IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

UNITED THERAPEUTICS CORPORATION,
Plaintiff,
v.
LIQUIDIA TECHNOLOGIES, INC.,
Defendant.

C.A. No. 20-755-RGA-JLH

Volume III

J. Caleb Boggs Courthouse
844 North King Street
Wilmington, Delaware

Wednesday, March 30, 2022
8:30 a.m.
Bench Trial

BEFORE: THE HONORABLE RICHARD G. ANDREWS, U.S.D.C.J.

APPEARANCES:

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BY: JACK B. BLUMENFELD, ESQUIRE
BY: MICHAEL J. FLYNN, ESQUIRE
BY: SARAH E. SIMONETTI, ESQUIRE

-and-

GOODWIN PROCTER LLP
BY: WILLIAM C. JACKSON, ESQUIRE
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- and -

APPEARANCES CONTINUED:

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BY: ERIK B. MILCH, ESQUIRE
BY: KYUNG TAECK MINN, ESQUIRE

For the Defendants

08:07:47
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*** PROCEEDINGS ***

08:29:50 DEPUTY CLERK: All rise. Court is now in session. The Honorable Richard G. Andrews presiding.

08:29:56 THE COURT: All right. Good morning, please be seated.

08:29:58

I'm not sure exactly what the order is here, but whoever is next, please do something.

MS. KIM: Good morning, Your Honor. Mandy Kim on behalf of UT. And we call Dr. Waxman to the stand.

MR. FLYNN: Your Honor, may I approach?

THE COURT: Sure.

DEPUTY CLERK: Please state and spell your full name for the record.

THE WITNESS: Aaron B. Waxman, A-A-R-O-N. Middle initial B. Last name W-A-X-M-A-N.

DEPUTY CLERK: Do you affirm that the testimony you are about to give to the Court in the case now pending will be the truth, the whole truth, and nothing but the truth, you do so affirm?

THE WITNESS: I do.

DEPUTY CLERK: Please speak in the microphone. Please make sure you speak into it.

THE COURT: Thank you.

MS. KIM: May I proceed, Your Honor?

THE COURT: Yes.

DIRECT EXAMINATION

BY MS. KIM:

Q. Good morning, Dr. Waxman. Please introduce yourself to the Court and what you do for a living.

A. My name is Aaron Waxman, and I'm a physician,

pulmonary critical care medicine, at the Brigham and Women's Hospital in Boston and Associate professor of medicine at Harvard Medical School. And I'm the executive director of the Center for Pulmonary Heart Disease and more specifically the director of the pulmonary vascular disease program at Brigham and Women's Hospital.

Q. What are your responsibilities in these positions?

A. So as the executive director, I oversee the broader pulmonary heart disease program, which includes all aspects of pulmonary vascular disease and right-heart failure and oversee eight faculty that work on the program as well as a large clinical trials and basic research program.

Q. Please briefly describe your educational background.

A. Undergraduate, I went to GW, George Washington University, in D.C. and then went on to get a Ph.D. in anatomy and neuroscience, and then after that, an M.D. at Yale University where I also did a number of research fellowships and then all my post-graduate training in internal medicine, pulmonary, and critical care medicine.

Q. And what area of medicine have you been focused on after medical school and fellowships?

A. Again, broadly speaking, I've practiced the full range of pulmonary and, specifically, critical care medicine and then more specifically pulmonary vascular disease and care of patients with pulmonary hypertension.

08:34:33 Q. How long have you been treating patients with pulmonary hypertension?
08:34:33 A. About 30 years.
08:34:33 Q. And treating those patients, have you used drugs by inhalation?
08:34:33 A. I have, yes.
08:34:33 Q. And how many pulmonary hypertension -- and I might interchangeably use that with just PH for short. Is that okay with you?
08:34:33 A. Yes.
08:34:33 Q. How many PH patients do you follow?
08:34:33 A. Me personally? About 800 patients.
08:34:33 Q. And how many PH patients does the Center for Pulmonary Heart Disease at the Brigham center does it follow?
08:34:33 A. So, we follow about 2,000 patients with pulmonary hypertension at the Brigham.
08:34:33 Q. Have you been involved in any clinical trials involving treatments for pulmonary hypertension?
08:34:34 A. I have. I mean, over the course of the years, pretty much any drug that's now approved, we were involved in those clinical trials. And we currently have about 16 clinical trials active in our program, of which some are investigator-initiated but most are industry sponsored.
08:34:34 Q. And do some of those involve UT?

08:34:34 A. They do, yes.
08:34:34 Q. Have you received any awards or honors in the course of your career?
08:34:34 A. I have received some. The most recent probably borne out of my work in the COVID ICU, the Distinguished Clinician Award at Brigham.
08:34:34 Q. Have you provided a CV in connection with your work in this case?
08:34:34 A. I have, yes.
08:34:34 Q. Please turn in your binder to PTX 506, and let me know when you have that in front of you.
08:34:34 A. I have it.
08:34:34 Q. Is this an accurate copy of your CV?
08:34:34 A. As of September of 2021, it is, yes.
08:34:34 MS. KIM: Your Honor, we move PTX 506 into evidence.
08:34:36 MR. DAVIES: No objection, Your Honor.
08:34:36 THE COURT: Admitted without objection.
08:34:37 (PTX Exhibit No. 506 was admitted into evidence.)
08:34:38 MS. KIM: Your Honor, I proffer Dr. Waxman as an expert in internal medicine pulmonary disease and critical care medicine and the treatment of pulmonary hypertension, including by inhalation.
08:34:38 MR. DAVIES: No objection.
08:34:40
08:34:43
08:34:46
08:34:49

08:34:51 THE COURT: All right. You may proceed.

08:34:52 MS. KIM: Thank you.

08:34:54 BY MS. KIM:

08:34:54 Q. Dr. Waxman, what were you asked to do in this case?

08:34:58 A. I was asked to review the '793 patent as well as a number of materials and provide my opinion as to infringement and validity of the UTC patent for inhaled Treprostinil.

08:35:09 Q. Have you worked with us to create a set of slides to help demonstrate your testimony here today?

08:35:14 A. I have, yes.

08:35:20 Q. And what does this slide show?

08:35:21 A. This slide shows the definitions provided by myself as well as Dr. Hill in regards to the definition of a person of ordinary skill in the art or a POSA.

08:35:33 Q. In your opinion, what is the definition of a person of ordinary skill in the art?

08:35:36 A. My definition is on the left side of that. It describes someone with a degree in either an M.D. or a Ph.D. and at least two years of experience in the field as well as experience with investigation and treatment of pulmonary hypertension and the development of the potential drug candidates.

08:36:00 Q. Did you apply this definition in connection with your analysis in this case?

08:36:03 A. I did, yes.
08:36:06 Q. Dr. Hill used a different definition. Would your
08:36:08 opinions change if you used his definition?
08:36:10 A. No.
08:36:11 Q. Were you a person of ordinary skill in the art as of
08:36:14 May 2006?
08:36:14 A. I was, yes.
08:36:16 Q. Please turn to JTX 3 in your binder, and let me know
08:36:23 when you're there.
08:36:23 A. I'm there.
08:36:25 Q. Do you recognize this document?
08:36:26 A. I do, yes.
08:36:29 Q. What is it?
08:36:29 A. This is the '793 patent.
08:36:32 Q. Have you reviewed this patent?
08:36:33 A. I have, yes.
08:36:36 Q. Can you generally describe the -- what the '793
08:36:39 patent is directed to?
08:36:40 A. The '793 patent describes a method of using
08:36:45 Treprostinil as inhaled therapy for the treatment of
08:36:48 patients with pulmonary hypertension.
08:36:50 Q. And what was your impression in reading the science
08:36:54 of the patent?
08:36:54 A. Well, I think it's very clear that inhaling
08:36:58 Treprostinil results in an effective response, as far as

08:37:03 reducing pulmonary artery pressure and reducing pulmonary
08:37:07 vascular resistance, which are the fundamental components of
08:37:11 pulmonary hypertension.
08:37:14 Q. And up on the slide, can you explain what we see over
08:37:20 on the left-hand side with respect to the Figure 10.
08:37:23 A. Yeah. The -- on the left of this slide shows the
08:37:27 graphic representation of the impact of inhaled Treprostinil
08:37:31 on pulmonary artery pressure in the upper left and the
08:37:35 pulmonary vascular resistance in the lower left compared to
08:37:38 the placebo.
08:37:41 Q. What are the asserted claims of the '793 patent in
08:37:44 this case?
08:37:46 A. The asserted claims have to do with treatment of
08:37:50 patients -- sorry. We can see them up there on the -- on
08:37:54 the slide. The asserted claims are 1, 4, 6, 7 and 8.
08:37:59 Q. What is Claim 1 directed to?
08:38:01 A. Claim 1 directs to the treatment of pulmonary
08:38:05 hypertension, specifically inhalational therapy for patients
08:38:10 suffering from pulmonary hypertension, delivered in a
08:38:13 therapeutically effective dose and through an inhalational
08:38:18 device in a single event therapeutically effective dose and
08:38:24 dose range of 15 to 90 micrograms that can be delivered in
08:38:29 one to three breaths.
08:38:31 Q. Have you prepared a demonstrative that summarizes the
08:38:33 opinions you'll be providing today?

A. Yes.
Q. And what are they?
A. As you can see up there, claim 1 of the '793 does provide an adequate written description of the invention such that the '793 patent enables those of us who are POSAs to be able to make the invention, and that Liquidia's accused product, the Liquidia '861, infringes on all aspects of the asserted claims of the patent.
Q. Thank you, Dr. Waxman. Before we get into your opinions regarding validity and infringement of the patent, I want to back up briefly and just provide some background as to the state of the art in May of 2006. What is pulmonary hypertension?
A. So, in the simplest definition is pulmonary hypertension simply describes an increased pressure in the blood vessels of the lung and then more specifically, we think of it as a complex disease that involves remodeling, and it's really a pathologic process that involves progressive change to the blood vessels of the lungs so they become thicker and stiffer. As they become thicker and stiffer, they increases the resistance to blood flow through the lung, and that results in increasing pressure and increasing pulmonary vascular resistance, and, ultimately, that leads to dysfunction of the right ventricle of the heart and, ultimately, failure of the right ventricle. And

that's what leads to the death of the patient.

Q. And are there different forms or classifications of pulmonary hypertension?

A. There are. I like to think of it in terms of pre and postcapillary disease because that really gets to the pathology, the pathophysiology, and the pathogenesis. And when we think about precapillary, we're really talking about all that remodeling that I was referring to in the pulmonary arterial bed.

There is postcapillary disease as well that we can breakdown into isolated postcapillary, which is really a passive drive for the pressure in the pulmonary arterial bed because of the increased pressure in the left heart. And then there is a mixed picture. As long as you have long-standing, untreated postcapillary disease. It drives remodeling of the pulmonary arterial bed so you end up with a combined pre- and post-capillary picture.

And then there are the groupings which the groups we think -- what used to be called WHO now called WSDH are, really, an arbitrary approach to categorizing the disease based on associated or comorbid conditions that go along with pulmonary hypertension.

Q. With respect to the WHO categories that you just mentioned, do all five of those categories exhibit elevated blood pressure as you just mentioned with respect to your

08:41:29 1 understanding of pulmonary hypertension?
08:41:31 2 A. So that is the unifying theme for all of them to call
08:41:34 3 them pulmonary hypertension. They all require a hemodynamic
08:41:38 4 assessment that shows elevated pressure in the pulmonary
08:41:41 5 arteries.
08:41:42 6 Q. And earlier, you said that the center -- excuse me --
08:41:45 7 center has over 2,000 pulmonary hypertension patients.
08:41:49 8 What's the breakdown of the forms for those patients?
08:41:52 9 A. So for us, to call a patient or at least diagnose a
08:41:57 10 patient with pulmonary hypertension requires that they've
08:42:00 11 had a right-heart catheterization. An echo is a good
08:42:05 12 screening tool, but it's not a diagnosis. Once we do it,
08:42:08 13 make the diagnosis, I would say our breakdown in our program
08:42:12 14 is around 25 to 28 percent of the patients will have what's
08:42:16 15 called group one disease. Probably about 35 to 40 percent
08:42:22 16 of the patients will have group two disease. And of those,
08:42:25 17 probably about two-thirds of them will have combined pre-
08:42:29 18 and postcapillary pulmonary hypertension. And then probably
08:42:33 19 about 25 percent of our patients will have group three
08:42:36 20 disease. Probably less than eight percent will have group
08:42:40 21 four disease. And the remainder will have group five, which
08:42:44 22 is really kind of a catchall basin for the rest of the
08:42:47 23 patients.
08:42:48 24 Q. And was that breakdown accurate also back in the year
08:42:51 25 2006?

08:42:52 A. Yes.
08:42:56 Q. Do you also have patients with mixed groups, such as,
08:42:58 like, group one and two or group one and group three?
08:43:03 A. Yeah, I think that illustrates the shortcomings of
08:43:06 the groupings, that it's pretty rare to find a patient that
08:43:09 just fits into one group. And I think that's one of the
08:43:13 drivers for our current investigation, like PVDOMICS, that
08:43:17 Dr. Hill and I were both involved in where we have patients
08:43:21 that have group one plus group two, group one plus group
08:43:24 three. If you have a patient with connective tissue disease
08:43:27 who smoked for 20 or 30 years, they're likely to have a
08:43:31 mixed picture. Somebody develops a malignancy, they could
08:43:35 end up with group five plus group one. So it's kind of a
08:43:38 whole mix and match of different groupings.
08:43:42 Q. And were there any treatments for pulmonary
08:43:46 hypertension as of May 2006?
08:43:47 A. There were treatments. It was somewhat limited at
08:43:51 that time, but, yes.
08:43:53 Q. What were they?
08:43:53 A. We can see them on the slide. They're really three
08:43:57 targeted pathways. The prostacyclin pathway, which at the
08:44:02 time we had three treatments -- three drugs available,
08:44:06 Flolan or epoprostenol was the first agent approved, and it
08:44:11 was -- I mean, it was a great drug and remains a great drug.
08:44:15 It's just it's very cumbersome. It's a very short

half-life, about two to six minutes, so it has to be given intravenously through a tunneled catheter, so an IV catheter that goes into the -- into the heart itself and delivered by an external pump. It was cumbersome for the patient, and it was also not stable at room temperature, so it had to be kept on ice. And the other important thing, because of the short half-life, the patient had disruption of delivery, it could be a medical emergency, and it's life-threatening.

Following that, I like to think of Treprostinil or Remodulin there as the second generation prostacyclin which was, I think a big step forward, in part because of safety because the half-life is longer at four and a half hours. And it's also stable at room temperature. So it made life easier for the patient but also safer.

And then Ventavis or iloprost was an inhaled formulation, which for us, was not particularly helpful because patients had to take it six to nine times a day, so not many of our patients were compliant. And also we had a lot of side effect issues with it.

And then on top of that, we had two oral drugs, bosentan, which is an endothelin antagonist and sildenafil, which was, essentially, repurposed Viagra, which is a phosphodiesterase-5 inhibitor.

Q. And we're talking about, again, the classifications or the forms of PH, what forms can Treprostinil treat?

08:45:53 A. Well, we would use it for any form of pulmonary
08:45:59 arterial or precapillary disease.
08:46:03 Q. And in May of 2006, were there any Treprostinil
08:46:06 therapies that were provided by inhalation?
08:46:10 A. Not at that time, no.
08:46:14 Q. Let's turn to your written description opinions
08:46:18 first. Have you prepared a summary slide regarding your
08:46:21 opinions on written description?
08:46:22 A. Yes.
08:46:25 Q. What are they?
08:46:25 A. Well, I think the '793 patent provides a clear and
08:46:31 appropriate description of the invention.
08:46:35 Q. And we just talked about kind of the background as to
08:46:38 what pulmonary hypertension was. In 2006, what would a POSA
08:46:43 have understood the term "pulmonary hypertension" to mean in
08:46:49 the context of this patent?
08:46:50 A. Well, in the context of this patent, based on the
08:46:52 examples that are in the patent, it's clear that it would
08:46:55 include pulmonary arterial hypertension or precapillary
08:47:02 pulmonary hypertension, as there are a number of
08:47:03 descriptions of various forms of precapillary disease.
08:47:06 Q. Is there any description in the patent that supports
08:47:09 your opinion?
08:47:10 A. Well, there's a description of treating patients with
08:47:14 idiopathic pulmonary arterial hypertension which would fit

into group one disease. There's description of patients with what they term in there PAH or pulmonary arterial hypertension other, which would overlap with group five disease. There's also a description of treating patients with chronic thromboembolic pulmonary hypertension, which is really defining group four disease. And then there's a description in there of treating patients with pulmonary hypertension and pulmonary fibrosis, which, again, is another form of precapillary pulmonary arterial disease that would fit into group three disease.

Q. Does this study that you're explaining right now include group two patients?

A. Not specifically, no.

Q. Okay. But would a POSA reading this study have understood that they can apply it to group two patients?

A. So again. With group two. We have two different subsets. We do have patients that who develop pulmonary arterial disease and remodel their pulmonary arterial beds, and in those patients, we would consider using a pulmonary vasodilator like Treprostinil.

Q. Do you recall Dr. Hill's testimony that a POSA would not have understood the inventors were in possession of a method of treating pulmonary hypertension for at least isolated postcapillary pulmonary hypertension patients?

A. Yes.

08:48:40 Q. Do you agree with his opinion?
08:48:42 A. Well, I would agree that in purely isolated
08:48:47 postcapillary disease, yeah, we would not consider any
08:48:50 pulmonary vasodilator in that setting because the mainstay
08:48:53 of treatment is a diuretic.
08:48:55 Q. Are there other forms or subclasses in group two that
08:48:59 one would be able to treat with?
08:49:02 A. So for those patients who have a remodel pulmonary
08:49:05 arterial bed, so combined pre- and postcapillary disease, we
08:49:10 would consider using pulmonary vasodilator therapy.
08:49:16 Q. Okay. So not all forms of group two patients fall
08:49:20 under this specific isolated postcapillary PH Dr. Hill was
08:49:25 talking about?
08:49:26 A. That's correct, no.
08:49:28 Q. And as of May 2006, would you have been able to treat
08:49:33 a patient with any form of PH based only on FDA approval?
08:49:37 A. Well, at the time, FDA had only approved those drugs
08:49:40 that we already reviewed for only group one disease. But, I
08:49:46 think as clinicians, we often will make use of those drugs
08:49:51 in an off-label approach when it makes sense
08:49:54 pathophysiologically.
08:49:56 Q. So would you have also been able to treat patients
08:50:00 that have pre- and post-capillary that would be classified
08:50:04 as pre- and post-capillary group two Dr. Hill mentioned?
08:50:08 A. So for the combined pre- and post-capillary disease,

yes.
Q. So reading Claim 1 in the context of the patent, would a POSA, in your opinion, know whether isolated postcapillary PH is within the scope of the claims?
A. I think a POSA would understand that isolated postcapillary disease, again, would be treated with a diuretic and not a pulmonary vasodilator.
Q. As of May 2006, would a POSA have understood that prostacyclins would not be -- would not likely work for isolated postcapillary PH patients?
A. Yes. I mean, essentially, any pulmonary vasodilator would probably not be needed.
Q. Thank you. Let's turn to enablement. Have you prepared a slide of your opinions on enablement?
A. Yes.
Q. What are your opinions -- what are your -- at a high level, what are your opinions on enablement?
A. So, I think that the information provided in the patent provides plenty of information to enable someone who's skilled in the art to be able to make the invention.
Q. And what's the basis for your opinions?
A. Well, in the examples that are in the patent, there's plenty of information as far as the patient population to treat, how to treat, as far as a single-event therapeutic dosing that results in improved hemodynamics. There's

information about delivering it as an inhaled therapy, and there's information, I think very importantly, on dosing to get that single-event therapeutic dose.

Q. And do you recall Dr. Hill opining that, once again, a POSA or the patent is not enabled because -- he used the same rationale of isolated postcapillary group two PH patients not being enabled with the description in this patent?

Do you recall that?

A. I recall that, yes.

Q. Do you agree with his opinions?

A. Well, I think, again, as I've said, I don't agree in the sense that we wouldn't treat a postcapillary disease with a pulmonary vasodilator of any kind.

Q. And does the patent support your opinions?

A. I think it does. Like I said, there's a description in there of treating idiopathic or group one, group five with PH other, chronic thromboembolic, group four, pulmonary fibrosis, group three, and if we look at that table up there, it does describe pulmonary hypertension, but you can see there's no pulmonary capillary wedge pressure listed anywhere, so we really don't know if anyone had combined pre- or postcapillary PH.

Q. Do you recall Dr. Hill also opined that in 2006 there was no evidence that prostacyclins could treat any group two

patients?

A. Well, I would say there was certainly no published evidence, but I think, again, as clinicians, we often use medications that are available in an off-label approach. And we were certainly using inhaled epoprostenol in the hospital for those very purposes.

Q. So, in your opinion, would a POSA reading the claims in the context of the patent be able to make and use the invention without undue experimentation?

A. Yeah, I think there's plenty of information in the patent to allow us to move forward to use the invention.

Q. And would a POSA also understand that they could not use the claimed invention for isolated postcapillary PH patients?

A. I think that's just very simple pathophysiology that all of us learn about and would practice.

Q. And do you recall Dr. Hill's testimony when he said it would be virtually unpredictable that a POSA would have found developing inhaled Treprostinil to treat group two patients?

A. I actually would disagree. I think it's predictable in the sense that if you have a patient with precapillary disease, you can see improvement upon treating that patient. So I would disagree in the combined pre- and postcapillary disease.

08:54:26 Q. And would it also have been predictable that one
08:54:28 cannot treat for isolated postcapillary PH patients?
08:54:32 A. Well, I think it would be consistent with our
08:54:37 understanding of pathophysiology that we would not treat an
08:54:41 isolated postcapillary disease patient.
08:54:45 Q. Dr. Waxman, can you summarize your opinions to the
08:54:48 Court with respect to validity.
08:54:49 A. Yeah, I think that it's clear to me, in reviewing the
08:54:53 patent, that it does provide adequate written description of
08:54:58 the invention as the inventors put forth. I also think that
08:55:03 it enables a POSA to be able to make the invention and make
08:55:08 use of it.
08:55:10 Q. Thank you, Dr. Waxman. Let's turn to your
08:55:13 infringement opinions next. Have you provided a slide
08:55:15 briefly summarizing the opinions that you're going to be
08:55:17 providing on infringement?
08:55:18 A. I have, yes.
08:55:19 Q. And what are they?
08:55:20 A. That the accused product, the Liquidia 861, infringes
08:55:27 on Claims 1, 4, 6, 7 and 8.
08:55:31 Q. What is Liquidia's accused product?
08:55:34 A. Liquidia 861 is -- is a dry-powder formulation of
08:55:39 Treprostinil for inhalation.
08:55:42 Q. And is that LIQ861?
08:55:45 A. Yes.

Q. Does it also go by the brand name of Yutrepia?
A. It does.
Q. And how did you determine or analyze whether Liquidia's LIQ861 infringes the asserted claims?
A. I reviewed a number of materials, including several package inserts, the new drug application that was submitted to the FDA, as well as instructional -- what do you call it -- inserts that were -- would have been provided to patients and clinicians.
Q. Thank you. Let's start with Claim 1.
Please turn to PTX 134 in your binder.
A. Okay.
Q. Let me know when you're there.
A. I am.
Q. Do you recognize this document?
A. I do. This is a package insert that was revised in April of 2021.
Q. Is this one of the documents that you reviewed in connection with your analysis?
A. It is, yes.
MS. KIM: Your Honor, I move PTX 134 into evidence.
MR. DAVIES: No objection, Your Honor.
THE COURT: Admitted without objection.
(PTX Exhibit No. 134 was admitted into

08:56:56 1 evidence.)
08:56:57 2 MS. KIM: Thank you.
08:56:57 3 BY MS. KIM:
08:56:59 4 Q. Can you explain to the Court how this document
08:57:00 5 relates to your opinions on infringements.
08:57:02 6 A. Sure. I mean, there are a number of things in here
08:57:05 7 that clearly infringe on the patent. If you look at
08:57:09 8 indications and usage, it talks about Treprostinil as a --
08:57:14 9 an inhalation powder prostacyclin vasodilator indicated for
08:57:20 10 the treatment of pulmonary arterial hypertension, and it
08:57:24 11 describes patients suffering from pulmonary hypertension
08:57:27 12 based on a functional Class II through III symptoms. We can
08:57:30 13 look at the dosage and administration and, again, it talks
08:57:33 14 about oral inhalation. And it also talks about single-event
08:57:41 15 dosing and inhaling it in one to two breaths. It also lists
08:57:46 16 dosages there in the range of 15 to 90 micrograms. And
08:57:51 17 that's also reiterated on the next two pages and throughout
08:57:58 18 the document.
08:58:00 19 Q. And can you walk us through this demonstrative that
08:58:02 20 you prepared.
08:58:06 21 A. Sure. This demonstrative illustrates from the
08:58:09 22 package insert what I just reviewed as far as this being an
08:58:14 23 inhalational treatment for pulmonary hypertension, a
08:58:18 24 dry-powder inhaler, single-event dosing and therapeutically
08:58:23 25 effective dosing based on those dose ranges that are shown

and delivered in one to three breaths.

Q. And so what does the April 2021 package insert demonstrate with respect to Claim 1?

A. That it infringes on all of the asserted claims within Claim 1.

Q. Have you reviewed any other versions of the label or the package insert?

A. I have, yes.

Q. Please turn to PTX 469 in your binder.

A. Okay.

Q. Do you recognize this document?

A. I do.

Q. Is this one of the other versions of the labels or package inserts that you were referring to?

A. Yes. This is a revised package insert from November of 2021.

Q. Did you review this November 2021 package insert in connection with your analysis?

A. I did, yes.

MS. KIM: Your Honor, I move PTX 469 into evidence.

MR. DAVIES: No objection, Your Honor.

THE COURT: All right. Admitted without objection.

(PTX Exhibit No. 469 was admitted into

08:59:23 evidence.)
08:59:23 BY MS. KIM:
08:59:24 Q. Dr. Waxman, can you explain to the Court how the
08:59:27 November 2021 package insert relates to your opinions?
08:59:30 A. Yeah, essentially, for the same reasons that I've
08:59:34 just went over for the April insert. This says pretty much
08:59:39 the same thing, as far as this being Treprostinil inhalation
08:59:43 powder, oral inhalation for the treatment of pulmonary
08:59:47 hypertension for patients suffering from pulmonary
08:59:49 hypertension, again, based on functional class description.
08:59:53 Describes a single-event dose. It describes a
08:59:56 therapeutically effective dose. It also describes providing
09:00:00 it in one to three breaths.
09:00:03 Q. And can you explain this slide that we see up on the
09:00:07 screen.
09:00:07 A. Again, the same thing I just went over, that it
09:00:11 overlaps with each of -- of the claims in Claim 1. Again,
09:00:16 treating pulmonary hypertension by inhalation with single,
09:00:22 therapeutically effective single-event dosing and dosing in
09:00:27 the range of 15 to 90 micrograms and delivered in one to
09:00:32 three breaths.
09:00:32 Q. So what does the November 2021 package insert
09:00:35 demonstrate with respect to your analysis of Claim 1?
09:00:38 A. That the asserted product, the accused product,
09:00:43 Liquidia 861, infringes on all aspects of Claim 1.

09:00:47 Q. Please turn to DTX 113 in your binder.
09:00:50 A. Which one?
09:00:51 Q. DTX 113.
09:00:55 A. DTX.
09:00:55 Q. Let me know when you're there.
09:00:57 A. Okay.
09:01:01 Q. Do you recognize this document?
09:01:02 A. I do, yes.
09:01:04 Q. What is it?
09:01:05 A. This is the teaching instructions that are for Liquidia 861 Treprostinil -- Treprostinil inhalational powder. And this is intended to instruct patients, clinicians, providers on how to use the dry-powder inhaler.
09:01:27 Q. Is this also one of the documents that you reviewed in your analysis?
09:01:30 A. Yes.
09:01:31 MS. KIM: Your Honor, I move DTX 113 into evidence.
09:01:34 MR. DAVIES: No objection, Your Honor.
09:01:34 THE COURT: Admitted without objection.
09:01:35 (DTX Exhibit No. 113 was admitted into evidence.)
09:01:37 BY MS. KIM:
09:01:38 Q. Can you explain to the Court how the instructions for use relate to your opinions.
09:01:39
09:01:40

09:01:42 A. Well, this document describes Treprostinil as an
09:01:46 inhalational powder. Again, it talks about a dry-powder
09:01:50 inhaler for oral inhalation. It talks about the number of
09:01:54 breaths being two breaths, so within the one to three
09:01:59 breaths. It also talks about a single-event dosing and the
09:02:03 dose range overlapping with the 15- to 90-microgram doses.
09:02:08 And it has pictures that actually illustrate the dry-powder
09:02:11 inhaler quite clearly on how to use it.
09:02:16 Q. And can you explain what this slide shows on the
09:02:18 screen.
09:02:19 A. The slide goes over what I just discussed, as far as
09:02:23 Treprostinil inhalation powder to treat pulmonary
09:02:27 hypertension. It also shows a dosing chart with the doses
09:02:31 that overlap with the 15 to 90 micrograms. It shows the
09:02:36 construct of the dry-powder inhaler and that it is dosed two
09:02:44 breaths per capsule.
09:02:47 Q. Thank you.
09:02:48 Please turn to PTX 573 in your binder.
09:02:52 A. PTX 573?
09:02:54 Q. 573. Let me know when you're there?
09:03:00 A. I'm there.
09:03:00 Q. Do you recognize this document?
09:03:01 A. I do, yes.
09:03:02 Q. What is it?
09:03:03 A. This is part of the new drug application that was

09:03:08 submitted by Liquidia regarding Liquidia 861 to the FDA in
09:03:13 2020.
09:03:14 Q. Is this also one of the documents that you reviewed?
09:03:16 A. It is, yes.
09:03:18 MS. KIM: Your Honor, I move PTX 573 into
09:03:20 evidence.
09:03:21 MR. DAVIES: No objection, Your Honor.
09:03:23 THE COURT: Admitted without objection.
09:03:24 (PTX Exhibit No. 573 was admitted into
09:03:25 evidence.)
09:03:25 BY MS. KIM:
09:03:25 Q. Dr. Waxman, can you explain how this section of the
09:03:28 NDA informed your opinions.
09:03:30 A. Yeah. This is a product overview that describes a
09:03:33 lot of the features of the product and specifically goes
09:03:36 into it being a treatment for pulmonary hypertension, that
09:03:40 it's Treprostinil inhalational powder. That it's a
09:03:44 dry-powder inhaler. It's inhaled. It talks about the
09:03:49 therapeutically effective single-event dosing. It talks
09:03:52 about the dosing. And it also talks about the number of
09:03:56 breaths being within the range of one to three.
09:04:01 Q. And in this NDA section, what did Liquidia represent
09:04:07 to the FDA with respect to therapeutically effective?
09:04:10 A. It -- you mean as far as the -- it -- it talks about
09:04:18 therapeutically effective single-event dosing using the dose

09:04:22 ranges that we've already reviewed of 15 to 90 micrograms.
09:04:26 Q. And did they rely on any data for showing efficacy?
09:04:29 A. So, a lot of the comparative data is based on
09:04:33 comparing the Liquidia product to TYVASO, which is an
09:04:38 identical molecule.
09:04:40 Q. And can you explain what this slide shows.
09:04:43 A. This slide just reviews what I just went over as far
09:04:47 as the -- the components within this document, the NDA,
09:04:53 that, again, describes Treprostinil as an inhalational
09:04:57 therapy inhalational powder via dry-powder inhaler for the
09:05:02 treatment of hypertension and that it is a single-event
09:05:09 dosing through that dry-powder inhaler and also reviews the
09:05:13 comparative safety data for TYVASO and the one to two
09:05:19 breaths as a single event.
09:05:23 Q. Thank you. Please turn to PTX 1213 in your binder.
09:05:29 A. Okay.
09:05:31 Q. Do you recognize this document?
09:05:32 A. I do, yes.
09:05:34 Q. What is it?
09:05:34 A. This was a paper that was published in Vascular
09:05:39 Pharmacology by Roscigno, et al., that is comparing the
09:05:45 bioavailability, which is a measure of certain aspects of
09:05:48 the pharmacology of inhaled Treprostinil, and specifically
09:05:52 they were comparing the Liquidia 861 version of inhaled
09:05:56 Treprostinil to TYVASO, and showing that, as expected, since

09:06:01 the molecules are identical, that the uptake and
09:06:04 bioavailability after a single-event therapeutically
09:06:08 effective dose is administered that they would have the same
09:06:11 bioavailability.
09:06:13 Q. And did you review this document?
09:06:14 A. Yes.
09:06:16 MS. KIM: Your Honor, I move PTX 1213 into
09:06:19 evidence.
09:06:20 MR. DAVIES: No objection, Your Honor.
09:06:21 THE COURT: All right. Admitted without
09:06:22 objection.
09:06:24 (PTX Exhibit No. 1213 was admitted into
09:06:24 evidence.)
09:06:24 BY MS. KIM:
09:06:26 Q. Can you explain in a little more detail what this
09:06:28 publication shows or demonstrates.
09:06:30 A. Yeah. So like I had just kind of rolled into there,
09:06:36 this is a -- an assessment of bioavailability, which
09:06:40 measures the -- kind of the uptake and the drug that's
09:06:43 available for having a therapeutic effect. If you provide
09:06:48 Liquidia 861, it works exactly the same way as TYVASO as far
09:06:52 as that uptake in bioavailability using a single-event
09:06:57 therapeutic dosing that you will see the same
09:07:00 bioavailability as you would with TYVASO.
09:07:04 Q. And did you prepare a slide that summarizes those

opinions?

A. I did, yes.

Q. And can you explain what this slide shows.

A. So this slide, again, shows that we're talking about Treprostinil as an inhaled treatment for pulmonary hypertension, and specifically a dry-powder inhaler, comparing it to TYVASO and equivalent therapeutically effective single-event dosing. And that, again, it shows the same bioavailability and safety profile as TYVASO.

Q. Now, bioavailability isn't necessarily the same thing or identical to therapeutic effectiveness; right?

A. No, therapeutically effectiveness speaks to the effect of the drug on target organ. Bioavailability simply refers to the uptake of the drug.

Q. Would a POSA, though, be able to take the bioavailability information and infer any information with respect to efficacy?

A. Well, there's two different questions. Bioavailability simply speaks to the pharmacology, and therapeutically effectiveness speaks to the effect of the drug on the target organ, which, in this case, the target organ being the pulmonary vasculature the pulmonary arterial side of that vascular and the ability to dilate the vessels, reduce the pulmonary artery pressure, and reduce the pulmonary vascular resistance.

09:08:34 Q. Could one expect for that to translate into
09:08:38 therapeutic efficacy?
09:08:38 A. Well, that would speak to therapeutically effective
09:08:41 dosing when you see a hemodynamic response. Yes.
09:08:45 Q. So, I want to briefly talk about one of the
09:08:47 limitations in Claim 1, a therapeutically effective
09:08:51 single-event dose. Can you explain to the Court what this
09:08:54 term means.
09:08:55 A. So, a single event therapeutically effective dose
09:08:59 refers to providing an effective dose of the drug in a
09:09:05 single sitting.
09:09:07 Q. And in your opinion, can a single-event dose be
09:09:10 therapeutically effective?
09:09:11 A. Well, especially in the case where we're talking
09:09:14 about a hemodynamic disease, you want to see a
09:09:17 therapeutically effective dose cause a positive change in
09:09:22 those hemodynamics. So any anything - -- a therapeutically
09:09:26 effective dose should cause a reduction in pulmonary artery
09:09:29 pressure and cause a reduction in pulmonary vascular
09:09:32 resistance, and one would expect then that that hemodynamic
09:09:35 effect would translate into a patient feeling better, doing
09:09:39 more, and probably living longer.
09:09:43 Q. Do you recall Dr. Hill's opinions in his expert
09:09:46 report regarding what "therapeutic effective" means?
09:09:50 A. I do, yes.

09:09:51 Q. What are his opinions, to your understanding?
09:09:53 A. His opinions are that a therapeutically effective
09:09:56 dose should make a patient feel better, do more, and live
09:10:00 longer.
09:10:01 Q. Do you agree with Dr. Hill's opinions?
09:10:03 A. Well, I think those opinions are taken from an FDA
09:10:06 mandate that came down, especially in pulmonary hypertension
09:10:10 clinical trial development, where the goal of these drugs
09:10:14 are to make patients feel better, live -- and do more and
09:10:18 live longer. But that applies to a clinical trial.
09:10:21 But when we're talking about the clinically
09:10:23 effective dose in a hemodynamic disease, it has to be able
09:10:28 to improve the hemodynamics, which then would translate into
09:10:32 all of those features: a patient feeling better, doing
09:10:35 more, and living longer.
09:10:37 Q. Even if the Court were to agree with Dr. Hill's
09:10:40 opinion with respect to therapeutically effective, in your
09:10:45 opinion, does Liquidia's LIQ861 product still meet this
09:10:49 claim limitation?
09:10:50 A. Yes. I mean, it's been compared nicely to TYVASO and
09:10:55 has the same -- same therapeutically effective single-event
09:11:00 dosing.
09:11:01 Q. Even just taking it once?
09:11:02 A. It -- taking it once impacts the hemodynamics in a
09:11:06 positive way that would translate into those three features

that I mentioned, feeling better, doing more, and living longer.

Q. Thank you Dr. Waxman.

Let's move on to Claim 4. Can you explain to the Court what the basis for your opinions with respect to Claim 4 are.

A. Well, Claim 4 describes an inhalation device as a dry-powder inhaler. And I think it's very clear from all the documents we just reviewed that Liquidia 861 is a dry-powder inhaler.

Q. And I think you have a slide on that. Can you explain some of the highlights from the documents that you looked at right now with respect to Claim 4.

A. Yeah. As I said, all of the documents describe -- especially the package inserts and the instructions to the patient -- specifically describe a dry-powder oral inhalation and provide it has a dry-powder inhaler, and it also speaks to the single-event dosing.

Q. Thank you. Let's move on to dependent Claim 6.

Can you explain the basis for your opinions.

A. Yeah. Essentially, the same as Claim 4, in that this is simply talking about the administration as a powder, and we've just reviewed how it's not only a powder, it is a dry-powder delivered through a dry-powder inhaler, and it is obviously Treprostinil.

09:12:33 Q. Thank you.

09:12:34 Let's move on to dependent Claim 7. Can you
09:12:37 explain the basis for your opinions.

09:12:39 A. Yes. So, here Claim 7 describes the particle size
09:12:44 being less than 5 microns in diameter.

09:12:51 Q. Can you turn to PTX 20 in your binder. And let me
09:12:55 know when you're there.

09:13:07 A. Okay.

09:13:09 Q. Do you recognize this document?

09:13:10 A. I do, yes.

09:13:12 Q. What is it?

09:13:12 A. It's -- so, this was another part of the new drug
09:13:15 application that was submitted to the FDA by Liquidia
09:13:20 regarding Liquidia 861 and submitted in 2020.

09:13:24 Q. Did you review this document?

09:13:25 A. I did, yes.

09:13:30 MS. KIM: Your Honor, I move PTX 20 into
09:13:31 evidence.

09:13:32 MR. DAVIES: No objection Your Honor.

09:13:33 THE COURT: Admitted without objection.

09:13:34 (PTX Exhibit No. 20 was admitted into evidence.)

09:13:35 BY MS. KIM:

09:13:36 Q. Can you explain what this section of the NDA shows.

09:13:39 A. Yeah, this is, essentially, a product summary of the
09:13:43 characteristics and features of the dry-powder or the

09:13:46 inhalational powder of Treprostinil.
09:13:54 Q. And how does this relate to your opinions on
09:13:59 infringement?
09:13:59 A. Well, this document, because it talks about the
09:14:03 chemical properties the physical properties of the drug, it
09:14:06 actually says a number of -- in a number of places in the
09:14:09 document, like on Page 12 and Page 62 and 63, it describes
09:14:15 the particle size of 1 to 5 microns and then specifically in
09:14:19 the tables on 62 and Page 62 and Page 63, it describes
09:14:24 particle size of being 3.5 microns.
09:14:28 Q. Thank you.
09:14:29 Let's move on to dependent Claim 8. Can you
09:14:31 explain to the Court what the basis for your opinions are?
09:14:34 A. So, in Claim 8, it describes the formulation as
09:14:39 containing no -- no metacresol which is a preservative that
09:14:44 is sometimes added, and it is not part of the formulation of
09:14:49 Treprostinil.
09:14:50 Q. What are the components that are identified in the
09:14:54 documents that you reviewed?
09:14:54 A. You can see here that on the demonstrative, it
09:15:00 describes the ingredients on top of Treprostinil as
09:15:05 trehalose polysorbate 80, L-leucine sodium citrate, and
09:15:09 sodium chloride.
09:15:12 Q. Thank you.
09:15:12 Dr. Waxman, do you have an opinion of whether

09:15:16 Liquidia induces infringement of the asserted claims?
09:15:17 A. I do yes.
09:15:19 Q. What are they?
09:15:20 A. I think it's pretty clear that they do induce
09:15:23 infringement.
09:15:24 Q. And what's the basis for your opinion?
09:15:30 A. Well, I think this instructions for use that we went
09:15:33 over earlier, the Liquidia 861 Treprostinil inhalational
09:15:39 powder instructions explain very clearly to a physician and
09:15:45 a clinician and, most importantly, the patients on how to
09:15:47 use the product and, therefore, instruct them on
09:15:51 infringement of the patent.
09:15:54 Q. Dr. Waxman, can you summarize your opinions for the
09:15:56 Court.
09:15:56 A. I think it's pretty clear from everything we've gone
09:16:00 over that the Liquidia 861 product infringes on all of the
09:16:04 asserted claims of the patent.
09:16:09 MS. KIM: Thank you. I have no further
09:16:09 questions.
09:16:12 THE COURT: Cross-examination.
09:16:14 MR. DAVIES: May I approach?
09:16:37 THE COURT: Yes.
09:16:49 MR. SUKDUANG: May I approach, Your Honor?
09:16:51 THE COURT: Sure.
09:16:51 CROSS-EXAMINATION

09:16:53 BY MR. DAVIES:

09:16:53 Q. Good morning, Dr. Waxman.

09:17:32 A. Good morning.

09:17:33 Q. It's good to see you again.

09:17:36 A. Just in real life.

09:17:37 Q. Pardon?

09:17:38 A. In real life.

09:17:39 Q. It does feel a little strange, doesn't it?

09:17:42 Dr. Waxman, I want to go back to your opinion
09:17:47 regarding the scope of pulmonary hypertension in Claim 1 of
09:17:51 the '793 patent. And this was the demonstrative that you
09:17:57 used with your counsel. Is it your opinion -- well, it is
09:18:04 your opinion now that pulmonary hypertension in Claim 1
09:18:08 includes group one; correct?

09:18:10 A. Well, again, as I've said repeatedly, that pulmonary
09:18:15 hypertension includes all formulations -- forms of pulmonary
09:18:18 hypertension that involve the pulmonary arterial bed.

09:18:22 Q. So, those would be groups, in your opinion, one,
09:18:24 three, four, and five?

09:18:26 A. As well as group two, but yes.

09:18:29 Q. Why didn't you list group two on here?

09:18:31 A. Well, because I was quoting what's in the -- the
09:18:36 specific example of what's in the patent.

09:18:38 Q. So your opinion today is that pulmonary hypertension
09:18:41 in the patent includes all of groups one, two, three, four

and five?

A. Well, I think as a POSA, I'm including group two. I don't think it says specifically anything about group two, but we -- like I said earlier, when we look at that table, it doesn't list wedge pressures or list the nature of the pressures, so we really don't know whether group two patients were included or not, but certainly I would consider treating them.

Q. And in the scope of pulmonary hypertension in the '793 patent, you were including both isolated and pre- and post-combined group two patients today?

A. Well, I'm not sure what you're asking. I'm not including isolated postcapillary patients as far as a subgroup that I would treat with a pulmonary vasodilator. I am including combined pre- and post-capillary disease as a group that I would consider treating.

Q. And you understand that Claim 1 of the '793 patent refers to a method of treating pulmonary hypertension?

A. Yes.

Q. And I'm just trying to be clear on the scope of patients that you're including in that. Are you including, with respect to group two, both isolated and pre- and post-combined?

A. Well, as I said consistently, I would treat and consider treating patients who have pulmonary arterial

09:20:02 1 involvement, which would include patients who have combined
09:20:05 2 pre- and post-capillary disease.
09:20:07 3 Q. And, Doctor, maybe you're not quite understanding
09:20:10 4 what I'm asking. In offering your opinions on written
09:20:12 5 description and enablement, you need to understand what the
09:20:15 6 full scope of the claim is; do you understand that?
09:20:17 7 A. Yes.
09:20:17 8 Q. Okay. So I'm going to ask you another time. For
09:20:20 9 Claim 1, which is to a method of treating pulmonary
09:20:23 10 hypertension, with respect to group two, did you include
09:20:27 11 both isolated and pre- and post-combined patients?
09:20:30 12 A. I included patients who have pulmonary arterial
09:20:35 13 involvement, so that would be the patients with combined
09:20:37 14 pre- and post-capillary disease.
09:20:39 15 Q. So for your understanding of Claim 1, you have
09:20:43 16 included all PH patients but have carved out the isolated
09:20:48 17 group two patients; correct?
09:20:49 18 A. Well, as I said, we would not consider treating an
09:20:53 19 isolated postcapillary patient with a pulmonary vasodilator
09:20:57 20 of any kind.
09:20:58 21 Q. And in fact, you've carved them out of your
09:21:00 22 definition of pulmonary hypertension that you applied to
09:21:03 23 Claim 1; correct?
09:21:03 24 A. Well, I have not carved them out of the definition of
09:21:06 25 pulmonary hypertension. I've simply carved them out of a

patient who has pulmonary arterial involvement and who you would consider treating with a pulmonary vasodilator.

Q. So then I'm still not clear. So, let's go to JTX 3, please. And please go to the claim which is on the last page.

And again, you see in Claim 1, it refers to a method of treating pulmonary hypertension; correct?

A. Yes.

Q. And I think we -- we understand that your opinion today is that WHO groups one, three, four, and five are included; correct?

A. Well, as I've said over and over again, the groupings really don't have a whole lot of bearing on who we decide to treat. They don't really speak to pathogenesis, pathology, or pathophysiology. It all comes down to, really, pre- versus postcapillary disease, and pulmonary hypertension simply defines an elevated pressure in the pulmonary arterial circuit.

Q. And I understand, Doctor, that today you referred to the grouping as arbitrary; correct?

A. I've always considered it somewhat arbitrary.

Q. But you then went on to identify percentages of your patient population that fell into each of those groups; correct?

A. Well, I was asked to break it down into how they

would fit into the WHO groups.

Q. And you're able to do that with respect to the WHO groups; correct?

A. I -- I am able to do that, yes.

Q. And the patent actually refers to the WHO groups in Column 1 of the patent; correct?

A. It does.

Q. Okay. So let's go back to the term "treating pulmonary hypertension." I'm going ask you one more time. For group two, did you include all of group two when you analyzed the full scope of the term "pulmonary hypertension" in Claim 1, or was there a particular subset that you carved out of your definition?

A. Well, as I've said, we would only be treating disease that affects the pulmonary arterial bed, and by that, really, we mean a patient who has an increased pulmonary vascular resistance. We wouldn't treat a patient whose pulmonary vascular resistance was normal, and in the isolated postcapillary disease state, the pulmonary vascular resistance is normal.

Q. So, I'm still not entirely clear.

THE COURT: Mr. Davies.

MR. DAVIES: Yes.

THE COURT: Why don't you move on. I understand what his medical opinion is. You can make legal arguments

later on.

MR. DAVIES: Understood, Your Honor.

BY MR. DAVIES:

Q. With respect to precapillary pulmonary hypertension, are all the groups that are included in Claim 1, in your opinion, precapillary?

A. Well, what's described in here as far as precapillary disease in the examples -- I'm sorry. Ask the question again.

Q. There's a reference of I couldn't -- I'm sorry. I apologize. I apologize.

If you look, there's a reference on your demonstrative to precapillary pulmonary hypertension.

A. Yes.

Q. And is it your opinion that only precapillary pulmonary hypertension patients are included within the definition of pulmonary hypertension for -- with respect to Claim 1?

A. Well, this gets to exactly what I've been saying over and over again, that "precapillary" implies disease in the pulmonary arterial bed. And patients with an increased pulmonary vascular resistance where there is disease, pathology, pathophysiology that reflects a change in blood flow through the pulmonary arterial circuit, would be candidates for treatment with pulmonary vasodilators.

09:25:16 Q. And Dr. Waxman, do you -- do you recall being deposed
09:25:19 in this case.
09:25:19 A. I do, yes.
09:25:20 Q. And you were deposed. You were asked questions about
09:25:22 the scope of pulmonary hypertension in Claim 1. Do you
09:25:25 recall that?
09:25:25 A. I do, yes.
09:25:29 MS. KIM: Before you put that up, can you let me
09:25:31 know what pages you're referring to so that I can see what
09:25:33 it is?
09:25:34 MR. DAVIES: I'm sorry. I'm on Page 117 of
09:25:36 Dr. Waxman's District Court deposition.
09:25:39 And, Dr. Waxman, there should be a copy in your
09:25:42 binder there as well. Just let me know once you're there.
09:25:44 THE WITNESS: What tab is it?
09:25:47 MR. DAVIES: It should be labeled Depo
09:25:48 Transcript District Court.
09:25:51 THE WITNESS: Okay.
09:25:53 MS. KIM: Your Honor, if I may, now that I know
09:25:55 what page he's referring to, I think I know what Mr. Davies
09:26:00 is going to use this for, and I would say it doesn't provide
09:26:03 the full context of Dr. Waxman's testimony at his
09:26:07 deposition. If Mr. Davies -- if we could hear some of the
09:26:10 other questions that he's not pointing to because I see that
09:26:13 he said Page 117.

09:26:14 THE COURT: All right. Well, why don't we see
09:26:17 what he does, and then you can make an objection in context.
09:26:23 MS. KIM: Thank you.
09:26:24 BY MR. DAVIES:
09:26:24 Q. And, Dr. Waxman, are you at Page 117?
09:26:26 A. Yes.
09:26:27 Q. And you can refer to Page 116 for some context, but
09:26:30 you'll see I'm asking you about the plain and ordinary
09:26:33 meaning that you applied to "pulmonary hypertension" of
09:26:36 Claim 1; correct?
09:26:37 A. Yes.
09:26:40 Q. Okay. And if you go to Page 117, you were asked, "In
09:26:47 your opinion, does it" -- talking about pulmonary
09:26:51 hypertension here -- "describe the treatment of group three
09:26:53 pulmonary hypertension?"
09:26:54 And your answer was "In this application, it
09:26:56 does not."
09:26:57 Do you see that?
09:26:58 A. I see that. Yes.
09:26:59 Q. And that was your testimony?
09:27:00 A. That was my literal testimony, yes.
09:27:05 THE COURT: All right. So you say it's your
09:27:08 literal testimony. What do you mean by that?
09:27:12 What's your explanation?
09:27:13 THE WITNESS: Sure. So, I think I was -- there

was a lot of questions about specific wording within the claims, and the claims themselves do not literally speak of group one, two, three, four or five. But when we look at the examples within the patent, it certainly describes a lot of examples of precapillary pulmonary hypertension, which I've kind of been focusing on quite a lot. And certainly, patients with pulmonary fibrosis, as are described in the patent, are a precapillary disease. Those would fit into a group three, it's just not literally spoken of in the claims.

BY MR. DAVIES:

Q. You were also asked "In your opinion, does Claim 1 describe treatment of group four?"

And again, your answer was no; correct?

A. Again, literally, it did not speak of group four, but again, I have kind of been pretty consistent about my description of precapillary disease, pulmonary arterial disease, and the examples within the patent also.

Q. And then you were asked about group five and, again, you said no.

A. And again, same answer in that it is described in the examples but not specifically or literally described in the claims.

Q. And so then you were asked "In offering your opinions in your expert declarations offered in this case, the only

group that you included within Claim 1's reference to pulmonary hypertension is group one pulmonary arterial hypertension; correct?"

And for that you responded, "The only group that I included is pulmonary arterial hypertension."

And I asked "Understood. That's group one; correct?" And you said that includes group one.

And then I said, "As of May 2006, would that have included any other groups?"

And you said, "No."

Correct?

A. Well, I think there, I'm speaking as a clinician and kind of got wrapped up in the pulmonary arterial hypertension, but, again, my emphasis was on pulmonary arterial hypertension and pulmonary -- excuse me pulmonary arterial disease.

THE COURT: And, Doctor, do you do much testifying in patent cases?

THE WITNESS: No.

THE COURT: Is this your first time?

THE WITNESS: In court, yes.

THE COURT: Thank you.

MS. KIM: And Your Honor, I'd like to re-raise my request to just show up on the screen.

THE COURT: You can do that on redirect.

09:29:47 MS. KIM: Okay. Thank you.
09:29:49 BY MR. DAVIES:
09:29:49 Q. Can we go, please, to PTX 1213.
09:29:55 And Dr. Waxman, this was a publication that you
09:30:15 talked about -- oh, I'm sorry. Just let me know once you're
09:30:19 there.
09:30:19 A. PTX 1213?
09:30:21 Q. I believe it's 1213. Yes, 1213. It's the Roscigno,
09:30:21 et al., paper?
09:30:32 A. That's in the other binder.
09:30:34 Q. This is in -- yes, I apologize. This is in counsel's
09:30:38 direct binder. I apologize. The white binder.
09:30:41 A. Oh, sorry.
09:30:42 Q. No problem. That was my fault.
09:30:46 A. Okay.
09:30:50 Q. And you acknowledge that this paper is a measure of
09:30:56 comparative bioavailability of both TYVASO and LIQ816;
09:31:01 correct?
09:31:01 A. Correct.
09:31:01 Q. And a the bioavailability that's being looking at
09:31:03 here is systemic bioavailability; correct?
09:31:06 A. Yes.
09:31:06 Q. And the blood levels that are being taken are being
09:31:09 taken from a systemic vein, not in the lungs; correct?
09:31:14 A. Peripheral vein, yes.

09:31:15 Q. And the site of action for Treprostinil in treating
09:31:19 PH is not in the systemic vasculature; correct?
09:31:22 A. Not in treating pulmonary hypertension pulmonary
09:31:25 hypertension. It would be in the lung.
09:31:25 Q. So this paper does nothing to measure the level of
09:31:29 either TYVASO or LIQ8619, the Treprostinil in those
09:31:33 products, at the actual site of action in the lungs;
09:31:37 correct.
09:31:37 A. Well, I wouldn't agree with that. I mean, if you
09:31:40 have a systemic level circulating throughout the body, it's
09:31:43 throughout the body. And it also has trans -- I would say
09:31:48 transferred across multiple membranes to get into the
09:31:52 systemic circulation. So it's certainly having an effect
09:31:57 because of those levels in the pulmonary arterial system.
09:32:01 Q. Understand that an artery would have to pass through
09:32:05 the pulmonary vasculature to get there, but this paper says
09:32:08 nothing about the relative levels that Treprostinil achieved
09:32:10 with these two products in the lungs; correct?
09:32:14 A. Well, again, blood is blood. It's throughout the
09:32:16 entire body, so if you're measuring what's bioavailable in a
09:32:24 peripheral stick or a peripheral blood sample, that is
09:32:26 reflective of the whole system, the whole body.
09:32:29 Q. But it doesn't tell you how much passed through the
09:32:32 lungs and the rate at which it passed through the lungs;
09:32:34 correct?

09:32:35 A. I mean, specifically, you're just measuring blood
09:32:38 levels, so that's what you're measuring.
09:32:43 Q. Bioavailability, I think you said, is not a measure
09:32:45 of therapeutic effectiveness; correct?
09:32:48 A. It is simply a measure of the quantity that's in --
09:32:52 available to the systems.
09:32:54 Q. And this study was done in healthy subjects not, PH
09:32:58 patients; correct?
09:32:59 A. Correct.
09:33:00 Q. Is there remodeling that goes on -- I think that you
09:33:03 discussed in PH patients -- that would not be addressed by
09:33:06 this bioavailability study?
09:33:08 A. I'm not sure what you're asking. I mean, there's
09:33:12 certainly remodeling that goes on in the pulmonary arterial
09:33:14 system of patients with pulmonary arterial disease and not
09:33:18 in normal, healthy controls. But bioavailability is
09:33:23 measuring the serum quantity of the drug in the blood.
09:33:28 Q. And this is measuring the serum quantity of the drug
09:33:31 of Treprostinil in healthy subjects and not PH patients;
09:33:34 correct?
09:33:35 A. In this case, yes.
09:33:38 Q. Bioavailability is not a measure of hemodynamics, is
09:34:13 it?
09:34:13 A. Not specifically, no.
09:34:23 Q. You said on direct that in your opinion, that

09:34:26 approximately two-thirds of the group two patients were pre-
09:34:28 and post- combined group two patients; is that correct?
09:34:31 A. In my programs, population of the patients who have
09:34:36 group two disease, about two-thirds of those had combined
09:34:40 pre- and post-capillary disease.
09:34:43 Q. Do you know whether in 2006 -- strike that.
09:34:49 In 2006 -- in 2006, is it your opinion that
09:35:01 isolated -- sorry, in 2006, would this two-thirds have also
09:35:05 applied to the percent of pre- and post-combined patients in
09:35:09 group two?
09:35:09 A. I would say that the breakdown of patients in our
09:35:15 program -- and I would say in 2006, I was actually at the
09:35:19 Mass General Hospital, not at the Brigham and Women's
09:35:23 Hospital, but it was, essentially, the same program. It
09:35:25 wasn't as big then, but it was certainly growing. But I
09:35:29 would say it's pretty much the same breakdown as far as the
09:35:34 percentages of patients who were in each subgroup.
09:35:38 Q. Can you go in the -- we're now in the black binder,
09:35:43 the one that we passed up. And there should be a tab in
09:35:46 there right before your depo transcript for an article
09:35:51 that's Assad 2016. And just let me know once you're there.
09:36:05 A. Okay.
09:36:09 Q. And this is in the major journal of the American
09:36:14 College of Cardiology --
09:36:14 A. Correct.

09:36:16 Q. -- correct, Doctor?
09:36:18 A. Yes.
09:36:18 Q. This article?
09:36:19 There's two authors that are listed. There's an
09:36:22 Anna R. Hemnes and a John H. Newman. Do you see them as two
09:36:27 authors of this article?
09:36:28 A. Hemnes and John Newman, yes.
09:36:33 Q. And you have eight published articles with both of
09:36:35 them?
09:36:35 A. Yes.
09:36:36 Q. And they're from the Division of Allergy, Pulmonary,
09:36:41 and Critical Care Medicine at Vanderbilt University School
09:36:41 of Medicine?
09:36:45 A. Yes.
09:36:45 Q. And that's a well-respected group?
09:36:47 A. Yes.
09:36:48 Q. Are you -- have you seen this article before?
09:36:50 A. I can't recall.
09:36:55 Q. Can you turn to Page 2529.
09:37:08 A. Okay.
09:37:10 Q. Can you bring that up, Derrick? And go under
09:37:13 results.
09:37:16 (Discussion held off the record.)
09:37:20 BY MR. DAVIES:
09:37:20 Q. 2529. The page number is in the corner. Go one

more.

Do you see, Dr. Waxman, the section on Demographic and Clinical Characteristics?

A. Yes.

Q. Do you see they looked at a 5,797 unique patients identified for right-heart cath?

A. Yes.

Q. And then do you see below that, they have a breakdown of the number that had pulmonary hypertension?

A. Yes.

Q. And that was 2,817?

A. Yes.

Q. Okay. And of those patients in this study, they classified 20 percent of them as having PAH?

A. Yes.

Q. And then they go on to say 13 percent had combined pre- and post-capillary pulmonary hypertension. Do you see that?

A. I do.

Q. And then they go onto say that 52 percent of the patients had isolated postcapillary pulmonary hypertension; correct?

A. Correct.

Q. Okay. And this was as of 2015?

A. Yes.

09:38:30 MR. DAVIES: Your Honor, I'd like to move this
09:38:31 article into evidence.
09:38:35 MS. KIM: No objections, although, counsel, is
09:38:37 this 2016 instead of 2015?
09:38:42 MR. DAVIES: Correct. It is 2016.
09:38:42 MS. KIM: Thank you.
09:38:43 THE COURT: Does it have an exhibit number?
09:38:45 MR. DAVIES: What is the next exhibit? PTX 2000
09:38:52 -- DTX 2000.
09:38:55 THE COURT: All right. Well, it's admitted
09:38:58 without objection.
09:38:58 (DTX Exhibit No. 2000 was admitted into
09:38:59 evidence.)
09:38:59 BY MR. DAVIES:
09:39:50 Q. With respect to therapeutically effective, Doctor,
09:39:53 it's your opinion that any improvement in the hemodynamic
09:39:56 measures PAP or PVR would constitute therapeutic
09:40:01 effectiveness in the '793 patent; correct?
09:40:04 A. Well, I think what I said earlier was that to be
09:40:07 therapeutically effective, there needs to be an important or
09:40:10 clinically important impact, and by that, I mean a reduction
09:40:14 in pulmonary artery pressure and improvement or reduction in
09:40:18 pulmonary vascular resistance.
09:40:21 Q. And what's your cutoff for what is clinically
09:40:26 important improvement?

09:40:27 A. Well, I think as we talked about in my deposition, we
09:40:32 had published previously that we had found that when you see
09:40:36 at least a 12 percent reduction, that that often translated
09:40:40 into a good response to therapy in the long term. And that
09:40:45 would translate into patients feeling better, doing more and
09:40:48 living longer.
09:40:51 Q. Can you turn to Page 200 of your district court
09:40:59 deposition. And I'm back in the black binder.
09:41:02 A. 200.
09:41:15 Q. And, Doctor, I think the improvement that you just
09:41:18 described is one that you apply in your clinical practice;
09:41:21 correct?
09:41:21 A. It is, yes.
09:41:23 Q. Okay. So in your deposition, you were asked "So in
09:41:25 your opinion, any improvement in PAP cardiac output and
09:41:30 pulmonary vascular resistance would be sufficient to
09:41:34 demonstrate therapeutically effective as that term is used
09:41:37 in the '793 patent." And you answered yes.
09:41:40 Correct?
09:41:40 A. That's correct. Yes.
09:41:42 Q. So, when you did your analysis in the patent, the way
09:41:46 you treated therapeutically effective was that any
09:41:49 improvement in those three measures satisfied
09:41:53 therapeutically effective; correct?
09:41:54 A. Well, I would say that in a disease that is dependent

on pressure being high to make the diagnosis, if you can bring that pressure down, that is therapeutically effective, yes.

Q. Dr. Waxman, you talked about single-event dose this morning. You would agree that a POSA would understand the term "single-event dose" to mean the amount of Treprostinil inhaled by a patient in a single treatment session?

A. I would -- well, I think we've left some stuff out there. A single-event dose is the -- the single event where you are delivering a therapeutically effective dose.

Q. So it's -- a single-event dose would mean the amount of Treprostinil inhaled by a patient in a single treatment session which also must be therapeutically effective?

A. Well, that would be a therapeutically effective single-event dose, yes.

Q. And you would agree that Claim 1 requires any single-event dose that's given to be therapeutically effective; correct?

A. I think Claim 1 states that there needs to be a single -- a therapeutically effective single-event dose delivered in one to three breaths.

Q. With respect to LIQ861, you recall looking at the approved prescribing information?

A. The approved prescribing information?

Q. Yes. You're aware that LIQ861 is tentatively

09:43:31 approved?
09:43:32 A. I -- when you talk about the prescribing
09:43:35 information --
09:43:46 Q. And back in your binder now, and I'm at PTX 469.
09:44:05 A. So the package insert?
09:44:06 Q. Correct. The package insert.
09:44:14 And if you turn to -- you see there's some Bates
09:44:16 numbers, Doctor, in the lower right-hand corner?
09:44:19 A. The lower right-hand where the -- you're talking
09:44:23 Liquidia 008?
09:44:24 Q. Yes.
09:44:25 A. Yes.
09:44:26 Q. Can you go to the Bates number ending 8824?
09:44:29 A. Yes.
09:44:30 Q. And do you see under dosage administration it states
09:44:35 Yutrepia should be administered three to five times per day?
09:44:38 A. Yes.
09:44:38 Q. So in your opinion, that would be three to five
09:44:41 single-event doses?
09:44:43 A. That's correct.
09:44:44 Q. The label never instructs giving only a single dose
09:44:47 of LIQ861 correct?
09:44:50 A. Well, the label says administer three to five times
09:44:53 per day, contents of each capsule can be inhaled in two
09:44:58 breaths.

Q. So it does not instruct that it only be given once; correct?

A. It does not say once. It simply says three to five per day of single-event dosing.

MR. DAVIES: I have no further questions at this time, Your Honor.

THE COURT: All right. Any redirect?

MS. KIM: Just briefly, Your Honor.

REDIRECT EXAMINATION

BY MS. KIM:

Q. And, Dr. Waxman, it will be brief. Earlier, counsel asked you about what your understanding of PH and PAH was and brought up some of your deposition testimony. I just wanted to provide some context. I don't think that was -- I think you've clearly stated to the Court that your testimony has been consistent in this case. If you could turn to your deposition transcript to Page 92.

A. Oh, thanks.

Q. And do you see there on Page 92?

A. Yes.

Q. You were asked "QUESTION: What plain and ordinary meaning did you apply to the term pulmonary hypertension?"

And what was your answer?

A. I said pulmonary hypertension, as I've said over and over again, implies elevation of the pressure inside the

09:46:32 blood vessels of the lung.
09:46:34 Q. Okay. And then if you could turn to Page 95. You
09:46:40 were asked: "Do all five categories of pulmonary
09:46:44 hypertension exhibit elevated blood pressure in the lungs?"
09:46:47 And what was your answer?
09:46:47 A. That they are defined by an elevated blood pressure
09:46:52 in the lungs.
09:46:52 Q. Thank you.
09:46:58 Just one -- a few more questions on
09:47:00 therapeutically effective single-event dose. Counsel was
09:47:03 asking you if there's anything in the Yutrepia label that
09:47:08 says that you do it once a day. Do you recall that?
09:47:10 A. Yes.
09:47:11 Q. And he pointed you specifically to the language that
09:47:13 said three to five times?
09:47:14 A. Yes.
09:47:16 Q. Is there anything in the patent that says such a dose
09:47:19 has to be given only once per day?
09:47:21 A. No.
09:47:22 Q. If we could put up Claim 1 of the '793 patent. Is
09:47:36 there anything in Claim 1 that requires that the
09:47:38 single-event dose be given only once per day?
09:47:41 A. No, there's nothing there about frequency of dosing.
09:47:46 Q. And in fact, if you go to the '793 patent Column 8,
09:47:53 lines 1, 2 what is the description there?

09:48:01 A. Column 8 lines 12. Treprostinil can be administered
09:48:20 a single time per day or several times per day.
09:48:30 Q. What is the half-life of Treprostinil?
09:48:32 A. Terminal half-life is about just shy of four and a
09:48:36 half hours.
09:48:36 Q. And is Treprostinil typically used for the long-term
09:48:39 treatment of pulmonary hypertension patients?
09:48:41 A. It is, yes.
09:48:44 Q. So, you would understand that Treprostinil could be
09:48:48 used multiple times a day for these patients; right?
09:48:51 A. Yes.
09:48:52 Q. All right. I have no further questions. Thank you.
09:48:54 THE COURT: All right. Doctor, did you and
09:48:58 Dr. Hill, the defendant's expert, have a lot of professional
09:49:03 interactions?
09:49:04 THE WITNESS: I guess it depends how you define
09:49:08 a lot. We certainly interact professionally, yes.
09:49:12 THE COURT: And you weren't here yesterday;
09:49:14 right?
09:49:14 THE WITNESS: I was in the cath lab yesterday.
09:49:18 THE COURT: Yeah, so, did you -- did your -- did
09:49:20 you read the transcript of Dr. Hill's testimony yesterday?
09:49:23 THE WITNESS: I did, yes.
09:49:24 THE COURT: And in terms of his medical opinions
09:49:27 that he gave during that, was there anything that you saw in

there that you disagreed with?

THE WITNESS: I -- I thought -- I think the -- well, from a medical opinion, it seemed like most of the opinions were really related to what we're talking about here, not strictly applicable to clinical practice.

THE COURT: Well, and, really, that's it because, you know, doctors testifying about legal things is kind of outside your area of expertise. And the things that are in your area of expertise, did you see anything that he said that you disagreed with?

THE WITNESS: No. I -- I mean, we clearly agreed on postcapillary disease as something we wouldn't be treating with a pulmonary vasodilator. I think we agreed that there was room for treatment in patients with combined pre- and post-capillary disease. I think it's just a matter of the patient at the time. So, I would say we -- it looked to me like we agreed from the standpoint of medical opinion, yeah.

THE COURT: All right. Thank you.

You're done. You can step down. Watch your step.

THE WITNESS: Thank you. Should I take these binders?

THE COURT: No, leave the binders. They'll take care of them.

09:50:43 THE WITNESS: Okay. Thank you.

09:51:14 MR. DAVIES: Your Honor, Defendants call Nicholas Hill.

09:51:18 THE COURT: All right. So, Dr. Hill, you're still sworn from yesterday, so you can just sit down. All right.

09:51:41 THE WITNESS: Oh. Thank you.

09:51:47 THE COURT: And before Mr. Davies begins, Dr. Hill, you heard the questions I just asked your opponent in this case; right?

09:51:55 THE WITNESS: Yes.

09:51:57 THE COURT: Did you hear him give any medical testimony that you disagree with?

09:52:03 THE WITNESS: Well, I think our view of treatment of pre- and post-capillary pulmonary hypertension is a little bit different. I did say that there's a rationale for doing -- for treating that group, but I -- I'm a little more concerned about the safety concerns that I raised yesterday, particularly the danger of inducing pulmonary hypertension. And so, I think we don't have enough evidence in that group to justify saying, well, we should just go ahead and treat with these pulmonary hypertension-specific drugs that are available. And in fact, none have been approved to date to treat the -- that entity. So they don't seem yet to be as responsive to these

drugs as, say, group one pulmonary hypertension.

THE COURT: All right. Go ahead, Mr. Davies.

MR. DAVIES: Thank you, Your Honor.

REDIRECT EXAMINATION

BY MR. DAVIES:

Q. Welcome back, Dr. Hill. Today, I'd like to turn to your opinions on non-infringement.

Do you remember yesterday that we spoke about your definition of a POSA?

A. Yes, we did.

Q. And with respect to your opinions on non-infringement, did you apply the same POSA that you discussed yesterday?

A. Yes, I did.

Q. Can you please turn to JTX 3 in the binder in front of you.

A. Yes, I'm there.

Q. This is a copy of the '793 patent?

A. Yes, it is.

Q. Can you turn to Claim 1 at the back of the patent, please.

A. I see it.

Q. And do you see that refers to a single-event dose?

A. Yes, it does.

Q. And do you have an understanding as to what the

meaning of single-event dose is in Claim 1?
A. I think it is a dose that achieves what would be a therapeutically effective treatment of -- either by applying multiple breaths or multiple pills at the same event.
Q. When you say it's in the same event, would it be the single-dose event?
A. Yes.
Q. But it can be delivered over multiple breaths?
A. Yes.
Q. There's no definition provided in the '793 patent of a single-event dose; correct?
A. There is not.
Q. Can a single-event dose include chronic dosing?
A. I don't think so.
Q. Why not?
A. In order to achieve chronic dosing, you would have to give multiple doses over a sustained period of time.
Q. So then can a single event include any kind of multiple dosing?
A. I don't think so.
Q. Does the '793 patent discuss frequency of dosing?
A. It does.
Q. Can you turn to Column 8 at line 1. Yeah, right at the top there.
And is this the discussion you were referring

09:55:16 to?
09:55:16 A. Yes.
09:55:17 Q. And what does this passage describe?
09:55:19 A. It says that Treprostinil can be administered in a
09:55:23 single time per day or several times per day.
09:55:25 Q. And of those two descriptions, which one applies to
09:55:29 the claim?
09:55:29 A. The single time per day.
09:55:37 Q. You mentioned chronic dosing. What is chronic
09:55:40 dosing?
09:55:40 A. Chronic dosing is multiple -- or sustained treatment
09:55:48 over an extended period of time.
09:55:51 Q. Can you turn to Example 1 of the patent. It should
09:55:55 begin at Column 8, line 59.
09:56:02 And does Example 1 describe acute or chronic
09:56:05 dosing?
09:56:06 A. Clearly, it states specifically acute dosing.
09:56:11 Q. It -- and what is acute dosing?
09:56:13 A. Acute dosing, it would be a -- an administration of
09:56:19 doses over a brief interval.
09:56:22 Q. Can you turn to Example 2.
09:56:28 A. That would be page or column?
09:56:30 Q. Column 16, line 56, I apologize.
09:56:33 A. Yes, I see it.
09:56:39 Q. And does this describe acute or chronic dosing?

09:56:42 A. Specifically acute effect.
09:56:46 Q. Do either of these examples describe the
09:56:49 administration of more than one dose?
09:56:51 A. No, they don't.
09:56:57 Q. Can we go back to Claim 1 of the patent. And blow it
09:57:07 up there.
09:57:08 Do you see the reference to therapeutically
09:57:12 effective single-event dose in Claim 1?
09:57:13 A. Yes, I do.
09:57:15 Q. And is the term "therapeutically effective" defined
09:57:18 anywhere in the '793 patent?
09:57:20 A. No, it's not.
09:57:21 Q. Do have you an opinion of how a POSA would view
09:57:23 "therapeutically effective" in the '793 patent?
09:57:25 A. My view is that "therapeutically effective" to a
09:57:33 POSA, either looking at this patent or in general use, is
09:57:37 that it is a treatment that achieves improvement in
09:57:46 symptoms, in function, and/or in survival.
09:57:50 Q. And in your opinion, is that the plain and ordinary
09:57:53 meaning of the term?
09:57:53 A. Yes.
09:57:55 Q. How did your clinical practice inform your
09:57:58 understanding of the term "therapeutically effective" in the
09:58:01 '793 patent?
09:58:02 A. Well, I think as a POSA, when I see a patient who

09:58:12 comes to me with pulmonary hypertension, they are
09:58:14 complaining of symptoms, most prominently shortness of
09:58:18 breath with exertion. They are complaining of limitation in
09:58:24 function. They may be having trouble climbing a flight of
09:58:29 stairs. And if I am successful in treating these patients,
09:58:37 I alleviate those problems. I have them feeling better. I
09:58:41 have them functioning better and -- and if I don't achieve
09:58:46 ends like that, regardless of what I do to the hemodynamics,
09:58:48 they are not happy.
09:58:50 Q. You just mentioned the word "hemodynamics," Doctor.
09:58:53 What are hemodynamics?
09:58:54 A. Well, the "hemo" part refers to blood. The
09:58:58 "dynamics" part refers to pressures and flow. So literally,
09:59:03 it literally means blood pressures and flows. And here
09:59:08 we're talking, of course, about pulmonary circulation.
09:59:12 Q. How are hemodynamics relevant to pulmonary
09:59:16 hypertension?
09:59:16 A. They're very relevant. You know, I do not discount
09:59:20 the value of assessing hemodynamics. In fact, we need to
09:59:26 check hemodynamics in order to make a diagnosis of pulmonary
09:59:30 hypertension. It is defined hemodynamically. It's
09:59:35 extremely important to do hemodynamics to differentiate
09:59:38 between the different groups because most of the groups
09:59:44 require the filling pressure of the left ventricle to be
09:59:48 normal whereas in group two, the filling pressures are

09:59:52 elevated. And to make that distinction accurately, you have
09:59:55 to do hemodynamics. They also can be in helpful in
10:00:00 monitoring patients. If a patient is deteriorating, they
10:00:03 could be very helpful in deciding specifically what kinds of
10:00:06 treatments you might want to select.
10:00:08 Q. Are hemodynamic measures themselves sufficient to
10:00:12 demonstrate therapeutic effectiveness?
10:00:15 A. I don't believe they are.
10:00:16 Q. Why not?
10:00:17 A. Because they don't necessarily reflect what is
10:00:23 happening systemically or with patient function or survival.
10:00:29 Q. You're aware that Dr. Waxman has taken the position
10:00:32 that "therapeutically effective" means any improvement in
10:00:36 certain hemodynamic measures; correct?
10:00:38 A. Yes.
10:00:39 Q. Do you agree with Dr. Waxman's definition?
10:00:41 A. I respectfully disagree.
10:00:43 Q. And why?
10:00:44 A. Well, as I was saying, I don't think there's a direct
10:00:49 relationship between what happens with -- with the
10:00:52 hemodynamics, especially acutely, and what happens
10:00:56 subsequently to therapeutic response. A fair number of
10:01:01 patients don't respond at all acutely and yet may have quite
10:01:04 robust responses later on. And we don't do -- we do acute
10:01:12 vasodilator testing commonly, but that would not prevent us

from using a treatment chronically, and often we will see a therapeutic response under those circumstances.

Also, even if you do see an acute vasodilator response that doesn't always translate into improved symptoms, function, and survival. And one example would be the study on the IV epoprostenol that we talked about yesterday, where there was an acute benefit in hemodynamics and yet, these patients had increased mortality and no improvement in quality of life after months period of time.

Q. Dr. Hill, have you formed an opinion whether the use of Liquidia's 861 product will infringe Claim 1 of the '793 patent?

A. Yes, I have that opinion.

Q. And what is your opinion?

A. I don't believe it will infringe on the patent.

Q. And why not?

A. Well, first of all, it doesn't call for a single-event dose. And secondly, I -- it doesn't impinge on the therapeutic effectiveness part because I don't believe a single-event dose is therapeutically effective.

Q. Have you reviewed the approved labeling for Liquidia's 861 product?

A. Yes, I have.

Q. In your opinion, does the approved labeling instruct or encourage a patient or physician to administer just a

10:02:55 single-event dose of Liquidia's 861 product?
10:02:58 A. It does not.
10:02:59 Q. Can you please turn to DTX 408 in your binder. And
10:03:05 let's go to Page 4, the letter on the front.
10:03:07 Dr. Hill, what's described at Page 4?
10:03:12 A. Page 4, we have highlights of the prescribing
10:03:18 information for Yutrepia, which is, of course, the brand
10:03:22 name for the Liquidia 861 product.
10:03:24 Q. And if you flip through the rest of the pages, do you
10:03:27 understand this to be the approved -- currently approved
10:03:30 labeling for Liquidia's 861 product?
10:03:34 A. That's my understanding, yes.
10:03:36 MR. DAVIES: Your Honor, I'd like to enter DTX
10:03:39 408 into evidence.
10:03:40 MR. JACKSON: No objection.
10:03:41 THE COURT: Admitted without objection.
10:03:42 (DTX Exhibit No. 408 was admitted into
10:03:43 evidence.)
10:03:43 BY MR. DAVIES:
10:03:44 Q. Dr. Hill, on Page 4, do you see the section under
10:03:48 dosage and administration?
10:03:50 A. I do.
10:03:50 Q. How many times does it instruct administration of
10:03:53 Yutrepia?
10:03:54 A. Three to five times a day.

10:03:57 Q. And if you turn to the next page at Section 2.1, it
10:04:03 should be usual dosage in adults.
10:04:07 Derrick on the next page, I think.
10:04:10 A. Yeah.
10:04:15 Q. Okay. Do you see that, Dr. Hill?
10:04:20 A. I do.
10:04:21 Q. And what does this section on dosage and
10:04:24 administration instruct with respect to the frequency of
10:04:27 dosing?
10:04:28 A. It states three to five times per day.
10:04:31 Q. Can we turn to Page 17 of the label.
10:04:41 A. I'm there.
10:04:42 Q. And what is at Page 17?
10:04:45 A. These are instructions for use of Yutrepia.
10:04:50 Q. And beginning on Page 16, are these the same
10:04:53 instructions for use that Dr. Waxman opined on during his
10:04:57 testimony?
10:04:57 A. They are.
10:04:59 Q. How many blister cards of capsules are included in
10:05:02 the Yutrepia carton?
10:05:04 A. In each carton, there are seven blister cards.
10:05:08 Q. And how many capsule in each blister card?
10:05:11 A. Four.
10:05:12 Q. And so how many total capsules are supplied in a
10:05:15 carton of -- will be supplied in a carton of LIQ861?

10:05:19 A. 28.
10:05:22 Q. Given these instructions in the description here,
10:05:24 would a patient administer only a single-event dose of
10:05:26 Liquidia's 861 patent?
10:05:27 A. I would think not.
10:05:30 Q. Why not?
10:05:30 A. It's pretty clear that the manufacturers have in mind
10:05:34 multiple doses over a period of time.
10:05:43 Q. Does this labeling for Liquidia's '861 product
10:05:50 provide any evidence that the product is therapeutically
10:05:53 effective after a single-event dose?
10:05:54 A. No, it doesn't.
10:05:57 Q. Let's look at Page 6 of 35 at the bottom, Derrick.
10:06:02 And let's look at Section 6.1 titled Clinical Trials
10:06:07 Experience.
10:06:09 A. Yes.
10:06:10 Q. Does this section of the label provide any evidence
10:06:13 that Liquidia's 861 product is therapeutically effective
10:06:16 after a single-event dose?
10:06:17 A. No, it doesn't.
10:06:19 Q. Do you see the INSPIRE trial?
10:06:21 A. Yes, I do.
10:06:22 Q. What is INSPIRE?
10:06:24 A. The INSPIRE trial was a safety and tolerability trial
10:06:31 that enrolled patients either who had been transitioned from

10:06:38 TYVASO, the United Therapeutics inhaled product, to Liquidia
10:06:45 861 and also patients who were on background pulmonary
10:06:52 hypertension therapies, and the Yutrepia was added to their
10:06:55 therapy.
10:06:57 Q. Does this section of the label say anything about the
10:07:00 therapeutic effectiveness from the INSPIRE trial?
10:07:04 A. No, it doesn't.
10:07:04 Q. Were you involved in the INSPIRE trial?
10:07:06 A. Yes, I was.
10:07:08 Q. Did the INSPIRE trial measure efficacy or therapeutic
10:07:13 effectiveness of Liquidia's 861 product?
10:07:15 A. The main reason for doing the study was to look at
10:07:20 safety and tolerability, but they did have some exploratory
10:07:23 endpoints looking at efficacy.
10:07:25 Q. Was efficacy ever assessed after a single-event dose
10:07:31 of Liquidia's 861 product?
10:07:32 A. No, it wasn't.
10:07:33 Q. Can you take again -- let's go back to the label and
10:07:36 go to Page 12. And I'd like to look at Section 14, titled
10:07:41 clinical studies.
10:07:42 Just let me know once you're there, Doctor.
10:07:46 A. I'm there.
10:07:46 Q. Okay. And there's a study here that's referred to as
10:07:50 the TRIUMPH 1 study. Do you see that?
10:07:52 A. Yes.

10:07:53 Q. And what is the TRIUMPH study?
10:07:54 A. The TRIUMPH trial was a trial undertaken by United
10:08:01 Therapeutics to do a formal large study on safety and
10:08:08 efficacy. It was a 12-week trial, and it randomized 235
10:08:13 patients between inhaled TYVASO and -- or an inhaled
10:08:21 placebo. And it established the efficacy of TYVASO, in
10:08:27 terms of improving six-minute walk distance.
10:08:30 Q. Was Liquidia's 861 product administered in the
10:08:33 Triumph trial?
10:08:34 A. No.
10:08:35 Q. Does the Triumph trial data in the label provide any
10:08:38 information as to whether Liquidia's 861 product is
10:08:41 therapeutically effective after a single-event dose?
10:08:44 A. No.
10:08:45 Q. And in the Triumph trial, how often was TYVASO
10:08:48 administered?
10:08:49 A. Four times a day.
10:08:51 Q. What was the number of breaths that was the target?
10:08:55 A. Well, the patients were titrated up to nine breaths a
10:09:00 day at the maximum dose as tolerated.
10:09:03 Q. Is that a single-event dose of TYVASO when it's given
10:09:06 four times per day?
10:09:07 A. No.
10:09:14 Q. When was therapeutic effectiveness measured in the
10:09:18 Triumph study?

10:09:20 A. Therapeutic effectiveness was measured with a
10:09:26 six-minute walk distance. It was measured after one day,
10:09:30 after six weeks, and after 12 weeks. And for the quality of
10:09:35 life score, it was after 12 weeks.
10:09:37 Q. After one day of administration of TYVASO, was TYVASO
10:09:41 therapeutically effective?
10:09:42 A. There was no change in the six-minute walk distance
10:09:47 after one day.
10:09:48 Q. So no evidence of therapeutic effectiveness after a
10:09:51 full day of dosing of TYVASO?
10:09:53 A. In terms of the six-minute walk distance, that's
10:09:56 correct.
10:09:56 Q. Does the label refer to any testing of therapeutic
10:09:59 effectiveness after a single-event dose of Liquidia's 861
10:10:02 product?
10:10:03 A. No, it doesn't.
10:10:04 Q. Does the label ever instruct dosing of a single-event
10:10:08 dose of Liquidia's 861 product?
10:10:10 A. No it doesn't.
10:10:13 Q. What would happen if a patient took only a
10:10:16 single-event dose of Liquidia's 861 product and then stopped
10:10:19 taking it?
10:10:20 A. There might be a transient improvement in
10:10:25 hemodynamics. There might be no effect on the hemodynamics,
10:10:28 but in the longer term, the effect would dissipate within

hours, and you would expect no therapeutic effect beyond those first few hours.

Q. Have you seen any evidence, even outside the label, that Liquidia's 861 product is therapeutically effective after a single-event dose?

A. No.

Q. To your knowledge, has Liquidia ever determined therapeutic effectiveness after a single-event dose of Liquidia's 861 product?

A. Not aware of that.

Q. To your knowledge, has Liquidia ever examined the results of hemodynamic responses after a single-event dose of Liquidia's 861 product?

A. There was a study referred to as the 201 study that was designed to look at the hemodynamic responses after an initial acute dose and then after 16 weeks of chronic dosing.

Q. And what's the status of that study, to your knowledge?

A. It was stopped as a consequence of the pandemic and it enrolled very few patients. I have seen no -- nothing of the results from that trial.

Q. Does the approved label for Liquidia's 861 product include any report of any hemodynamics obtained after administration of Liquidia's 861 product?

10:12:00 A. No.
10:12:12 Q. In Dr. Waxman's testimony, do you recall that he
10:12:15 compared TYVASO to 861 in offering his opinions on
10:12:20 infringement?
10:12:22 A. I do.
10:12:23 Q. Is Liquidia's 861 product a generic of TYVASO?
10:12:26 A. No, it is not.
10:12:27 Q. How are the products different?
10:12:29 A. Well, one is delivered in a liquid form via a
10:12:36 nebulizer, and it creates a mist that the patient then
10:12:41 inhales. And the LIQ -- the Liquidia 861 is a dry-powder
10:12:52 for inhalation.
10:12:54 Q. Can you turn to DTX 576 in your binder.
10:13:06 A. I'm there.
10:13:09 Q. And what is DTX 576?
10:13:12 A. Well, this is the bioavailability study that
10:13:17 Dr. Waxman commented on in his direct testimony.
10:13:21 MR. DAVIES: Your Honor, I'd like to enter DTX
10:13:24 576 into the record.
10:13:26 MR. JACKSON: No objection, Your Honor.
10:13:26 THE COURT: All right it's admitted without
10:13:29 objection.
10:13:29 (DTX Exhibit No. 576 was admitted into
10:13:29 evidence.)
10:13:29 BY MR. DAVIES:

10:13:30 Q. What is bioavailability?
10:13:32 A. It refers to the absorption of a pharmacological
10:13:39 agent into the bloodstream. And as Dr. Waxman said, it's
10:13:44 measured in peripheral veins periodically after the dosing.
10:13:52 So they look at samples every number of minutes to get a
10:13:58 curve of the level of drug that is in the blood.
10:14:02 Q. Is bioavailability a measure of therapeutic
10:14:06 effectiveness for TYVASO?
10:14:06 A. It's not in this study.
10:14:08 Q. Is bioavailability in this publication a measure of
10:14:11 therapeutic effectiveness for Liquidia's 861 product?
10:14:14 A. No, it's not.
10:14:15 Q. Do the systemic blood levels that are seen in this
10:14:19 paper reflect the levels of drug that are seen in the lung
10:14:23 for inhaled TYVASO or Liquidia's 861 product?
10:14:26 A. Well, in order to get into the bloodstream with an
10:14:32 inhalation agent, it has to go into the airways. It has to
10:14:36 cross the walls of the airways and then into the substance
10:14:41 of the lung. The idea with both of these agents is to relax
10:14:49 the smooth muscles in the walls of the vessels and open them
10:14:53 up. But exactly what the concentration is at the target,
10:14:58 which is those small arteries, there's no way of directly
10:15:03 measuring that, and we don't know for sure.
10:15:08 Q. Can measurements of bioavailability -- oh, these
10:15:12 subjects in the study, were they healthy subjects or PH

10:15:16 patients?
10:15:16 A. They were healthy subjects.
10:15:20 Q. In your opinion, what would a clinician conclude about therapeutically effective -- let me try that again. Strike that.
10:15:26 In your opinion, what would a clinician conclude about therapeutic effectiveness of Liquidia's 861 product from this study?
10:15:34 A. I don't think you can conclude anything about the therapeutic effectiveness from the study.
10:15:37 MR. DAVIES: Your Honor, I have no further questions at this time.
10:15:45 THE COURT: All right. Well, let's take the morning break of ten minutes. So, we'll be back shortly.
10:15:46 DEPUTY CLERK: All rise.
10:15:47 (Recess was taken.)
10:16:07 DEPUTY CLERK: All rise.
10:28:52 THE COURT: All right. Let's resume here. Cross-examination.
10:28:58 CROSS-EXAMINATION
10:29:01 MR. JACKSON: Good morning, Your Honor.
10:29:01 THE COURT: Good morning.
10:29:04 BY MR. JACKSON:
10:29:05 Q. Good morning, Dr. Hill.
10:29:06 A. Good morning, Mr. Jackson.
10:29:07
10:29:08

10:29:10 Q. So, you offered the opinion -- two opinions today.
10:29:16 One is on single-event dose and one was on therapeutic
10:29:20 effectiveness correct?
10:29:20 A. That's correct.
10:29:21 Q. And all of the other opinions offered about the label
10:29:24 and about Liquidia's -- whether or not Liquidia infringes
10:29:28 the patent is based on those two definitions, just
10:29:33 therapeutically effective and single-event dose; correct?
10:29:34 A. Yes.
10:29:35 Q. Everything else flows from those two; right?
10:29:37 A. That's right.
10:29:38 Q. Okay. Now, your definition of therapeutically
10:29:41 effective, the counsel didn't show you any documents
10:29:44 supporting it, did they?
10:29:45 A. No.
10:29:47 Q. Okay. And counsel didn't -- strike that.
10:29:55 Let's talk for a second about the disease and
10:29:57 the drug that we're -- that's at issue here.
10:30:00 You agree that hemodynamics is the blood
10:30:05 pressure flows in the pulmonary circulation; correct?
10:30:08 A. Yes.
10:30:09 Q. In fact, that's the testimony I elicited out of you
10:30:12 yesterday; correct?
10:30:13 A. Yes.
10:30:14 Q. And so you agree that pulmonary hypertension is the

10:30:18 constriction and thickening of the vessels that narrows the
10:30:21 channels of the heart and lungs; right?
10:30:23 A. That's one of the causes of it. Literally pulmonary
10:30:29 hypertension is elevation of pulmonary artery pressure.
10:30:33 Q. And you agree that pulmonary hypertension is based on
10:30:37 the measurements of the hemodynamics of the patient and, in
10:30:41 particular, an elevation of pulmonary arterial pressure over
10:30:45 normal levels; right?
10:30:47 A. That's correct.
10:30:48 Q. And in fact, that's in the patent; right?
10:30:50 That language is in the patent; right?
10:30:52 A. Yes.
10:30:54 Q. And you agree that using a -- the goal of using a
10:30:58 vasodilator such as Treprostinil is to reduce the pulmonary
10:31:02 arterial pressure and/or pulmonary vascular resistance;
10:31:06 correct?
10:31:06 A. Yes.
10:31:08 Q. And you also agree that the '793 patent contains
10:31:13 details of hemodynamic and gas exchange experiments;
10:31:16 correct?
10:31:17 A. Say that again, please.
10:31:18 Q. You agree that the '793 patent contains details of
10:31:23 hemodynamic and gas exchange experiments; correct?
10:31:27 A. Yes, I think so.
10:31:33 Q. And looking at Example 1, on Column 8 through 11, the

10:31:37 1 patent itself talks about the relative changes of
10:31:40 2 hemodynamic and gas exchange parameters compared to
10:31:44 3 baseline; correct?
10:31:44 4 A. Correct.
10:31:47 5 Q. And those calculations are the hemodynamics
10:31:51 6 parameters, such as a pulmonary arterial pressure and
10:31:54 7 pulmonary vascular resistance, among other things; right?
10:31:57 8 A. Right.
10:31:59 9 Q. And at the bottom of column 11 starting at line 62,
10:32:05 10 let's pull that, up please.
10:32:07 11 Do you agree that it says the application of an
10:32:09 12 effective amount of Treprostinil in only a few or even one
10:32:14 13 single breath was achieved with a highly concentrated
10:32:17 14 Treprostinil sodium solution; right?
10:32:20 15 A. I see that, and I agree. Yes.
10:32:23 16 Q. And so that -- that's the patent itself uses the word
10:32:27 17 that administration was effective; right?
10:32:29 18 A. It did say that, yes.
10:32:31 19 Q. Okay. And so, the patent is teaching based on the
10:32:37 20 results that are described in Example 1, which measures
10:32:41 21 pulmonary arterial pressure and pulmonary vascular
10:32:43 22 resistance, among other hemodynamic parameters, that an
10:32:48 23 effective amount of Treprostinil was achieved in a few or
10:32:52 24 even one single breath; correct?
10:32:55 25 A. That's what it says, yes.

10:32:56 Q. Okay. And so, you will agree with me that the '793
10:33:01 patent shows that there's hemodynamic effectiveness from
10:33:03 Treprostinil; correct?
10:33:04 A. I agree with that, yes.
10:33:07 Q. And on -- the average patient, a single
10:33:11 administration of Treprostinil to someone suffering from
10:33:13 pulmonary hypertension results in a beneficial reduction of
10:33:18 pulmonary arterial pressure and/or vascular resistance;
10:33:22 correct?
10:33:23 A. On average, yes. These are all populations, and not
10:33:26 every patient is going to have that kind of response.
10:33:30 Q. Now, you would agree with me that the examples in the
10:33:32 patent don't purport to measure long-term things like change
10:33:37 in walk distance over time or the survival rates over a
10:33:41 longer period of time; correct?
10:33:42 A. That's true.
10:33:44 Q. Instead, the patent we just looked at measures --
10:33:46 talked about an effectiveness -- an effective dose from --
10:33:50 an effective amount of a single-event dose; right?
10:33:53 A. Effective in improving hemodynamics, yes.
10:34:00 Q. And you would agree that a person of ordinary skill
10:34:04 in the art -- you would agree that a person of ordinary
10:34:06 skill in the art would have understood that for patients
10:34:08 with pulmonary hypertension, changes in hemodynamic
10:34:14 properties or parameters would have an association with

survival; correct?

A. Not necessarily.

Q. Okay. Let's pull up your deposition on January 4th, and let's look at Page 114, lines 1 through 6.

Right. Where you were asked this exact same question. "So people of ordinary skill in the art understood that changes in hemodynamic properties or parameters have an association with survival in connection with pulmonary hypertension patients; correct?"

And your answer there was yes; correct?

A. That is correct.

Q. And that was truthful testimony; right?

A. Yes.

Q. And in fact, Liquidia has begun an acute and/or -- strike that.

Liquidia began an acute and chronic hemodynamic study on LIQ 861 which is called LI -- LTI 201; right?

A. That's correct.

Q. And so, let's pull up PTX 59, please.

And this is that study; right?

It's in your binder, but it also might be easier on the screen as well.

A. Yes. This is -- this is a description of the study.

Q. Okay.

MR. JACKSON: Move to admit PTX 59.

10:35:36 MR. DAVIES: No objection, Your Honor.

10:35:37 THE COURT: Admitted without objection.

10:35:39 (PTX Exhibit No. 59 was admitted into evidence.)

10:35:39 BY MR. JACKSON:

10:35:40 Q. And you agree that the primary efficacy purpose of this study was -- for LIQ861 -- was to assess the hemodynamic parameters; correct?

10:35:51 A. That's correct.

10:35:55 Q. Now, you agree with me that as of 2006, a person of ordinary skill would have known that the half-life of Treprostinil in the body was roughly three to four hours; correct?

10:36:06 A. That's correct.

10:36:08 Q. And you agree with me that you would not be able to dose somebody once a day with Treprostinil as a result; correct?

10:36:15 A. To apply a therapy over time, yes.

10:36:22 Q. Okay. So, all things being equal, would you expect that you'd be able to dose somebody once a day with an active ingredient that has a three- to four-hour half-life?

10:36:33 A. It would not be a once-a-day therapeutic agent.

10:36:38 Q. So you have to dose probably somewhere between three and four times a day; right?

10:36:42 A. That's about right.

10:36:44 Q. Now, let's turn for a minute to the single-event

dose. Your definition of a single-event dose is the dose that is delivered in a single session; right?

A. That is correct.

Q. So for example, the Yutrepia tells you to take multiple breaths right?

A. It does.

Q. And so it's that multiple breaths that would be a single-event dose; correct?

A. Yes, it would.

Q. Okay. Now, were you here when Dr. Rubin's deposition was played yesterday?

A. Yes, I was.

Q. And so during that deposition, Dr. Rubin commented that if you need to take two blood pressure pills four times a day, each of those administration of the two pills would be a single-event dose; right?

That's what he testified?

A. I recall that, yes.

Q. And you agree with that definition, right?

A. I do.

Q. And so that's true even though you're taking two pills four times a day; right?

A. Yes.

Q. Okay. So each of those separate four-times-a-day sessions is a single-event dose; right?

10:37:46 A. I don't see it that way, no.
10:37:50 Q. Okay. So --
10:37:51 A. I think each administration of the two pills is a
10:37:54 single-event. And then have you to do that four times a
10:37:58 day.
10:37:58 Q. Yes, I think we're on the same page. Thank you.
10:38:01 That was helpful.
10:38:02 And so, let's look at PTX 134, which I believe
10:38:08 your -- counsel for Liquidia showed to you. This is the
10:38:14 April 2021 label; right?
10:38:16 A. Yes.
10:38:17 Q. And you agree with me that -- let's turn to -- you
10:38:28 agree -- you agree with me that it -- the label provides
10:38:31 that the dosing is -- is 15 point -- 26.5, 53 milligrams,
10:38:42 79 milligrams, 106 milligrams, et cetera. There are sort of
10:38:47 dosings in there; right?
10:38:48 A. Those are the -- that's the amount of drug in -- in
10:38:51 the different capsule size.
10:38:53 Q. And that's the amount of drug that's going to be
10:38:55 administered in that dosing session; right?
10:38:58 A. Right. And you can combine these capsules to get
10:39:01 higher levels. But that -- that would be the single event,
10:39:05 yes.
10:39:05 Q. And you would agree that a number of those -- a
10:39:08 number of those calculations fall within 15 to

10:39:11 90 micrograms; correct?
10:39:12 A. They do.
10:39:13 Q. Okay. And again, each of the -- and again,
10:39:24 Yutrepia's label -- strike that.
10:39:26 Liquidia's label states that each capsule should
10:39:29 be taken in one to two breaths; right?
10:39:31 A. That's correct.
10:39:32 Q. And each of those one to two breaths would be a
10:39:35 single-event dose; right?
10:39:36 A. Well, again, if you have multiple capsule, you might
10:39:39 end up taking one or two breaths for each capsule, but that
10:39:43 would be a single-event dose. It might be more -- more
10:39:48 breaths.
10:39:48 Q. In fact, the label specifically says always inhale
10:39:52 each capsule two times to make sure you get your full dose;
10:39:55 right?
10:39:56 A. I don't know if that's what is said literally, but
10:40:01 they do say two breaths encouraged.
10:40:07 Q. Let's pull up PTX 61, please.
10:40:10 A. Actually, if I read it, it says the contents of each
10:40:14 capsule can be inhaled in one to two breaths. That's what
10:40:18 it says right there.
10:40:19 Q. Okay. But it's not just can be. The instructions
10:40:22 for use actually is instructing always inhale at least two
10:40:26 breaths or always inhale two breaths; right?

10:40:28 A. I just read that right out of the highlight.
10:40:31 Q. Okay. So let's take a look at PTX 61. You've seen
10:40:35 this document before; right?
10:40:36 A. Yes.
10:40:37 Q. Okay. And it is the instructions for use; right?
10:40:41 It's a letter to the FDA, and it includes the
10:40:43 label; correct?
10:40:44 A. Right. That's the letter, and then the instructions
10:40:47 are starting on Page 4.
10:40:48 Q. Okay. So, let's go to Bates Number 836, please.
10:40:53 You've seen this before; right?
10:40:54 A. Yes.
10:40:56 Q. Okay. And so these are the instructions for use for
10:40:58 Liquidia's product; right?
10:40:59 A. That is correct.
10:41:00 Q. Now, about three -- about four or five bullets up
10:41:04 to -- up from the bottom, do you see where it says "always
10:41:07 inhale"?
10:41:07 A. Right.
10:41:09 Q. So it says, "Always inhale each capsule two times to
10:41:11 make sure you get your full dose of Yutrepia; right?
10:41:15 A. That's what it says there, yes.
10:41:18 Q. Now, let's go back to a second to the '793 patent.
10:41:24 Counsel for Liquidia focused on language on top of Column 8,
10:41:29 lines 1 to 2. Do you recall that?

10:41:30 A. I'm not up with you yet.
10:41:34 Q. Fair enough. It's Treprostinil can be administered a
10:41:36 single time per day or several times per day.
10:41:38 A. Yes. Okay.
10:41:39 Q. And counsel pointed this language to you; right?
10:41:41 A. Yes. And we have -- we've looked at it twice today
10:41:43 already, yes.
10:41:48 Q. Nothing in the '793 patent provides that it addresses
10:41:52 only acute treatment; correct?
10:41:54 A. Well, the examples are looking at acute treatment.
10:42:03 Q. But -- agreed. But that's because they're looking at
10:42:06 the various examples of what the effect on the given patient
10:42:11 was after taking this dose; right?
10:42:13 A. Right.
10:42:14 Q. Okay.
10:42:14 A. So maybe I'm not understanding your question. I'm
10:42:16 sorry.
10:42:16 Q. Yeah, so let me help if I can clarify. The patent
10:42:21 doesn't specifically say it's -- this is only about acute
10:42:25 treatment; correct?
10:42:26 A. Well, what it says is a single-event dose. That's
10:42:33 what it says.
10:42:34 Q. Okay. I understand it says single-event dose. I
10:42:37 understand it says therapeutically effective; right?
10:42:40 A. Yes.

10:42:40 Q. But we've already agreed that you can have
10:42:43 multiple -- like with the blood pressure example we went
10:42:47 through a couple minutes ago, you can have multiple
10:42:50 single-event doses per day; right?
10:42:51 A. Yes, you can.
10:42:54 Q. Okay. And each single-event -- if the drug has a
10:43:01 effect on hemodynamics in the patient, that is a therapeutic
10:43:07 effect on the patient; right?
10:43:08 A. Say that again, please.
10:43:10 Q. I'll come back to it in a second.
10:43:12 Would you agree with me that nothing in the
10:43:16 patent precludes more than one single-event dose per day?
10:43:22 A. Right. Yeah, and I -- let me just say that it is
10:43:27 true that these are multiple single events, but I think the
10:43:31 term "single event" refers to a single event. I would just
10:43:34 call that multiple events in a day. I think, you know, what
10:43:40 this says is it's -- it can be a single time or several
10:43:43 time.
10:43:43 Q. Right. So multiple single-event doses per day. Is
10:43:47 that what you're talking about?
10:43:48 A. Well, I don't know -- it seems to me to be calling
10:43:52 those single events is a little redundant. They're multiple
10:43:56 events.
10:43:56 Q. Okay. You'll agree with me that Liquidia is relying
10:44:00 on TYVASO, the United Therapeutics TYVASO, safety and

efficacy data to support the approval of Liquidia's product; right?

A. Yes.

Q. And you agree that TYVASO and Liquidia and LIQ861 involve the same molecule; right?

A. They do.

Q. And you would agree with me that you would be surprised if LIQ 861 was significantly different than TYVASO for the reduction of pulmonary arterial pressure and pulmonary vascular resistance; correct?

A. I would expect them to be quite similar, yeah.

Q. And you would agree -- and you would agree that you would be surprise by any differences because the molecules are the same; right?

A. Well, the formulation is quite different. And TYVASO was liquid. The LIQ861 is a dry-powder, and exactly how they behave might be different. This is why this INSPIRE study was done, to establish, especially for the FDA, that there was safety and tolerability of this different formulation.

Q. Would you agree with me that you would be surprised -- strike that.

You agree with me that you would be surprised by any differences because the molecules of TYVASO and LIQ are the same; right?

10:45:22 A. Yes.

10:45:24 MR. JACKSON: No further questions.

10:45:26 Thank you, Your Honor.

10:45:27 THE COURT: All right. Any redirect?

10:45:28 MR. DAVIES: Nothing, Your Honor.

10:45:29 THE COURT: All right. Dr. Hill, you can step down. Watch your step.

10:45:32 THE WITNESS: Thank you, Your Honor.

10:46:26 MR. SUKDUANG: Your Honor, at this time -- I'm sorry to interrupt.

10:46:28 THE COURT: No, I'm listening.

10:46:29 MR. SUKDUANG: At this time, Defendants call Dr. Igor Gonda, who will be discussing the issues of the invalidity of the '793 patent.

10:46:39 THE COURT: All right.

10:46:40 DEPUTY CLERK: Please state and spell your full name for the record.

10:46:42 THE WITNESS: Igor, I-G-O-R, Gonda, G-O-N-D-A.

10:46:48 DEPUTY CLERK: Do you affirm that the testimony you are about to give to the Court in the case now pending will be the truth, the whole truth, and nothing but the truth, you do so affirm?

10:46:55 THE WITNESS: Yes, I do.

10:46:56 DEPUTY CLERK: Thank you, Doctor. Here's the microphone on top of the computer. Just make sure you speak

10:47:01 up.

10:47:01 IGOR GONDA, the witness herein, after having been duly sworn under oath, was examined and testified as follows:

10:47:02 THE WITNESS: Yes.

DIRECT EXAMINATION

BY MR. SUKDUANG:

10:47:03 Q. Hello, Dr. Gonda.

10:47:04 A. Hello.

10:47:05 Q. Can you please state your full name for the record?

10:47:07 A. Igor Gonda.

10:47:11 Q. And where are you currently employed?

10:47:12 A. I'm employed in Respidex, LLC.

10:47:17 Q. And what is your title at Respidex?

10:47:19 A. I'm the founder and CEO.

10:47:21 Q. What types of services does Respidex provide?

10:47:25 A. We provide a variety of services for multiple organizations that develop, obviously, the products as well as the pharmaceutical industry, particularly in the field of inhalation products and products for nasal delivery.

10:47:42 Q. Do you have a CV, Dr. Gonda?

10:47:44 A. Yes, I do.

10:47:45 Q. Could you can we please turn to DTX 722.

10:47:50 Is this a copy of your CV?

10:47:53 A. Yes, it is.

10:47:53 MR. SUKDUANG: Your Honor, I'd like to offer DTX
10:47:58 722 into evidence.
10:47:59 THE COURT: Admitted without objection.
10:48:00 (DTX Exhibit No. 722 was admitted into
10:48:01 evidence.)
10:48:01 BY MR. SUKDUANG:
10:48:02 Q. Dr. Gonda, where do you go to graduate school?
10:48:04 A. I went to graduate school at University of Leeds in
10:48:07 England.
10:48:08 Q. And what degree did you get?
10:48:10 A. I received a Ph.D. degree in physical chemistry, and
10:48:15 prior to that, a bachelor of science in chemistry.
10:48:17 Q. And what year did you receive your Ph.D.?
10:48:20 A. In 1974.
10:48:24 Q. Over the course of your career, what's been the focus
10:48:26 of your scientific work?
10:48:28 A. The focus of my scientific work has been therapeutic
10:48:33 inhalation and diagnosing inhalations. That's been the
10:48:38 focus.
10:48:38 Q. And how long have you been working on inhalations and
10:48:42 therapeutic inhalations?
10:48:44 A. It's about 46 years.
10:48:47 MR. SUKDUANG: Your Honor, we'd like to offer
10:48:48 Dr. Gonda as an expert in the field of inhaled drugs,
10:48:52 inhaled drug formulations, and inhalation devices as well as

their development.

MR. CARSTEN: No objection, Your Honor.

THE COURT: You may proceed.

BY MR. SUKDUANG:

Q. Dr. Gonda, I'd like to just discuss at a very high level what your opinions in this case are. Can you provide the Court what are your opinions regarding the invalidity of '793 patent?

A. I think it is invalid.

Q. And for what reasons?

A. I think that it lacks enablement, and it lacks possession of the invention.

Q. And with respect to the '793 patent claim, what aspect of those claims are your opinions based on?

A. Can you please repeat the question.

Q. Sure. Are your opinions focused on the formulations disclosed in Claim 1?

A. Yes, they are.

Q. And do are they focused on a particular type of formulation within the scope of Claim 1?

A. Yes, they are particularly focused on the powder formulations.

Q. Now, I'd like to talk about the different types of inhalations devices. Have you prepared a demonstrative?

A. Yes, I have.

10:50:05 Q. Can we bring up DDX 5.1, please. Is this a
10:50:08 demonstrative you prepared?
10:50:09 A. Yes, it is.
10:50:10 Q. So can you just describe what, generally, this
10:50:13 demonstrative shows?
10:50:14 A. So, this demonstrative shows the four fundamental
10:50:20 types of inhaled devices and formulations. So the first one
10:50:27 is a nebulizer, which is a device that they take
10:50:33 formulations of the typically water which are placed in the
10:50:37 nebulizer, and the power to form the aerosol comes from
10:50:40 compressed air from a compressed air cylinder composition
10:50:46 similar to the one on the top. And that energy is used to
10:50:50 disperse the liquid into fine droplets and push the aerosol
10:50:55 out of the device into the mouthpiece from which the patient
10:50:58 is inhaling.
10:51:01 Q. And with respect to the nebulizer and the liquid
10:51:05 formulation on the top left, does TYVASO use a nebulizer?
10:51:09 A. Yes, TYVASO uses a nebulizer.
10:51:13 Q. On the top right, you have pressurized metered dose
10:51:17 inhaler. What kind of -- can you describe how a pressurized
10:51:20 metered dose inhaler works?
10:51:22 A. Sure. So the energy to get the aerosol out of the
10:51:28 device and disperse it into small particles comes from the
10:51:32 compressed air which comes liquified inside the cartridge
10:51:36 that goes into the device and then the patient actuates this

device. The compressed air will push the dose out of the device, and it will also disperse the energy, disperse it into small droplets that will be inhaled by the patient.

Q. What type of formulation is used within a pressurized metered-dose inhaler.

A. It's a liquid.

Q. Okay. And is the, like, a typical asthma inhaler an example of when a pressurized metered-dose inhaler would be?

A. Yes, a typical asthma inhaler would be a typical device.

Q. On the bottom left side, have you a soft mist inhaler. Could you describe how that soft mist inhaler works.

A. Yes, I can. So the energy for that device comes typically from a compressed spring, and when the patient actuates the device, the spring will expand to push a liquid typically against a water solution of the drug. So through some form orifice which will form the fine droplets, and the energy of that will also push the aerosol out of the device and then the patient will inhale the aerosol.

Q. And what type of formulation is used within a soft mist inhaler?

A. It is typically an aqueous solution. It's a liquid of the drug in water.

Q. And then the last device on the right-hand side, I

know we've talked about that earlier, but in the case, what is a dry-powder inhaler and how does that work?

A. So, a dry-powder inhaler is quite different in at least two respects from the other inhalers. It uses a dry-powder formulation. It doesn't use the liquids. And also the energy to get the dose out of the inhaler and disperse it into small particles that would be suitable for inhalation comes from the patient's ability to -- from the energy of the patients, the muscles in the lungs to create the air flow that will then get the dose out of the device and disperse into particles of small size.

Q. And again, what type of formulation was used in the dry-powder inhaler?

A. It's a dry-powder formulation.

Q. Could you use a liquid in a dry-powder formulation?

Excuse me. Can you use a liquid formulation in a dry-powder inhaler?

A. No, you could not.

Q. Could you use a powder formulation in a nebulizer?

A. No, you could not.

Q. Would it be fair to say that the dry-powder inhaler is the only inhalation device that uses a patient's own power to bring the drug into the body?

A. As far as I know, it's the only device of that nature, yes.

10:54:20 Q. Are you aware of any papers that discuss the energy
10:54:26 needed by a patient in order to use a dry-powder inhaler?
10:54:30 A. Yes, I am.
10:54:32 Q. Could we turn to DTX 268, please. And is this one of
10:54:39 the publications you considered?
10:54:40 A. Yes, it is.
10:54:42 Q. And what's the title of the publication?
10:54:43 A. It's called Medical Aerosol Inhalers: Past, present
10:54:47 and future.
10:54:48 Q. Okay. And who is the author?
10:54:50 A. It's A. R. Clark.
10:54:52 Q. And is he is one of UT's expert in his this case?
10:54:55 A. Yes, I believe he is.
10:54:57 Q. And when was this paper published?
10:54:59 A. It was published in 1995.
10:55:02 MR. SUKDUANG: Your Honor I'd like to enter DTX
10:55:04 268 into evidence.
10:55:05 MR. CARSTEN: No objection, Your Honor.
10:55:06 THE COURT: Admitted without objection.
10:55:07 (DTX Exhibit No. 268 was admitted into
10:55:08 evidence.)
10:55:08 BY MR. SUKDUANG:
10:55:08 Q. Could we -- could you turn to Page 12 of 19 for me.
10:55:11 And there's a paragraph that begins paradoxically.
10:55:15 Did you consider this paragraph?

10:55:17 A. Yes.
10:55:17 Q. And what does this passage state?
10:55:20 A. This was a very profound statement that the world
10:55:24 follows. And it says in 1995, all currently available DPIs
10:55:29 utilize the energy in the patient's inspiration as the power
10:55:32 source for aerosol generation. Therefore, their delivery
10:55:36 and dispersion performance and, hence, the dose which they
10:55:40 deliver to the lung is affected by a patient's ability to
10:55:43 inhale at a suitably high flow rate.
10:55:46 Q. What does "inspiration" mean in the context of
10:55:50 dry-powder inhalers?
10:55:51 A. Well, as I mentioned, in dry-powder inhalers, it's
10:55:55 the patient's inspiration is the inhalation through the
10:56:00 dry-powder inhaler. It's the ability to have adequate
10:56:03 inspiration for it at any specific volume that is required
10:56:07 for dry-powder inhalers.
10:56:09 Q. So, in laymen's terms what is this -- what is the
10:56:12 Clark paper telling persons of ordinary skill in the art to
10:56:16 do with respect to dry-powder inhalers?
10:56:19 A. Well, it says that you have to pick the device that
10:56:23 your target population of patients, in this case, pulmonary
10:56:27 arterial hypertension patients, a device and test it whether
10:56:30 the patients can use it, how can they use it, and whether
10:56:33 it's going to be the right combination of the patient's
10:56:36 disease with the device and the formulation to get the

adequate dose and the adequate particle size distribution.

Sorry. If you can't follow me. Just --

Q. She'll let you know. She's fantastic. If she can't get you, she'll -- she'll tell you, Dr. Gonda.

So let's turn to the drugs -- the drug that's involved in this case, Treprostinil. Are you aware that Treprostinil is used in Liquidia's LIQ861 product?

A. Yes, I am.

Q. Are there any inhaled Treprostinil products in the market? Inhaled Treprostinil products --

A. Yes.

Q. -- in the market?

And what is that?

A. It's TYVASO.

Q. And who markets TYVASO?

A. United Therapeutics.

Q. Today, are there any dry-powder formulations of Treprostinil on the market?

A. No.

Q. Are you are you aware of any companies that are develop developing dry-powder inhalers?

A. Yes, I am.

Q. And what are those companies?

A. They are Mannkind and Liquidia, Mannkind and Liquidia.

10:57:39 Q. With respect to Mannkind, how do they make their
10:57:43 dry-powder formulation of Treprostinil?
10:57:45 A. So, MannKind takes Treprostinil and they use the
10:57:51 proprietary technology -- in fact, two proprietary
10:57:54 technologies. They use the Technosphere, which a propriety
10:57:59 technology, to make particles suitable for inhalation. And
10:58:04 then they use the proprietary inhaler called Dreamboat which
10:58:08 they combine together to form the product of Treprostinil
10:58:13 dry-powder inhaler.
10:58:15 Q. Does Liquidia use a proprietary process to make their
10:58:19 dry-powder formulation?
10:58:20 A. Yes. Liquidia uses a proprietary process which is
10:58:25 called PRINT, and in the process, they take Treprostinil.
10:58:29 They take a particular type of salt, Treprostinil salt.
10:58:33 They dissolve the salt. They form the solution of that salt
10:58:38 with other materials. Then they power that solution into
10:58:43 the PRINT technology equipment. They evaporate the solution
10:58:46 to form the small particles, and then they dry the particles
10:58:50 and store them in appropriate conditions.
10:58:54 Q. Do you understand that Liquidia filed a new drug
10:58:56 application for their Liquidia LIQ861 product?
10:59:00 A. Yes, I do.
10:59:01 Q. Have you seen a press release relating to that?
10:59:04 A. Yes, I have.
10:59:05 Q. Can we bring up DTX 369, please.

10:59:07 And on the top right corner what is this,
10:59:13 Dr. Gonda?
10:59:14 A. It is the announcement that Liquidia submits the new
10:59:19 drug applications for the product Treprostinil inhalation
10:59:24 powder to the U.S. FDA for the treatment of pulmonary
10:59:28 arterial hypertension.
10:59:28 Q. And when did Liquidia publicly announce that they
10:59:31 filed their new drug application for LIQ861?
10:59:34 A. They published it on January 27th, 2020.
10:59:38 MR. SUKDUANG: Your Honor, I'd like to enter DTX
10:59:41 369 into evidence.
10:59:41 MR. CARSTEN: No objection, Your Honor.
10:59:42 THE COURT: All right. Admitted without
10:59:44 objection.
10:59:44 (DTX Exhibit No. 369 was admitted into
10:59:45 evidence.)
10:59:45 BY MR. SUKDUANG:
10:59:46 Q. Dr. Gonda, are you aware that UTC is currently
10:59:49 working on a Treprostinil dry-powder formulation?
10:59:51 A. I am aware that they are working to together with
10:59:55 Mannkind on such a product.
10:59:57 Q. Have you seen any documentation related to UTC's
11:00:00 collaboration with Mannkind?
11:00:01 A. Yes, I have.
11:00:02 Q. Can we bring up DTX 389 in your binder.

11:00:08 Is this the press release that you saw?
11:00:10 A. Yes, it is.
11:00:12 Q. And, Dr. Gonda, what type of agreement does UTC have
11:00:19 with Mannkind with respect to the Treprostinil dry-powder
11:00:22 formulations?
11:00:23 A. So, it is an exclusive license for this product
11:00:28 Treprostinil Technosphere. That includes $95 million in
11:00:32 upfront and milestone payments. And also Mannkind is
11:00:37 entitled to receive world royalties for the product once
11:00:42 it's on the market.
11:00:42 MR. SUKDUANG: Your Honor, I'd like to enter in
11:00:44 DTX 389 into evident evidence.
11:00:46 MR. CARSTEN: No objection.
11:00:47 THE COURT: All right. Admitted without
11:00:48 objection.
11:00:48 (DTX Exhibit No. 389 was admitted into
11:00:48 evidence.)
11:00:48 BY MR. SUKDUANG:
11:00:49 Q. Does UTC have an FDA approval for their dry-powder
11:00:53 formulation that they're developing with Mannkind?
11:00:56 A. Not as far as I know.
11:00:59 Q. Are you aware of if Liquidia has tentative approval
11:01:03 for their dry-powder formulation, LIQ861?
11:01:06 A. Yes, I am.
11:01:07 Q. And does Liquidia have tentative approval?

A. Yes.

Q. Dr. Gonda, have you provided a definition of a person of ordinary skill in the art for the '793 patent as of May 2006?

A. Yes, I have.

Q. And have you prepared a demonstrative that addresses that?

A. Yes, I did.

Q. Can we bring up DDX 5.2, please. Thank you.

Dr. Gonda, is this your definition of a person of ordinary skill in the art?

A. It is.

Q. And how have you defined a POSA for the '793 patent as of May 2006 with respect to the formulation aspects?

A. So, with respect to the subject of the '793 patent, it would be somebody with a Ph.D. in pharmaceutical science or a related discipline like chemistry or medicinal chemistry plus two years of experience in pharmaceutical formulations including inhaled products. Alternatively, it could be somebody, again, with respect to the same issues, somebody who holds a master's in the same fields plus five years of experience in pharmaceutical formulations, including inhaled products.

Q. Did you apply this definition of a POSA in rendering your opinion in this case?

11:02:22 A. Yes, I did.
11:02:24 Q. Are you aware that UTC's experts provided their own
11:02:27 definition of a POSA for the '793 patent?
11:02:30 A. Yes, some of them did.
11:02:33 Q. Would your opinions change if the Court adopts UTC's
11:02:39 definition of a POSA?
11:02:39 A. No.
11:02:43 Q. Could we turn to the '793 patent. And could we look
11:02:46 at the first page, please -- or excuse me. Could we go to
11:02:50 the claims, and that's JTX 3 for the record.
11:02:58 Generally, what does Claim 1 of the '793 patent
11:03:01 relate to?
11:03:02 A. Well, Claim 1 is a claim that states a method of
11:03:06 treating pulmonary hypertension comprising administering by
11:03:09 inhalation to a human suffering from pulmonary hypertension
11:03:13 a therapeutically effective single-event dose of a
11:03:16 formulation comprising Treprostinil or a pharmaceutically
11:03:21 acceptable salt of Treprostinil with an inhalation device
11:03:26 wherein the therapeutically effective single-event dose
11:03:29 comprises from 15 to 90 micrograms of Treprostinil or a
11:03:33 pharmaceutically acceptable salt thereof delivered in one to
11:03:37 three breaths.
11:03:38 Q. In forming your opinions regarding powdered
11:03:43 formulations of Treprostinil, are you requiring the claims
11:03:47 of the '793 patent to meet some FDA requirement for

11:03:50 approval?
11:03:51 A. No.
11:03:57 Q. The claims do require a method of actually treating a
11:04:00 patient with pulmonary hypertension, though; is that right?
11:04:02 A. Well, the claim says that it should be a
11:04:06 therapeutically effective.
11:04:07 Q. For a pulmonary hypertension patient?
11:04:09 A. For -- that's correct. For the particular indication
11:04:12 for pulmonary hypertension.
11:04:13 Q. If you take a look at Claim 1, there's a phrase
11:04:17 "formulation comprising Treprostinil." Do you see that?
11:04:19 A. Yes, I do.
11:04:20 Q. What types of formulations are encompassed by the
11:04:24 formulations formulation comprising Treprostinil?
11:04:29 A. So, this is a very general claim that covers any
11:04:32 formulation.
11:04:33 Q. And what types of formulations would that include?
11:04:36 A. Well, it would be liquid formulations or solid
11:04:40 formulations.
11:04:40 Q. And with respect to solid formulations, would that
11:04:43 include powders?
11:04:44 A. Yes, of course.
11:04:49 Q. Further down in Claim 1, you it you had mentioned
11:04:52 that it refers to an inhalation device. Do you see that?
11:04:54 A. Yes, I do.

11:04:57 Q. And what types of inhalation devices would be covered by Claim 1?
11:05:00 A. Again, this is a very general claim, and the way that the POSA would understand it, it would be any formulation.
11:05:01 Q. Would it include the four inhalation devices that you expressed in the beginning of your testimony?
11:05:08 A. Yes, it would.
11:05:13 Q. That would be a nebulizer, pressure metered-dose inhaler or soft mist inhaler and a dry-powder inhaler?
11:05:15 A. That is correct.
11:05:16 Q. Now I'd like to discuss your opinion regarding whether the inventors had possession of a dry-powder formulation of Treprostinil as of 2006.
11:05:18 Generally speaking, Dr. Gonda, what's your opinion as to whether a POSA, a person of ordinary skill in the art, reading the '793 patent would understand if the inventors were in possession of a dry-powder formulation of Treprostinil?
11:05:21 A. A POSA would have concluded, in my -- in my view, that they were not in possession of the invention.
11:05:29 Q. And why is that?
11:05:32 A. Well, there is no evidence of that in the patent.
11:05:36 Q. Now, did you read the '793 patent in rendering your opinions?
11:05:43 A. Yes, I did.

11:06:20 Q. Does the '793 patent contain a mention of inhaled
11:06:24 powders or a dry-powder inhaler?
11:06:26 A. Yes, it does.
11:06:27 Q. Can we turn to Column 7, lines 22 to 26 at page 230
11:06:34 of the '793. And can we blow that up, please, Derrick?
11:06:39 Thank you.
11:06:39 Is this the reference to powders and dry-powder
11:06:43 inhalers you previously mentioned?
11:06:44 A. That is the reference in the specifications.
11:06:48 Q. And just briefly, what does that '793 patent state?
11:06:51 A. It says the inhalation device can be also a
11:06:55 dry-powder inhaler. In such case, the respiratory drug is
11:06:59 inhaled in solid formulation, usually in the form of a
11:07:03 powder with particle size less than ten micrometers in
11:07:07 diameter or less than five micrometers in diameter.
11:07:11 Q. Other than these two sentences, does the '793 patent
11:07:15 contain any other discussion of a dry-powder or a dry-powder
11:07:18 inhaler?
11:07:19 A. Only in the claims.
11:07:21 Q. But not in the body of the patent itself?
11:07:23 A. No.
11:07:26 Q. Other than these two -- do these two sentences tell a
11:07:30 POSA how to make a dry-powder formulation of Treprostinil?
11:07:33 A. No, they do not.
11:07:35 Q. Do they tell a POSA what dry-powder inhalers would be

11:07:40 suitable for patients with pulmonary hypertension?
11:07:42 A. No, it does not.
11:07:49 Q. Do you recall if there are examples in the '793 patent?
11:07:51 A. Yes, there are examples.
11:07:54 Q. Can we go to Example 1? It's the bottom of Column 8. Again, also on Page 20.
11:08:00 Can you blow that up, please, Derrick. Thank you.
11:08:04 What type of inhaler did Example 1 utilize?
11:08:07 A. It was a soft mist inhaler.
11:08:11 Q. And what type of formulation is used in a soft mist inhaler?
11:08:16 A. It would be a liquid, typically, an aqueous solution of the drug.
11:08:20 Q. It would not -- a soft mist inhaler would not use a powder; is that correct?
11:08:25 A. No.
11:08:26 Q. Can you go to Example 2. It starts at Column 12. And could you blow that up, please?
11:08:37 Dr. Gonda, what type of inhaler was utilized in Example 2 of the patent?
11:08:42 A. Example 2 used an ultrasonic nebulizer.
11:08:48 Q. And what type of formulation is used in an ultrasonic nebulizer?
11:08:52

11:08:53 A. It is, again, a liquid, and it can typically -- an
11:08:56 aqueous of the drug in water.
11:09:02 Q. And can you use a powdered formulation in an
11:09:04 ultrasonic nebulizer?
11:09:06 A. No, you cannot.
11:09:12 Q. Did either of these examples mention the use of a
11:09:16 dry-powder formulation of Treprostinil?
11:09:18 A. No, they don't.
11:09:20 Q. Do these either of these examples actually administer
11:09:23 a dry-powder formulation of Treprostinil?
11:09:25 A. No, they don't.
11:09:27 Q. Do either of these examples utilize a dry-powder
11:09:30 inhaler?
11:09:31 A. No.
11:09:39 Q. Now, did you consider testimony from the inventors of
11:09:43 the '793 patent in forming your opinions?
11:09:46 A. I considered three testimonies in this -- regarding
11:09:51 this from Drs. Roscigno, Rubin, and Seeger.
11:09:56 Q. And what did their testimony -- or how did their
11:10:01 testimony impact your opinions in this case?
11:10:04 A. Well, they confirmed that these investors -- these
11:10:11 inventors did not have possession of the dry-powder device
11:10:15 or dry-powder formulation.
11:10:17 Q. And how did they confirm that they did not have
11:10:20 possession of a dry-powder formulation or a dry-powder

inhaler?

A. So Dr. Seeger and -- Dr. Seeger and Dr. Rubin, in my recollection, said that they did not -- they explicitly said that they did not work or have possession of the invention. And Dr. Roscigno could not remember. That's my recollection.

Q. Did you see any evidence that the inventors of the '793 patent were actually working on a dry-powder formulation of Treprostinil as of May 2006?

A. No, I didn't see any evidence that they would have worked on a dry-powder inhaler.

Q. Did you see any evidence that the inventors of the '793 patent were actually working on trying to use a dry-powder inhaler for inhaled therapies of Treprostinil to treat pulmonary hypertension patients as of May 2006?

A. I couldn't see any evidence of it, no.

Q. Now, do you understand that United Therapeutics has asserted claims in addition to Claim 1 against Liquidia?

A. Yes, I'm aware of that.

Q. Can we go back to the claims at the end.

Do you understand that UT has also asserted Claims 4, 6, 7, and 8?

A. Yes, I know that.

Q. And do Claims 4, 6, 7, and 8 depend from Claim 1?

A. Yes, they are the dependent claims.

11:11:48 Q. Based on this dependency, do Claims 4, 6, 7, and 8 require either a dry-powder formulation or a dry-powder inhaler?

11:11:56 A. So, Claims 4, 6, and 7 specifically require a dry-powder formulation. Claim 8 is a very general claim that covers, also, dry-powder formulations.

11:12:07 Q. The opinions you provided with respect to Claim 1 and your opinion that the inventors, a POSA, would not consider the inventors to be in possession of a dry-powder formulation of Treprostinil for the treatment of pulmonary hypertension, would that apply to Claims 4, 6, 7, and 8 as well?

11:12:29 A. Yes.

11:12:31 Q. I'd like to move to your second opinion, which relates to whether the '793 patent would enable a POSA to make a dry-powder formulation of Treprostinil for treating pulmonary hypertension in May 2006. Can you generally describe what your opinion is with respect to that aspect.

11:12:58 A. Yes.

11:13:00 Q. Could you please describe that.

11:13:01 A. Yes. Sorry. Yes. I don't think that the patent, the claims have been met.

11:13:10 Q. And why is that?

11:13:11 A. I see -- I see that it would have been very difficult. It would have required undue experimentation to

11:13:23 actually develop those kind of products.
11:13:26 Q. And what do you mean by "undue experimentation"?
11:13:29 A. By "undue experimentation," I mean that it would take
11:13:32 a group, a team, a fairly large team of experts in different
11:13:37 fields and a number of years to develop the formulation and
11:13:43 device that would be consistent with Claim 1.
11:13:47 Q. Have you prepared a demonstrative that describes the
11:13:50 various parameters and processes POSAs would need to
11:13:53 undertake to develop a dry-powder formulation of
11:13:56 Treprostinil for the treatment of pulmonary hypertension?
11:13:58 A. Yes, I have.
11:14:01 Q. Can we pull up DDX 5.3, please.
11:14:03 Is this the demonstrative?
11:14:04 A. Yes, it is.
11:14:07 Q. Could you describe what this demonstrative depicts.
11:14:11 A. Yes. So this demonstrative, in a very sort of
11:14:16 schematic way, depicts a -- what a POSA would do in 2006 in
11:14:24 order to develop the kind of product that is described in
11:14:28 Claim 1, and specifically a powder product. So, in the
11:14:33 first place, a POSA would have need to find -- to make the
11:14:38 active pharmaceutical ingredient, which in this case would
11:14:41 be Treprostinil or a pharmaceutically acceptable salt of
11:14:46 Treprostinil, that would be suitable to make into a
11:14:51 dry-powder inhaler. So you would look at the physical and
11:14:56 chemical stability of that you would be -- you would, of

course, look to prior literature, and prior literature taught that you would have to pick, preferably, a material with a fairly high melting point. You would look then at whether the material can exist in different solid form being in the known crystalline, or various types of crystals, or maybe some hydrates, or solvates in the material. And you would then check whether those materials are physically and chemically stable at the time of manufacturing, during storage, during manufacturing of the final product, and then during storage and used in real life.

Q. So and that's the first box you had API?

A. That's the very first thing. You would be looking for a suitable form of the active pharmaceutical ingredient that, based on the prior art, as I mentioned hygroscopicity, stable solid form, would be suitable for that kind of product.

Q. Now, Dr. Gonda, I'd like you to talk now -- that's your first box API. What is your second box, carrier excipient relates to developing dry-powder formulations of Treprostinil?

A. So, just to explain Treprostinil is a very potent drug. In other words, you use a very small quantity. For example, instructions. Therefore, you cannot use just Treprostinil just alone. You have to dilute it somehow. You have to put it into a bulking agent, which we call a

carrier or an excipient. So you would then have to pick a carrier that you would think or you would know is safe; right? And again, stable during manufacturing and during storage. And you would then take that and check whether that carrier is compatible physically and chemically at the time of mixing them, during manufacturing, right, and then during storage and -- and you would also check whether during, you know, real use that kind of a mixture could be used and can be stable.

Q. And now after you look at the API and the carrier, what is your third box at the top, inhalation device? How does that relate to developing a dry-powder formulation of Treprostinil for treating pulmonary hypertension?

A. So, we would have known from prior art, you know, which was, you know, started up with the article by Dr. Clark that you would need to be sure that the device that you select for this can be actually used in a proper way by the patients and that the patients would be able to inhale with sufficient effort, meaning how quickly can they inhale, what is the acceleration, what is the peak flow that you get and how much volume, how much volume they could generate with a particular device. So you have to make sure that you have the device that would be capable of delivering dose of the right particle size distribution to the patients with the disease that they're going to be treating.

11:18:02 Q. And as of May 2006, a POSA looking to make a dry-powder formulation of Treprostinil to treat pulmonary hypertension, they would take into consideration these three factors?

11:18:14 A. Yes, they would.

11:18:15 Q. Now, in terms of testing the device in your third box at the top, with patients, would the drug or the powder formulation actually have to be in the device to do that?

11:18:27 A. No. You still -- you wouldn't need to check the capability of the device in the patients with the drug in the device, no.

11:18:35 Q. And did the '793 patent provide any information regarding any of these factors as they applied to making a dry-powder formulation of Treprostinil for a pulmonary hypertension?

11:18:47 A. No, no it did not.

11:18:49 Q. Now, do you know that UTC has enlisted an expert of Dr. Smyth in this case?

11:18:57 A. Yes, I know.

11:18:58 Q. And do you understand that Dr. Smyth conducted testing to try to make a dry-powder formulation of Treprostinil?

11:19:03 A. Yes, he did.

11:19:06 Q. Generally, what type of testing did Dr. Smyth conduct?

11:19:09 A. So, I mean, I can describe briefly what it is. So
11:19:15 Dr. Smyth did not have to source or make the different forms
11:19:22 of the active pharmaceutical ingredient he received them
11:19:25 from the other documents. And there was three types of
11:19:31 solids. They were Treprostinil, the acid itself, the drug
11:19:36 itself there were Treprostinil sodium, and then he -- which
11:19:40 is a salt. And then he had to search for which was
11:19:46 diethanolamine, the salt form, or salt of Treprostinil. And
11:19:50 then he took those three forms and he milled them, and he
11:19:55 picked the most common and widely used excipient as of
11:20:02 May 2006, which was lactose, lactose powder. He then
11:20:08 blended, mixed, the lactose powder with these three
11:20:14 different types of solid forms of Treprostinil. He then
11:20:17 took an inhalation device and then he put all of these
11:20:23 things together, went into the laboratory, and in the
11:20:27 laboratory, he tested the dose delivered and the particle
11:20:30 size distribution of the -- of -- so, essentially, those
11:20:33 were the elements of the experiments that Dr. Professor
11:20:37 Smyth conducted.
11:20:38 Q. And in your opinion, do those experiments establish
11:20:42 that as of May 2006, a POSA would have been able to, based
11:20:46 on the '793 patent, make a dry-powder formulation of
11:20:50 Treprostinil for treatment of pulmonary hypertension?
11:20:52 A. No, not according to Claim 1. No.
11:20:57 Q. Let's talk about one of the active ingredients or the

11:21:00 APIs that Dr. Smyth used, Treprostinil sodium. Does
11:21:04 Treprostinil sodium have any characteristics that would
11:21:07 impact its ability to be used as a dry-powder?
11:21:10 A. Yes. It's one of the properties which is mentioned
11:21:15 in prior art that the POSA would have to be careful about,
11:21:18 and that is hygroscopicity.
11:21:20 Q. What is hygro -- hygro --
11:21:22 A. Hygroscopicity.
11:21:24 Q. What is hygroscopicity?
11:21:27 A. So hygroscopicity is the property, the attribute,
11:21:31 whereby a solid material would have a tendency to pick up
11:21:35 water from the environment and incorporate water in the
11:21:40 structure. In the case of Treprostinil sodium, the property
11:21:45 is actually so, so extensive that if you pick up -- you will
11:21:51 pick up so much water that in ordinary room conditions, if
11:21:54 you leave it sitting on the bench. It was not to be --
11:21:59 meaning that it picks up so much water that it actually
11:22:02 forms a liquid.
11:22:03 Q. Now, was Dr. Smyth able to make a dry-powder
11:22:05 formulation of Treprostinil sodium?
11:22:09 A. No, he failed in his laboratory to do so.
11:22:13 Q. And why did he fail?
11:22:13 A. Well, I think that it was because it was so
11:22:17 hygroscopic that eventually picked up so much water that the
11:22:20 product failed.

11:22:21 Q. And did Dr. Smyth note that in his expert report and
11:22:25 notebooks, the hygroscopicity of Treprostinil sodium?
11:22:29 A. Well, he did mention that he was unable to control
11:22:32 relative humidity to the extent that he would have been able
11:22:35 to make -- to make the product.
11:22:37 Q. Now, if Treprostinil sodium is hygroscopic at room
11:22:43 temperature, is it physically stable at room temperature?
11:22:46 A. Well, based on what I know, and for a POSA would have
11:22:51 known or would have found out by experimentation, it would
11:22:53 not have been stable.
11:22:55 Q. And does Dr. Smyth's experiments establish that?
11:22:58 A. Well, the fact that he failed to make a formulation
11:23:03 indicates to me that, yes, it confirmed that.
11:23:05 Q. Can we go back to JTX 3, please, the '793 patent.
11:23:09 And Column 6, do you see do you see a structure
11:23:14 there, Dr. Gonda?
11:23:15 A. Yes, I do.
11:23:17 Q. And what is that structure?
11:23:18 A. It is Treprostinil sodium.
11:23:21 Q. So within the '793 patent -- excuse me -- is this a
11:23:25 Treprostinil sodium that Dr. Smyth failed to make a
11:23:30 dry-powder formulation out of?
11:23:31 A. This is the chemical formula because this doesn't
11:23:36 tell me anything about the solid structure of this compound,
11:23:39 but it's the same formula.

11:23:40 Q. Now, you had mentioned that Liquidia used Treprostinil sodium for their dry-powder formulation; correct?

11:23:46 A. Yes, that's correct.

11:23:48 Q. And how were they able to make a dry-powder formulation when Dr. Smyth could not?

11:23:52 A. Well, they -- they overcome the problem by using completely different process, so they didn't mill the Treprostinil sodium and mix it with lactose. Instead, they actually dissolved Treprostinil sodium. They put it into a solution, and then they added a number of other excipients, a number of other substances, to the formulation. Then they pull the formulation using the proprietary PRINT Process. They evaporate the formulation then it forms a solid. They dry it, and then they use the small particles in their product.

11:24:28 Q. Was Liquidia's PRINT Process available to a person of ordinary skill in the art as of May 2006?

11:24:33 A. I -- I don't think so.

11:24:38 Q. Now I'd like to talk about the second form of Treprostinil Dr. Smyth used, Treprostinil free acid. Okay. Did you consider any documents discussing the characteristics of Treprostinil free acid that might impact its ability to be used in a dry-powder formulation?

11:25:01 A. Yes, I did.

11:25:02 Q. Can we go to DTX 674, please.

11:25:06 Is this a document you reviewed?

11:25:07 A. Yes. It's a highly confidential document from United
11:25:10 Therapeutics.

11:25:11 Q. And do you understand there it says salts of
11:25:15 Treprostinil and UT-15. Do you understand what UT-15 is?

11:25:19 A. UT-15 is Treprostinil.

11:25:21 Q. And is that Treprostinil free acid?

11:25:23 A. Well, Treprostinil is the free acid, that's right.

11:25:28 MR. SUKDUANG: Your Honor, I'd like to move DTX
11:25:29 674 into evidence.

11:25:31 MR. CARSTEN: No objection, Your Honor.

11:25:31 THE COURT: Admitted without objection.

11:25:33 (DTX Exhibit No. 674 was admitted into
11:25:33 evidence.)

11:25:33 BY MR. SUKDUANG:

11:25:33 Q. Can you please turn to Page 4 of 291. And what
11:25:37 does -- there's a section titled Initial Development at
11:25:40 United Therapeutics. Do you see that?

11:25:42 A. Yes, I do.

11:25:43 Q. What does this paragraph tell you about the
11:25:46 properties of UT-15, the Treprostinil free acid?

11:25:49 A. So just to put it into context, it says that already
11:25:54 in 2001, United Therapeutics began a project to determine a
11:25:57 suitable oral formulation of Treprostinil. So they were

11:26:00 trying to make tablets and also the solid form of -- for
11:26:05 making tablets. And it says that because of the instability
11:26:08 and propensity of UT-15 free acid, meaning Treprostinil, to
11:26:14 form dimers at ambient temperature, it was thought that a
11:26:17 salt form of UT-15 might be more stable.
11:26:21 Q. Now, would a person of ordinary skill in the art as
11:26:23 of May 2006 want to use a form of Treprostinil that would
11:26:28 form dimers at room temperature or ambient temperature?
11:26:30 A. No, no. A POSA wouldn't want to use that kind of a
11:26:34 form because it's -- it's a chemically different form, and
11:26:38 it could cause efficacy problems as well as safety problems.
11:26:43 Q. Now, outside of this document, if a POSA had
11:26:47 Treprostinil free acid, a sample of Treprostinil free acid,
11:26:52 and they were determining whether they can use it to make a
11:26:57 dry-powder formulation of Treprostinil, what would they do
11:27:01 first?
11:27:03 A. So that would be the very first stage, selecting a
11:27:07 suitable solid form of Treprostinil. You would want to make
11:27:11 sure that that substance is stable, physically and
11:27:16 chemically, during processing and during storage.
11:27:20 Q. And if a POSA conducted the experiments that you
11:27:24 described in your demonstrative on Treprostinil free acid in
11:27:28 trying to make a dry-powder formulation, what would they
11:27:30 find out?
11:27:31 A. Well, I expect that they would have found out the

same thing as United Therapeutics did, that -- that even during storage at room temperature, they would form dimers of Treprostinil, which a POSA would not wish to have in their active pharmaceutical ingredient.

Q. Now, did Dr. Smyth conduct studies on Treprostinil free acid to determine whether it would remain stable at the temperatures for processing and actually making a Treprostinil free acid powder form?

A. I didn't see any experiments to -- to that perform that.

Q. Referring to that, did Dr. Smyth process the Treprostinil free acid in a particular way to mix it with the lactose that you described?

A. Yes. He used he first -- he first made it into jet milling. First made it into small particles using jet milling and then he mixed those particles with lactose.

Q. And does jet milling result in micronizing the Treprostinil free acid?

A. Yes. Jet milling is using the energy of compressed air to -- to make smaller particles from big particle, yes.

Q. I'd like to talk about the last Treprostinil form that Dr. Smyth used in his experiments, Treprostinil diethanolamine. Do you recall whether Dr. Smyth also mixed Treprostinil diethanolamine with lactose?

A. Yes, he did.

11:29:16 Q. And as of May 2006, would a POSA have actually selected lactose to use with Treprostinil diethanolamine?
11:29:19
11:29:25 A. Probably not.
11:29:25 Q. And why not?
11:29:26 A. Well, a POSA should have known that lactose reacts with amines by a so-called Maillard reaction.
11:29:31
11:29:38 M-A-I-L-L-A-R-D reaction. And therefore, a POSA would have been reluctant to use lactose with -- with that kind of a salt.
11:29:40
11:29:46
11:29:46 Q. Is Treprostinil diethanolamine an amine?
11:29:50 A. Yes, it is.
11:29:51 Q. Is there any literature as of May 2006 that discusses this Maillard reaction that you mentioned?
11:29:55
11:29:58 A. Yes, there is.
11:29:58 Q. Can we go to DTX 481.
11:30:01 Is this the reference you were referring to, Dr. Gonda?
11:30:06
11:30:06 A. Yes, it is.
11:30:07 Q. And when was this published?
11:30:09 A. This was published in 1998, I think is when it was, yes.
11:30:15
11:30:15 Q. And what is the title?
11:30:16 A. It's called sorry, I misspelled it. It's double L. I'm sorry.
11:30:22
11:30:22 Q. That's fine.

11:30:23 A. Maillard reaction of lactose and fluoxetine
11:30:26 hydrochloride, a secondary amine.
11:30:31 MR. SUKDUANG: Your Honor, I'd like to enter DTX
11:30:35 481 into evidence.
11:30:36 MR. CARSTEN: No objection.
11:30:36 THE COURT: All right. Admitted without
11:30:38 objection.
11:30:38 (DTX Exhibit No. 481 was admitted into
11:30:38 evidence.)
11:30:38 BY MR. SUKDUANG:
11:30:39 Q. Did you review this document, this reference,
11:30:41 regarding the compatibility of Treprostinil diethanolamine
11:30:44 with lactose?
11:30:44 A. Yes, I did.
11:30:46 Q. Can you can turn to the top right column of Page 1.
11:30:50 And what does this say with respect to amines
11:30:54 and compounds like lactose?
11:30:56 A. Well, it says that earlier on, it was believed that
11:31:01 only primary aromatic amine were capable of this reaction,
11:31:04 but subsequent research has shown that near nearly all
11:31:08 primary and secondary amines, aromatic or aliphatic, are
11:31:12 capable of this reaction.
11:31:13 Q. What type of amine is Treprostinil diethanolamine?
11:31:16 A. It's an aliphatic type.
11:31:19 Q. And is it a primary or a secondary aliphatic?

11:31:22 A. Sorry, it's a secondary. Secondary aliphatic.
11:31:27 Q. And what would this reference teach a POSA as of 2006
11:31:31 about combining a secondary aliphatic amine like
11:31:37 diethanolamine with lactose?
11:31:39 A. It says that -- that there was a likelihood, and
11:31:46 fairly high likelihood, that such a reaction would take
11:31:49 place.
11:31:49 Q. Now, as part of your demonstrative discussing
11:31:53 carriers, you mentioned that POSAs would conduct studies to
11:31:57 determine compatibility of the API they selected and the
11:32:02 carriers or the excipients that they wanted to use in the
11:32:05 powder formulation.
11:32:06 Do you recall that?
11:32:06 A. Yes, I do.
11:32:07 Q. Did Dr. Smyth conduct any experiments assessing the
11:32:11 compatibility of diethanolamine with lactose?
11:32:15 A. No, he didn't. And just to put it into context, I
11:32:19 mean, all of the experiments that I, in my demonstrative,
11:32:23 would be done by a POSA even before going into animal
11:32:28 experiments. So this would be way ahead of any kind of
11:32:30 clinical trials. You wouldn't want to take a risk that your
11:32:33 product was unlikely to be suitable for this patient
11:32:39 population before you could even go into patients, you would
11:32:41 have to test it in animals for safety. So, a POSA would
11:32:45 really want to do all of this work before even conducting

11:32:49 1 animal experiments. And Professor Smyth didn't look at the
11:32:53 2 compatibility of lactose with this particular salt.
11:32:58 3 Q. Did he look at the compatibility with lactose in any
11:33:01 4 of the forms of Treprostinil that he studied?
11:33:03 5 A. No, he did not do such studies, no.
11:33:07 6 Q. Is --
11:33:07 7 A. He did not do it at the beginning. He did not do it
11:33:10 8 during storage or after manufacturing or under conditions of
11:33:15 9 use by the patient.
11:33:15 10 Q. Now I'd like to talk about the last part of your
11:33:18 11 demonstrative, the device. When selecting a dry-powder
11:33:25 12 inhaler, what would a -- what -- would a POSA need to know
11:33:31 13 the patient population the device is to be used for?
11:33:35 14 A. Yes.
11:33:37 15 Q. And why is that important?
11:33:38 16 A. Well, because for dry-powder inhalers, it is the --
11:33:44 17 the interaction of the patient with the device and, in
11:33:48 18 particular, how much air flow, how far, how -- you know, how
11:33:53 19 hard they can inhale on the inhaler, and embodies the volume
11:33:57 20 of the air that will impact the dose. So a POSA would want
11:34:00 21 to know what is the interaction between the patient and the
11:34:03 22 device before testing the formulation with the device in the
11:34:09 23 laboratory in order to make sure that the device is tested
11:34:12 24 in the laboratory and at the correct conditions.
11:34:14 25 Q. If a pulmonary hypertension patient could use a

11:34:17 nebulizer like TYVASO uses, does that mean they could use a
11:34:21 dry-powder inhaler?
11:34:22 A. No.
11:34:26 Q. Are you aware of any publications that discuss the
11:34:28 use of dry-powder inhalers in pulmonary hypertension
11:34:31 patients?
11:34:31 A. There are two recent papers on the subjects. They
11:34:36 are -- they were both published in 2021.
11:34:38 Q. Let's look at one of them, DTX 468. Is this one of
11:34:44 the references, Dr. Gonda?
11:34:44 A. Yes, it is.
11:34:46 Q. And what is the title?
11:34:47 A. It is Inspiratory Flow Patterns with Dry-Powder
11:34:51 Inhalers of Low and Medium Flow Resistance in Patients with
11:34:56 Pulmonary Arterial Hypertension.
11:34:57 Q. And who's the last named author?
11:35:00 A. The last named author is Dr. Aaron B. Waxman.
11:35:05 Q. And is he the Dr. Waxman that we heard earlier today?
11:35:07 A. I believe it is.
11:35:10 MR. SUKDUANG: Your Honor, I'd like to move DTX
11:35:12 468 into evidence.
11:35:13 MR. CARSTEN: No objection Your Honor.
11:35:14 THE COURT: Admitted without objection.
11:35:16 (DTX Exhibit No. 468 was admitted into
11:35:16 evidence.)

11:35:16 BY MR. SUKDUANG:

11:35:18 Q. Can you turn to the abstract, please.

11:35:21 And what was the goal of the study conducted by Dr. Waxman and his colleagues?

11:35:28 A. So, the investigators wanted to see whether two dry-powder inhalers, when used by patients with pulmonary arterial hypertension -- they wanted to know what is the inspiratory flow pattern, meaning the inspiratory flow rate, the acceleration of inspiration, and the spike body, the amount of air that they take, how they could do it, what were these results in the patients that were intended for the therapy with these dry-powder inhalers.

11:36:03 Q. Okay. And there's -- with respect to the inhalers, the dry-powder inhalers, if you can highlight that, there's two mentioned, RS01-L and RS01-M. What does the L stand for?

11:36:20 A. The L stands for low resistance.

11:36:24 Q. And what does that mean?

11:36:25 A. So, as Dr. Clark mentioned in 1995, different devices will have different resistance. And so they will require different kind of collaboration, different effort, and maybe different volumes. So, the RSOL means it is a low-resistance device that one in the art obtains, so they can test both in order to see how well the patients can use them.

11:36:49 Q. So in more simplistic terms, what does it mean to
11:36:51 have a device that has low resistance versus a device that
11:36:55 has moderate resistance?
11:36:58 A. Okay. So if I tried to breathe through this, that's
11:37:01 high resistance. If I try to breathe through that, that's
11:37:04 low resistance, so there is -- it's easier to breathe
11:37:07 through a low-resistance device.
11:37:12 Q. What type of patient -- oh, you mentioned -- did
11:37:15 Dr. Waxman, in his study, look at pulmonary arterial
11:37:19 hypertension patients?
11:37:19 A. Yes.
11:37:21 Q. Can we turn to the Table 2 on Page 4. And can you
11:37:26 blow that up, please, Derrick. Thank you.
11:37:29 Now, what does Dr. Waxman and his colleagues'
11:37:33 results show with respect to pulmonary arterial hypertension
11:37:38 patients and the use of dry-powder inhalers?
11:37:40 A. Yeah, so just to explain, so this was looking at the
11:37:45 complete inspiratory flow pattern in patients with pulmonary
11:37:52 arterial hypertension. There were 20 patients.
11:37:54 When we look at the top row, below the title are
11:38:00 two devices, RS01-L, low resistance, and RS01-M, which is
11:38:06 the medium resistance, so these devices are different.
11:38:09 Different resistance. And if you take a quick look between
11:38:14 the two columns, you will see that the results in the two
11:38:18 columns are different.

11:38:19 Q. Could you focus in on inspiratory effort and inhaled
11:38:22 volume?
11:38:22 A. Sure. So. The inspiratory effort, which is the
11:38:28 fact, you know, how hard you can inhale is that particular
11:38:33 variable there. And we see that for the RS01, the low
11:38:37 resistance, it is 2.6 kilopascals plus minus 1.2, which is
11:38:43 the term of deviation, standard deviation, meaning that the
11:38:46 patients who has more bigger problems with their lungs could
11:38:51 only inhale at an even lower. This is -- the mean volume is
11:38:56 2.6 minus 1.2 would be one point -- would be 1.4. So, they
11:39:02 could only have a relatively low effort.
11:39:06 And vice versa, the people who are the
11:39:09 healthiest would be able to do it -- be better than that.
11:39:12 So, it just -- and knowing a little bit about -- with normal
11:39:17 healthy individuals, this is much lower than the result.
11:39:20 Q. Where it says inhaled volume, what does that inhaled
11:39:24 volume mean?
11:39:24 A. So, the inhaled volume is the total volume that the
11:39:27 patients would be inhaling through the device. So, if they
11:39:29 get the device and they start inhaling, it's how much air
11:39:32 they can get into -- into their lungs when they're inhaling
11:39:37 from the particular device.
11:39:39 Q. With respect to the RS01-L device, what inhaled
11:39:43 volume did Dr. Waxman and his colleagues find out?
11:39:47 A. So, they found that the mean volume was 1.4. And

again, the -- some patients were a little bit higher and some patients were a little bit lower.

Q. Did Dr. Smyth conduct testing on inhaled -- let me rephrase.

Did Dr. Smyth conduct testing of this powdered formulation with a dry-powder inhaler?

A. Yes, he did.

Q. Did you create a demonstrative describing that?

A. Yes.

Q. Can we bring up DDX 5.4, please. And, Dr. Gonda, what type of DPI or dry-powder inhaler did Dr. Smyth use?

A. Well, it was the same DPI as one of the DPI, the low-resistance DPI in the publications that we have just reviewed.

Q. So he used an RSO1-L which was the same as Dr. Waxman's device in his paper?

A. Yes, he did.

Q. And with respect to the inspiratory effort, what inspiratory effort did Dr. Smyth use?

A. He used four kilopascal.

Q. And how does that compare to the inspiratory effort that Dr. Waxman found for pulmonary arterial hypertension patients?

A. Well, it's obviously much higher.

Q. And with respect to inhaled volume, how much -- what

was the inhaled volume that Dr. Smyth used?

A. It was about three times as high, almost three times as high as the volume, as the mean volume.

Q. And how did the differences in inspiratory effort and inhaled volume that Dr. Smyth used compare to Dr. Waxman in PAH patients impact his testing?

A. Well, I mean, firstly, it is questionable whether he had used the bodies from the paper, whether they would have got any dose out of the device. So, and if they got any dose out of the device, I would expect that the dose would have been lower and the particle size would have been higher. It wouldn't have been dispersed as well as with the bodies that he was using in the report.

Q. Now, did Dr. Smyth actually test his dry-powder and dry-powder inhaler in humans?

A. No, he did not.

Q. Did he test it in PAH patients?

A. No.

Q. Did he test it using a machine?

A. Yes, he used it on the bench. He used a pump to -- pump to create the flow through the device.

Q. Based on the experiments Dr. Smyth conducted on the API, the carrier, making the dry-powder formulation and testing it in the RS01-L dry-powder inhaler, in your opinion, does his experiments establish that a POSA, as of

May 2006, would have been enabled, based on the patent, to make a dry-powder formulation of Treprostinil for treating PH?

A. No.

Q. Now, do you understand Dr. Smyth is saying that he was able to do this so quickly, it's only in three weeks?

A. Yes, I know that he says that he did it in three weeks.

Q. If a colleague came to you and said, I developed a dry-powder formulation of Treprostinil that could be administered to a patient for pulmonary hypertension in three weeks, what would you say?

A. I would have said it's impossible.

Q. Why?

A. Because the elements that I mentioned before, choosing the suitable solid form, in the first place, or making it -- making sure that it satisfies the criteria that would be defined by POSAs in prior art, right, he wouldn't have been able to do that in three weeks.

And then on top of it, some of the experiments, which is the compatibility studies, when you're looking at stability and in general, I'm saying all of this would be done by a POSA even before going into animals; right? You would just -- you just -- it just takes much longer to do all of these steps. The stability studies take a lot longer

than three weeks.

Q. So, if Dr. Smyth says, Oh, I didn't see any compatibility problems within the three weeks, what would that say to you?

A. I would say show me the data. He -- he certainly did not present any of the data. I would just say it's impossible to get that kind of data over such a short period of time.

Q. Now, do your opinions with respect to the enablement of dry-powder formulations of Treprostinil to make -- to treat pulmonary hypertension, would they also apply to Claims 4, 6, 7, and 8 of the '793 patent?

A. Yes.

MR. SUKDUANG: Thank you, Your Honor.

Dr. Gonda. No further questions.

THE COURT: All right. So we'll take a ten-minute break and then we'll come back.

DEPUTY CLERK: All rise.

(Recess was taken.)

DEPUTY CLERK: All rise.

THE COURT: Let's be seated.

Mr. Carsten.

MR. CARSTEN: Your Honor, may I proceed?

THE COURT: Yeah.

MR. CARSTEN: Thank you.

CROSS-EXAMINATION

BY MR. CARSTEN:

Q. Good morning, Dr. Gonda.

A. Hello.

Q. My name is Doug Carsten. I don't think we ever formally met before. I'm going to be asking you some questions today, if that's okay.

A. Sure.

Q. Great. Now, the claims, you may have covered this with Mr. Sukduang, but I want to make sure. The claims of the '793 patent don't require FDA approval, do they?

A. No.

Q. Okay. And they don't require optimized formulations, do they?

A. No.

Q. And the claims don't require a particular polymorphic form?

A. No, they cover any -- any polymorphic form, yes.

Q. They don't require any particular polymorphic form; right?

A. It should be a pharmaceutically acceptable salt.

Q. I believe you testified that in your view, undue experimentation meant any number of years of work. Isn't that what you said earlier today?

A. Well, I wouldn't say any number of years. I said

substantial period of time.
Q. A substantial period of time. So a lot of work?
A. A lot of work. Yes.
Q. Now, in -- as of 2006 -- well, you put up a chart that had three items. It had active ingredient, it had carrier, and then it had inhaler device, right?
A. Yes, I did.
Q. As of 2006, there were numerous dry-powder inhalers options available to a person of skill in the art; correct?
A. Yes.
Q. There is the Dura/Spiros; correct?
A. Well, the Dura/Spiros was never approved. So -- and it was approved -- it was disapproved, not allowed to be used, by FDA, so a POSA would have been very reluctant to use a device that FDA refused to approve.
Q. But you just told me the claims don't require FDA approval; right?
A. No, but -- but a POSA would not have chosen a device where FDA would have stated very clearly why they didn't want it to approve it.
Q. Okay. But it was a publicly known dry-powder device. You agree with me on that at least; right?
A. It was a publicly available device, yes.
Q. The Exubera device was publicly known?
A. Sorry?

11:58:38 Q. Exubera?
11:58:39 A. Yes, Exubera was known. Yes.
11:58:41 Q. Now the Exubera device, that's a dry-powder inhaler
11:58:44 device; right?
11:58:45 A. It is.
11:58:46 Q. And that's an active dry-powder inhaler device, isn't
11:58:49 it?
11:58:49 A. That is correct.
11:58:51 Q. So it's not the passive device that you were
11:58:54 depicting with the Plastiape device that you showed on your
11:58:57 demonstratives right?
11:58:58 A. That is correct.
11:58:59 Q. Okay. So this one would actually assist a patient in
11:59:04 taking dry-powders; correct?
11:59:06 A. It would -- that's correct. It would assist the
11:59:09 patient. Will patients.
11:59:11 Q. And then you showed an image of a Plastiape device.
11:59:16 Am I saying that correctly?
11:59:16 A. That's good enough. I can't -- I can't say it any
11:59:20 better.
11:59:20 Q. Well, if it's good enough for you, it's good enough
11:59:23 for me, Doctor. It's P-L-A-S-T-I-A-P-E; right.
11:59:27 A. That is correct.
11:59:28 Q. Italian company?
11:59:29 A. Sorry?

11:59:30 Q. Italian company?
11:59:31 A. Yes, correct.
11:59:32 Q. And Plastiape inhalation devices, they've been
11:59:38 available since the 1970s; correct?
11:59:40 A. That is correct.
11:59:40 Q. Now, you understand that as of 2006, Remodulin was an
11:59:46 approved drug product; correct?
11:59:48 A. Yes.
11:59:49 Q. And the active ingredient of Remodulin was
11:59:52 Treprostinil; correct?
11:59:53 A. That is correct.
11:59:56 Q. Now, you believe that a person of skill in the art
12:00:02 would have had some challenges in terms of identifying
12:00:07 whether Treprostinil or a salt of Treprostinil would have
12:00:10 been appropriate for taking into dry-powder inhalation
12:00:16 development; correct?
12:00:17 A. Yes.
12:00:19 Q. Okay. Now -- and you pointed to an internal
12:00:24 confidential document from United Therapeutics pertaining to
12:00:28 characteristics of various salt forms; correct?
12:00:31 A. Yes, I did.
12:00:33 Q. Now, that wouldn't have been available to a person of
12:00:37 skill in the art; right?
12:00:39 A. Not unless if they worked at United Therapeutics.
12:00:41 Q. And the hypothetical person of skill in the art,

there isn't a criteria that says you worked internally at United Therapeutics; is there?

A. No, no, of course.

Q. Okay. Fair enough. So, doing that kind of screening, though, of salt formation and properties, that was routine as of 2006, wasn't it?

A. Yes.

Q. And you could have hired a lab to go ahead and do that for you; right?

A. Yes.

Q. And it wouldn't be an expensive, long challenge, none of those things, would it?

A. I didn't say that. It could have been challenging. I mean, it would have depended on how quickly you would have found the right salt and studied all the attributes of that salt or the material that would was defined by POSAs. You know, what would be the properties that would be required for a suitable API form for a dry-powder inhaler.

Q. Right. And there were publications available as of 2006 that set forth the kind of desired wish list for an API or an active pharmaceutical ingredient to be developed for a dry-powder inhaler; correct?

A. Yes, correct.

Q. Okay. Now, you pointed out hygroscopicity -- maybe I said that right, maybe I didn't -- as a concern, and you

criticized some of Dr. Smyth's work in the case on that basis; correct?

A. Yes, I did.

Q. Okay. Now, you understand, however, that a person of skill in the art could use temperature and humidity controls and controlled environments to try to address hygroscopicity; correct?

A. That is correct.

Q. And that was true as of 2006?

A. Yes.

Q. And those techniques were at -- or were readily available; correct?

A. Yes, they would have been in industrial laboratories, yes.

Q. And you understand that Dr. Smyth was not using an industrial laboratory for his prospecting experiments. Instead, he was using his own laboratory; right?

A. Well, he was supposed to be emulating what a POSA would do.

Q. Right. But he wasn't working in a pharmaceutical company with that kind of facility that you're aware of; right?

A. I -- I really don't know how, you know, what kind of laboratory -- I really don't know what is the quality of the laboratory with respect to production. So -- I just don't

12:03:00 1 know.
12:03:00 2 Q. Fair enough. But you're comfortable criticizing the
12:03:03 3 Treprostinil sodium experiments of Dr. Smyth having not
12:03:06 4 known anything about the laboratory -- laboratories in which
12:03:09 5 he was conducting his experiments; right?
12:03:11 6 A. I'm saying that he provides no evidence that
12:03:15 7 Treprostinil sodium could have been manufactured under
12:03:18 8 whatever conditions he was using in his laboratory.
12:03:21 9 Q. Okay. Well, Dr. Smyth will get a chance to say
12:03:25 10 exactly what he did and how he did it.
12:03:27 11 Let's turn to the -- the middle box. That was
12:03:29 12 the carrier box. Do you remember that?
12:03:31 13 A. Yes, I do.
12:03:31 14 Q. Now, at the time, roughly 2006, lactose was an
12:03:38 15 approved carrier for dry-powder formulations; correct?
12:03:41 16 A. That's correct.
12:03:43 17 Q. In fact, it was the only approved carrier at that
12:03:45 18 time in the United States for dry-powder inhalation
12:03:48 19 formulations; correct?
12:03:49 20 A. As far as I know, you are correct. It was the only
12:03:52 21 excipient.
12:03:52 22 Q. Okay. But glucose was also approved as a dry carrier
12:03:57 23 -- as a dry-powder carrier in Europe at that time. Isn't
12:04:00 24 that right?
12:04:00 25 A. I really, really don't know, but I -- I believe you

when you say that. I -- I'm in the aware of that. I read that it was, but I have not checked it.

Q. You don't know one way or another whether there was a second carrier that was approved anywhere in the world as of the priority date?

A. I read about the fact. I actually haven't checked the approval, no.

Q. You remember reading that glucose was an approved carrier in Europe at that time, don't you?

A. Yes.

Q. Okay.

A. Yes.

Q. And you have no reason sitting here today to doubt that, do you?

A. No.

Q. You're here as an expert; right?

A. Yes.

Q. Okay. All right. And you also understand that compounds like mannitol, as of that time, had been shown to be feasible alternatives to lactose, and POSAs expected that they would, ultimately, be approved; correct?

A. Well, I think we need to be very careful about it particularly with respect to automation. Exubera was made with mannitol formulation. And it had a label that it was not recommended for patients with lung disease.

12:05:03 Q. I'm sorry. It was not --
12:05:05 A. So Exubera was a product, the Exubera device was --
12:05:10 an Exubera device with a specific formulation which
12:05:13 contained mannitol; right? And it had a label for approval
12:05:18 that it should not be used in patients with lung disease.
12:05:24 So when it says mannitol, I mean, you have to be
12:05:26 very careful. Again, bearing in mind what kind of
12:05:30 population of patient you are going to be using the
12:05:32 materials with.
12:05:33 Q. Okay. But you do understand that man -- the
12:05:36 formulations including mannitol were ultimately approved
12:05:39 drug products; right?
12:05:40 A. For other drugs, yes.
12:05:42 Q. Okay. And by for other drugs you mean not
12:05:45 Treprostinil?
12:05:46 A. That's correct.
12:05:51 Q. You talked about some concerns about the Maillard
12:05:57 reaction.
12:05:57 A. Yes, I did.
12:05:58 Q. And you say that a person of skill in the art at the
12:06:01 time wouldn't pursue the use of a lactose carrier with
12:06:05 amine-containing compounds, amine, A-M-I-N-E?
12:06:09 A. Yes.
12:06:09 Q. Out of concern about some safety issues; is that
12:06:14 right?

12:06:14 A. Well, it wouldn't be my first choice or a POSA's
12:06:18 choice to use the excipient unless you would say, well, I
12:06:21 really don't have that many choices, so I have to pick this
12:06:25 one. Yes, and then I would study all the aspects that I
12:06:28 mentioned, the compatibility during manufacturing up to
12:06:34 storage and up to real use before I would decide whether it
12:06:36 is a suitable material.
12:06:42 Q. Okay. So let's see if I can get an answer to my
12:06:45 question, sir, if I could.
12:06:46 A. Yes.
12:06:46 Q. I think we may have lost that in the bidding here.
12:06:51 You say that a person of skill in the art would not pursue
12:06:54 use of a lactose carrier with an amine-containing material
12:06:58 out of concern out of safety concerns; is that right?
12:07:00 A. No, all I said was that a POSA would have had two
12:07:04 choices. A POSA would have said, well, I will use lactose,
12:07:08 but now I will study whether the lactose is compatible with
12:07:12 my materials through all of these steps that I mentioned
12:07:16 before a POSA would come to the conclusion that lactose is a
12:07:19 suitable carrier.
12:07:20 Q. Okay. And that's true even though lactose was the
12:07:24 only approved carrier as of 2006 in the United States;
12:07:28 correct?
12:07:29 A. Well, a POSA would have had the choice, as we have
12:07:35 found out that Mannkind and Liquidia, to say, I am not going

12:07:39 to use lactose because I worry about this, and I'm going to
12:07:42 develop my own formulation which should be a new whole new
12:07:49 formulation, a revolutionary step not based on prior art.
12:07:50 Q. Right. Somebody could do that; right?
12:07:52 A. Yeah.
12:07:52 Q. Okay. Now, I believe that counsel -- this is -- let
12:07:57 me see.
12:07:57 This is the '793 patent. This is the patent
12:07:59 that you studied in this case; right, Dr. Gonda?
12:08:02 A. Yes, of course.
12:08:02 Q. And this is the compound Treprostinil; right?
12:08:06 A. It's Treprostinil sodium.
12:08:08 Q. Right.
12:08:09 A. It's a salt.
12:08:10 Q. The sodium is that little NA plus there; right?
12:08:12 A. Yes, it is.
12:08:13 Q. Okay. And if this were going to be just Treprostinil
12:08:16 free acid, you wouldn't have that little minus sign, you
12:08:19 would have an H there instead and none of this NA business;
12:08:22 right?
12:08:22 A. I agree.
12:08:23 Q. Okay. Great.
12:08:24 Now, you would agree with me, Dr. Gonda,
12:08:26 wouldn't you, that the Treprostinil molecule contains no
12:08:30 amines; right?

12:08:31 A. That's correct.
12:08:34 Q. So the concerns about a Maillard formulation have
12:08:39 nothing to do with the Treprostinil molecule itself but
12:08:43 rather the particular salt form here was a diethanolamine,
12:08:48 which that's the concern for using lactose; right? The
12:08:52 amine and the counter ion?
12:08:54 A. Yes, in this particular case that is the concern,
12:08:56 yes.
12:08:57 Q. And there are other salt forms available that which
12:09:00 don't have that amino group in the counter ion; correct?
12:09:03 A. I'm not sure that there were other salts available.
12:09:10 Q. Okay. If that's your testimony.
12:09:13 The diethanolamine counter ion, we talked about
12:09:17 primary amines and secondary amines. Do you remember that
12:09:20 testimony?
12:09:20 A. Yes, I do.
12:09:22 Q. All right. And the counterion here is a secondary
12:09:26 amine, if you're classifying it; right?
12:09:29 A. That is correct.
12:09:30 Q. And it's not even really a secondary amine. It's a
12:09:33 secondary ammonium ion if we're being specific; right?
12:09:37 A. Well, you know, you're really testing my chemistry.
12:09:41 I say I really can't -- yeah. But it's a diethanolamine.
12:09:48 Q. You can't say one way or the other whether it's a
12:09:50 diethanolamine, a secondary amine, or a diethanol ammonium

ion? You don't know?
A. I don't know the distinction. Yeah, I don't.
Q. Fair enough. Okay.
You yourself were involved, however, as of the priority date, in formulating a dry-powder using DNase; right?
A. That is right.
Q. And DNase is a protein; right?
A. Yes.
Q. And proteins contain primary amines?
A. Yes.
Q. And that contained lactose, didn't it?
A. Yes.
Q. It was approved drug product?
A. Not the dry-powder, no.
Q. In fact, you worked on that product with Dr. Clark; right?
A. Yes, I did.
Q. There are a lot of reunions of experts in this case?
A. Yes, happy days.
Q. Now, Dr. Gonda, you could have done a test yourself, couldn't you?
A. Can you be specific. What kind of test?
Q. Sure. You could have sat down with a batch of Treprostinil of one sort or another and some lactose and

actually given it a shot and seen if applying the level of ordinary skill in the art in 2006 that a person of skill would have had success without undue experimentation; right?

A. Well, again, it all depends on what you define as undue experimentation. These experiments take months because you would want to know whether, during the storage of the product and during the use, you would -- you would want to be pretty sure that you're not going to get the reaction because you would want to do it before you go into animal, long before you go into human.

Q. Understood.

A. So I -- it would take several months, at least.

Q. Sure. I apologize. I didn't mean to step on your words, sir, I want to make sure you complete your answer.

Stability testing was routine as of 2006; right?

A. Yes.

Q. And the reason it would take months is the stability testing. You have to let it sit in order to test whether it's stable after a certain period of time; right?

A. That is correct.

Q. Okay. Let me make sure I got an answer to my question, though. There was nothing preventing you from going ahead and actually trying this yourself as part of your work in this case; correct?

A. That is correct. The POSA would have studied this.

12:12:28 Q. Yeah, they would have. You chose not to. Instead, you were looking at Dr. Smyth's information. You didn't try that test yourself; right?

12:12:38 A. Well, we tried it for DNase.

12:12:40 Q. Sure, for DNase. You didn't try it with any Treprostinil in connection with your work in this case; is that right?

12:12:45 A. No, I did not.

12:12:46 Q. Okay. Let's turn to written description, if we could.

12:12:53 You agree with me, at least, that -- well, maybe I shouldn't do it, but there's a Latin expression that says in forma verbis. It means the words themselves. You agree with me that in forma verbis, the words themselves, that dry-powder appears in this patent; right? Dry-powder inhaler?

12:13:15 A. Yes, it does.

12:13:16 Q. They're there in Column 7?

12:13:18 A. Yes, in the highlighted text, yes.

12:13:23 Q. Right. And dry-powder with a particular particle size of less than 5 micrometers in diameter is also there in words themselves; right?

12:13:34 A. Yes, it is.

12:13:36 Q. And that's in the specification at Column 7?

12:13:39 A. That's correct.

12:13:40 Q. Okay. Now, you think that it doesn't -- that this is
12:13:46 insufficient written description because there's got to be
12:13:50 more; right?
12:13:53 A. Yes. I mean that's one aspect of it, yes.
12:13:56 Q. That's the only aspect of it. It's written
12:13:58 description. You have to look within the four corners of
12:14:00 the document through the filter of a person of skill in the
12:14:03 art and determine whether the inventor had possession of the
12:14:07 -- of the invention or not; right?
12:14:09 A. Yes.
12:14:11 Q. That's the standard you applied?
12:14:12 A. Yes. I mean, yes. I did look whether the patent
12:14:19 had -- what information it had about dry-powder inhalers and
12:14:24 dry-powder processes.
12:14:25 Q. And in terms of your written description analysis --
12:14:28 we're talking about written description now -- is it your
12:14:32 understanding that to satisfy written description, a person
12:14:37 of skill in the art must be able to piece together the
12:14:40 information that is provided in the patent and then be able
12:14:44 to develop the product or method in the patent?
12:14:46 A. Yes.
12:14:48 Q. Okay. And that's the standard you applied as well as
12:14:50 the possession test; right?
12:14:52 A. No, I did not use the form.
12:14:55 Q. I'm sorry.

12:14:56 A. I did not use the same standard for possession.
12:15:01 Q. I'm sorry, sir. I missed it.
12:15:02 A. So I did not see any evidence that the inventors
12:15:05 would have the possession, and I couldn't see how, based on
12:15:09 this patent and the prior art, a POSA would have been able
12:15:14 to make a dry-powder inhaler with dry-powder formulation of
12:15:18 Treprostinil without undue experimentation.
12:15:21 Q. I understand. I'm asking a very specific question.
12:15:23 A. Yes.
12:15:24 Q. Your understanding and the standard for written
12:15:28 description that you applied here included whether the
12:15:33 written description, using that description, a person of
12:15:36 skill in the art would be able to piece together the
12:15:39 information that is provided in the patent and then be able
12:15:43 to develop the product or method in the patent.
12:15:46 A. Yes, I did it. As I said, my basis for enabling was
12:15:53 that -- that a POSA would not have been able to do this
12:15:56 without undue experimentation.
12:15:58 Q. I understand you applied that for enablement.
12:16:01 A. Yes.
12:16:01 Q. Again, third time, and I'll be done really soon, I
12:16:05 promise. You also considered that to be the standard for
12:16:08 written description, didn't you?
12:16:09 A. Well, I mean, honestly, I'm not a lawyer, and I
12:16:16 really can't give you a straight answer to this. No.

12:16:19 Q. I understand and appreciate that. Let me just show a
12:16:27 segment of your deposition, if I could, sir. You remember
12:16:31 you were deposed in this case?
12:16:32 A. Several times.
12:16:34 Q. Well, in this case, it was just once. There were
12:16:36 some IPRs in which --
12:16:37 A. Yes.
12:16:38 Q. -- you were deposed as well, and my colleague Art
12:16:42 Dykhuis took your deposition; right?
12:16:43 A. Yes, he did.
12:16:46 Q. You have this in your binder as well.
12:16:49 A. Yes.
12:16:49 Q. But I'm turning to Page 50, and I'll put it up on the
12:16:53 board as well.
12:16:54 MR. SUKDUANG: Can you tell me which transcript.
12:16:56 MR. CARSTEN: It's the District Court deposition
12:16:58 at page 50.
12:17:00 THE WITNESS: So that would be the January 7th?
12:17:07 BY MR. CARSTEN:
12:17:07 Q. Let me check.
12:17:08 A. 2022? Yes.
12:17:11 Q. January 7th.
12:17:11 A. Yes, correct.
12:17:12 Q. Okay.
12:17:14 A. And it's page?

12:17:16 Q. It's going to be at Page 50 onto Page 51. And I've got it on the screen if you need it.

12:17:23 A. Okay. That may be easier.

12:17:25 Q. It may be easier, and if you need me to blow something up, you just let me know. Okay?

12:17:29 A. Yes, thank you.

12:17:30 Q. So Mr. Dykhuis asked you "Is undue experimentation" -- excuse me. "Is the lack of undue experimentation also a requirement for a written description as you understand it?"

12:17:42 And you answered -- there was an objection. You answered, "Well, they are not exactly the same. I mean, as I said, I'm not a lawyer." And then you went on to say, "You know, I think that they are similar; right? But clearly there is a -- there is a distinction between the two. So the enablement is defined by undue experimentation." Right?

12:18:00 At the top, it continues and you said, "My understanding of written description is that it needs to be adequate for a person of ordinary skill in the art to be able to piece together the information that is provided in the patent and then be able to develop the product or the method in the claims of the patent. So, the enablement is specifically defined in terms of undue experimentation. But, I mean, from my perspective, they are related. They're not identical requirements, but they are related."

Is that correct?
A. Yes, I did say that.
Q. That was your answer then; correct?
A. Except for the under. I said the text says under experimentation. It should be undue experimentation.
Q. Right. That's an error in the transcript; right?
A. Yes.
Q. Now, you relied in connection with your undue -- with your written description analysis in the case on some deposition testimony from Dr. Seeger, Dr. Rubin, et cetera; correct?
A. Yes, I relied on that. I relied upon my own knowledge, yes. They were -- and the information that was also presented to me during this -- during the preparation.
Q. Understood. Now, you were here in court when Dr. Rubin's video was played?
A. Yes, I was.
Q. Okay. And you heard Dr. Rubin talk about a lunch he had with UTC's Martine Rothblatt, did you?
A. Yes, I did.
Q. And you heard him say that I told Dr. Rothblatt at that point that we ought to pursue a dry-powder inhaler for Treprostinil; right?
A. Yes, I heard that.
Q. Was there any doubt in your mind that -- when you

heard that Dr. Rubin had clear possession in his head of a dry-powder formulation including Treprostinil?

A. Well, I think that a statement "it would be nice to have a dry-powder inhaler" does not indicate to me that he was in possession of the invention.

Q. Fair enough. I understand that, sir. Thank you so much.

MR. CARSTEN: I have no further questions, Your Honor.

MR. SUKDUANG: No redirect, Your Honor.

THE COURT: All right. Dr. Gonda, thank you. You may step down. Watch your step.

THE WITNESS: Thank you.

MR. SUKDUANG: Your Honor, Dr. Gonda was our last witness, so we close our case on --

THE COURT: All right.

MR. CARSTEN: Your Honor this is my colleague Harry Gunn. He would like to make a an oral motion under Rule 52(c).

THE COURT: All right. Knock yourself out.

MR. GUNN: All right. So there's two categories of arguments here. The first one is arguments Defendant disclosed in the Pretrial Order that they didn't present any evidence whatsoever at trial for. And the second argument is for where they presented evidence but it's not sufficient

12:21:02 to meet their burden.

12:21:03 So we'll start with the '066 patent. Defendants
12:21:07 have not presented any evidence of obviousness of the '066
12:21:10 patent. And then with respect to 112, defendants have only
12:21:14 presented two of their 13 arguments. The 11 arguments they
12:21:18 have not presented at trial include the following: Written
12:21:21 description. They haven't presented arguments with respect
12:21:23 to the salt limitation, with respect to the storage
12:21:26 limitation, with respect to the permission of a column
12:21:29 chromatography limitation between alkylation and salt
12:21:32 formation, and with respect to permission of an isolation
12:21:35 between hydrolysis and salt formation.

12:21:37 With respect to enablement, they haven't
12:21:40 presented argument with respect to the salt limitation, with
12:21:42 respect to the storage limitation, with respect to the
12:21:45 permission of column chromatography between alkylation and
12:21:48 salt formation, and with respect to isolation between
12:21:51 hydrolysis and salt formation.

12:21:53 And with respect to indefiniteness, the
12:21:56 defendants have not presented any evidence with respect to
12:21:59 the impurities limitation.

12:22:02 And next, on to the second category of
12:22:05 arguments. Defendant has failed to meet their burden of
12:22:08 clear and convincing evidence. Defendant has failed to show
12:22:12 by clear and convincing evidence that the '066 patent is

12:22:15 invalid as a product-by-process claim because they have not
12:22:18 shown publicly available information showing that the
12:22:20 product produced according to the Moriarty JOC article is
12:22:24 the same as the product produced according to the Chicago
12:22:27 process to make Remodulin. Dr. Winkler relies only on
12:22:31 confidential information submitted by UTC to the FDA, and a
12:22:35 POSA would not have had access to this information prior to
12:22:37 the priority date.

12:22:38 With respect to their 112 arguments, Defendant
12:22:44 has failed to meet its burden to demonstrate clear and
12:22:47 convincing evidence that the inventors were not in
12:22:49 possession of the impurities limitation. Dr. Winkler's
12:22:52 analysis reads out the word "steps" from the impurities
12:22:55 limitation. He instead focuses on highly specific
12:22:59 blackboard chemistry where the I am impurities can only come
12:23:02 from the single molecule BTO. This is not aligned with the
12:23:05 real-world reaction processes disclosed in the patent. And
12:23:08 in doing so, he fails to consider that colored impurities
12:23:12 are created after the alkylation and hydrolysis steps, and
12:23:16 those colored impurities are removed in the salt formation
12:23:18 step.

12:23:18 With respect to the definiteness of the storage
12:23:23 limitation, Liquidia -- Defendant Liquidia has, again,
12:23:26 failed to meet its burden of clear and convincing evidence
12:23:28 that a POSA would not have been able to discern with

reasonable certainty the scope and meaning of the storage limitation. The disagreement between this Court and the PTAB on the meaning of "storage" does not provide sufficient evidence to meet that burden.

Turning next to the '793 patent, again, there's these two categories where they didn't present any arguments that were disclosed in the Pretrial Order. Those arguments that they didn't present any 102 arguments and no obviousness arguments with respect to the '793 patent.

With respect to the 112 arguments, Liquidia has failed to meet its burden of clear and convincing evidence that the inventors did not possess a method of treating all five groups of pulmonary hypertension. The patent describes treating patients with mixed pre- and post-capillary group two hypertension, and as Dr. Hill explained, a POSA would have understood that Treprostinil cannot be used to treat purely postcapillary group two hypertension as explained by Dr. Hill.

THE COURT: All right. Thank you, Mr. Gunn. I'll grant the part about the Section 112 indefiniteness argument relating to the storage limitation for the '066 patent. Otherwise, I'll take it all under advisement. So, let's proceed.

MR. GUNN: Thank you, Your Honor.

MR. CARSTEN: Thank you, Your Honor. United

Therapeutics calls as its next witness, Mr. Dean Bunce of United Therapeutics.

And Mr. Burrowbridge will be conducting the examination.

THE COURT: All right. Thank you.

DEPUTY CLERK: Please state and spell your full name for the record.

THE WITNESS: Dean Bunce, D-E-A-N B-U-N-C-E.

DEPUTY CLERK: Do you affirm that the testimony you are about to give to the Court in the case now pending will be the truth, the whole truth, and nothing but the truth, you do so affirm?

THE WITNESS: I do affirm.

DEAN BUNCE, the witness herein, after having been duly sworn under oath, was examined and testified as follows:

DEPUTY CLERK: Thank you. You can be seated, and there's the microphone on top of the computer, so make sure you speak into it.

MR. BURROWBRIDGE: May I approach?

THE COURT: Yes.

DIRECT EXAMINATION

BY MR. BURROWBRIDGE:

Q. Good morning, Mr. Bunce.

A. Good morning.

12:26:30 Q. Can you please introduce yourself to the Court.
12:26:33 A. I'm Dean Bunce, executive vice president global
12:26:36 regulatory affairs for United Therapeutics.
12:26:39 Q. When did you first start work at UTC?
12:26:41 A. In August 1999.
12:26:43 Q. Have you been the head of regulatory since you
12:26:48 started with UTC?
12:26:49 A. I have, and I was also head of compliance for a time.
12:26:54 Q. What are your responsibilities as executive vice
12:26:57 president global regulatory affairs?
12:26:58 A. I'm responsible for all interactions and submissions
12:27:02 to regulatory agencies including the FDA.
12:27:06 Q. When was the original Remodulin NDA submitted to the
12:27:10 FDA?
12:27:11 A. October 2000.
12:27:13 Q. And when was the original Remodulin NDA approved?
12:27:16 A. In May 2002.
12:27:19 Q. Where was the Treprostinil used in Remodulin
12:27:22 manufactured at the time of the original NDA submission?
12:27:25 A. In Chicago.
12:27:28 Q. And when was the original TYVASO NDA application
12:27:32 submitted to the FDA?
12:27:33 A. In June 2008.
12:27:36 Q. When was the original TYVASO NDA approved?
12:27:39 A. In July 2009.

12:27:41 Q. Was the material made according to the TYVASO NDA
12:27:46 ever available to the public before the time of the FDA
12:27:49 approval?
12:27:50 A. No, we cannot sell any product until we have
12:27:54 approval.
12:27:55 Q. Was UTC's process for manufacturing Remodulin under
12:27:58 its original NDA submission publicly known at the time?
12:28:01 A. No, what we put in the submission is proprietary.
12:28:07 Q. Was the process information, analytical methods, and
12:28:10 details of the COAs publicly available before the TYVASO
12:28:17 approval in 2009?
12:28:18 A. It was not. Again, we can't provide -- the
12:28:21 information we put into an application is proprietary
12:28:25 information.
12:28:25 Q. If UTC were to change the process used to manufacture
12:28:29 the Treprostinil Remodulin, would that be reported to the
12:28:33 FDA?
12:28:33 A. Yes. Any change in process is required to be
12:28:35 submitted to the FDA and approved before we can use that
12:28:39 change.
12:28:40 Q. Did UTC ever seek approval for a change in its
12:28:43 Treprostinil manufacturing process?
12:28:44 A. Yes, we did.
12:28:47 Q. When did UTC seek approval for a change in its
12:28:50 manufacturing process?

12:28:50 A. That was in 2008.
12:28:56 Q. And what prompted that change?
12:28:58 A. A couple of things. A change of the site from
12:29:02 Chicago to Silver Spring and improvements in the process
12:29:06 when we went to Silver Spring.
12:29:08 Q. And when was the move to the Silver Spring facility?
12:29:10 A. It opened in 2007.
12:29:16 Q. When did the FDA approve commercial batches
12:29:18 manufactured by the new process in Silver Spring?
12:29:20 A. In May 2009.
12:29:25 Q. With respect to characterizing the quality of the
12:29:28 drug substance, what is provided to the FDA?
12:29:30 A. We provide information on how it's manufactured,
12:29:35 certificates of analysis from test batches, and stability
12:29:38 data.
12:29:40 Q. How does the FDA regulate the purity of the drug
12:29:42 substance being reported?
12:29:44 A. Saying through -- we are required to submit
12:29:48 analytical updates to the FDA with results of testing and
12:29:52 annual batches that go on stability.
12:29:56 Q. Does that include assay purity?
12:29:58 A. It does.
12:29:59 Q. Has UTC ever updated its purity assay specification?
12:30:03 A. Yes, we have.
12:30:05 Q. I'd like to turn to DTX 07.

12:30:08 A. Okay.
12:30:18 Q. You have it in front of you as well.
12:30:20 A. Yes.
12:30:20 Q. What is this document?
12:30:22 A. This was our --
12:30:30 Q. Seven.
12:30:30 Go ahead, you can use the document in front of
12:30:32 you.
12:30:32 A. This is our response to our pre-approval supplement
12:30:36 for the change in Chicago and the manufacture that we
12:30:39 submitted to the FDA in 2009.
12:30:47 Q. I'd like to direct you to FDA comment two. Do you
12:30:50 see that?
12:30:50 A. Yes.
12:30:55 Q. What was the FDA asking you, UTC, to do in this
12:30:59 comment?
12:30:59 A. To provide justification for specifications and for
12:31:05 the change in -- in the Treprostinil drug substance
12:31:09 specification.
12:31:09 Q. What was UTC's justification for typing the release
12:31:16 specification?
12:31:16 A. When we did the change in process, we found that the
12:31:20 purity of the drug substance we were making was -- was more
12:31:24 pure than before or closer to 100 percent with assay
12:31:29 variability of plus or minus two percent. We found that

some of the batches from Chicago would have been out of spec if we did not get a change in the specification closer to 100 percent.

Q. And does this document describe the shift in the release specification?

A. Yes, it does.

Q. And when was that shift?

A. In the changing from 97 to 101 percent to 98 to 102 percent.

Q. Do you also see the paragraph above FDA comment two?

A. Yes.

Q. There's a statement "API produced by the new process in Silver Spring are of the same high quality and purity as the commercial lots of API produced at the existing process at the Chicago facility."

Do you see that?

A. Yes, I do.

Q. What does that statement mean in the context of this FDA correspondence?

A. For FDA, when we submit a regulatory change, FDA wants the change to be the same or better than what's currently available. They like -- we can't introduce new impurities or that the level of impurities are lower than what was previously there. So in this change, they -- going up to 99 percent -- or excuse me. Target of 100 percent

purity was a change that the FDA would have liked, and they did. They approved it.

Q. And so, is it fair to say that this was/is showing that the new process was above the minimum -- minimal requirements -- excuse me -- the minimum requirements that the FDA had previously required?

A. Yes.

MR. BURROWBRIDGE: Plaintiff offers DTX 70 into evidence.

MR. SUKDUANG: No objection.

THE COURT: Admitted without objection.

(DTX Exhibit No. 70 was admitted into evidence.)

BY MR. BURROWBRIDGE:

Q. Has UTC ever updated its approval specifications to the FDA?

A. Yes.

Q. Please turn to PTX 1552. What is this document?

A. This is an information request letter from the FDA during its review of the TYVASO NDA asking for various things.

Q. If you look at comment two in this document, what is the FDA requesting?

A. Based on the data submitted, they're asking us to tighten our total related substances specification, and provide justification.

12:34:06 Q. Is it normal for the FDA to request tightening of
12:34:09 specifications?
12:34:10 A. Yes, it is. The FDA reviews all the data for new
12:34:16 process or a change in process. FDA wants the
12:34:19 specifications as tight as possible. And the lower -- and
12:34:24 the fewest impurities or lowest level of impurities in a
12:34:27 product because those impurities can/could have an
12:34:30 unintended effect for a patient.
12:34:37 Q. And is it normal for the FDA to request tightening of
12:34:40 the specification even if the product is already within the
12:34:43 specification?
12:34:43 A. Yes. And through -- either through another
12:34:48 supplement or through annual reports, FDA reviews that data
12:34:52 and -- if the process supports a tightening of the
12:34:55 specifications. Yes, they often will request the change.
12:34:59 Q. And looking back at question two, is the FDA
12:35:04 asking -- excuse me. Can you, again, explain what the FDA
12:35:11 is asking here with regard to impurity limits.
12:35:14 A. So, we had a specification limit of not more than
12:35:19 three percent for total related substances. FDA says that
12:35:22 wasn't justified. So showing that our impurities were quite
12:35:27 a bit lower this time, so they're asking us to tighten that
12:35:30 criteria.
12:35:31 Q. And why does the FDA care about impurity limits?
12:35:34 A. In -- impurities can have unintended side effects for

patients, and so FDA wants the lowest levels that's in there going -- you know, going forward for all patients.

MR. BURROWBRIDGE: I'd like to offer PTX 1552 into evidence.

MR. SUKDUANG: No objection.

THE COURT: Admitted without objection.

(PTX Exhibit No. 1552 was admitted into evidence.)

BY MR. BURROWBRIDGE:

Q. Please turn to PTX 1553. 1553.

Do you have it, Mr. Bunce?

A. Yes.

Q. And what is this document?

A. This is our response to FDA's request to tighten the specifications, among other topics.

Q. And how did UTC respond to the FDA comment two?

A. We -- we disagreed that we could, based on the process and the data, that we could tighten our specifications.

MR. BURROWBRIDGE: UTC offers PTX 1553 into evidence.

MR. SUKDUANG: No objection.

THE COURT: Admitted without objection.

(PTX Exhibit No. 1553 was admitted into evidence.)

12:36:44 BY MR. BURROWBRIDGE:
12:36:44 Q. How does FDA monitor the stability of the drug
12:36:50 substance?
12:36:51 A. We're required to put at least one batch on stability
12:36:56 a year and present those results of that batch and other
12:37:00 batches that are ongoing to FDA annually.
12:37:03 Q. And why are stability studies important to the FDA?
12:37:06 A. Again, it shows that the product is stable -- stable
12:37:09 over the approved expiration date. And that the impurities
12:37:16 are not -- not increasing or going out of spec.
12:37:20 Q. Is the data submitted to the FDA representative of
12:37:23 what you intend to sell?
12:37:25 A. Yes, it is.
12:37:26 Q. Let's pull up PTX 1564.
12:37:37 A. Okay.
12:37:37 Q. What is this document?
12:37:39 A. It is our 2015 submission of stability data FDA in
12:37:44 one of our annual reports.
12:37:46 Q. It was 1564.
12:37:50 If we turn to Page 3, what does this page show?
12:37:55 A. It's -- Page 3 shows the stability data for
12:38:05 Treprostinil drug substance manufactured in Silver Spring,
12:38:07 Maryland, in 2009 and the 60-month stability time frame.
12:38:13 Q. Was this submitted to the FDA as representative of
12:38:15 the product manufactured in Silver Spring?

12:38:17 A. Yes, it was.

12:38:19 MR. BURROWBRIDGE: Plaintiff moves to admit PTX 1564.

12:38:21 MR. SUKDUANG: No objection.

12:38:22 THE COURT: Admitted without objection.

12:38:24 (PTX Exhibit No. 1564 was admitted into evidence.)

12:38:24 BY MR. BURROWBRIDGE:

12:38:24 Q. Based on your interactions with the FDA, how do you understand the FDA views impurities and drug substances in drug products?

12:38:32 A. The FDA would like those to be as low as possible again so there's less chance of unintended side effects from those impurities.

12:38:42 MR. BURROWBRIDGE: Pass the witness.

12:38:46 MR. SUKDUANG: No questions, Your Honor.

12:38:47 THE COURT: All right. Mr. Bunce, thank you. You may step down.

12:39:03 MR. CARSTEN: Your Honor, United Therapeutics calls Dr. David Walsh to the stand.

12:39:07 THE COURT: Okay.

12:39:08 MR. CARSTEN: My colleague Art Dykhuis is going to be handling this examination.

12:39:15 THE COURT: All right.

12:39:39 DEPUTY CLERK: You can stand. Please state and

spell your full name for the record.

THE WITNESS: My name is David Allan Walsh. D-A-V-I-D A-L-L-A-N W-A-L-S-H.

DEPUTY CLERK: Do you affirm that the testimony you are about to give to the Court in the case now pending will be the truth, the whole truth, and nothing but the truth, you do so affirm?

THE WITNESS: I do.

DAVID WALSH, the witness herein, after having been duly sworn under oath, was examined and testified as follows:

DEPUTY CLERK: Thank you.

MR. DYKHUIS: May I approach, Your Honor?

THE COURT: Yes.

MR. FLYNN: May I approach, Your Honor?

THE COURT: Yes.

DIRECT EXAMINATION

BY MR. DYKHUIS:

Q. Good afternoon, Dr. Walsh.

A. Good afternoon.

Q. Could you please introduce yourself to the Court.

A. My name is David Walsh.

Q. Have you ever worked for United Therapeutics?

A. Yes, I worked for them from 1999 to 2015.

Q. And can you generally describe the roles and

responsibilities you had at UT?

A. When I started at UT, I was responsible for their Chicago manufacturing facility, making sure enough Treprostinil was produced to meet current needs, and to make sure the facility would pass the FDA inspection.

Q. And with respect to passing an FDA inspection, does that involve aspects of quality?

A. Yes.

Q. What other locations, if any, did you work at United Therapeutics?

A. In 2006 to '07, a new manufacturing facility was built in Silver Spring, Maryland, and we moved from Chicago to Silver Spring.

Q. And did any of your work at UT lead to patents?

A. Yes, several patents.

Q. If we could please pull up JTX 2.

And, Dr. Walsh, you have a copy in your binder as well, but it will be on the screen. Do you recognize this patent, Dr. Walsh?

A. Yes, this is one of the patents on which I'm an inventor.

Q. And does that -- just at a general level, what is this patent about, just at a high level?

A. It generally describes a new process to prepare Treprostinil.

12:42:05 Q. And how was the process that you developed and
12:42:11 performed at UT, the new process, different from the old
12:42:15 process that you performed at UT?
12:42:17 A. Well, the main difference was we formed a salt of the
12:42:22 Treprostinil free acid.
12:42:25 Q. And in the work that led to this patent, what kind of
12:42:27 problems from you facing?
12:42:28 A. Well, in the move to Silver Spring, it was a larger
12:42:33 facility, and we needed to scale up. Many of the reaction
12:42:39 processes were fairly dangerous on large scale. So, we had
12:42:46 to find a process that would fit into Silver Spring
12:42:52 facility.
12:42:55 Q. Did the old process involve the use of solvents in
12:42:58 any way?
12:42:59 A. Yes, many of the purifications were by column
12:43:03 chromatography. They required large volumes of solvents and
12:43:08 they -- the zoning restrictions in the Silver Spring
12:43:12 facility didn't allow us to use those large volumes of
12:43:15 solvents.
12:43:15 Q. And how did implementing a salt formation step
12:43:18 address any of these problems?
12:43:21 A. Well, when we moved to Silver Spring, we outsourced
12:43:24 many of the early steps in the process to contract
12:43:28 manufacturers. And so, we didn't have to do the dangerous
12:43:32 steps in Silver Spring. And salt formation allowed us to

not have to use column chromatography and purifications. So we didn't need to have the large volumes of solvents.

Q. Did implementing the salt formation step affect handling ability for the operators?

A. Yes, it was much safer for the operators because Treprostinil itself, when dried, is a cotton-like material, fibrous, and it's staticky and it jumps out of the trays and it's very difficult to handle. And Treprostinil is a very potent drug, and our operators on occasion would be exposed to this. But the salt form is a nice granular crystalline material like sugar, and so it was much easier to handle.

Q. Did you ever perform any impurity and stability testing on Treprostinil made from the new process?

A. Yes.

Q. What were the results of that testing?

A. Well, when I got the results back, I was pleasantly surprised because in the salt form, there's much fewer impurities than in the free acid. Plus, upon looking at the stability data, it was much more stable at room temperature then free acid.

Q. You said you reviewed testing results for the new process. Did you also review stability and impurity data for the Treprostinil made from the old process at UT?

A. Yes. I was responsible for sending out each lot we prepped for testing. And so, when we -- reports came back,

and I reviewed all the data.

Q. What fraction or percentage of batches made by UT did you review their quality?

A. Up to about 2012, I reviewed all -- every lot that went out during my tenure there.

Q. I want to talk about the Chicago and Silver Spring facilities. So when did UT manufacture Treprostinil out of each location?

A. It manufactured from about '98 to 2006 in the Chicago facility.

Q. And the Chicago facility was the old process?

A. Yes.

Q. When did you move to the Silver Spring?

A. In the 2006, 2007 time frame.

Q. And how were you involved in that move from Chicago to Silver Spring?

A. Well, initially, I was involved in the design of the new labs in Silver Spring, and then I oversaw the move of the production facility from Chicago to Silver Spring.

Q. And as far as inventory goes, were you able to manufacture in Chicago until that closed and immediately start up in Silver Spring?

A. No. We prepared a three-year inventory in Chicago to use while the Silver Spring facility was being validated and approved by the FDA.

12:46:56 Q. And then what did you do with that stockpile?
12:46:59 A. Well, we moved it to Silver Spring and then used it
12:47:03 until it was gone.
12:47:05 Q. And then did you ever sell the old process of
12:47:08 Treprostinil made by the old process and Treprostinil made
12:47:11 by the new process at the same time?
12:47:13 A. I don't believe so, no. We used up the old material
12:47:16 first, and then once the facility was approved for
12:47:21 manufacture, we used the new material, and the old material
12:47:24 was gone.
12:47:25 Q. I want to talk a little more about stability testing
12:47:29 results. If we could call up PTX 1563, please. And you
12:47:33 have a copy in your binder, Dr. Walsh. It will also be on
12:47:36 the screen. We can look at Page 2.
12:47:38 What is this document, Dr. Walsh?
12:47:41 A. I was writing a treatise on UT-15 at the time, and
12:47:48 this is a chapter that summarized stability studies for
12:47:55 compounds in the process, including Treprostinil.
12:48:01 MR. BURROWBRIDGE: Your Honor, we would move to
12:48:02 admit PTX 1563.
12:48:05 MR. SUKDUANG: No objection.
12:48:06 THE COURT: Admitted without objection.
12:48:08 (PTX Exhibit No. 1563 was admitted into
12:48:09 evidence.)
12:48:09 BY MR. DYKHUIS:

12:48:10 Q. If I can direct you, Dr. Walsh, to the page with -- it's got a production number at the bottom ending in 7298. We can call that up on the screen as well.

12:48:41 It's up on the screen now, Dr. Walsh, if that's easier.

12:48:44 A. Yes.

12:48:45 Q. And so what is this describe -- page describing?

12:48:51 A. This is the results data from stability study on Treprostinil lot UT15-000701.

12:49:01 Q. And have you seen this data before?

12:49:03 A. I have.

12:49:07 Q. When would you have seen this data, Dr. Walsh?

12:49:09 A. When it was generated, when these lots were tested, and then, again, when I wrote this chapter.

12:49:19 Q. And was it your practice to review stability testing results when they were received?

12:49:24 A. I reviewed all stability data through 1999 to about 2012.

12:49:34 Q. And then on the left, there's a column that says attributes. What is that describing?

12:49:38 A. Those are potential impurities that were seen in the Treprostinil.

12:49:44 Q. And then how about those columns on the right?

12:49:47 A. That's the data that was obtained from the time points and month from the stability testing.

12:49:50

12:49:56 Q. Dr. Walsh, have you prepared some slides to eight to
12:49:59 assist with the testimony today?
12:50:00 A. Yes.
12:50:00 Q. Let's look at slide number two, please. Now, what
12:50:07 does this slide show, Dr. Walsh?
12:50:08 A. These are -- the top table is stability data from
12:50:18 three lots of Treprostinil prepared at the Chicago facility.
12:50:24 These happen to be the three lots that were submitted for
12:50:27 NDA. For the NDA.
12:50:30 Q. And then what were the temperature and the humidity
12:50:33 conditions?
12:50:33 A. Well, the first table is for an impurity 3AU09 at
12:50:42 25 degrees and 60 percent relative humidity, which is room
12:50:47 temperature.
12:50:48 Q. And then how about the bottom table?
12:50:50 A. And these are the same lot's data for a different
12:50:56 impurity profile. It's the total related substances for --
12:51:01 at the same temperature and relative humidity.
12:51:04 Q. And where does this data come from?
12:51:06 A. It comes from stability reports.
12:51:11 Q. Let's look at slide three, please.
12:51:12 What does this slide slow, Dr. Walsh?
12:51:17 A. These are data at room temperature for material made
12:51:23 by the new process at Silver Spring. And these are three
12:51:26 typical lots of Treprostinil.

12:51:30 Q. And then the top table mentions 3AU90. What is
12:51:36 3AU90?
12:51:37 A. That's one of the impurities which is an isomer of
12:51:40 Treprostinil.
12:51:42 Q. Let's look at Slide 4, please. What is shown on
12:51:47 Slide 4, Dr. Walsh?
12:51:49 A. This is the old process from Chicago, the same
12:51:55 date -- same type of data you saw before only at a six
12:51:59 months in that refrigerated temperature.
12:52:05 Q. Let's call up Slide 5, please. What does this slide
12:52:10 show, Dr. Walsh?
12:52:11 A. This is an -- a graphical representation of the data
12:52:20 I just showed you. This is for 3AU90 at 25 degrees ambient
12:52:31 -- ambient -- 25 degrees temperature, relative ambient
12:52:34 relative humidity.
12:52:35 Q. And what is that top blue line?
12:52:40 A. That's the amount -- that's a graphical
12:52:48 representation of 3AU90 from the old process.
12:52:56 Q. And what is that bottom orange line?
12:52:58 A. That's a graphical representation of 3AU90 amounts
12:53:04 from the new process at six months.
12:53:20 Q. Thank you, Dr. Walsh.
12:53:21 If we could just go back for a moment. I want
12:53:24 to be clear on something. Could we call up Slide 2?
12:53:35 Which document, Dr. Walsh, is the underlying

data that's reflected on Slide Number 2?

A. It came from PTX 1563.

Q. Thank you.

And then if I could turn to Slide 3, please. And then which document is the underlying data that's reflected on slide number three, Dr. Walsh?

A. That's PTX 1564.

MR. DYKHUIS: And then just to confirm, Your Honor we'd move 1563 and 1564 into evidence.

MR. SUKDUANG: No objection.

THE COURT: All right. Admitted without objection.

MR. DYKHUIS: Let's go to Slide Number 6, please.

(PTX Exhibit Nos. 1563 and 1564 were admitted into evidence.)

BY MR. DYKHUIS:

Q. Dr. Walsh, what is shown on Slide Number 6?

A. This is a comparison of the two impurities of -- from the old and new process at six months.

Q. And so, what are the two bars that are shown on the left?

A. Well, the blue bar is 3AU90 at six months from the old process and the orange bar, which is at baseline, is the new process at six months and at room temperature. The old

process we had to store the Treprostinil at -- in the refrigerator at 5 degrees C.

Q. And then how about those two bars on the right? What do those describe?

A. Those are the total related substances for the old process in blue and the new process in orange.

Q. And thinking back to your time at United Therapeutics, did you compare impurities and stability data for Treprostinil made by the new process with that same data for Treprostinil made by the old process?

A. Yes, that -- that was part of my responsibilities.

Q. And how did the data compare?

A. Well, when I saw the data on the salt of Treprostinil, I was really pleasantly surprised because we were making batches that were much fewer impurities in them than the old process. In fact, some batches we made we couldn't see any impurities at all. I mean, I've never, in my 40 years' experience, seen an API that had no other impurities in it.

MR. DYKHUIS: Thank you, Dr. Walsh. We'll pass the witness.

THE COURT: All right. Cross-examination.

CROSS-EXAMINATION

BY MR. SUKDUANG:

Q. Hello, Dr. Walsh. Sanya Sukduang. Nice to meet you.

12:56:29 In your exhibits, you use color coding. For the old process blue, and color coding for the new process orange; is that right?

A. Correct.

Q. Is the blue Treprostinil free acid?

A. Yes.

Q. Is the orange Treprostinil diethanolamine salt?

A. Yes.

Q. So you're comparing a free acid stored stability and impurity profile against a salt impurity and stability profile?

A. Correct.

Q. Let's look at what the purity is of the Treprostinil free acid. Can we bring up JTX 002 which is the '066 patent?

And can you go to column -- this is your patent; correct?

A. Yes.

Q. Can you go to Column 13 and -- excuse me, Column 14.

And this is taking the Treprostinil diethanolamine salt and converting it back to Treprostinil free acid; is that right?

A. Yes.

Q. Can you go to the bottom of Column 14? Do you see analytical testing of the Treprostinil diethanolamine salt

12:57:43 to Treprostinil? Do you see that table?
12:57:46 A. Yes.
12:57:50 Q. And this is HPLC purity data; correct?
12:57:54 A. I believe so. Yes.
12:58:02 Q. And this is the purity data of the Treprostinil free
12:58:05 acid after it's being converted from the diethanolamine
12:58:08 salt; is that correct?
12:58:09 A. Yes.
12:58:10 Q. And the purity of the Treprostinil free acid is --
12:58:17 goes from 99.8 percent or 99.9 percent or 99.7 percent;
12:58:25 correct?
12:58:25 A. Yes.
12:58:26 Q. And that's compared -- that's the purity of the
12:58:29 Treprostinil free acid, not the Treprostinil diethanolamine
12:58:36 salt; correct?
12:58:36 A. Yes.
12:58:37 Q. And the Treprostinil diethylamine salt is a different
12:58:40 compound than Treprostinil free acid?
12:58:42 A. It's a different physical structure, yes.
12:58:47 MR. SUKDUANG: No further questions, Your Honor.
12:58:48 THE COURT: All right. Any redirect?
12:58:50 MR. DYKHUIS: No redirect, Your Honor.
12:58:51 THE COURT: All right. Dr. Walsh, thank you.
12:58:53 Watch your step as you're stepping down. Okay?
12:58:55 THE WITNESS: All right. Thank you.

12:58:59 THE COURT: All right. So, why don't we break
12:59:00 for lunch here, and we'll come back at 2 o'clock. We'll be
12:59:07 in recess.
12:59:08 DEPUTY CLERK: All rise.
12:59:11 (Recess was taken.)
01:59:08 DEPUTY CLERK: All rise.
01:59:12 THE COURT: I'll be right back.
01:59:37 All right: Let's go ahead, Ms. Wu.
01:59:43 MS. WU: Plaintiff calls Dr. Karl Scheidt. May
01:59:50 I approach?
01:59:55 THE COURT: Sure.
01:59:58 DEPUTY CLERK: How are you?
01:59:59 THE WITNESS: Good.
01:59:59 DEPUTY CLERK: Please state and spell your full
02:00:02 name for the record.
02:00:03 THE WITNESS: Karl Andrew Scheidt K-A-R-L
02:00:06 A-N-D-R-E-W S-C-H-E-I-D-T.
02:00:12 DEPUTY CLERK: Do you affirm that the testimony
02:00:15 you are about to give to the Court in the case now pending
02:00:18 will be the truth, the whole truth, and nothing but the
02:00:20 truth, you do so affirm?
02:00:21 THE WITNESS: I affirm. Thank you.
02:00:21 KARL SCHEIDT, the witness herein, after having
02:00:21 been duly sworn under oath, was examined and testified as
02:00:24 follows:

02:00:24 DEPUTY CLERK: Dr. Scheidt, just make sure you
02:00:27 speak into the microphone.
02:00:27 THE WITNESS: I will.
02:00:28 THE COURT: Thank you.
02:00:31 DIRECT EXAMINATION
02:00:31 BY MS. WU:
02:00:33 Q. Please state your name for the record.
02:00:34 A. Carl Andrew Scheidt.
02:00:36 Q. Did you prepare any materials to assist in your
02:00:39 testimony today?
02:00:40 A. Yes, I did.
02:00:41 Q. Where are you currently employed?
02:00:42 A. Currently employed at Northwestern University. It's
02:00:46 just north of Chicago in Evanston, Illinois.
02:00:49 Q. Please tell us about your education.
02:00:51 A. I -- my formal education, I received a bachelor's of
02:00:55 science from the university of Notre Dame in South Bend,
02:00:57 Indiana. After that, I earned Ph.D. in 1999 from Indiana
02:01:03 University in Bloomington, Indiana. And after that, I was
02:01:05 an NIH post-doctoral fellow at Harvard University from 1999
02:01:09 until 2002 and then came back to the mid -- or excuse me
02:01:14 went back to the Midwest where I assumed my position in
02:01:17 Northwestern at 2002.
02:01:19 Q. Are you currently employed by Northwestern?
02:01:21 A. Yes, I am.

Q. What's your position?
A. My position at Northwestern, I'm a professor of chemistry and pharmacology.
Q. Do you specialize in any particular area?
A. Yes. My specialty is organic chemistry and medicinal chemistry. My laboratory is involved in the development of catalysis, asymmetric synthesis, and investigating and making bioactive molecules to understand and treat disease.
Q. Can you take a look in your binder at PTX 512. Do you recognize this document?
A. Yes, I do.
Q. What is it?
A. It's my CV.
Q. Does this document accurately reflect your credentials?
A. Yes, it does.
MS. WU: Your Honor, I move to admit PTX 512.
THE COURT: Admitted without objection.
(PTX Exhibit No. 512 was admitted into evidence.)
MS. WU: At this time, Plaintiff tenders Dr. Karl Scheidt as an expert in the field of organic and medicinal chemistry organic.
MS. KANNAPPAN: No objection.
THE COURT: All right. You may proceed.

BY MS. WU:

Q. What testimony will you be providing today?

A. The testimony I'll -- I'm providing today is to -- that the asserted claims of the '066 patent are valid.

Q. What -- from what perspective to did you evaluate the 066 apparently?

A. I evaluated the '066 patent from the perspective of a POSA.

Q. What is a level of skill of a POSA for the '066 patent?

A. So I believe this is the same slide that Dr. Nuckolls used on Monday, and I am applying the same standards for POSA.

Q. What materials did you review in forming your opinions?

A. In forming my opinions, I considered the four corners of the '066 patent.

Q. Can you provide an overview of the issues you will address today.

A. Yes, next slide, please.

Today, I'm going to be providing opinions around Dr. Winkler's argument around written description and specifically the impurities limitation, and I was going to speak to indefiniteness of storage, but I believe I no longer have to do that.

02:03:22 Q. So, let's talk about the impurities limitation. What
02:03:27 were the impurities limitations you analyzed?
02:03:31 A. So if we go to the next slide, the impurities
02:03:32 limitation in Claim 1 here states providing a starting batch
02:03:35 of Treprostinil having one or more impurities resulting from
02:03:39 prior alkylation and hydrolysis steps. Wherein said
02:03:42 alkylation is alkylation of benzindene triol. And secondly,
02:03:46 a level of one or more impurities found in the starting
02:03:48 batch of Treprostinil is lower in the pharmaceutical
02:03:51 composition.
02:03:53 Q. Have you seen Dr. Nuckolls's slide providing an
02:03:56 overview of impurities as described in Claim 1?
02:03:59 A. Yes, I have. Next slide, please.
02:04:04 Q. Now, have you adapted this slide based on your review
02:04:07 of the '066 patent?
02:04:10 A. Yes, I have. I've taken this sort of generic green
02:04:12 color and utilized specific mention of color in the
02:04:15 specification. I have a more refined overview of the
02:04:18 overall process.
02:04:22 Q. Dr. Nuckolls detected at the presence of impurities
02:04:24 in his BTO batch. You do as well. Why?
02:04:27 A. Well, right. So this little square here is an
02:04:30 impurity in BTO. And as we've learned this week, that every
02:04:33 reaction produces impurities and that no compound is
02:04:38 100 percent pure, so I wanted to account for that in the

starting material of BTO.

Q. And you have assigned a white color to your BTO batch. How would a POSA have known the color of BTO as of 2007?

A. So, as of 2007, a POSA would understand that BTO was colorless because BTO has a very similar structure to Treprostinil and neither one has a chromophore, and so Treprostinil is known to be white or colorless. So a POSA would understand that the BTO would also be the same -- have the same lack of color.

Q. Can you walk us through slide PDX 7.6 to explain what you're depicting.

A. Yes, certainly. So, it's an overall process, and the beakers represent reaction containers. So you BTO, which we've heard a quite a bit about, and you undergo an alkylation step. And I want to be very clear about this. This is not a chalkboard or a piece of paper. This is really -- with a single reaction on it. It's the entirety of BTO plus the reagents plus the solvent. And you do an alkylation step which generates the light brown material which I'll get to in a minute.

After you -- the alkylation product is formed, it then undergoes hydrolysis, which generates a starting batch which is pale yellow color. And then that starting batch is then -- undergoes a salt formation step, which

produces Treprostinil as an off-white material.

Q. So, what, if anything, does the '066 patent tell a POSA about alkylation impurities?

A. If we go to the next slide, please. Here is Example 1. It is the alkylation of benzindene triol, and you take -- what I've done is separated the beakers slide. Starting with BTO, it undergoes an alkylation step. What I've done is selected some from the specification. Here is sort of the recipe for this reaction. Here are all the reactions components save the Celite, which they use later. But they take these colorless materials -- and again, I also want to note that this third line here, this chloroacetonitrile Is used in two-fold excess. What they do is they combine it and they do an alkylation step not just on a single molecule or only a molecule of BTO, but everything is in the flask.

And let's sort of work through this text here. So after completion of the reaction, the reaction mixture was filtered with or without C light. That's to remove some of the impurities that were generated in the reaction. Then in this green box here, the filtrate was concentrated. You just pull a vacuum to remove some solvent, and what you're left with is a light brown viscous liquid benzidine nitrile indicated here. That's why I've used light brown in my slides, and a POSA would understand that this light brown

indicates the generation of impurities from the alkylation step. And this last sentence here, the crude benzidine nitrile, crude means it's unpurified meaning it has impurities, and they use this in the next step without purification.

Q. I see you've also made some blue highlighting the progress of the reaction was monitored by TLC. Why did you highlight that?

A. It's really important here. So the progress of the reaction was monitored by TLC. We've heard a little bit about chromatography over the last three days. This is thin layer chromatography. It's a very useful and important technique in chemistry.

Q. Can you explain how TLC works?

A. Yes, I provided -- yes, on the next slide, please.

I provided a little tutorial, so with permission. Thin layer of chromatography is what POSAs or chemists use to monitor reactions. So what we have here are three -- I guess these are pickle jars or just jars, what you can do here. I have represented at the beginning of the reaction and then we'll see something in the middle of the reaction and then finally at the end.

Now, at the beginning of the reaction, you take a thin layer chromatography plate and you have an authentic standard of the starting material and an authentic standard

of the product, and in this middle lane, you have the reaction that you sample. And so you place it in the liquids, and by capillary action, the solvent front moves up. And chromatography can -- is the separation of components from a mixture.

And at the very start of the reaction, you have no desired product. You obviously have almost all your starting material, but what I have here in this yellow -- represented by this yellow dot is the presence of an impurity in the starting material possibly. I want to note that these colors are just representative to be -- so we can see them. Many times chemists use either UV light or staining so that the compounds will change color. So starting materials are not always blue and starting products are not all red, so this is at the beginning of the reaction.

At the middle of the reaction, so let's say four hours or six hours or 12 hours later, you're not sure if the reaction is done yet or not. Here you've got your standard on the left and your standard on the right, and you start taking an aliquot of the reaction and you run this middle lane, and you see a difference. What you see is now the reaction is proceeding, so you're generating some of the product. Some of your starting material has now dissipated. You can actually qualitative it assess amounts in TLC.

Maybe not down to the thousandths place, but you can see whether or not things are changing in a qualitative sense. But importantly, what I have here is you can notice possibly that there are impurities that are generated from the reaction because you have a standard here that you know what you brought into the reaction at the start. Now, take another TLC maybe 24, 48 hours later, and that's on the far right of the slide.

So a POSA knows when a reaction is finished when they run a TLC plate like this. And here, again, we have the same mobility of the starting material, and it's no longer -- it's to longer in this lane here. It's disappeared. We could possibly see the generation of more impurities, we could see other things, but the point is that thin layer chromatography is a very useful and enabling way to monitor reactions.

Q. Were you why in the courtroom when Dr. Winkler provided his testimony?

A. I was, yes.

Q. Did you hear Dr. Winkler testify that there is too little material to identify a measure of impurities via TLC?

A. I did hear that.

Q. Do you agree with his opinion?

A. I don't agree with that. I think that Dr. Winkler might have been comparing apples to oranges here. So the

impurities that I heard about were very small impurities from isolated materials. Not reaction mixtures. So this -- these TLC plates were taken directly out of the reaction. There's no finished product where we're assessing purity levels.

So as I mentioned, they use a full two-fold excess of one of the reagents. That's still in the reaction that you're sampling. So there are impurities that are generated during alkylation. You would be able to visualize that.

Q. Were you in the courtroom when Dr. Batra's video was played?

A. I was, yes.

Q. Did you hear his testimony about TLC?

A. I did.

Q. Now, how, if at all, does his testimony impact your opinions?

A. I think it agrees with mine since I recall he said that TLC can be used to visualize impurities.

Q. And when I were you in the courtroom when Dr. Tuladhar's video was played?

A. I was.

Q. And did you hear Dr. Tuladhar testify that impurities from the alkylation step comes from the reagent?

A. I did hear that, yes.

02:11:50 Q. And how, if at all, does that testimony impact your
02:11:54 opinions?
02:11:54 A. That agrees with my testimony that impurities that
02:11:56 are generated in the alkylation step with possibly the
02:12:00 reagent, you would be able to see those by TLC and they
02:12:04 would be generated in that reaction step.
02:12:06 Q. Can the alkylation step take place without the
02:12:09 reagent?
02:12:09 A. No, it cannot.
02:12:12 Q. All right. Let's move on from alkylation impurities.
02:12:14 What, if anything, does the '066 patent tell a POSA about
02:12:19 hydrolysis impurities?
02:12:19 A. So, next slide, please. So here is Example 2 of the
02:12:25 hydrolysis of the benzindene nitrile. And I've highlighted,
02:12:28 again, that the inventors used TLC to monitor the progress
02:12:31 of the reaction. So they're use that same technique that I
02:12:33 just had that tutorial on.
02:12:35 At the top of the second column here in purple,
02:12:38 it says the aqueous layer was diluted with water and
02:12:41 extracted with ethyl acetate to remove impurities soluble in
02:12:49 ethyl acetate. To me, that indicates that during this
02:12:51 reaction, impurities are generated. Some of them are
02:12:54 removed, but importantly, they are generated during the
02:12:56 alkylation and hydrolysis steps.
02:13:00 In the blue box it says -- it states to the

02:13:03 solution of Treprostinil in reactor was added activated
02:13:06 carbon. Activated carbon is a material that POSA -- a POSA
02:13:10 knows can remove some, but not all, impurities, indicating
02:13:14 that impurities have been generated in this reaction.
02:13:18 Lastly, in the yellow box, it says the filtrate,
02:13:22 which is pale yellow and it's pretty important to a POSA
02:13:25 here, was reduced to a volume and you -- for direct use in
02:13:29 the next step, and this is where we now have the starting
02:13:32 batch of Treprostinil. So we've gone from the brown,
02:13:36 alkylated material. It's undergone a hydrolysis step, and
02:13:39 there's been some impurities removed, but some impurities
02:13:42 remain because it's light yellow in color.
02:13:47 Q. Claim 1 requires a lowering of one or more impurities
02:13:50 found in the starting batch. What, if anything, does the
02:13:53 '066 patent tell a POSA about lowering impurities from the
02:13:57 starting batch?
02:13:58 A. Next slide, please.
02:14:01 So, here, in the Example 5, it's quite explicit.
02:14:04 The conversion of Treprostinil diethanolamine salt to
02:14:08 Treprostinil. They take the starting batch which we've --
02:14:11 which a POSA would understand is pale yellow from the
02:14:14 specification and undergoes a salt formation step which
02:14:18 generates an off-white solid. So, the yellow color is
02:14:23 removed, indicating a lowering of impurities of the starting
02:14:26 batch.

02:14:28 Q. Is there any other disclosure in the patent about
02:14:30 lowered impurities?
02:14:31 A. Yes, I believe there is. Next slide, please.
02:14:35 The specification directly teaches the
02:14:38 impurities limitation. And I have highlighted here the
02:14:41 impurities carried over from intermediate steps, that is
02:14:44 alkylation of triol and hydrolysis of benzidine nitrile, are
02:14:47 removed during the carbon treatment and salt formation step.
02:14:52 Q. Where is this disclosure?
02:14:53 A. This is in column 17 of the '066 patent, lines 27
02:14:58 through 40.
02:14:59 Q. Did you hear Dr. Winkler's testimony about this
02:15:02 passage?
02:15:02 A. I did hear that testimony.
02:15:04 Q. Do you agree with his interpretation of this passage?
02:15:06 A. I don't agree with his interpretation.
02:15:09 Q. Why not?
02:15:09 A. I think Dr. Winkler is being very specific and
02:15:14 restrictive about his application of only BTO being
02:15:16 alkylated. It's an alkylation step, and it encompasses all
02:15:20 the components of the reaction, including reagents and
02:15:23 solvents.
02:15:24 Q. Did you hear Dr. Winkler testify that the patent
02:15:27 lacks written description because the specification does not
02:15:30 describe the identification or measurement of specific

impurities?

A. I did hear that testimony, yes.

Q. Do you agree with him?

A. I disagree with that.

Q. Why do you disagree?

A. Let's go to the next slide, please.

I've just put up, again, for the Court, this overall process tracking color changes. Your eyes are very, very powerful -- or I guess very good qualitative analytical tools. We go from -- a POSA would understand you go from a colorless material. After you do an alkylation, it generates something that's brown. And after that brownness, then there's some material that's removed but not all, since the starting batch is pale yellow. And then the salt formation step then lowers that color. So, a POSA would understand that there's a generation of impurities and then a lowering of impurities from the starting batch to Treprostinil.

Q. Does the specification of the '066 patent convey to a POSA that the inventors were in possession of the impurity limitations of Claims 1, 2, 3, and 6?

A. Yes.

MS. WU: I pass the witness.

THE COURT: All right. Cross.

CROSS-EXAMINATION

BY MS. KANNAPPAN:

Q. Dr. Scheidt, you just opined that color changes could indicate purity changes; right?

A. Yes, I did.

Q. And when we talked about this during your deposition, you agreed that color changes do not identify which impurities were changed; correct?

A. That's correct.

Q. And color changes do not identify the level of specific impurities that were changed; correct?

A. I believe that they would indicate the level of overall impurities changed, not specific impurity changes.

Q. And if we could go to PTX 201 at the Bates ending in 781. That's going to show up on your screen, Dr. Scheidt.

A. Mm-hmm.

Q. Do you see that BTO up here --

MS. WU: What page?

MS. KANNAPPAN: It's not in the binder, but it is your PTX exhibit.

BY MS. KANNAPPAN:

Q. If you want to look at other pages, you can, Dr. Scheidt, but I just wanted to point you to a very specific disclosure here. Do you see that it says BTO appearance can be white to pale yellowish powder?

A. Yes, I see that.

02:17:55 Q. And then if we go to your demonstratives, PDX 7.7 and
02:18:00 PDX 7.9, this is Example 1 and Example 2 from the patent;
02:18:06 correct?
02:18:06 A. That's correct. Yes.
02:18:08 Q. And you pointed to some ethyl acetate Celite pad
02:18:11 steps and activated carbon steps in these examples; correct?
02:18:14 A. Yes, that's correct.
02:18:16 Q. And you testified that those were a purification
02:18:18 steps; right?
02:18:18 A. That's correct.
02:18:21 Q. And these steps happened before the pale yellow
02:18:24 filtrate comes out at the end of Example 2; right?
02:18:26 A. Yes.
02:18:28 Q. And there's no disclosure in these examples of how
02:18:32 much of any particular impurity was removed by the Celite
02:18:35 pad step, the ethyl acetate steps, or the activated carbon
02:18:39 steps; right?
02:18:39 A. There's no specific amounts.
02:18:42 Q. And you also talked a little bit about TLC. The
02:18:45 patent does not disclose using TLC to identify or measure
02:18:50 impurities; correct?
02:18:50 A. I disagree with that.
02:18:52 Q. Okay. What the literal sentence says is the progress
02:18:55 of the reaction was monitored; correct?
02:18:57 A. It does say monitored, yes.

02:18:59 Q. Does it use the word -- or does it say that there's
02:19:01 identification or measurement of impurities by TLC, the
02:19:04 patent?
02:19:05 A. The patent uses monitored by TLC, and I think the
02:19:09 demonstrative I had indicated what one can do when they're
02:19:13 monitoring a reaction by TLC.
02:19:14 Q. And in TLC, you can measure the amounts of very
02:19:18 specific impurities? Is that your testimony?
02:19:20 A. My testimony is that, as I've shown on my slide, is
02:19:22 that you can get a qualitative assessment of the amounts of
02:19:25 whatever it is that you're developing using that
02:19:28 chromatographic technique.
02:19:29 Q. So qualitative but not quantitative; correct?
02:19:31 A. Qualitative, correct.
02:19:34 Q. But not quantitative?
02:19:34 A. Not quantitative. Qualitative.
02:19:38 Q. And until your testimony today, you had not
02:19:41 considered any inventor testimony in your written
02:19:44 description analysis; correct?
02:19:44 A. Could you could you restate the question, please.
02:19:47 Q. Sure. Until your direct examination today, you had
02:19:52 not considered any inventor testimony in your written
02:19:56 description analysis; correct?
02:19:57 A. Have I considered? I've got to -- sorry. I've got
02:20:08 to think. One more time, please. I apologize. I want to

make sure.

Q. Maybe I'll do it simpler.

A. Okay.

Q. When you did your written description analysis, you only looked at the four corners of the patent for your reports; correct?

A. That's correct. Thank you.

Q. And you specifically said "I didn't want to look at the inventor testimony that Dr. Winkler referred to"; right?

A. I didn't say -- I didn't say that specifically.

Q. Did you consider the inventor testimony in your written description analysis in your reports?

A. I considered the four corners of the '066 patent.

Q. So is that a no?

A. I considered the four corners of the '066 patent.

Q. But not the inventor testimony?

A. I -- I considered the four corners of the '066 patent.

Q. Okay. All right. Sorry, Dr. Scheidt.

MS. KANNAPPAN: No further questions, Your Honor.

THE COURT: All right. Any redirect?

MS. WU: Nothing from Plaintiff.

THE COURT: All right, Dr. Scheidt. Watch your step.

THE WITNESS: Thank you, sir.

MR. CARSTEN: Hello, Your Honor. United Therapeutics calls Dr. Andrew Clark to the stand as its next witness, please.

THE COURT: Okay.

DEPUTY CLERK: Please states and spell your full name for the record.

THE WITNESS: Andrew Clark. Surname is C-L-A-R-K.

DEPUTY CLERK: Do you affirm that the testimony you are about to give to the Court in the case now pending will be the truth, the whole truth, and nothing but the truth, you do so affirm?

THE WITNESS: Yes, I do.

ANDREW CLARK, the witness herein, after having been duly sworn under oath, was examined and testified as follows:

DEPUTY CLERK: Just make sure you speak into the microphone the best you can.

MR. CARSTEN: May I proceed, Your Honor?

DIRECT EXAMINATION

BY MR. CARSTEN:

Q. Good afternoon, Dr. Clark.

A. Good afternoon.

Q. Would you please introduce yourself to the Court.

A. Yes, my name is Andrew Reginald Clark.
Q. Could you spell it, please.
A. C-L-A-R-K is the surname.
Q. Okay. What do you do for a living, Dr. Clark?
A. I am currently president and general manager of the Aerogen Pharma Corporation which I helped found in 2015.
Q. Do have you a binder in front of you?
A. I do.
Q. Would you turn in that to PTX 505, please. And get your glasses out. Is your eye okay?
A. Oh, yeah. The eye is fine.
PTX 005?
Q. PTX 505. Please, Dr. Clark.
A. PTX 505. Yes.
Q. What is that?
A. That's my Curriculum Vitae.
Q. True and correct copy of it?
A. Yes, it is, as far as I can see.
MR. CARSTEN: Your Honor, we move to admit PTX 505.
THE COURT: Admitted without objection.
(PTX Exhibit No. 505 was admitted into evidence.)
MR. CARSTEN: Thank you, Your Honor.
BY MR. CARSTEN:

02:22:49 Q. How long have you been working in the pharmaceutical
02:22:54 industry, Dr. Clark?
02:22:54 A. I joined the industry in 1980, so 41, 42 years.
02:23:04 Q. Have you been working in inhalation product for that
02:23:08 entire time?
02:23:08 A. Oddly enough, yes.
02:23:10 Q. Have you ever worked on any drugs pertaining to
02:23:15 pulmonary hypertension?
02:23:15 A. Yes, recently I acted in a role as chief technical
02:23:21 officer at Respira Therapeutics. We were developing a
02:23:24 powder formulation of the PD5 inhibitor for acute therapy in
02:23:29 PAH patient.
02:23:30 Q. Any others?
02:23:31 A. The current role I have, we were developing
02:23:36 epoprostenol, and the target indication was for delivery of
02:23:41 epoprostenol by aerosol on ventilators in patients
02:23:44 recovering from heart surgery and cardiopulmonary bypass.
02:23:49 Q. What other types of inhalation products have you
02:23:51 worked on in the course of your 40 years in the industry?
02:23:53 A. If I could refer to Dr. Gonda's demographic, all of
02:23:58 them. I've been involved in designing nebulizers, MDIs,
02:24:03 dry-powder inhalers, and I did some original work even on
02:24:07 the small mist inhalers. On formulations for all of those
02:24:11 inhaler forms.
02:24:13 Q. Have you worked on any products that have secured FDA

approval?

A. So far in the inhalation space five.

Q. By 2006, how familiar are you with the process of developing a dry-powder for a dry-powder inhalation?

A. 26 years long. Very familiar.

MR. CARSTEN: Your Honor, we'd move to admit Dr. Clark as an expert in inhaled drug -- inhaled drugs, formulations, and devices and their development including dry-powder formulations and dry-powder inhalers.

MS. KANNAPPAN: No objection.

THE COURT: All right. You may proceed.

MR. CARSTEN: Thank you, Your Honor.

BY MR. CARSTEN:

Q. Dr. Clark, have you formed any opinions in this case?

A. Yes.

Q. Okay. Have you prepared demonstratives to help assist the explanation of your testimony today?

A. Yes.

Q. PDX 10.2. This is -- what is this, Dr. Clark?

A. This is the '793 patent.

Q. Does it look familiar to you?

A. It does, yes.

Q. Have you spent much time with this one in the work of your case?

A. Yes, I have read it several times.

02:25:22 Q. Were you instructed to apply any particular filter or
02:25:25 frame of reference when you considered the '793 patent?
02:25:28 A. The filter is, essentially, what a person of ordinary
02:25:38 skill in the art of the date of 2006 patent would read into
02:25:43 and see and understand from the patent.
02:25:46 Q. And what was your definition of person of ordinary
02:25:50 skill in the art that you applied here?
02:25:51 A. Somebody who's got an M.D. or a Ph.D. and at least a
02:25:56 couple years' experience in terms of developing inhaled
02:26:00 formulations. I also put in some understanding of pulmonary
02:26:06 hypertension and treatment of it.
02:26:07 Q. Now, you understand that Dr. Gonda, the expert on the
02:26:11 other side that you're going to be addressing, he also
02:26:15 provided a level of ordinary skill in the art; is that
02:26:18 right?
02:26:18 A. That's correct.
02:26:19 Q. Do you guys have the same level of ordinary skill?
02:26:21 A. Not quite. I think they're very similar, apart from
02:26:26 the requirement for some understanding or understanding of
02:26:33 treatments of pulmonary hypertension.
02:26:34 Q. Okay. Regardless of which of those two level of
02:26:38 ordinary skills that you applied here, would your opinions
02:26:41 change?
02:26:41 A. No.
02:26:42 Q. Would you qualify as a level -- as having a level of

ordinary skill in the art for either one?

A. In 2006, I would have greatly exceeded a POSA of ordinary skill in the art.

Q. Now, that raises an interesting point, Dr. Clark. How was it that you were able to apply the level of ordinary skill in the art as of 2006 when you yourself were more qualified than that as of that date?

A. By reviewing publications that were around at that time and actually by trying to put myself in the position where I was a POSA with this level of skill, which is actually back in 1980s.

Q. You mentioned that you had looked at a couple of or several references from the rough timeframe of 2006 to help guide your analysis. What references were they?

A. The two major ones were the Labiris, which is actually referenced in the '793 patent. And a publication by Telko and Hickey, which describes, essentially, the things to look for and how to develop pulmonary dry powder formulation.

Q. Would you turn in your binder to PTX 905. Let me know when you're there.

A. Yeah. It's open.

Q. What is this?

A. This is the paper by Telko and Hickey describing, essentially, the essential elements to look at and the

processes for developing a dry-powder formulation from a molecule.

MR. CARSTEN: Your Honor, we'd move PTX 905 into evidence.

MS. KRICKL: No objection.

THE COURT: Admitted without objection.

(PTX Exhibit No. 905 was admitted into evidence.)

BY MR. CARSTEN:

Q. So, can you just give us an overview on what Telko and Hickey, dated 2005, PTX 905, teaches to a person of ordinary skill in the art who's interested in developing a dry-powder formulation as of 2006?

A. Essentially teaches the general requirements for the molecule that was being developed as a dry-powder formulation. It has some highlights and issues to look out for during that development, the methods for actually size-reducing the material for blending the material, and then for testing those materials appropriately to show that the dry-powder formulation was acceptable.

Q. And you mentioned another article that you had considered in connection with your work in this case, the Labiris reference. Would you please turn in your binder to PTX 271.

A. 271.

Q. What's that, Dr. Clark?
A. This is the publication by Labiris and Dolovich.
Q. And is this the publication that you considered in connection with your work in this case?
A. Yes.
MR. CARSTEN: Your Honor, we'd introduce PTX 271 into evidence.
MS. KRICKL: No objection.
THE COURT: Admitted without objection.
(PTX Exhibit No. 271 was admitted into evidence.)
BY MR. CARSTEN:
Q. So can you describe, similar to what you just did with Telko with respect to Labiris, what did that help a person of ordinary skill in the art do in terms of understanding how to develop a dry-powder formulation as of 2006?
A. This publication had reasonable descriptions of the available dry-powder inhaler technology at the time. And again, reiterated or repeated some of the information in the Telko and Hickey publication in terms of methods of manufacture and testing.
Q. Now, let's go back to the '793 patent, if we could. Did you prepare any opinions pertaining to written description in this case?

02:30:46 A. Yes.
02:30:47 Q. And what legal standard did you apply for your
02:30:50 written description analysis here?
02:30:52 A. Whether a POSA at the time is -- could read the
02:30:58 specification, the claims in the patent, and understand that
02:31:01 the inventors were in possession of the invention.
02:31:06 Q. What claims did you consider in connection with your
02:31:09 work in the case?
02:31:10 A. 1, 4, 6, 7, 8.
02:31:18 Q. Now, you heard -- you were in Court when Dr. Gonda
02:31:21 testified; right?
02:31:21 A. I was, yes.
02:31:22 Q. You heard his opinions pertaining to written
02:31:24 description?
02:31:24 A. Yes.
02:31:24 Q. Do you agree with them?
02:31:25 A. No.
02:31:26 Q. Why not?
02:31:26 A. My reading of the patent is that the inventors
02:31:33 actually performed what's given as Example 1 and Example 2,
02:31:36 but Example 2 actually has more than one set of clinical
02:31:40 data in it, but what the inventors were trying to show was
02:31:43 that you could essentially reduce the time and deliver a
02:31:47 bolus of Treprostinil, still get efficacy, and not generate
02:31:52 any tolerability issues. So in that sense, they were in

possession of the demonstration that you could deliver a bolus of Treprostinil. They further went on to give some examples of how you would do that. The recipe is one of small mist inhaler is what was used in one of the examples. They also mentioned pressurized metered dose and, that is, of course, dry-powder.

Q. And those two example, those were liquid formulations; right?

A. That is correct.

Q. How does that help a person of skill person of skill in the art who's been directed to make a dry-powder formulation?

A. Essentially, what was specified is the dose and the time which -- over which you would deliver it.

Q. And why is that relevant?

A. That's generally the starting point for developing a powder formulation. You need to know the dose, and, of course, in this particular case, you need to know that it's safe to deliver it in a single bolus, which is what a dry-powder inhaler would do.

Q. I thought Dr. Gonda said you have to start with a whole bunch of pre-clinical stuff before you can even start to think about preparing a dry-powder inhalation formulation; is that right?

A. It's semi-right. I just question a whole bunch of

02:33:03 stuff that you just stated.

02:33:06 Generally, the patent is Treprostinil
02:33:09 pharmaceutically acceptable salts thereof and derivatives
02:33:12 thereof. And a POSA at the time of the patent would have
02:33:16 had access to preformulation laboratory where that sort of
02:33:21 screenings were advised on which was the best salt form or
02:33:25 crystalline form of the polymorph was available to the
02:33:28 formulator.

02:33:28 Q. Okay. Let's get back to written description. Is
02:33:31 there anything in the patent aside from the claims that
02:33:35 actually tells a person of skill in the art that we're
02:33:38 interested in a dry-powder?

02:33:40 A. Yeah, there's a statement about a dry-powder inhaler
02:33:43 with a dry-powder formulation consisting of particles less
02:33:47 than five microns.

02:33:50 Q. If I could have PDX 10.6, please. And where is this
02:33:58 from?

02:33:58 A. Let me find it. The statement on the right is from
02:34:10 within the specification on the patent, and the statement on
02:34:13 the left, number four, is actually one of the claims.

02:34:20 Q. Now, there isn't, you'd agree, a specific operational
02:34:26 detailed example in the patent specification of a dry-powder
02:34:31 formulation, is there?

02:34:32 A. Correct. There isn't.

02:34:34 Q. Is that relevant to your analysis here in terms of

02:34:37 written description?
02:34:38 A. No, I -- it was -- I was essentially instructed by
02:34:42 counsel that that was not required.
02:34:44 Q. What was not required?
02:34:44 A. What you've just stated in terms of there is no
02:34:48 example of a particular formulation in the patent.
02:34:56 Q. Based upon the presence of the two examples you
02:34:59 talked about, Examples 1 and 2, the disclosure at Column 7,
02:35:06 how strong is your confidence that a person of skill in the
02:35:09 art reading this as of 2006 would have understood that the
02:35:13 inventors had possession of a dry-powder formulation of
02:35:16 Treprostinil that met the claims that you considered?
02:35:19 A. I have no doubt that they would have understood it.
02:35:33 Q. Now, there was some -- we've been talking about the
02:35:39 formulation. Claim 4 says dry-powder inhaler. That's not
02:35:45 the formulation, is it?
02:35:46 A. Correct.
02:35:48 Q. What is a dry-powder inhaler?
02:35:50 A. It's a device you would put the drug or blend or
02:35:54 formulation into that the patient would then use to inhale
02:35:58 from. In other words, it's the delivery mode.
02:36:02 Q. And the patent also discloses dry-powder inhalers?
02:36:05 A. It does.
02:36:06 Q. And what dry-powder inhalers would a person of skill
02:36:09 in the art have understood existed as of 2006?

02:36:11 A. There were numerous examples of commercial products.
02:36:20 There were numerous examples of products that were in
02:36:23 development.
02:36:26 Q. Now, we went through a list of some of them with
02:36:29 Dr. Gonda. It was Exubera device and so forth. Do you
02:36:34 remember that?
02:36:34 A. Yes, I was part of the development of Exubera.
02:36:37 Q. With respect to Dr. Gonda's testimony earlier, he
02:36:41 suggested or at least presented as if you're starting with
02:36:45 selecting a dry-powder inhaler, the device, and then you
02:36:48 create the formulation for it. Was that the way that things
02:36:50 worked?
02:36:51 A. Not strictly true. You would manufacture blends and
02:36:57 most likely take an inhaler that was available at the time,
02:37:00 rather than actually kind of physically choosing it for a
02:37:12 patient population.
02:37:12 Q. With respect to the claims, the claims that you
02:37:15 considered, you're confident that a person of skill in the
02:37:19 art would have understood these inventors possessed these
02:37:23 inventions as of 2006; is that right?
02:37:25 A. Yes.
02:37:28 Q. Now, let's switch gears a little bit to enablement.
02:37:34 Did you prepare any opinions concerning enablement,
02:37:37 Dr. Clark?
02:37:37 A. Yes.

02:37:38 Q. And what was the legal standard that you applied there?
02:37:40 A. That there was sufficient description in the specification of the patent for a POSA in 2006 to take that information and develop the formulation or the product.
02:37:50 Q. Is -- and was what's your opinion pertaining to enablement?
02:37:55 A. I think given what's specified, a POSA at the time would have been able to take that information about Treprostinil and salts thereof, about the dose, and about being a dry-powder of a specific size and develop an example of the dry-powder formulation inhaler combination.
02:38:02 Q. Now, Dr. Gonda talked a lot this morning about undue experimentation, that phrase. Do you remember him saying that?
02:38:26 A. I do, yes.
02:38:30 Q. What's your understanding of the phrase "undue experimentation"? What does that mean?
02:38:30 A. So, the first thing I would say is I wouldn't decry that there's a reasonable amount of work involved in terms of developing one of these formulations. And we can talk about that in a few minutes. But by 2006, the processes and the issues around developing dry-powder inhalers were actually well known, and the process of developing formulation usually used pretty routine techniques, both in
02:38:34
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02:39:03

terms of analysis and in terms of manufacturing.

Q. What is your understanding, for purposes of enablement, about whether a patent has to include things that a person of ordinary skill in the art would know about the field of invention?

A. As far as I am aware, instructed by counsel, that's not necessary.

Q. Now, Dr. Gonda started with the particular inhalers. He had the four categories of inhalers. Would a person of skill in the art have had any difficulty as of 2006 choosing a dry-powder inhaler?

A. I don't believe so. There were fairly good examples and fairly accessible examples of dry-powder inhalers that could be used.

Q. Okay. Did you prepare a demonstrative to explain the steps that are involved in preparing a dry-powder?

A. Yes, I did.

Q. Can we have PDX 10.8, please. All right.

So, Dr. Clark, would you please just step through this process briefly for the Court.

A. Yes. So Step 1 would be selecting an API. Now, because in terms of the pharmaceutical, could be doing research selecting the API, yes, it's for medical chemists. In the case of the '793 patent, we're already told that API is Treprostinil. As part of selecting the API, there's also

select, of course, selecting the salt thereof and, if necessary, the polymorph, and that would be a standard screening exercise in nearly every pharmaceutical company I ever worked for.

Having chosen the API, we had a discussion about manufacturing of Treprostinil. Generally, the last stage of API manufacturing is the crystallization. At crystallization, usually makes material that is too large to be considered for delivering to the airways. In other words, it would get stuck in the mouth. It wouldn't get into the lungs. So the second step is actually size reduction. And the classic way of doing that, which has been around since before I joined the industry, is jet milling. And jet milling is used because it uses air jets and the comminution or reduction in size is actually generated by the air jets making the crystals impact with each other, rather than having a hammer or a pin or, you know, like a kitchen weapon. So it's much preferred because it -- it -- it is very unlikely it will introduce any impurities or metals from the micronizing jet milling, et cetera.

Having jet milled it, the next step is to check, of course, that you've got the size reduction; right? And that it's sufficiently small to be considered in that respiratory range of less than 5 microns or so.

02:42:06 The next step is then to blend with the carrier, and I think Dr. Gonda actually summarized it quite well this morning that these sorts of doses of micrograms -- actually putting micrograms of material into an inhaler and expecting it to come out of the inhaler is -- is really a bit of an over-expectation. You have to bulk it in some way. And it's for two reasons. One is so that it will flow and come out of the inhaler, and the other is you have to actually put it into a container in the inhaler. 12 micrograms in a gelatin or an HPLC capsule, for example, would really just coat the walls. So what's done is a carrier is used, and the Treprostinil is actually blended and mixed with the carrier and it adheres to the carrier surface.

I guess two things. Gets you bulk so that you can actually dispense it, and it gets you a powder that will actually flow reasonably well so that when the patient inhales, the powder will flow and it will come out with the inhaler into the patient as a delivered dose.

Then the final part, of course, is to put it together with an inhaler. Typically, as this graphic shows at the bottom, the most common one these days used by lots of people is the Plastiape device. Uses a capsule with a blend in. The patient pierces it and inhales and the active inhalation actually fluidizes the pathway in the capsule and the aerosol gets delivered to the mouthpiece. At that

point, you need to check that you've got the air the required delivered dose and that the aerosol is of reasonable quality to be able to get into the lungs anyways.

Q. Thank you. We'll step through each of those briefly. But in terms of selecting the API, was that the pre-clinical kind of step that Dr. Gonda was talking about?

A. Yes. Because in this case, we wouldn't be selecting API. What we would be doing would be selecting the particular form of the API, which is Treprostinil.

Q. And if you wanted to do salt selection, are there labs that can do screening of salts for suitable characteristics?

A. Major pharmaceutical companies do that very routinely for almost every NC that they ever manufacture.

Q. Is it standard practice to actually do salt screens and polymorph testing?

A. Yes. I would consider that relative -- I mean, relative -- it's routine within pharmaceutical companies.

Q. Routine as of 2006?

A. Absolutely. Routine for the last four decades that I've been involved.

Q. So, let's go to the next demonstrative, if we could, PDX 10.9, Step 1 selection of API. For a person of skill in the art looking at the claim, what would they have to do in order to move forward with the selection of API?

02:44:56 A. They would take a look at Treprostinil and the salts
02:45:02 and derivatives thereof. Now, at the time of the 2006
02:45:06 patent, there was a previous patent by Phares that actually
02:45:10 describes some of the salts and some of their salts
02:45:13 characteristics, which is where a POSA would start.
02:45:17 Q. And now, let's turn to Step 2. Once you've gotten
02:45:26 the particular active and salt form that you're going to
02:45:30 proceed with, what's the next step?
02:45:32 A. Size reduction. Because invariably the
02:45:36 crystallization that creates the active solid makes it too
02:45:42 big to be used directly in the formulation, so it needs to
02:45:48 be micronized. This is a graphic of a micronized polymer.
02:45:52 Q. Did Dr. Gonda talk at all about the jet milling or
02:45:55 any complexities with respect to jet milling?
02:45:58 A. I believe he talked somewhat about having a high
02:46:04 enough melting point that the micronizing wouldn't melt or
02:46:08 create issues with a amorphous content or whatever in micron
02:46:12 material.
02:46:19 Q. Is jet milling, as of 2006, is that routine?
02:46:22 A. It has been routine for decades before 2006.
02:46:26 Q. Once you've got -- is there anything you need to do
02:46:39 after you build the particles to assess whether they're the
02:46:42 right size?
02:46:43 A. Yeah, you have to measure the size.
02:46:45 Q. How do you do that?

02:46:46 A. Typically these days, that's done by laser
02:46:49 diffraction, which was also around in 2006. This -- you
02:46:55 suspend the material in some non-solvent, shine the laser
02:46:59 beam through it and the diffraction pattern is indicative of
02:47:02 the size of the material that's suspended.
02:47:04 Q. What does the patent teach you about what the right
02:47:07 size of these particles out to be?
02:47:09 A. It's less than ten and specifically less than five.
02:47:12 Q. Was that pretty commonly understood as of the
02:47:14 priority date 2006?
02:47:15 A. Yes.
02:47:19 Q. Once you've gotten the particles the right size,
02:47:21 what's next step?
02:47:22 A. Blending with a carrier. So to bulk the material up
02:47:26 so that, A, you can fill it into a capsule or an inhaler
02:47:30 and, B, to get a powder that will actually fluidize and flow
02:47:35 appropriately when the patient inhales from the device or
02:47:39 when the device actually actuates, if it's not passive
02:47:42 inhaler.
02:47:43 Q. And now there's -- there's an images at the bottom
02:47:46 here of sheer -- high-sheer blending and low-sheer blending.
02:47:49 What is that?
02:47:50 A. Those are two forms of blending that actually
02:47:54 occurred used now currently used back in 2006. The one on
02:47:58 the left, probably the best analogy is the kitchen blender.

02:48:04 The kitchen blenders were a little bit too severe. Essentially have a set of blades within the powder that rotates and mixes the powder. Maybe a kitchen mixer is a better way of saying it.

The low-sheer on the left is actually tumbled with the blend or the lactose and the active into a container and the container is tumbled. Back in the '80s, we sometimes did that by making a nice jar of water and walking around the lab, or although now machines would have been around for again decades. And would actually do that for you automatically.

Q. Now, you've shown lactose at the top of this screen as the carrier here. Why did you select lactose?

A. Lactose, at the time in 2006, was the only approved carrier in the U.S.

Q. Now, Dr. Gonda talked about concerns about proceeding with lactose with any compound or salt that contained an amine moiety. Is that was that a legitimate concern?

A. It's a legitimate concern in terms of paying attention, but I believe there were numerous inhaler products with amines and I think there were probably 70 or so pharmaceutical products with amines that have actually been formulated with lactose.

Q. What would you do if you were concerned about the Maillard reaction? Would you just stop and say I'm not

02:49:27 going to develop a formulation?
02:49:28 A. No, we'd try it and see what happens.
02:49:31 Q. Okay.
02:49:31 A. A bit like the DNase particle we were talking about
02:49:35 this morning.
02:49:37 Q. That's right. You -- I had mentioned the DNase
02:49:38 product with Dr. Gonda. You were on that too?
02:49:40 A. Absolutely.
02:49:41 Q. And when was that product developed?
02:49:42 A. Early '90s.
02:49:46 Q. And how long were you working on than that with
02:49:48 Dr. Gonda?
02:49:48 A. Three years. Not specifically on the powder because
02:49:52 we were also finishing off getting the nebulizer product
02:49:56 approved by FDA, and the powder was going to be a follow-on
02:49:59 product. It would have been more convenient for patients.
02:50:02 Q. So once you've actually made this blended powder,
02:50:06 what do you do with it? Do you have to test it?
02:50:08 A. Yes, and you would put it in into the capsules or the
02:50:12 containers for the inhaler. And this is a graphic of an
02:50:17 instrument called a cascading impactor. These have been
02:50:19 used in the industry -- I guess since I joined the industry
02:50:23 back in the '80s. Different designs, but essentially the
02:50:28 same principles. The aerosol is drawn out through the
02:50:31 inhaler, so the -- fluidizes in the capsule container. The

drug gets drawn out through the container. And the cascade impactor actually separates the aerosol out into different aerodynamic size fractions. With aerodynamic size being the important determiner to where it would head in the air. Course at one end and the fractions just get finer and finer. And what we're looking for here is the quality of that aerosol, i.e., that there's sufficient aerosol less than five microns could be able to get into the airways.

Q. Now, so, and at this point, you have some understanding as to whether you had a successful dry-powder formulation sufficient to carry forward?

A. Correct. Or an understanding that you need to tune the binding or change the lactose carrier size which would all be kind of routine optimization.

Q. So, soup to nuts from selection of the API to going through the cascade impactor or getting sufficient testing to have an idea as to whether you had something that was worth carrying forward, how long do you think that would have taken a person of ordinary skill in the art as of 2006?

A. So a starting point of knowing the API, way before back in the '80s. Dr. Russo would have compound. Took me about six weeks to develop a manufacturing process and it probably would have been acceptable to take into clinical manufacturing so that you could have manufactured it and used it in humans. So that's six weeks to maybe two months

to get a reasonable confidence that you've got a process and a product that would then, of course, require the reasonable amount of work, but routine work, to get to a product that you would be able to put into people.

Q. Would a person of ordinary skill in the art consider six to eight weeks of development undue experimentation?

A. No.

Q. And with all this information and these opinions, what is -- what's your opinion about the -- whether the '793 patent and the disclosure enables a person of skill in the art to practice the -- each and every one of the asserted claims in this case?

A. I believe it does.

Q. Any doubt in your mind on that?

A. No.

MR. CARSTEN: Pass the witness.

THE COURT: All right. Cross-examination.

CROSS-EXAMINATION

BY MS. KRICKL:

Q. Hello there, Dr. Clark. Good to see you again. You may not recall, but my name is Lauren Krickl.

Dr. Clark, do you agree that the '793 patent does not disclose any method for making a powder formulation of Treprostinil?

A. Yes.

02:53:13 Q. And you just testified on direct examination that a
02:53:17 POSA could have developed a dry-powder formulation of
02:53:20 Treprostinil using routine techniques in 2006; right?
02:53:23 A. Yes.
02:53:25 Q. 2006 was 16 years ago; right?
02:53:27 A. Yes.
02:53:30 Q. Yet, you understand that even as of today, 16 years
02:53:33 later, UTC does not have an FDA-approved dry-powder and any
02:53:38 other product on the market, does it?
02:53:39 A. It doesn't.
02:53:41 Q. To your knowledge, no company has ever sold a powder
02:53:44 formulation of Treprostinil; right?
02:53:45 A. As far as I know, yes.
02:53:48 Q. You understand that the '793 patent only has two
02:53:52 examples; right?
02:53:53 A. No, you will have to clarify that.
02:53:59 Q. I believe you testified on direct examination that
02:54:01 the '793 patent has two examples.
02:54:03 A. Oh, wording of DPI formulations in the patent, yes.
02:54:07 Q. Sorry. Can you repeat that.
02:54:09 A. The wording in the patent --
02:54:10 Q. Yeah. Within the patent?
02:54:12 A. -- specifying dry-powder remains in formulations.
02:54:16 Q. Sorry. Can you repeat that again.
02:54:18 A. Yeah. So within the patent, it is mentioned twice.

02:54:22 Q. Okay. My question was a little different. I'm
02:54:27 asking if you understand that -- whether the '793 patent has
02:54:30 two examples.
02:54:32 A. Yes, the two examples are the Respimat and the
02:54:46 Optineb which was used in post delivery medicine.
02:54:49 Sorry a little bit of an accent.
02:54:52 Q. And those two examples describe liquid formulations
02:54:56 of Treprostinil; right?
02:54:57 A. Correct.
02:54:59 Q. And you also testified today that the patent does not
02:55:04 close -- not disclose that a powder formulation was actually
02:55:07 made; right?
02:55:08 A. Correct.
02:55:10 Q. You mentioned that Treprostinil powder has a carrier
02:55:13 material; right?
02:55:14 A. The most logical way of formulating into in 2006
02:55:19 would have been with a carrier. There were alternatives in
02:55:23 2006, but they were more earlier in development. Let's put
02:55:28 it that way.
02:55:30 Q. Let's take a look at JTX 003, the '793 patent.
02:55:35 A. In the binder, yeah.
02:55:37 Q. And turn to Claim 1. And it will be on the screen as
02:55:41 well, Dr. Clark.
02:55:43 A. Okay.
02:55:51 Q. The claim is not limited to any specific excipient

carrier material, is it?
A. No.
Q. The claims are not limited to a specific dry-powder formulation; right?
A. No.
Q. It can be any dry-powder formulation; right?
A. Yes.
Q. Dr. Clark, you've never developed a dry-powder formulation of Treprostinil; right?
A. Correct.
Q. You published papers that discuss the use of medical inhalers; right?
A. And formulation development and interaction with patients and clinical trials, et cetera, et cetera.
Q. In general, when designing medical inhalers, you'd agree that problems can arise if the drug and excipient are not chemically compatible; right?
A. It would be very unusual to see a chemical incompatibility between the formulation and the device.
Q. I apologize can you repeat that again.
A. Said it would be very unusual to see a chemical incompatibility between a formulation and a device.
Q. You heard Dr. Gonda testify earlier; right?
A. I did, yes.
Q. He talked about a paper you published in 1995 called

Medical Aerosol Inhalers Past, Present, and Future?

A. Yes.

Q. Let's look at DTX 268 on the screen, please. And this is that paper; right?

A. Yes, it looks like it is.

Q. Let's turn to Page 2. And do you see the paragraph starting with however?

A. Yeah, if you -- you -- you're going to blow it up, I'll read it. Yeah. Okay.

Q. And on -- do you see the last sentence of the paragraph says, "In this respect, problems can arise if the drug substance and/or excipients are not suitably isolated from the external environment or if the drug and excipient are not chemically compatible"; right?

A. Right. Yes. True statement.

Q. This was true in 1995, the dates of this paper?

A. Oh, yeah. For sure. It's still true now.

Q. And it was true in 2006?

A. Yes.

Q. Dr. Clark, before 2021, there were no reported inhalation profiles to support the use of DPI in patients with PAH; correct?

A. When I testified at my deposition, I believed that to be the case. I've since seen or become aware of a paper in 2005 that details the pressures that PAH can form when they

make extreme effort.

MS. KRICKL: No further questions.

THE COURT: All right. Any redirect?

MR. CARSTEN: Just a moment, Your Honor.

THE COURT: Sure.

MR. CARSTEN: May I proceed, Your Honor?

THE COURT: Yeah.

MR. CARSTEN: Thank you.

MR. SUKDUANG: Can we see it first, Mr. Carsten?

MR. CARSTEN: Yeah, they're getting a copy right now. May I proceed? Thank you.

CROSS-EXAMINATION

MR. CARSTEN:

Q. Dr. Clark, on your cross-examination, you were asked about whether you were aware of a paper that allowed you to conclude something about the inspiratory pull of pulmonary hypertension patients?

A. I was, yes.

Q. What was that article that you found?

A. An article by Meyer, et al.

Q. I'm putting up on the screen --

A. Sorry. Yeah. I'll lean forward a little bit apologies. I'm getting too relaxed.

Q. You're also feeding us back.

A. Yeah. Okay. Sit back a little bit.

03:00:32 Q. Putting up on the screen what's been marked as PTX 1980. Does this look familiar to you?
03:00:37 A. Yes, it does.
03:00:38 Q. Is this the paper that you were referring to?
03:00:40 A. Yes, it is. I became aware of this after my original deposition.
03:00:45 Q. Okay. And just in very broad terms, what does this paper, as of the priority date, tell a person of ordinary skill in the art about the inspiratory pull pressure of those suffering from pulmonary arterial hypertension?
03:01:00 A. I believe the numbers in here were something like five KPA for females and 6.2 KPA for males.
03:01:11 Q. I'm going to zoom in on the abstract here.
03:01:14 A. Yes, please.
03:01:15 Q. Maybe we all can read it without glasses.
03:01:20 And --
03:01:22 A. Actually 5.3 and 6.8.
03:01:25 Q. You're one step ahead of me, Dr. Clark.
03:01:29 I'm going to highlight a sentence there from the abstract. I may have gone over -- I may have overshot.
03:01:36 Would you explain to the Court -- would you read that sentence into the record and then would you tell the Court what that's saying?
03:01:42 A. Maximum inspiratory pressure was lower in the female patients than in 20 controls, 5.2 versus 8.2. In male

patients, PI max was lower than in 25 controls, 6.8 versus 10.5.

Q. Okay. Now, what is this -- how would a person of skill in the art consider these maximal inspiratory pressure numbers?

A. So, in -- sorry. In line a little bit with what Dr. Gonda was saying this morning, generally lung disease in itself does not determine what pressures patients PDCF or PH patients can actually manage to exert, how strong their respiratory muscles are. And what this is a measure of is that respiratory muscle strength and its ability to pull a pressure the way these tests usually do is against a hollow or dead stock, but it tells one skilled in the art what pressure these patients should be able to pull on the end of a dry-powder inhaler.

Q. And how do these numbers compare to the numbers that Dr. Gonda presented earlier pertaining to inspiratory pressures of those separate proponent hypertension which came years after the priority date here?

A. They are much higher.

MR. CARSTEN: Your Honor, I'd offer PTX 1980 into evidence.

MS. KRICKL: Objection.

THE COURT: What's the basis.

MS. KRICKL: He never produced and considered

this publication.

MR. CARSTEN: They opened the door Your Honor.

THE COURT: You asked him about it on cross. If you didn't want him to bring it up, why did you bring it up on cross?

MS. KRICKL: Okay.

THE COURT: All right. So it's admitted over objection.

(PTX Exhibit No. 1980 was admitted into evidence.)

MR. CARSTEN: Thank you.

No further questions, Dr. Clark. Thank you so much.

THE COURT: All right. I think you're done, Dr. Clark. So you can step down and watch your step.

THE WITNESS: Thank you, Judge.

MS. KRICKL: Oh, we have a re-cross.

THE COURT: All right. You're not done.

RECROSS-EXAMINATION

BY MS. KRICKL:

Q. Were' going to take a look at DTX 468.

Do you recognize this paper, Dr. Clark?

A. I do. That's a paper that was recently published with Aaron Waxman's name on.

Q. And it's published in 2021?

A. Yes.
Q. And this is a peer-reviewed paper; correct?
A. Correct. I assume so. It's Pulmonary Circulation, which has a peer-review process.
Q. And you see the first sentence says inhalation profiles to support the use of dry-powder inhalers for drug delivery in patients with pulmonary arterial hypertension have not been reported?
A. Yes.
MS. KRICKL: No further questions.
THE COURT: All right. I think you can step down now.
THE WITNESS: Thank you, Your Honor.
MR. JACKSON: Good afternoon, Your Honor. Plaintiffs call Hugh Smyth to the stand. Dr. Hugh Smyth.
DEPUTY CLERK: Please state and state spell your full name for the record.
THE WITNESS: Hugh David Charles Smyth H-U-G-H space S-M-Y-T-H.
DEPUTY CLERK: Do you affirm that the testimony you are about to give to the Court in the case now pending will be the truth, the whole truth, and nothing but the truth, you do so affirm?
THE WITNESS: I do.
HUGH SMYTH, the witness herein, after having

been duly sworn under oath, was examined and testified as follows:

DEPUTY CLERK: Doctor, just make sure you speak in the mike as best as you can.

MR. DYKHUIS: Your Honor, may I approach?

MR. JACKSON: May I proceed.

THE COURT: Yes.

DIRECT EXAMINATION

BY MR. JACKSON:

Q. Good afternoon, Dr. Smyth.

A. Good afternoon.

Q. Could you please introduce yourself to the Court and spell your name for the court reporter.

A. My name is Hugh Smyth. It's spelled H-U-G-H, S-M-Y-T-H, and I'm professor at University of Texas at Austin.

Q. And in any particular department at the University of Texas at Austin?

A. I'm employed in the College of Pharmacy.

Q. And what type of work or research do you focus on at the University of Texas?

A. My lab does drug delivery research and primarily focuses on inhalation aerosols, including dry-powder inhalers.

Q. What about your teaching responsibilities if any?

A. I teach in the pharm D program as well as the graduate pharmaceutical sciences program.

Q. Okay. In your binder, do you have -- could you open up and look at PTX 507. And could we put that up on the screen, please.

Do you recognize this document?

A. Yes, this is my CV.

Q. And is it current?

A. Reasonably current, I imagine.

MR. JACKSON: Okay. Move to admit PTX 507.

THE COURT: Admitted without objection.

(PTX Exhibit No. 507 was admitted into evidence.)

BY MR. JACKSON:

Q. Now, would you say -- do you have any particular area of expertise in terms of drug formulation or drug delivery?

A. Yes, as I mentioned, inhalation aerosols is one of the area that is I focus on in my research.

Q. Does that include dry-powder inhalers?

A. It does. I've worked on those for many years.

Q. Does that also include metered-dose inhalers?

A. Yes.

Q. Nasal sprays?

A. Yes.

Q. Transdermal drug delivery?

A. It does.

Q. And formulations as well?

A. Yes, formulating all those different types of products.

MR. JACKSON: Your Honor, United Therapeutics offers Dr. Smyth as an expert in the field of inhaled drugs, formulations, and devices, their development, including dry-powder formulations and dry-powder inhalers.

MR. SUKDUANG: No objection.

THE COURT: All right. You may proceed.

BY MR. JACKSON:

Q. So, have you -- did you render -- you rendered some opinions in this case.

A. Yes.

Q. And have you prepared a demonstrative outlining what you were asked to consider?

A. Yes.

Q. So, can we take a look at that?

So, what exactly were you asked to consider?

A. I was asked to perform some testing from the point of view of the POSA in May of 2006 to see whether or not a development of a dry-powder inhaler containing Treprostinil could be done within the claim limitations of the '793 patent without undue experimentation.

Q. Now, what claims did you consider when performing

your analysis?

A. Claims 1, 4, 6, and 7 and not really 8, but that goes in there.

Q. And what particular criteria or characteristics were -- or limitations were you seeking to meet in the test -- testing that you were performing?

A. That, first of all, a dry-powder formulation of Treprostinil for the use in dry-powder inhaler that could be dosed within the 15 to 90 micrograms range in one to three breaths, and I think with the powder being -- comprising powders less than five microns in time.

Q. Now, Dr. Smyth, were you here when Dr. Gonda provided an opinion with respect to the amount of experimentation that would be required to practice these claims?

A. Yes.

Q. And do you agree with him that it would have required undue experimentation to prepare a dry-powder consistent with these claims?

A. No, consistent with these cases.

Q. So did you agree or disagree?

A. I disagree that it would not -- it would include undue experimentation.

Q. And why?

A. Based on my own experimentation that I conducted over the course of a few weeks as well as my knowledge of

development of dry-powder inhalers.

Q. Okay. Now, you indicated that you did this from the perspective of a person of ordinary skill in the art; is that right?

A. That's correct.

Q. So, can we go to the next slide. And what did you define as your -- as the -- what did you use as your definition of a person of ordinary skill?

A. I used the definition that Drs. Waxman and Clark used. It's up there on the slide on the left.

Q. And could you just read what the test is.

A. It would have -- the POSA would have had a graduate degree in medicine or a field related to drug development that would have been M.D. or Ph.D. with at least two years of experience in either investigation or treatment of pulmonary hypertension or in the development of potential drug candidates for -- to be delivered by inhalation.

Q. Now, you're aware that Dr. Gonda has a slightly different formulation of the person of ordinary skill; is that right?

A. Yes.

Q. Would your opinion about this -- about the amount of experimentation required change if you were to use Dr. Gonda's definition?

A. No.

Q. So, what would a person of ordinary skill in 2006, under either definition, know about formulating a dry-powder formulation with a dry-powder inhaler?

A. As Dr. Gonda and Dr. Clark mentioned, there was lots of references and literature and prior art available to a POSA about the development of dry-powder inhalers at that point.

Q. Now, did you review any particular documents to make sure you understood what a person of ordinary skill would know as of 2006?

A. Yeah, there was one particular reference that I relied on, which has been mentioned already, the Telko and Hickey reference.

Q. Okay. So let's pull up the PTX 905. Is this the Telko and Hickey reference?

A. It is.

Q. Okay.

MR. JACKSON: I believe, Your Honor, it is already in evidence as a result of Dr. Clark.

BY MR. JACKSON:

Q. So what would a person of ordinary skill know from the Telko and Hickey article?

A. We can see from this demonstrative there's, you know, pretty large table of contents. This review article goes over a lot of different aspects including, you know, the

development of DPIs, particle sizing, formulation excipients, processing methods, things of that nature.

Q. Now, what did you do to assess the degree of experimentation that would be required as of 2006 to practice the claims based on the teachings of the patent?

A. I -- I did some experimentation myself in my lab.

Q. And did you prepare a demonstrative that summarizes those steps?

A. Yes.

Q. So can we go to that. So, can you tell me what this demonstrative shows.

A. This is a calendar from -- I think it's October. Yeah, this is October of last year starting October 20th when we began experiments, myself and a post-doctoral fellow in my lab. And I've got little icons on there that sort of indicate what kind of experiments were being done on what day of the week.

And so you can see we're doing some powder milling, powder blending, aerosol testing, things like Dr. Gonda and Dr. Clark have already talked about.

Q. Okay. So the grinding, the gear shift wheels, do you see those a number of places?

A. Yes.

Q. Those are powder milling, so you did that on October 22nd, the 26th, the 28th, the 29th and November 2nd;

correct?
A. Yes.
Q. Okay. And then the bowl stirring thing, powder blending, is that the mixing you mentioned?
A. That's right.
Q. Okay. And so you did that on the 26, the 3rd, and -- 26th of October, the 3rd, and 6th of November; right?
A. Yes.
Q. And then aerosol testing, that's the other icon; right?
A. Yes.
Q. And so you did that on the 28th of October, and the 7th of November, and the 9th of November; is that right?
A. Yes.
Q. So, I want to take you through -- we're going to walk through each of those steps, the milling, the blending, and the aerosol testing.

Looking first at that first step, the milling or the grinding thing, can you -- did you prepare a demonstrative of what that's all about.
A. Yes, a schematic.
Q. So can we go to that.

So are these -- are these the steps you took?
A. Right. Yeah, I had three specific steps, kind of as Dr. Clark mentioned, milling, taking the micronized powder

of the right size, blending it with the lactose, taking that blended powder, putting it in a capsule, and putting that in an inhaler and testing the aerosol.

Q. And your testing, on the side it says three weeks in time. Is that how long it took?

A. Roughly.

Q. So, the micronizing by jet milling, what is that?

A. As Dr. Clark had his demonstrative, it's basically using a compressed gas to break up particles into smaller particles, which is grinding them up like a salt grinder or coffee grinder or something like that.

Q. And then how do you measure the particle size following the milling or micronization process?

A. We used laser diffraction.

Q. And how does laser diffraction work?

A. Essentially, as Andy or Dr. Clark mentioned, if you shine a laser through your particles, the diffraction patterns that result from the interaction of light with particles can be converted back into a particle size distribution. And it allows you to figure out how much size of your particles you have.

Q. So, once you have the micronized particles that you've measured the size of, what did you do next?

A. So, then we did that Step 2, which was blending of the micronized material, Treprostinil, with lactose.

Q. And why did you choose lactose?
A. Again, from a perspective of a POSA from 2006, this was the most common excipient for use in dry-powder inhalers.
Q. Okay. So, let me -- let's -- can I pull up PTX 47, please.
Do you recognize this document?
A. Yes.
Q. And what is it?
A. It's a research article on -- focused on Maillard reaction.
MR. JACKSON: Move to admit PTX 47.
MR. SUKDUANG: No objection.
THE COURT: Admitted without objection.
(PTX Exhibit No. 47 was admitted into evidence.)
BY MR. JACKSON:
Q. Okay. So can we go to the second page of this and look at the first full paragraph.
Sorry. First full paragraph on the right-hand side. Okay. So can you read that first sentence?
A. "Although the Maillard reaction is a widely recognized drug-excipient interaction, lactose, the reducing sugar used most widely as an excipient, is frequently used to formulate amine drugs."
Q. And then can you read the next sentence, please.

A. The database of Physicians Desk Reference gives 72 entries in which amine drugs are formulated with lactose.

Q. So, that's -- that's an article that describes 72 entries in which amine drugs are formulated with lactose; is that right?

A. Yeah, and the Physicians Desk Reference is generally those products which were approved.

Q. Okay. So now let's go back to your testing process. Did you prepare a demonstrative to show how you blended the Treprostinil and lactose?

A. Yes.

Q. All right. So let's go to that. So, actually, let's go back one just for a second. Can you tell me what this jet mill -- air jet mill thing is?

A. This is just a -- you know cartoon showing big particles going into the jet mill, and after one cycle, you get reduction of the particle size.

Q. So they bounce around in side the jet mill and then pop out?

A. They go around at high speeds colliding with each other and with the walls of the mill.

Q. And then after you have the micronized powder, you said you blended it with lactose; right?

A. That's right.

Q. Can you explain that process on the next slide?

03:18:45 A. I do, yeah. So we use this geometric. So we're
03:18:49 trying to mix a very small amount of powder with a large
03:18:52 amount of powder, pharmacists use this method as kind of --
03:18:55 it's called geometric dilution or geometric pre-blending.
03:19:01 Basically, you take your smaller amount of drug, which in
03:19:04 this case is the micronized Treprostinil, and you add an
03:19:07 equal amount of the lactose. And then you mix that and then
03:19:12 you add -- now you have, like, 25 milligrams of -- of total
03:19:20 powder. You add 25 milligrams of lactose. You mix that.
03:19:24 And now you have 50 of the blend, and you add 50 more of the
03:19:28 lactose and you just continue on until you achieve the
03:19:32 desired quantity of powder that you wanted to mix with.
03:19:37 Then you take that pre-blended material and throw it into
03:19:40 this low-shear Turbula blender.
03:19:44 Q. Let me just check. You keep doubling the volume; is
03:19:47 that right?
03:19:47 A. That's right.
03:19:48 Q. And so you keep adding the equal amount of whatever
03:19:51 you've got in there to -- so for example, the -- you're
03:19:54 adding 50 milligrams of lactose to 50 milligrams of the
03:19:58 previously blended solution, then you've got 100, and then
03:20:01 to that you are area adding another 100; right?
03:20:03 A. That's right.
03:20:03 Q. Is that why the blue gets progressively lighter?
03:20:07 A. That's right.

Q. And then so, you said you put it in a Turbula blender. What happens then?
A. That basically is just a tumble mixer, and it tosses the powder back and forth, and we did it for about 30 minutes.
Q. And then what did you do after the blending process?
A. So then we tested to see whether or not the drug had been adequately blended or homogenized within this lactose to see if it was uniform throughout that powder.
Q. Okay. Can we go to the next slide. And what does this slide shows show?
A. This is, essentially, the testing that we did to -- to test for blend uniformity. We took ten samples of the bulk powder and analyzed it for Treprostinil content and then we compared those ten results of Treprostinil amounts against each other to see if they were variable or uniform.
Q. And then have you prepared a demonstrative of what you did after this, after you did this testing for blend uniformity?
A. Yes.
Q. What was the next step you took?
A. So, once we established that blend uniformity was good, then we filled HPLC capsules with 20 milligrams of that blend and then tested, using the Plastiape RS01 or Aerolizer device, the aerosol performance and dose delivery

03:21:36 characteristics.
03:21:40 Q. And then what's the -- it says after the Plastiape
03:21:43 device, it says an arrow to the cascade impactor. What does
03:21:46 that mean?
03:21:47 A. Yes, this is the -- the instrument that I was using
03:21:50 to characterize aerodynamic particle size distribution which
03:21:53 was Dr. Clark had just gone over. Essentially, it
03:22:00 classifies aerosols by their aerodynamic diameter.
03:22:06 Q. And in the context of the '793 patent, what sort of
03:22:09 emitted dose would a person of ordinary skill be looking to
03:22:13 see from this aerosol test?
03:22:15 A. So this is the 15 to 90 micrograms of Treprostinil
03:22:22 limitation in the '793 patent.
03:22:26 Q. And is that the emitted dose you were looking for?
03:22:27 A. That's how I understood it.
03:22:28 Q. Okay. And so here you have testing results of
03:22:31 emitted dose. Do you see that?
03:22:33 A. Yes.
03:22:33 Q. And it shows for Treprostinil sodium -- could you
03:22:36 read what the emitted dose was.
03:22:38 A. Yeah, 47.15 for Treprostinil sodium. Treprostinil
03:22:43 free acid 47.72, and Treprostinil diethanolamine 20.88.
03:22:50 Q. And tell me what you said -- also I have a column
03:22:53 there that says fine particle dose. Do you see that?
03:22:55 A. Yes.

Q. Why were you looking at fine particle dose?
A. That's representative of the quality of the aerosol as Dr. Clark introduced earlier. It essentially represents the proportion of the aerosol that would be considered respirable.
Q. And so what steps at all did you take next?
A. Well, based on these results -- these are the averages by the way. Individually, we saw quite a bit of variability in the -- how each capsule performed and plus the fine particle dose, as you can see, it was fairly low in some cases. So, I made a couple modifications to the jet milling and then the lactose that we used as well.
Q. Okay. So tell me what modifications you did for the jet milling process.
A. So instead of a single cycle jet mill, we put it through the jet mill three times to get a more uniform and narrowly particle-sized Treprostinil powders.
Q. So, I want to have you look at Exhibit 1314 in your binder. And could we pull that up on the screen.
Can you tell me what this is.
A. Yeah, this is a particle size distribution that are obtained using the laser diffraction.
Q. And is the document, I believe, labeled TR3XJM_TRA-H. Can you tell me what that means?
A. Yes. This is the particle size for the Treprostinil

free acid that was micronized three times.

Q. And now I'd like you to pull up Exhibit 1313, please. I believe this is entitled he will 3XJM_TRE-DA. Can you tell me what this is.

A. So this is the particle size distribution of the three times jet milled Treprostinil diethanolamine salt showing that, you know, you've got a lot of particles less than 5 microns.

Q. And now I'd like to you point up 1319, please, which I believe is the Document 3XJM-TRE-NA. Can you tell me what this is.

A. So this is the particle size distribution of the three times jet milled Treprostinil sodium, and you can see there that actually we were, in my lab, unsuccessful in jet milling that substantially below 5 microns.

MR. JACKSON: Okay. And so I move to admit Exhibits 1314, 1313, and 1319.

MR. SUKDUANG: No objection.

THE COURT: Admitted without objection.

(PTX Exhibit Nos. 1313, 1314, and 1319 were admitted into evidence.)

BY MR. JACKSON:

Q. What did you conclude from these jet milling results?

A. At least the Treprostinil free acid and the Treprostinil diethanolamine were going to be suitable for

formulating drug.

Q. Those were the Exhibits 1313 and 1314 where you showed the graph; is that right?

A. Yes.

Q. And then have you prepared a slide about -- identifying what you did next after the jet milling process?

A. Yes.

Q. What did you do?

A. Essentially took the same thing as before. We blended it what with lactose. In this round of experiments, we had adjusted the lactose composition to include some lactose fine as well as the original coarse lactose to improve the flowability of the drug.

Q. So you used two different kinds of lactose; is that right?

A. That's right.

Q. And then what did you do after pre-blending the lactose?

A. We pre-blended it using that dilution method. And then put it in the Turbula mixer for exactly the same time and then we did the blend uniformity measurement.

Q. And what results would a person of ordinary skill look for in determining whether the blend uniformity was successful?

A. Typically, you want low variability in my lab.

Person of ordinary skill in the art would look at variability as less than 10 percent or 15 percent. We used a 10 percent cutoff in this these experiments.

Q. I'd like to show you what's been marked as 1347, please.

This is a labeled 3XJMTRE-H Blend Uniformity 3 November, 2021. Do you see that?

A. Yes.

Q. And tell me, -- can you tell me what this is.

A. This is an Excel spreadsheet summarizing the blend uniformity results. And if you look down at the bottom box, right at the bottom of the slide, there's in very small print percent CV. That's the percent variability. We call percent variation.

Q. And that's what we're -- that's the little box down in at the middle bottom?

A. Yes.

Q. Little box. There you go. Thank you.

And so what does percent CV stand for?

A. That is the percent coefficient of variation. It's the standard deviation divided by mean times 100.

Q. And so what number were you looking for that number to be?

A. Less than ten.

Q. And so it's just less than two; is that right?

A. That's right.

MR. JACKSON: Move to admit PTX 1437.

MR. SUKDUANG: No objection.

THE COURT: Admitted without objection.

(PTX Exhibit No. 1347 was admitted into evidence.)

BY MR. JACKSON:

Q. I'd like to show you 1342 as well. Can you tell me what this is?

A. So, this is the blend uniformity of the Treprostinil diethanolamine. Just went through that that we made. And here you can see in red in that box down below the rate of uniformity was too high. It was 20 percent.

Q. Okay. And so what did you do next on this batch?

A. Essentially, we took this powder, put it through a sieve, and reblended it and tested the blend for uniformity again.

Q. And now I'd like to show you what's been marked as 1343. And what does this show -- or what document -- what's this document?

A. This is the reblended -- the sieved and reblending Treprostinil diethanolamine formulation showing a percent CV of around about 5.

Q. So the previous you one you looked at with the 20 percent, you sieved and reblended and this was the

result?

A. That's right.

MR. JACKSON: Move to admit 1342 and 1343, please.

MR. SUKDUANG: No objection.

THE COURT: Admitted without objection.

(PTX Exhibit Nos. 1342 and 1343 were admitted into evidence.)

BY MR. JACKSON:

Q. Now, did you prepare a demonstrative to show the next step in your testing?

A. I think so.

Q. So what did you do?

A. We took those powders which had passed through the blend uniformity test and put them in the capsule again. Used the Plastiape and tested them using the cascade impactor the aerosol and test performance.

Q. And so I'd like to show you what's been marked as 1345. Can you tell me what this document is?

A. It is an Excel spreadsheet which summarizes the results of that next-generation impacted impactor air seal test.

MR. JACKSON: Move to admit 1345.

MR. SUKDUANG: No objection.

THE COURT: Admitted without objection.

(PTX Exhibit No. 1345 was admitted into evidence.)

BY MR. JACKSON:

Q. Now, this was the results of your testing; right?

A. Yes.

Q. So, what does it show for what did you get for the emitted dose on these?

A. So we'll go down the bottom. There's a table. Yeah. In each one of the columns, columns 2, 3, and 4, represent different capsules that were tested. So for capsule 1, 52.42 micrograms of Treprostinil, 53.70 for the second one and 54.5 for the third.

Q. And those were emitted doses; right?

A. That's right.

Q. And then what was the fine particle dose of each?

A. That's the line directly below, the 17.23, 16.81, and 21.55.

Q. Okay. Now, I'd like to show you what's been marked as 1344. What's this document?

A. This is another Excel spreadsheet of which I presume is the -- I can't -- yeah, this is the Treprostinil diethanolamine formulation that we ran that had -- yeah, it looks like it had about 100-micrograms loading in the capsule. And these are the emitted doses and fine doses.

Q. And so what were the emitted doses?

A. 52.85, 50.3, 54.67.

Q. And what were the fine particle doses?

A. 14.83, 15.1, and 14.91.

Q. And this is the thing -- this is the set of results after that sieving and reblending; is that right?

A. That is correct.

Q. Okay. So let's go back to your demonstrative, please. Are those the numbers you show in your demonstrative from the 13 -- actually, let me just check.

MR. JACKSON: Move to admits 1344. I don't think I've done that yet.

MR. SUKDUANG: No objection.

THE COURT: Admitted without objection.

(PTX Exhibit No. 1344 was admitted into evidence.)

BY MR. JACKSON:

Q. So, back here, so are these the results of those tests you just superimposed here?

A. Yes.

Q. And so what did you find?

A. I found that -- that the emitted doses were within the limitation of the claims.

Q. Now, did you reach a conclusion following your testing about the degree of experimentation that would be required to practice these claims?

A. Based on this, you know, three weeks of testing and optimized systems, I thought it would be -- there would not be undue experimentation to develop a drug dry-powder and have a formulation to meet those limitations of the '793 patent.

Q. And, again, you did all that in about three weeks; is that right?

A. That's right.

MR. JACKSON: Pass the witness, Your Honor.

THE COURT: All right.

CROSS-EXAMINATION

BY MR. SUKDUANG:

Q. Hello, Dr. Smyth. Nice to see you again.

A. Yeah, hi.

Q. You received Treprostinil, Treprostinil sodium, and Treprostinil diethanolamine salt, and Treprostinil free acid from UTC; correct?

A. I did, yes.

Q. And UTC, they shipped Treprostinil sodium and Treprostinil free acid to you under cold-pack conditions; correct?

A. I believe so, yes.

Q. Can you look at DTX 618. It's on the screen for you. It will be on the screen for you, Dr. Smyth.

And can you turn to Page 18 for me. And Page 18

is your shipping from your lab, your receipt of the Treprostinil sodium and Treprostinil free acid; correct?

A. That's correct.

Q. And it says on the shipping temp cold pack; correct?

A. Yes, I see that.

Q. And that's not ambient temperature; is that correct?

A. That's not ambient.

Q. And when you received the Treprostinil sodium from United Therapeutics, after you unpacked it, you put the Treprostinil sodium in the refrigerator; correct?

A. One of the people in my lab did, yes.

Q. Right. And you didn't keep it in ambient temperature; correct?

A. Correct.

Q. That's because when you received it cold pack, it tells you as a scientist, hey, I need to refrigerate this because it was shipped this way; correct?

A. That's correct.

Q. Now, you tested Treprostinil sodium, is that right, and as one of your examples?

A. Yes.

Q. And you found when you tested Treprostinil sodium, it was too hygroscopic to create a powder blend; correct?

A. In my lab, yes. It was -- we could see it, basically taking it out of the bottle, jet milling it, trying to

collect it, it was starting to take on moisture. It was very hygroscopic.

Q. And you just look at -- again, before you jet mill, you could look at the Treprostinil sodium that you were going to use and based on visual inspection, you saw there was hygroscopicity?

A. I'm not sure if it was before we jet milled, but definitely after -- after we jet milled, yes.

Q. And you tried to make a powder blend. I think you testified you used a one-time jet mill with the three forms of Treprostinil you received?

A. That's right.

Q. And a one-time jet milled through all three forms of Treprostinil didn't provide suitable dispersion and particle size; correct?

A. I thought it could be improved, so I did the -- the three times jet milled.

Q. Right. It wasn't suitable enough. You had to improve it; correct?

A. It wasn't going to be too hard for me to three times jet mill it, so I thought let's do the three times jet mill and get even better results.

Q. Sure. So, one time wasn't suitable enough for you. You had to three-time jet mill it?

A. I saw a -- quite a bit of variability, at least, with

the one-time experiments that we did.

Q. And you didn't even try to three time jet mill the Treprostinil sodium; correct?

A. We jet milled it, but then, you know, we couldn't get -- as you saw on the laser diffraction -- diffractogram, the sizes were, at least by that method, weren't very small. So I decided I had to devote my efforts to the free acid and diethanolamine.

Q. Right. So, after -- and you're correct. After three times jet milling the Treprostinil sodium, there was too much variability in the particle size, so you decided to not focus on that and instead focus on the free acid and the diethanolamine; correct?

A. Yes, in the conditions in my lab, which in Austin, Texas, we don't have humidity control. So, it was probably pretty pointless for us to continue with that Treprostinil sodium.

Q. Now, with the Treprostinil sodium, you actually tried to use a dry box, didn't you, to control humidity?

A. We -- we did. It's not really a dry box, but a -- it was a glove box.

Q. A glove box, yes. And you used a glove box during your experimentations with the Treprostinil sodium to control humidity; correct?

A. Certain parts of that preparation process we could do

in the dry box or in the glove box. Other parts of that process, we couldn't because the equipment wouldn't fit inside of that dry box.

Q. And even with using the glove box to control humidity, you weren't able to make a suitable dry-powder formulation because of the hygroscopicity of the Treprostinil sodium?

A. Right. During jet milling, it's a mill. It doesn't fit inside of a glove box. I forgot --

Q. Go ahead. I'm sorry.

A. I was just going to say that the -- when we're doing the jet milling, it doesn't fit inside the glove box. And then -- then that's when you're breaking down the particles and creating a lot of surface air. That's where a lot of moisture can be found.

Q. So, during what you considered normal processing, you weren't able to control the hygro -- hygroscopicity. I'm going to get that by the end of the day. By the time -- during the normal processing you were using, you could not control the hygroscopicity of the Treprostinil sodium such that the jet milling provided suitable particle sizes?

A. Right. In our lab, the high humidity, you know, we couldn't do jet milling of the sodium salt properly.

Q. Now, you have a lab notebook that you recorded your experiments in; correct?

A. That's right.
Q. And in your lab notebook, which I believe is DTX 600, you actually noted the humidities when you conducted the experiments; correct?
A. Well, what I told my post-doc is to write down the humidity and the temperature in the lab that -- at the start of the experiment.
Q. And there's no humidity in your notebook, DTX 600, above about 43 percent; correct?
A. That would be correct. But during the course of the day, the humidity would climb in our lab, and I noted that there were relative humidities higher than that.
MR. SUKDUANG: Okay. I'd like to admit DTX 600 into evidence.
MR. JACKSON: No objection, Your Honor.
THE COURT: Admitted without objection.
MR. SUKDUANG: And DTX 618, which was a shipping receiving information --
(DTX Exhibit No. 600 was admitted into evidence.)
MR. SUKDUANG: -- into evidence.
MR. JACKSON: No objection.
THE COURT: All right. Admitted without objection.
(DTX Exhibit No. 618 was admitted into

evidence.)

BY MR. SUKDUANG:

Q. And the claims of the seven -- hold on. You don't have -- although you say that humidity increased, what you actually wrote in your notebook didn't note that humidity increase; is that correct?

A. That's correct.

Q. When you conducted your testing with the dry-powder inhaler, you did not test it in pulmonary arterial hypertension patients; correct?

A. That's correct.

Q. You did not test it in healthy subjects; correct?

A. That's correct.

Q. You used a machine to do that testing; correct?

A. The next generation testing.

Q. Now, I asked you during the deposition and I took your deposition, you had -- you had no more formulations left in the capsule by the time you were deposed; correct? You had no more of the powder blends in capsules that were left?

A. Yeah, I wasn't sure if we had any left in the lab or not.

Q. And I asked you that, if you did have more of those Treprostinil formulations sitting in your lab, and if you stored them properly, you would not advise giving those

formulations to pulmonary hypertension patients without conducting more studies on that formulation; isn't that correct?

A. I think that's fair, yes.

MR. SUKDUANG: No further questions. Your Honor.

THE COURT: All right. Any redirect?

MR. JACKSON: Nothing, Your Honor. Thank you.

THE COURT: All right. Dr. Smyth, thank you. You can step down.

MR. JACKSON: Your Honor, United Therapeutics rests.

THE COURT: Okay.

MR. JACKSON: Thank you.

THE COURT: All right. And Liquidia, are you done?

MR. SUKDUANG: I'm sorry. I was talking to counsel. They rested? They closed their case?

THE COURT: Yes.

MR. SUKDUANG: Then yes, we are finished, Your Honor.

THE COURT: Okay. Great.

All right. So we have summations scheduled tomorrow morning; right?

So, they're scheduled for 8:30. I think I'd

like to move them back to 9 o'clock. Is that all right?

MR. JACKSON: As you wish, Your Honor.

MR. SUKDUANG: That's fine.

THE COURT: Okay. Did I set how long they were going to be?

MR. SUKDUANG: You said 30 minutes, 30-ish minutes each, but you didn't --

THE COURT: All right.

MR. SUKDUANG: -- definitively say.

THE COURT: Well, 30 minutes seems reasonable. So, I can't remember because I did this last week, too. I'm not looking for a slide show tomorrow. Did I give you that speech?

MR. SUKDUANG: Yes.

THE COURT: Okay. All right.

So, if you can all talk to each other about post-trial briefing overnight so that after we're finished with the argument, we can discuss that subject. Or did I already decide that?

MR. JACKSON: No, we've actually started the conversations already, Your Honor, but we will -- we're working on it.

THE COURT: Well --

MR. JACKSON: We'll have that conversation tomorrow.

THE COURT: Yeah. Okay.

Anything else you want to talk about now?

MR. SUKDUANG: Just a question on closings. You had indicated previously, like, you want to have a conversation.

THE COURT: Well, when I say "conversation," I don't mean that the 30 minutes is going to be question and answer. I mean, it's a closing argument like I'm a juror.

MR. SUKDUANG: Okay.

THE COURT: But it's possible that when you're done with the summation, I might have some questions, but I might not. It depends.

MR. SUKDUANG: That clarifies. I just wanted to make sure it wasn't just we're going to sit down and you ask us questions.

THE COURT: No, no, no. It's your chance to persuade me how you won the case.

And -- okay. Anything else?

MR. JACKSON: Not from Plaintiffs, Your Honor.

THE COURT: Thank you. All right.

Okay. Well, thank you. I will see you tomorrow morning. Have a good evening.

MR. SUKDUANG: Thank you, Your Honor.

DEPUTY CLERK: All rise.

(Court was recessed at 3:44 p.m.)

I hereby certify the foregoing is a true and accurate transcript from my stenographic notes in the proceeding.

/s/ Heather M. Triozzi
Certified Merit and Real-Time Reporter
U.S. District Court