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P R O C E E D I N G S

[10:03 a.m.]

CHIEF JUSTICE REHNQUIST: We'll hear argument  
now in the Merck KGaA v. Integra Lifesciences.

Mr. Rosenkranz.

ORAL ARGUMENT OF E. JOSHUA ROSENKRANZ

ON BEHALF OF PETITIONER

MR. ROSENKRANZ: Thank you, Your -- Mr. Chief  
Justice, and may it please the Court:

Your Honors, there is no dispute among the  
parties, nor among the 19 amicus briefs presented before  
the Court today. As to the answer to the threshold legal  
question, everyone agrees that the FDA exemption does,  
indeed, apply, with full course, to the sorts of  
experiments that are conducted and that would be relevant  
to the FDA in consideration of an Investigational New Drug  
application, a so-called IND. So the battleground now  
shifts to Integra's alternative arguments in support of  
the judgement --

JUSTICE O'CONNOR: Well, would you just clarify  
something for me as we start to consider the case? I  
guess this thing went to the jury under an instruction  
that tried to come to grips with the definition under the  
statute in some way. Was that instruction one to which  
Merck preserved an objection?

1           MR. ROSENKRANZ: No, Your Honor. We did not  
2 object to the core of the jury's instructions stating the  
3 legal standard. And we --

4           JUSTICE O'CONNOR: Do you think it was properly  
5 stated in that instruction?

6           MR. ROSENKRANZ: The core of the instruction,  
7 yes, Your Honor, was --

8           JUSTICE O'CONNOR: That's as good as we could  
9 do.

10          MR. ROSENKRANZ: Your Honor, I believe -- the  
11 answer is, the core was as good as this Court can do, and

12

13          JUSTICE O'CONNOR: All right. And, under that,  
14 you think that Merck was entitled to a directed verdict --

15          MR. ROSENKRANZ: Yes, Your Honor.

16          JUSTICE O'CONNOR: -- from the evidence?

17          MR. ROSENKRANZ: It was entitled to a verdict as  
18 a matter of law, but let me just --

19          JUSTICE O'CONNOR: Okay, but the Court of  
20 Appeals for the Federal Circuit did not address the case  
21 in -- by looking at the evidence and whether a directed  
22 verdict should have been given --

23          MR. ROSENKRANZ: Your Honor, the --

24          JUSTICE O'CONNOR: -- or not?

25          MR. ROSENKRANZ: -- the Federal Circuit did

1 understand that this was a JMOL case --

2 JUSTICE O'CONNOR: No, but it seemed to decide  
3 the case based on its view of the statute as just applying  
4 to generic drugs or something --

5 MR. ROSENKRANZ: That is absolutely correct,  
6 Your Honor.

7 JUSTICE O'CONNOR: So it didn't, in fact, come  
8 to grips with the evidence.

9 MR. ROSENKRANZ: It absolutely did not come to  
10 grips with the evidence, nor did it grapple with the  
11 alternative arguments that Integra was presenting --

12 JUSTICE O'CONNOR: Yeah, so --

13 MR. ROSENKRANZ: -- so they --

14 JUSTICE O'CONNOR: -- maybe all we have to do is  
15 deal with whether that court should have addressed the  
16 evidence.

17 MR. ROSENKRANZ: That would be one answer, Your  
18 Honor, reverse and not addressing the alternative legal  
19 grounds, but I would urge this Court to address the  
20 alternative grounds, because they raise --

21 JUSTICE O'CONNOR: All of them? You mean, like  
22 the research tools problem?

23 MR. ROSENKRANZ: No, Your Honor, because the  
24 research tools problem was never presented --

25 JUSTICE O'CONNOR: No.

1           MR. ROSENKRANZ:  -- as an issue before the jury  
2 or before the District Court.  And --

3           JUSTICE O'CONNOR:  Or the Tripps Treaty?

4           MR. ROSENKRANZ:  No, Your Honor.

5           JUSTICE O'CONNOR:  No.

6           MR. ROSENKRANZ:  In fact, that's not even raised  
7 by Respondents.  It's raised by --

8           JUSTICE O'CONNOR:  All right.  And how about the  
9 common-law research --

10          MR. ROSENKRANZ:  I would -- I would urge the  
11 Court not broach the subject of any of the questions that  
12 are not properly presented --

13          JUSTICE O'CONNOR:  Okay, so --

14          MR. ROSENKRANZ:  -- to this Court.

15          JUSTICE O'CONNOR:  -- all we're doing is looking  
16 at the statute.

17          MR. ROSENKRANZ:  We're --

18          JUSTICE O'CONNOR:  Thank you.

19          MR. ROSENKRANZ:  Yes, Your Honor, we're looking  
20 at the statute --

21          JUSTICE O'CONNOR:  Okay.

22          MR. ROSENKRANZ:  -- but it is an -- it is  
23 important, in answer to the very first question, to  
24 embellish a bit, because the lower courts need this  
25 Court's guidance, because every one of the theories on

1 which Integra defends the judgement below raise exactly  
2 the same problems that the Federal Circuit's opinion  
3 raises. They defy the plain language of the statute  
4 Congress passed. They are equally at odds with the  
5 purpose that Congress had in mind when it passed the FDA  
6 exemption.

7 CHIEF JUSTICE REHNQUIST: What are the  
8 alternative grounds that you're discussing now passed on  
9 by the Federal Circuit?

10 MR. ROSENKRANZ: Your Honor, they were not  
11 passed on by the Federal Circuit, except perhaps to the  
12 extent that the Federal Circuit may have concluded that  
13 all -- or that, excuse me -- that safety is the only issue  
14 before the FDA when it is considering an Investigational  
15 New Drug application, or that a drug innovator may not  
16 harbor additional purposes in an experiment beyond the FDA  
17 exemption, or that the -- excuse me -- beyond FDA  
18 regulatory purposes -- or, third, that the exemption does  
19 not cover efforts to optimize the drug candidate after  
20 it's identified and that candidate is, in fact, the lead  
21 candidate.

22 Those are the three legal theories, Your Honors,  
23 on which Integra is resting its defense of the judgement  
24 below. And every single one of them is either incorrect  
25 as a matter of law or immaterial as a matter of law. If

1 this Court were to ask Integra to come up with a single  
2 genuine issue of fact that does not relate to one or  
3 another of those three propositions, it will not be able  
4 to do so, save a footnote to be addressed later about the  
5 credibility of witnesses on a topic on which Integra never  
6 argued the witnesses were not credible.

7           Just beginning with the safety question, and  
8 I'll defer to the Government on that, because the  
9 Government can speak better than anyone else as to what it  
10 is that is relevant to the FDA in consideration of an IND,  
11 suffice it to say that the regulations say, as a matter of  
12 law, that safety is not the only consideration before the  
13 FDA as it considers an IND. The FDA cares very much about  
14 whether a drug will work: efficacy. The FDA cares very  
15 much about how it works: mechanism of action. It cares  
16 about what the body does to that drug: pharmacokinetics.  
17 And it cares very much about what that drug does to the  
18 body: pharmacology. And Integra's position before the  
19 jury, and before this Court, depends upon the proposition  
20 that it can bring in a witness to argue that the law is  
21 other than what the law clearly is. And the same thing  
22 goes for the so-called GLP studies that the FDA considers  
23 in connection with safety data, but need not limit itself  
24 to GLP studies when it's considering those other IND-  
25 relevant topics.

1 JUSTICE GINSBURG: Mr. Rosenkranz, just one  
2 piece of information. Because the IND is so important at  
3 this point, is it in the record -- do we have a copy of  
4 the IND?

5 MR. ROSENKRANZ: The IND, Your Honor, is not in  
6 the record, because it was excluded from evidence, which  
7 may be why the jury reached the wrong conclusion. But, I  
8 hasten to add, that will not be uncommon in these sorts of  
9 cases, because there are many circumstances in which a  
10 preclinical study begins and fails, and the IND will never  
11 materialize. There are circumstances in which a  
12 preliminary injunction is brought and won, and the  
13 research stops cold, so an IND never materializes.

14 And, again, it's important to understand, as one  
15 assesses the FDA exemption, that the inquiry is always ex  
16 ante, it is always, "What is a reasonable drug innovator?  
17 What does that drug innovator or scientist know at the  
18 point in time at which it is about to perform the next set  
19 of experiments?" So you always reflect back to a point in  
20 time before the IND materializes.

21 JUSTICE SCALIA: Mr. Rosenkrantz, the items you  
22 listed earlier seemed to me to more narrow than what I  
23 took to be the point of your opening brief, which was that  
24 the decision below was wrong because the Federal Circuit  
25 simply excluded all consideration of materials prepared

1 for purposes of the IND, as opposed to materials prepared  
2 for the -- for the drug application, later on. Are you  
3 abandoning that more expansive position?

4 MR. ROSENKRANZ: No, Your Honor.

5 JUSTICE SCALIA: Because I don't read the  
6 opinion that way. I don't think that opinion has to be  
7 read to say that they're not going to allow in anything  
8 that goes to the IND.

9 MR. ROSENKRANZ: Your Honor, there is certainly  
10 a way to read the Federal Circuit's opinion -- and this is  
11 also in response to Justice O'Connor's earlier question --  
12 in which it did grapple with the very questions we're  
13 talking about now, and did answer the questions about  
14 whether it's just safety -- and I believe the Federal  
15 Circuit believed that only safety data were relevant; that  
16 is certainly what it indicated in oral argument -- and  
17 also that dual purposes are not permissible.

18 So let me now turn to the dual-purpose question,  
19 because it's another major theme of --

20 JUSTICE SCALIA: Have you answered my question?  
21 You're abandoning the assertion that the Federal Circuit  
22 did not consider anything that didn't go to the IND --  
23 that didn't go to the --

24 MR. ROSENKRANZ: The --

25 JUSTICE SCALIA: -- drug application.

1           MR. ROSENKRANZ: No, Your Honor. I believe that  
2 there are two ways to read the Federal Circuit's opinion.  
3 To the extent that the Federal Circuit said nothing before  
4 the clinical stage is relevant to the FDA exemption -- if  
5 that is what the Federal Circuit held, we are -- we are  
6 not abandoning the position that that is wrong. I  
7 understand that there is another way to read the Federal  
8 Circuit's opinion that grapples with the subsidiary  
9 questions that we're discussing here, which are all fairly  
10 presented in our question presented. And that's what I'm  
11 addressing myself to now.

12           JUSTICE GINSBURG: So your first answer, are you  
13 relying what the Federal Circuit said in its opinion --  
14 and it's in 10a of our cert petition appendix -- that is,  
15 the Federal Circuit's statement of the question presented,  
16 whether the preclinical research conducted under Scripps-  
17 Merck agreement is exempt from liability for infringement  
18 of Integra's patents.

19           MR. ROSENKRANZ: Yes, Your Honor. And then, two  
20 pages later, on 12a, the Federal Circuit states its  
21 conclusion, and I quote, "Thus, the Scripps work sponsored  
22 by Merck was not solely for use as reasonably related to  
23 clinical testing for the FDA."

24           JUSTICE SCALIA: Yeah, but it -- it's not at all  
25 clear in the opinion that the Court was using preclinical

1 and clinical in the very technical sense that you were --  
2 that you use it, which means "clinical" is stuff submitted  
3 for the drug application, and "preclinical" is for the  
4 earlier application. That is not at all --

5 MR. ROSENKRANZ: Your Honor, it's not at all  
6 clear. And, just as in Boyle, when this Court faced a  
7 situation where it wasn't clear what the Federal -- or,  
8 excuse me -- what the Court of Appeals held, the Court --,  
9 "The best thing for this Court to do is to address what  
10 appears to be the threshold question that the Court of  
11 Appeals decided," but then also to address the subsidiary  
12 questions on the basis of which Integra is defending the  
13 judgement below.

14 JUSTICE SOUTER: Well, Mr. Rosenkranz --

15 CHIEF JUSTICE REHNQUIST: A moment ago -- a  
16 moment ago, you were reading from 12(a). Was it the first  
17 sentence you were reading from?

18 MR. ROSENKRANZ: I believe it was the first  
19 paragraph, and I was reading from the end of that  
20 paragraph, Your Honor, the -- which begins, "Thus," three  
21 lines -- really two -- the word "thus" is at the end of  
22 the third line from the bottom of that paragraph, Your  
23 Honor.

24 CHIEF JUSTICE REHNQUIST: Thank you.

25 MR. ROSENKRANZ: And so, I was saying earlier

1 that a critical component of Integra's case revolves  
2 around the notion that the use may not have more than one  
3 purpose, and that purpose can only be FDA directed. That  
4 argument is also incorrect as a matter of law. And one  
5 way we can tell that is that there is no such thing as a  
6 preclinical course of study that has only one purpose.  
7 When one is studying mechanism of action, a scientist is  
8 deeply interested, not just in how this drug works, but in  
9 how the disease works. And the language of the statute  
10 is, of course, the touchstone here. The statute is  
11 triggered by uses. The use, in this context, is an  
12 experiment. And the statute covers, provides a safe  
13 harbor for, experiments that develop the sorts of  
14 information that are relevant to the FDA. If that --

15 JUSTICE KENNEDY: Would that -- would that --  
16 would that be explained by the research-tool doctrine, or  
17 not?

18 MR. ROSENKRANZ: No, absolutely not, Your Honor.  
19 The research-tool question -- let me begin by saying,  
20 these were not research tools; these RGD peptides were the  
21 objects of study.

22 JUSTICE KENNEDY: I guess what I was asking,  
23 Would you ever use the peptide as a research tool, was my  
24 -- was my question.

25 MR. ROSENKRANZ: Oh, yes, Your Honor. There are

1 circumstances in which these peptides could be used as  
2 research tools to stunt the growth of blood vessels and  
3 study what happens next with other compounds, but they  
4 were emphatically not used as research tools in this case.  
5 In this case, they were the objects of study, and Integra  
6 won a jury verdict based upon that presentation. In fact,  
7 never argued to any court or to the jury that there is a  
8 resource tool carve out. So, I was just talking about the  
9 subjective purpose earlier, and it is -- again, it's  
10 important to note that the information can be used for  
11 other purposes. There's nothing in the statute that  
12 prohibits that.

13           Now, let me turn, just briefly then, to what is  
14 often one of the most important questions in these FDA  
15 exemption cases, which is the timeline question. At what  
16 point in the arc of drug development is it unreasonable  
17 for a jury to conclude that the FDA is an inappropriate  
18 audience for the next set of experiments? Our position --  
19 and people may differ, as a matter of law, as to whether  
20 it earlier -- but our argument is, at a bare minimum, at  
21 the point in time at which a drug developer has a known  
22 structure and cures a disease in an animal with that known  
23 structure, all eyes turn to drug development; which is to  
24 say, all eyes turn to the FDA. As a matter of law,  
25 everything after that, so long as it's relevant to the

1 FDA, is FDA -- is appropriate to view as FDA directed.

2 JUSTICE SOUTER: Do you agree then that at  
3 whatever period, however you want to describe the period,  
4 at which the researcher is basically trying to figure out  
5 what drug to concentrate on, that that period is too far  
6 back in time to come within the exception?

7 MR. ROSENKRANZ: No, Your Honor. That's exactly  
8 the trigger moment. If it has a structure, and it's  
9 investigating analogs of that structure to figure out  
10 which of these various structures are the best ones to  
11 move forward, everything from that point on is FDA  
12 directed.

13 JUSTICE SOUTER: Okay, here's what -- here's the  
14 problem I have with your argument. I can understand that  
15 argument more easily under the statute, under the text of  
16 the statute as it is written, than I can understand it  
17 under the instruction that you agreed to, because the  
18 instruction that you agreed to had a limitation, a textual  
19 limitation which is not in the statute itself, that refers  
20 to "relatively directly" as describing the relationship  
21 between this information and its object. And if we decide  
22 this case on the basis of the statute, and we read the  
23 statute more broadly than the instruction, then you're  
24 getting something that you're not entitled to, because you  
25 agreed to the instruction. If we decide this issue by

1     construing the statute as if your instruction is correct,  
2     then we're making an assumption about the proper  
3     construction of the statute that has not been argued here.

4             MR. ROSENKRANZ:   Well, Your Honor --

5             JUSTICE SOUTER:   It seems to me that the law of  
6     the case, as to what the statute means for your case, is  
7     set by the instruction, and that is why I am reluctant to  
8     get into the issue that you raise here, because I think  
9     we're rather -- you are limited, and we are tied in what  
10    we can do as a result of your agreement with the  
11    instruction.

12            MR. ROSENKRANZ:   Your Honor -- and I see my time  
13    is running out; I'd like to reserve it for rebuttal, so  
14    let me, just briefly.   Under *Praprotnik*, of course, this  
15    Court is not bound by law of the case by the instruction.  
16    But the instruction, as I understand it, says exactly what  
17    the statute says.   "Reasonably directly" is simply another  
18    way of saying, "Are these activities reasonably related to  
19    the FDA purposes?"   And every one of the comparative  
20    experiments is relevant to the FDA's inquiry, whether this  
21    drug or that is the optimum drug.   Every experiment that  
22    is involved here -- and there were only 10 percent that  
23    were comparative in nature -- develops information about  
24    the lead drug candidate, including understanding why this  
25    one works, rather than that one.

1           So, if it's all right, Your Honors, I'd like to  
2 reserve the remainder of my time for rebuttal.

3           CHIEF JUSTICE REHNQUIST: Very well, Mr.  
4 Rosenkranz.

5           Mr. Joseffer.

6           ORAL ARGUMENT OF DARYL JOSEFFER  
7 FOR UNITED STATES, AS AMICUS CURIAE,  
8 SUPPORTING THE PETITIONER

9           MR. JOSEFFER: Mr. Chief Justice, and may it  
10 please the Court:

11           We believe the question before the Court is the  
12 proper construction of the statute, and we believe the  
13 lower courts committed three important legal errors that  
14 should be corrected.

15           The first is in drawing the clinical/preclinical  
16 distinction. And, understanding that, Justice Scalia, I  
17 think the important thing to understand is that clinical  
18 studies refer to studies conducted on humans, and at the  
19 IND stage, the whole question is to decide whether studies  
20 should be conducted on humans. So at that point in time  
21 the only information that's available is the preclinical  
22 studies on animals and in test tubes. So when the Court  
23 distinguished between preclinical and clinical, it was  
24 essentially saying, you cannot do the information that's  
25 necessary to submit an IND, necessary to do clinical

1 trials, necessary to get your drug approved. And that's  
2 why we -- it seems to us that that's clearly wrong.

3 CHIEF JUSTICE REHNQUIST: Do you have to have  
4 the FDA's permission to start clinical testing?

5 MR. JOSEFFER: Yes, that's the purpose of an IND  
6 application, is -- the whole -- the only thing that FDA is  
7 looking at, at that point, is whether to permit human  
8 clinical trials to proceed.

9 The second important legal error committed by  
10 the Federal Circuit was in apparently concluding that only  
11 tests regarding the compounds ultimately submitted to FDA  
12 in an IND are subject to the protection. Now, the problem  
13 with that is that a company can decide which specific  
14 compound to submit only by first comparing -- doing  
15 studies on that compound and on others in order to  
16 determine which would be the best compound to submit,  
17 which would strike the best balance between obtaining  
18 health effects or reporting safety concerns. So, if the  
19 exemption only --

20 JUSTICE O'CONNOR: Would you state again what  
21 you say the second error was?

22 MR. JOSEFFER: The second error, we believe, is  
23 that the Federal Circuit indicated that only studies  
24 undertaken on the single compound ultimately submitted in  
25 an IND are protected by the exception. And the problem

1 with that is that I can't figure out what that one  
2 compound is until I've done studies on it and on other  
3 compounds to determine --

4 JUSTICE SCALIA: That --

5 MR. JOSEFFER: -- which is the best to submit.

6 JUSTICE SCALIA: But that might well determine  
7 whether the research was relatively directly related. I  
8 mean, if I were a juror, I would -- I would say it's  
9 relatively directly related if it relates to that  
10 particular compound which is ultimately submitted, and not  
11 relatively directly related if it was preliminary, trying  
12 to found out which compound to submit.

13 MR. JOSEFFER: We would -- we would look at it  
14 this way. If I'm -- say I have 12 compounds that I'm  
15 going to test and decide which is best and go forward  
16 with. At the time I'm doing a test on any one of those  
17 compounds, if those tests succeed, it's reasonably  
18 foreseeable I'll submit an IND for that compound.

19 JUSTICE SCALIA: Yes, I understand all that.  
20 But --

21 MR. JOSEFFER: And the --

22 JUSTICE SCALIA: -- I'm just saying that that is  
23 certainly one interpretation of "reasonably directly."  
24 And if that is so, then you are erroneous in your  
25 assumption that the question before this Court is the

1 meaning of the statute. It might not be. It might be --  
2 it might be the meaning of the instruction.

3 MR. JOSEFFER: Well, I think we would disagree  
4 with that, for two reasons. The first is that the Federal  
5 Circuit, as Justice O'Connor noted, reserved -- resolved  
6 these questions entirely as a matter of law, based on a de  
7 novo interpretation of the statute, without regard to the  
8 jury instruction. And that's the holding that's now  
9 before this Court.

10 JUSTICE O'CONNOR: What's your position on the  
11 jury instruction? Does it correctly state the law?

12 MR. JOSEFFER: We think that it's -- if it's  
13 construed correctly, we think that it's correct, but just  
14 too general to be of assistance to the courts in  
15 addressing the more specific questions of the issue here.  
16 And this is -- remember, Merck has sought judgement as a  
17 matter of law. And when a party seeks judgement as a  
18 matter of law, the courts are not constrained to only  
19 applying the law that's found in the jury instruction;  
20 they can also articulate and apply -- and do all the time  
21 -- other legal principles that are relevant. *Praprotnik*  
22 *v. St. Louis* is a great example of a case where this Court  
23 did that.

24 Now, there would be a problem if the jury  
25 instruction was inconsistent with the correct rule of law,

1 because then there could be a waiver concern. But we  
2 don't see that at issue here, because the jury  
3 instruction, we think, was just too general to speak to  
4 these issues.

5 But getting back to my point about why it can't  
6 be limited to that single compound --

7 CHIEF JUSTICE REHNQUIST: If in fact the jury  
8 instruction is too general. I mean, if both parties  
9 agreed to it, aren't they, in a sense, bound by it?

10 MR. JOSEFFER: We think that the Petitioner  
11 should not, and is not, arguing inconsistently with the  
12 jury instruction. The point is just that juries, being  
13 lay people, tend to be instructed --

14 CHIEF JUSTICE REHNQUIST: The Petitioner said he  
15 agreed with the core of the instruction, whatever that is.

16 MR. JOSEFFER: I think that's just with the  
17 general principles. Take, for example, a negligence case.  
18 Jurors are instructed all the time that the Defendant has  
19 a duty of ordinary care. And then courts, on appeal, will  
20 determine more specific legal questions, whether entire  
21 classes of conduct do or do not comply with the ordinary  
22 care, in much greater detailed instructions to the jury.  
23 And example of a case where this Court did that would be  
24 *Shenker v. B&O Railroad*, at 374 U.S. 1. And we think that  
25 in a -- in determining whether a Petitioner is entitled to

1 judgement as a matter of law, this Court should just  
2 articulate and apply the specific legal principles here;  
3 they're not inconsistent with the jury --

4 JUSTICE O'CONNOR: Was the court below wrong in  
5 saying that the statute was enacted only to help generic-  
6 drug development?

7 MR. JOSEFFER: Yes. In fact, this Court already  
8 held in *Eli Lilly v. Medtronic* that the statute is not  
9 limited to generic drugs. In fact, it's not even limited  
10 to drugs, but also applies to things like medical devices,  
11 food additives, color additives. And it's a very  
12 important point, because the Federal Circuit thought the  
13 statute to be construed in an artificially narrow manner  
14 in light of a supposed focus on generic drugs, which is  
15 just inconsistent with this Court's authoritative  
16 construction of --

17 JUSTICE SOUTER: Is that going to be your third  
18 point, the third error that the court supposedly  
19 committed?

20 MR. JOSEFFER: No, the third is the error  
21 committed by the District Court and relied on by  
22 Respondents here, which is the statement that FDA only  
23 considers safety, and not efficacy, in determining whether  
24 to permit human clinical trials to proceed. It's a very  
25 important point, because at the IND stage the question for

1 FDA is whether a drug should be given to human beings.  
2 And because there's no such thing as an absolutely safe  
3 drug, because all drugs entail at least some safety risks,  
4 FDA will not let human clinical trials proceed unless  
5 there's some reason to believe that the study could be  
6 useful. It's a -- it's a benefit-risk analysis. The  
7 Court looks to whether the potential benefits of the test  
8 would outweigh the risks of the test; and if not, the  
9 Court will not let a test proceed.

10 Now, Congress charged FDA with doing that by  
11 instructing FDA to determine whether the drug would pose  
12 an unreasonable risk to the health and safety of humans.  
13 And FDA has construed that, as I said, to mean the  
14 benefit-risk.

15 The most express articulation of that comes in  
16 the guidance document that FDA has put out regarding the  
17 preparation of the investigators brochure, which is a  
18 required part of the 9d submission. And the investigators  
19 -- and the guidance document explains that the  
20 investigators brochure must provide sufficient information  
21 for the -- for the reader to, quote, "make his/her own  
22 unbiased risk-benefit assessment of the proposed  
23 clinical." That's set forth on the bottom of page 10 of  
24 our brief. And --

25 CHIEF JUSTICE REHNQUIST: What are the

1 consequences if someone goes ahead and conducts a clinical  
2 trial without the approval of the FDA?

3 MR. JOSEFFER: That's contrary to federal law.  
4 I -- certainly would be severe civil consequences. And my  
5 guess is there are criminal consequences for doing that,  
6 too.

7 JUSTICE GINSBURG: Your time is short, so could  
8 you tell us how far back you think, under the statute, you  
9 can go and not -- and be within the safe harbor?

10 MR. JOSEFFER: Yes. We think that the proper  
11 test looks to whether a company is trying to develop a  
12 particular drug, by which we mean a substance with  
13 particular characteristics designed to achieve particular  
14 objectives. To explain that, we recognize that basic  
15 scientific research into human biology and disease  
16 processes is not protected. That's just too far down the  
17 stream of causation. But once I get a particular concept  
18 for a drug, this says I'm going to treat the disease in a  
19 particular way by targeting a particular part of the  
20 disease process. Then we think that the work done, going  
21 forward, with includes comparing different substances to  
22 figure out which would be the best active ingredient, is  
23 protected. To provide a concrete example --

24 JUSTICE SCALIA: Why isn't that basic research?  
25 I mean, I want to -- I want to treat this disease by

1 stifling the development of blood cells around it, or  
2 something like that, and then you ask yourself, "Gee, what  
3 would stifle the production of blood cells?" And let's  
4 assume there hasn't been any research done in that field  
5 before. You wouldn't consider that basic research, so  
6 long as the idea I have in my -- in my head is, I want to  
7 create a drug to treat this disease that will stifle blood  
8 cells?

9 MR. JOSEFFER: No. And here's why. The basic  
10 insight, and then I'll explain it, is that the first time  
11 a study -- a study is run on a particular substance, if  
12 that's -- first study is not protected, then the exemption  
13 is worthless, because I'd have to commit that infringing  
14 study before I came to the protection of the exemption.

15 So, we would say that the -- in this case, for  
16 example -- I think it's easier on particulars -- that  
17 basic research was figuring out that the key to cancer is  
18 -- the key to the growth of tumors is angiogenesis, and  
19 the key to blocking angiogenesis is blocking the alpha v  
20 beta 3 receptors. That's the basic research into how the  
21 body works. But once I then start trying to figure out  
22 which substance would best block an alpha v beta 3  
23 receptor, it's very specific, because I know what that  
24 receptor is, I know what it's like, I know what  
25 characteristics I'm going to need in a drug to block that.

1 And when I try different things out to block that, that  
2 first experiment, at that point, has to be protected,  
3 because, otherwise, I'd have to commit the infringement  
4 before I could get --

5 JUSTICE KENNEDY: Did the earlier process that  
6 you described, the basic research, is that within the  
7 common law research exemption?

8 MR. JOSEFFER: The -- it would be if it was  
9 noncommercial.

10 JUSTICE KENNEDY: How does the common law of  
11 research exemption figure into this case, if at all?

12 MR. JOSEFFER: It's not directly you, Your  
13 Honor, because Petitioner has not relied on it at all, and  
14 for good reason, which is that the courts have  
15 consistently held that the common law research exception  
16 applies only to noncommercial activity. The most obvious  
17 example would be kids in their basements. But when a drug  
18 company, that its entire business is developing and  
19 manufacturing drugs, undertakes the activity, that's  
20 commercial, and that's never been considered protected by  
21 the common law exception.

22 JUSTICE KENNEDY: Does Scripps -- is Scripps in  
23 the business, too?

24 MR. JOSEFFER: I see my red light is on, if I  
25 could answer the question.

1           Some of Scripps' work, when it's working  
2 directly for Merck, certainly is, we would think, you  
3 know, tied closely to Merck's commercial activities.  
4 Scripps may also do some other --

5           CHIEF JUSTICE REHNQUIST: Thank you, Mr.  
6 Joseffer.

7           Mr. Flores.

8           ORAL ARGUMENT OF MAURICIO A. FLORES

9           ON BEHALF OF PETITIONER

10          MR. FLORES: Mr. Chief Justice, and may it  
11 please the Court:

12          This Court stated, in Black versus Cutter  
13 Laboratories, which is cited on page 27 of our brief, as  
14 follows, "At times, the atmosphere in which an opinion is  
15 written may become so surcharged that unnecessarily broad  
16 statements are made. In such a case, it is our duty to  
17 look beyond the broad sweep of the language and determine  
18 for ourselves precisely the ground on which the judgement  
19 rests."

20          This is such a case. The judgement of the  
21 Federal Circuit was its order affirming the District  
22 Court's denial of motion for judgement as a matter of law.  
23 The precise grounds for the Federal Circuit's opinion is  
24 set forth in page 14a in the appendix attached to Merck's  
25 petition for certiorari. And there the Federal Circuit

1 said that it upheld the denial of Merck's motion for  
2 judgement as a matter of law because the Federal Circuit  
3 discerned no error in the District Court's interpretation  
4 of section 271(e)(1), which raises the question --

5 JUSTICE GINSBURG: Where is this? Page 14a --

6 MR. FLORES: Yes, Your --

7 JUSTICE GINSBURG: What are you quoting from?

8 JUSTICE KENNEDY: Is it just before the letter  
9 "b" on 14a?

10 MR. FLORES: Yes, Your Honor.

11 JUSTICE BREYER: What are the first few words of  
12 the sentence there that you quoted?

13 MR. FLORES: "Because the language and context  
14 of the safe harbor do not embrace the Scripps-Merck  
15 general biomedical experimentation, this Court discerns no  
16 error" --

17 JUSTICE BREYER: Exactly. And so, they are  
18 saying that they're wrong on their ground for thinking  
19 that the language and context don't embrace it. Since  
20 they used the wrong standard, they never got to the  
21 question of whether the evidence warranted a directed  
22 verdict. So I don't see how we avoid looking at all of  
23 what you'd call the atmospheric.

24 MR. FLORES: The precise holding and the  
25 reasoning of the Federal Circuit was, they found no error

1 in what the District Court's --

2 JUSTICE BREYER: Because they interpreted the  
3 statute in a particular way. Isn't that right? I'm  
4 asking. I'm not --

5 MR. FLORES: No, Your Honor.

6 JUSTICE BREYER: No?

7 MR. FLORES: The only interpretation of the  
8 statute that can be found in the District Court's order  
9 denying Merck's motion for judgement as a matter of law is  
10 the standard articulated in the jury instruction.

11 JUSTICE SCALIA: No, but I think -- I think the  
12 Justice was asking whether it was the Court of Appeals  
13 that --

14 JUSTICE BREYER: Yes.

15 JUSTICE SCALIA: -- that applied a particular  
16 standard. And certainly it had to have been. Didn't the  
17 Court of Appeals have a particular standard as to what  
18 constituted general biomedical experimentation, as opposed  
19 to the kind of experimentation that's covered by the -- by  
20 the safe harbor exemption? It must have had. I mean, how  
21 could you -- how could you rule on the question before you  
22 unless you have, in your head, a notion of what the safe  
23 harbor consists of and what is beyond it?

24 MR. FLORES: The question before the Federal  
25 Circuit was whether the District Court erred by not

1 applying the rational predicate interpretation of section  
2 271(e), which was the sole focus of Merck's appeal to the  
3 Federal Circuit.

4 JUSTICE GINSBURG: Why should we say that's the  
5 question, when the Federal Circuit, itself, said what I  
6 read before from 10a?

7 MR. FLORES: We're -- on page 10a, the Federal  
8 Circuit said, "Thus" -- and this is in the -- the last  
9 sentence in the middle paragraph of the page -- "Thus,  
10 this Court must determine whether section -- the section  
11 271(e) safe harbor reaches back down the chain of  
12 experimentation to embrace development and identification  
13 of new drugs that will, in turn, be subject to FDA  
14 approval."

15 JUSTICE BREYER: That would answer that question?

16 MR. FLORES: It does not. The Federal Circuit  
17 answered that in the negative. The Federal Circuit  
18 rejected the interpretation advanced by Merck, which was  
19 the rational predicate standard, which was basically a  
20 causal test, and held that the District Court's  
21 interpretation, under the Intermedics standard that's  
22 given in the jury instruction, that Merck now concedes is  
23 the correct standard.

24 JUSTICE BREYER: So they say that does not --  
25 the safe harbor does not reach, among other things, back

1 down the chain of experimentation to embrace the  
2 development of new drugs that will be subject to FDA  
3 approval. In your opinion, is that statement, as I read  
4 it -- I left out the word "identification" -- as I read  
5 it, is that statement a correct statement of the law, or  
6 incorrect statement?

7 MR. FLORES: That is a correct statement of the  
8 law.

9 JUSTICE BREYER: That is a correct statement of  
10 the law. So then, I take it, the other thinks that it  
11 isn't, because, for example, you could have a situation  
12 where you are developing drugs, and, in developing drugs,  
13 you do some experiments and you get some information that  
14 would be useful to the FDA and the IND process, and,  
15 therefore, they are within the safe harbor.

16 MR. FLORES: No, Your Honor. I believe the  
17 Solicitor General agrees with this aspect of the Federal  
18 Circuit's opinion and makes that clear at the bottom of  
19 page 15 and onto page 16 of the Solicitor General's brief.  
20 Merck no longer challenges this aspect of the Federal  
21 Circuit's opinion. Merck concedes that there are  
22 experiments in the basic research phase, that, although  
23 they're necessary in the chain of causation, are not  
24 exempt. The rational -- Merck has abandoned the rational  
25 predicate standard that the Federal Circuit rejected here.

1 JUSTICE GINSBURG: Mr. Flores, when I asked you  
2 about the sentence on page 10, I intended, not the one  
3 that you read, but an earlier one that precedes it, and  
4 that is, "The questioning arising in this case is whether  
5 the preclinical research" -- that is, the research on  
6 animals, as distinguished from humans -- "conducted under  
7 the Scripps-Merck agreement is exempt from liability for  
8 infringement of Integra's patents."

9 Now, if you just took that as the question, then you  
10 would say it -- this Circuit is drawing the line between  
11 clinical and preclinical. It's not a crystal-clear  
12 opinion, by any means, but that is one question presented  
13 that they've identified. And how do they answer that  
14 question?

15 MR. FLORES: Your Honor, I disagree. I think  
16 the operative language in this sentence is the reference  
17 to "the Scripps-Merck" -- is to "research conducted under  
18 the Scripps-Merck agreement."

19 JUSTICE SCALIA: That's the way I read it. It  
20 -- the -- and this is why I was disagreeing with counsel  
21 from the other side. It -- well, counsel ultimately  
22 conceded, you could read it not to draw the line between  
23 clinical and preclinical. And the way you read this  
24 sentence is -- the question, they say, is not whether  
25 preclinical research falls under 271(e)(1); it's whether

1 the "preclinical research conducted under the Scripps-  
2 Merck agreement." And then the next sentence explains  
3 what that means. The experiments did not supply  
4 information for submission to the United States Food and  
5 Drug Administration, but, instead, identified the best  
6 drug candidate.

7           So, I think what they're describing as the  
8 question presented is whether preclinical research that is  
9 -- that is not directed to supplying information for  
10 submission to the Food and Drug Administration, but,  
11 instead, to selecting the drug candidate, whether that  
12 type of preclinical research is within the safe harbor.

13           MR. FLORES: Yes. In fact, Justice Scalia, if  
14 this opinion by the Federal Circuit were interpreted to  
15 hold that preclinical experiments are categorically  
16 excluded from the scope of the exemption, that holding  
17 would be inconsistent with the District Court's  
18 interpretation of the law, because the District Court's  
19 interpretation of the law was that preclinical experiments  
20 are potentially eligible, and the District Court submitted  
21 the question to the jury.

22           So the Federal Circuit would be completely  
23 inconsistent, if, on the one hand, it categorically  
24 excluded preclinical experiments, and, on the other hand,  
25 it approved the District Court's --

1 JUSTICE BREYER: All right, this very dialogue  
2 makes me able to ask a question that I think will reveal  
3 better to you what I need an answer to.

4 Reading this, and listening to the discussion,  
5 and your use of the word "atmospherics," suggests that the  
6 opinion below is pretty foggy. We have Merck, the Food  
7 and Drug Administration, the Government, the entire  
8 biotechnology industry, the drug industry of the United  
9 States, and everybody else telling us that they are wrong  
10 in the way they stated the standard. And you, yourself,  
11 urge us to look beyond the way they stated it. So, what's  
12 the harm, and why wouldn't we, given this and the  
13 unclarity, just try to do a better job at stating the  
14 standard, say, "That's the standard," and then send it  
15 back, and then you can make all your arguments there about  
16 how it applies.

17 MR. FLORES: The reason it would not be  
18 appropriate for the Court to do so is because no standard,  
19 other than the Intermedics standard that was applied by  
20 the District Court, was ever suggested to the District  
21 Court. There was only one standard ever considered.

22 CHIEF JUSTICE REHNQUIST: We're not reviewing the  
23 District Court's opinion? We granted certiorari as to the  
24 particular question which will deal with what was the  
25 Court of Appeals opinion. We don't ordinarily simply

1 compare the Court of Appeals' opinion with the District  
2 Court's opinion to see if they parse.

3 MR. FLORES: Yes, Your Honor. But in this case  
4 the issue before the District Court was whether the  
5 District Court erred in denying a motion for judgement as  
6 a matter of law.

7 JUSTICE O'CONNOR: Well, don't you think that  
8 the Federal Circuit may have focused too much on generic  
9 drug applications? Do you think it was right about that?

10 MR. FLORES: I think the Federal Circuit was  
11 right, as a factual matter, describing the impetus for  
12 Congress adopting section 271(e).

13 JUSTICE O'CONNOR: Well, it seemed to be driven  
14 by its very narrow focus on generic drug development. Do  
15 you -- do you think that the efficacy of the drug being  
16 suggested plays a role in the IND application?

17 MR. FLORES: No, Your Honor, it does not.

18 JUSTICE O'CONNOR: See, I think there may be a  
19 difference there, because I think the other side thinks  
20 that how the drug is expected to work, in practice, and  
21 whether it, in fact, will attack a certain disease, is  
22 part of what the FDA looks at. Apparently, the Government  
23 takes that position, as narrowly as I could determine.  
24 But you reject that, as well.

25 MR. FLORES: Yes, Your Honor. I think the

1 answer to that is in the statute. It's a -- it's section  
2 -- it's 21 United States Code 355(i)(3)(B)(i). And in  
3 that --

4 JUSTICE O'CONNOR: Can you repeat that 355 what?

5 MR. FLORES: (i) --

6 JUSTICE O'CONNOR: -- (i) --

7 MR. FLORES: -- (3) --

8 JUSTICE O'CONNOR: Uh-huh.

9 MR. FLORES: -- (B)(i) again. And, in this  
10 section, Congress is telling the FDA what are the  
11 considerations that the FDA has to weigh in making the  
12 safety decision, the decision whether to allow clinical  
13 trials in humans --

14 JUSTICE GINSBURG: Is this text that you're  
15 referring to, is it someplace -- is the text someplace  
16 where we can look at it while you're explaining this to  
17 us?

18 MR. FLORES: No, Your Honor, it's not in the  
19 appendix, unfortunately. Let me read that statute,  
20 because it's instructive about what Congress told FDA to  
21 weigh for the --

22 JUSTICE O'CONNOR: But does the -- does the  
23 statute -- is that the only place we would look to decide  
24 whether safety is the only consideration for the FDA?

25 MR. FLORES: No, Your Honor. The regulations, I

1 believe, address that. And the regulations are 312.22(a),  
2 which is in the appendix attached to Integra's brief on  
3 the merits. And I'll read that. It says --

4 JUSTICE O'CONNOR: But you do --

5 JUSTICE SOUTER: What are you --

6 JUSTICE O'CONNOR: -- you do agree, do you not,  
7 that the Government does not agree with you on this point?

8 MR. FLORES: The Government disagrees, Your  
9 Honor.

10 JUSTICE O'CONNOR: Right.

11 JUSTICE SOUTER: What are you reading from?

12 MR. FLORES: Page 3a in the addendum to  
13 Integra's brief.

14 JUSTICE SOUTER: Okay.

15 MR. FLORES: That's 21 C.F.R. Section 312.22(a).  
16 It states that, "The FDA's primary objectives in reviewing  
17 an IND are, in all phases of the investigation, to assure  
18 the safety and rights of subjects, and, in phase two and  
19 three, to help assure that the quality of the scientific  
20 investigation of the drugs is adequate to prevent an  
21 evaluation of the drug's effectiveness and safety."

22 JUSTICE SOUTER: Okay, that talks about the  
23 primary concern. There is certainly going to be concern  
24 with efficacy to this extent. They are going to want to  
25 know, before they allow clinical trials, whether the drug

1 that it is proposed to give cancer patients has some  
2 relationship to cancer, as opposed to the common cold.  
3 Admittedly, at the clinical trial they're trying to find  
4 out how effective it is on human beings, but there's got  
5 to be some threshold showing of effectiveness. They can't  
6 simply ignore effectiveness and look at safety entirely  
7 prior to that point.

8 JUSTICE STEVENS: In fact, that paragraph refers  
9 to effectiveness, as I read it.

10 MR. FLORES: Yes, it does, Your Honor. But it  
11 does -- it refers to it in the context of phases two and  
12 three. And the simple fact is that until there's clinical  
13 trials in humans, there's no way tell whether this drug a  
14 going to be effective.

15 JUSTICE SOUTER: But there is at least --  
16 there's got to be some way to tell whether it even  
17 addresses the disease. That is essentially a threshold  
18 effectiveness question.

19 MR. FLORES: The FDA statutes and regulations do  
20 not use the term "efficacy" to describe that. In section  
21 355(i)(3)(B)(i), when Congress listed the factors to  
22 consider, what it listed was not efficacy. Efficacy is  
23 not --

24 JUSTICE SOUTER: Congress described the need  
25 that there be some relationship between the consequences

1 of taking the given drug and the disease which is supposed  
2 to be addressed by taking the drug. If they didn't use  
3 the word "efficacy," what word did they use?

4 MR. FLORES: They --

5 JUSTICE STEVENS: They used the word  
6 "effectiveness," which is pretty close.

7 [Laughter.]

8 MR. FLORES: No, Your Honor, they used the word,  
9 in the statute, "the condition for which the drug is to be  
10 investigated."

11 JUSTICE BREYER: That's important. They say they  
12 want to know the pharmacological action of the drug in  
13 relation to its proposed therapeutic indication. The  
14 reason, I take it, the word "efficacy" is not there  
15 directly is because that word has a history, the Kefauver  
16 hearings, and it was involving drugs that don't do  
17 anything. Safety is a different matter. But of course  
18 when you consider whether something is safe, you must  
19 know, since, for example, cancer drugs poison people, the  
20 extent to which that poisoning is outbalanced by its  
21 effect in curing people. So how could you possibly,  
22 particularly where cancer is at issue, know whether this  
23 is an appropriately safe drug, without knowing how  
24 effective it is, as well as knowing the side effects that  
25 are -- that are harmful? If I knew that there was any

1 answer to that question at all, I might be tempted to  
2 agree with you, because it doesn't use the word. But  
3 what's the answer?

4 MR. FLORES: The answer is that the FDA  
5 considers what information is available to it. It does  
6 not have information about the effectiveness of the drug,  
7 because clinical trials have not taken place; and,  
8 therefore, the regulations and the statutes say you do the  
9 -- what you can. You look at the condition for which the  
10 drug --

11 JUSTICE GINSBURG: But why wouldn't it have  
12 information about effectiveness on animals? I mean, if  
13 the -- you show that the -- all the FDA's interested in is  
14 that it didn't kill the animal, never mind whether it was  
15 effective to cure the tumor?

16 MR. FLORES: The FDA is concerned with safety in  
17 animals. And there may be some cases in which there is a  
18 known safety risk to a drug, and there will be a  
19 heightened look at potential benefits in order to balance  
20 that out. But the regulations focus on safety. And in  
21 this particular --

22 JUSTICE O'CONNOR: Yeah, but it's absolutely  
23 clear, I thought, that the FDA, at the end of the day in  
24 some of these drug applications, ends up looking at not  
25 only safety, but how effective it is. And sometimes if

1 the safety risk is minimal but the effectiveness is great,  
2 I understood at least, that could affect the decisions.  
3 So, I would think that you would want to encourage the  
4 exemption to cover those matters.

5 MR. FLORES: Your Honor, of course FDA is very  
6 concerned about efficacy, and it -- but concerned about  
7 that after it gets data from human clinical trials.  
8 That's the -- that is the basis of --

9 JUSTICE O'CONNOR: No, I'm not sure. If there's  
10 data earlier, at IND stage, as a result of the lab tests  
11 and the animal tests, I would think that would be part of  
12 the exemption.

13 MR. FLORES: If efficacy -- or some information  
14 about what benefits the drug might have, is probably a  
15 better way to phrase it -- is considered at the safety  
16 stage as part of the safety balancing, then it's got to be  
17 done under good laboratory practices, because --

18 JUSTICE BREYER: Suppose that we concluded --  
19 well, I don't want to cut you off. Go ahead, please. I  
20 cut you off.

21 MR. FLORES: If -- I believe the Solicitor  
22 General's point is that the safety decision is a practical  
23 one, and you've got to look at both sides of the ledger --  
24 potential harm, potential benefit -- I don't believe it's  
25 proper to call that "efficacy." But whatever you call it,

1 if it's part of the safety balancing it has to be done  
2 under good laboratory procedures. That, I think, is clear  
3 from the FDA regulations. And, as a matter of policy, it  
4 wouldn't make any sense for the FDA to say that half of  
5 the safety equation need not be done under good laboratory  
6 practices. Both parts of the safety equation have to be  
7 done under that.

8 JUSTICE SCALIA: I don't -- so what? I don't  
9 understand what conclusion that leads to.

10 MR. FLORES: Well, Justice Scalia, let me say  
11 that I think that this whole discussion about the  
12 interpretation of the FDA law is really somewhat off the  
13 point here.

14 JUSTICE SCALIA: I was beginning to think that,  
15 too.

16 [Laughter.]

17 MR. FLORES: And the reason I say that is  
18 because we're not here to judge the legality of an FDA  
19 action in its discretion, saying we want to consider  
20 preclinical --

21 JUSTICE BREYER: Yeah, but the reason you  
22 brought it up is because the particular certificate that  
23 is for a safety-certified lab is not applicable to the lab  
24 that used this stuff. That's why you brought it up, I  
25 think.

1 MR. FLORES: That is correct.

2 JUSTICE BREYER: And I understand that. And  
3 you'd have to conclude, for them to win -- but suppose I  
4 did conclude -- suppose, for hypothetical -- the sake of  
5 -- for -- as a hypothetical, suppose I thought, yes, this  
6 does include the safety part, looking at how effective  
7 drugs are, too. Suppose I concluded that the statute  
8 meant sometimes you could do that, in an ordinary  
9 laboratory that didn't have the special certificate?  
10 Suppose I concluded that, indeed, you could look well in  
11 advance of the clinical test period to get the information  
12 for the IND? And suppose I concluded that sometimes,  
13 where it was reasonably related, you could, in fact, look  
14 at other drugs, too, that are related to the ones you do.  
15 If I concluded that -- and I'm not saying I would -- then  
16 would you concede that a directed verdict would have been  
17 appropriate against you?

18 MR. FLORES: No, Your Honor.

19 JUSTICE BREYER: Because? And what's your  
20 strongest argument that it wouldn't?

21 MR. FLORES: Well, Your Honor, there's numerous  
22 admissions in the record that Merck made which would  
23 indicate that they've -- that the program carried out at  
24 Scripps was not reasonably related to the FDA, that the  
25 real FDA work was being done in Germany, that the majority

1 of these experiments conducted by Scripps were conducted  
2 on chicken embryos, which Merck's own scientists agree  
3 have nothing to do with safety, and, by logical extension,  
4 they can't tell you much about efficacy, either. Merck  
5 agreed that a significant portion of these experiments in  
6 which Merck was looking for non-peptide compounds as  
7 possible drug candidates, is something that --

8 JUSTICE O'CONNOR: Well, we don't -- I hope we  
9 don't have to, at this Court, look at all the evidence and  
10 try to sort it out that way. What we have to focus on is  
11 whether the Court of Appeals for the Federal Circuit was  
12 in error in articulating the scope of the exemption.

13 MR. FLORES: Your Honor, this Court does not  
14 have to get into Rule 50 review of the evidence here --

15 JUSTICE O'CONNOR: No.

16 MR. FLORES: -- because there's no dispute about  
17 the legal standard. We've all heard that this morning.  
18 The only other possible issue is Rule 50 review. But  
19 Merck has failed --

20 JUSTICE O'CONNOR: Well, I thought the issue was  
21 whether the Court of Appeals for the Federal Circuit  
22 correctly determined the scope of the exemption. If they  
23 were wrong about it, then it is open to us to correct that  
24 and send it back.

25 MR. FLORES: Your Honor, the Federal Circuit

1 didn't determine the scope of the invention. There's --  
2 it's --

3 JUSTICE O'CONNOR: Exemption. The statutory  
4 exemption. I thought that was what we were looking at.

5 MR. FLORES: Yes, that's what I was referring  
6 to. The Federal Circuit didn't articulate a standard for  
7 that. The Federal Circuit approved the District Court's  
8 use of the Intermedics standard, under which preclinical  
9 experiments are potentially --

10 JUSTICE O'CONNOR: Well, but it's certainly --  
11 that the FDA considers only safety, and nothing else, that  
12 it was directed at generic drugs, not others, and that  
13 there was a cutoff point earlier than that argued by the  
14 Government and the Petitioner for what is exempt  
15 preclinical trial information.

16 MR. FLORES: The Federal Circuit's opinion, I  
17 believe -- the Federal Circuit's opinion rejects the  
18 rational predicate theory. It does not articulate an  
19 alternative standard to that. It merely ----

20 CHIEF JUSTICE REHNQUIST: They spent about ten  
21 pages in the appendix trying to do that.

22 MR. FLORES: But Federal Circuit didn't do that.  
23 That was discussion in there. It gave a lot of background  
24 about the statute, which may not have been necessary for  
25 its ultimate holding. But the Federal Circuit, when it

1 comes down to it, didn't do anything other than approve  
2 the District Court's interpretation.

3           Now, if the Federal Circuit did something  
4 different than that, which we just -- which is -- Integra  
5 does not believe is the case, its judgement should be  
6 upheld on the grounds articulated, that it could discern  
7 no error in the District Court's judgement -- in the  
8 District Court's denial of Merck's motion for judgement as  
9 a matter of law.

10           To respond to one of Justice O'Connor's earlier  
11 questions, "Does this Court have to get into a Rule 50  
12 review," the answer is no, because Merck failed to  
13 preserve its right to Rule 50 review. In the District  
14 Court, in the Federal Circuit, the -- Merck argued the  
15 rational predicate standard as a matter of law. That was  
16 rejected.

17           Rule 50 review, under the Intermedics standard,  
18 is an entirely different argument, and Merck never raised  
19 that argument in -- before the Federal Circuit. In its  
20 brief, Merck relies, on pages 50 and 51 of its brief to  
21 the Federal Circuit, saying there it argued substantial  
22 evidence. But what it argued there was, the experiments  
23 are rational predicates. Merck never argued, before the  
24 Federal Circuit, that the verdict can't be sustained under  
25 Rule 50, under the Intermedics standard, as opposed to the

1 rational predicate standard, so it's not entitled to that  
2 review here.

3 JUSTICE GINSBURG: The dissenting judge did not  
4 -- the dissenting judge, Judge Newman, did not read the  
5 Court's opinion the way you do. Is that correct?

6 MR. FLORES: That is correct, Your Honor.

7 JUSTICE GINSBURG: Maybe we should take that  
8 into account, to some extent, that someone who  
9 participated on the bench had a different take on what her  
10 colleagues were saying?

11 MR. FLORES: That is certainly a consideration,  
12 but we disagree with Judge Newman on that point.

13 JUSTICE KENNEDY: Is there a difference between  
14 you and Merck concerning the scope and extent of the  
15 common law research exemption? And if there is, does that  
16 even enter into our case?

17 MR. FLORES: That issue hasn't entered into the  
18 case, so there's been no differences articulated, Your  
19 Honor.

20 And to get back to the point that Merck did not  
21 preserve its right to Rule 50 review under the Intermedics  
22 standard, even if it had raised that issue before the  
23 Federal Circuit, clearly the Federal Circuit didn't reach  
24 that issue. And if the Federal Circuit didn't reach an  
25 issue that was properly presented before it, that was

1 error, and Merck would have had to seek relief from that  
2 error. And it did not do so in its petition for  
3 certiorari. So, I do not believe this Court even needs to  
4 address the issue of Rule 50 review.

5           There is no dispute in this case as to the  
6 substantive standard that governs the scope of Section  
7 271(e)(1), and Merck, having failed to preserve its rights  
8 to Rule 50 review under the Intermedics standard, there  
9 is no controversy for this Court to decide.

10           If the Court does reach the issue of Rule 50  
11 review under Intermedics, it is -- the case should be  
12 decided under the basic principles that it is the  
13 exclusive province of the jury to weigh the evidence and  
14 to determine the credibility of the witnesses.

15           And my time is up, but -- almost -- but I'll say  
16 one thing. After 25 days of trial, the District Judge, in  
17 his denial of Merck's motion for judgement as a matter of  
18 law, expressly said that the jury had reasonable cause to  
19 disregard the testimony of Merck's main witness, Dr.  
20 Cheresh. And, on that ground alone, the judgement with  
21 the Federal Circuit should be sustained. Merck can't be  
22 rescued from the jury's verdict unless this Court  
23 determines, as a matter of law, that the jury was required  
24 to believe the testimony of Dr. Cheresh. And Merck can't  
25 show that, and hasn't even attempted to show that.

1 Unless there are any questions --

2 CHIEF JUSTICE REHNQUIST: Thank you, Mr. Flores.

3 Mr. Rosenkranz, you have two minutes remaining.

4 REBUTTAL ARGUMENT OF E. JOSHUA ROSENKRANZ

5 ON BEHALF OF PETITIONER

6 MR. ROSENKRANZ: Thank you, Your Honor.

7 With my two minutes, I want to make one  
8 overarching important point, and it's really in response  
9 to a question Justice Scalia asked.

10 The emphasis in the statute is about the use, so  
11 let's get past labels about, Is this drug discovery or  
12 basic research, or is it, as Merck says, optimization on  
13 the lead drug candidate, and look at exactly what was  
14 occurring here. Here, this was not a, "Gee, we'd like to  
15 see what affects angiogenesis." Merck knew what affected  
16 angiogenesis. It had a structure. And if you look at  
17 page 42 of the supplemental appendix, you will see that  
18 structure. It knew exactly what that structure did and  
19 how it did it. It then tweaked it by changing, literally,  
20 three atoms to compare that activity with other activity,  
21 exactly the sorts of research that any drug innovator  
22 would do to verify that they have the best and most  
23 effective candidate. Then, with -- and with every single  
24 one of its experiments, it was examining information that  
25 was relevant to mechanism of action, pharmacology,

1 pharmacokinetics, and efficacy. With 10 percent of the  
2 experiments, it was also running them in parallel with a  
3 series of analogs that were designed to look exactly like  
4 the RGD peptides, and to work exactly like the RGD  
5 peptides. And no rational drug innovator ever proceeds to  
6 clinical trials, nor does the FDA want it to, without  
7 conducting that research, because you don't spend millions  
8 of dollars for expensive toxicology studies until you know  
9 you've got the safest and most effective drug candidate.  
10 The FDA reviews that evidence, because it wants to know  
11 why you're proceeding with that candidate. And if you  
12 shift midstream to another lead, as Merck, in fact, did in  
13 this very case, the FDA wants to understand why.

14           So each of those experiments, even in  
15 comparison, developed information that is relevant to the  
16 FDA.

17           Thank you, Your Honors.

18           CHIEF JUSTICE REHNQUIST: Thank you, Mr.  
19 Rosenkrantz. The case is submitted.

20           [Whereupon, at 11:03 a.m., the case in the  
21 above-entitled matter was submitted.]

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