UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE PATENT TRIAL AND APPEAL BOARD

WATSON LABORATORIES, INC., Petitioner,	)	
vs.	)	IPR NO. 2017-01621
UNITED THERAPEUTICS CORP., Patent Owner.	)	IPR NO. 2017-01622

The videotaped deposition of MAUREEN DONOVAN, Ph.D., called as a witness for examination, taken pursuant to the Federal Rules of Civil Procedure of the United States District Courts pertaining to the taking of depositions, taken before ANDREA L. KIM, a Certified Shorthand Reporter of said state, CSR No. 84-3722, at Suite 4800, 35 West Wacker Drive, Chicago, Illinois, on the 4th day of April, A.D. 2018, at 9:37 a.m.

Job No: 54284

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REPORTED BY: ANDREA L. KIM,
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I N D E X

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I N D E X

MAUREEN DONOVAN, Ph.D.

THE VIDEOGRAPHER: We are now on the record. This marks the beginning of media number 1 in the deposition of Maureen Donovan in the matter of Watson Laboratories, Inc., versus United Therapeutics Corporation in the U.S. District Court, District of New Jersey.

This deposition is being held at 35 West Wacker Drive, Chicago, Illinois on April 4th, 2018, and the time is now 9:41 a.m.

Will attorneys please identify themselves.

MR. MATHAS: Good morning. Kurt Mathas from Winston & Strawn on behalf of the petitioner Watson Pharmaceuticals, Inc., and the witness Dr. Donovan, and for the record, I would note that the caption read on was the district court caption. We are actually here today in proceedings in two IPRs, IPR No. 2017-1621 and 1622 titled Watson Laboratories, Inc., v. United Therapeutics Corp.

MS. ASCARRUNZ: Good morning. My name is Veronica Ascarrunz from the law firm Wilson Sonsini Goodrich & Rosati in Washington, D.C. here representing the patent owner. With

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me are co-counsel Stephen Maebius and Natash Iyer of Foley & Lardner in Washington, D.C. also representing the patent owner.

THE VIDEOGRAPHER: Will the court reporter please swear in the witness.

(WHEREUPON, the witness was duly sworn.)

MAUREEN DONOVAN, Ph.D.,

called as a witness herein, having been first duly sworn, was examined and testified as follows:

EXAMINATION

BY MS. ASCARRUNZ:

Q. Good morning, Dr. Donovan.

A. Good morning.

Q. Could I get you to state your full name for the record, please.

A. Maureen Donovan.

Q. And you have been deposed before, correct?

A. Yes, I have.

Q. Approximately how many times?

A. About 11 times.

Q. Have you been deposed in an

IPR proceeding before?

A. Yes, I have.

Q. And, therefore, I -- I know you understand the ground rules. I'm going to go over just a few of the most important ones to make sure we are on the same page.

You understand that you are here today to testify truthfully because you are under oath just as if you were in a courtroom or in front of the Board?

A. Yes.

Q. And because we have a court reporter taking down our questions and answers, I would ask that you wait until I finish asking my question before you begin to answer.

Is that fair?

A. Yes.

Q. And if you don't understand one of my questions, will you please let me know?

A. Okay.

Q. Otherwise, if you answer my question, I will assume that you understood it.

Is that fair?

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A. Yes.

Q. We will probably take a few breaks about on the hour or a little bit longer than an hour. If you need to take a break any time before I call for one, please just let me know.

A. Okay.

Q. The only thing I will ask is if there's a question pending, let's answer the question first, and then we can take a break.

A. Sure.

Q. Are you aware of anything that prevent you from providing complete and truthful answers today?

A. No.

Q. I will start by handing you the first exhibit which is marked Exhibit 1002 in case IPR 2017-01622.

(WHEREUPON, a certain document was marked Deposition Exhibit 1002, for identification, as of 4/4/18.)

BY MS. ASCARRUNZ:

Q. Dr. Donovan, is this a copy of

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your expert declaration provided in case IPR 2017-01622 in connection with Patent No. 9,339,507?

A. It appears to be, yes.

Q. And does this declaration bear your signature on page 105 of 105?

A. Yes, it does.

(WHEREUPON, a certain document was marked Deposition Exhibit 1002, for identification, as of 4/4/18.)

BY MS. ASCARRUNZ:

Q. And for the record, the court reporter has just handed you Exhibit 1002 in IPR proceeding 2017-01621.

Dr. Donovan, is this exhibit your expert declaration provided in case IPR 2017-01621 in connection with Patent No. 9,358,240?

A. It appears to be, yes.

Q. And does this bear your signature on page 91 of 91?

A. Yes, it does.

Q. So I notice that the two

declarations have obviously different page numbers. I understand that there are also a number of other differences between the two declarations?

A. There's several differences, yes.

Q. Okay. One of the major differences is that you rely on the Chaudry reference in connection with the '507 patent, but not the '240 patent, correct?

A. I believe that's correct, yes. I could double check, but that's correct.

Q. Okay. Since the '507 patent declaration contains additional pages and the discussion of Chaudry, is it fair to characterize that declaration as containing more information than is provided in the '240 declaration?

A. Well, the declaration for the '507 addresses issues that aren't pertinent to the '240. So it contains additional information.

Q. Okay. Apart from those differences and additional sort of differences

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in wording, et cetera, that are found between the two, is your opinion between the '240 declaration and the '507 declaration consistent?

MR. MATHAS: Object to the form.

BY THE WITNESS:

A. I guess there's a number of items in each of these reports that I express an opinion about. So I think it probably would be most helpful to step through each one of those individual items and describe whether my opinion is consistent or not.

BY MS. ASCARRUNZ:

Q. Okay. And we will. Where I am trying to go here is I don't want to ask you seven hours of questions on one and then seven hours of questions on the other. I would like to be able to use your testimony today to encompass both declarations, and where the differences are important, we can articulate those. Either I will do so in my question or if you feel the need to do so, you would do so as well.

So that's the context of sort

of where I am going with this. I am not trying to do like sort of a gotcha of, you know, equating the two together.

So is it fair to characterize the two declarations as being related?

A. Yes.

Q. Okay. And as having some degree of overlap?

A. Yes, they is speak to many of the same issues.

Q. Perfect. Okay.

MS. ASCARRUNZ: So Kurt with that context and background, can we agree that this transcript will be used in both proceedings?

MR. MATHAS: We can agree that the transcript will be used in both proceedings, yes.

BY MS. ASCARRUNZ:

Q. And as I said, Dr. Donovan, where I -- where my questions are specific to one patent or the other, I will try to make that clear, and I would ask that you do the same. If your opinion would different depending on which patent we are talking about,

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please let me know.

A. Okay.

Q. So that you have them in front of you should you need them during the deposition, I will go ahead and give you the patents now.

(WHEREUPON, certain documents was marked Deposition Exhibit 1001, 1001, for identification, as of 4/4/18.)

BY MS. ASCARRUNZ:

Q. So, Dr. Donovan, the court reporter has now handed you two exhibits. For the record, one is marked Exhibit 1001 in IPR proceeding 01622, and the other is also Exhibit 1001 in IPR proceeding 01621.

Do you have those in front of you?

A. I have things that are marked one and two.

Q. Okay. So --

A. If that's adequate, then, yes.

Q. Okay. The two items at the top of your table there, the two patents, both

of which are Exhibits 1001. Are those the two patents that are at issue in your declaration?

A. Oh, I see what you mean by exhibit number.

Actually, both of them are at the -- the bottom numbers are listed as 1001.

Q. Correct.

A. Okay.

Q. And you will notice -- thank you for the clarification there. It's important to note at the bottom in the dark bold is the exhibit number as well as the proceeding and the page number.

So when I am referring to page numbers, I'll typically refer to those.

A. Okay.

Q. So you noted that they were both marked Exhibit 1001, correct?

A. That's correct.

Q. And you will notice that one is in connection with one of the proceedings, and one is in connection with the second proceeding. That's the distinction.

A. Yes. Okay.

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Q. You are familiar with these patents, correct?

A. Yes, I am.

Q. Treprostinil is a component in all of the claims of those two patents, correct?

A. Well, in the '507 treprostinil is mentioned in claim 1 and in claim 2, and all the rest of the claims are either dependent on one, two, or six, and six is dependent on two. So it's mentioned -- treprostinil is mentioned or dependent in all of the claims of the '507. And similarly for the '240, treprostinil is mentioned in claims 1 and 2 -- or actually claim 1. None of the other claims are dependent on claim 1, and for claim 2 and claim 6, treprostinil is also mentioned in those.

Q. Okay. You are using the word mentioned. Is treprostinil a limitation of all of the claims?

A. I think you would have to explain to me what you mean by a limitation in a claim.

Q. Do you not have an independent

understanding of what a limitation in a patent claim is?

A. I don't keep track of legal requirements for terminologies. I have looked at others to instruct me how to use those terms when necessary.

Q. Okay. Fair enough. We can move on.

You recall that I deposed you in this building in June of last year in connection with the district court action between the same parties involved in this proceeding, correct?

A. Yes.

Q. And your testimony in that other case included, among others, discussion about the same two patents that you have in front of you as Exhibits 1001, correct?

A. Correct.

Q. And at the time of that deposition, you were under oath and endeavored to answer my questions truthfully, correct?

A. Yes.

Q. Have you reviewed that

deposition testimony in connection with your work on this IPR?

A. I have.

Q. When was the last time you reviewed your deposition testimony?

A. Yesterday.

Q. And we previously talked about some of your expertise at that deposition. So I wouldn't rehash all of it today, but there are some issues that are probably important to discuss for these proceedings.

You are an expert in pharmaceutics, correct?

A. Yes.

Q. But you don't claim to be an expert in the law, correct?

A. No, I do not.

Q. And you are not a medical doctor, correct?

A. No, I am not.

Q. And you do not claim to be an expert in the treatment of pulmonary hypertension, correct?

A. No.

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Q. And you have not researched pulmonary hypertension in your professional experience outside of this and the prior case between the parties, correct?

A. Not to any significant extent.

Q. Have you researched pulmonary hypertension in your professional experience to any extent?

A. I was -- both in my professional and my personal experiences, I am familiar with pulmonary hypertension and have looked at treatments and disease state progression information.

Q. Okay. You have not been involved in any clinical trials related to pulmonary hypertension, correct?

A. That's correct.

Q. And before the district court case between the parties, you were not familiar with TYVASO, correct?

A. Not to any extent, no.

Q. And before your involvement in the district court case between the parties, you were not familiar with treprostinil in any

form from a professional standpoint, correct?

A. No.

Q. And you have never published on prostacyclins, correct?

A. No, I have not.

Q. And you don't claim to be an expert in pulmonary hypertension, correct?

A. No.

Q. And you haven't developed any products that have been approved or submitted for approval to the FDA for the treatment of a disease, correct?

A. That's correct.

Q. And you have not developed any drug device combinations that have been approved or submitted for approval to the FDA, correct?

A. That's correct.

Q. And you are not an expert in the design of nebulizers, correct?

A. That's correct. I have an understanding of nebulizer design, but I wouldn't lead that to I am not in an expert in the design of.

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Q. And you have testified a number of times in patent cases, correct?

A. Yes, I have.

Q. And in all the cases in which you have testified at trial or in deposition, they were all on behalf of a generic company, correct?

A. I am trying to recall, but I actually think my very first deposition was on behalf of the brand owner.

Q. Was that in Canada?

A. Yes, it was.

Q. In all cases in which you have testified at trial or deposition in the United States, they were all on behalf of a generic company, correct?

A. Yes, they were.

Q. In the course of your professional career, you have multiple publications, correct?

A. Yes, I do.

Q. And are any of those review articles?

A. Yes.

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Q. Are any of those abstracts?

A. Certainly, yeah.

Q. When you publish papers, you frequently have to perform literature research and cite to the publication of others, correct?

A. Yes, that's true.

Q. When you are performing the research for such endeavors, what steps do you take to find relevant sources?

A. Are you speaking -- are we speaking currently? Are we speaking ever since I started publishing work?

Q. Why don't we think back to 2004.

A. Okay. So in 2004, there were sort of probably multiple avenues in the area that I was likely to be publishing in I already had familiarity with. So I probably had some key references. Maybe I had an extensive collection and was just trying to make sure that it was completely up to date, but regardless I certainly start with key references -- well, let me back up.

Starting with an online

literature search is certainly a process that either immediately or initially or as a follow up to a couple of key references would take place.

I would look at databases that -- that are designed to have or give easy access to literature, and most of them -- many of them are linked in my library, and I have -- then I can figure out whether my library owns that material that I am interested in or whether I need to request it as loan material or whatever.

So I will do several literature searches. In 2004 there were probably -- and even currently -- probably about three. Maybe in 2004 there were even four databases that I would typically search if I were looking for -- it depends on what I was looking for, but if I was looking for a pretty extensive cross-section of information, and then often times if I have a key piece of literature I have identified or review article or something else or there is something I want to follow up on, I will look at the references

that are in that particular piece of literature.

I will follow up on those. I will follow up on the particular key piece by looking at who has cited that literature and sort of expand the search in that manner when I find actual papers or review articles or something that I think are particularly valuable that I want to know who else followed up on those.

Q. Okay. And you mentioned that there were four databases in 2004 that you might consult.

What databases are those?

A. I would certainly consult with PubMed. I would consult with a database that was called International Pharmaceutical Abstracts. I would consult with what probably at the time even was the SciFinder database for the American Chemical Society, and I would look at the Web of Science database.

Q. If you were performing a similar search in 2006, would there be any major changes to what you've just described?

A. No.

Q. Is it your opinion that a person of ordinary skill in the art as you have defined that person in this proceeding in 2006 would go about performing research in a similar manner?

A. Yes.

Q. You have indicated that you have published some abstracts, correct?

A. Well, abstracts that I have presented have been published.

Q. Okay. And what was the purpose of publishing those abstracts?

A. Often times the abstracts that -- the abstracts that are published are abstracts of presentations that were made at a national meeting. The organizations that sponsor those meetings often times have associations with particular publications, and as part of publishing agreements and so forth, often times the abstracts appear in that publication post the -- post their presentation.

As time has gone on, that --

in particular one of the organizations that I present at most frequently, they have -- they now house the abstract -- the abstracts at the national meetings on their own website.

Q. And what would be the purpose of putting the abstracts for the national meetings on the website?

A. I -- I am going to suppose this just because I knew about the association's agreements with their previous publishers that it just became a matter of the next negotiation with the publishers of the journals that they were associated with that the association felt that it better served their members to house the abstracts on their website, and that they didn't need to be associated with any particular journal.

The association had developed interactions with a number of journals. I think a number of them had different publishers. So I think it became an issue of which journal, which publisher, how do you make this all work. So given somewhat of the interdisciplinary nature of the particular

organization and the meeting and the materials that are presented there, it became I think easier for their members to access that information via the association's website than it did to select a particular publisher and journal to house those.

Q. In the discussion of how you might have or a person of ordinary skill in the art might have gone about performing research or I guess just going back to that discussion. If you were searching for works in 2006 about treating pulmonary hypertension, would you pick up every issue of a certain periodical for the last two years and leaf through it because that periodical happened to deal with, for example, medicine?

MR. MATHAS: Object to the form.

BY THE WITNESS:

A. I'm going to -- well, I'm going to answer that as a person who is interested in -- in pharmaceuticals, pharmaceutics aspects. Leafing through medical journals sometimes is a great way to actually get new ideas for potential new dosage forms or

improvements to current dosage forms. So it's not out of the question that that might happen.

I don't do it on a regular basis, and if I am looking for general information in a particular therapeutic area, that probably wouldn't be how I would start, but I am not going to exclude that it wouldn't be something -- especially I would choose probably a focused journal in the area to get an idea of the variety of art.

The reason is that, you know, databases are dependent on the words I put into them in their search, and sometimes I want to know what the vocabulary is that I am not aware that I could be using in my search terms. So I might actually go and look at see what people are publishing currently or talking about.

BY MS. ASCARRUNZ:

Q. Okay. Of the four databases we discussed, is there one in particular that you think is the most popular among persons of ordinary skill in the art as you have defined that person in 2006?

A. I guess that's how you go

about searching and what you're comfortable with and what you use is more of an -- not necessarily an individual preference, but it often times -- you know, it can be influenced by what access you have to those materials. So it's really difficult for me to speak for all POSAs on the matter.

Q. Okay. Sorry to jump around. I had realized that I forgot to ask some questions before.

So going back to abstracts now, you agree with me that abstracts are not peer reviewed, correct?

A. No, I don't agree. When I submit an abstract for presentation, it's reviewed before it's accepted for presentation.

Q. Okay. Are abstracts indexed and searchable?

A. Many times they are, yes.

Q. Is that helpful if they are?

A. Yes. It's helpful for people who weren't able to actually attend the physical presentation to be able to access, and I cite abstracts in a number of my

publications. So, yes, it's helpful to have them indexed and accessible.

Q. When you cite abstracts in your publication, how do you go about finding them?

A. Many times they show up in my searches. If -- again, they are -- if they are abstracts that I actually saw the presentation to, you know, I where to go look. I know which journal supplement the particular abstract is in based on what meeting I was at and what year it was during, but otherwise in many cases they actually are -- those citations show up in a literature search.

Q. Okay. Have you ever published an abstract where preliminary data was conveyed, but the data did not pan out further into a full research study?

A. Can you ask that again?

Q. Sure. Let me ask it a different way. That probably wasn't the most articulate question.

Have you ever published an abstract where you presented preliminary data

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and then were disappointing in how further research evolved from that point?

MR. MATHAS: Object to the form.

BY THE WITNESS:

A. Well, I don't know that I am ever really disappointed in how the research evolves. It is what it is. It may not actually corroborate the hypothesis I had to start with, and as a result, I don't know, I may change my hypothesis and change the approach. I may decide to discontinue. I may identify that I need to do work that requires me to find a collaborator and that doesn't -- doesn't either work out, or I am not able to identify a collaborator at the time to move that on at the right time.

There's all sorts of things that would cause an area of research to not continue to be pursued, and I have a number of abstracts that the full body of work hasn't resulted in a -- in a publication. Some of the work ends up being resident in my students' thesis instead, and that's the appropriate place for that information.

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Q. Okay. Those were exactly the types of things that I was trying to get to, and you articulated them way better that I could have. So thank you.

In this case you provided some opinions about a person of ordinary skill in the art, correct?

A. Yes.

Q. And the person of ordinary skill in the art in this particular case, and by this particular case I mean the two IPR proceedings, were interested in the treatment of pulmonary hypertension, correct?

A. I have to find where my --

Q. If it helps to direct you to a paragraph I had in mind. In paragraph 112 of the shorter declaration is sort of what I had in mind when I asked that question.

So I will restart and ask a different question now that we have that in front of us.

A. Okay.

Q. You start off that paragraph by indicating that: "Given that a POSA wished

to treatment pulmonary hypertension, it would have been obvious," and then you continue on in the paragraph. So I am just focused on that first part where you indicate that a POSA wished to treat pulmonary hypertension.

Do you agree with that?

A. Well, I think that is somewhat of a shorthand in the -- in this particular declaration regarding the claims in these patents. The POSA that I have defined is a drug development expert, and so they are wishing to develop a therapy to treat pulmonary hypertension.

Q. Okay.

A. Somewhat could have added that, but given the context of the other 111 paragraphs that precede it, I think it's in keeping with the context of the report.

Q. Okay. Fair enough.

Now, you pointed out that you have defined a person of ordinary skill in the art, and I believe that is starting around paragraph 72 of this declaration, and one of the statements you make in paragraph 72 is:

"In this case, the earliest priority date to which the asserted claims of the '240 patent a claim is made 15, 2006. Thus, a POSA would have knowledge of all the relevant art as of that time."

Are you taking an expert opinion in this case as to the earliest priority date, or is that information that was provided to you by counsel?

A. Well, it's a combination. I mean, I could look at the information provided on the face pages of the patents and identify that date, similar dates, and that would be my first estimate.

Now, I also don't clearly understand continuations, abandoned patents, and As and Bs and so forth very well. So that's when I ask counsel to either confirm that the date I have identified is actually the priority date or whether there's something that I don't appreciate out of the history that changes that.

Q. Okay. And in this case have you done any detailed assessment of when the

inventors conceived of or invented the claims in the patents?

A. Can you be more specific about that question?

Q. Yes. Have you done an independent assessment to try to put a date to when the inventors conceived the invention?

A. Well, I don't know that I necessarily have access to the appropriate information to do that. So I have -- I look at the dates certainly on the patents, and I am left to, you know, essentially believe that that's the date of conception or that -- actually that's the date that the complete descriptions about the invention that they want to disclose is identified, but, you know, clearly there are -- there's art that goes into building towards what somebody discloses in a patent.

So, you know, which specific idea, which specific part of a claim, which specific thing, you know, when those are conceived is not something that's very -- is necessarily easy for another person to identify

which is why I think it's the inventors' responsibility to define or describe when that was as they're filing the patent application. That's sort of my understanding of they have to document when the invention conception took place.

Q. Okay. And I am just trying to get at you weren't tasked with performing a detailed analysis of those particular dates, correct?

A. I don't know that I have the capabilities to do that accurately in, you know, United States patent timing, no.

Q. Okay. Who are the inventors of the two patents at issue here?

A. Well, the inventors are listed on the face pages. So Horst Olschewski, Robert Roscigno, Lewis Rubin, Thomas Schmehl, Werner Seeger, Carl Sterritt, and Robert Voswinckel are listed as the inventors on the '507 patent. And Horst Olschewski, Robert Roscigno, Lewis Rubin, Thomas Schmehl, Werner Seeger, Carl Sterritt, and Robert Voswinckel are also listed as the inventors on the '240 patent.

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Q. So the same set of inventors for both patents, correct?

A. It appears to be based that on the face pages.

Q. Prior to this case and the district court case between the parties, had you heard of any of these individuals?

A. Not to my recollection.

Q. Do you know the education level of these individuals?

A. Not specifically, no.

Q. Do you know what the problem the inventors were attempting to solve was?

A. I believe it's, you know, somewhat identified in the titles of the patents that they were -- they were using treprostinil via inhalation, and when you read further into the details of the patent or in the specification, they talk about the disease state that they think that would be appropriate for use.

Q. Okay. At paragraph 73 of the '240 declaration, you list some numbered items there.

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Do you see that?

A. Yes.

Q. And you understand these to be factors to be considered in determining the level of skill in the art, correct?

A. Yes.

Q. Did you consider each of these?

A. At various levels, yes.

Q. What did you consider with respect to item 2 the types of problems encountered in the art?

A. Well, as a pharmaceutical scientist, the art that this speaks to is inhalation administration. I'm quite familiar with the delivery systems and issues sometimes that face those delivery systems in developing materials, dosage forms for inhalation delivery.

So I, you know -- I am quite familiar with the problem encountered in the art regarding -- or problems encountered in the art regarding inhalation delivery. So, you know, I didn't have to do a lot of work to find

those particular issues. Those are things that I deal with at -- you know, frequently. I am certainly aware of, follow to some extent utilizing my own research.

Q. Okay. And did you consider any similar types of problems specifically with respect to prostacyclins?

A. Well, again, I am aware of prostacyclins, some of their similar analog compounds just by virtue of the family of materials has been around and considered for quite a few years. And so in keeping with that, there were specific pieces of information like the structure of treprostinil. Some of its chemical characteristics were certainly things that I was sure that I had more familiarity with than just sort of my casual background, but it becomes a consideration of what the chemistry is of those compounds, what their compatibilities are, what their stabilities are, and so forth.

A POSA would certainly include those in their understanding of what the -- both the level of skill in the art somebody

interpreting that information and what the art was at the time.

Q. Okay. And did you consider any types of problems specifically with respect to the treatment of pulmonary hypertension?

A. Again, needing -- you need a knowledge of what the disease state is, what the -- where the target is for treatment, where the target that the particular therapeutic entity that you are using or potentially considering using, where those targets might be, how you go about getting the drug to those targets.

Look at -- certainly in the art, you start investigating how others may be delivering similar materials or how in the therapeutic area, how other treatments are currently being utilized to again look at what the level of -- where the art is at the time and where it has been up until that time.

Q. Okay. What is the target of treatment for pulmonary hypertension?

A. Well, the most obvious target is or region of pathology is in the lungs. I

don't know that we even at this point, certainly not in -- at the priority date of these patents does everybody understand the actual molecular mechanisms behind pulmonary hypertension.

So there may be other organs involved. There may be other targets within the body, but the manifestation and the region that certainly could benefit from some therapeutic interventions initially are the lungs. So that would be certainly one of the initial targets that one would assess.

Q. So you identified the lungs as the region of pathology and also a region that could benefit from some therapeutic interventions.

Is there a particular part of the lungs that you had in mind?

A. Well, the disease itself appears to be an issue regarding the pulmonary vasculature and the resistance through the pulmonary vasculature, and that means that you are likely going to need to target a pretty broad spectrum of the lung tissue because it's

well perfused on high populations of capillaries and arterials and venials.

The other side to that knowing about lung anatomy is there's a lot of ability for materials that enter the bloodstream to actually contact a lot of those tissues without you actually contacting them directly. The bloodstream is pretty effective about moving things through those tissues. So I wouldn't be halted as a POSA knowing that I couldn't actually reach every single cell in the lung with my delivery system.

Q. Returning to paragraph 73 and the numbered items, what did you consider with respect to No. 4 the rapidity with which innovations were made?

A. I think that becomes an area where in my knowledge of what is going on in inhalation delivery in particular, I am aware of and typically attend meetings at least annually where if presentations are being given where there's new innovations, significant innovations in the area, they're likely to be being discussed at those particular meetings.

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And so my context sort of reviewing this at the time of -- in the near 2006 is the recollection of how many technologies were known at the time and whether there was a significant change in the number of those or the knowledge of how one delivers materials via inhalation was changing around the time of 2006.

Q. Is it your opinion that this area is one in which innovations were made rapidly?

A. Well, to be honest in the world of drug development, nothing is as rapid as we want it to be. There's a lot of work and effort that goes into actually bringing any idea into the commercial space certainly if that's your end point for innovation or even just bringing about a change in direction.

So in drug development I don't really qualify anything as rapid. Were there new ideas being discussed? In the mid 2000s there were -- yeah, there were new ideas, but they weren't paradigm changing ideas.

Q. Okay. Are you a POSA as you

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define that person in your declaration?

A. That's what I was looking for before. I was trying to find where I placed my definition of POSA. I know it's in here.

Q. If you will permit me, I think it's at paragraph 74.

A. All right. I was looking for a heading so. And, yes, I believe I was a POSA as described in paragraph 74.

Q. And were you a POSA as of May of 2006?

A. Yes.

Q. Are you aware that the patent owner in this case has a different view on what a POSA is?

MR. MATHAS: Object to the form.

BY THE WITNESS:

A. Yeah, I mean, I am aware that there have been different interpretations of the definition of POSA and different rulings from the court regarding that and different acceptances of different versions of definition of POSA. So if you want me -- I don't know. I think I need to see something specifically and

then agree that I have seen that and you place it in time and place regarding what it means regarding this particular discussion.

BY MS. ASCARRUNZ:

Q. Okay. Let me ask this instead.

In your opinions the POSA that you had in mind was the POSA as you have defined it in paragraphs 72 through 74, correct?

A. Well, in developing my opinions initially in the previous case, more likely when I became aware of the other possible definitions of POSA I recognized those. I evaluated whether my opinions would really change based on that, and I don't -- and they wouldn't, but I still believe that my definition of POSA is accurate.

Q. Okay. And your definition of a POSA is not different with respect to which of the two patents we are talking about, correct?

A. No, it's not.

Q. Okay. Okay. In your

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declaration you talk about several prior art references. Today I am only going to ask you about four of them: The Voswinckel reference, the Ghofrani reference, the Patton reference, and the Chaudry reference.

When I use those names, do you understand what I am referring to?

A. As long as you are referring to the ones that I have described in brief in my declarations, I will recognize that those are what you mean.

Q. Great. I am trying to use the names that you gave them so.

A. Right.

Q. Okay.

THE VIDEOGRAPHER: Going off the record at 10:31 a.m.

(WHEREUPON, discussion was had off the record.)

THE VIDEOGRAPHER: Going on the record. The time is 10:32 a.m.

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(WHEREUPON, a certain document was marked Deposition Exhibit 1003, for identification, as of 4/4/18.)

BY MS. ASCARRUNZ:

Q. So I have handed you what's been marked as Exhibit 1003, and that's the same exhibit number in both IPR proceedings.

Do you recognize this as what you refer to as the Voswinckel reference?

A. Yes, I do.

(WHEREUPON, a certain document was marked Deposition Exhibit 1004, for identification, as of 4/4/18.)

BY MS. ASCARRUNZ:

Q. I have now handed you what's marked as Exhibit 1004 in both proceedings.

Do you recognize this as what you refer to as the Chaudry reference?

A. Yes, I do.

MR. MATHAS: Just a point of clarification. The Chaudry that you have handed is in IPR 1621. I think it's the same

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number in both, but it may not be. So just to be -- for clarity of the record, it is 1004 in 1621.

MS. ASCARRUNZ: Yes, so it is the same number in both --

MR. MATHAS: Okay. Thank you.

MS. ASCARRUNZ: -- which is what I think I tried to represent on the record.

MR. MATHAS: Thank you.

(WHEREUPON, a certain document was marked Deposition Exhibit 1005, for identification, as of 4/4/18.)

BY MS. ASCARRUNZ:

Q. The most recent exhibit that's been handed you to is Exhibit 1005, and that's the same exhibit in both proceedings.

Do you recognize this to be the Ghofrani -- a translation of the Ghofrani reference?

A. Yes.

Q. Okay. And then the last of the four --

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(WHEREUPON, a certain document was marked Deposition Exhibit 1012, for identification, as of 4/4/18.)

BY MS. ASCARRUNZ:

Q. -- is Exhibit 1012 in both proceedings, and do you recognize this to be the Patton reference?

A. Yes.

Q. Were these four references provided to you by counsel, or did you personally locate any of these four references?

A. These were provided to me by counsel. I know how to locate most of them, but the translation in particular was provided by counsel.

Q. Okay. Are you providing an expert opinion that the Voswinckel reference was publicly accessible to a person of ordinary skill in the art, or is that an assumption that you were given by counsel?

A. No, I found that particular abstract citation myself. So I know it's publicly -- or it was certainly publicly

available to me when I looked.

Q. Where did you find that particular abstract citation yourself?

A. I looked in Web of Science.

Q. So I am not sure that answered my question.

So are you providing an expert opinion that Voswinckel was publicly accessible to a person of ordinary skill in the art?

A. Well, I am telling you that I looked for it. I found it using a database that was certainly available at the -- in 2004, 2005 when this probably appeared on the database, but I don't have actual direct knowledge that -- I didn't search it in 2004, 2005. So I can't absolutely say, but knowing the Web of Science and what they abstract and how they go about approaching what's on -- in their database, they have maybe a six-week lag time in getting new material into that database.

I have no reason to expect that if I can find it in their database in 2018 or 2017, that I wouldn't have found it shortly

after it had been published.

Q. You didn't include any of the discussion of your search and what you found in your declaration, correct?

A. I didn't feel I needed to. I mean, they were available in hard copy. They are available in libraries. The fact that I could go and find it on Web of Science and access it or at least know that it was available in my library didn't seem to be something that rose to the level of needing to be in my report.

Q. Okay. Are you providing an expert opinion that any of the other three references: The Ghofrani reference, the Chaudry reference, or the Patton reference was publicly accessible to a person of ordinary skill in the art?

A. Yes, in the same manner. I know how to search patent publications and could have found both the Chaudry and the Patton publications in 2018 or whenever they appear in the databases according to their dates, and, again, I did look to see whether I

could access the Ghofrani publication.

I did find it in the collection in my library, but I didn't actually pursue whether I needed to inter-library loan that or how I would have actually gone about obtaining that, but in the same manner I -- both the electronic source that my library subscribes to had this journal available electronically before 2005. And so I am -- I'm perfectly willing to believe that if I had looked in 2005 or any time after that, I would have been able to find this and obtain a copy of the original paper.

Now, whether -- whether I needed to then have it translated or not, depended on -- would depend on what information I needed from the particular publication.

Q. Okay. You have stated that you were willing to believe that had you looked in 2005, you would have been able to find and obtain a copy of the original paper.

In your declaration you did not detail any steps that you took or that a person of ordinary skill in the art would take

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to locate that reference, correct?

A. I didn't but these are -- the Ghofrani reference in particular Herz is a recognized journal --

Q. I am just asking what was in your declaration. That was not in your declaration, correct?

MR. MATHAS: Object to the form. You have got to let her answer, and then you can ask your question again.

You may continue with your original answer.

BY THE WITNESS:

A. Okay. Well, I was just going to say that this was a well-known journal, and patent publications are well known to be publicly available. In my description of information in my declaration, I -- it was -- it was a belief that everybody reading that would appreciate that these were -- you know, were publicly available.

They are in well-recognized journals. Circulation a well-recognized journal. There was no reason to believe that

somebody interested in a -- a particular POSA interested in the area wouldn't be able to access this information.

BY MS. ASCARRUNZ:

Q. Nowhere in your declaration do you assess whether Voswinckel was searchable by a subject or a key word, correct?

A. I don't recall that being a -- you know, the actual searching of the information that I described as contemporary prior art, how that was searchable isn't the topic of this declaration and is typically not the topic of any of my opinions or declarations in most of the patent cases that I have been involved in.

Q. I want to talk for a minute about objective indicia.

You understand what I mean when I say that?

A. I have a general understanding of that, yes.

Q. Let's look at paragraph 207 in your '240 declaration.

A. 207?

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Q. Yes, and actually since this is a little bit of a change in gear in topics, we have been going for a little over an hour. Would you like to take a break?

A. I would, yes.

THE VIDEOGRAPHER: Going off the record. The time is 10:43 a.m.

(WHEREUPON, a recess was had at 10:43 a.m. until 10:55 a.m.)

THE VIDEOGRAPHER: Going on the record. This marks the beginning of media number 2. The time is now 10:55 a.m.

BY MS. ASCARRUNZ:

Q. Dr. Donovan, before we went on the break, I started to have you turn to paragraph 207.

A. Yes.

Q. And in that paragraph you indicate quote: "Assuming the myriad teachings of Voswinckel and Ghofrani are overcome, the evidence of secondary considerations presented during prosecution of the '240 patent does not change my opinions."

What did you mean by that

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statement?

A. Well, it means that secondary considerations are something that should also be evaluated when looking at obviousness, but that none of the secondary considerations identified during the prosecution of the '240 patent were of a level that were -- that would overcome what was already in the prior art and known to a POSA.

Q. Okay. In the tail end of that paragraph, what you say does not change my opinions.

Is it fair to say then that you looked at the prior art, formed your opinions on obviousness, and then looked to the secondary considerations that were provided to see if they changed your opinions?

MR. MATHAS: Object to the form.

BY THE WITNESS:

A. Not in that particular order. I mean, just based on my own experiences, I have a lot more knowledge without even looking further into the prior art about a lot of things about inhalation delivery. So I start

with that knowledge base.

I expand it regarding the prior art that's available regarding these particular topics, and certainly the secondary considerations aspects go into that to help me sort of identify whether there are other things in the art that I need to become familiar with or things that -- that -- again, just areas that I perhaps need to be -- to broaden my information that I am evaluating to form my opinion, and then I form my opinion. So it's not -- I don't really do things in a first this, then that serial method.

BY MS. ASCARRUNZ:

Q. Okay. In the district court proceeding, you did not consider objective indicia in your opening report, correct?

MR. MATHAS: Object to the form.

BY THE WITNESS:

A. I don't recall. I would have to take a look at my opening report to refresh my memory.

BY MS. ASCARRUNZ:

Q. Okay. In -- at page 84 in

the -- I guess the header that is for the section in which paragraph 207 was included, the header there says: "Objective indicia of non-obviousness do not overcome the strong showing of obviousness."

What did you mean by that header?

A. I think it's just another way of essentially saying what's also said in paragraph 207 that evaluating the objective -- the objective indicia of non-obviousness that the rest of the prior art demonstrating the obviousness of the claims, those objective inertia which are not necessarily searchable in the databases that I would look at don't overcome -- don't replace, don't cause me to evaluate in a -- I am trying to think of the right way to say this, but knowing what those objective indicia were that the plethora of information in the art, those other issues didn't rise to overcome or to make them a significant consideration in light of what was already available in the art that was obvious.

Q. Okay. What did you mean when

you said the objective indicia are not necessarily searchable in the databases that you would look to?

A. Well, one of the objective indicia is commercial success, and I can't find information about commercial success of products in Web of Science.

Q. Okay. In paragraph 209 you indicate that: "The benefits that patients have experienced from TYVASO cannot be attributed to the specific nebulizer."

Do you see that?

A. I see where it says that, yes.

Q. Isn't it a fact that there's a single patient who has received TYVASO since it was approved by the FDA that did not use the specific nebulizer UTC developed for it?

A. I have no way of being able to answer that. I actually suspect that there may be patients who have used something other than the nebulizer that it was approved for use but that's outside of the FDA approval. I don't know that it's common, but I wouldn't dismiss it as a possibility.

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Q. Why do you suspect that there may be patients who have used something other than the nebulizer that TYVASO was approved with?

A. You know, things happen. Something happens to a patient's nebulizer for their -- that their supposed to use with TYVASO and they need a dose of the drug, and they are 100 miles away from being able to find another nebulizer yet they have a different brand. I would suspect that somebody would at least attempt to use a different nebulizer for that. I don't know but things happen.

Q. Are you aware that TYVASO is approved by the FDA not as a stand-along drug, but as a drug device combination?

A. That's my understanding, yes.

Q. You indicated that certain UT patents effectively blocked anyone outside of UTC from pursuing an inhalable drug product containing treprostinil, correct?

A. I recall that being in one of my reports, declarations.

Q. Well, let me ask it this way.

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Is it your opinion that certain United Therapeutics patents effectively block anyone outside from United Therapeutics from pursuing an inhalable drug product containing treprostinil?

MR. MATHAS: Object to the form.

BY THE WITNESS:

A. Well, I think somebody outside of UTC who was aware of those patents yet wanted to commercialize something that involved areas covered by those patents would -- could work with UTC for a royalty potentially, but from a -- from a free ability to commercialize without having to do that, that would likely be an element that they would decide that, you know, they can't work in that area based on those patents.

BY MS. ASCARRUNZ:

Q. Okay. You talked about freedom to commercialize.

Would someone outside of UT be free to investigate and develop inhalable therapy containing treprostinil?

MR. MATHAS: Object to the form.

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BY THE WITNESS:

A. I am a lot less familiar with the requirements for essentially freedom to use, and I know how I approach it as an academic because typically those legal standards aren't typically enforced against academics because we are not -- the work that we are doing isn't directly linked to trying to move something into a commercial marketplace, but the other individuals who have other goals or missions have other constraints.

I know they exist. I just don't know enough about them to be able to know what they really can do and can't do, but I understand that there -- the abilities to freely operate are limited and prescribed.

BY MS. ASCARRUNZ:

Q. You are aware that the individuals at the University of Giessen, in fact, did pursue research into the inhalable treatment with treprostinil, correct?

A. Well, I am going to refer to the Voswinckel abstract, and those individuals were located at Giessen in a number of -- even

in my declaration, I refer to other people referring to them as the group in Giessen. Yet the abstract indicates that the work was supported by Lung Rx which tells me that in addition to their own independent work, somehow they were either provided funding or some other way of achieving doing this work.

Q. In coordination with Lung Rx?

A. Yes.

Q. Are you aware that Lung Rx is a subsidiary of United Therapeutics?

A. I am vaguely aware that Lung Rx has some relationship to what's currently known as United Therapeutics.

Q. At page 31 of your '240 declaration, you start your discussion of obviousness of the '240 patent, and if I could direct your attention specifically to paragraph 71, you state that it is your opinion that the asserted claims of the '240 patent would have been obvious to a POSA in view of the teachings of certain specific combinations of prior art.

Do you see that?

A. Well, I give specific examples

of those combinations, but, yes, that my opinion was that those claims would have been obvious to a POSA.

Q. Okay. And you list three bullet points there of certain combinations of prior art, correct?

A. That's correct.

Q. Are you aware that the Patent Trial and Appeal Board instituted this trial only as to one of those three grounds?

A. Yes, I am somewhat aware of that.

Q. And it is your opinion that the claims of the '240 patent are obvious over Voswinckel in view of Patton and Ghofrani, correct?

A. Yes, that's my opinion.

Q. And with respect to the '507 patent, it is your opinion that the claims of that patent are obvious over Voswinckel in view of Patton and Ghofrani and Chaudry, correct?

A. Yes.

Q. One of the references you refer to is the Voswinckel reference?

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A. Correct.

Q. And one place that you refer to Voswinckel is paragraph 56, and you indicate there in the last sentence that: "Voswinckel's findings gained immediate interest as they were cited in a 2005 paper by Sulica and Poon in Expert Review of Cardiovascular Therapy."

Do you see that?

A. I do.

Q. Why did you find that to be relevant?

A. Well, it tells me that people were interested in what Voswinckel had reported about inhaled treprostinil, and that they saw the information that was presented by Voswinckel either at the American Heart Association meeting or read the abstract and felt it was -- there was a reason to include it in a review of the recent therapies that were being investigated for pulmonary hypertension.

Q. Do you find it relevant that no other reference has cited Voswinckel?

MR. MATHAS: Object to the form.

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BY THE WITNESS:

A. It's my recollection that after this abstract, Voswinckel published a number of additional papers. He found -- he seems to be a pretty prolific author, and my -- typically as a POSA, if there are publications that have more information in them, more details and so forth on a particular study that may have been described in an abstract, that the actual publication is the reference that's cited instead of citing the abstract.

BY MS. ASCARRUNZ:

Q. Why is that?

A. Again, the publication contains more extensive information. Perhaps has some graphs, has some other information included in it, and it makes it from a -- from a reference citation standpoint something that a writer could rely on for perhaps more than just one or a few facts that are stated in the abstract.

It gives people the opportunity to look at more further methods, descriptions, and so forth to learn how the

particular study was done perhaps, and that's just -- ends up being -- there's more information often times, and so the actual paper publication gets cited when it actually appears in publication.

Q. Okay. Do you know for a fact that the study in Voswinckel resulted in a paper publication?

A. I have seen some of Voswinckel's later works. I can't recall specifically whether pieces of this study were included in some of those papers. It's referred to in other papers certainly.

Q. Is it your opinion that the study in Voswinckel established the safety, tolerability, and clinical efficacy of treating pulmonary hypertension with inhaled treprostinil?

A. Well, I believe what their goal statement was that, as Voswinckel describes it, their goal of this study was to assess safety, tolerability, and clinical efficacy in patients with severe pulmonary hypertension, and the rest of the abstract goes

on to describe that under the conditions that they used, it was safe, the patients tolerated it quite well, and they had patients that did well enough and requested compassionate use that they remained on the therapy outside of the particular study. So I think they accomplished their preliminary goals.

Q. So, yes, is it your opinion that the study in Voswinckel established the safety, tolerability, and clinical efficacy of treating pulmonary hypertension with inhaled treprostinil?

A. Yes, certainly under the conditions of the investigation that they conducted.

Q. Voswinckel was primarily an acute study, right?

A. You mean acute a one-time therapy. For most of the patients that received it and for the portion of the study where the actual pulmonary vascular resistance and other measures were being made, yes, that was a -- as reported here at least, appears to be a one-time exposure for most of the

patients, but, again, at least two of the patients remained on that therapy for a long period of time without continued, constant evaluation of their pulmonary vascular resistant and some of the other measures that were clinically observed.

Q. And those two patients were receiving compassionate treatment under the study, correct?

A. That's what the authors refer to it as, yes.

Q. What is compassionate treatment?

A. Well, in -- I mean, my understanding in human clinical evaluation and Germany's requirements for human clinical evaluation probably differ from the United States, and I have a much better understanding of what the regulations are in the United States, but typically for human investigations, you need to have protocols approved, and they are very clear about the number of times a person would receive an investigational agent. What would be happening to them while they

received it. What follow-up care perhaps would be provided to them. A whole number of things.

And so at the time that these authors likely identified what they were going to do to conduct the study that involved the Swan-Ganz catheretization and so forth, they had not included a long-term follow-up leg or follow-up treatment leg in their protocol, and so since it appears that two of the patients either requested or needed or everybody felt that continuing that therapy was in their best interest, the compassionate treatment arms become an ability on an individual patient basis to allow use of an investigational agent outside of an approved protocol and current clinical study.

I am sure that person -- a person who is expert in compassionate use could tell me that I am slightly generous in some of my descriptions of how that works, but I think that's a reasonable layperson's description of what compassionate use was and in keeping with this particular information in this abstract.

Q. Okay. In paragraph 80 you

state that you understand -- sorry, I will give you a chance to get there.

You indicate there that you understand that the October 2004 issue of Circulation in which Voswinckel was published was made available in libraries by at least December 2004, and then you cite a footnote there that I will represent to you is the declaration of a Dr. Scott Bennett.

Do you see that?

A. Yes.

Q. Is it your own expert opinion that the abstract issue of Circulation containing Voswinckel was published and made available in libraries by at least December 2004, or are you simply relying on Dr. Bennett for that point?

A. Well, while I rely on Dr. Bennett for the details, I look at the materials provided with the Voswinckel abstract, and in particular it includes the journal face page, in essence, or the journal cover, and the date on the journal tells me that it was published and available October 26,

2004.

So I mean it was published before that. It became widely available by at least October 26, 2004 to subscribers. The libraries -- my library, for example, is a subscriber. At the time probably received this in hard copy. Mailing times and so forth, who knows when they really got there, and by the time it's indexed and put on the shelf, there may be a couple of week lag.

So by at least December of 2004 is certainly in keeping with all of my experience regarding how journals arrived in libraries, how they were indexed, and when they get to shelves or when they got to the, you know, sort of new journal area often times before they were actually shelved with the rest of the collection.

Q. Okay. In the last part of that paragraph, you indicate that materials were given to all attendees at the conference or after the conference.

How do you know that?

A. I have seen a press release

that indicates that, you know, that all -- that there's -- that the journal abstracts or the -- the meeting presentation abstracts were provided as -- in a CD-ROM format. They were available online to meeting attendees, and that they were -- they certainly appear in hard copy as a supplement to the journal. And so the press release tells me what the meeting attendees got, and they got online access in some manner for at least a year, I believe, and then they actually got a CD-ROM of the material.

Q. Okay. I'd like to turn your attention to paragraph 108, and starting in that section you begin your discussion of why the preamble of claim 1 is met, correct, or is obvious I should say -- let me strike that and start again.

Starting in paragraph 108, you begin your discussion of the preamble of claim 1, correct?

A. I am just trying to get placed in where I am in my declaration or where we are discussing in my declaration. Okay.

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Can I ask you to repeat the question just to make sure that I am answering the question that I thought I heard?

Q. Sure. Starting at paragraph 108, you begin your discussion of the preamble of claim 1, correct?

A. Yes, in paragraph 108 it's a subset of the first phrase in claim 1.

Q. Which is quote: "A method for treating pulmonary hypertension," correct?

A. Correct.

Q. And the only reference you cite to in this section is Voswinckel, correct?

A. In those specific paragraphs, yes, but the other art that I rely on also would have sufficed, but the information in Voswinckel was very clear and is used as a -- as a -- one of the three articles in the '240 that I use to support my opinions.

Q. Okay. In paragraph 109 you state in the second sentence that: "The 17 patients received a three-breath inhalation treatment four times per day using a pulsed ultrasonic nebulizer from Nebutech and a

formulation comprising 600 micrograms per mil of treprostinil."

Do you see where I am?

A. I do, yep.

Q. When you refer to these 17 patients, you are referring to the 17 patients in Voswinckel, correct?

A. Well, there were 17 patients in the Voswinckel initial study. The patients who received the treatment four times a day I think are the subset of the two compassionate use patients from that.

Q. Okay. This statement as written here is incorrect; is that right?

A. Two of the 17 patients received that three breath inhalation treatment four times a day. The other 17 -- the other 15 received a three breath inhalation treatment as part of the monitored portion of that study.

Q. So the part that states here quote: "These 17 patients received a three breath inhalation treatment four times per day" is incorrect?

A. There should have been some

additional information included in that sentence to make it clear.

Q. Okay. In fact 17 patients did not receive three breath inhalation treatments four times per day, correct?

A. As written in the abstract, the 17 patients received the treatment using an ultrasonic nebulizer as the treatment of three breaths and were observed for two hours and then two additional patients received compassionate use using four inhalations per day after the acute test was over.

Q. These 17 patients that received a single treatment of three breaths did so while they were there was pulmonary artery catheter inserted into their heart taking measurements, right?

A. That's my understanding of the study design.

Q. So they weren't receiving treatment and walking around their daily routines, correct?

A. Not in this study, no.

Q. In the last part of paragraph

110, you state that: "Voswinckel did actually teach a treatment for pulmonary hypertension."

Do you see that?

A. Yes, I see that.

Q. And that was based on the conclusion that long-term treatment effects in Voswinckel were promising, correct?

A. Or very promising, yes, based in their statement that says exactly that.

Q. Only two patients in Voswinckel actually received non-acute treatment for pulmonary hypertension, correct?

A. In this particular study as described, yes.

Q. And Voswinckel is actually silent on the number of breaths or device that was used for those two patients, isn't it?

A. Well, I believe that Voswinckel tells us that they received the same three breath treatment four times a day.

Q. Can you quote me where it says that?

A. Well, what it says is that the two patients with idiopathic pulmonary

hypertension or PAH received compassionate treatment with four inhalations of TRE per day after the acute test, and when I refer back to what they define as a TRE inhalation, it's the use of the pulsed OptiNeb ultrasound nebulizer three breaths TRE solution 600 micrograms per mil.

Q. So is it an assumption that you are making that the two patients were treated with three breaths four times per day?

A. I am reading this as a POSA would read an abstract and anticipate that if they received a different treatment regimen, that that information would also be included in the abstract. Yet there's sufficient information in the abstract here for me to use their own controlled vocabulary and understand what the inhalation of treprostinil per day was in that compassionate use study.

Q. Would it make sense to treat the 17 acute patients who were catheterized with the same device that was being used to treat chronically the two patients that were treated for long-term?

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MR. MATHAS: Object to the form.

BY THE WITNESS:

A. Yeah, I don't understand the question.

BY MS. ASCARRUNZ:

Q. I will withdraw it.

Does Voswinckel identify the device that was used on the two compassionate use patients?

A. Well, again, in keeping with how the acute use inhalation is described with the use of the pulsed OptiNeb ultrasound nebulizer, that same inhalation is described or terminology is used for the compassionate use. So it is in keeping that those two patients used the pulsed OptiNeb ultrasound nebulizer.

Q. If I could direct your attention to paragraph 121, you agree that Voswinckel does not expressly state that the nebulizer generated a fixed amount per pulse, correct?

A. Yes, as stated in that paragraph.

Q. If you could go to paragraph

104, it's your opinion that Voswinckel discloses the delivery of three distinct pulses or breaths, correct?

A. That the Voswinckel describes that their administration of treprostinil came from a 600 microgram per mil solution using the pulsed OptiNeb ultrasound nebulizer, and the patients inhaled three breaths from that nebulizer.

Q. So I am referring to the first paragraph where you use the terminology: "Device in three distinct pulses (breaths)."

Do you see that?

A. I see that.

Q. Okay. Are you equating pulses with breaths?

A. Well, in the case of the pulsed OptiNeb ultrasound nebulizer, the pulses are associated with the output of the device which means that the time the user should be breathing in to receive the medication.

Q. How do you know that based on the disclosure in Voswinckel?

A. Again, Voswinckel tells me

that it's a pulsed OptiNeb ultrasound nebulizer. A POSA is well aware of what a pulsed ultrasound nebulizer is and the operating principles behind it and when one breathes and one is emitting a dose. So it's clear to a POSA from that description how that was being administered.

Q. And is it clear to a POSA based on simply the use of the terminology pulsed ultrasonic nebulizer that there is to be one breath for one pulse?

A. That's the traditional method that one would use a pulsed ultrasonic nebulizer.

Q. When you say traditional, what do you base that on?

A. Based on other nebulizers available, both ultrasound, jet, other technologies that were being evaluated at the time that if there was a -- a time of aerosol delivery and a time of -- a period of time where the aerosol wasn't being emitted from the mouthpiece, that the person was instructed to inhale in the aerosol being formed during the

time that the nebulizer was sending that aerosol out the mouthpiece, and some people have now started or were referring to that as a pulse of the aerosol.

Q. Okay. We will definitely talk a little more through some of that a little bit later.

Right now I want to turn to Ghofrani and your paragraph 85. In that paragraph you indicate that you understand that the June 2005 issue of Herz in which Ghofrani was published was made available in libraries and online by at least July of 2005.

Do you see that?

A. I see that.

Q. Is that in your expert opinion or are you relying on Dr. Bennett's expert assessment for that point?

A. Well, I both used Dr. Bennett's more familiar opinion regarding how library -- how fast libraries actually index and maybe hard copy available. I am aware that Herz is available online. Its 2005 year was available or is available to me

online, and my search told me that -- I don't remember the exact year, but it was several years before 2005 that that journal was available online. So almost immediately assessable whenever the publisher made those publications available relative to the print version.

Given that this is listed as the fourth volume of 2005, I would have to go back and look at what the fourth volume in date referred to in Herz, but I'm certainly willing to believe given -- just sitting here, I mean, I could refer to Dr. Bennett's information. I think he is more clear about this, but number four would probably strike me as it was probably April but -- which means it would certainly have been catalogued and in the library but July of 2005.

And if number four means something different as far as what month or series of dates it was published, it would be with -- this article would have been available probably within four to six weeks at the very longest and probably earlier than that in hard

copy in a library, and it would have been online again as soon as the hard copy was published or even before.

Q. Okay. The testimony that you just gave and your observations about the online availability of Herz were not detailed in either of your declarations, correct?

A. I didn't expressly describe how I went about looking at how to obtain the art that I used in my -- and referred to in my declaration. Yet there was no reason to anticipate that it was any different than any art -- other art that is normally obtained that I obtain and use. Databases and libraries and the dates on these are certainly with -- prior to the priority date that we are discussing for these two patents.

Q. Are you aware that Dr. Bennett admitted he was mistaken about the July 2005 date at his deposition last week?

MR. MATHAS: Object to the form.

BY THE WITNESS:

A. Not specifically aware of that, no.

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BY MS. ASCARRUNZ:

Q. Have you had any conversations with Dr. Bennett?

A. I have not.

Q. Were you aware of any of his deposition testimony from last week?

A. I think I understood that he had been deposed, but that's my level of awareness.

Q. And you did not review his deposition testimony from last week?

A. No.

Q. Let's look at paragraph 136. You begin paragraph 136 by stating quote: "Ghofrani further appears to describe" -- then in italics -- "the very same study as Voswinckel."

Do you see that?

A. I see that.

Q. But Voswinckel is not cited in Ghofrani, correct?

A. You mean -- are we talking about the abstract that we have been talking about labeled as Voswinckel?

Q. Yes, correct.

A. Let me double check, but my recollection is that it's -- the abstract is not in the citation list. There's an earlier Voswinckel reference, but the abstract in Circulation is not in the literature list in Ghofrani but, yeah.

Q. Now, what is your basis to conclude that it's the very same study?

A. Well, because the abstract or the information -- the Voswinckel information that's cited and that's number six, and number six is used as a reference in the section in Ghofrani about inhaled treprostinil.

My recollection is that that -- the European Heart Journal information publication is -- used a six-minute exposure from a nebulizer for the patients in that study, and there were a different number of patients in that study. So I know that in the -- when Ghofrani then goes on to describe in his first study 17 patients were treated and goes on to describe some other things about it, I know that it's not describing the work that

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was conducted under the citation number six which precedes that sentence.

Q. So the discussion in Ghofrani cites to a reference numbered six that you indicated you reviewed, correct?

A. Yeah, I have seen it, and again I'm pretty sure, but I would appreciate the opportunity to review it if we are going to continue to talk about it that that used a different dosing strategy compared to the Voswinckel abstract in Circulation.

(WHEREUPON, a certain document was marked Deposition Exhibit 1046, for identification, as of 4/4/18.)

BY MS. ASCARRUNZ:

Q. I have just handed you what's marked as Exhibit 1046 in both proceedings. Is this the Voswinckel reference that's cited in Ghofrani as reference number six?

A. Yes. I'm sorry, yes, it is.

Q. Okay. And this reference -- is it your testimony that Ghofrani's discussion

of initial trials in Giessen which cites to this document, in fact, should be read as citing to Voswinckel?

MR. MATHAS: Object to the form.

BY THE WITNESS:

A. Well, I understand that the -- I mean both I understand and I am looking at citation number six, and what citation number six from Ghofrani the Voswinckel European Heart Journal abstract doesn't describe the conditions that are being described in the -- in the portion of that paragraph where the one sentence starts "in this first study," and it ends with occurring. So bracketed between those two bracket sixes.

So a POSA would understand that it's been mistakenly cited and that sometimes happens, and so I wouldn't look to the information in the Europe Heart Journal abstract as being the study that's being described in that section of that paragraph.

Q. On which basis do you conclude that it's been mistakenly cited?

A. Well, again, it describes a

different set of dosing conditions and a different number of patients are the two quantitative obvious differences.

Q. Okay. What is the inconsistency of the different -- strike that.

What do you mean by different set of dosing conditions?

A. Well, in the European Heart Journal abstract, they are describing using an OptiNeb ultrasound nebulizer using different concentrations of treprostinil solution 16, 32, 48, and 64 micrograms per milliliter and provide some information about how many patients received each of those and the measurement time over which they looked at various of the experimental pulmonary hypertension outcome measures that they chose.

And just the dose strategy is very different than the dose strategy which in the section in Ghofrani that we are -- we are focused on talks about a 15 microgram inhalation and the ability to dose up to 90 micrograms, and neither of those absolute doses are even included in the description in the

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European Heart Journal abstract.

Q. Both references the Ghofrani and this 1046 exhibit include treatments with 15 micrograms per inhalation, correct?

MR. MATHAS: Object to the form.

BY MS. ASCARRUNZ:

Q. Actually, strike that.

Why do you say that the two dosing strategies are very different?

MR. MATHAS: Object to the form.

BY THE WITNESS:

A. Well, in the study being described in Ghofrani, they only mention a single dose that is being provided to the patient. So 15 micrograms per inhalation.

In the European Heart Journal abstract, they are looking at an escalating dose study. They increase the concentration of treprostinil and provide that as a nebulized solution for inhalation for a certain period to the patients in the study.

BY MS. ASCARRUNZ:

Q. Okay. So you testified that the Ghofrani reference talks about a single

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dose to patients of 15 micrograms per inhalation, correct?

A. That's how Ghofrani is describing it.

Q. Okay. So I think that we have established that the citation to reference six in Ghofrani may not be fully supported or consistent with the Voswinckel 1046 reference.

Is that fair?

MR. MATHAS: Object to the form.

BY THE WITNESS:

A. Well, I think there's other information that's in Ghofrani that cites six that uses the information from the European Heart Journal abstract, but the citation to six for the source of information about the 15 microgram per inhalation greater than 180 minutes up to 90 micrograms section of that paragraph, that information did not come from the abstract that was published in the European Heart Journal.

BY MS. ASCARRUNZ:

Q. Okay. So that information which includes, as you said, the 15 microgram

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per inhalation greater than 180 minutes up to 90 micrograms is not supported in Ghofrani by any citation, correct?

MR. MATHAS: Object to the form.

BY THE WITNESS:

A. I actually didn't look at all of the citations in Ghofrani, but it's my -- I -- based on dates and so forth, I think that Ghofrani intended on citing something else besides the European Heart Journal for that section, and there are descriptions of trials -- of these trials being conducted in Giessen that are several sentences before the area that we are starting, and since Ghofrani at the time was in Giessen based on the author list on this paper, he certainly had good knowledge of those trials, but he mistakenly cited the wrong abstract for a published form of that information.

BY MS. ASCARRUNZ:

Q. Okay. The 1046 Voswinckel reference used an ultrasound nebulizer in continuous mode producing a constant stream of aerosol for six minutes, correct?

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A. That's how a POSA would read those methods, yes.

Q. That is not pulsed, correct?

A. It doesn't indicate that they used it in a pulsed mode.

Q. What do you mean used it in a pulsed mode?

A. Well, the OptiNeb ultrasound nebulizer in some version of its history was a continuous -- it produced aerosol on a continuous basis, but how patients interacted with that to limit wasting of the nebulized aerosol and so forth could have been modified pretty easily.

So but I don't -- there's nothing in the abstract that makes me begin to think that anything else besides the typical operation of the OptiNeb ultrasound nebulizer as described that it didn't operate in continuous fashion for six minutes in this particular study.

Q. Do you agree with me that a pulse cannot last for six minutes?

A. No, I don't agree with that.

Q. Why not?

A. The definition of -- or I mean a pulse is however long the designer of that pulse period designs -- describes it to be.

Q. Okay. So let me clarify. Actually, let's come back to this. Okay.

Patton is another one of the references you discuss in your declaration, correct?

A. Yes, it is.

Q. And since, again, this is a little bit of a change in gears, I haven't kept track on how long we have been on this session, but I assume it's about it an hour.

Do you want to take a break now?

A. It depends. I mean, we are approaching noon. We can go for another 20, 30 minutes or so if that's a reasonable amount of time and then break for lunch, or we can take a break now, go for another hour, break for lunch. I am open to however you --

Q. So I can do both of those things. I think the person whose comfort

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matters the most here is you.

A. I am comfortable going for another 20 minutes or so but not much longer than that.

Q. Okay. Let's shoot for that then. Okay.

So I started to talk about Patton is one of the references you discuss in your declaration, correct?

A. Yes.

Q. And it's your opinion that Patton teaches strategies to deliver a pulsed dose precisely and efficiently, correct?

A. I take it that you must be reading something from a paragraph I have written. So if you could --

Q. Well, just speaking in the general abstract, is it your opinion that Patton teaches strategies to deliver a pulsed dose precisely and efficiently?

MR. MATHAS: Object to the form.

BY THE WITNESS:

A. Again, if I used those specific words, I'd appreciate being pointed to

what paragraph they are in. I have another paragraph open at the moment where I describe that a -- describes a nebulizer that generates a defined amount of medicament in a preselected amount of compressed air from the compressor.

BY MS. ASCARRUNZ:

Q. Okay. Let's look at the last paragraph of -- I mean, the last sentence of paragraph 105.

A. 105. Okay. Would you like to reask the question then?

Q. Yes. Is it your opinion that the Patton teaches strategies to deliver a pulsed dose precisely and efficiently?

A. Yes, it is.

Q. Could you point me to all of the evidence you provide in Patton that teaches anything at all about pulsed delivery?

MR. MATHAS: Object to the form.

BY THE WITNESS:

A. Well, Patton describes the ability to place a -- the dose of aerosol that's available for an individual to inhale from a device, and Patton provides the

opportunity for that activity to be repeated to -- as many times as necessary to receive the amount of drug that the patient is supposed to receive.

And Patton -- Patton's descriptions which, you know, I can go through here page by page if you would like talk in detail about the precision, the accuracy of the dose that's placed into the device, and the efficiency description is really always attributed to there isn't any aerosol produced that's lost to the atmosphere, that's lost to other non-device areas. So we are not losing any of the drug solution or dry powder in the case of Patton also to -- that could never, ever be administered to the patient.

That's what Patton's wording on efficiency really is, but back to pulsed dose, it is just a repetition of doses, and Patton describes being able to give or utilize the device in a manner where you would reload and reinhale as frequently as needed to get the number of doses that were intended, and on his microprocessor there's the ability to count the

number of doses that were placed into the chamber. There's a number of other things that in this describe being able to use this in essence in a pulsed fashion where pulse describes the repetition of dose availability.

Q. So is it your opinion that Patton provides a teaching about pulsed dose because it provides for a repetition of doses?

A. Well, Patton's device allows for a user to inhale a series, you know, or a specific aerosol containing a specific amount of drug is made available for inhalation. If a patient needs an integer based increase off of that amount, they are able to use the device in a -- and inhale, reactivate, place the aerosol, make it available for inhalation, and then reinhale. It's just a sequential availability of aerosol.

And during -- between the times that -- that that is happening then the time that the patient needs to then re -- to tell the inhaler that they want another amount aerosolized, there is a pause. There is no aerosol being formed, nor is there any aerosol

being lost out of the system, and that is -- that describes what many in the art describe as a pulse, a pulsed dose.

Q. You indicated that between the times that drug is made available for inhalation that there is a pause where there is no aerosol being formed.

How long is that pause?

A. In the Patton device?

Q. (No audible response.)

A. It is as long as the individual or whoever the operator is chooses that to be.

Q. Could it be a minute?

A. Again, there's no information provided in Patton about how long it actually takes to accomplish the aerosolization activity, but a POSA's knowledge in the area and certainly in the -- in some of the further work that also was reported by Patton, it doesn't take long.

It's not a -- that's not a limitation to this device. So one could assume that it only takes a few seconds to actually

form that aerosol and place it ready. So it could be less than a minute. It depends on the patient's interaction with the device and the instructions for use.

Q. If a patient using the Patton device inhales the drug that's made available for inhalation and then takes ten seconds to get the device ready to prepare the next bolus of inhalation, and once that's done takes the second dose of inhalation, is that using the device in a pulsed manner?

A. Well, it's receiving two separate doses or two separate amounts of the drug in this case in one -- what do I usually call that in -- well, anyway, two separate -- two separate amounts of the drug considered as a -- the amount to achieve the desired dose for that individual per -- per administration. So, yes, it could easily be considered two pulses.

Q. Patton does not discuss treating pulmonary hypertension, correct?

A. Patton's description is far broader than -- than the development of -- or the use of his invention for a specific disease

in the pulmonary airways. So I mean he doesn't limit any of the use to any particular disease in the claims in particular or even in most of the description he provides I think a couple of example diseases, but it's a broader use. It could be used for many treatments intended to be directed to the lungs.

Q. So there's no express discussion in Patton specifically of pulmonary hypertension, correct?

A. That's my recollection, yes.

Q. Is it your opinion that Patton teaches about accuracy of dosing?

A. Well, I think he certainly acknowledges that, and I am looking at paragraph with the line speaking to that at the moment that precision in dose delivery was a serious problem, and he was trying to address that. Whether he addressed precision in a manner that everybody would agree was accurate, I think there's less detail provided in the in Patton -- Patton written description.

Yet really what he is able to accomplish is reproducibility, and in the world