THE COURT: YOU MAY PROCEED.

MR. PASAHOW: YOUR HONOR, PERHAPS I SHOULD BEGIN BY INTRODUCING OUR ADDITION TO COUNSEL TABLE AS WELL. THE GENTLEMEN AT THE END OF OUR COUNSEL TABLE IS DR. KARY MULLIS.

THE COURT: THANK YOU.

MR. PASAHOW: LADIES AND GENTLEMEN, IN THE SPRING OF 1983, THE EXACT DATE IS NOT KNOWN, DR. KARY MULLIS BEGAN A TRIP UP HIGHWAY 101 TO A CABIN HE RENTED IN MENDOCINO. THE TRIP PROVED TO BE A VERY IMPORTANT ONE, BOTH FOR DR. MULLIS PERSONALLY AND BIOTECHNOLOGY BECAUSE IT WAS ON THAT TRIP THAT DR. MULLIS INVENTED THE TECHNIQUE THAT'S KNOWN KNOWN AS POLYMERASE CHAIN REACTION.

AFTER DR. MULLIS RETURNED TO CETUS AND REDUCED THE INVENTION THAT HE THOUGHT OF DURING THAT TRIP TO A METHOD HE COULD SHOW OTHER HE WORKED WITH, HIS COLLEAGUES, TO INVENT VARIOUS APPLICATIONS OF THAT TECHNIQUE. SOME OF THOSE VERY IMPORTANT APPLICATIONS WERE USING IT TO DETECT DISEASES, DISEASES THAT INFLICT HUMANS.

IN PARTICULAR DISEASES THAT ARE KNOWN AS GENTIC DISEASE. GENTIC DISEASES ARE CAUSED BY ERRORS IN OUR DNA, IN OUR GENES ONE OF THOSE FOUR BASIS MR. FIGG POINTED OUT SOMETIMES ARE WRONG. IF ONE OF THE FOUR BASIS IS WRONG WE CAN SUFFER VARIOUS DISEASES.

THE CETUS SCIENTISTS WE'RE LOOKING FOR A PRACTICAL, SIMPLE WAY TO MAKE IT POSSIBLE FOR DOCTORS AND HOSPITALS TO

DETECT THOSE GENTIC DISEASES. THAT IS WHAT IS THE SUBJECT MATTER OF ONE OF THE TWO PATENTS.

CETUS' EVIDENCE WILL SHOW YOU THAT THE UNITED STATES PATENT AND TRADEMARK OFFICE PROPERLY UNDER THE LAW ISSUED PATENTS TO CETUS FOR THE WORK ITS SCIENTISTS DID IN INVENTING PCR AND IN INVENTING THESE VERY IMPORTANT APPLICATIONS OF THE REVOLUTIONARY PCR TECHNIQUE.

INDEED YOU'LL SEE THAT'S EXACTLY THE CONCLUSION THE PATENT OFFICE ITSELF CAME TO LAST YEAR WHEN DU PONT TOOK ALL THE ARGUMENTS IT WANTED TO TAKE TO THE PATENT OFFICE AND ASKED THE EXPERTS THERE TO RE-EXAMINE THE PATENTS AND SEE IF THEY MADE A MISTAKE IN THE FIRST PLACE WHEN THEY ALLOWED THE PATENTS IN 1967.

YOU'LL SEE THAT FOLLOWING CONSIDERATION OF THE ARGUMENTS DU PONT CHOSE TO MAKE -- REVIEWING THE PRINTED PUBLICATIONS THAT DU PONT CHOSE TO PUT BEFORE THE PATENT OFFICE, THE EXPERTS IN THE PATENT OFFICE CONCLUDED THE PATENTS WERE PROPERLY ISSUED IN 1987. SO THEY REAFFIRMED EACH AND EVERY ONE OF THE CLAIMS IN BOTH OF THE TWO PATENTS.

NOW, BEFORE DR. MULLIS CAME TO WORK AT CETUS' EMERYVILLE LABORATORY, HE HAD GONE THROUGH THE USUAL COURSE OF STUDY OF A BIOCHEMIST. FIRST, HE HAD SPENT THE TIME GETTING A PHD DEGREE AT THE UNIVERSITY OF CALIFORNIA AT BERKLEY, STUDYING SEVERAL YEARS THERE, AND THEN LIKE MANY BIOCHEMISTS HE FOLLOWED THAT UP WITH A POST-DOCTORAL RESEARCH PROGRAM. IN HIS CASE HE

SPENT SEVERAL YEARS WORKING WITH A MORE SENIOR SCIENTISTS AT THE UNIVERSITY OF CALIFORNIA HERE IN SAN FRANCISCO.

AFTER THAT DR. MULLIS WAS HIRED BY CETUS. IN 1983 THE FOCUS OF DR. MULLIS' WORK WAS MAKING THE SHORT PIECES OF DNA THAT WERE USED AS PRIMERS AND PROBES BY OTHER SCIENTISTS IN THE CETUS LABORATORY.

BUT YOU'LL HEAR THAT DR. MULLIS HAD CREATED A LABORATORY THAT WAS SO EFFICIENT AT THAT PROCESS, THAT HE HAD EXTRA TIME ON HIS HANDS AND HE CHOSE TO USE THAT EXTRA TIME, WITH THE CONCURRENCE OF HIS SUPERVISORS, TO HELP OTHER SCIENTISTS WITH ROAD BLOCKS THEY WERE HAVING IN WORK THEY WERE DOING.

IN EARLY 1983 THE PROJECT THAT CAUGHT DOCTOR MULLIS' ATTENTION, IN ADDITION TO THE MAKING OF THESE DNA PIECES, WAS WORK THAT WAS GOING ON IN THE LABORATORY OF DOCTOR HENRY ERLICH THE SAME HAVE RESPECTED SCIENTIST THAT MR. FIGG SPOKE OF.

YOU'LL HEAR DOCTOR ERLICH'S LABORATORY WAS FOCUSING ON COMING UP WITH A PRACTICAL SIMPLE METHOD OF DETECTING GENETIC DISEASES, ONE THAT COULD BE USED BY DOCTORS AND HOSPITALS AND DIDN'T REQUIRE A HEAVILY TRAINED BIOCHEMIST OR MOLECULARBIOLOGIST.

YOU'LL HEAR IN 1983 FROM TIME TO TIME DOCTOR MULLIS DISCUSSED THE WORK GOING ON IN THAT LABORATORY WITH THE SCIENTISTS THERE. YOU'LL HEAR THAT HE SUGGESTED IDEAS TO THEM AND HE DISCUSSED THEIR WORK WITH THEM.

YOU'LL HEAR THAT HE, AS HE TOOK THAT DRIVE UP 101 TO THE CABIN IN MENDOCINO THAT DAY, HIS THOUGHTS WERE ON THIS PROBLEM THAT WERE PLAGUING THE CETUS SCIENTISTS AT WORK. THE PROBLEM HOW DO YOU MAKE THE TEST MORE SENSITIVE. HOW DO YOU MAKE IT SO IT CAN BE SIMPLY USED, USED BY PEOPLE WHO ARE NOT TRAINED LABORATORY BIOCHEMIST AND MOLECULARBIOLOGIST.

THE SOLUTION DR. MULLIS THOUGHT OF IS WHAT'S NOW KNOWN AS POLYMERASE CHAIN REACTION. YOU'LL HEAR DR. MULLIS WAS VERY EXCITED ABOUT HIS THOUGHTS EVEN THAT WEEKEND. HE CAME BACK TO THE EMERYVILLE LABORATORY THE NEXT MONDAY AND THE FIRST THING HE DID WAS ASK THAT A LITERATURE SEARCH BE DONE WITH A COMPUTER BY THE LIBRARIAN AT CETUS. HE WANTED TO FIND OUT IF ANYONE ELSE HAD EVER TRIED THIS IDEA BEFORE.

THE RESULT CAME BACK TO HIM. HE LOOKED THROUGH THE RESULTS OF THE SEARCH. HE CONCLUDED, NO, NO ONE ELSE HAD TRIED IT BEFORE. SO THEN DR. MULLIS BEGAN RESEARCHING HOW ONE MIGHT ACTUALLY GO ABOUT DOING THIS.

NOW, A LOT OF RESEARCH HAD TO BE DONE BEFORE HE COULD EVEN TRY THE FIRST EXPERIMENT. HE HAD TO FIGURE OUT WHAT CHEMICALS TO PUT IN; HOW MANY POLYMERASE; WHAT POLYMERASE. HE HAD TO FIGURE OUT HOW MUCH OF THE TARGET, THAT IS, THE TEMPLATE DNA HE WAS DRYING TO COPY.

HE HAD TO FIGURE OUT HOW MANY PRIMERS AND WHAT THE RELATIVE CONCENTRATIONS OF ALL OF THESE THINGS SHOULD BE. HE HAD TO FIGURE OUT THE TIMES AND TEMPERATURES FOR RUNNING THE

REACTION.

DR. MULLIS RESEARCHED ARTICLES BY OTHERS WHO HAD DONE THINGS WHICH HE THOUGHT MIGHT GIVE CLUES FOR HIS REACTION AND HE DID CALCULATIONS AND HE DID SOME EXPERIMENTS, AND FINALLY IN SEPTEMBER 1983 HE WAS READY TO TRY HIS FIRST EXPERIMENT. AND YOU'LL HEAR FROM DR. MULLIS THAT THAT FIRST EXPERIMENT WAS JUST PLAINLY A FAILURE. THERE WAS NO INDICATION AT ALL THAT THE PROCESS WORKED.

SO DR. MULLIS WENT BACK TO THE DRAWING BOARD, IF YOU WILL, AND HE CHANGED HIS HE IDEA ABOUT HOW THE REACTION MIGHT WORK CONSIDERABLY AND ABOUT A MONTH LATER IN OCTOBER 1983 HE TRIED AGAIN, AND AGAIN HE FAILED. THERE WAS NO INDICATION IN THAT REACTION EITHER HE WAS GETTING ANY AMPLIFICATION WHATSOEVER.

NOW, BETWEEN THIS TIME AND THE NEXT EXPERIMENT DR. MULLIS DID TWO THINGS: FIRST, HE THOUGHT MORE HOW HE MIGHT DO PCR, BUT HE ALSO THOUGHT ABOUT THE PROBLEM OF DETECTING WHAT WAS LIKELY TO BE IN THE FIRST INSTANCE A VERY WEAK REACTION. AND THE SCHEME HE HIT UPON WAS ONE THAT WAS CAUSED PROOF THE REACTION WAS WORKING, A LINE OR A BAND TO FORM ON AN X RAY FILM IN A PARTICULAR SPOT.

SO IN DECEMBER 1983 HE SET UP TO DO THE EXPERIMENT AGAIN. WE'RE NOW ABOUT A WEEK BEFORE CHRISTMAS IN 1983. HE DID THE EXPERIMENT THE THIRD TIME. THIS IS THE TIME THAT THE DU PONT WITNESSES SOMETIMES CALL THE FIRST SUCCESSFUL USE OF PCR BY

MR. MULLIS. HE HIMSELF WAS ACTUALLY RATHER MORE MODEST ABOUT IT AND YOU'LL BOTH HEAR HIS TESTIMONY AND HAVE A CHANCE TO SEE WHAT HE WROTE IN HIS LABORATORY NOTEBOOK.

YOU'LL RECALL THE TEST OF WHETHER OR NOT IT WORKED WAS GOING TO BE THE BAND ON THIS FILM AND WHAT DR. MULLIS GOT IS A VERY FAINT BAND PERHAPS, AND SO HE PUT THE PIECE OF FILM OR PRINT OF IT IN HIS LABORATORY NOTEBOOK AND HE PUT THIS NOTE NEXT TO IT.

AND THE NOTE YOU SEE SAYS: THERE WAS AN ARROW THERE, HE WROTE ARROW MARKS THE SPOT WHERE TRUE BELIEVERS SEE A BAND. THAT IS VERY FAINT AND MAYBE WITH A LITTLE BIT OF SQUINTING AND IMAGINATION YOU SEE THE BAND.

WELL, DR. MULLIS KNEW THAT WASN'T GOING SO WORK TO SHOW OTHER SCIENTISTS THAT PCR WORKED, SO HE KEPT WORKING AT THE PROCESS. HE WORKED TO MAKE IT MORE ROBUST TO GET STRONGER INDICATIONS AND HE WORKED ON OTHER METHODS OF DETECTING WHETHER THE PROCESS WORKED. THESE EFFORTS OCCUPIED HIM THROUGH THE SUMMER OF 1985. I'M SORRY, THROUGH THE SUMMER OF 1984.

DURING THAT TIME DR. MULLIS KEPT TELLING OTHERS IN THE COMPANY ABOUT THE PROCESS HE WAS WORKING ON. HE SHOWED THEM THE EVIDENCE HE WAS GETTING AND HE KEPT HEARING, WELL, MAYBE, OR IT WILL NEVER WORK, OR THINGS OTHER THAN, YES, I SEE, I AGREE.

NOW, IN THE SUMMER OF 1984 YOU'LL HEAR THERE WAS A MEETING OF ALL THE SCIENTISTS AT CETUS WHERE THEY GOT TOGETHER AND SHOWED EACH OTHER THEIR WORK AND DR. MULLIS SHARED THE

RESULTS HE HAD AT THAT TIME. AND YOU'LL HEAR THAT AFTER THAT MEETING THE CETUS MANAGEMENT MADE THE DECISION ABOUT PCR WHICH PROVED TO BE VERY IMPORTANT.

THEY DECIDED THEY HAD TO KNOW WHETHER OR NOT IT WORKED, AND THAT OTHER SCIENTISTS WERE GOING TO HAVE TO BE PUSHED TO EVALUATE IT. SO WHAT THEY DECIDED WAS THAT DR. MULLIS SHOULD START DIRECTLY WORKING WITH DOCTOR HENRY ERLICH'S LAB ON THIS EFFORT TO COME UP WITH A SIMPLE, PRACTICAL METHOD OF DETECTING GENTIC DISEASES. SO THE TWO LABORATORY DID START WORKING TOGETHER.

IN NOVEMBER THEY CAME UP WITH A JOINT EXPERIMENT WHICH WAS PROBABLY THE FIRST EXPERIMENT THAT CAUSED THE SIGNIFICANT NUMBER OF OTHER SCIENTISTS, NON-TRUE-BELIEVERS IF YOU WILL, TO START BELIEVING THAT PCR COULD BE MADE TO WORK.

WHAT HAPPENED IN THAT EXPERIMENT WAS DR. MULLIS' LABORATORY TOOK SOME DNA FROM A PERSON WHO WAS INFLICTED WITH SICKLE CELL ANEMIA. IT WAS AN EXPERIMENTAL BATCH OF DNA AND DR. MULLIS' LABORATORY DID PCR ON THAT TO TRY AND AMPLIFY THE PART OF THE DNA FROM THIS PERSON WHICH WOULD HAVE THE SICKLE CELL GENE. THEY THEN GAVE THAT AMPLIFIED PRODUCT TO THE SCIENTISTS AND DOCTOR ERLICH'S LABORATORY.

THE SCIENTISTS IN DOCTOR ERLICH'S LABORATORY SUBJECTED THAT AMPLIFIED DNA TO THE TEST THEY HAD DEVELOPED FOR TRYING TO FIND OUT WHETHER OR NOT SOME DNA HAD THE SICKLE CELL GENE IN IT. THEY FOUND THAT THERE WAS A VERY STRONG DRAMATIC SIGNAL. FAR

STRONGER THAN ANYTHING THEY HAD EVER SEEN BEFORE.

THE SCIENTISTS WHO DID THE WORK WENT AROUND AND SHOWED OTHERS THIS AND SUDDENLY THEY BEGAN TO BELIEVE THAT THE SECRET COMING UP WITH THE TEST FOR SICKLE CELL AND OTHER BETWEEN ETHIC DISEASES THAT THEY WERE SEARCHING FOR WOULD INVOLVING MARRYING THE PCR PROCESS TO THEIR OWN DETECTION SYSTEM WHICH WAS CALLED OLIGOMER RESTRICTION.

THE TWO LABORATORIES CONTINUED TO WORK ON THIS THROUGH THE END OF THAT YEAR AND INTO 1985 AND BY THE SPRING THEY CAME UP WITH A METHOD THEY FELT WAS REPRODUCIBLE, RELIABLE, ONE THEY WERE PREPARED TO TELL THE OTHER SCIENTIFIC COMMUNITY ABOUT. THAT'S JUST WHAT THEY DID.

THEY WROTE AN ARTICLE AND THEY PUT THEIR EXPERIMENTAL RESULTS IN IT, THE DETAILS OF HOW THEY DID THE PCR AND THE OR, AND THEY SUBMITTED THAT MANUSCRIPT TO A PRESTIGIOUS SCIENTIFIC MAGAZINE MAYBE THE MOST PRESTIGIOUS IN THIS COUNTRY, SCIENCE. IT WAS ACCEPTED BY SCIENCE AS THE PRINCIPAL ARTICLE FOR DECEMBER 1985 ISSUE AND THAT'S WHERE IT PUBLISHED.

IN THAT ARTICLE THE PRINCIPAL FOCUS WAS ON USING A METHOD OF DETECTING SICKLE CELL ANEMIA AND SHOWING THEY NOW HAD A METHOD THAT WOULD DO THAT. A GOAL THAT SEVERAL SCIENTISTS WERE WORKING FOR AT THE TIME.

IN FACT, YOU'LL HEAR DURING THIS TRIAL FROM ANOTHER OF THOSE SCIENTISTS, ONE OF DU PONT'S WITNESSES DOCTOR BRUCE WALLACE, HAD ALSO SPENT MANY YEARS TRYING TO COME UP WITH A

PRACTICAL METHOD OF DETECTING SICKLE CELL ANEMIA. AND YOU'LL HEAR DR. WALLACE IN HIS WRITINGS AFTER HE LEARNED OF THE CETUS METHOD WAS VERY CONGRATULATORY OF THEM FOR HAVING INVENTED PCR AS A METHOD WHICH WOULD ACCOMPLISH THIS.

BUT TO GET BACK TO SCIENCE MAGAZINE. IN THIS SCIENCE MAGAZINE IN 1985 THE CETUS SCIENTISTS LAID OUT THE DETAILS OF HOW TO DO PCR. THERE WAS A VERY DETAILED DISCLOSURE, A RECIPE, IF YOU WILL, THAT SCIENTISTS IN ANY LABORATORY COULD FOLLOW AND DO PCR.

THIS RECIPE WAS PUT INTO ONE OF THE CAPTIONS TO ONE OF THE EXPERIMENTAL RESULTS WHICH IS WHAT THEY DID AND IT TOLD OTHER SCIENTISTS EXACTLY HOW MUCH PRECISELY EACH INGREDIENT TO PUT IN. IT TOLD THEM EXACTLY HOW LONG AND AT WHAT TEMPERATURE TO DO THE VARIOUS STEPS AND IT WAS MUCH LIKE A VERY COMPLICATED CAKE BAKING RECIPE, IF YOU WILL. AS LONG AS YOU FOLLOWED EVERY STEP, YOU DID EXACTLY WHAT WAS THERE, YOU WOULD SUCCESSFULLY ACCOMPLISH PCR.

NOW, YOU WILL HEAR FROM DU PONT ABOUT A MEMORANDUM THAT DOCTOR ERLICH WROTE TO HIS COLLEAGUES AT CETUS. IN FACT, THAT'S ONE YOU'VE ALREADY SEEN HERE THIS MORNING. AND DU PONT WILL SUGGEST THERE WAS SOME DISPUTE ABOUT PUBLISHING THIS ARTICLE, THAT'S WHAT THE MEMORANDUM IS ABOUT. YOU'LL SEE THE MEMORANDUM YOURSELF AND YOU'LL SEE THE MEMORANDUM HAD NOTHING TO DO WITH THAT AT ALL. YOU'LL SEE THAT MEMORANDUM FROM DOCTOR ERLICH ESSENTIALLY SAYS THIS:

THIS ARTICLE, THE ONE WITH THIS DETAILED RECIPE HAD ALREADY BEEN SENT TO SCIENCE MAGAZINE. IT WAS ALREADY SENT AND GOING TO BE PUBLISHED. THEY'VE ALREADY BEEN TOLD BY SCIENCE THIS DETAILED RECIPE WAS GOING TO BE PUBLISHED.

NOW, THERE WAS A SECOND MANUSCRIPT, ONE THAT DR. MULLIS AND HIS LABORATORY ASSISTANT, MR. FRED FALOONA, HAD PREPARED. THE CONTROVERSY WAS NOT ABOUT PUBLISHING THIS DETAILED RECIPE, BUT WHETHER OR NOT MR. FALOONA AND MR. MULLIS COULD PUBLISH THEIR ARTICLE.

AND YOU'LL HEAR WHAT MR. ERLICH WAS TELLING HIS COLLEAGUES, HE'LL EXPLAIN THIS HIMSELF. HE WAS TELLING HIS COLLEAGUES WHAT'S IN THIS CAPTION WE'VE ALREADY TOLD SOMEONE HOW TO DO IT. WE LAID IT OUT IN EXCRUCIATING DETAIL. THERE'S NO REASON NOT TO PUBLISH THE MULLIS' PIECE. SURE IT TELLS PEOPLE OTHER THINGS THEY CAN DO WITH IT, BUT ANY GOOD MOLECULAR BIOLOGIST WOULD BE ABLE TO FIGURE THOSE OTHER THINGS OUT NOW THAT WE'VE TOLD PEOPLE HOW TO DO IT.

YOU WON'T SEE ANY ADMISSION BY DOCTOR ERLICH THAT SOME VAGUE NOTION OF HOW TO DO THIS WOULD HAVE ENABLED HIM. HE WILL TESTIFY IT'S HIS VIEW YOU HAVE TO GIVE THE DETAILS AND THE MANNER THAT YOU SAW IN THAT CAPTION TO ENABLE OTHER PEOPLE TO DO IT.

NOW, AMONG THE PEOPLE WHO SAW THIS DECEMBER 1985 PUBLICATION IN SCIENCE MAGAZINE WAS ONE OF THE DEANS OF THE BIOTECHNOLOGY MOVEMENT, DOCTOR JAMES WATSON WHO RUNS A VERY

FAMOUS LABORATORY IN COLD SPRING HARBOR, NEW YORK.

DOCTOR JAMES WATSON TOOK NOTE OF THE ARTICLE AND RECOGNIZED IN IT THE POWER OF PCR, EVEN THOUGH THE ARTICLE ITSELF DIDN'T SPELL IT OUT. DOCTOR WATSON BECAUSE OF THE ARTICLE INVITED DOCTOR KARY MULLIS TO COME AND SPEAK AT A PRESTIGIOUS GATHERING OF THE ELITE OF THE PROFESSION, IF YOU WILL, THAT TAKES PLACE ANNUALLY. THIS ONE WAS IN JUNE 1986.

SO IN JUNE 1986 DR. MULLIS TRAVELED TO COLD SPRING HARBOR, NEW YORK AND ALONG WITH HIS PIECE HE PRESENTED HIS PAPER, A PAPER ON PCR AND A PAPER THAT WENT FAR BEYOND THE SICKLE CELL NOTION.

IN THAT PAPER YOU'LL SEE DR. MULLIS SPELLED OUT A LOT OF THE OTHER THINGS HE HAD DONE AND A LOT OF THE IDEAS HE HAD BEYOND USING THE CYCLE CELL TEST. THAT IS, THAT PCR WAS A POWERFUL TOOL WITH A LOT OF USES.

YOU'LL HEAR THAT THE AUDIENCE AT THAT MEETING WAS VERY IMPRESSED BY DR. MULLIS' DISCLOSURE. AFTER HE SPOKE HE FOUND HIMSELF SURROUNDED BY A GROUP OF SCIENTISTS WHO WANTED MORE DETAILS THEN AND THERE SO THEY COULD START USING PCR TO HELP THEM IN THEIR WORK.

NOW, THIS JUNE 1986 MEETING WAS THE FIRST OF MANY TIMES THAT DR. MULLIS AND, IN FACT, MANY OF THE CETUS SCIENTISTS FOUND THEMSELVES SPEAKING ABOUT PCR AND BEING CONGRADULATED BY THEIR PEERS. SINCE THAT TIME SEVERAL OF THEM HAVE BEEN HONORED BY THEIR PEERS IN VARIOUS ORGANIZATIONS AND YOU'LL HEAR ABOUT THAT,

BUT THE SERIES OF HONORS WAS PROBABLY BEST CAPPED OFF BY SCIENCE MAGAZINE IN LATE 1989. SCIENCE MAGAZINE DECIDED IT WOULD START NAMING A DEVELOPMENT OF THE YEAR. THE DEVELOPMENT THAT PEOPLE AT SCIENCE MAGAZINE THOUGHT WAS MOST LIKELY TO HAVE AN IMPACT ON HISTORY.

FOR THE FIRST OF THESE AWARDS THE EDITORS OF SCIENCE CHOSE THE POLYMERASE CHAIN REACTION. SO THE DECEMBER 1989 ISSUE OF SCIENCE HAD THIS COVER AND THEN INSIDE THEY PUBLISHED AN ARTICLE ABOUT THE MOLECULE OF THE YEAR EXPLAINING THAT THIS YEAR'S AWARD GOES TO THE DNA POLYMERASE MOLECULE AND TECHNIQUE CALLED POLYMERASE CHAIN REACTION.

PCR AS IT'S CALLED THEY SAID HAS DEVELOPED INTO ONE OF THE MOST POWERFULL TOOLS OF MODERN BIOLOGY. THEY SAID ITS REVOLUTIONIZING THE APPROACHES RESEARCHERS ARE TAKING TO MANY PROBLEMS IN BIOLOGY. THEN THEY WENT ON IN A SEPARATE ARTICLE ABOUT PCR TO POINT OUT OTHER OF ITS ATTRIBUTES.

LET ME SWITCH SIDES HERE. THEY POINTED OUT THE PCR PAPERS WERE FIRST PUBLISHED IN 1985, IN FACT, IN AN EARLIER ISSUE OF SCIENCE AND THAT SINCE THAT TIME PCR HAD GROWN INTO AN INCREASINGLY POWERFUL AND VERSATILE AND USEFUL TECHNIQUE.

THEY EXPLAINED WHAT PCR DID WAS TAKE TINY BITS OF EMBEDDED, OFTEN HIDDEN GENETIC INFORMATION AND AMPLIFIED IT INTO LARGE QUANTITIES OF ACCESSIBLE, IDENTIFIABLE AND ANALYZABLE MATERIAL. SO WITH THIS AWARD PCR ESSENTIALLY WAS HONORED BY THE PROFESSION AS THE MOST IMPORTANT OF THE DEVELOPMENTS THAT WAS

AROUND AT THE TIME.

NOW, WITH THIS KIND OF A CLAIM THERE REALLY SHOULDN'T BE ANY QUESTION ABOUT THE IMPORTANCE OF PCR AND THAT IT WAS A REVOLUTIONARY TECHNIQUE, WHICH WOULD HAVE BEEN IMPORTANT AT ANY TIME. IT WOULD HAVE BEEN IMPORTANT IN 1972, IN 1980, IN 1990. IN FACT, THE DU PONT SCIENTISTS HAD BEEN AS QUICK AS ANYONE TO TALK ABOUT THE REVOLUTIONARY NATURE OF PCR.

IN 1989 ONE OF THE DU PONT MANAGER SCIENTISTS WROTE THIS MEMORANDUM TO HIS BOSS. AS YOU CAN SEE HE, TOO, THOUGHT THAT PCR HAD ALREADY REVOLUTIONIZED THE THINKING OF BIOTECHNOLOGY RESEARCH COMMUNITY AND HE ADDED THAT PROMISES TO HAVE A MAJOR IMPACT IN DIAGNOSTICS. THAT IS, THE USE OF A PCR FOR DIAGNOSING GENTIC AND OTHER DISEASES.

OTHER SCIENTISTS AT DU PONT ADD TO THAT. A GROUP HAD BEEN FORMED AT DU PONT TO TRY TO DECIDE WHETHER OR NOT DU PONT WANTED TO LICENSE PCR. WHETHER IT WAS WORTH THE EFFORT IN THE LIKELY COST. THAT GROUP HAD A MEETING WHERE THEY PREPARED A SERIES OF SLIDES.

DURING THE TRIAL WE'LL SHOW YOU SEVERAL OF THEM. THIS WAS ESSENTIALLY THEIR SUMMARY. IT BEGAN THE OPPORTUNITY POINTED OUT CETUS CORPORATION HAD DEVELOPED A PROPRIETARY METHOD FOR AMPLIFICATION OF A NUCLEIC ACID TARGET. IT THEN GOES ON AND TALKS ABOUT WHAT IT IS PCR CAN DO IN MUCH THE SAME LANGUAGE OF THE OTHER LAUDATORY REMARKS THAT HAD BEEN WRITTEN.

IT ALSO CONCLUDED CRITICAL PATENT REVIEW CONFIRM

UNIQUENESS OF THE TECHNOLOGY, THAT IS OF THE PCR TECHNOLOGY. THIS WAS WHAT THE DU PONT SCIENTISTS WERE WRITING BEFORE DU PONT DECIDED TO BRING THIS SUIT.

NOW, THIS REAL WORLD EVIDENT THE STATEMENT OF SCIENTISTS OUTSIDE THIS COURTROOM, STATEMENTS THEY MADE TO THEIR COLLEAGUES AS THEY WERE TRYING TO DO REAL SCIENTIFIC WORK AN IMPORTANT PART OF THE EVIDENCE THAT WE WILL PRESENT TO YOU. YOU WILL SEE THAT THIS REAL WORLD EVIDENCE THROUGH THE TIME THAT DU PONT DECIDED TO BRING THIS SUIT WAS UNIVERSAL IN APPLAUDING PCR AND APPLAUDING THE CETUS SCIENTISTS WHO BROUGHT IT TO THE SCIENTIFIC COMMUNITY.

NOW, AFTER DU PONT DECIDED TO BRING THIS SUIT SOME SCIENTISTS HAVE SAID OTHER THINGS. LET ME GIVE YOU AN EXAMPLE. ONE SCIENTISTS YOU'LL HEAR FROM A DU PONT WITNESS DOCTOR IAN MOLINEUX. DOCTOR MOLINEUX WORKED IN THE LABORATORY OF DOCTOR KHORANA AND NOW A PROFESSOR DOWN IN TEXAS.

YOU'LL HEAR FROM DOCTOR MOLINEUX KNEW HE WAS WELL AWARE PCR FROM THE VARIOUS CETUS REPORTS AND ALL THE OTHER ATTENTION THE REACTION WAS GETTING. HE CERTAINLY KNEW IT WAS THERE AND HE KNEW IT WAS QUITE IMPORTANT. IN FACT, YOU'LL HEAR HE WAS TEACHING IT TO HIS STUDENTS THERE AT THE UNIVERSITY.

AND YOU WILL HEAR THAT, ALTHOUGH DOCTOR MOLINEUX WAS FULLY AWARE OF PCR, HE DIDN'T THINK IT RELATED TO ANYTHING THAT HE HAD DONE IN DOCTOR KHORANA'S LABORATORY. OR AT LEAST HE DIDN'T THINK THAT UNTIL HE WAS VISITED BY ONE OF THE DU PONT

SCIENTISTS AND -- I'M SORRY, ONE OF THE DU PONT LAWYERS, AND THE TWO OF THEM HAD A CONVERSATION AND THEN MR. MOLINEUX TELLS US HE REALIZED THAT, YES, IN MR. KHORANA'S LABORATORY HE HAD DONE PCR.

THE SAME IS TRUE OF OTHER SCIENTISTS, BOTH THOSE IN AND OUT OF DOCTOR KHORANA'S LABORATORY. SINCE DU PONT'S FILED ITS SUIT IT HAS BEEN SUCCESSFUL IN GETTING A SMATTERING OF SCIENTISTS TO SIGN ON TO THE NOTION THAT PCR IS THE SAME AS WHAT WAS GOING ON IN DOCTOR KHORANA'S LABORATORY.

LET ME GIVE YOU ONE MORE EXAMPLE OF THAT. ONE OF THE SCIENTISTS WHOSE DECLARATIONS THAT DU PONT PRESENTED TO THE PATENT OFFICE WAS A SCIENTIST NAMED SAMBROOK, AND DOCTOR SAMBROOK WAS ONE OF A GROUP OF THREE SCIENTISTS WHO FROM TIME TO TIME WROTE A LARGE MANUAL OF ALL THE USEFUL TECHNIQUES THAT BIOTECHNOLOGY MIGHT -- PEOPLE WORKING IN BIOTECHNOLOGY MIGHT NEED. AND THESE CHARGED CONPENDIUMS OF TECHNIQUES WERE PUBLISHED IN 1982, THEN MUCH EXPANDED VERSION IN 1989.

NOW, IN 1982 PCR WASN'T IN THE MANUAL. IN 1989 THERE'S A WHOLE CHAPTER IN THE MANUAL ABOUT IT. DOCTOR SAMBROOK AND HIS CO-AUTHORS WROTE A PREFACE IN WHICH THEY POINTED OUT THAT NEW SECTIONS HAD BEEN ADDED TO THE 1989 MANUAL TO DEAL WITH RECENTLY INVENTED TECHNIQUES, SUCH AS AMPLIFICATION OF DNA BY THE POLYMERSE CHAIN REACTION.

NOW, SOMETIME AFTER DOCTOR SAMBROOK WROTE THAT YOU'LL SEE HE BEGAN TO SERVE AS AN EXPERT FOR DU PONT AND HE THEN TOLD THE PATENT OFFICE THE NEXT YEAR IN 1990 THAT, IN FACT, PCR

WASN'T RECENTLY INVENTED AS HE SAID THERE IN THE PREFACE. HE'LL SAY PCR WAS OLD, IT WAS IN THE ARTICLES FROM THE 1970'S FROM THE KHORANA LABORATORY. SO THAT'S THE KIND OF CHANGED VIEW OF SCIENTISTS THAT HAPPENED AFTER DU PONT DECIDED TO FILE THIS SUIT AND YOU'LL SEE SEVERAL EXAMPLES OF THAT.

NOW, DURING THE TIME OTHER REAL WORLD EVIDENCE YOU'LL HEAR WILL BE REAL WORLD EVIDENCE ABOUT THE RELATIONSHIP OF EVENTS AND THE TIME PERIODS THAT HAPPEN BETWEEN THEM. LET ME BE SPECIFIC. DOCTOR KHORANA DID HIS WORK BACK IN THE EARLY 1970'S, AND WE'VE GOT VARIOUS INDICATIONS HERE. THIS IS THE DATE WHEN DOCTOR KJELL KLEPPE HAD SOME NOTEBOOK ENTRIES THAT DU PONT IS GOING TO PRESENT AS BEING EVIDENCE OF PCR.

THIS IS THE DATE OF PUBLICATION OF THE FIRST OF THE ARTICLES, THE ARTICLE THAT'S CALLED KLEPPE ET AL., IT'S IN 1971. THESE VARIOUS KHORANA ENTRIES CONTINUE THROUGH 1973 OR 1975, THEN THEY END.

NOW, EVEN IF ONE ASSUMES THAT IN 1975 SOMETHING WAS MISSING TO MAKE PCR CONVENIENT OR EASY, TIME PASSES AND WE GET TO THE END OF THE 1970'S AND IN THE END OF THE 1970'S, CERTAINLY BY THE BEGINNING OF THE 1980'S EVERYTHING NECESSARY TO DO PCR WAS AVAILABLE TO ANYONE WHO WANTED IT, AND YET STILL NOBODY IS DOING PCR.

WE COME TO 1983 AND THAT IS, AS I TOLD YOU EARLIER, WAS WHEN MR. MULLIS HAD HIS INSPIRATION AND DID THE FIRST PCR EXPERIMENTS. STILL NOBODY IS DOING PCR EXCEPT THE SCIENTISTS AT

CETUS. BETWEEN 1983 AND 1985 THE SCIENTISTS AT CETUS MADE PCR INTO A SIMPLE EASY TECHNIQUE. THEY DEVELOPED A RECIPE FOR DOING IT. STILL NOBODY ELSE WAS DOING PCR EXCEPT THE SCIENTISTS AT CETUS.

IN DECEMBER 1985 THE ARTICLE WAS PUBLISHED IN SCIENCE. SUDDENLY YOU'LL SEE THERE'S AN EXPLOSION OF USE OF PCR. THERE'S THE KIND OF LAUDATORY COMMENTS WE'VE SEEN. PCR STARTING WITH THIS PUBLICATION IN 1975, QUICKLY IS THE ARTICLES PUT IT REVOLUTIONIZES BIOLOGY. IT REVOLUTIONIZES THE APPROACH THAT PEOPLE WORKING IN THIS FIELD CAN TAKE BECAUSE IT'S SUCH A SIMPLE POWERFUL TECHNIQUE. YET, THROUGHOUT ALL THIS TIME WHEN YOU'RE GOING TO HEAR FROM WITNESSES PCR WAS KNOWN, NOBODY IS DOING IT.

NOW, IT CERTAINLY ISN'T TRUE THAT THERE WAS NOBODY DURING THAT TIME WHO COULD HAVE BENEFITED FROM PCR. YOU'LL HEAR FROM SOME SCIENTISTS WHO WILL TELL YOU HOW DESPERATELY THEY COULD HAVE USED THE TECHNIQUE, WHAT PCR DOES.

AGAIN, I'M JUST GOING TO CHOSE ONE EXAMPLE. DOCTOR FRENCH ANDERSON IS THE HEAD OF A LABORATORY AT THE NATIONAL INSTITUTES OF HEALTH IN WASHINGTON D.C. IT'S A GOVERNMENT LABORATORY. DOCTOR ANDERSON IS A RARE INDIVIDUAL EVEN AMONG THE WORLD CLASS SCIENTISTS YOU'LL SEE IN THIS COURTROOM.

HE FOR YEARS AND YEARS AND YEARS, LONG BEFORE EVEN CONCEIVABLY WAS POSSIBLE HAS STRUGGLED TO BRING TOGETHER THE BITS AND PIECES OF BIOTECHNOLOGY WHICH MIGHT BE USED TO TREAT GENTIC DISEASES. NOT JUST TO DETECT THEM LIKE THE CETUS

SCIENTISTS AND OTHERS WERE DOING, BUT TO ACTUALLY DO TREATMENT, GENE THERAPY TREATMENT.

YOU'LL HEAR FROM DOCTOR ANDERSON IT NOW APPEARS HE'S HOPEFULLY ON THE VERGE OF SUCCESSES, RECEIVED CONSENT FROM THE FOOD AND DRUG ADMINISTRATION TO ADMINISTER THE FIRST OF THESE THERAPIST TO A YOUNG GIRL WHO'S SUFFERING FROM SKIDS, THE IMMUNE SYSTEM DISEASE THAT MAKES CHILDREN SUBJECT TO INFECTION AND DEATH.

NOW, DOCTOR ANDERSON WILL TELL YOU THAT AS HE STRUGGLED TO PUT TOGETHER THE BITS AND PIECES NECESSARY TO DO GENE THERAPY, ONE OF THE BIG HOLES WAS HAVING A DETECTION METHOD HE COULD USE SO HE COULD TELL WHETHER OR NOT THE THERAPY WAS WORKING. HE NEEDED SOMETHING SO HE COULD TAKE A SAMPLE FROM THE PATIENT AND AMPLIFY IT UP TO HUGE QUANTITIES WITH THE RESULT THAT HE COULD DETECT THAT HE WAS ACTUALLY GETTING SOME RESULTS. HE'LL TELL YOU THE ABSENCE OF SUCH AN AMPLIFICATION TECHNIQUE WAS A BIG PROBLEM.

NOW, DOCTOR ANDERSON CERTAINLY KNEW ALL ABOUT THE KIND OF PRIMER EXTENSION REACTION, THE REPLICATION REACTIONS THAT WERE GOING ON IN THE EARLY 1970'S. IN FACT, HE PUBLISHED SOME REPLICATION REACTION WORK HIMSELF. HE USED PRIMER EXTENSIONS IN HIS WORK REPEATLY. HE ENOUGH HOW TO DO THEM. HIS PEOPLE IN HIS LABORATORY DID THEM ROUTINELY.

YET, DOCTOR ANDERSON WILL TELL YOU HE DIDN'T THINK FROM THAT WORK THAT DOING SOMETHING LIKE PCR WAS POSSIBLE. AND, IN

FACT, HE'LL TELL YOU HE WAS ABSOLUTELY CONVINCED IT WAS IMPOSSIBLE AND HE'LL GIVE YOU SOME OF THE REASONS WHY.

HE'LL TELL YOU HE WAS SO CONVINCED IT WAS IMPOSSIBLE, EVEN AFTER HE READ THE ARTICLE THAT THE CETUS SCIENTISTS PUBLISHED HE THOUGHT THEY MADE A MISTAKE. HE THOUGHT THERE WAS SOMETHING WRONG WITH THEIR DETECTION SYSTEM AND WIND UP BEING EMBARRASSED FOR PUBLISHING WHAT HE THOUGHT TO BE A RIDICULOUS CLAIM.

IN TIME DOCTOR ANDERSON WAS CONVINCED. ONE OF THE PEOPLE WHO WORKED IN HIS OWN LABORATORY AND DID PCR AND REPORTED BACK TO HIM IT REALLY WORK. NOW, DOCTOR ANDERSON LIKE THOUSANDS OF OTHER SCIENTISTS USES PCR IN HIS LABORATORY IN ORDER TO ACCOMPLISH HIS WORK.

LET HE ME TALK FOR A MINUTE ABOUT SPECIFICALLY WHY PCR IS SO IMPORTANT. NOW, AS WE'VE TALKED ABOUT THE IDEA OF HAVING A PRIMER EXTENSION REACTION WAS WELL-KNOWN FROM THE EARLY 1970'S, THAT'S THE KIND OF WORK DOCTOR KHORANA PUBLISHED. IT WAS KNOWN THAT YOU COULD USE A PRIMER EXTENSION REACTION TO COPY A STRAND OF DNA.

BUT THERE'S AN IMPORTANT DIFFERENCE. THE PRIMER EXTENSION REACTION, THE REPAIR REPLICATIONS REACTIONS THEY WERE CALLED BACK THEN, COPIED STRANDS ONE AT A TIME. SO YOU MAKE COPY AND THEN YOU GO BACK YOUR ORIGINAL TEMPLATE, FROM THE ORIGINAL TEMPLATE YOU MAKE ANOTHER COPY. THEN YOU DO ANOTHER CYCLE WITH THE ORIGINAL TEMPLATE AND MAKE ANOTHER COPY.

SO AFTER ONE CYCLE YOU GET TWO COPIES. AFTER TWO CYCLES YOU HAVE THREE COPIES, THE ORIGINAL PLUS THE TWO YOU MADE. PCR IS DRAMATICALLY DIFFERENT AND PARTICULARLY ONCE YOU GET INTO THE NUMBERS LIKE FIVE OR TEN, WE HAVE A CHART WHICH SHOWS THIS.

THE CHART ON YOUR LEFT SHOWS WHAT HAPPENS IN AN AMPLIFICATION. YOU CAN SEE THAT -- MAYBE WE COULD SET THESE UP. YOU CAN SEE THAT YOU HAVE ONE STRAND TO BEGIN WITH AND AFTER ONE CYCLE YOU GOT THE ORIGINAL STRAND PLUS ONE. AFTER TWO CYCLES YOU'VE GOT THE ORIGINAL STRAND PLUS TWO.

THEN MOVING DOWN AFTER TEN CYCLES YOU GOT THE ORIGINAL STRAND PLUS TEN, AFTER 30 CYCLES YOU GOT THE ORIGINAL STRAND PLUS 30 COPIES, SO GOING THROUGH 30 CYCLES IS GIVING YOU 31 COPIES. NOW, PCR IS QUITE DIFFERENT.

AND WHAT HAPPENS IN PCR IS THAT AT LEAST THE AMOUNT OF STRANDS YOU MAKE DOUBLES IN EVERY CYCLE. SO IN THE FIRST ROUND AGAIN YOU MAKE ONE AND HAVE TWO, BUT AFTER THE SECOND CYCLE YOU'VE GOT FOUR, AFTER THE NEXT CYCLE YOU'VE GOT EIGHT, AND ALL THAT ONCE YOU GET TO TEN CYCLES BECAUSE THEN INSTEAD OF HAVING 11 STRANDS YOU GOT 1,000 AND AFTER 20 CYCLES INSTEAD OF HAVING 21 STRANDS YOU HAVE APPROXIMATELY A MILLION AND AFTER 30 CYCLES WHICH IS ABOUT THE PRACTICAL LIMIT OF PCR, INSTEAD OF 31 STRANDS YOU HAVE SOMETHING LIKE A BILLION COPIES. THAT IS ENORMOUSLY POWERFUL AMPLIFICATION TECHNIQUE.

NOW, THIS IS WHAT THE CETUS PATENT, WHAT MAKES THE

AMPLIFICATION EXPONENTIAL IN PCR, IS THAT IN EACH CYCLE OF PCR THE PRODUCT THAT YOU MADE FROM THE PRIOR CYCLE IS USED AS TEMPLATE IN THE NEXT CYCLE. SO IN THE FIRST CYCLE YOU USE YOUR ORIGINAL DNA AND MAKE ONE COPY.

IN THE NEXT CYCLE BOTH OF THOSE STRANDS, THE ORIGINAL ONE AND THE COPY ARE BOTH COPIED AND SO AFTER THEY'RE EACH COPIED YOU GOT FOUR. IN THE NEXT CYCLE EACH OF THOSE FOUR IS COPIED AND YOU GET EIGHT, AND YOU GET TO NUMBERS LIKE 1,000, A MILLION, A BILLION, BECAUSE THAT'S THE POWER OF MULTIPLYING TWO BY ITSELF TEN TIMES, 20 TIMES, 30 TIMES.

NOW, WHAT CETUS PATENTED WHEN IT PATENTED PCR WAS NOT THE USE OF A PRIMER EXTENSION REACTION TO MAKE A COPY, BUT THE USE OF A REACTION WHICH USES THE PRODUCT OF EACH CYCLE IN ORDER TO BE TEMPLATE AND LATER CYCLES WITH THE RESULT THAT YOU GET EXPONENTIAL AMPLIFICATION. AS YOU WILL SEE THE CLAIMS AND HAVE THEM ANALYZED FOR YOU THIS WILL BECOME VERY CLEAR TO YOU.

LET US JUST SHOW YOU THE ONE PATENT, THE BASIC AMPLIFICATION PATENT AS AN EXAMPLE. THIS IS A PATENT CLAIM WHICH AS IT SAYS COVERS THE PROCESS FOR AMPLIFYING AND IT AMPLIFIES AT LEAST ONE SPECIFIC NUCLEIC ACID SEQUENCE. THAT IS YOU GOT A TARGET OUT THERE THAT YOU'RE TRYING TO AMPLIFY AND THIS SPECIFICALLY COPIES WHAT IT IS YOU'RE TRYING TO COPY.

WELL, IT WILL BE AN IMPORTANT POINT LATER. IT MAKES THAT COPY IN AWAY SUCH THAT THE PRODUCTS SYNTHESIZED IN ONE CYCLE IS SEPARATED FROM ITS OTHER HALF AND THEN THAT PRODUCT CAN

SERVE AS A TEMPLATE IN LATER ROUNDS AND THE CLAIM GOES ON THEN TO THE NEXT CYCLE AND SAYS IN THE LATER ROUND YOU, IN FACT, USE THE PRODUCT THAT WAS SYNTHESIZED ABOVE IN ORDER TO PRODUCE ANOTHER STRAND.

THAT IS THE CLAIMS SPECIFICALLY READ ON THIS EXPONENTIAL COPYING TECHNIQUE, NOT LINEAR BUT ONLY EXPONENTIAL. THE ONLY KIND OF COPYING THAT COMES WITHIN THE PCR PATENT A COPYING EXPONENTIAL IT USES THE PRODUCT OF ONE STRAND AS TEMPLATE IN LATER REACTIONS. IT'S A POINT YOU'LL HEAR US AND OUR WITNESSES TALKING A LOT ABOUT.

NOW, AS LONG AS I'VE GOTTEN INTO THE PATENTS LET ME SAY A FEW WORDS ABOUT THE PATENT PROCESS AND HOW WE GOTTEN TO WHERE WE ARE. THE ORIGINAL PATENTS WERE ISSUED BY THE UNITED STATES PATENT AND TRADEMARK OFFICE IN 1987 AND YOU'LL HEAR HOW THE PROCESS INVOLVED ABOUT TWO YEARS.

THEY WERE FILED IN 1985 AND THEN THERE WAS VARIOUS COMMUNICATIONS BACK AND FORTH BETWEEN THE CETUS LAWYERS AND SCIENTISTS AND THE PATENT EXAMINER AND IN THE END THE PATENT EXAMINER DECIDED THE CLAIMS THAT ARE IN THESE PATENTS ARE PROPER UNDER THE LAW.

YOU'LL HEAR THE PATENT EXAMINER WHO MADE THAT DECISION IS AN EXPERT. HE'S AN EXPERT BOTH IN PATENT LAW AND HE'S AN EXPERT SCIENTIST, A MAN WHO HIMSELF HAS A PHD.

AND AFTER HIS CAREFUL REVIEW THIS EXPERT SCIENTISTS HIS NAME IS DR. MARTINELL CONCLUDED THE CETUS CLAIMS PROPERLY WERE

PATENTABLE AND HE ISSUED THE PATENTS.

NOW, YOU'LL HEAR THAT THAT INITIAL APPLICATION WAS FILED WITH REFERENCE TO PRIMER EXTENSION REACTIONS, BUT NOT SPECIFICALLY TO DR. KHORANA'S WORK, AND THAT'S BECAUSE NO ONE KNEW AT THE TIME DU PONT WAS GOING TO LATER MAKE THE CLAIM THAT IT WAS THE KHORANA WORK WHICH INVALIDATED THE PATENTS.

WHAT COULD HAVE BEEN A VERY DIFFICULT ISSUE FOR US, THOUGH, IS NOT. THAT'S BECAUSE THE PATENT OFFICE WAS SPECIFICALLY ASKED, DOES THIS KHORANA WORK MAKE A DIFFERENCE AND THEY SPECIFICALLY ANSWERED, NO, IT DOESN'T.

THAT CAME ABOUT UNDER A SPECIAL PROCEDURE THAT CONGRESS CREATED CALLED THE RE-EXAMINATION PROCEEDING THERE WERE TWO OF THEM HERE. THE FIRST WAS BROUGHT BY CETUS LICENSEE HOFFMAN-LA ROCHE. WHAT HOFFMAN-LA ROCHE DID, THEY SAW THIS LAWSUIT HAD BEEN FILED, IN THIS LAWSUIT DU PONT WAS MAKING CLAIMS THAT CERTAIN PUBLICATIONS INVALIDATED THE PATENT.

HOFFMAN-LA ROCHE WANTED TO GET THE VIEWS OF THE EXPERT EXAMINERS AT THE PATENT OFFICE ON THAT QUESTION. SO IN A VERY UP FRONT WAY HOFFMAN-LA ROCHE WENT TO THE PATENT OFFICE AND SAID WE ARE CETUS' LICENSEE, DU PONT HAS FILED A LAWSUIT IN WHICH IT CLAIMS THESE WRITTEN PUBLICATIONS INVALIDATE THE PATENT. WE WANT TO KNOW YOUR VIEWS. PLEASE RE-EXAMINE THE PATENT AND TELL US WHETHER OR NOT IT IS VALID IN LIGHT OF THESE PUBLICATIONS FROM THE KHORANA LABORATORY.

AS THAT PROCEEDING WAS GOING ON DU PONT DECIDED THAT

IT, TOO, WANTED TO GET THE VIEWS OF THE EXPERT AT THE PATENT OFFICE. SO IT, TOO, FILED THE RE-EXAMINATION REQUEST. IN THAT REQUEST DU PONT WAS ENTITLED TO FILE WHATEVER PRINTED ART IT WANTED. IT CHOSE WHAT IT WANTED TO FILE AND IT CHOSE WHAT IT WANTED THE PATENT OFFICE TO RULE ON.

IT CHOSE NOT THE NSF GRANT PROPOSAL THAT DU PONT WILL BE PUTTING IN EVIDENCE IN THIS LAWSUIT, IT CHOSE ANOTHER GRANT DOCUMENT. DOCTOR KHORANA'S LABORATORY AND THE PATENT OFFICE SAID THE OTHER GRANT DOCUMENT DOESN'T INVALIDATE THE PATENT, BUT THE PARTICULAR ONE THAT'S INVOLVED IN THIS SUIT WAS NOT PUT BEFORE THE PATENT OFFICE BY DU PONT.

IT ALSO WASN'T PUT BEFORE THE PATENT OFFICE BY HOFFMAN-LA ROCHE BECAUSE IT WASN'T PART OF THE ISSUES IN THIS LAWSUIT AT THE TIME THAT HOFFMAN-LA ROCHE WENT TO THE PATENT OFFICE AND SAID THESE ARE THE PRINTED PUBLICATIONS THAT DU PONT IS ARGUING INVALIDATE THE PATENT.

NOW, IN THE FIRST STEP IN THE PATENT OFFICE THE PATENT EXAMINER LOOKS AT THE NEW MATERIAL THAT'S SUBMITTED. IN THE FIRST STEP IS FOR THE PATENT EXAMINER TO ASK IS THERE ANY SUBSTANTIAL LIKELYHOOD THAT A REASONABLE PATENT EXAMINER COULD FIND THAT THIS MATERIAL WOULD HAVE AN EFFECT ON THE VALIDITY OF THESE PATENT CLAIMS.

AND THE THEORY APPARENTLY IS, IF IT DOESN'T PASS THAT TEST, NO REASONABLE PATENT EXAMINER COULD THINK THEY WERE MATERIAL THEY'RE NOT GOING TO GO WITH IT AND REQUIRE A STATEMENT

FROM THE PATENT OWNER IN OTHER PROCEEDINGS. YOU'LL HEAR THAT IN THE HOFFMAN-LA ROCHE PROCEEDING AND IN THE DU PONT PROCEEDING.

AT THIS VERY FIRST STEP THE ONLY QUESTION IS COULD ANY REASONABLE EXAMINER THINK THIS, MOST OF DU PONT'S ARGUMENTS WERE THROWN OUT. INCLUDED IN THE STUFF THAT WAS THROWN OUT WAS EVERY SINGLE ARGUMENT IT WOULD HAVE BEEN OBVIOUS TO ONE ORDINARILY SKILLED IN THE ART, BASED UPON THE KHORANA PUBLICATIONS TO DO PCR. THEY WERE THROWN OUT AT THIS VERY FIRST STAGE BY THE EXPERTS IN THE PATENT OFFICE.

NOW, AFTER THIS FIRST STAGE CETUS WAS ENTITLED TO FILE ITS PATENT OWNERS STATEMENT AND IT FILED ONE, IT FILED IT IN THE HOFFMAN-LA ROCHE PROCEEDING. BY THE TIME THE DU PONT PROCEEDING HAD GOTTEN TO THE POINT WHERE CETUS COULD FILE ONE, THE TWO WERE IDENTICAL. THE PATENT EXAMINER HAD SAID THEY WERE THE SAME. BECAUSE THEY WERE THE SAME THERE WAS OBVIOUSLY NO POINT IN FILING A SECOND IDENTICAL PATENT OWNERS STATEMENT AT THIS POINT TO MAKE SURE THE RELEVANT ARGUMENTS WERE ALL PUT TOGETHER AND DECIDED AT ONCE.

CETUS ASKED THE TWO PROCEEDINGS BE COMBINED THAT INSURED IN DECIDING THE HOFFMAN LA ROCHE PROCEEDING ALL THE DU PONT ARGUMENTS WOULD BE CONSIDERED, ALL THE MATERIAL DU PONT PUT BEFORE THE PATENT OFFICE WOULD BE CONSIDERED. THERE INCLUDED THE VARIOUS PUBLICATIONS, SOME PATENTS, THE GRANT DOCUMENT THEY CHOSE AT THAT TIME AND ALSO SOME WRITTEN TESTIMONY FROM SOME SCIENTISTS THAT IT RECRUITED.

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ONE OF THOSE SCIENTISTS WAS DOCTOR SAMBROOK, THE MAN WHO WROTE THE PREFACE TO THE BOOK WE LOOKED AT A MOMENT AGO. THE OTHER IS DOCTOR ARTHUR KORNBERG THE STANFORD SCIENTISTS WHO MR. FIGG HAS INDICATED IS GOING TO BE TESTIFYING HERE AT TRIAL.

SO THE PATENT OFFICE LOOKED AT ALL OF THIS, INCLUDING THE TESTIMONY FROM THE SCIENTISTS THAT DU PONT PUT BEFORE IT AND THE PATENT EXAMINER DECIDED NONE OF THIS MATTERS, THE PATENTS ARE STILL VALID.

SO THE PATENT OFFICE ISSUED WHAT ARE CALLED RE-EXAMINATION CERTIFICATES. THESE RE-EXAMINATION CERTIFICATES DO TWO THINGS THAT ARE IMPORTANT FOR WHAT I'M TALKING ABOUT RIGHT NOW:

FIRST, THEY LIST THE SPECIFIC ART THAT THE PATENT OFFICE HAS CONSIDERED. HERE YOU SEE THERE'S THE KLEPPE ARTICLE, HERE'S THE THE ARTICLE AND HERE'S THE VARIOUS OTHER PIECES OF ART THAT DU PONT CHOSE TO DECIDE AT THAT TIME.

THERE'S ALSO ANOTHER ARTICLE BY DOCTOR KHORANA WHICH WAS INVOLVED BACK THEN. BASED UPON ALL OF THAT THE PATENT EXAMINER IN THE PATENT OFFICE DECIDED THAT ALL OF THE CLAIMS ARE CONFIRMED. HERE IT'S ONE THROUGH 26 AND THERE ARE 26 CLAIMS.

NOW, THE PATENT OFFICE DIDN'T JUST HAVE DOCTOR MARTINELL EXPERT EXAMINER LOOK AT THIS. YOU'LL HEAR THAT IN ADDITION DOCTOR MARTINELL'S SUPERVISOR LOOKED AT IT AND HE, TOO, SIGNED THE DECISION WHICH LED TO THE ISSUANCE OF THESE CERTIFICATES.

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YOU'LL HAVE A CHANCE TO SEE THE OPINIONS OF THE PATENT EXAMINER AND HIS SUPERVISOR AND THEIR DETAILED EXPLANATIONS AND TECHNICAL TERMS OF WHY IT IS THAT THE ART FROM THE KHORANA LABORATORY JUST DOESN'T EQUAL PCR.

IN GENERAL WHAT YOU'LL HEAR THEM SAY IS THAT THE MATERIAL FROM THE KHORANA LABORATORY IS VAGUE, GENERAL AND IT'S IMPOSSIBLE TO TELL FROM IT EXACTLY WHAT WAS DONE. BUT IT CERTAINLY ISN'T POSSIBLE TO USE THAT TO DO PCR. IT WOULD NOT HAVE BEEN POSSIBLE FOR ONE ORDINARILY SKILLED IN THE ART TO HAVE USED THAT VAGUE AMBIGUOUS LANGUAGE IN THOSE ARTICLES TO DO PCR BACK AT THE TIME IN 1984 WHEN CETUS MADE ITS INVENTION.

NOW, IT'S ALSO TRUE YOU'LL HEAR THAT THE PATENT OFFICE DID NOT CONSIDER THE EXPERIMENTS THAT WERE DONE AND WERE NEVER PUT INTO ANY PUBLICATION. THESE WERE THE EXPERIMENTS THAT WERE DONE FIRST BY DOCTOR KLEPPE AND THEN BY DOCTOR MOLINEUX. EXPERIMENTS DOCTOR KHORANA AND HIS COLLEAGUES DECIDED DIDN'T MERIT PUBLICATION. THAT THEY DIDN'T COME UP TO THE STANDARDS OF RELIABILITY, ACCURACY, REPRODUCABILITY TO BE PUBLISHABLE EXPERIMENTS. SO IN ADDITION TO THE PRINTED MATERIAL DU PONT WILL PRESENT EVIDENCE OF THESE EXPERIMENTS. IT'S TRUE THE PATENT OFFICE DID NOT CONSIDER THEM.

WHAT YOU'RE GOING TO SEE IS THAT THE EVIDENCE OF THESE EXPERIMENTS CERTAINLY NO MORE COMPELLING THAN THE DESCRIPTIONS IN THESE ARTICLES AS EVIDENCE THAT PCR WAS EVER DONE IN DOCTOR KHORANA'S LABORATORY.

LIKE DU PONT, IN ADDITION TO THE REAL WORLD EVIDENCE WE'LL BE PRESENTING TO YOU, WE WILL BE PRESENTING SOME EXPERT WITNESSES. SOME WITNESSES WHO WILL COME TO YOU, REVIEW THE ARTICLES, REVIEW THE EXPERIMENTS AND TELL YOU WHAT THEY MEAN AND WHAT THEY DON'T MEAN.

ONE OF THESE SCIENTISTS IS A VERY SPECIAL PERSON. THERE'S AS LABORATORY IN ENGLAND THAT IS, IF YOU WILL, THE BIRTH PLACE OF BIOTECHNOLOGY. IT IS AT THIS LABORATORY IN ENGLAND CAMBRIDGE WHERE DOCTOR WATSON AND DOCTOR KLUG FIGURED OUT THE STRUCTURE OF DNA.

THEY FIGURED OUT IT HAD THESE BUILDING BLOCKS THAT FIT TOGETHER. THEY FIGURED OUT THE BASE PAIRING. THEY FIGURED OUT IT ACTUALLY WRAPS AROUND ITSELF IN A HELICAL STRUCTURE.

THIS LABORATORY HAS AMONG ITS ALUMNI A SERIES OF PEOPLE WHO WERE AWARDED NOBEL PRIZES FOR THE WORK THEY DID THERE. IT'S THE MOST IMPORTANT BIOTECHNOLOGY LABORATORY IN THE WORLD WITHOUT DOUBT. THE HEAD OF THIS LABORATORY IS A SCIENTIST NAMED SIR AARON KLUG. HE'S ONE OF THE MANY NOBEL PRIZE WINNERS FROM THE LABORATORY.

DR. KLUG'S TESTIMONY WILL BE PRESENTED TO YOU. DOCTOR KLUG'S HEALTH DIDN'T ALLOW HIM TO COME TO SAN FRANCISCO, SO ONE OF THE DU PONT LAWYERS, ONE OF MR. FIGG'S PARTNERS AND I TRAVELED TO CAMBRIDGE TO GET HIS TESTIMONY. AND WE DID THE USUAL QUESTION AND ANSWER FORMAT. IT WAS ALL WRITTEN DOWN AND WE'LL HAVE A CHANCE TO READ THAT TO YOU.

ANOTHER OF THE SCIENTISTS WHO WILL BE PRESENTING IS DR. JAMES DAHLBERG. DR. DAHLBERG IS A PROFESSOR AT THE UNIVERSITY OF WISCONSIN, A MAN WHO HAS BEEN CHOSEN BY HIS PEERS TO LEAD VARIOUS CONFERENCES IN THE BIOTECHNOLOGY FIELD. HE'S A SCIENTIST WHO USED TO COLLABORATE WITH DR. KHORANA.

IN FACT, YOU'LL SEE DR. KHORANA SAYS THAT THE PRINCIPLE BEHIND REPLICATION REACTIONS IS A PRINCIPLE THAT WAS BEING USED OR WAS BEING USED IN THE WORK THAT DR. DAHLBERG WAS DOING.

DR. DAHLBERG WILL BE HERE AND HE WILL ANALYZE FOR YOU IN DETAIL THE EXPERIMENTS THAT WERE DONE AND THE EVIDENCE OF THOSE EXPERIMENTS THAT YOU'LL SEE.

WHAT THESE SCIENTISTS, DR. KLUG, DR. DAHLBERG AND SOME OTHERS, WILL TELL YOU WILL BE CLEAR AND UNEQUIVOCAL AND IT WILL BE THIS: DR. MULLIS INVENTED PCR. THEY'LL TELL YOU THAT PCR WAS NOT OBVIOUS AT THE TIME THAT IT WAS INVENTED BY DR. MULLIS IN 1984.

THEY'LL TELL YOU THAT THIS WORK THAT WAS DONE IN DR. KHORANA'S LABORATORY, WHETHER IT'S REFLECTED IN ARTICLES, LETTERS, OR WHETHER IT'S REFLECTED IN THE EVIDENCE WE HAVE IN THE EXPERIMENTS, DOES NOT SHOW PCR WAS DONE AND COULD NOT HAVE BEEN USED BY SCIENTISTS IN 1984 OR ANY OTHER TIME TO FIGURE OUT HOW TO DO PCR.

INDEED YOU'LL HEAR FROM THE SCIENTISTS THAT THE DU PONT ARGUMENTS ARE BASED UPON GROSSLY OVERSIMPLIFYING PCR AND WHAT IT TAKES TO MAKE PCR WORK. THERE ARE MANY PROBLEMS THEY'LL TELL

YOU THAT WOULD HAVE PREVENTED ANYONE FROM JUST SITTING DOWN WITH THE KIND OF VAGUE THINGS IN THESE ARTICLES AND TRYING TO DO PCR.

THE PROBLEMS IN FACT WERE REASONABLY WELL-KNOWN. THEY HAVE TECHNICAL TERMS LIKE PRIMER, STRAND SWITCHING. THEY HAD PROBLEMS RE ANNEALING OF COMPLIMENTARY STRANDS, THINGS LIKE THAT, THINGS WE WILL SHOW YOU THROUGH OUR SCIENTISTS IN WHAT WE HOPE WILL BE A CLEAR AND SIMPLE EXPLANATION.

WHILE THE PROBLEMS WERE WELL-KNOWN, THE SOLUTIONS WERE NOT KNOWN. THEY WEREN'T KNOWN UNTIL THEY WERE EXPLAINED BY DR. MULLIS AND EXPLAINED FIRST IN THE PRINTED PUBLICATION IN THE DECEMBER 1985 ARTICLES, THEN EXPLAINED IN MORE DETAIL IN THE PATENTS THAT ARE IN YOUR BOOK.

ONE LAST POINT ABOUT THIS WORK FROM DOCTOR KHORANA'S LABORATORY, THEN I'M ALMOST DONE. THAT POINT IS THIS: THE EVIDENCE THAT WILL BE PUT BEFORE YOU WHAT HAPPENED IN DR. KHORANA'S LABORATORY IS VERY INCOMPLETE. IT'S INCOMPLETE THROUGH NO FAULT OF ANYONE REALLY, BUT IT IS INCOMPLETE.

THE NOTEBOOKS OF DR. MULLIS WHICH WOULD HAVE SHOWN THE DETAILS OF WHAT HE DID ARE JUST GONE. NO ONE KNOWS WHAT HAPPENED TO THEM. SO THERE ARE NO DETAILED RECORDS OF DR. MULLIS NEW WORK AT ALL.

DR. KLEPPE, AS MR. FIGG POINTED OUT, UNFORTUNATELY DIED A COUPLE OF YEARS AGO. DR. KHORANA HAS CHOSEN NOT TO TESTIFY, SO WE WON'T HAVE THE BENEFIT OF HIS RECOLLECTION AND VIEWS ON THESE SUBJECTS.

THIS INCOMPLETE RECORD IS NOT GOING TO PRESENT ANY CLEAR AND CONVINCING EVIDENCE THE EXPERIMENTS DONE IN THAT LABORATORY CONSTITUTED PCR. WHAT YOU ARE GOING TO SEE AS TO THE GRANT PROPOSALS IS THAT THERE WERE A SERIES OF REPORTS BY DR. KHORANA TO THE GOVERNMENT ABOUT HIS WORK.

YOU WILL SEE THAT IN NONE OF THOSE REPORTS DR. KHORANA EVER CLAIMED I HAVE SUCCESSFULLY ACHIEVED REPAIR REPLICATION PCR OR ANY OF THESE OTHER COPYING METHODS. HE AT VARIOUS TIMES SAYS I HAVE THIS PROPOSAL OR THIS MIGHT WORK, AND EXPERIMENTS ARE IN PROGRESS THAT WE'RE WORKING ON.

ALL OF THIS ENDS YOU'LL SEE IN 1985 WHEN DR. KHORANA REPORTED TO THE GOVERNMENT THAT HIS EFFORTS TO CREATE THIS METHOD AND MAKE IT WORK HAD FAILED. HE TOLD THE GOVERNMENT THAT IT HAD PROVEN TO BE IMPOSSIBLE TO GET EITHER EXTENSIVE OR COMPLETE COPIES OF THE DNA HE WAS TRYING TO MAKE COPIES OF.

OBVIOUSLY, IF HIS METHOD DIDN'T MAKE A COMPLETE COPY IT WAS WORTHLESS BECAUSE THE PARTIAL COPY COULDN'T BE USED IN PLACE OF THE ORIGINAL. DR. KHORANA HIMSELF REPORTED TO THE GOVERNMENT IN 1975 THAT HE WAS UNABLE TO MAKE COMPLETE COPIES AND THAT'S THE LAST THING HE SAID ABOUT USING THE REPAIR REPLICATION AS A COPYING METHOD.

WHEN A FEW WEEKS FROM NOW WE CONCLUDE, YOU HAVE SEEN NO EVIDENCE THAT JUSTIFIES TAKING THE REMARKABLE DISCOVERY OF PCR FROM DR. MULLIS. YOU WILL SEE NO EVIDENCE THAT SHOWS YOU CLEARLY AND CONVINCINGLY OR SHOWS YOU AT ALL DR. MARTINELL AND

HIS COLLEAGUES AT THE PATENT OFFICE EITHER IN GRANTING THE PATENT OR RECONFIRMING THE PATENT WHEN THEY WERE ASKED TO LOOK AT IT AGAIN BY DU PONT LAST YEAR. YOU'LL SEE NO EVIDENCE ON THE BASIS OF WHICH YOU WOULD INVALIDATE THESE PATENTS OR ANY OF THEIR CLAIMS.

THE COURT: THANK YOU, MR. PASAHOW. I THINK WE HAVE TEN MINUTES LEFT. HARDLY ENOUGH TIME TO GET ANY TESTIMONY IN; IS THAT RIGHT?

WE HAVE A FEW OTHER MATTERS WE CAN TAKE UP IN ANY EVENT.

LADIES AND GENTLEMEN, WE'LL RECESS FOR THE DAY AND WE RECONVENE TOMORROW MORNING AT 8:00 O'CLOCK AND THAT'S WHEN WE WILL BEGIN HEARING THE TESTIMONY OF WITNESSES IN THIS CASE.

PLEASE FOLLOW THE INSTRUCTIONS THAT I'VE GIVEN YOU. MY CLERK HAS JUST CALLED TO MY ATTENTION THE FACT THAT INDEED I GUESS THERE MAY BE SOME THINGS IN THE LOCAL PRESS. I TRUST NOT EVERY DAY, BUT WHO KNOWS.

IN ANY EVENT, YOU ARE NOT TO READ ANYTHING ABOUT THE CASE, SO YOU SEE A HEADLINE THAT LOOKS LIKE IT HAS SOME RELATIONSHIP TO THIS CASE JUST IGNORE IT AND READ SOMETHING ELSE.

OKAY. THANK YOU. HAVE A VERY PLEASANT AFTERNOON AND EVENING. SEE YOU TOMORROW MORNING AT 8:00 O'CLOCK.

(PROCEEDINGS HELD IN OPEN COURT, JURY NOT PRESENT:)

THE COURT: WHO ARE YOU GOING TO BE CALLING TOMORROW?

MR. FIGG: OUR FIRST WITNESS WILL BE MR. DE GRANDI.

THE COURT: THEN?

MR. FIGG: AFTER THAT DR. KORNBERG.

THE COURT: ABOUT HOW LONG DO YOU EXPECT MR. DE GRANDI WILL BE?

MR. FIGG: I THINK HIS DIRECT EXAMINATION WILL PROBABLY TWO AND A HALF HOURS, SOMETHING ALONG THAT LINE.

THE COURT: OKAY. ANYTHING ELSE WE NEED TO TAKE CARE OF TODAY?

MR. LEWIS: YOUR HONOR, I WOULD LIKE A POINT OF CLARIFICATION IN CONNECTION WITH MR. DE GRANDI'S TESTIMONY. AT THE PRETRIAL CONFERENCE IN NOVEMBER I THOUGHT YOU HAD INDICATED THERE SHOULD NOT BE ANY TESTIMONY ABOUT PATENT MONOPOLIES, ANY COMPETITIVE EFFECTS. MR. FIGG'S OPENING IT SOUNDED LIKE THAT MIGHT BE PART OF THE PLAN. IT WOULD HELP IF WE CAN CLARIFY THAT.

MR. FIGG: I DON'T REMEMBER THAT AT ALL, YOUR HONOR. YOU SIMPLY INDICATED THAT -- I DON'T REMEMBER --

THE COURT: I DON'T KNOW WHAT THE RELEVANCY OF THAT, IN ANY EVENT. THE QUESTION IS THE VALIDITY OF THE PATENTS. WHAT EFFECT IT MAY HAVE IF SOMEONE HAS A PATENT, WHAT THE COMMERCIAL EFFECT MAY BE OR THE FINANCIAL IMPACT MAY BE IS REALLY NOT RELEVANT.

MR. FIGG: NO. OUR POINT IS SIMPLY TO POINT OUT THE BREADTH OF THE CLAIMS IS WHAT DEFINES SCOPE OF THE PATENT AND

THE EFFECT OF THE PRIOR ART ON THE PATENT WHICH WE WILL DO THROUGH MR. DE GRANDI'S TESTIMONY.

I THINK WHAT MR. LEWIS MIGHT BE TALKING ABOUT WE SPOKE ABOUT PRESENTING MR. QUISENBERRY AS A WITNESS. WE HAVE DROPPED HIM FROM OUR WITNESS LIST NOW.

THE COURT: WELL, AS LONG AS WE UNDERSTAND THAT THE COMPETITIVE OR ANTICOMPETITIVE EFFECT IMPACT ON THE PATENT REALLY IS NOT AN ISSUE, IS NOT RELEVANT TO THE ISSUES HERE.

I'M SOMEWHAT CONCERNED, SO FAR YOU'VE BEEN CAREFUL WHEN YOU'VE BEEN TALKING ABOUT THE SCOPE OR THE BREADTH OF THE CLAIMS TO TIE IT UP WITH THE PRIOR ART, AND I ASSUME OPPOSING COUNSEL IS GOING TO BE ON THEIR GUARD WITH RESPECT TO SNEAKING IN 112, SECTION 112 MATERIAL, BUT IT'S GOING TO HAVE TO BE CONNECTED TO THE PRIOR ART. YOU UNDERSTAND THAT GIVEN THE COURT'S EARLIER RULING?

MR. FIGG: YES. WE'RE NOT GOING TO TALK ABOUT 112 EXCEPT INSOFAR AS THAT WAS INVOLVED IN THE PROSECUTION OF THE PATENT.

THE COURT: YOU WOULDN'T BE THE FIRST LAWYER TO TRY TO SNEAK SOMETHING IN BY THE BACK DOOR.

MR. LEWIS: I'LL BE ON MY TOES, YOUR HONOR.

THE COURT: OKAY. THERE IS ONE RULE SINCE WE HAVE A HOST OF ATTORNEYS HERE, THAT IS THAT THERE'S NO DOUBLE-TEAMING. WHOEVER IS GOING TO EXAMINE A WITNESS EXAMINES THAT WITNESS AND WHOEVER IS GOING TO CROSS-EXAMINE IS THE ONE TO ASSERT ANY

OBJECTIONS. SO IF THE WRONG COUNSEL ASSERTS AN OBJECTION YOU MAY FIND YOURSELF CROSS-EXAMINING A WITNESS YOU WEREN'T PREPARED FOR. SO JUST KEEP THAT IN MIND. OKAY.

MR. LEWIS: APPRECIATE THE WARNING, YOUR HONOR.

THE COURT: ANYTHING SO YOU RESTRAIN YOURSELF IN CASE YOUR CO-COUNSEL FAILS TO OBJECT YOU THINK HE OR SHE SHOULD HAVE.

ANYTHING ELSE I SHOULD BE AWARE OF?

PROBABLY A LOT OF I SHOULD BE AWARE OF. ANYTHING I NEED TO KNOW BEFORE TOMORROW FOR THIS CASE?

MR. LEWIS: I DON'T THINK SO, YOUR HONOR. WE WILL -- LET'S SEE, IF YOU'RE GOING TO PUT DR. KORNBERG ON, MR. FIGG, WE WILL NEED TO BE MOVING IN THE NEW EQUIPMENT TODAY. WILL WE HAVE ACCESS LATE THIS AFTERNOON OR CAN WE ARRANGE --

THE COURT: YES, CERTAINLY. I THINK WE HAVE JUST ONE SHORT PROCEEDING IN HERE THIS AFTERNOON, SO WE'RE ALL RIGHT. AND EVEN DURING THAT I DON'T THINK THERE WILL BE A PROBLEM IF YOU NEED TO GET IN.

WERE YOU ABLE TO LOCATE THE COPY OF THE ORDER? APPARENTLY THERE WAS SOME PROBLEM ABOUT THE COPY OF THE ORDER.

MR. KURZ: WE WERE LOOKING FOR THAT AND WE GOT IT FROM OPPOSING COUNSEL.

THE COURT: FINE. ALSO, DID YOU HAVE ANY OBJECTIONS TO DU PONT'S DESIGNATIONS OF ANY PORTION OF DOCTOR KLUG'S DEPOSITION?

MR. LEWIS: LET ME JUST CLARIFY THAT. NO, THERE ARE