

1 (OPEN COURT, JURY PRESENT, AT 10:24 A.M.:)

2 THE COURT: MR. FIGG.

3 MR. FIGG: THANK YOU, YOUR HONOR.

4 OPENING STATEMENT BY

5 MR. FIGG: LADIES AND GENTLEMEN OF THE JURY, LET ME
6 INTRODUCE ONE OTHER PERSON WHO IS SITTING AT COUNSEL TABLE NOW
7 WHO WASN'T THERE AWHILE AGO, MISS CELINE JIMINEZ, WHO IS AN
8 ATTORNEY WITH MY FIRM AND IS HELPING US OUT WITH THE CASE.

9 AS JUDGE PATEL TOLD YOU, WHAT WE'RE DOING NOW ARE THE
10 OPENING STATEMENTS, AND THE PURPOSE OF THE OPENING STATEMENT IS
11 TO GIVE YOU A BIRD'S EYE VIEW OF WHAT WE THINK THE EVIDENCE IS
12 GOING TO SHOW.

13 I'M NOT GOING TO SAY "THE EVIDENCE WILL SHOW" OR
14 "DU PONT'S EVIDENCE WILL PROVE" BEFORE EACH COMMENT THAT I MAKE
15 DURING MY OPENING STATEMENT, BUT YOU WILL UNDERSTAND THAT WHAT I
16 AM TELLING YOU IS WHAT WE EXPECT THE EVIDENCE TO SHOW AS IT
17 COMES IN DURING THE COURSE OF THE TRIAL.

18 WHAT IS THIS CASE ABOUT? YOU'VE HEARD IT'S A PATENT
19 CASE. WE ARE ASKING THE COURT TO DECLARE THAT TWO
20 CLOSELY-RELATED PATENTS OWNED BY CETUS CORPORATION ARE INVALID.

21 IN ITS SIMPLEST ASPECT, THE QUESTION IN THIS CASE IS
22 WHETHER, THROUGH ITS PATENTS, CETUS HAS WITHDRAWN SUBJECT
23 MATTER, WITHDRAWN VALUABLE TECHNOLOGY, FROM THE PUBLIC WHICH THE
24 PUBLIC ALREADY OWNED. THIS TECHNOLOGY HAD BEEN DEDICATED TO THE
25 PUBLIC YEARS BEFORE CETUS' PATENTS BY A FAMOUS SCIENTIST BY THE

1 NAME OF H. G. KHORANA. YOU'LL BE HEARING A LOT ABOUT PROFESSOR
2 KHORANA DURING THE COURSE OF THE TRIAL.

3 CETUS' PATENTS RELATE TO THE FIELD OF BIOTECHNOLOGY.
4 IN PARTICULAR, THEY RELATE TO A WAY OF AMPLIFYING DNA. DNA IS
5 THE GENETIC MATERIAL THAT'S FOUND IN VIRTUALLY ALL LIVING
6 THINGS, AND AGAIN YOU WILL BE HEARING A LOT ABOUT DNA, AND WE
7 WILL HAVE EXPERTS WHO WILL EXPLAIN TO YOU WHAT DNA IS AND WHAT
8 THIS PROCESS INVOLVES.

9 AS LONG AS CETUS' PATENTS STAND, ONLY CETUS AND ITS
10 LICENSEES, SUCH AS THE SWISS PHARMACEUTICAL COMPANY HOFFMANN-LA
11 ROCHE, CAN USE THE TECHNOLOGY COVERED BY THE CETUS PATENTS AND
12 COMMERCIALIZED PRODUCTS BASED ON THAT TECHNOLOGY.

13 WELL, MOST OF YOU HAVE HEARD OF A PATENT, BUT WHAT
14 REALLY IS A PATENT? A PATENT IS A RIGHT THAT'S GRANTED BY THE
15 GOVERNMENT. IT IS A RIGHT THAT IS PROVIDED AS AN INCENTIVE FOR
16 THOSE WHO CONTRIBUTE SOMETHING NEW, USEFUL AND UNOBSVIOUS.

17 IN RETURN FOR A FULL DISCLOSURE OF AN INVENTION OR A
18 DISCOVERY, THE PUBLIC GRANTS THE INVENTOR OR THE PATENTEE A
19 17-YEAR RIGHT TO EXCLUDE ALL OTHERS FROM MAKING, USING OR
20 SELLING THE SUBJECT MATTER THAT'S COVERED BY THE PATENT. THE
21 INVENTOR CAN SELL OR LICENSE THE RIGHT UNDER THE PATENT AND, AS
22 YOU WILL LEARN, THAT HAS OCCURRED IN THIS CASE.

23 THE SUBJECT MATTER OF THIS CASE IS VERY COMPLEX, BUT IT
24 IS UNDERSTANDABLE, AND IT IS ALSO VERY INTERESTING.

25 THE PLAINTIFF IS DU PONT, AS YOU'VE HEARD. DU PONT

1 WILL SHOW THAT CETUS' PATENTS ARE VERY BROAD. IN EFFECT,
2 DU PONT CONTENDS THAT THE PATENTS ARE INVALID BECAUSE THEY ARE
3 SO BROAD THAT THEY COVER TECHNOLOGY OR A PROCESS THAT WAS IN THE
4 PRIOR ART; IN OTHER WORDS, THAT WAS ALREADY KNOWN.

5 DU PONT ASKS THIS COURT AND YOU TO HOLD THAT CETUS'
6 PATENTS ARE INVALID SO THAT THIS VALUABLE TECHNOLOGY WILL BE
7 AVAILABLE TO DU PONT, IT WILL BE AVAILABLE TO CETUS, AND IT WILL
8 BE AVAILABLE TO ALL OTHERS INVOLVED IN BIOTECHNOLOGY RESEARCH,
9 WHETHER THEY BE MOTIVATED BY ACADEMIC INTERESTS OR BY THE PROFIT
10 MOTIVE.

11 THE DEFENDANT IS CETUS. CETUS WILL CONTEND THAT THE
12 PATENTS ARE VALID AND WILL TELL YOU THAT A BIOTECHNOLOGY PROCESS
13 COVERED BY THE PATENTS KNOWN AS PCR HAS RECEIVED WIDESPREAD
14 ACCLAIM, AND THEY WILL TELL YOU THAT THIS TECHNOLOGY HAS BEEN
15 PRAISED IN THE SCIENTIFIC COMMUNITY AND RECEIVED A LOT OF
16 ATTENTION.

17 DU PONT DOES NOT DISPUTE THE VALUE OF THE TECHNOLOGY
18 COVERED BY THE PATENTS. THIS IS TECHNOLOGY -- YOU WILL HEAR THE
19 WORD "PCR" AND WE'LL TALK ABOUT THAT LATER. IF IT WERE NOT
20 VALUABLE TECHNOLOGY, DU PONT WOULD NOT BE INVOLVED IN THIS
21 LAWSUIT.

22 DU PONT SEEKS TO MAKE THIS PATENT, THIS TECHNOLOGY,
23 AVAILABLE TO ITSELF THROUGH THIS LAWSUIT AND, IN THE COURSE OF
24 DOING SO, WILL MAKE IT AVAILABLE TO OTHERS. CERTAINLY DU PONT'S
25 SCIENTISTS HAVE SAID THAT THIS IS VALUABLE TECHNOLOGY AND INDEED

1 1 BEFORE DU PONT KNEW OF THE PRIOR ART AND THE WORK OF DR.
2 KHORANA, WHICH YOU ARE GOING TO HEAR ABOUT, MANY AT DU PONT
3 BELIEVED THAT THE SUBJECT MATTER WAS PATENTABLE.

4 WELL, WHY DOES DU PONT FEEL THAT THE PATENTS ARE
5 INVALID? THIS IS BEST EXPLAINED BY DESCRIBING THE SCIENTIFIC
6 EVENTS THAT OCCURRED OVER THE DECADE OR SO PRECEDING THE
7 PATENTS. AND IT BEGINS -- THE STORY BEGINS IN THE LATE 1960'S
8 IN THE LABORATORY OF DR. KHORANA.

9 AT THIS TIME, DR. KHORANA WAS WORKING AT THE UNIVERSITY
10 OF WISCONSIN. HE WAS A PROFESSOR AT THE UNIVERSITY OF
11 WISCONSIN. LATER ON, HE WENT TO THE MASSACHUSETTS INSTITUTE OF
12 TECHNOLOGY.

13 IN THE LATE '60'S, DR. KHORANA HAD JUST COMPLETED THE
14 WORK FOR WHICH HE WOULD RECEIVE THE NOBEL PRIZE, WHICH IS THE
15 HIGHEST PRIZE IN A SCIENCE. AND THIS WORK INVOLVED DECIPHERING
16 THE GENETIC CODE; IN OTHER WORDS, DETERMINING WHAT IT IS IN THE
17 GENES THAT ACCOUNTS FOR THE MESSAGE THAT IS CARRIED BY THE DNA
18 IN THE GENES. THIS WORK OF DR. KHORANA'S WAS THE FOUNDATION FOR
19 THE VERITABLE EXPLOSION OF BIOTECHNOLOGY THAT OCCURRED DURING
20 THE '70'S AND '80'S.

21 AFTER DR. KHORANA FINISHED HIS WORK ON THE GENETIC
22 CODE, HE BEGAN A NEW PROJECT, AND THAT NEW PROJECT INVOLVED THE
23 CHORE OF SYNTHESIZING A GENE, A PIECE OF DNA, IN THE LABORATORY.

24 NOW, THAT -- THAT TASK THAT DR. KHORANA SET OUT FOR
25 HIMSELF, BY TODAY'S STANDARDS, WOULD NOT BE A PARTICULARLY

2
1 DIFFICULT THING TO DO. IN FACT, IT'S NOT UNREASONABLE TO THINK
2 THAT AN UNDERGRADUATE SCIENCE STUDENT MIGHT BE ABLE TO DO THAT
3 WORK TODAY. BUT IN THE EARLY 1970'S, IT WAS A MONUMENTAL TASK
4 AND THE . . . THE TECHNOLOGY AT THAT TIME WAS RELATIVELY
5 PRIMITIVE AND CUMBERSOME, AND DR. KHORANA WORKED OUT THE
6 PROCEDURES AND TECHNIQUES THAT WOULD ALLOW HIM TO ACCOMPLISH IT.

7 I'D LIKE TO DIGRESS JUST A MOMENT TO EXPLAIN WHY THAT
8 WAS A DIFFICULT TASK, AND I'VE PUT ON THE STAND HERE THIS
9 PICTURE OF DNA, AND BASICALLY TO EXPLAIN IN A NUTSHELL WHAT DNA
10 IS, AND OUR EXPERTS WILL EXPLAIN THIS MUCH MORE THOROUGHLY LATER
11 ON.

12 EACH OF THE -- THE HUMAN BODY IS COMPOSED OF CELLS, AS
13 IS VIRTUALLY EVERYTHING THAT IS ALIVE. THE CELLS CONTAIN A
14 NUCLEUS, AND WITHIN THE NUCLEUS ARE THESE STRUCTURES CALLED
15 CHROMOSOMES. CHROMOSOMES ARE WHAT CARRY THE GENETIC BLUEPRINT
16 FOR LIFE. THEY ARE WHAT SAYS -- TELLS WHETHER YOU HAVE BLUE
17 EYES OR BROWN EYES, WHETHER YOU'RE TALL OR SHORT.

18 WITHIN THE CHROMOSOMES ARE DNA, AND DNA IS DEPICTED BY
19 THIS LINE HERE (INDICATING). IT IS A DOUBLE-STRANDED FILAMENT
20 OF MATERIAL THAT IS MADE UP OF A SERIES OF BUILDING BLOCKS
21 CALLED NUCLEOTIDES.

22 THERE ARE FOUR NUCLEOTIDES, A'S, T'S, C'S, AND G'S, AND
23 THOSE NUCLEOTIDES ARE THE ALPHABET OF THE GENETIC INFORMATION,
24 IF YOU WILL. IT IS THE SEQUENCE IN WHICH THOSE NUCLEOTIDES ARE
25 PUT TOGETHER THAT DETERMINES THE CODE THAT'S CARRIED IN A

2
1 PARTICULAR SEGMENT OF DNA.

2 A GENE IS LIKE A CHAPTER IN A BOOK. IT CONTAINS A
3 STRETCH OF NUCLEOTIDES, A STRETCH OF THIS ALPHABET WHICH IS
4 WRITTEN OUT TO CODE FOR A PARTICULAR FUNCTION OR A PARTICULAR
5 PROTEIN. FOR EXAMPLE, THE PROTEIN INSULIN CIRCULATES IN OUR
6 BODY HAS A GENE THAT HAS A SEQUENCE OF AMINO ACID -- EXCUSE
7 ME -- A SEQUENCE OF THESE NUCLEOTIDES THAT CODES FOR THAT.

8 TWO STRANDS OF THE DNA ARE HELD TOGETHER BY BONDS
9 BETWEEN THESE NUCLEOTIDES. AN IMPORTANT FACTOR THAT YOU WILL
10 HEAR ABOUT AND WANT TO KEEP IN MIND DURING THE COURSE OF THIS
11 TRIAL IS THAT THERE ARE SPECIFIC RULES FOR THE WAY THESE BOND
12 TOGETHER: T'S AND A'S CAN ONLY BIND WITH ONE ANOTHER; AND C'S
13 AND G'S CAN ONLY BIND WITH ONE ANOTHER. THE SPECIFIC WAY IN
14 WHICH THE BUILDING BLOCKS OF THE TWO STRANDS OF DNA COMBINE WITH
15 EACH OTHER AND ARE HELD TOGETHER IS A PART OF WHAT ALLOWS THE
16 DNA TO BE REPLICATED, BOTH IN THE BODY AND IN THE LABORATORY.

17 WELL, HOW DID DR. KHORANA PROPOSE TO ACCOMPLISH THE
18 GOAL OF SYNTHESIZING A GENE?

19 FIRST OF ALL, TODAY, THERE ARE THOUSANDS OF GENES WHOSE
20 SEQUENCES ARE KNOWN. I MENTIONED INSULIN. THAT SEQUENCE IS
21 KNOWN. GROWTH HORMONE, MANY, MANY THINGS THAT ARE CIRCULATING
22 IN OUR BODIES, THE SEQUENCES ARE KNOWN.

23 BUT IN THE LATE '60'S AND EARLY '70'S WHEN DR. KHORANA
24 WAS DOING HIS WORK, THERE WERE ONLY A FEW GENES WHOSE SEQUENCES
25 WERE KNOWN. AND HE SET OUT TO SYNTHESIZE ONE OF THESE GENES,

2 1 WHICH WAS A GENE FROM A YEAST CELL, LIKE BAKER'S YEAST, THAT
2 CODED FOR A PARTICULAR MATERIAL THAT'S CALLED TRNA. YOU DON'T
3 HAVE TO KNOW WHAT TRNA IS, BUT THAT IS THE NAME OF THE GENE THAT
4 DR. KHORANA SET OUT TO SYNTHESIZE.

5 HE HAD ASSEMBLED A LARGE LABORATORY OF SCIENTISTS,
6 POST-DOCTORAL STUDENTS AND OTHER SCIENTISTS, TO WORK IN HIS
7 LABORATORY. SOME OF THESE SCIENTISTS WERE ORGANIC CHEMISTS WHO
8 COULD CHEMICALLY SYNTHESIZE DNA IN THE TEST TUBE. OTHERS WERE
9 SKILLED AT GROWING UP BACTERIAL CELLS AND BACTERIAL CULTURES AND
10 EXTRACTING FROM THOSE CULTURES ENZYMES THAT THEN COULD BE USED
11 TO REPAIR AND LINK TOGETHER THE FRAGMENTS OF DNA THAT WERE
12 CHEMICALLY SYNTHESIZED.

13 IN THIS WAY, THE LAB INTENDED TO SYNTHESIZE THE GENE
14 BIT BY BIT AND PUT IT TOGETHER.

15 I MENTIONED THE WORD "ENZYME." WHAT IS AN ENZYME?
16 THAT'S SOMETHING YOU WILL HEAR FROM THE EXPERTS AND YOU NEED TO
17 KNOW FOR THIS CASE.

18 AN ENZYME IS LIKE A LITTLE WORKER. THE LIVING CELLS,
19 INCLUDING THE CELLS IN OUR BODIES, CONTAIN MANY THOUSANDS OF
20 ENZYMES, AND AN ENZYME IS SIMPLY A MOLECULE THAT IS CAPABLE OF
21 BRINGING CHEMICAL MATERIALS TOGETHER AND CAUSING THEM TO REACT
22 IN A VERY SPECIFIC WAY.

23 THERE ARE THOUSANDS OF DIFFERENT ENZYMES, AND WE HAVE
24 LEARNED -- SCIENTISTS HAVE LEARNED THAT THEY CAN BE ISOLATED
25 FROM CELLS AND USED TO CARRY OUT REACTIONS IN THE TEST TUBE OR

3 1 IN THE LABORATORY. AND THAT'S REALLY THE SUBJECT OF THE PROCESS
2 THAT WE ARE DEALING WITH IN THIS LAWSUIT.

3 IN THE EARLY 1970'S, DR. KHORANA'S LABORATORY WAS THE
4 ONLY ONE IN THE WORLD THAT WAS CAPABLE OF CHEMICALLY
5 SYNTHESIZING DNA. THIS WAS A VERY DIFFICULT TASK, IT WAS VERY
6 CUMBERSOME, AND SCIENTISTS IN HIS LAB WORKED MONTHS AND
7 SOMETIMES EVEN YEARS TO SYNTHESIZE SMALL PIECES OF DNA THAT
8 WOULD BE USED TO CREATE THIS GENE.

9 AS THE BITS AND PIECES OF THE DNA WERE FORMED, DR.
10 KHORANA REALIZED THAT IT WOULD BE DESIRABLE TO HAVE A WAY OF
11 REPLICATING THOSE BITS AND PIECES SO THAT THEY WOULDN'T HAVE TO
12 BE CHEMICALLY SYNTHESIZED EVERY TIME ADDITIONAL MATERIAL WAS
13 NEEDED.

14 HIS ULTIMATE GOAL WAS TO STUDY THE WAY THIS GENE --
15 THIS SYNTHETIC GENE WOULD FUNCTION IN LIVING CELLS, AND HIS GOAL
16 WAS TO HAVE ENOUGH THAT HE COULD PUT IT IN LIVING CELLS, LIKE
17 BACTERIAL CELLS, AND DETERMINE HOW IT WORKED.

18 JUST AS THERE WAS NO WAY TO CHEMICALLY SYNTHESIZE DNA
19 BEFORE DR. KHORANA DISCOVERED THE PROCESS, THERE WAS ALSO NO WAY
20 TO REPLICATE THE GENE IN THE LABORATORY PRIOR TO HIS WORK.

21 DR. KHORANA HAD CAREFULLY FOLLOWED THE WORK OF ANOTHER
22 FAMOUS SCIENTIST, DR. ARTHUR KORNBERG. YOU WILL HEAR FROM DR.
23 KORNBERG. HE WILL BE CALLED AS AN EXPERT WITNESS BY DU PONT.

24 DR. KORNBERG IS A PROFESSOR EMERITUS OF STANFORD
25 UNIVERSITY AND WAS THE HEAD OF THE DEPARTMENT OF BIOCHEMISTRY IN

3 1 THE MEDICAL SCHOOL AT STANFORD FOR MANY, MANY YEARS. BACK AT
2 THIS TIME, DR. KORNBERG HAD WON THE NOBEL PRIZE FOR HIS
3 REMARKABLE DISCOVERY OF THE WAY DNA REPLICATES IN LIVING CELLS.

4 AND DR. KORNBERG DISCOVERED AN ENZYME CALLED DNA
5 POLYMERASE. DR. KORNBERG DISCOVERED THAT THIS WAS THE ENZYME
6 RESPONSIBLE FOR SYNTHESIZING DNA IN LIVING CELLS, AND HE ALSO
7 DISCOVERED HOW YOU COULD USE THAT ENZYME FOR SYNTHESIZING DNA IN
8 THE TEST TUBE.

9 NOW, DR. KHORANA CAREFULLY FOLLOWED THIS WORK OF DR.
10 KORNBERG'S. DR. KHORANA AND DR. KORNBERG WERE VERY CLOSE
11 FRIENDS, AND THEY COLLABORATED, AND DR. KHORANA OFTEN WORKED IN
12 DR. KORNBERG'S LABORATORY.

13 SO THROUGH THIS COLLABORATION, DR. KHORANA LEARNED HOW
14 TO USE THE ENZYME DNA POLYMERASE TO SYNTHESIZE DNA.

15 SOME OF THESE WORDS MAY SEEM DAUNTING TO YOU, BUT OFTEN
16 THEY'RE JUST MADE UP OF COMPONENT PARTS THAT IS QUITE LOGICAL.
17 "POLYMERASE" SIMPLY MEANS THAT IT IS AN ENZYME THAT CAUSES THE
18 FORMATION OF A POLYMER, DNA. "POLYMER" BECAUSE IT IS MADE UP OF
19 MANY COMPONENT PARTS. THE WORD -- THE SUFFIX "ASE" IS USED TO
20 INDICATE THAT IT IS AN ENZYME.

21 DR. KHORANA'S POST-DOCTORAL STUDENTS, SOME OF WHICH YOU
22 WILL HEAR FROM DURING THE COURSE OF THIS TRIAL, WORKED OUT
23 CONDITIONS FOR REPLICATING SEGMENTS OF SYNTHETIC DNA MANY FOLD
24 USING THIS ENZYME DNA POLYMERASE. THE PROCESS THAT THEY
25 DISCOVERED INVOLVED MULTIPLE CYCLES OF A PROCEDURE THEY CALLED

3
1 REPAIR REPLICATION.

2 AND WHAT THEY FOUND WAS THAT BY USING THIS MULTIPLE
3 CYCLE REPAIR REPLICATION PROCESS, THEY WERE ABLE TO TAKE A PIECE
4 OF DNA THAT HAD BEEN SYNTHESIZED IN THE LABORATORY AND REPLICATE
5 IT, AND WITH EACH CYCLE OF REPLICATION, THEY WERE ABLE TO GET A
6 100 PERCENT INCREASE IN THE AMOUNT OF DNA THAT THEY STARTED
7 WITH; IN OTHER WORDS, THEY DOUBLED THE AMOUNT WITH EACH CYCLE.
8 SO IF THEY STARTED OUT WITH ONE MOLECULE, AFTER ONE CYCLE, THEY
9 WOULD HAVE TWO; AFTER TWO CYCLES, THEY WOULD HAVE FOUR; AFTER
10 THREE CYCLES, THEY WOULD HAVE EIGHT, AND SO FORTH. THIS IS
11 CALLED EXPONENTIAL AMPLIFICATION.

4
12 DR. KORNBERG WILL DESCRIBE DR. KHORANA'S MULTI-CYCLE
13 AMPLIFICATION PROCESS TO YOU AND WILL SHOW YOU THAT IT IS
14 IDENTICAL TO THE PROCESS THAT IS COVERED IN THE CETUS '202
15 PATENT.

16 YOU WILL LEARN FROM THE SCIENTISTS WHO WORKED IN DR.
17 KHORANA'S LAB THAT THIS PROCEDURE OF AMPLIFYING DNA WAS CARRIED
18 OUT SUCCESSFULLY IN DR. KHORANA'S LABORATORY. THEY DESCRIBED IT
19 IN THEIR PUBLICATIONS, AND TWO OF THE PUBLICATIONS THAT WE WILL
20 SEE AND WHICH ARE IN YOUR JURY'S BOOK ARE AN ARTICLE BY KLEPPE,
21 ET AL., WHICH WAS PUBLISHED IN 1971, AND AN ARTICLE BY PANET,
22 KHORANA, PUBLISHED IN 1974.

23 INCIDENTALLY, IT IS VERY COMMON FOR SCIENTISTS TO REFER
24 TO SCIENTIFIC PUBLICATIONS BY THE FIRST AUTHOR, SO THIS ONE YOU
25 WILL HEAR FREQUENTLY REFERRED TO AS THE KLEPPE PAPER, OR THE

1 KLEPPE, ET AL. -- MEANING "AND OTHERS" -- PAPER. IT ACTUALLY
2 HAD SEVERAL AUTHORS AND TWO OF THE AUTHORS ARE GOING TO TESTIFY
3 HERE AT THE TRIAL. THE LAST AUTHOR ON THE KLEPPE PAPER IS DR.
4 KHORANA AND THE LAST AUTHOR NAMED ON THE PANET PAPER IS DR.
5 KHORANA. IT WAS CUSTOMARY FOR THE LEAD SCIENTIST OR THE SENIOR
6 SCIENTIST TO HAVE HIS NAME LAST IN ORDER.

7 NOT ONLY DID DR. KHORANA'S LAB DESCRIBE THIS
8 MULTI-CYCLE AMPLIFICATION PROCESS IN THEIR PUBLICATIONS, THEY
9 DESCRIBED IT TO GOVERNMENT FUNDING AGENCIES TO WHICH THEY SOUGHT
10 FUNDING TO SUPPORT THEIR RESEARCH.

11 AND A VERY IMPORTANT DOCUMENT THAT YOU WILL SEE IS AN
12 APPLICATION THAT WAS SUBMITTED TO THE NATIONAL SCIENCE
13 FOUNDATION. THAT'S A GOVERNMENT AGENCY THAT FUNDS SCIENTIFIC
14 RESEARCH. AND DR. KHORANA AND HIS GROUP DESCRIBED THEIR
15 MULTI-CYCLE AMPLIFICATION PROCESS IN THEIR APPLICATION TO THE
16 NATIONAL SCIENCE FOUNDATION.

17 DR. KHORANA'S SCIENTISTS ALSO DISCLOSED THEIR WORK WITH
18 THIS MULTI-CYCLE AMPLIFICATION PROCESS IN SEMINARS THAT WERE
19 REGULARLY GIVEN IN THE KHORANA LAB. THEY WERE GIVEN ONCE A
20 WEEK, AND YOU WILL HEAR ABOUT THOSE SEMINARS DURING THE COURSE
21 OF THE TRIAL.

22 AN IRONIC ASPECT OF DR. KHORANA'S MULTI-CYCLE
23 AMPLIFICATION PROCESS IS THAT, ALTHOUGH IT WAS DESIGNED TO
24 AMPLIFY THESE PRECIOUS SEGMENTS OF DNA THAT HAD BEEN SYNTHESIZED
25 BY LONG, TEDIOUS PROCEDURES BY HIS SCIENTISTS, THE PROCESS

4
1 ITSELF REQUIRED LARGE EXCESSES OF SHORT SYNTHETIC PIECES OF DNA
2 CALLED PRIMERS.

3 DR. KORNBERG WILL EXPLAIN TO YOU HOW THIS ENZYME DNA
4 POLYMERASE WORKS, AND HE WILL EXPLAIN THAT FOR DNA POLYMERASE TO
5 SYNTHESIZE A PIECE OF DNA, IT REQUIRES A TEMPLATE OR A STRAND OF
6 DNA, IF YOU WILL, ONE STRAND LIKE THE BOTTOM STRAND HERE
7 (INDICATING) OF DNA, UPON WHICH TO SYNTHESIZE, BUT IT ALSO
8 REQUIRES A PRIMER. IT WON'T START FROM SCRATCH. IT HAS TO HAVE
9 SOMETHING TO SORT OF PRIME THE PUMP.

10 AND IT WAS THE FACT THAT DR. KHORANA'S REPAIR --
11 MULTI-CYCLE REPAIR REPLICATION PROCESS REQUIRED THESE LARGE
12 EXCESSES OF PRIMERS THAT MADE THIS PROCESS OF LIMITED PRACTICAL
13 VALUE IN THE EARLY 1970'S. AND THE REASON IT WAS OF LIMITED
14 PRACTICAL VALUE WAS, AS I SAY, IT TOOK THE CHEMISTS MONTHS AND
15 SOMETIMES EVEN YEARS TO SYNTHESIZE THIS DNA, AND ANYTHING THAT
16 REQUIRED LARGE EXCESSES OF SOMETHING THAT WAS THAT DIFFICULT TO
17 GET WAS NOT IDEAL.

18 FORTUNATELY AT ABOUT THIS SAME TIME, OTHER TECHNOLOGY
19 CAME ON THE SCENE, AND THAT WAS TECHNOLOGY CALLED CLONING. MOST
20 OF YOU HAVE PROBABLY HEARD THE WORD "CLONING." CLONING HAS
21 FORMED THE BASIS OF THE EXPLOSION IN THE BIOTECHNOLOGY BUSINESS
22 AND GENETIC ENGINEERING YOU'VE HEARD ABOUT OVER THE LAST MANY
23 YEARS. CLONING BASICALLY BEGAN AT ABOUT THIS TIME, IN THE EARLY
24 '70'S, AND DEVELOPED THROUGH THE LATE '70'S AND THE '80'S.

25 THROUGH CLONING, DR. KHORANA WAS ABLE TO AMPLIFY HIS

4 1 DNA, AND HE WAS ABLE TO ALSO HAVE IT IN A LIVING CELL, WHICH WAS
2 HIS ULTIMATE GOAL, TO STUDY THE DNA IN THE LIVING CELL.

3 SO ALTHOUGH CLONING WAS A MUCH MORE PRACTICAL METHOD,
4 AT THAT TIME, FOR DR. KHORANA TO AMPLIFY OR REPLICATE HIS DNA,
5 YOU WILL SEE THAT HIS LABORATORY SUCCESSFULLY PRACTICED THIS
6 MULTI-CYCLE REPAIR REPLICATION PROCESS AND THEY USED IT
7 SUCCESSFULLY IN THE LATE '60'S AND EARLY '70'S.

8 AS I'VE INDICATED, MUCH OF THE WORK THAT DR. KHORANA
9 DID WAS SUPPORTED BY TAXPAYERS' MONEY, THROUGH GRANTS FROM THE
10 NATIONAL SCIENCE FOUNDATION AND ELSEWHERE. DR. KHORANA DID NOT
11 PATENT HIS WORK. HE DEDICATED IT TO THE PUBLIC.

12 DURING THE YEARS FOLLOWING DR. KHORANA'S DISCOVERY AND
13 USE OF THIS MULTI-CYCLE AMPLIFICATION PROCESS, THERE WAS A
14 VERITABLE REVOLUTION IN THE TECHNOLOGY OF BIOTECHNOLOGY.

15 WHAT WAS OF INTEREST TO ONLY A FEW PEOPLE IN THE LATE
16 '60'S AND EARLY '70'S WAS THE DARLING OF WALL STREET IN THE
17 EARLY 1980'S. SCIENTISTS IN THE EARLY '80'S WERE TAKING
18 ADVANTAGE OF FUNDAMENTAL DISCOVERIES THAT HAD BEEN MADE DURING
19 THE PREVIOUS DECADES AND APPLYING THEM TO PRACTICAL PROBLEMS,
20 LIKE SYNTHESIZING PHARMACEUTICAL PRODUCTS USING GENETIC
21 ENGINEERING OR RECOMBINANT DNA. MANY OF THESE PROJECTS BECAME
22 HEADLINE NEWS AND WERE REPORTED IN PLACES LIKE THE WALL STREET
23 JOURNAL IN THE BUSINESS SECTION OF THE PAPER.

24 AS THE TECHNIQUES IN BIOTECHNOLOGY ADVANCED DURING THE
25 1970'S, THE USES OF DNA POLYMERASE MULTIPLIED. RATHER THAN

5
1 GROWING UP BACTERIA AND EXTRACTING THE ENZYME FROM THE BACTERIA,
2 PURIFYING IT, IN THE EARLY -- AS DR. KHORANA AND DR. KORNBERG
3 HAD TO DO, IN THE EARLY 1980'S, THE -- ALL YOU HAD TO DO WAS
4 WRITE TO A LABORATORY SUPPLY HOUSE AND ORDER THE ENZYME AND IT
5 WOULD ARRIVE ON YOUR DOORSTEP THE NEXT MORNING.

6 IN CONTRAST TO THE LENGTHY ARDUOUS PROCEDURES THAT DR.
7 KHORANA'S LAB HAD TO USE TO SYNTHESIZE THE PRIMERS TO MAKE THE
8 MULTI-CYCLE PROCEDURE WORK, IN THE EARLY 1980'S, MACHINES HAD
9 BEEN DEVELOPED, AND THEY WOULD SYNTHESIZE THESE PRIMERS
10 AUTOMATICALLY, AND LITERALLY YOU COULD PUSH A BUTTON AND GO TO
11 LUNCH AND COME BACK AND YOU WOULD HAVE YOUR PRIMERS.

12 SO ALTHOUGH DR. KHORANA'S MULTI-CYCLE AMPLIFICATION
13 PROCEDURE WAS NOT A PRACTICAL PROCEDURE FOR AMPLIFYING DNA IN
14 THE EARLY 1970'S, BY THE EARLY 1980'S, IT WAS A PRACTICAL,
15 FEASIBLE PROCESS, AND THE REASON FOR THIS IS BECAUSE ALL OF THE
16 ASSOCIATED TECHNOLOGY THAT WAS REQUIRED TO MAKE IT WORK
17 CONVENIENTLY, NOT TO MAKE IT WORK, BUT TO MAKE IT CONVENIENT TO
18 THE -- TO THE SCIENTISTS USING IT, THAT WORK HAD CAUGHT UP.

19 DR. KHORANA AND THE PEOPLE WORKING IN HIS LABORATORY
20 WERE TRULY AHEAD OF THEIR TIME IN THE EARLY 1970'S WHEN THEY
21 CAME UP WITH THIS PROCESS.

22 WELL, AGAINST THIS BACKGROUND OF THE EXPLOSIVE PROGRESS
23 IN BIOTECHNOLOGY IN THE LATE 1970'S AND THE EARLY 1980'S, CETUS
24 REDISCOVERED DR. KHORANA'S MULTI-CYCLE AMPLIFICATION PROCESS.

25 YOU WILL MEET DR. KARY MULLIS, THE SCIENTIST THAT CETUS

5 1 CREDITS WITH THE DISCOVERY OF THIS AMPLIFICATION PROCEDURE.

2 DR. MULLIS WILL DESCRIBE TO YOU HOW HE THOUGHT OF THE
3 IDEA OF EXTENSIVELY SYNTHESIZING DNA USING THIS MULTI-CYCLE
4 PROCEDURE, AND HOW HE WENT TO THE LABORATORY AND, WITH COMMONLY
5 AVAILABLE MATERIALS AND TECHNOLOGY THAT WAS BEING USED BY OTHERS
6 FOR MANY DIFFERENT REASONS, HE WAS ABLE TO MAKE THE PROCESS WORK
7 ON HIS SECOND OR THIRD TRY.

8 NOW, CETUS REDISCOVERED THE MULTI-STEP REPAIR
9 REPLICATION PROCESS WHICH DR. KHORANA HAD DESCRIBED MORE THAN 10
10 YEARS EARLIER, AND THEY GAVE IT A DIFFERENT NAME. THEY CALLED
11 IT THE POLYMERASE CHAIN REACTION, OR PCR. POLYMERASE CHAIN
12 REACTION, COMMONLY ABBREVIATED PCR. IT'S CALLED THE POLYMERASE
13 CHAIN REACTION, "POLYMERASE" BECAUSE IT USED DR. KORNBERG'S
14 ENZYME, DNA POLYMERASE, AND "CHAIN REACTION" BECAUSE IT USES THE
15 MULTIPLE CYCLES THAT DR. KHORANA HAD DISCOVERED.

16 CETUS WOULD HAVE YOU BELIEVE THAT IT WOULD HAVE BEEN
17 VERY DIFFICULT FOR A SCIENTIST OF ORDINARY SKILL IN THE EARLY
18 1980'S TO FOLLOW THE PROCEDURES THAT WERE DESCRIBED IN DR.
19 KHORANA'S PUBLICATIONS AND MAKE THIS REACTION WORK. BUT LET'S
20 TAKE A LOOK AT SOME OF THE THINGS THAT CETUS HAS SAID OUT OF THE
21 CONTEXT OF THIS LITIGATION.

22 THIS IS AN EXCERPT FROM A PUBLICATION WRITTEN BY DR.
23 MULLIS REGARDING CETUS' DISCOVERY OF THE POLYMERASE CHAIN
24 REACTION. AND THIS, RATHER THAN DESCRIBING THIS AS A COMPLEX
25 PROCEDURE THAT IT'S DIFFICULT TO MAKE IT WORK, DR. MULLIS

5 1 DESCRIBES IT AS "AN ENZYMATIC REACTION AS SIMPLE TO PERFORM AS
2 IT IS INTELLECTUALLY SATISFYING TO CONTEMPLATE."

3 HE SAYS THAT "PCR IS SURPRISINGLY ROBUST AND IT IS
4 DIFFICULT TO FIND SITUATIONS IN WHICH IT WILL NOT WORK, AND IT
5 DERIVES FROM A COMBINATION OF THREE FAMILIAR PHENOMENA." IN
6 OTHER WORDS, THREE PHENOMENA THAT AT THE TIME OF ITS DISCOVERY
7 WERE WELL-KNOWN TO SCIENTISTS THAT WERE SKILLED IN THIS FIELD.

8 ANOTHER IMPORTANT DOCUMENT IS A MEMO THAT AN ESTEEMED
9 SCIENTIST AT CETUS WROTE BACK IN 1985, LONG BEFORE ANYONE
10 THOUGHT ABOUT THIS LITIGATION.

11 WHAT WAS BEING DISCUSSED IN THIS MEMO WAS WHETHER IT
12 WAS A GOOD IDEA FOR CETUS TO PUBLISH AN ARTICLE THAT WAS TO
13 APPEAR IN SCIENCE MAGAZINE. NOW, THAT ARTICLE WAS GOING TO
14 CONTAIN SOME FAIRLY DETAILED INFORMATION ON HOW TO RUN THIS
15 REACTION THAT CETUS CALLED PCR, DR. KHORANA'S MULTI-STEP
16 AMPLIFICATION REACTION.

17 AND THE DEBATE IN CETUS WAS: SHOULD WE REALLY PUBLISH
18 THIS AND LET THE CAT OUT OF THE BAG, OR SHOULD WE KEEP THIS TO
19 OURSELVES?

20 WELL, DR. MULLIS HAD GIVEN A TALK A SHORT TIME BEFORE
21 THIS, AND IN THAT TALK, HE HAD DESCRIBED THE BASIC PRINCIPLE OF
22 PCR. HE HADN'T GIVEN THIS DETAILED INFORMATION, BUT HE
23 DESCRIBED HOW THE REACTION IS CARRIED OUT.

24 THE CONCERN BY SOME AT CETUS WAS: WELL, HE GAVE THE
25 FUNDAMENTAL PRINCIPLE, BUT WE'VE GOT TWO FIGURES IN THIS

6 1 PUBLICATION THAT'S GOING TO APPEAR IN SCIENCE THAT HAVE LONG
2 LEGENDS UNDER THEM, AND THEY GIVE DETAILS OF HOW TO MAKE THE
3 REACTION WORK. SHOULD WE REALLY LET THAT CAT OUT OF THE BAG?

4 BUT DR. ERLICH, WHO WAS THE HEAD OF THE DEPARTMENT AND
5 IS ONE OF THE MOST FAMOUS SCIENTISTS IN THIS FIELD, SAID THE
6 FOLLOWING: BASICALLY, HE SAID, I SEE NO PROBLEM OF PUBLISHING
7 THIS ARTICLE.

8 "ONCE THE FUNDAMENTAL PRINCIPLE OF PCR HAS
9 BEEN DISCLOSED, ANY GOOD MOLECULAR BIOLOGIST WILL BE
10 AWARE OF THE RELEVANT PARAMETERS TO EXPLORE. FOR
11 EXAMPLE, TIME OF INCUBATION, REAGENT, PRIMERS,
12 ENZYMES, AND SO FORTH. EVEN THE APPROACHES THAT ARE
13 ONLY SEMIOBVIOUS WILL BE APPARENT EVENTUALLY."

14 SO DR. MULLIS -- DR. ERLICH IS SAYING: DR. MULLIS
15 ALREADY LET THE CAT OUT OF THE BAG WHEN HE DESCRIBED THE
16 FUNDAMENTAL PRINCIPLE. ALL OF THESE DETAILS THAT ARE IN THE
17 SCIENCE ARTICLE ARE THINGS THAT ANY GOOD MOLECULAR BIOLOGIST IS
18 GOING TO BE ABLE TO FIGURE OUT.

19 WELL, YOU WILL LEARN FROM DR. KHORANA -- EXCUSE ME --
20 DR. KORNBERG AND OTHER DU PONT WITNESSES THAT THE FUNDAMENTAL
21 PRINCIPLE OF THIS REACTION AND MUCH MORE WERE DISCLOSED IN THE
22 PUBLICATIONS AND THE WORK OF DR. KHORANA.

23 IN THE EARLY AND MID-1980'S, WHEN CETUS REDISCOVERED
24 DR. KHORANA'S MULTI-CYCLE AMPLIFICATION PROCEDURE, THE FIELD OF
25 BIOTECHNOLOGY WAS VASTLY DIFFERENT.

6 1 AS I SAID, WHERE IT TOOK DR. KHORANA'S LAB MONTHS AND
2 SOMETIMES EVEN YEARS TO SYNTHESIZE THESE LARGE EXCESSES OF
3 PRIMERS THAT THEY NEEDED, YOU COULD GET THEM IN A FEW HOURS WHEN
4 IT WAS REDISCOVERED IN THE EARLY 1980'S.

5 WHERE DR. KHORANA'S LAB HAD TO PAINSTAKINGLY EXTRACT
6 THE ENZYME AND PURIFY IT IN THE EARLY 1980'S WHEN CETUS
7 REDISCOVERED THE PROCESS, YOU COULD BUY THE ENZYME FROM A LAB
8 SUPPLY HOUSE. IN FACT, THE CHANCES ARE THE ENZYME WOULD HAVE
9 BEEN AVAILABLE IN THE FREEZER IN THE LAB BECAUSE IT WAS BEING
10 USED FOR SO MANY OTHER THINGS IN THOSE DAYS.

11 WHERE IN THE LATE '60'S AND EARLY '70'S, WHEN DR.
12 KHORANA'S LAB WAS DOING THIS WORK, IT WAS ONE OF THE FEW LABS IN
13 THE WORLD, ONE OF THE FEW IN THE WORLD THAT HAD ANY PRACTICAL
14 USE FOR THIS REACTION AT ALL, BUT IN THE EARLY 1980'S, WHEN DR.
15 MULLIS AND CETUS CLAIMED TO HAVE REDISCOVERED PCR, THE
16 TECHNOLOGY HAD CAUGHT UP AND THE REACTION HAD MANY, MANY USES
17 AND APPLICATIONS. SO IT MADE IT A MUCH MORE INTERESTING
18 REACTION TO THE SCIENTIFIC WORLD.

19 WHERE IN THE LATE 1960'S AND EARLY '70'S, WHEN DR.
20 KHORANA'S LAB WAS DOING THIS WORK, ONLY A HANDFUL OF SCIENTISTS
21 HAD ANY EXPERIENCE OR USE FOR THE ENZYME DNA POLYMERASE, DR.
22 KHORANA'S LAB, DR. KORNBERG'S LAB, AND VERY FEW OTHER
23 LABORATORIES, IN THE EARLY TO MID-1980'S WHEN CETUS REDISCOVERED
24 THIS PROCESS, THAT ENZYME WAS BEING USED BY SCIENTISTS ROUTINELY
25 FOR A WIDE VARIETY OF DIFFERENT APPLICATIONS. AND YOU'RE GOING

6 1 TO HEAR ABOUT THOSE APPLICATIONS FROM THE EXPERT WITNESSES WHO
2 WILL APPEAR.

3 IN THE LATE '60'S AND EARLY '70'S, WHEN DR. KHORANA'S
4 LAB WAS DOING THIS WORK, ANALYTICAL PROCEDURES FOR DETECTING
5 WHAT YOU'VE GOT AFTER YOU'VE AMPLIFIED THE DNA WERE VERY CRUDE
6 AND INSENSITIVE. BY THE EARLY 1980'S WHEN CETUS REDISCOVERED
7 THIS PROCESS, THOSE TECHNIQUES HAD BEEN DEVELOPED TO THE POINT
8 WHERE YOU COULD SENSITIVELY ANALYZE AND DETECT VERY SMALL
9 AMOUNTS OF DNA, SO THE REACTION WAS MUCH MORE EASY TO DEAL WITH
10 IN THOSE DAYS.

11 DESPITE THESE OBSTACLES, DR. KHORANA'S LAB SUCCESSFULLY
12 USED IN THE 1969-TO-'72 TIME FRAME THE MULTI-CYCLE AMPLIFICATION
13 PROCESS THAT CETUS NOW CALLS PCR AND WHICH IS THE SUBJECT MATTER
14 CLAIM IN THE '202 PATENT.

15 WELL, UNLIKE DR. KHORANA, WHEN CETUS REDISCOVERED
16 THE -- DR. KHORANA'S PROCESS, CETUS PATENTED IT. THUS, THEY
17 TOOK AWAY FROM THE PUBLIC TECHNOLOGY WHICH DR. KHORANA HAD
18 DEDICATED TO THE PUBLIC.

19 FOLLOWING DR. MULLIS' REDISCOVERY OF PCR, CETUS
20 CONTINUED TO OPTIMIZE THE TECHNIQUE AND APPLY IT TO NEW
21 APPLICATIONS. CETUS HAS BEEN WIDELY CREDITED WITH DEVELOPING
22 THIS TECHNIQUE FOR MANY DIVERSE USES, SUCH AS DIAGNOSING CERTAIN
23 DISEASES, INVOLVING CRIME, AND SO FORTH.

24 YOU WILL HEAR THE TERM "PCR" OVER AND OVER. BUT YOU
25 SHOULD KEEP IN MIND THAT PCR, AS IT IS KNOWN TODAY, REALLY HAS

6 1 VERY LITTLE TO DO WITH THIS LAWSUIT. WHAT THE LAWSUIT ABOUT --
2 IS ABOUT IS NOT THE PCR PROCESS THAT'S PRACTICED BY SCIENTISTS
3 TODAY.

4 THE LAWSUIT IS ABOUT THE PROCESS THAT IS COVERED BY THE
5 CLAIMS OF THE CETUS PATENTS, AND THOSE CLAIMS ARE MUCH BROADER
6 THAN WHAT IS DESCRIBED AS PCR. REFINEMENTS AND IMPROVEMENTS IN
7 THE PROCESS THAT HAVE OCCURRED SINCE THE PATENTS ISSUED AND
8 WHICH ARE NOT LIMITATIONS OR THINGS THAT ARE REFLECTED IN THE
9 CLAIMS OF THE PATENT ARE REALLY IRRELEVANT TO THE QUESTION
10 RAISED IN THIS LAWSUIT.

11 WELL, CETUS OBTAINED THE TWO PATENTS COVERING THE DNA
12 AMPLIFICATION PROCESS FROM THE PATENT & TRADEMARK OFFICE
13 INITIALLY WITH THE PATENT & TRADEMARK OFFICE KNOWING NOTHING AT
14 ALL ABOUT DR. KHORANA'S WORK. AND FOR THAT REASON, IT'S NOT
15 SURPRISING THAT THOSE PATENTS ISSUED WITH CLAIMS IT ACTUALLY
16 COVERED OR ENCOMPASSED DR. KHORANA'S WORK.

17 AS JUDGE PATEL TOLD YOU, THESE PATENTS ARE U.S. PATENTS
18 4,683,202, WHICH WE WILL REFER TO AS THE '202 PATENT, AND
19 4,683,195, WHICH WE WILL REFER TO AS THE '195 PATENT. AND THESE
20 PATENTS ARE -- COPIES OF THEM ARE IN THE BOOKS THAT WERE PLACED
21 ON YOUR CHAIRS.

22 ONE OF OUR WITNESSES IS MR. JOSEPH DE GRANDI. MR.
23 DE GRANDI IS A HIGHLY-RESPECTED PATENT ATTORNEY. MR. DE GRANDI
24 HAS BEEN SELECTED BY HIS PEERS TO HEAD TWO OF THE LARGEST
25 ORGANIZATIONS OF PATENT ATTORNEYS IN THE UNITED STATES. HE HAS

7
1 BEEN SERVED -- HE HAS SERVED ON COMMISSIONS THAT HAVE REPORTED
2 TO THE PRESIDENT. HE HAS SERVED ON COMMITTEES AND ADVISED THE
3 PATENT & TRADEMARK OFFICE ABOUT PROBLEMS THAT MIGHT EXIST WITH
4 THE PATENT SYSTEM.

5 MR. DE GRANDI WILL EXPLAIN THAT ALTHOUGH THE PATENT
6 SYSTEM HAS BEEN VERY GOOD FOR STIMULATION INNOVATION, THE
7 PATENTS CAN ALSO HAVE A NEGATIVE EFFECT. BY ITS VERY NATURE, A
8 PATENT IS ANTICOMPETITIVE SINCE IT GIVES THE OWNER OF THE PATENT
9 THE RIGHT TO EXCLUDE OTHERS FROM MAKING, USING OR SELLING THE
10 PATENTED INVENTION.

11 THE EXTENT TO WHICH THE PATENT CAN BE USED TO PREVENT
12 COMPETITION DEPENDS ON THE SCOPE OF ITS CLAIMS. AND THE CLAIMS,
13 MR. DE GRANDI WILL EXPLAIN TO YOU, ARE THE NUMBERED PARAGRAPHS
14 THAT APPEAR AT THE END OF THE PATENT, AND THEY APPEAR AT THE END
15 OF EVERY PATENT AND AT THE END OF THESE TWO PATENTS.

16 THE CLAIMS ARE THE MEETS AND BOUNDS OF THE PATENT, IF
17 YOU WILL. THEY DRAW AN IMAGINARY PROPERTY LINE AROUND WHAT THE
18 PATENTEE REGARDS AS THE INVENTION.

19 NOW, DR. KORNBERG WILL EXPLAIN THAT THE CLAIMS OF THE
20 '202 AND THE '195 PATENTS ARE EXTREMELY BROAD. PRESENT-DAY PCR
21 TYPICALLY USES 20 TO 30 OF THESE MULTIPLE CYCLES THAT DR.
22 KHORANA DISCOVERED, WHICH MIGHT RESULT IN AMPLIFICATIONS OF THE
23 DNA BY A MILLION-FOLD OR MORE. BUT THE CLAIMS OF THE '202
24 PATENT COVER THE USE OF TWO AMPLIFICATION CYCLES OR, AT MOST,
25 THREE AMPLIFICATION CYCLES.

7 1 NOW, THEY ENCOMPASS USING MORE CYCLES THAN THAT, BUT IF
2 YOU USE TWO CYCLES OR IF YOU USE THREE CYCLES, YOU FALL WITHIN
3 THE SCOPE OF THOSE CLAIMS. THAT'S WHAT WE MEAN BY SAYING THE
4 CLAIMS ARE SO BROAD. IT'S NOT ONLY MODERN-DAY PCR; IT'S
5 VIRTUALLY ANY MULTIPLE CYCLE AMPLIFICATION PROCESS THAT THE
6 CLAIMS COVER.

7 SO PCR, YOU WILL HEAR, WILL GIVE YOU AMPLIFICATIONS OF
8 DNA BY A MILLION-FOLD OR MORE, BUT THE CLAIMS THEMSELVES
9 ENCOMPASS PROCESSES WHERE YOU USE TWO CYCLES, SO YOU GET
10 FOUR-FOLD AMPLIFICATION, OR, AT MOST, THREE CYCLES, WHICH GIVE
11 YOU EIGHT-FOLD AMPLIFICATION.

12 PCR, AS IT'S KNOWN TODAY, IS OFTEN USED FOR AMPLIFYING
13 UP A PIECE OF DNA THAT MIGHT BE ASSOCIATED WITH -- WITH A
14 CERTAIN CHARACTERISTIC, AND IT OCCURS IN A COMPLEX MIXTURE OF
15 DNA. IT'S AMPLIFIED UP FROM ITS COMPLEX MIXTURE.

16 BUT THE CLAIMS AREN'T LIMITED TO THAT SORT OF A
17 REACTION. THE CLAIMS COVER AMPLIFYING UP A SMALL PURE SEGMENT
18 OF DNA. IT DOESN'T REQUIRE THIS COMPLEX MIXTURE.

19 SO YOU MUST KEEP IN MIND THAT THE SCOPE OF THE CLAIMS
20 ARE WHAT DETERMINE THE EXTENT OF THE COVERAGE OF THE PATENT AND
21 ALSO DETERMINE HOW YOU COMPARE THE PATENT TO THE PRIOR ART. IN
22 OTHER WORDS, THE CLAIMS ARE BROAD ENOUGH TO COVER THE PRIOR ART,
23 THEN THEY TAKE AWAY FROM THE PUBLIC SOMETHING THAT THE PUBLIC
24 HAD.

25 "PRIOR ART" IS A TERM THAT PATENT LAWYERS USE SIMPLY TO

7 1 MEAN THAT WHICH WAS KNOWN BEFORE THE PATENT ISSUED, AS JUDGE
2 PATEL EXPLAINED.

3 NOW, DR. -- MR. DE GRANDI WILL EXPLAIN THAT THE UNITED
4 STATES PATENT SYSTEM IS MADE UP OF MANY COMPONENT PARTS. THE
5 CONSTITUTIONAL PURPOSE OF THE PATENT SYSTEM IS TO PROMOTE
6 PROGRESS OF SCIENCE, BUT IT'S RECOGNIZED THAT THIS
7 ANTICOMPETITIVE EFFECT OF THE PATENT IS ONLY JUSTIFIED IF THE
8 PATENTEE DOES PROVIDE SOMETHING TO THE PUBLIC THE PUBLIC DID NOT
9 HAVE BEFORE.

10 THEREFORE, THE PATENT SYSTEM HAS A NUMBER OF CHECKS AND
11 BALANCES, BECAUSE IT'S IMPORTANT THAT THE PUBLIC MAKE SURE THAT
12 IT'S GETTING SOMETHING NEW BEFORE IT GIVES UP THIS 17-YEAR RIGHT
13 TO EXCLUDE OTHERS. AND ONE OF THE COMPONENT PARTS OF THE UNITED
14 STATES PATENT AND TRADEMARK SYSTEM IS THIS COURT. THIS COURT
15 DECIDES WHETHER OR NOT THE PATENT & TRADEMARK OFFICE MADE THE
16 RIGHT DECISION IN GRANTING THESE PATENTS OR THE WRONG DECISION.

17 NOW, AFTER DU PONT BROUGHT THIS LAWSUIT TO HAVE CETUS'
18 '202 AND '195 PATENTS DECLARED INVALID, CETUS' EXCLUSIVE
19 LICENSEE IN THE MEDICAL DIAGNOSTICS AREA, HOFFMANN-LA ROCHE,
20 ASKED THE PATENT & TRADEMARK OFFICE TO INITIATE PROCEEDINGS
21 CALLED RE-EXAMINATION.

22 HOFFMAN-LA ROCHE'S REQUEST FOR RE-EXAMINATION DID NOT
23 ASK THE PATENT & TRADEMARK OFFICE TO REVOKE CETUS' PATENTS.
24 WHAT THEY ASKED THE PATENT & TRADEMARK OFFICE TO DO WAS TO
25 REAFFIRM THE PATENTABILITY OF THE PROCESS COVERED BY THOSE

8 1 PATENTS OVER CERTAIN PRIOR ART. HOFFMANN-LA ROCHE TOLD THE
2 PATENT & TRADEMARK OFFICE ABOUT SOME BUT NOT ALL OF DR.
3 KHORANA'S PRIOR ART.

4 DU PONT FELT THAT THE HOFFMANN-LA ROCHE RE-EXAMINATION
5 REQUEST WAS MISLEADING AND DID NOT FAIRLY REPRESENT DR.
6 KHORANA'S WORK AND HIS PUBLICATIONS, AND FOR THIS REASON DU PONT
7 ALSO ASKED THE PATENT & TRADEMARK OFFICE TO RE-EXAMINE CETUS'
8 PATENTS.

9 THE PATENT & TRADEMARK OFFICE RULES, YOU WILL HEAR FROM
10 MR. DE GRANDI, ARE DESIGNED TO PROVIDE VERY LITTLE PARTICIPATION
11 BY AN ADVERSE RE-EXAMINATION REQUESTER. IN THIS CASE, DU PONT
12 HAD ONE OPPORTUNITY TO PRESENT ITS VIEWS ON EACH OF THE CETUS
13 PATENTS.

14 CETUS AND ITS PARTNER HOFFMANN-LA ROCHE TEAMED UP TO
15 SUBMIT HUNDREDS OF PAGES OF ARGUMENTATION AND EXPERT
16 DECLARATIONS TO THE PATENT & TRADEMARK OFFICE WHILE COORDINATING
17 THEIR EFFORTS TO MAKE SURE THAT DU PONT WOULD HAVE NO FURTHER
18 OPPORTUNITY TO REPLY OR TO REBUT THE ARGUMENTS THAT CETUS AND
19 HOFFMANN-LA ROCHE WERE MAKING TO THE PATENT & TRADEMARK OFFICE.

20 NOW, WE AREN'T SAYING THAT CETUS AND HOFFMANN-LA ROCHE
21 VIOLATED THE RULES. THEY TOOK ADVANTAGE OF THE RULES. THE
22 SYSTEM ITSELF PROVIDES VERY LITTLE OPPORTUNITY FOR AN ADVERSE
23 PARTY CHALLENGING A PATENT, SUCH AS DU PONT, TO PARTICIPATE IN
24 THE RE-EXAMINATION PROCEDURE.

25 THE PATENT EXAMINER WAS PERSUADED BY CETUS AND

8 1 HOFFMANN-LA ROCHE THAT THE SUBJECT MATTER CLAIMED IN THEIR
2 PATENTS WAS PATENTABLE OVER TWO OF DR. KHORANA'S PUBLICATIONS,
3 THE KLEPPE AND PANET PAPERS.

4 THE PATENT EXAMINER REACHED THE WRONG RESULT. DR.
5 KORNBERG WILL SHOW YOU THAT EACH AND EVERY STEP OF THE CLAIMS OF
6 THE '202 PATENT IS DESCRIBED IN DR. KHORANA'S PUBLICATIONS AND
7 WAS WORK DONE BY DR. KHORANA.

8 THE TEST FOR WHETHER SOMETHING IS OBVIOUS OR WHETHER
9 SOMETHING IS DESCRIBED IN THE PRIOR ART IS WHETHER THE PRIOR ART
10 WAS SUFFICIENT TO TELL A PERSON OF ORDINARY SKILL IN THE ART HOW
11 TO CARRY IT OUT.

12 NOW, DR. ERLICH THOUGHT THAT THE PERSON OF ORDINARY
13 SKILL COULD CARRY IT OUT. HE SAID ANY GOOD MOLECULAR BIOLOGIST
14 WILL BE AWARE OF HOW TO DO IT.

15 BUT WHAT WAS THE LEVEL OF ORDINARY SKILL IN THIS ART IN
16 THE EARLY 1980'S WHEN CETUS REDISCOVERED DR. KHORANA'S PROCESS?
17 THE AVERAGE SCIENTIST WORKING IN THIS FIELD HAD USUALLY A
18 BACHELOR'S DEGREE OR AN UNDERGRADUATE DEGREE IN SCIENCE SUCH AS
19 CHEMISTRY OR BIOLOGY. THIS AVERAGE SCIENTIST THEN WENT ON TO
20 GRADUATE SCHOOL, AND PROBABLY WENT TO SCHOOL FOR ANOTHER FOUR TO
21 FIVE YEARS TO GET A PH.D. DEGREE, A DOCTORATE DEGREE, TYPICALLY
22 IN A FIELD OF SCIENCE LIKE MOLECULAR BIOLOGY.

23 THE SCIENTIST MIGHT ALSO HAVE GONE THROUGH MEDICAL
24 SCHOOL AND GOTTEN HIS TRAINING IN BIOCHEMISTRY AND MOLECULAR
25 BIOLOGY THAT WAY.

8 1 AFTER GETTING THE DOCTORATE DEGREE, THOUGH, THE
2 EDUCATION OF THE AVERAGE SCIENTIST IN THIS FIELD DOESN'T END.
3 THE SCIENTIST USUALLY THEN GOES TO WORK AS WHAT IS CALLED A
4 POST-DOCTORAL STUDENT FOR ANOTHER TWO OR THREE YEARS UNDER THE
5 DIRECTION OF A SENIOR SCIENTIST.

6 NOW, THIS IS THE PERSON WHO HAS ORDINARY SKILL IN THE
7 FIELD OF SCIENCE THAT WE'RE TALKING ABOUT. THESE ARE VERY
8 HIGHLY-TRAINED INDIVIDUALS.

9 YOU'RE GOING TO HEAR FROM ANOTHER EXPERT WITNESS THAT
10 DU PONT WILL CALL, DR. BRUCE WALLACE, WHO IS A WORLD RENOWNED
11 SCIENTIST AT THE CITY OF HOPE RESEARCH INSTITUTE DOWN IN THE LOS
12 ANGELES AREA. DR. WALLACE IS A LEADING FIGURE IN THE FIELDS OF
13 SCIENCE TO WHICH THE '202 PATENT AND THE '195 PATENT RELATE.

14 DR. WALLACE WILL EXPLAIN THAT ALL OF THE TEACHINGS, ALL
15 OF THE TECHNIQUES OF THE DNA AMPLIFICATION PROCEDURE DESCRIBED
16 AND CLAIMED IN THE '202 PATENT WERE COMMONLY AND ROUTINELY USED
17 BY MOLECULAR BIOLOGISTS IN THE EARLY 1980'S PRIOR TO THE CETUS
18 INVENTION.

19 HE WILL EXPLAIN THAT A SKILLED SCIENTIST COULD HAVE
20 READILY FOLLOWED THE TEACHINGS OF DR. KHORANA'S PUBLICATIONS AND
21 SUCCESSFULLY USED THE PROCESS DESCRIBED IN THE CETUS PATENTS.
22 DR. WALLACE WILL ALSO EXPLAIN TO YOU THE '195 PATENT.

23 NOW, THE '202 PATENT COVERS THIS AMPLIFICATION
24 PROCEDURE THAT WE'VE BEEN TALKING ABOUT. THE '195 PATENT COVERS
25 EXACTLY THE SAME AMPLIFICATION PROCESS, AND YOU WILL SEE THAT

9 1 THE TWO PATENTS ARE VIRTUALLY IDENTICAL. THE REASON FOR THAT IS
2 THAT THEY BOTH WERE DIVIDED OUT OF A COMMON PATENT APPLICATION.

3 THE '195 PATENT DIFFERS FROM THE '202 PATENT IN THAT IT
4 HAD -- IT INVOLVES, IN ADDITION TO THE AMPLIFICATION, AN
5 ADDITIONAL STEP OF DETECTING THE DNA THAT HAS BEEN AMPLIFIED.
6 AND THE WAY THAT THIS IS DETECTED IS USING A TECHNIQUE CALLED
7 PROBE HYBRIDIZATION, OR PROBING.

8 DR. WALLACE WAS ONE OF THE PIONEERS OF THE USE OF THIS
9 TECHNIQUE OF PROBING TO IDENTIFY DNA. DR. WALLACE WORKED OUT
10 THESE PROCEDURES IN THE LATE '70'S AND HE PUBLISHED HIS WORK IN
11 VERY IMPORTANT SCIENTIFIC JOURNALS.

12 DR. WALLACE'S WORK BECAME QUITE WELL-KNOWN, AND, IN
13 FACT, THE USE OF PROBES OR PROBING TO IDENTIFY DNA IN COMPLEX
14 MIXTURES BECAME SORT OF THE BACKBONE OF THE WAY TO FIND DNA IN
15 GENETICALLY-ENGINEERED MICROORGANISMS TO ASSIST WITH GENE
16 SPLICING EXPERIMENTS AND SO FORTH.

17 DR. WALLACE WILL EXPLAIN THAT, BY 1984, WHEN CETUS
18 REDISCOVERED THE PROCESS OF AMPLIFICATION OF DNA, THAT THE
19 TECHNIQUE OF PROBING WAS THE METHOD OF CHOICE FOR IDENTIFYING
20 DNA AND, IN THE '195 PATENT, ALL THAT CETUS HAS DONE IS COMBINED
21 A WELL-KNOWN TECHNIQUE FOR DETECTING DNA WITH DR. KHORANA'S
22 AMPLIFICATION PROCEDURE, AND DR. WALLACE WILL EXPLAIN TO YOU
23 THAT IT WAS VERY OBVIOUS TO COMBINE THESE TWO TECHNIQUES.

24 WELL, THE EXAMINER IN THE RE-EXAMINATION, LED BY THE
25 OVERWHELMING SUBMISSIONS BY HOFFMANN-LA ROCHE AND CETUS, DID NOT

9 1 CORRECTLY COMPARE DR. KHORANA'S PRIOR WORK WITH THE CLAIMS OF
2 THE CETUS PATENT.

3 DU PONT'S PATENT LAW EXPERT, MR. DE GRANDI, WILL
4 EXPLAIN, AS I'VE SAID, THAT IT IS THE CLAIMS OF THE PATENT THAT
5 DETERMINE WHAT THE PATENT COVERS AND THE BROADER THE CLAIMS OF
6 THE PATENT, THE MORE LIKELY IT IS THE CLAIMS WILL COVER
7 SOMETHING IN THE PRIOR ART.

8 DR. KORNBERG WILL EXPLAIN THAT WHEN THE PATENT EXAMINER
9 WAS LOOKING AT THE CETUS PATENTS, HE DID NOT ANALYZE THE CLAIMS.
10 HE FOCUSED ON THINGS THAT HE THOUGHT WERE MISSING FROM DR.
11 KHORANA'S PUBLICATIONS, THINGS LIKE THE LENGTH OF THE PRIMERS
12 THAT ARE USED, OR THE LENGTH OF THE DNA THAT IS USED FOR
13 AMPLIFICATION.

14 DR. KORNBERG AND DR. WALLACE WILL EXPLAIN THAT BOTH OF
15 THESE THINGS WERE WELL-KNOWN TO SCIENTISTS WORKING IN THE FIELD
16 OF MOLECULAR BIOLOGY IN THE EARLY 1980'S. MOREOVER, AND VERY
17 IMPORTANTLY, THESE FEATURES THAT THE PATENT EXAMINER RELIED ON
18 ARE NOT IN THE CLAIMS OF THE PATENT, SO IT WAS ERROR FOR THE
19 PATENT EXAMINER TO DISTINGUISH THE CLAIMS OF THE PATENT OVER THE
20 PRIOR ART WHEN THE CLAIMS DID NOT HAVE THE VERY THINGS IN THEM
21 THAT THE EXAMINER WAS CRITICIZING THE PRIOR ART FOR NOT HAVING.

22 PERHAPS THE MOST IMPORTANT DEFECT IN THE RE-EXAMINATION
23 IS THAT THE EXAMINER SIMPLY DIDN'T HAVE ALL OF THE INFORMATION
24 BEFORE HIM.

25 CETUS AND ITS PARTNER, HOFFMANN-LA ROCHE, ARGUED TO THE

9 1 PATENT OFFICE DURING THE RE-EXAMINATION PROCEEDINGS THAT THE
2 KHORANA PUBLICATIONS WERE VAGUE AND THAT THEY DID NOT
3 SPECIFICALLY DESCRIBE HOW THE COMPONENTS OF THE AMPLIFICATION
4 REACTION WOULD INTERACT WITH ONE ANOTHER. YOU'LL HEAR A MORE
5 EXPLICIT STATEMENT OF HOW THE EXAMINER ANALYZED THE CLAIMS OF
6 THE PATENT.

7 WHAT CETUS DIDN'T TELL THE PATENT EXAMINER WAS THAT
8 THERE WAS ANOTHER PIECE OF PRIOR ART WHICH CETUS HAD OBTAINED
9 WHILE THE RE-EXAMINATION WAS ONGOING.

10 DURING THE RE-EXAMINATION, CETUS OBTAINED A COPY OF DR.
11 KHORANA'S NSF GRANT APPLICATION. THIS IS THE DOCUMENT I
12 REFERRED TO EARLIER.

13 THE POSTER I'VE PLACED ON THE EASEL HERE IS AN EXCERPT
14 FROM DR. KHORANA'S NSF GRANT APPLICATION.

15 NOW, CETUS ARGUED THAT THE LANGUAGE IN THE OTHER PRIOR
16 ART THAT WAS BEFORE THE EXAMINER WAS VAGUE AND YOU COULDN'T TELL
17 HOW THESE BITS AND PIECES WOULD FIT TOGETHER WITH ONE ANOTHER TO
18 MAKE THE REACTION WORK. BUT DR. KORNBERG AND DR. WALLACE AND
19 OTHERS WILL TELL YOU THAT THAT SIMPLY ISN'T SO.

20 HERE IS A PIECE OF LITERATURE, A PIECE OF PRIOR ART,
21 THAT NOT ONLY TELLS YOU IN STRAIGHTFORWARD LANGUAGE HOW THE
22 REACTION IS CARRIED OUT, BUT IT DRAWS YOU A PICTURE OF HOW THE
23 REACTION WAS CARRIED OUT, AND IT SHOWS YOU HOW THE COMPONENTS OF
24 THE REACTION INTERACT.

25 I DON'T EXPECT YOU TO UNDERSTAND ALL OF THE LANGUAGE OF

10

1 THIS NOW, BUT THE WITNESSES WILL EXPLAIN TO YOU HOW THIS
2 REACTION WORKS, AND THEY WILL SHOW YOU THAT THE STEPS AND THE
3 DIAGRAM ON HERE DESCRIBE PRECISELY THE AMPLIFICATION PROCESS
4 THAT IS DESCRIBED IN CLAIM 1 OF CETUS' '202 PATENT.

5 MR. DE GRANDI WILL EXPLAIN THAT A PATENT APPLICANT HAS
6 AN UNCOMPROMISING DUTY TO INFORM THE PATENT & TRADEMARK OFFICE
7 OF ANY INFORMATION THAT THE PATENT APPLICANT HAS THAT MIGHT BE
8 IMPORTANT TO THE EXAMINER IN EXAMINING A PATENT APPLICATION.

9 THE REASON FOR THIS IS, THE EXAMINER IS SITTING IN AN
10 OFFICE IN WASHINGTON, D.C., AND DOESN'T HAVE THE RESOURCES TO GO
11 OUT AND LOOK FOR EVERYTHING, AND MANY TIMES THE PATENT APPLICANT
12 KNOWS MORE ABOUT THE PRIOR ART AND KNOWS MORE ABOUT THE THINGS
13 THAT MIGHT AFFECT THE PATENTABILITY THAN THE PATENT APPLICANT
14 HIMSELF -- OR THE PATENT EXAMINER HIMSELF, AND THEREFORE THE
15 RULES THAT WE FOLLOW, THE PATENT APPLICANT HAS TO BE CANDID WITH
16 THE PATENT OFFICE. IT HAS TO TELL THE PATENT OFFICE ABOUT
17 IMPORTANT INFORMATION.

18 NOTWITHSTANDING THIS UNCOMPROMISING DUTY, CETUS NEVER
19 TOLD THE PATENT EXAMINER ABOUT THIS DOCUMENT UNTIL AFTER THE
20 RE-EXAMINATION PROCEEDINGS WERE CONCLUDED.

21 AFTER THE EXAMINER ISSUED HIS DECISION AND AFFIRMED THE
22 PATENTABILITY, CETUS THEN SENT THE DOCUMENT ALONG TO THE PATENT
23 EXAMINER SAYING, "OH, HERE'S ANOTHER ONE." THE PATENT OFFICE
24 SAID, "WE'RE SORRY. IT'S TOO LATE. YOU SAID YOU HAD THIS OVER
25 A MONTH AGO. YOU CAN'T GET IT CONSIDERED IN THIS

10 1 RE-EXAMINATION."

2 MR. DE GRANDI WILL ALSO EXPLAIN THAT THERE ARE ISSUES
3 THAT CAN BE -- THAT THE ISSUES WHICH CAN BE CONSIDERED DURING
4 RE-EXAMINATION OF A PATENT ARE VERY LIMITED. IN EFFECT, A
5 RE-EXAMINATION CAN ONLY CONSIDER PATENTABILITY OVER PRIOR
6 PRINTED PUBLICATIONS. THE REASON FOR THIS IS, THE PATENT OFFICE
7 WANTS TO KEEP THE RE-EXAMINATION PROCEDURES STREAMLINED.

8 BUT THERE ARE MANY ISSUES OTHER THAN PRIOR PRINTED
9 PUBLICATIONS THAT AFFECT THE PATENTABILITY OF AN INVENTION. AND
10 THOSE ISSUES ARE GOING TO BE VERY IMPORTANT IN THE CASE THAT YOU
11 ARE GOING TO HEAR.

12 FOR EXAMPLE, PRIOR KNOWLEDGE OF A PROCESS BY OTHERS IS
13 PRIOR ART THAT CAN RENDER A PATENT INVALID. THE PATENT EXAMINER
14 COULD NOT -- BY THE RULES, HE COULD NOT CONSIDER THE QUESTION OF
15 WHETHER THE PRIOR KNOWLEDGE BY THE SCIENTISTS WHO WERE WORKING
16 IN DR. KHORANA'S LABORATORY HAD ANY EFFECT OR IMPACT ON THE
17 PATENTABILITY OF THE CETUS PATENTS, SO THAT WAS NEVER CONSIDERED
18 BY THE PATENT EXAMINER.

19 PRIOR USE, AGAIN, IS A TYPE OF PRIOR ART OR AN ISSUE
20 THAT THE PATENT EXAMINER SIMPLY CANNOT CONSIDER BECAUSE OF THE
21 RULES. THE PRIOR USE BY THE SCIENTISTS IN DR. KHORANA'S
22 LABORATORY OF THIS AMPLIFICATION PROCESS WAS NEVER CONSIDERED BY
23 THE PATENT EXAMINER.

24 SIMILARLY, PRIOR INVENTION BY OTHERS IS PRIOR ART THAT
25 THE -- THAT WILL RENDER OR CAN RENDER THE PATENT INVALID, BUT

10

1 UNDER THE RULES OF THE RE-EXAMINATION PROCEDURE, PRIOR INVENTION
2 CANNOT BE CONSIDERED BY THE EXAMINER, AND SO HE NEVER KNEW THAT
3 DR. KHORANA HAD INVENTED THE SUBJECT MATTER CLAIMED IN CETUS'
4 '202 PATENT WHILE HE WAS CARRYING OUT THE RE-EXAMINATION
5 PROCEDURE.

6 THE EXAMINER NEVER CONSIDERED THE QUESTION OF
7 OBVIOUSNESS. WHAT WE'RE TALKING ABOUT IN THE RE-EXAMINATION IS
8 WHETHER THE CLAIMS WERE IDENTICALLY ANTICIPATED, AND THE
9 EXAMINER SAID, NO, THEY WEREN'T IDENTICALLY ANTICIPATED. BUT
10 THE CLAIMS CAN ALSO BE INVALID IF THE SUBJECT MATTER WAS OBVIOUS
11 OVER WHAT WAS BEING DESCRIBED IN THE PRIOR ART. THE EXAMINER
12 NEVER CONSIDERED OBVIOUSNESS.

13 AND LAST AND CERTAINLY NOT LEAST, THE PATENT EXAMINER
14 NEVER HAD THE OPPORTUNITY TO CONSIDER DR. KHORANA'S NSF GRANT
15 APPLICATION, WHICH YOU WILL FIND IS A MOST IMPORTANT PIECE OF
16 PRIOR ART.

17 YOU'RE GOING TO HEAR TESTIMONY FROM THREE SCIENTISTS
18 WHO WORKED IN DR. KHORANA'S LABORATORY IN THE LATE '60'S AND
19 EARLY '70'S. THE FIRST OF THESE SCIENTISTS IS DR. RUTH KLEPPE.

20 DR. KLEPPE IS A PROFESSOR AT THE UNIVERSITY OF BERGEN
21 IN NORWAY. SHE WORKED OVER ~~WAS~~ IN DR. KHORANA'S LAB AS A
22 POST-DOCTORAL STUDENT IN THE LATE '60'S AND EARLY '70'S. DR.
23 KLEPPE UNTIL RECENTLY WAS A MEMBER OF THE NORWEGIAN PARLIAMENT.

24 THE OTHER SCIENTISTS -- ANOTHER SCIENTIST FROM DR.
25 KHORANA'S LABORATORY THAT YOU WILL HEAR FROM IS DR. IAN

10 1 MOLINEUX. DR. MOLINEUX IS NOW A PROFESSOR OF BIOCHEMISTRY AT
2 THE UNIVERSITY OF TEXAS AT AUSTIN, TEXAS.

3 AND YOU WILL ALSO HEAR FROM DR. HANS VAN DE SANDE,
4 AGAIN A POST-DOCTORAL STUDENT IN DR. KHORANA'S LAB IN THE LATE
5 '60'S, EARLY '70'S, WHO IS NOW THE CHAIRMAN OF THE DEPARTMENT OF
6 BIOCHEMISTRY AT THE UNIVERSITY OF CALGARY IN CANADA.

7 DR. KLEPPE IS GOING TO DESCRIBE HOW DR. KHORANA'S LAB
8 WAS ORGANIZED. SHE'S GOING TO DESCRIBE THE PROCEDURES THAT DR.
9 KHORANA'S LAB USED FOR DISSEMINATING THEIR INFORMATION THROUGH
10 THEIR SEMINARS, THROUGH THEIR PUBLICATIONS. SHE'S GOING TO
11 DESCRIBE HOW THEY RECORDED THEIR INFORMATION IN THEIR NOTEBOOKS
12 AND SO FORTH.

11 13 DR. KLEPPE'S HUSBAND, DR. KJELL KLEPPE, WAS ALSO A
14 SCIENTIST IN DR. KHORANA'S LAB. DR. KJELL KLEPPE PERFORMED SOME
15 OF THE FIRST AND THE SUCCESSFUL EXPERIMENTS WITH DR. KHORANA'S
16 MULTI-CYCLE AMPLIFICATION PROCESS.

17 UNFORTUNATELY, DR. KJELL KLEPPE DIED A FEW YEARS AGO,
18 BUT DR. RUTH KLEPPE WILL EXPLAIN THAT DR. KJELL KLEPPE'S
19 NOTEBOOKS HAVE BEEN RETAINED, AND WE HAVE THEM HERE, AND YOU
20 WILL SEE THE NOTEBOOKS THAT DESCRIBE THE WORK THAT DR. KLEPPE
21 DID WITH THE AMPLIFICATION PROCESS.

22 DR. MOLINEUX WILL DESCRIBE THE WORK THAT HE DID, HIS
23 OWN HANDS, WITH THE AMPLIFICATION PROCESS OF DR. KHORANA'S IN
24 THE EARLY '70'S.

25 AND DR. VAN DE SANDE WILL DESCRIBE THE WORK DONE BY DR.

11

1 KJELL KLEPPE. HE WILL SHOW YOU EXPERIMENTS SET FORTH IN DR.
2 KLEPPE'S NOTEBOOKS, AND HE WILL DEMONSTRATE TO YOU THAT DR.
3 KJELL KLEPPE WAS USING THE SAME EXACT PROCESS AS IS NOW CLAIMED
4 IN THE '202 PATENTS.

5 DR. VAN DE SANDE WILL ALSO COMPARE DR. KLEPPE'S WORK
6 WITH THE WORK THAT DR. MULLIS DID SOME 10 OR 15 YEARS LATER, AND
7 DR. -- DR. VAN DE SANDE WILL SHOW YOU THAT DR. KLEPPE'S WORK IN
8 MANY WAYS WAS MORE CAREFULLY CONTROLLED, WAS MORE CAREFULLY
9 PERFORMED, AND MORE CERTAINLY DEMONSTRATED THE FEASIBILITY OF
10 THIS REACTION THAN DR. MULLIS' EARLIER EXPERIMENTS WITH IT.

11 IT WILL BECOME CRYSTAL CLEAR TO YOU THAT IF DR. KHORANA
12 WERE TO REPEAT TODAY THE EXPERIMENTS THAT HIS POST-DOCTORAL
13 STUDENTS DID IN THE EARLY 1970'S, DR. KHORANA WOULD INFRINGE
14 CETUS' PATENTS. THAT SIMPLY ISN'T RIGHT, AND THAT IS A
15 CONCLUSIVE TEST THAT THE PATENTS COVER WHAT DR. KHORANA DID AND
16 THEREFORE ARE INVALID.

17 THE PATENT EXAMINER, WHEN HE ISSUED THESE PATENTS AND
18 ISSUED THE RE-EXAMINATION, NEVER KNEW ABOUT THE WORK THAT WAS
19 BEING DONE IN DR. KHORANA'S LABORATORY. BUT YOU'RE GOING TO
20 HEAR ABOUT IT, AND YOU CAN MAKE AN INDEPENDENT JUDGMENT ON
21 WHETHER OR NOT DR. KHORANA AND HIS ASSISTANTS AND HIS SCIENTISTS
22 KNEW OF AND PERFORMED AND PUBLISHED THE REACTION THAT'S NOW
23 COVERED BY THE CETUS PATENTS; IN OTHER WORDS, YOU CAN DECIDE:
24 DO THESE PATENTS TAKE SOMETHING AWAY FROM THE PUBLIC THAT THE
25 PUBLIC ALREADY HAD BY VIRTUE OF DR. KHORANA'S WORK?

11 1 THANK YOU FOR YOUR ATTENTION.

2 THE COURT: THANK YOU, MR. FIGG.

3 MR. PASAHOW: YOUR HONOR, WE'LL NEED A FEW MINUTES TO
4 CHANGE THE SCENE HERE.

5 THE COURT: OKAY. I -- THERE'S A GENTLEMAN BY THE
6 DOOR. MAYBE ONE OF THE ATTORNEYS. COULD YOU GO OUTSIDE AND SEE
7 IF THERE'S A GRAND JURY OUTSIDE? YOU CAN TELL. YOU'LL SEE A
8 U.S. ATTORNEY AND A LOT OF PEOPLE.

9 I UNDERSTAND A GRAND JURY'S ABOUT TO RETURN AT 11:30,
10 SO THIS IS A GOOD TIME, AND I MAY HAVE TO TAKE A LITTLE BIT
11 LONGER THAN A 10-MINUTE BREAK.

12 NO SIGN?

13 MR. NEWLAND: NO.

14 THE COURT: WELL, WE'LL TAKE A BREAK AND WE'LL TRY TO
15 TRACK THEM DOWN. IT MAY TAKE US A LITTLE BIT LONGER, BECAUSE I
16 HAVE ANOTHER MATTER I'M GOING TO HAVE TO TAKE CARE OF IN THE
17 INTERIM.

18 SO WE'LL TAKE A BRIEF RECESS AND THE CLERK WILL LET YOU
19 KNOW WHEN WE'RE READY TO PROCEED AGAIN.

20 PLEASE FOLLOW THE INSTRUCTIONS I GAVE YOU EARLIER, AND
21 WE'LL SEE YOU AT THE CLOSE OF THE RECESS.

22 I THINK MR. FIGG DID MENTION -- I NEGLECTED TO TELL
23 YOU -- THAT DURING THE EARLIER RECESS, THEY PUT THE JURY BOOK ON
24 YOUR SEATS, AND THAT HAS THE PATENTS THEMSELVES AND SOME OTHER
25 DOCUMENTS IN THERE.

11 1 IF YOU DON'T WANT TO LUG THOSE BACK AND FORTH DURING
2 THE TIME THAT WE'RE IN SESSION, YOU CAN JUST TAKE THEM BACK AT
3 THE END OF THE DAY. YOU CAN LEAVE THEM ON YOUR OWN CHAIR.
4 THAT'S FINE.

5 AND WE'LL RECESS FOR A FEW MOMENTS. THANK YOU.

6 (JURY EXCUSED)

7 (RECESS TAKEN AT 11:23 A.M.)
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25 (CONTINUED ON NEXT PAGE - NOTHING OMITTED)