN THE REACTION.

6 SO THAT THE -- IF YOU SIMPLY MELT APART THE TWO STRANDS
7 OF THE GENE, THERE'S A VERY HIGH PROBABILITY THAT THOSE TWO
8 STRANDS COULD SIMPLY COME BACK TOGETHER AGAIN.

9 EVEN IF PRIMER BOUND -- IF YOU LOOKED AT THE CONDITIONS
10 OF ANNEALING WHICH ARE OF THE LENGTH OF AN HOUR OR SO, EVEN IF
11 PRIMER BOUND, YOU COULD STILL JOIN THE GENE TOGETHER AND IT
12 WOULD DISPLACE THE PRIMER OVER THE PERIOD OF AN HOUR.

13 SO THAT, AGAIN, THE POST-DOCTORAL FELLOW THAT WE'RE
14 TALKING ABOUT HERE WOULD, I THINK, MAKE THE LOGICAL ASSUMPTION
15 THAT THAT WOULD BE A SERIOUS PROBLEM.

16 Q. (BY MR. PASAHOW) NOW, THE ARTICLE SAYS THAT THAT SHOULD --
17 OR SUGGESTS THAT:

18 "IF THIS TENDENCY COULD NOT BE CIRCUMVENTED
19 BY ADJUSTING PRIMER -- BY ADJUSTING THE CONCENTRATIONS
20 OF THE PRIMERS" --

21 A. UH-HUH.

22 Q. -- "SOMETHING ELSE SHOULD BE DONE."

23 NOW, WHAT WOULD THIS 1984 POST-DOCTORAL FELLOW
24 UNDERSTAND BY THE PHRASE "ADJUSTING THE CONCENTRATIONS OF THE
25 PRIMERS"?

8

1 A. I THINK THE -- SINCE THERE WAS CONCERN ABOUT THE COMPETING
2 ANNEALING OF THE TEMPLATE, THE NATURAL ASSUMPTION WOULD BE THAT
3 ONE WOULD INCREASE THE AMOUNT OF PRIMER TO TRY TO MAKE IT MORE
4 FAVORABLE FOR THE PRIMER TO BIND TO THE TEMPLATE.

5 Q. THROUGH WHAT KIND OF A RANGE WOULD YOU EXPECT THE 1984
6 POST-DOCTORAL FELLOW TO TRY TO ADJUST THE CONCENTRATION OF THE
7 PRIMERS?

8 A. WELL, IN THE LITERATURE, ONE COULD SEE VALUES UP AROUND
9 30-FOLD EXCESS, BUT I -- I DON'T THINK THAT WOULD ALLEVIATE THE
10 PROBLEM, BECAUSE IN THIS PAPER, THEY'RE DESCRIBING ANNEALING
11 TIMES OF AN HOUR OR SO, WHICH WOULD ALLOW PLENTY OF TIME FOR
12 DISPLACEMENT OF THOSE PRIMERS TO FORM THE MORE STABLE, FULL
13 ANNEALED GENE.

14 REMEMBER, THE PRIMER IS ONLY A SHORT SEGMENT, WHEREAS
15 THE GENE WOULD PAIR OVER THE WHOLE LENGTH. IT'S A MUCH MORE
16 STABLE STRUCTURE. IT WOULD TEND TO DISPLACE THOSE PRIMERS, EVEN
17 IF THEY WERE IN HIGHER CONCENTRATION.

18 Q. WELL, DO YOU THINK THE 1984 POST-DOCTORAL FELLOW WE'VE BEEN
19 TALKING ABOUT WOULD BE ABLE TO FIND A SITUATION WHERE HE COULD
20 ADJUST THE PRIMERS TO OVERCOME THE RE-ANNEALING PROBLEM?

21 (PAUSE IN PROCEEDINGS)

22 THE WITNESS: I DON'T THINK HE COULD SOLVE THE PROBLEM,
23 FRANKLY, NOT . . .

24 (PAUSE IN PROCEEDINGS)

25 THE WITNESS: CERTAINLY NOT WITH THE KINDS OF

8
1 CONCENTRATIONS OF -- OF TEMPLATE THAT ARE MENTIONED IN THIS
2 ARTICLE. HE WOULD HAVE TO DO HIS OWN EXPERIMENTATION. HE
3 CERTAINLY COULD NOT DERIVE IT FROM THIS PAPER.

4 MR. PASAHOW: YOUR HONOR, THIS MIGHT BE AN APPROPRIATE
5 TIME TO BREAK.

6 THE COURT: THIS IS A GOOD TIME FOR YOU? FINE.

7 OKAY. DR. SMITH, YOU MAY STEP DOWN, IF YOU'D LIKE, AND
8 WE'LL SEE YOU TOMORROW MORNING.

9 AND, LADIES AND GENTLEMEN, YOU ARE EXCUSED.

10 PLEASE FOLLOW THE INSTRUCTIONS I'VE GIVEN YOU ABOUT NOT
11 DISCUSSING THE CASE AMONGST YOURSELVES OR WITH ANYONE ELSE, AND
12 WE'LL SEE YOU TOMORROW MORNING AT 8:00 O'CLOCK. THANK YOU.

13 (JURY EXCUSED)

14 (OPEN COURT, JURY NOT PRESENT:)

15 THE COURT: OKAY. NOW, THE ISSUES THAT YOU WANTED TO
16 TAKE UP AT THIS TIME, WHICH IS THE MORE CRITICAL? WE'LL DEAL
17 WITH THAT FIRST.

18 MR. LEWIS: I THINK IT'S THE MOTION CONCERNING DR.
19 MARTINELL'S QUALIFICATIONS.

20 THE COURT: WHICH YOU HAD HOPED TO ELICIT THROUGH DR.
21 ANDERSON OR -- IS THAT CORRECT?

22 MR. LEWIS: YES, YOUR HONOR. IT WOULD CERTAINLY
23 INCLUDE THAT.

24 THE COURT: WELL, WHAT HAPPENS IF YOU ELICIT THAT
25 TESTIMONY? THEN I ASSUME THAT PLAINTIFFS WILL WANT TO CALL

9
1 SOMEONE ON REBUTTAL TO GO MORE DEEPLY INTO IT?

2 MR. FIGG: WELL, I THINK WE WOULD CERTAINLY BE ENTITLED
3 TO CALL PEOPLE WHO HAD WORKED WITH DR. MARTINELL, CRITIQUE HIS
4 PAPERS, CRITIQUE HIS EDUCATION, HOW HE DID IN SCHOOL. I THINK
5 YOU OPEN UP THE WHOLE THING.

6 THE COURT: GO BACK TO KINDERGARTEN?

7 MR. FIGG: WE MIGHT.

8 MR. LEWIS: WELL, YOUR HONOR, AFTER ALL, IT'S NOT WE
9 WHO PROPOSED TO OPEN THIS SUBJECT. IT'S DU PONT WHO OPENED IT
10 BY DR. KORNBERG'S COMMENTS SAYING THAT DR. MARTINELL DIDN'T KNOW
11 WHAT HE WAS TALKING ABOUT --

12 MR. FIGG: WELL --

13 MR. LEWIS: -- THAT HE WAS NOT FAMILIAR WITH THE PRIMER
14 EXTENSION REACTION; WAS NOT FAMILIAR WITH THE PRIMER EXTENSION
15 REACTION.

16 NOW, WE HAD SOME CROSS, AND I WOULD HOPE IT DISPELLED
17 SOME OF THAT IMPRESSION, BUT AS OF NOW, WE HAVE NO EVIDENCE
18 REBUTTING THAT AND I THINK WE ARE ENTITLED TO REBUT IT.

19 MR. FIGG: YOUR HONOR --

20 THE COURT: WELL, WHAT ABOUT --

21 MR. FIGG: -- IT WAS OPENED BY MR. PASAHOW'S OPENING
22 STATEMENT WHEN HE POINTED OUT THAT DR. MARTINELL HAD A PH.D.; HE
23 HAD PUBLISHED SCIENTIFIC ARTICLES HIMSELF, AND SO FORTH.

24 DR. KORNBERG DREW CONCLUSIONS FROM WHAT DR. MARTINELL
25 HAD WRITTEN AND THE WAY DR. MARTINELL HAD ANALYZED THE PRIOR ART

9
1 AND, FROM HIS ANALYSIS OF THAT INFORMATION, DREW CONCLUSIONS
2 ABOUT WHETHER DR. MARTINELL UNDERSTOOD THE TECHNOLOGY OR NOT.

3 THAT'S FAR DIFFERENT FROM SAYING THAT DR. MARTINELL DID
4 NOT HAVE A PROPER EDUCATION OR WHATEVER.

5 THE COURT: WELL, WE ALSO HAVE MR. DE GRANDI'S
6 TESTIMONY AS WELL --

7 MR. FIGG: MR. DE GRANDI DID NOT MAKE ANY --

8 THE COURT: -- ABOUT THE MATTER AND MANNERS IN WHICH
9 THESE APPLICATIONS ARE HANDLED AND THE PEOPLE WHO -- TYPES OF
10 PEOPLE -- RATHER CATEGORICAL STATEMENTS ABOUT THE TYPES OF
11 PEOPLE WHO HANDLE THEM.

12 MR. FIGG: MR. DE GRANDI WAS PROVIDING BACKGROUND
13 INFORMATION ABOUT THE WAY THE PATENT OFFICE IS ORGANIZED, AND I
14 WOULD FULLY EXPECT THAT CETUS CAN DO THE SAME.

15 DOCTOR -- MR. DE GRANDI DID POINT OUT THAT PATENT
16 EXAMINERS OFTEN COME TO THE PATENT OFFICE WITH TECHNICAL
17 EDUCATIONS AND THAT SOME HAVE PH.D.'S.

18 MR. LEWIS: YOUR HONOR, THE ONLY POSSIBLE PURPOSE OF
19 MR. DE GRANDI'S GIVING THAT TESTIMONY IS TO CAST SOME
20 IMPLICATION ON THE QUALIFICATIONS OF THE EXAMINER IN THIS CASE.

21 THE COURT: OKAY.

22 MR. FIGG: WELL --

23 THE COURT: BUT I DON'T WANT TO RETRY -- OR TRY
24 ESSENTIALLY AN ANCILLARY ISSUE, MR. MARTINELL'S QUALIFICATIONS.

25 WHY CAN'T WE HAVE A STIPULATION AS TO WHAT HIS

9
1 BACKGROUND, EXPERIENCE, TRAINING WAS, IF HE -- YOU KNOW, WHERE
2 HE GOT HIS PH.D., WHEN, IN WHAT FIELD, WHAT LABS HE WORKED IN,
3 THE TYPE OF WORK THAT HE PERFORMED, PAPERS WRITTEN, OR WHATEVER,
4 WITHOUT REGARD TO THE KIND AND QUALITY OF HIS WORK?

5 MR. FIGG: WELL, YOUR HONOR, I THINK THAT WOULD BE
6 VERY, VERY PREJUDICIAL. IT WOULD CAST A SPOTLIGHT ON EXAMINER
7 MARTINELL'S BACKGROUND, WHICH IS THE VERY THING THAT THE FEDERAL
8 CIRCUIT HAS --

9 THE COURT: WELL, BUT YOU OPENED THE DOOR.

10 MR. FIGG: I DON'T BELIEVE WE DID, YOUR HONOR. WE DID
11 NOT ASK ANY OF OUR WITNESSES ANYTHING ABOUT DR. MARTINELL'S
12 BACKGROUND.

13 DR. KORNBERG DREW CONCLUSIONS ABOUT HIS UNDERSTANDING
14 OF THE TECHNOLOGY FROM WHAT HE READ IN THE PAPERS.

15 CETUS IS CERTAINLY ENTITLED TO ASK THEIR WITNESSES
16 WHETHER THEY BELIEVE DR. MARTINELL UNDERSTOOD THE TECHNOLOGY
17 FROM HIS -- FROM THE WAY THEY READ DR. MARTINELL'S PUBLICATIONS,
18 BUT DR. MARTINELL'S SPECIFIC BACKGROUND IS NOT APPROPRIATE HERE.

19 AND, IN CONNECTION WITH WHAT MR. DE GRANDI SAID, CETUS
20 IS PERFECTLY ENTITLED TO ASK THEIR PATENT LAW EXPERT, MR.
21 ANDERSON, WHETHER SOME EXAMINERS HAVE MORE EXPERIENCE THAN THAT
22 THAT MR. DE GRANDI SPOKE ABOUT.

23 BUT I THINK IF WE GET INTO TRYING MAKING IT AN ISSUE OF
24 THIS CASE WITH THIS SPECIFIC EXAMINER MORE QUALIFIED OR LESS
25 QUALIFIED THAN HE SHOULD HAVE BEEN, IT'S GOING TO INTERJECT AN

9
1 ENTIRELY NEW ISSUE IN THE PATENT LITIGATION THAT'S NEVER BEEN
2 THERE BEFORE. PRESUMABLY, THE PRESUMPTION OF VALIDITY WILL BE
3 HIGHER OR LOWER DEPENDING UPON THE QUALIFICATION OF A PARTICULAR
4 EXAMINER.

5 MR. LEWIS: WELL, YOUR HONOR, IF I MAY SPEAK TO THAT.

6 THE COURT: YES, UH-HUH.

7 MR. LEWIS: THE PROBLEM THAT WE HAVE IS NOT ONE OF OUR
8 MAKING. IT'S ONE OF MR. FIGG'S MAKING, BECAUSE HE ASKED MR.
9 DE GRANDI THINGS LIKE, "WHAT KIND OF EDUCATION AND TRAINING DO
10 THE EXAMINERS HAVE?", AND ELICITED IN TESTIMONY THAT APPEARED TO
11 BE FAIRLY HIGHLY SCRIPTED THAT THEY COME STRAIGHT OUT OF
12 COLLEGE, OR SOMETHING LIKE THAT.

13 WE NEED TO RESPOND TO THAT, IN PART BECAUSE THAT
14 TESTIMONY WAS PUT ON, AND I WILL CONFESS IN PART BECAUSE I
15 OFFERED TO LAY A FOUNDATION WITH LATER WITNESSES, TO WHICH MR.
16 FIGG MADE NO OBJECTION, AND I THINK THE JURY IS GOING TO FIND IT
17 VERY PREJUDICIAL IF WE DON'T COME THROUGH WITH THAT FOUNDATION.

18 MR. FIGG: WELL, I THINK THE FOUNDATION WAS LAID WITH
19 THE LATER WITNESSES. I DID OBJECT.

20 AND AGAIN WE HAVE TO GO BACK TO MR. PASAHOW'S OPENING
21 STATEMENT. IT SAYS:

22 "HE'S AN EXPERT, BOTH IN PATENT LAW, AND HE'S
23 AN EXPERT SCIENTIST, A MAN HIMSELF WHO HAS A PH.D."

24 AND --

25 MR. LEWIS: YOUR HONOR, THE --

10

1 MR. FIGG: -- CETUS IS THE ONE WHO HAS OPENED THIS
2 ISSUE.

3 THE COURT: DID YOU OBJECT AT THAT TIME?

4 MR. FIGG: NO, YOUR HONOR, I DIDN'T OBJECT --

5 THE COURT: UH-HUH.

6 MR. FIGG: -- BECAUSE I DIDN'T -- DIDN'T WANT TO
7 INTERRUPT MR. PASAHOW'S OPENING STATEMENT.

8 BUT WE DID OBJECT WHEN COUNSEL BEGAN TO ASK OUR
9 WITNESSES THE SAME QUESTION.

10 THE COURT: UH-HUH. WHY WOULDN'T A STIPULATION SERVE
11 YOUR PURPOSES?

12 MR. LEWIS: YOUR HONOR, I . . . IT -- PERHAPS IT MIGHT.
13 I DON'T THINK THAT IT ADEQUATELY REDRESSES TESTIMONY FROM DR.
14 KORNBERG, WHOM YOU YOURSELF OBSERVED WAS A VERY GOOD WITNESS,
15 WHO SAYS THAT THIS EXAMINER EVIDENTLY DOESN'T UNDERSTAND THE
16 NITTY-GRITTY OF THE REACTION, OR SOMETHING LIKE THAT.

17 I THINK WE AT LEAST NEED TO PUT IN THE ARTICLES THAT
18 DR. MARTINELL HAS WRITTEN THAT SHOW THAT HE HAS, IN FACT, DONE
19 PRIMER EXTENSION REACTIONS AND WORKED IN THIS VERY FIELD THAT
20 WE'RE TALKING ABOUT.

21 THE COURT: WELL --

22 MR. FIGG: THE PROBLEM --

23 THE COURT: -- THE PROBLEM -- THE PROBLEM I HAVE WITH
24 THAT IS, THAT OPENS THE DOOR EVEN FURTHER THAN IT'S OPENED NOW,
25 TO GOING INTO AND CROSS-EXAMINING SOMEONE, IF, IN FACT, THEY CAN

10

1 BE CROSS-EXAMINED, OR CALLING WITNESSES TO TESTIFY AS TO THE
2 DEPTH AND EXTENT OF HIS KNOWLEDGE.

3 (PAUSE IN PROCEEDINGS)

4 THE COURT: AND HOW GOOD HE IS AT WHAT -- AT WHAT HE
5 DOES, ET CETERA.

6 I'M GOING TO INSTRUCT YOU TO COME UP WITH A STIPULATION
7 AS TO WHAT HIS BACKGROUND AND EXPERIENCE AND TRAINING IS, AND
8 LIST OF THE PAPERS, ET CETERA --

9 MR. FIGG: WELL, YOUR HONOR, I WOULD --

10 THE COURT: -- AND --

11 MR. FIGG: I'M SORRY.

12 THE COURT: AND IF YOU CAN'T COME UP WITH A
13 STIPULATION, YOU SUBMIT TO ME IN TERMS OF WHAT -- HIS CV AND
14 WHATEVER OTHER INFORMATION THAT'S OBJECTIVELY VERIFIABLE, AND
15 NOT QUALITATIVE IN TERMS OF HIS -- YOU KNOW, THE QUALITY OF HIS
16 WORK, AND I'LL FRAME MY OWN, WHICH SHOULD SEND SHIVERS INTO THE
17 HEARTS OF BOTH OF YOU.

18 MR. FIGG: WELL, YOUR HONOR, I WOULD SUBMIT THAT SUCH A
19 STIPULATION MIGHT BE APPROPRIATE IF DIRECTED TO THE GENERAL
20 BACKGROUNDS OF EXAMINERS, WHICH SEEMS TO BE THE POINT THAT MR.
21 LEWIS IS OBJECTING TO.

22 THE COURT: NO. IT GOT VERY -- IT GOT PERSONALIZED IN
23 THIS CASE.

24 MR. FIGG: WELL, ONLY THROUGH WHAT CETUS ASKED.

25 THE COURT: WELL --

10 1 MR. FIGG: WE DID NOT PERSONALIZE EXAMINER MARTINELL AT
2 ALL.

3 THE COURT: BUT THROUGH YOUR OWN -- THROUGH YOUR OWN
4 WITNESS.

5 NO. COME UP WITH A STIPULATION. I'M REALLY NOT GOING
6 TO TRY AN ANCILLARY CASE; NAMELY, THE QUALIFICATIONS OF DR.
7 MARTINELL.

8 SO YOU COME UP WITH A STIPULATION. IF YOU DON'T, YOU
9 SUBMIT TO ME WHAT I ASKED FOR, AND I WILL FRAME MY OWN.

10 MR. LEWIS: MAY I HAVE A POINT OF CLARIFICATION, YOUR
11 HONOR?

12 THE COURT: YES.

13 MR. LEWIS: WE BELIEVE THAT THE PAPERS, WHICH I DON'T
14 THINK ARE A DISPUTED MATTER, DEMONSTRATE THAT DR. MARTINELL HAS
15 PARTICIPATED IN EXPERIMENTS USING PRIMER EXTENSION REACTIONS.
16 MAY WE INCLUDE SOMETHING LIKE THAT IN OUR PROPOSAL TO STIPULATE?

17 MR. FIGG: WELL, YOUR HONOR, THAT --

18 THE COURT: WELL, AGAIN, THEN WE GET INTO HIS
19 QUALIFICATIONS. YOU CAN INCLUDE THE LIST OF HIS PUBLICATIONS --

20 MR. LEWIS: BUT --

21 THE COURT: -- AND THAT'S IT.

22 MR. LEWIS: (NODDING HEAD.)

23 THE COURT: OKAY. NOW, IF THEY'RE REFUTATORY ON THEIR
24 FACE, FINE. IF NOT, THEN SO BE IT.

25 MR. LEWIS: WOULD YOUR HONOR CONSIDERING INSTRUCTING

10

1 THE JURY TO DISREGARD DR. KORNBERG'S TESTIMONY ABOUT DR.
2 MARTINELL'S QUALIFICATIONS?

3 (PAUSE IN PROCEEDINGS)

4 MR. LEWIS: BECAUSE I -- THE REASON I ASK THAT, QUITE
5 SERIOUSLY, BECAUSE THE TESTIMONY WE HAVE FROM THIS EMINENT
6 SCIENTIST IS THAT DR. MARTINELL DOES NOT UNDERSTAND THE
7 NITTY-GRITTY OF THESE REACTIONS, AND I DON'T THINK THERE'S A
8 BASIS FOR THAT, AND I THINK WE COULD MAKE A CASE, A VERY STRONG
9 CASE, SHOWING THAT HE DOES, IN FACT, UNDERSTAND THAT.

10 THE COURT: IN LIEU OF A STIPULATION -- IN LIEU OF AN
11 INSTRUCTION OR A STIPULATION, OR . . .

12 MR. FIGG: YOUR HONOR, WHY CAN'T THEY JUST ADDRESS THAT
13 IN THEIR CASE IN CHIEF?

14 DR. KORNBERG DIDN'T --

15 THE COURT: THEY'RE TRYING TO, AND YOU OBJECTED.

16 MR. FIGG: NO, NO, NO, NO.

17 DR. KORNBERG DID NOT SAY EXAMINER MARTINELL DOESN'T
18 UNDERSTAND THIS BECAUSE HE WAS POORLY EDUCATED OR BECAUSE HE
19 STUDIED AT THE WRONG SCHOOL. DR. KORNBERG SAID, "I HAVE READ
20 WHAT DR. MARTINELL WROTE, AND FROM THAT, I CONCLUDE THAT DR.
21 MARTINELL DID NOT ADEQUATELY UNDERSTAND THIS SCIENCE."

22 CETUS CAN ASK THEIR WITNESSES TO READ WHAT DR.
23 MARTINELL WROTE AND THEY CAN DRAW THEIR OWN CONCLUSIONS ABOUT
24 DR. MARTINELL'S UNDERSTANDING OR LACK OF IT.

25 THE COURT: WELL, IF YOU WISH, IN LIEU OF A

10 1 STIPULATION, I WILL GIVE -- I WILL GIVE A STIPULATION -- I WILL
2 GIVE AN INSTRUCTION, AND I WILL GIVE SUCH AN INSTRUCTION AND
3 ALSO SOME INSTRUCTION WITH RESPECT TO THE BACKGROUND OF THE --
11 4 WELL, THE PRESUMPTIONS THAT ATTACH AND THAT THE BACKGROUNDS ARE
5 REALLY NOT IN ISSUE.

6 IF YOU WANT TO PREPARE AN INSTRUCTION, I WILL DO THAT.

7 MR. LEWIS: ALL RIGHT.

8 THE COURT: OTHERWISE, I'LL GIVE A STIPULATION.

9 MR. LEWIS: LET US CONSULT WITH MR. FIGG. WE'LL SEE IF
10 WE CAN DO A STIPULATION OR AGREE ON AN INSTRUCTION.

11 THE COURT: OKAY. NOW, AS TO THE EXHIBITS, I ASSUME
12 THAT THE EXHIBITS THAT YOU'RE REFERRING TO ARE THE FOUR EXHIBITS
13 THAT ARE REFERRED IN ONE OF THE PAPERS SUBMITTED, B-87, 88 --

14 MR. LEWIS: YES, YOUR HONOR.

15 THE COURT: -- B-113, OR SOMETHING ON THE ORDER, AND
16 B-124.

17 MR. LEWIS: 113 HAS BEEN ADMITTED, SO THAT'S NO LONGER
18 ON THE LIST.

19 THE COURT: OKAY.

20 MR. LEWIS: AND 124.

21 (PAUSE IN PROCEEDINGS)

22 THE COURT: NOW, ARE YOU SEEKING TO ADMIT ALL OF B-1 --
23 EXCUSE ME -- B-87? AND, IF SO, HOW WILL -- WHAT WILL THE JURY
24 DO WITH A LOT OF THIS?

25 MR. LEWIS: THE B-87 CONTAINS A NUMBER OF STATEMENTS

11

1 SHOWING DU PONT'S ANALYSIS OF THE IMPORTANCE OF PCR, AND I ADMIT
2 IT'S NOT A SIMPLE NARRATIVE DOCUMENT.

3 BUT I WOULD EXPECT THAT, IF IT IS ADMITTED INTO
4 EVIDENCE, WE WILL DO SOME EXPLAINING OF IT IN CLOSING
5 STATEMENTS.

6 THE COURT: AND IS THERE ANY QUESTION OF THE
7 AUTHENTICATION OF THIS DOCUMENT?

8 MR. FIGG: WELL, OUR NOTATION INDICATES THAT IT WAS NOT
9 AUTHENTICATED. THE WITNESS COULDN'T IDENTIFY IT.

10 I'M TAKEN A LITTLE BIT BY SURPRISE BY THIS TODAY.
11 PERHAPS I SHOULDN'T HAVE BEEN, BUT -- BUT I AM, AND I DON'T --

12 THE COURT: WELL, DO YOU WANT TO SEE IF YOU CAN WORK
13 THESE THREE OUT?

14 MR. FIGG: I'M SORRY. THEY WERE B-87, B-88 AND . . .

15 THE COURT: B-124. APPARENTLY 113 HAS BEEN RESOLVED.

16 MR. LEWIS: THAT'S CORRECT, YES.

17 THE COURT: AND IT SEEMS TO ME THAT B-124 IS, IN
18 FACT -- IS THAT NOT THE SAME AS A PAGE IN B-87, OR DOES IT JUST
19 LOOK THE SAME?

20 MR. LEWIS: YES, IT IS, YOUR HONOR. THE DIFFERENCE IS
21 THAT A WITNESS DID SPECIFICALLY AUTHENTICATE THIS PAGE.

22 (PAUSE IN PROCEEDINGS)

23 MR. FIGG: I THINK IT -- WE'LL TRY TO WORK IT OUT. I'M
24 REALLY NOT PREPARED TO TALK ABOUT THE DETAILS OF THESE.

25 THE COURT: OKAY. WELL, WHY DON'T YOU SEE IF YOU CAN

11

1 WORK IT OUT AND, IF YOU'RE NOT ABLE TO, TAKE IT UP WITH ME
2 TOMORROW --

3 MR. FIGG: OKAY.

4 THE COURT: -- AT THE END OF THE MORNING. OKAY?

5 MR. LEWIS: OKAY.

6 THE COURT: ANYTHING FURTHER?

7 MR. FIGG: WELL, WE STILL HAVE SOME EXHIBITS THAT HAD
8 NOT BEEN ENTERED, YOUR HONOR, AND --

9 THE COURT: OH, THIS IS FROM . . .

10 MR. KURZ: FROM THE OTHER DAY.

11 THE COURT: FROM THE CASE IN CHIEF. DO WE HAVE THEM
12 RESOLVED?

13 MR. KURZ: WE DON'T HAVE THEM ENTIRELY RESOLVED, AND
14 THERE'S A FOURTH ONE I BELIEVE THE OTHER SIDE IS STILL TRYING TO
15 DETERMINE WHETHER THEY WANT TO OBJECT OR NOT.

16 MR. LEWIS: THERE'S A FOURTH ONE MR. KURZ TOLD ME ABOUT
17 AT THE BREAK THAT WE HAVEN'T HAD A CHANCE TO EXAMINE YET.

18 THE COURT: WHY DON'T WE TAKE THEM ALL UP, ALL OF THE
19 EXHIBITS, TOMORROW AND GET THEM ALL RESOLVED.

20 MR. FIGG: OKAY.

21 THE COURT: NOW, YOU'LL BE CONTINUING WITH DR. SMITH
22 TOMORROW.

23 MR. LEWIS: THAT'S CORRECT, YOUR HONOR.

24 THE COURT: AND THEN WHO WILL BE NEXT?

25 MR. PASAHOW: DR. KARY MULLIS, YOUR HONOR.

11 1 THE COURT: OKAY. AND I ASSUME THAT WILL TAKE US THE
2 REST -- THROUGH THE REST OF TOMORROW, AT LEAST.

3 MR. PASAHOW: IT COULD.

4 THE COURT: OKAY. FINE.

5 MR. FIGG: YOUR HONOR, THERE'S ONE MORE ITEM --

6 THE COURT: YES.

7 MR. FIGG: -- I HAVE TO BRING UP, WHICH IS THE TIMING
8 AT WHICH WE ARE GETTING DEFENDANT'S EXHIBITS.

9 SOME OF THESE LARGE POSTERS AND THINGS OBVIOUSLY HAVE
10 BEEN PREPARED FOR A LONG TIME. WE RECEIVED A COPY OF ONE TODAY
11 THAT HAD A FAX DATE ON THE TOP OF IT OF JULY. WE GOT MOST OF
12 THEM AFTER SEVERAL REMINDERS LAST WEEK. THEY SHOULD HAVE BEEN
13 IN BEFORE THE NOVEMBER TRIAL DATE WAS SET.

14 THE COURT: ARE THESE THE LARGE POSTERS YOU'RE
15 REFERRING TO OR --

16 MR. FIGG: YES, SOME OF THESE. THIS -- NOT THIS
17 PARTICULAR ONE, BUT SEVERAL OF THEM.

18 THE COURT: UH-HUH.

19 MR. FIGG: AND I WOULD JUST LIKE TO HAVE AN
20 UNDERSTANDING THAT IF THERE ARE MORE OF THESE THAT ARE BEING
21 USED IN THE CASE IN CHIEF, WE SHOULD GET COPIES OF THEM RIGHT
22 AWAY.

23 THE COURT: HAVE YOU GOT MORE POSTERS --

24 MR. PASAHOW: WELL, YOUR HONOR, WE --

25 THE COURT: -- VISUAL AIDS?

11 1 MR. PASAHOW: WE ARE PREPARING SOME POST -- THE NEW
2 MATERIAL -- LET ME STRIKE AND START AGAIN:

3 LIKE MR. FIGG, WE WILL BE BLOWING UP PAGES OF THINGS AS
4 WE GO ALONG, AND I DON'T THINK THAT'S THE PROBLEM.

5 WHAT HE'S TALKING ABOUT ARE THESE GRAPHICAL THINGS.

6 THE COURT: UH-HUH.

7 MR. PASAHOW: AND WE ARE IN THE PROCESS OF PREPARING
8 SOME THAT RESPOND TO THE TESTIMONY OF DR. MOLINEUX AND DR.
9 VAN DE SANDE CONCERNING SOME OF THE EXPERIMENTS THAT WERE DONE
10 IN THE LABORATORY, AND WE WILL ENDEAVOR TO GET THOSE TO MR. FIGG
11 AS SOON AS THEY'RE FINALIZED. WE WILL GET THEM TO MR. FIGG AS
12 SOON AS THEY'RE FINALIZED.

13 THE COURT: WOULD YOU PLEASE DO THAT. AND ALSO, IN ANY
14 EVENT, PROVIDE HIM WITH COPIES AT LEAST BY THE AFTERNOON BEFORE,
15 AND EARLIER, IF POSSIBLE.

16 NOW, ADMITTEDLY, IF -- YOU KNOW, IF THAT'S THE FIRST
17 THAT IT'S READY, THAT'S ANOTHER MATTER. BUT IF YOU'RE ABLE TO
18 PROVIDE THEM WITH COPIES BEFORE, PLEASE DO, BUT AT LEAST BY THE
19 AFTERNOON OF THE DAY BEFORE WHICH IT'S GOING TO BE USED.

20 MR. PASAHOW: ABSOLUTELY, YOUR HONOR. AND WE HAVE BEEN
21 MEETING THAT DEADLINE EASILY PRIOR TO TODAY.

22 MR. FIGG: WELL --

23 THE COURT: OKAY?

24 MR. FIGG: -- THERE WAS ONE YOU USED TODAY THAT I HAD
25 NEVER SEEN BEFORE.

12 1 THANK YOU, YOUR HONOR.

2 MR. PASAHOW: I DON'T THINK THAT'S RIGHT. I THINK IT
3 WAS DELIVERED TO YOUR OFFICE YESTERDAY.

4 THE COURT: THEY'RE BEGINNING TO LOOK ALIKE, MAYBE? I
5 DON'T KNOW.

6 (LAUGHTER)

7 THE COURT: YOU'LL HAVE TO USE SOME DIFFERENT COLORS
8 THE NEXT TIME.

9 MR. PASAHOW: THERE REMAINS THE MATTER OF WHEN WE'RE
10 GOING TO MAKE OUR MOTION FOR A DIRECTED VERDICT.

11 IT IS NOT A GRAND MOTION, TO MAKE THE POINT CLEAR. IT
12 GOES TO SPECIFIC CLAIMS AS TO WHICH WE THINK THERE'S JUST BEEN A
13 FAILURE OF THE REQUIRED EVIDENCE UNDER EITHER 102 OR 103 OR, IN
14 SOME CASES, BOTH.

15 I DON'T THINK ANY OF THE EXHIBITS WE'RE GOING TO TALK
16 ABOUT CHANGE ANY OF IT.

17 THE COURT: WELL, IF YOU'RE GOING TO PARTICULARIZE IT
18 IN THAT FASHION, WHY DON'T YOU SUBMIT IT IN WRITING?

19 MR. LEWIS: WE HAVE IT. WE WILL SUBMIT IT IN WRITING.
20 WE WERE WAITING FOR THE TIME.

21 THE COURT: YOU HAVE -- YEAH. OKAY.

22 YOU HAVEN'T SUBMITTED IT YET; HAVE YOU? AT LEAST, I
23 HAVEN'T SEEN IT.

24 MR. LEWIS: NO, BUT WE'RE PREPARED TO SUBMIT IT.

25 THE COURT: WHY DON'T YOU, BUT KEEP IT SHORT AND TO THE

12

1 POINT.

2 AND THEN HOW MUCH TIME AFTER YOU RECEIVE A COPY DO YOU
3 NEED TO RESPOND TO IT IN WRITING?

4 MR. FIGG: YES. I NEED TO SEE IT FIRST, YOUR HONOR.
5 AT LEAST A FEW DAYS.

6 THE COURT: WE MAY BE FINISHED BY THAT TIME. I DON'T
7 KNOW.

8 MR. LEWIS: I CAN PROVIDE IT NOW.

9 THE COURT: ARE YOU GOING TO GET IT FILED TODAY?

10 MR. LEWIS: I CAN CERTAINLY FILE IT AS SOON AS WE
11 ADJOURN.

12 THE COURT: OKAY. WHY DON'T WE SAY, BY . . . CAN YOU
13 GET IT DONE BY THURSDAY, DO YOU THINK?

14 MR. FIGG: WE'LL TRY TO DO THAT.

15 THE COURT: OKAY. IT LOOKS -- LET'S SAY THURSDAY, AND
16 IF YOU HAVE A PROBLEM WITH THAT, LET US KNOW TOMORROW; OKAY?

17 MR. FIGG: OKAY.

18 THE COURT: FINE. THEN WE'LL SEE YOU TOMORROW MORNING.
19 THANK YOU.

20 MR. PASAHOW: THANK YOU, YOUR HONOR.

21 MR. FIGG: THANK YOU.

22

23

24

25

(COURT ADJOURNED AT 1:19 P.M. TO RECONVENE

TUESDAY, FEBRUARY 5, 1991, AT 8:00 O'CLOCK A.M.)