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

ELYSIUM HEALTH, INC., Petitioner,	
vs.	Case IPR2017-01795
TRUSTEES OF DARTMOUTH COLLEGE, Patent Owner.	

DEPOSITION of ZHAOHUI SUNNY ZHOU, Ph.D.
Thursday, August 2, 2018
9:00 a.m.
Foley Hoag, LLP
Boston, Massachusetts

Reported By:
Michael D. O'Connor, RMR, CRR, CRC

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Thursday, August 2, 2018
9:00 a.m.

DEPOSITION of ZHAOHUI SUNNY ZHOU, Ph.D., held at Foley Hoag, LLP, 155 Seaport Boulevard, Seaport West, Boston, Massachusetts, pursuant to notice, before Michael D. O'Connor, Registered Merit Reporter, Certified Realtime Reporter, Certified Realtime Captioner, and Notary Public in and for the Commonwealth of Massachusetts.

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I N D E X

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E X H I B I T S

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P R O C E E D I N G S
ZHAOHUI SUNNY ZHOU, Ph.D.
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having been satisfactorily identified by the production of his driver's license, and duly sworn by the Notary Public, was examined and testified as follows:

EXAMINATION
BY MR. YOUNKIN:

Q. Can you please state your name for the record.

A. Yes. My first name is Zhaohui, Z-h-a-o-h-u-i, middle name Sunny, S-u-n-n-y, last name Zhou, Z-h-o-u.

Q. How do you pronounce your last name?

A. Pronounced just like J-o-e. Zhou.

Q. Dr. Zhou, you're here as an expert on behalf of Dartmouth, correct?

A. That's right.

Q. And you prepared a declaration in these proceedings?

A. Yes, I did.

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Q. Okay. I'm going to hand it to you so you have it in front of you. I've handed you what has been marked previously as -- well, I will just call it Exhibit 2002. Do you see that on the bottom right-hand corner?

A. Yes, I do.

Q. Is this your declaration?

A. Yes.

Q. Okay. I'm going to hand you another declaration that was previously submitted in this case, the declaration of Joe Bauer. That's Exhibit 1002.

Do you have that document in front of you?

A. Yes, I do.

Q. You read Dr. Bauer's declaration before you drafted yours; is that correct?

A. Yes, I did read his declaration before mine.

Q. If you could turn to Page 4 of his declaration, please. So that's Exhibit 1002 at Page 4.

A. Page 4 of Dr. Bauer's declaration?

Q. Right.

A. Yes.

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Q. Do you see there that there is a bullet point list of articles that are discussed in Dr. Bauer's declaration?

A. Yes.

Q. Do you see that?

A. I see that list.

Q. And that list carries on to Page 5 and even on to Page 6, correct?

A. That's right.

Q. Okay. Did you read all of these articles that are cited in Dr. Bauer's declaration?

A. I did read all of them, yes.

Q. Okay. Had you read any of those articles before you began to work on this case?

A. I cannot recall whether I read some articles, because I have interest in NAD+ myself. So I know the work of this pathway, but I cannot recall whether I read some of the articles before. I might have, but I cannot recall.

Q. Okay. Let me ask you some specific questions. Firstly, when did you begin working on this case, do you recall?

A. If I recall, it's early this year.

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Q. Early in 2018?

A. 2018. March perhaps.

Q. Okay. And so before you began working on the case, can you recall reading any of the articles written by Joseph Goldberger?

A. No, I cannot recall I read any paper by him.

Q. Okay. Can you recall reading any papers by Charles Brenner before you began working on this case?

A. That's a paper. His work, I was aware of. So I cannot recall whether I read the exact paper or not.

Q. You can't remember whether you actually read the Brenner paper before you began work on the case?

A. I can't recall whether I read it or not, but I was aware of his work.

Q. Okay. How were you aware of his work?

A. Because I told you, I'm interested invite minutes in general, and this new pathway as it relates to NAD+, and I have an interest in NAD+ chemistry, chemistry, biology myself.

Q. Have you published any articles on

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nicotinamide riboside?
A. No, I have not published any paper on NR.
Q. Have you published any articles on NAD biosynthesis?
A. I studied several enzymes using NAD as a co-factor or substrate. I studied vitamin metabolism for many years and many of the pathways involved in NAD+.
Q. Okay. But have you published any articles on the NAD+ pathway?
A. Yes. I published the papers that involved that enzyme, also the enzyme using NAD+.
Q. Okay.
A. I did publish papers on that.
Q. Okay. Have you published any articles on any NAD+ precursors?
A. I cannot recall exactly whether in the paper I published mentioned that or not.
Q. Have you received any grants to study NAD biosynthesis?
A. I have received a grant to study a pathway involved in NAD, because metabolic cycles involves many enzymes and co-factors,

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vitamins. Some of these steps involve NAD+.
Q. What particular pathway do you study?
A. So the pathway studies are two pathways. One is transmethylation pathway, and the other one is transsulfuration pathway. It's a sulfur amino acid metabolic pathway. Many of the steps in these two pathways involve NAD.
Q. Okay. But you haven't received a grant to study the synthesis of NAD from an NAD precursor, correct?
A. So to clarify, your question is, I studied two pathways, transmethylation and transsulfuration pathways. So NAD is part of this pathway, yes.
Q. Have you attended any conferences that focus on NAD?
A. No, I haven't attended any conferences that focus on NAD.
Q. Have you given any lectures on NAD precursors?
A. Yes.
Q. Okay. Which precursors?
A. The whole pathway, nicotinamide

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riboside, nicotinic acid included in NR and NAD+, NADH and NADP. That's a different form of NAD+.
Q. What was the context of these lectures? Were they conferences or classes?
A. Lectures to my students why as it relates to their biosynthesis. The other one is their biological function, particularly in posttranslational modification of proteins involve NAD+.
Q. You understand that we're here today to discuss the '086 patent, correct?
A. '086 patent, yes.
Q. Why don't I hand it to you so you have it in front of you. This is previously marked as Exhibit 1001.
Were you aware of the '086 patent before you began work on this case?
A. No, I wasn't aware of this specific patent.
Q. Have you attended any talks by Charles Brenner before you began to work on this case?
A. Not that I can recall.
Q. Have you spoken with Dr. Brenner?

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A. No.
Q. Do you know that the '086 patent has been licensed to a company called ChromaDex?
MR. ABRAMIC: Objection. Scope.
A. In the context I learned this after I was involved in the case.
Q. After you became involved in the case you learned that the '086 patent has been licensed to ChromaDex?
A. I can't remember the name, but that sounds right.
Q. So you learned it had been licensed to a company?
A. Yes.
Q. Do you have any relationship with the company ChromaDex?
A. Not that I can think about.
Q. Dr. Zhou, what does the word "comprising" mean in patent law?
A. Comprising?
Q. Yes. The word "comprising."
A. In patent law?
Q. Yes. When the word "comprising" is used in a claim, what does that mean?

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MR. ABRAMIC: Objection to form.
A. Which specific claim are you talking about?
Q. Do you understand the word "comprising" to have a special meaning in patent law?
A. I understand that the special meaning goes with the context of the word.
Q. What do you mean you understand the special meaning goes with the context of the word?
A. For example, phrases used. This is a very common word, "comprising."
Q. Okay. So you're not aware that the word "comprising" is a special term of art in patent law?
A. I was instructed to study this patent and the claims in this patent, and within this context, I focused my understanding of "comprising" in this patent in the claims. I haven't studied all the comprising in all the patents, being all the context.
Q. Were you given any information about the meaning of the word "comprising" under U.S. patent law?

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A. No, not from this case. I have myself involved filing patents myself. So during those process, we talked about the word, and I was an expert witness in previous case. So the word "comprising" comes up in those cases as well.
So within those contexts of those patents, I was explained the meaning of "comprising" in those patents and my own patent filing.
Q. Based on your own prior experience, then, whether as an inventor on a patent application or a prior expert witness, did you come to understand that the word "comprising" has a special meaning in patent law?
A. Yes. If you're sitting here or in general, a patent in a broad sense, it means to include something, yes.
Q. It means to include something?
A. Yes.
Q. And is that the definition that you applied when you were reviewing the '086 patent?
A. That's a different issue, because

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the patent comprising is part of that claim, part of that phrase. So I interpret the meaning of "comprising" in that context, the claim of the patent.
Q. Okay. So let ask it this way. Am I correct that you understood when you began on this case that the word "comprising" in patent law means including; is that right?
MR. ABRAMIC: Objection to form.
A. In a very broad sense, without any context, that's my -- that's my interpretation I can use, yes.
Q. Is the word "comprising" defined in the '086 patent? Is there a definition provided of that word?
A. Not that I can recall.
Q. Did you depart from your understanding that "comprising" means including, did you depart from that concept when you were interpreting the '086 patent?
MR. ABRAMIC: Objection to the characterization.
A. No, not from the general sense. But because of the claim I look at the context, that's consistent with my general understanding

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of the word "comprising" in patent law.
Q. Assume that a patent claim is a pharmaceutical composition comprising calcium sulfate. Okay. What would you understand that claim to mean?
A. Can you repeat that?
Q. Certainly. So assume that a claim is directed to a pharmaceutical composition comprising of calcium sulfate. How would you interpret that claim?
A. There's no other -- so to answer your question, there's no other limitation for that phrase?
Q. That's the entirety of the claim, those words.
A. Okay.
Q. Pharmaceutical composition comprising calcium sulfate?
MR. ABRAMIC: And you're just giving him the claim?
MR. YOUNKIN: I'm giving him the claim.
A. And there's no other limitation on that claim?
Q. That's the entirety of the claim,

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yes.
MR. ABRAMIC: Objecting to the hypothetical.
Q. What does that claim mean?
A. So sitting here, you asked me to analyze right away, that means the pharmaceutical composition is a -- pharmaceutical means has a therapeutic or preventative effect. Composition means chemical compound that has active ingredient or active agent. In this case it's calcium -- did you say sulfate or chloride?
Q. I said calcium sulfate.
A. Yes.
Q. So you would interpret that claim to mean that it's to require the presence of calcium sulfate as an active ingredient; is that right?
A. So repeat. Sorry.
Q. I want to make sure that I understand your interpretation of the hypothetical claim that I've given you.
Am I correct that you would interpret that claim to mean that -- sorry.
Am I correct that you would

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require -- try that again.
Am I correct that you would interpret that claim to require that calcium sulfate be an active ingredient?
MR. ABRAMIC: Objection to the hypothetical.
A. So the claim says is a composition, is a compound or chemical, has therapeutic or preventative effect. That's what pharmaceutical means. And has active ingredient and active ingredient is calcium sulfate.
Q. Let me give you a different hypothetical claim. Imagine that the claim says a pharmaceutical composition comprising tryptophan. How would you interpret that claim?
MR. ABRAMIC: Again, you're just giving him claim, no patent specification?
MR. YOUNKIN: Yeah. I would appreciate it if we could just keep the objections to one word and the grounds for the objection.
MR. ABRAMIC: Trying to make the

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question clear.
MR. YOUNKIN: I'm comfortable with the clarity of the question.
Q. Let's try it again. So here's the hypothetical claim. A pharmaceutical composition comprising tryptophan. How would you interpret that claim?
A. Again, without any limitation, just sitting here, that would be the same interpretation as I had with the calcium sulfate.
Q. Okay. Meaning the tryptophan is the active ingredient, correct?
A. Active ingredient for some preventative and therapeutic effects.
Q. Okay. I'm going to give you a third hypothetical.
A pharmaceutical composition comprising calcium sulfate and tryptophan. How would you interpret that claim?
MR. ABRAMIC: Same objection.
A. Without any limitation?
Q. Those are all of the words of the claim, a pharmaceutical composition comprising calcium sulfate and tryptophan.

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A. First, I haven't thought about this with two components in the past. Also, all the cases I've been involved is only a single active ingredient. So I'm not sure I can exactly answer your question when I have two components.
Q. Okay.
A. Without any limitation from the patent.
Q. What is an active ingredient?
A. Active ingredient is a compound or chemical that conferred the activity observed for the composition of the drug.
Q. What do you mean when you say "the activity observed"?
A. Observed? Activity, basically means activity. You have to observe activity to see whether it's active or not.
Q. What sort of activity does an ingredient have to have in order for it to be considered an active ingredient?
MR. ABRAMIC: Objection to form.
A. So that -- so again, activity with no context. Are we talking about what kind of activity? In patent law, a vacuum activity or

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are we talking about pharmaceutical activity here? Sorry, I'm not clear about your question.

Q. Okay. Let's turn to Paragraph 31 of your declaration, which is on Page 10.

A. My declaration?

Q. Yes.

A. Paragraph 31?

Q. Yes. So the first sentence of Paragraph 31 of your declaration says, "A pharmaceutical composition, at its most basic level, contains an active ingredient," right?

A. In Paragraph 31, first sentence, yes.

Q. Okay. What does the word "active ingredient" mean as you used it in Paragraph 31?

MR. ABRAMIC: Asked and answered.

A. "Active ingredient" in the pharmaceutical composition, using the whole sentence, means it exhibits or confers certain therapeutic or preventative effects.

Q. Does the '086 patent show that NR has therapeutic or preventative effects?

MR. ABRAMIC: Objection to form.

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A. In the patent of '086, whether it shows --

Q. Yes. Does the '086 patent show that NR exhibits or confers certain therapeutic or preventative effects?

MR. ABRAMIC: Objection to form. Vague.

A. As I sit here, I cannot recall specific whether they mention a specific therapeutic effect. The patent is to have a claim of NR used as a pharmaceutical composition. So I cannot recall whether they specifically mention any pharmaceutical effect of NR in the patent.

Q. But you interpret the claim to require a pharmaceutical composition to have a therapeutic or preventative effect, correct?

MR. ABRAMIC: Objection to form.

A. Can you repeat the question?

Q. Sure. Is it your understanding that the claims of the '086 patent require the claimed pharmaceutical composition to have a therapeutic or preventative effect?

A. Sorry. Can you clarify the question?

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Q. Sure. In your declaration you opine on the meaning of Claim 1, correct?

A. Yes, I did opine on Claim 1 in the patent.

Q. Okay. But you opined specifically on what Claim 1 means, correct?

A. Yes. I was asked to do that.

Q. How a person of ordinary skill in the art would understand Claim 1, right?

A. Yes, that's correct.

Q. Okay. So is it your opinion that a person of ordinary skill in the art would understand Claim 1 to require that the pharmaceutical composition of Claim 1 brings about a therapeutic or preventative effect?

MR. ABRAMIC: Objection to form.

A. My understanding of patent law, in general, is you can claim something may be with or without its showing the intended use of a composition.

Q. Okay.

A. That's where my confusion comes from when you say "required."

Q. Okay. So let's discuss this a little bit further. So is it your opinion that

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the part of the claim that is -- the pharmaceutical -- the reason you're saying that an active ingredient has to have a therapeutic or preventative effect is because the claim is directed to a pharmaceutical composition; is that right?

MR. ABRAMIC: Objection to the characterization and the form of the question.

Q. Is that true?

A. Sorry, can you repeat the question. I was interrupted by counsel.

Q. The reason that you believe that the active ingredient -- sorry, let me rephrase that.

The reason that you believe that Claim 1 requires a -- well, let me try that yet one more time.

You're interpreting the words "pharmaceutical composition" to connote a substance that has a therapeutic or preventative effect, correct?

MR. ABRAMIC: Objection to the characterization.

A. So my understanding of patent law

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is you can claim -- so the Claim 1 said nicotinamide riboside, NR, in Claim 1 is the active ingredient for that pharmaceutical composition. That's what Claim 1 says.

Q. Okay. So how do you know whether or not NR is an active ingredient in a pharmaceutical composition?

A. How do I know it's an active ingredient?

Q. Yes.

A. So this experimentally someone can test out, because -- related to this patent, Claim 1 does not specify any therapeutic area or indication. But in the patent itself, it talks about different potential indications, different disease. So scientists study that with or without NR, for example, and see whether the fact, you know, are observed or not and that the person will establish whether NR is responsible to the observed activity.

Q. So in order to determine whether or not NR in a pill, for example, is an active ingredient, you would need to establish that the NR in the pill does what?

MR. ABRAMIC: Objection to the

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form and scope.

Q. In other words, imagine this. Imagine I came to you and said, Dr. Zhou, here is a pill that has NR in it. I would like you to tell me whether or not the NR is an active ingredient. How would you answer that question?

MR. ABRAMIC: Same objection.

A. So to answer that question, we need to know what we want to find out, whether NR is active for what? And the "what" part is what we have to define first, active for treating disease, to prevent disease?

So we need to know what the ultimate outcome of what we want to measure in terms of activity.

Q. And the amount of NR that would be needed to bring about a therapeutic effect would vary with whatever it is that you're treating; is that correct?

MR. ABRAMIC: Objection to form and scope.

A. That's not something I was asked to opine on.

Q. Do you believe that to be true?

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MR. ABRAMIC: Same objection.

A. If you ask me to answer that question, can you repeat it, because I wasn't asked to opine on that.

Q. Okay. Let me ask you a different question.

Is it your opinion that the pharmaceutical composition requires that there be an effective amount of NR in the composition?

MR. ABRAMIC: Objection. Same objection.

A. So first, I wasn't asked to opine on that.

Q. Okay. But I'm asking you today. Is that your understanding of Claim 1, that it requires that there be an amount that can be deemed an effective amount, meaning that it causes a certain effect with respect to a disease state?

MR. ABRAMIC: Objection. Scope.

A. When you ask me that question, I think that's not part of Claim 1 at all. Sorry, I said this very bluntly. I think maybe you confused the concept of the patent claim

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and the ultimate drug. That's maybe where the confusion comes from.

Q. Okay. But you said that Claim 1 requires the NR to be the active ingredient in the pharmaceutical composition, right?

A. If a composition, pharmaceutical composition is active, and then in that case NR is the active ingredient.

Q. And in order to know whether or not the NR is active, you first need to establish what activity you're trying to bring about; is that right?

MR. ABRAMIC: Objection. Asked and answered.

A. So, yes, we talked about this before, when we talk about specific therapeutic index or therapeutic area, therapeutic activity, then one has to do this experimental testing to show, in that particular case, that particular indication, how much activity NR exhibits.

Q. In your opinion, Claim 1 requires that NR be present as an active ingredient, correct?

MR. ABRAMIC: Asked and answered.

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A. So again, Claim 1 is about a composition, and the composition has therapeutic or preventative effect, and NR is the active ingredient.

Q. Does the NR need to be in an amount sufficient to effectively bring about that therapeutic or preventative effect?

MR. ABRAMIC: Objection. Asked and answered. Scope.

A. As I said, that's not part of Claim 1. And the patent did describe the process to establish maybe the amount for each individual indication or disease -- amount required to treat certain disease or indication.

Q. But if NR is the active ingredient in a pharmaceutical composition that brings about a therapeutic effect, isn't it the case that the amount of the NR in that composition is sufficient to bring about that therapeutic effect?

I'm not understanding how those two things can't be true.

MR. ABRAMIC: Same objection.

A. So my understanding of patent law

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is you can have a claim, and those limitations, those are for the limitation of a claim, and very common myself and other people see the claim is this claim like Claim 1, it just claims the entity, the chemical entity itself, without specifying the dose or amount in the pill as you were discussing.

Q. But your interpretation of active ingredient means that the composition actually has a function, right? It brings about an effect?

A. Yes. So a pharmaceutical composition -- active ingredient must bring some effect. The active ingredient must have an effect, otherwise it won't be called active ingredient.

Q. Right. So there must be enough active ingredient in the pharmaceutical composition in order to bring about the effect, correct?

MR. ABRAMIC: Objection. Asked and answered. Scope.

A. Again, I think where maybe we're maybe the drug development concept here and the patent mixed together. So my understanding --

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I'm sorry to say it that way.

My understanding here, we're talking about a patent case. In a patent case they talk about a chemical entity, a molecule in some sense. It's a concept, that structure, one would develop the drug, and each drug is approved by the FDA. It requires dosing amount in the pill for a certain disease.

By the way, here we're talking about patent is my understanding I was asked to opine on, is the chemical entity active ingredient, which in this case is NR.

So the reason I couldn't answer your question is the dosing is related to a specific drug, in my view, for drug development. That's related to the patent, but not the patent Claim 1 about, in my opinion.

Q. Do you know how much NR must be present in the composition for the NR to be an active ingredient?

MR. ABRAMIC: Objection. Asked and answered.

A. I think we talked about this before. As a drug, not in a patent case, but in a drug development case, the amount of NR

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required to treat a certain disease or prevent certain conditions may vary, and that needs to be found out by experimental approach.

Again, in my view, that's not part of Claim 1.

Q. I want to return to a hypothetical question I asked before, because I don't think the record is clear on this.

If I came to you with a pill, and I said I'm trying to figure out whether or not this pill falls within the scope of Claim 1, whether it's covered by Claim 1 or not, what sort of experiments would you do to answer that question? How would you tell?

MR. ABRAMIC: Objection to form.

A. Whether a pill is covered in Claim 1 or not?

Q. Yes.

A. Again, I'm not one to ask to opine on, I guess it's called infringement or whatever, right? So I'm not asked to do that.

Q. Okay. Well, imagine the pill is in the prior art, then. Okay? And I say, I found this prior art pill, and I'm trying to figure out whether or not this pill anticipates

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Claim 1. Okay? Here's the pill. Can you help me figure that out? What would you do?

A. That's an interesting question. So what I -- first, I would fully understand Claim 1. Then to understand the prior art, I need to see whether NR is present in the pill, whether it is available, and whether conferred activity people reported or observed.

Q. And what sort of activity would need to be reported or observed for you to feel that the pill could be covered by Claim 1?

A. That's not for me to decide activity. It's what they want to claim or report the activity. Then I need to show evidence whether the experimental procedure shows NR, without NR. There are many, many complicated experiments one has to conduct to see, for example, whether NR, in the absence of NR, whether the same effect is observed or not. It's, you know, hundreds and thousands of experiments one has to conduct, and there's always caveats how to interpret the data.

But one experiment I think one must do is to remove NR from that pill, and they have everything else in that pill, and

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test it, and see whether the same activity is still being observed and whether it's the same degree of activity.

That's, at least, I think scientifically that's a requirement to establish whether that pill has the activity of NR.

MR. YOUNKIN: Why don't we take a five-minute break.

(Recess taken at 9:40 a.m. and reconvening at 9:53 a.m.)

BY MR. YOUNKIN:

Q. Dr. Zhou, I'd like to ask you a few more hypotheticals.

A. Sure.

Q. Okay. Imagine that I come to you with a pill that has ten milligrams of NR in it. Okay? And the question is, does this pill anticipate Claim 1? Okay?

You run some experiments and determine that my ten milligram pill does not have any kind of therapeutic or preventative effect. Okay? You would conclude, am I right, that the pill does not anticipate Claim 1?

MR. ABRAMIC: Objection to the

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hypothetical.

A. Since it's a hypothetical question, I want to make sure I understand the question first. So you're saying that you would -- there's a pill with a certain amount of NR in it?

Q. Ten milligrams.

A. Ten milligrams. And it did not show any effect -- did or did not show any effect?

Q. Did not. Your testing established that there is no therapeutic or preventative effect brought on by taking this pill.

A. So this is a very broad question. I think I probably cannot answer that question, because therapeutic effect is not just one term. Therapeutic effect has many, many indications.

Q. But why can't you answer the question?

A. Because when you say therapeutic effect, there's no generic term for therapeutic effect. Therapeutic effect, there's always some specific indication of disease. So I cannot answer that question, even hypothetical.

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Q. I want you to assume as part of the hypothetical that you concluded that there is no therapeutic or preventative effect.

A. As I said, the scientific rationale won't allow me to conclude that way.

Q. So you're saying you could never reach the conclusion that a pill does not have an active -- that a pill does not bring about a therapeutic or preventative effect?

MR. ABRAMIC: Objection to form. Scope.

A. It's not whether I cannot or can. The question, the term "therapeutic effect" is used too broadly or too narrowly in this case. I'm not sure whether it's broadly or narrowly.

So the hypothetical question is not well defined, the question to me.

Q. Well, you used the phrase "therapeutic or preventative effect" in your testimony today, right?

A. Yes.

Q. And what do you mean by that?

A. Again --

MR. ABRAMIC: Objection. Asked and answered.

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A. Again, this is a general term, and the term "therapeutic effect" is for a certain preventative effect or therapeutic effect. But those effects are shown by specific indication or disease.

Q. Let me try to add a little more detail to the hypothetical.

Let's say that I give you my ten milligram of NR pill, and I say the question is whether or not this pill is an effective treatment of cancer. Okay? And you run your tests and conclude that the ten milligram pill has no effect on cancer. Okay?

Would you conclude that the pill does not have an active ingredient that is effective to treat cancer?

MR. ABRAMIC: Objection to form.

A. Again, I know this is a hypothetical question you asked me. You said that already. I wasn't asked to opine on that.

So sitting here, to think about your question, ten milligrams of a pill has ten milligrams of NR in it, is shown not effective treating cancer? Is that the hypothetical?

Q. Correct.

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A. Okay. And the question is whether NR is active pharmaceutical composition?

Q. The question is whether or not that ten milligram pill is covered by Claim 1?

MR. ABRAMIC: Same objection.

A. Again, I think -- again, I was not asked to opine on that. Sitting here, my feeling is maybe the question confuses the concept of patent claim with drug development.

Q. Okay. Let me be clear. I'm only interested in the patent claims. I'm not interested in drug development.

A. Right.

Q. So the only question that I have here today is whether or not this hypothetical pill that I'm talking about would or would not be covered by the claim under patent law? It's not a drug development question.

Do you understand the question?

A. I think. Repeat the question one more time.

Q. So this is our ten milligram -- our pill with ten milligrams of NR. You have concluded that the ten milligram pill is not effective in treating cancer. Okay?

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And the question is whether or not the ten milligram pill falls within the scope of Claim 1 or not?

Can you answer that question?

MR. ABRAMIC: Objection to form.

A. What do you mean "falls within the scope of Claim 1"?

Q. It means that it is a pharmaceutical composition comprising nicotinamide riboside as claimed in Claim 1.

A. The question said NR was not active treating cancer?

Q. Correct.

A. I'm also not clear about your question cover in the scope?

Q. Okay. You were asked to opine whether or not the prior art anticipates Claim 1, correct?

A. Right.

Q. And you understand what it means for a prior art reference to anticipate Claim 1, correct?

A. Right. Yes, I understand.

Q. Okay. So imagine that my pill is a piece of prior art. It was something that

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was sold ten years ago. Okay? Or 20 years ago. And that pill has been shown to be not effective in treating cancer. Okay?

So now my question is, does the pill anticipate Claim 1?

MR. ABRAMIC: Objection to the hypothetical.

A. So again, for that hypothetical question, sitting here, because the pill showed no activity, and the claim has NR as active ingredient. So this is a hypothetical case that did not describe elements of the claim.

Q. Now, what if the prior art showed that two of these pills, so 20 milligrams, was effective in treating cancer. Okay?

So would the two pills together anticipate Claim 1?

MR. ABRAMIC: Objection. Scope. Hypothetical.

A. Two pills together?

Q. Right. So we began with a ten milligram pill, and now I'm saying that what patients were taking in the prior art were two of those pills, 20 milligrams, and that when they took 20 milligrams, it was shown to be

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effective in treating cancer.
In that case, would the two ten milligram pills together anticipate Claim 1?
MR. ABRAMIC: Same objections.
A. Again, so it's a hypothetical question. And sitting here thinking about it, I think the issue here is not dosing. It's whether -- because Claim 1, there's no limitation of amount. It's the fact it's a chemical entity, which is NR, is active for some therapeutic indication. In this case, you already limit that to cancer treatment, without other details of the treatment regime.
So regardless of the dosing, if the chemical entity has an effect, sitting here now, I may consider that falls to the described element in Claim 1.
Q. So you would think that the taking of two ten milligram doses of NR would anticipate Claim 1 --
MR. ABRAMIC: Objection.
Q. -- under that hypothetical?
MR. ABRAMIC: Objection to the form and characterization.
A. So again, the question here is not

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about the dosing. In my view, it's a certain dose, certain dose, shows an effect of NR in treating cancer. That's a relevant effect.
Q. Do you have an opinion about whether or not the 20 milligram dose would anticipate Claim 1 under the hypothetical that I've given you?
MR. ABRAMIC: Same objections.
A. Again, it's not a dosing part. It's the fact that -- Claim 1 is nothing about dosing. Claim 1 is about whether this chemical entity, a certain dose, of course it's implied, that a certain dose has a certain effect.
Q. And if it was shown that the chemical entity had an effect at a dose of 20 milligrams in the prior art, that would anticipate Claim 1, right?
MR. ABRAMIC: Same objections.
A. Again, with all of these caveats, this compound is available, it's a responsible tool to cancer treatment and it's not other things. Sitting here, without -- I didn't have time to think through that, I would say it feels like it, the fact that NR at a certain dose has a therapeutic effect for the described

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elements of Claim 1.
Q. What is NR effective at treating or preventing?
A. Say that again.
Q. What is NR effective at treating or preventing?
A. Sorry, I didn't get your question?
Q. What can nicotinamide riboside treat or prevent?
A. Again, that's not what I was asked to opine on.
Q. Do you know the answer to that question?
A. So the patent describes -- some specification of the patent describes certain diseases that may be treated by NR, but that's not part of the patent claims.
Q. Does the patent claim show that the diseases that are mentioned in the specification can, in fact, be treated with NR?
MR. ABRAMIC: Objection to form.
A. I know we talked about this before. My understanding of patent law is, you can claim a chemical entity with the idea it may reach certain disease or indications, and

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then whether they can treat and what dosing, those are figured out later on, and can be as a source for the limitation. And again, that goes into the drug development process, not a patent.
Q. I'm not asking you about your understanding of patent law. I'm asking you about your interpretation of the patent itself, the document.
A. Okay.
Q. Does the patent, the '086 patent, show that the diseases that are mentioned in the specification can, in fact, be treated with NR? Do you think that the specification shows that?
MR. ABRAMIC: Objection. Form. Vague.
A. I cannot recall exactly whether NR can treat any disease, just mentioning the patent.
Q. You don't remember whether or not there were any experiments showing that NR does or does not treat cancer or some other disease, you don't remember whether that was in the specification?

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A. I don't remember specifically whether the disease treatment was shown in the patent. I do remember it mentioned certain disease potentially can be treated by NR. They also mention a general process of how to do that, for example, by varying amount and experimenting with the dosing, things like that.

Q. Okay. Your declaration cites dictionary definitions of the term "pharmaceutical," right?

A. Yes, it did.

Q. Let's look at Paragraph 30, for example, of your declaration.

A. Paragraph 30?

Q. Yes. So in that paragraph, you cite to the McGraw-Hill Dictionary of Scientific and Technical Terms, correct?

A. Yes.

Q. And you cite a definition that defines pharmaceutical as "'a chemical produced industrially (medicinal drug), which is useful in preventive or therapeutic treatment of a physical, mental, or behavioral condition'."

Do you see that?

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A. Yes.

Q. Would you agree with me the '086 patent does not disclose any chemicals that are produced industrially?

MR. ABRAMIC: Objection to form.

Do you mean the entire patent?

MR. YOUNKIN: Yes. I mean the entire patent.

A. What do you mean "industrially"?

Q. Well, you're the one who cited this definition. So what did you understand this to mean?

A. In fact, I tried to understand the word "industrially," and looked it up in the dictionary myself. My understanding of "industrially" is to opposite of recreationally. It means there's a purpose, and to me it doesn't mean to me to produce tons and tons of large, larger scale. It means it's produced with a purpose for utility.

Q. Okay. Is the McGraw-Hill Dictionary of Scientific and Technical Terms, is that something you consult in your research?

A. I do look up scientific terms among different dictionaries, and this is

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probably one of the dictionaries I come across.

Q. Do you have this dictionary in your office, for example?

A. I don't have a hard copy anymore. It's all an online.

Q. But this is a dictionary you can recall consulting this particular dictionary in your work?

A. This comes up when I searched online, I Google, we all are using that very often, and this is one of the results that come up. This is the dictionary that's more scientific than just layman's dictionary, and I thought this is a good definition in this context.

Q. But the actual dictionary definition was provided to you by Dartmouth's lawyers, right?

A. No. We talk about this when I came up with this one myself as well. Plus I search lots of dictionaries myself, and the attorneys ask me to come up with a definition during this process, that this is important, and this is one of the dictionaries, several of the ones, that I used.

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Q. Let me hand you a copy of the dictionary that you provided with your report. It's Exhibit 2004. You can see from the front page that this document is from the Steptoe & Johnson LLP library, right?

A. Right. For the lawsuit, it was still based on paper, and we needed to find the paper form, such as the Remmington compendium of pharmacy. We cannot just do a screen shot. We needed a paper form, and they produced it. It seems they have a hard copy of this dictionary and they made a copy of it to be included in my declaration.

Q. Do you dispute nicotinamide riboside is present in milk?

A. Which milk?

Q. Let me just ask you generally. If I say to you, do you agree or disagree with this statement; milk is a source of NR.

MR. ABRAMIC: Objection. Vague.

Q. Is that true or false?

MR. ABRAMIC: Objection. Vague.

A. So in science, we always need to look at the conditions. So what I would say, milk, in general, as in general, milk, may or

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may not contain NR.
There are cases that show certain milk contains NR. But other milk, sample, we call that, individual sample, may not contain NR.
Q. Can you tell me the name of any journal article that concluded that milk does not contain NR?
MR. ABRAMIC: Objection to form.
A. No, I cannot recall any article saying that.
Q. Okay.
A. But I can also not find any article established that exhaustively tests all the milk samples.
Q. Okay. So there's no article that's tested every single milk sample that's ever been produced in the world, ever, right?
A. Right.
Q. And because of that, you believe that you cannot conclude that NR is in milk?
MR. ABRAMIC: Objection to form.
A. As I said, NR may or may not be in certain milk samples.
Q. What is the basis for your opinion

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that NR may not be in milk samples?
A. I think I described it in my declaration, because NR can be degraded by many pathways. The known pathway is by bacterial and other microbes, such as fungi, are either a part of the milk or be contaminated with milk. And the literature article showed that such bacteria exists and such pathways exist.
Q. But every single one of those articles also shows that despite some degradation, NR is present in the milk samples that were tested, right?
MR. ABRAMIC: Objection to form.
A. Again, that was only a few, very few, limited, papers talk about NR content in milk.
Q. But in every single one of those papers, every single milk sample that was tested shows the presence of NR, correct?
MR. ABRAMIC: Objection. Vague.
A. Only one I could find, no more than ten papers, and all recent papers.
Q. But is the answer to that question yes? Let me ask it again, because this is important and I want it to be clear.

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In every single paper that you have read that studies the presence of NR in milk, the researchers concluded that milk contained NR, correct?
MR. ABRAMIC: Objection. Vague.
A. Yes. In the paper I read, which are limited in number, where they measure NR content in milk, and milk NR was present, yes.
Q. I'd like to direct your attention to the Trammell 1 article, and I'll give you a copy of it. It's Exhibit 1007.
A. Thank you.
Q. You read this paper in connection with your work on this case; is that right?
A. Yes, I did.
Q. Okay. This paper was coauthored by Charles Brenner, correct?
A. I see that, yes.
Q. And he is the sole inventor on the '086 patent, right?
A. I know he is -- yes, he's a sole inventor on the patent.
Q. I'd like to direct your attention to the paragraph that bridges the first and second pages of the paper.

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A. The first and second page?
Q. Right. So it's the paragraph that begins, "It has long been known."
A. Yes, I see that.
Q. And then in the second sentence he says or the authors say, "More recently, it has been discovered that milk also contains nicotinamide riboside (NR), another salvageable NAD+ precursor vitamin."
Do you see that?
A. Yes, I see that sentence.
Q. And you would agree with me that this article does not say that milk may or may not contain NR, right?
A. Of course, as I said, it is based on the report that some milk tested has NR. That's the report that...
Q. But the title of this article is "Nicotinamide Riboside is a Major NAD+ Precursor Vitamin in Cow Milk," right?
A. Yes. In science we leave lots of limitations or conditions out of a title, and also leave out of the paper, and that's why for the sake of easy to read. We can't have all the information in the title.

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Q. So you think that the only conclusion that one can draw from this paper is that there was NR in the particular samples that were tested, and that's it?
A. Science is evidence based. So we can only say that much. If we test a sample and we see NR present in that sample, we can say this sample contains NR.
Q. What does "bioavailable" mean?
A. Bioavailable means many things at different contexts. Maybe you can give me the context.
Q. Well, in the context of this patent, I believe a few times in your testimony you've used the phrase or the word "available" in talking about NR, that you would be interested in knowing whether or not the NR is available.
So what does that mean to you, when the NR is available?
A. "Available" to me means if it's present and will convert or transport whatever a process, right, we end up to the endpoint of that process. If I have water in this bottle that's available to me, I can drink it into my

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mouth. If it's closed, the cap is closed, it's not available for me to drink.
Q. Okay. In your opinion, is the nicotinamide riboside in milk orally bioavailable?
MR. ABRAMIC: Objection. Vague.
A. I don't think there is evidence that shows that.
Q. So you don't know one way or the other?
A. I don't think there's evidence to show the bioavailable of NR, if present in milk, if it's available to humans, for example.
Q. Okay. Let me ask you a different way. Let me start with a fundamental question.
Do you have an opinion -- this is a yes or no question. Do you have an opinion about whether nicotinamide riboside in milk is orally bioavailable?
MR. ABRAMIC: Objection. Vague.
Q. That's just a yes or no question. Let's first see if you have an opinion on it.
A. Based on this evidence I've seen so far, I think NR is not available.
Q. Okay. So you do have an opinion,

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and you believe that NR in milk is not bioavailable?
A. It may not be available.
Q. I want to make sure that I understand the "may" part of this. Is it your opinion that NR is not bioavailable in milk or may not be bioavailable in milk?
MR. ABRAMIC: Objection.
A. There's no evidence to show either way.
Q. So what's the answer to the question?
A. What's the question again? Sorry.
Q. Sure. Is it your opinion that the NR in milk is not orally bioavailable?
MR. ABRAMIC: Objection. Vague.
Q. That's a yes or no question.
MR. ABRAMIC: Vague. Asked and answered.
MR. YOUNKIN: We didn't get a clear answer.
MR. ABRAMIC: You're trying to make him answer yes or no to a vague question. You can't dictate what his answer is going to be to your question.

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Q. Is it your opinion that the NR in milk is not orally bioavailable?
MR. ABRAMIC: Same objection.
A. As an expert witness here and a scientist, my opinion only comes from scientific evidence. There's no scientific evidence to show either way NR in milk is bioavailable or not.
Q. Okay. So then is it your opinion that the NR in milk may or may not be orally bioavailable?
MR. ABRAMIC: Same objection.
A. So based on the evidence, yes, there's no evidence to show either way.
Q. Okay.
A. In milk, NR in milk.
Q. And what is the basis for your opinion that the NR in milk may not be orally bioavailable?
A. So first, as a scientist, there's a well-established experimental procedure or a set of experimental procedures to test whether a molecule in the mixture is bioavailable. In this case, whether NR in milk is bioavailable.
I don't feel pretty clearly that

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that experiment has not been conducted, and then whether the experiment has been conducted, has not been exclusively show whether NR is available or not.

Furthermore, there is experimental evidence shown in this paper suggests NR may not be bioavailable.

Q. Okay. Let's start with the first part of that answer. What is the nature of the well-established experimental procedure to test whether a molecule in a mixture is bioavailable?

A. There's many experiments, and all the single set of experiments can have caveats. So that's why we often need multiple sets of experiments. So just to give you one limited set of experiments I can think about now.

One has to establish NR is present in milk, and then we have to label it, to distinguish that from some other precursors of, for example, NAD. Then we can use, perhaps, NAD as an endpoint reading to see whether NR uptake by human and then convert to NAD+. It's just one possible experiment one can do.

Q. The second part of your answer

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stated that there is experimental evidence shown in this paper, referring to Trammell 1, I believe, that suggests that NR may not be bioavailable.

Can you explain what you mean by that?

A. Yes. So the evidence suggests that NR in milk may not be bioavailable, as described in my declaration. One piece of evidence is from this paper shown that in Figure 2, that NR, NR added to milk, that shows NR binds to certain components in milk, and often there's been quite a lot of time discussed of this fact.

So once a molecule binds to what's also called protective factor, I think, in the paper, and that is evidence that suggests that once you bind the molecule, NR binds to multiple molecules, the nature of the molecule NR binds to remains unclear, based on this paper.

So that evidence suggests to me, very strong evidence, that NR may not be available to human, for example.

Q. Okay. So the way that this

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experiment worked is they had samples of milk, and then they added NR to the samples; is that right?

A. Yes. They prepared an NR molecule and added to milk.

Q. And then they showed the NR bound to the milk, right?

A. Yes.

Q. And you conclude from that that the data may show that NR is not bioavailable in milk, right, because of the binding?

A. Yeah, because of the binding of NR to a component of milk suggests that NR in milk may not be bioavailable.

Q. Did the authors of Trammell 1 articulate any conclusions about the bioavailability of NR in milk?

A. I think they mentioned that in some of the texts, and I disagree with their statement it's available, because they haven't conducted experiments I mentioned earlier to really firmly establish that it is available.

Q. So you agree with me that the authors of Trammell 1 concluded that the NR in milk is orally bioavailable, correct?

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A. I cannot recall exactly whether they mentioned the bioavailability in the paper. I think they mentioned that. But they have no experiment to conclude that.

If they ever say something about that, they are a hypothesis, not a summary of experimental data.

Q. Let's look at the last paragraph of Trammell 1.

A. In the text?

Q. In the "Discussion" section. I'd like to direct your attention to the middle sentence of the very last paragraph. I'll read it.

"The ability of milk to bind and preserve the integrity of NR makes dairy products potentially good sources of supplemented NR."

Do you see that?

A. Yes.

Q. Do you disagree with that statement?

A. I think he's a careful scientist. He used the word "potentially good sources." I can read the sentence again. "The ability of

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milk to bind and preserve the integrity of NR makes dairy products potentially good sources of supplemented NR."

Before I go to the word "potentially," I want to just go back one step. So all the experiment has done is NR was added to the milk. He didn't do any experiment about what NR in the milk sample they studied. So that's a caveat we need to be mindful of. I think they are mindful of that as well.

So here that word they use "potentially good sources." So they haven't demonstrated in this paper, in my view, scientific evidence that NR in milk is a source of supplement NR at all. So that's why they use the word "potentially," because there's no evidence.

Q. But the authors of the article concluded that the binding that they observed was potentially beneficial to the oral bioavailability of milk, correct?

MR. ABRAMIC: Objection to form.

A. So I need to go back to this one, because this is an important point.

First, whether they ever studied

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NR added to the milk, it's not NR present in the milk. So there's a big caveat there.

The second one is, they use the word "preserve the integrity of NR." I'm not even sure of the word "preserve the integrity of NR" was accurate, because the chemical shift may actually change the structure of NR.

Q. So you disagree with this statement, right?

MR. ABRAMIC: Objection to form.

A. They are very good scientists. They use the word "potentially." So that suggests to me this is a hypothesis. It would be first tested, and based on the scientific evidence, and this potential may not be true. It may be true, but you need evidence to support that in the future.

Q. Are you aware of any data correlating NMR data, like the data shown in Figure 2, with the bioavailability with a nutrient?

A. I cannot recall an exact NMR experiment to link bioavailability of nutrient by NMR study. An NMR study here is a common tool to study binding or interaction between

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two molecules.

So the data presented by NMR here to me quite clearly shows the binding or interaction between NR with a known component in the milk.

Q. Are you aware of any publication stating that NR in milk is not orally bioavailable?

A. As I said, I'm not aware of any study that's been done about NR in milk, the bioavailability. So I don't think there's any evidence to say anyway. I'm not aware of any literature or report of bioavailability of NR in milk.

Q. Did you review the prosecution history of the '086 patent?

A. I was not asked to review that. I don't remember being asked to review that. That's in a file I may have read somewhere, but I don't remember I was asked to review the file.

Q. You understand the prosecution history means the back and forth between the patent applicant and the patent office in the process of getting a patent, right?

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A. Yes.

Q. I will point out that the prosecution history was marked as an exhibit earlier in the case, but it may not have been cited earlier, so let me just give it to you. This is Exhibit 1003.

What I'd like to do is direct your attention to Page 133 of this exhibit. Let's start on Page 132.

MR. ABRAMIC: I want to make the record clear. Are you suggesting that this is a file history for this patent?

MR. YOUNKIN: This is a file history for the patent application from which this is a continuation of.

MR. ABRAMIC: Okay. I just wanted to make the record clear.

Q. Do you see on Page 132, there's what's called a Rule 132 declaration? Do you see that?

A. I see Rule 132 declaration.

Q. And then if you turn to Page 135, you'll see that it's signed by Dr. Charles Brenner?

A. Yes, I see his signature here.

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Q. Okay. Have you reviewed this declaration before? Have you seen this before?
A. I cannot recall exactly now whether I reviewed this. I did remember reviewing a declaration by Dr. Brenner.
Q. Okay. Why don't you take a minute to take a look at it, and see if it refreshes your recollection about whether you reviewed this before.
A. The whole document?
Q. No, no. It's just on Page 132 to 135.
A. Okay. This is what I can recall now. I remember, as I recall, I see data similar to Figure 1 and Figure 2. I cannot recall exactly what this document formats or not, but I see some data similar to this.
Q. Do you see in this declaration Dr. Brenner explains that he prepared compounds of nicotinamide riboside in milk; is that right?
A. I see that, yeah, on Page 132, he mentioned each compound was prepared in 20 milliliter of lactaid milk.
Q. And then he writes in Figure 1, "I show that nicotinamide riboside is stable for

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at least 24 hours at room temperature in milk," right?
A. Yes, I see that.
Q. Okay. And then in Paragraph 3, he says, "Each formulation was ingested by a human subject"?
A. Yes.
Q. And in Paragraph 5, at the end, he concludes from the experimental data that NR is orally bioavailable, correct?
A. Where?
Q. In Paragraph 5 he says, "From the confirmatory data provided herein, it can be concluded that NR is detectable in plasma, NR increases within the first ten minutes after ingestion, and NR unexpectedly is more orally available than nicotinamide to produce NAD and NADP in white blood cells in the 80-minute experiment."
Do you see that?
A. Yes. That's what I explained before. In this case he labeled NR and NR was added to the milk. So what the data really showed here is NR added to the milk is orally available shown on this experiment or NR added

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to the milk is not -- may or may not be the same NR originally present in the milk. That's why the experiment is not conclusive.
Q. But the binding that was shown in the Trammell paper that we just discussed did not interfere with the bioavailability of the NR in milk, correct?
MR. ABRAMIC: Objection to form.
A. I'm not sure that's the same milk or not. Again, in that experiment and in this study, both NR are added to the milk. I just want to make sure that's clear, that NR was added to the milk, and that's different than NR in the milk.
Q. I understand that. I'm asking about the binding. I understood you to be suggesting that the Trammell article showed binding, and that you thought that the binding might interfere with the oral bioavailability of milk; is that right?
A. Might, yes.
Q. And the Brenner declaration shows that the binding of -- any binding that occurs between milk and the added NR does not interfere with the oral bioavailability of NR?

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MR. ABRAMIC: Objection to form. Vague.
A. No. The data shows here is more orally available than nicotinamide. NR is more orally available than nicotinamide.
I need to go back and look back at this more carefully whether they had done that. The question is whether NR binds the milk is still available, but maybe less available, whether it interferes with the availability. I need to go back and look at the data.
But the statement here, if I just restate his statement, is more orally available than nicotinamide.
So what he said there, binding may not prevent from being available, but whether binding interfered with availability, I don't know whether from the data that shows that or not.
Q. The binding did not destroy the bioavailability, correct?
A. The looks from this data shows that, yes, the added NR.
Q. This is a new exhibit that we're marking. We've labeled it 1025.

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(Document marked as Exhibit 1025 for identification)

Q. So we've given you a document that's been labeled Exhibit 1025. It's an article by Katrina Bogan and Charles Brenner entitled "Nicotinic Acid, Nicotinamide, and Nicotinamide Riboside: A Molecular Evaluation of NAD+ Precursor Vitamins in Human Nutrition."

Do you see that?

A. I see that.

Q. Is this a document you've ever read before?

A. As I said, I don't recall whether I read this specific article. I was aware of Dr. Brenner's work.

Q. Okay. I'd like to turn your attention to a sentence in here in particular, and see whether you agree with it or not. So this is on Page 11 of the paper.

A. Page 11 of the paper?

Q. Yes. Do you see there's a section called "Prospects for NR as a Supplement"?

A. Yes, I see that section.

Q. Okay. The second sentence of that section says, "Like Na and Nam, NR is a natural

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product found in milk, which is incorporated into the intracellular NAD+ pool, and thus could be used as a general supplement, potentially for people who have adverse reactions to Na or Nam."

Do you see that?

A. I see that sentence.

Q. Okay. Do you agree with that sentence?

MR. ABRAMIC: Objection. Form.

A. Not completely. As I said, there's a certain set of experiments. So there's a lot of limitation of this statement not expressed here. There are certain steps that can be done more to the nature of the NR or NR environment not mentioned here. So there's lots of steps.

This particular statement there's some leap of steps in here. It can be true if only certain conditions are included in this statement.

Q. And what conditions need to be included?

A. There's lots of things. For one is, I mentioned before, whether NR is naturally

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present in milk, if it's there, whether it's bioavailable, there's no data to show that.

When NR is released from milk, which people have done this by harsh treatment to milk, that NR outside of the environment of milk has been shown -- or even added back to milk -- has shown to be bioavailable.

But if you show NR in the milk is incorporated into intracellular NAD+ pool as people or human, I don't think such experiments have been conducted. So that conclusion cannot be drawn or maybe the statement should be more -- has more limitation to it.

Q. I'd like to draw your attention to the Goldberger article that's the subject of your declaration, but I can give you a copy of it.

Do you recall whether or not the Goldberger article discusses how the milk that was given to the dogs was prepared?

A. Maybe I should see that. I remember one of the articles, there are two Goldberger articles. One is Goldberger and Goldberger and Tanner. One of the articles I can recall is mentioned such like homemade,

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fresh made. I cannot recall exactly which paper it was mentioned or mentioned in both papers.

Q. Okay. Let's look at this one, the one that I've given you. This is 1005. And let's look at Page 20 of 71.

A. We refer to this as Goldberger, right or Goldberger or Tanner?

Q. This one is just Goldberger.

A. On Page 20?

Q. 20 of 71.

A. This is for a dog?

Q. Correct. You'll see that in experiment 7, he says that it was a test of fresh skim milk, right?

A. Yes.

Q. And he goes on to say, "The milk when delivered to us was freshly separated," right?

A. Yes.

Q. And he said that "this milk in a two-quart glass jar was allowed to stand in an icebox for not more than 24 hours before being used," right?

A. Yes.

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Q. Is it your opinion that contaminants in the milk used by Goldberger completely degraded the NR in the milk during this 24-hour period?

MR. ABRAMIC: Objection. Form.

A. There's no determination or experiment that was done to determine whether NR was present, and there's no experiment reporting this whether NR -- whether it's being degraded or being measured in this paper.

Q. And without such experiments, you can't say one way or another whether or not the NR was present in the milk; is that right?

A. There's no experiments that were done to measure NR content.

Q. And because of that, you cannot say one way or another whether or not there was NR in milk; is that right, NR in the milk?

A. As I said, there's no measurement.

Q. I know that you know there wasn't a measurement. I'm trying to understand the implication of that on your opinion.

So because there was no measurement, it's your opinion, is it not, that you cannot say one way or another whether or

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not the milk that was used in this experiment contained NR?

A. Right, I cannot say whether the milk contains NR. I cannot say how much of degradation of NR occurs under these conditions. It can still occur, because ice, microbes, can still act on NR if NR is there.

Q. Do you recall that we saw in the Brenner declaration that was filed in the patent office that Brenner reported that nicotinamide riboside is stable for at least 24 hours at room temperature in milk?

A. In what milk? In the lactaid milk?

Q. Well, he doesn't say what milk. He says in milk.

A. He said lactaid milk. I'm not sure what source of lactaid milk. Can I go back?

Q. Sure. It's Exhibit 1003, Page 132.

A. As I said, here it says only 20 mLs of lactaid milk. I'm not sure what's the source of lactaid milk. Is that from a store or from a farm. I'm not sure exactly what

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lactaid milk is.

Q. But the sentence about stability is, "I show nicotinamide riboside is stable for at least 24 hours at room temperature in milk," right?

A. This means the milk, in particular, lactaid milk.

Q. That's not what he says, right?

A. This is how scientist state, because given the context, when we say milk, it doesn't mean every milk. It means the milk he uses in this experiment. That's the only thing we can say in science.

Right here, in milk, this milk is the lactaid milk they use in the experiments.

Q. I'm going to give you a new exhibit. This is 1023.

(Document marked as Exhibit 1023 for identification)

A. So to answer your question --

Q. There's no question pending.

So we've given you a new document that has been marked 1023. I'll just direct your attention to the first page. This is a document that was submitted with the Food and

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Drug Administration.

A. I don't recall...

Q. You haven't seen these.

A. Okay.

Q. But just to sort of orient you a little bit, this is a document that was submitted to the Food and Drug Administration by ChromaDex.

A. Okay.

Q. Have you ever been involved in these sort of regulatory filings in the course of your work?

A. Not from my work, but I work with a pharmaceutical company, and also in the other lawsuits, I have seen some of these documents.

Q. Okay. I'd like to turn your attention to Page 22 of this document, using the typed in numbers.

A. The very bottom one?

MR. ABRAMIC: The bottom right.

Q. I'm sorry, I meant the times new Roman in the center. It has been stamped 35. The stamping was not done by us. This is how the document existed as FDA.

A. Okay.

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Q. So you can see that in this section, it's called "History of Use and Intended Use," right?

A. Yes.

Q. And the first section is "History of Use: Natural Occurrence of Nicotinamide Riboside (NR) in Foods and Dairy Products," right?

A. Yes, I see that.

Q. And if you skip down to the third sentence, this document that was filed with the FDA says, "Moreover, NR levels in milk do not change significantly when milk is stored at room temperature for 24 hours (Brenner, unpublished)."

Do you see that?

A. Yes, I see that.

Q. Okay. And there's nothing in this statement that limits the stability to lactaid, for example, right?

A. Again, any kind of statement like this, this otherwise is not scientific. It only applies to the milk samples it tested. If they haven't tested, you cannot do that. We don't know actually what happened to the milk

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that was processed.

I actually spent some time to learn about the milk industry myself during this course. The milk process varies dramatically from years back, a different process of treatment.

So this is very important, because I think their document shows in milk NR could be degraded by bacteria. So there are reports of that. So milk contamination, we know that's an issue, milk recalls in this country.

So the statement only scientifically means the milk has been tested. There's a supplemental material somewhere with the FDA filing and they have to tell where the milk is from and they have to tell the history of the samples, the history of the store, from what vendor, maybe which cow to some degree.

Q. That's not what they are saying to the FDA. They are saying to the FDA that relying on Brenner's unpublished data, they're telling FDA that NR levels in milk do not change significantly when milk is stored at room temperature for 24 hours.

A. So for this one, there will be an

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FDA examiner, and I am familiar with this process. The sample history has to be documented where this milk is from, how that process, it should be documented. If it were not documented, I'm sure the FDA examiner will ask that. So the information may be in this document or other documents.

Q. Let me ask you this question, then. Is it your opinion that one could never make the broad statement that NR levels in milk do not change significantly when milk is stored at room temperature for 24 hours?

MR. ABRAMIC: Objection to form.

A. I should not make that broad statement. One can say if this milk, for example, the exhaustive tests of a sample meet a certain FDA requirement, for example, just give example, one company has an FDA approved or agriculture department approved the process, and they have all of these monitoring processes in place, and refrigeration and such, conditions like that are met, then we have some certainty that such milk also had been tested for stability of NR in that milk, and then this statement there's always a limitation

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associated with such a statement.

If I have my own milk cow in my farm, I would not make that statement to my cow unless I tested or I have literature report of a cow or any cow or the cow raised my way in my such environment in Massachusetts, in Wellesley, back yard or Newton for that matter, right, and meet that requirement, otherwise I won't make that statement. I won't extrapolate this information to the cow in my back yard, for example.

Q. The first sentence of this section says, "Humans are exposed to NR via dietary sources such as milk."

Do you see that?

A. So this in general. If NR in some milk, as we know that. So human -- some people don't drink milk. Some humans are never exposed to NR in milk. They're intolerant. So some humans exposed to some milk which may have NR and that's what the statement about.

If a human is exposed to some milk and that milk has NR, that's a statement. It doesn't say everybody has been exposed to milk, right. So not every single human being has

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been exposed to NR in milk.
Q. But the sentence, does it say some humans are exposed to milk which may or may not contain NR, right?
A. That's really what it says, right.
Q. Well, that's not what it says. It says, "Humans are exposed to NR via dietary sources such as milk," right?
A. As an FDA examiner, as a scientist, that's how the sentence should be interpreted.
Q. Okay. Let's look at the last sentence of this section or before the table. "Thus, the estimated amount of NR ingested by humans from the equivalent of 710 milliliters per day (three cups) of cow's milk, is approximately" 345 "micrograms per day," right?
MR. ABRAMIC: I think it says "545."
Q. Oh, yes. 545. Sorry.
A. Yes. That's the statement.
Q. So the statement is extrapolating, right, and drawing a conclusion about the amount of NR ingested by humans when they drink three cups of cow's milk, right?

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A. Yes, it's about. We know or you know we have documents that shows different milk, organic and different vendors of milk have different amounts of NR. So this is about. That's why it says "about" there.
MR. YOUNKIN: Why don't we take a break.
(Recess taken at 11:02 a.m. and reconvening at 11:19 a.m.)
BY MR. YOUNKIN:
Q. Dr. Zhou, do you agree that pellagra is caused by a deficiency in NAD+?
A. I'm not a medical doctor. That's my understanding, deficiency of NAD is at least linked to pellagra. I'm not exactly sure it's causing that or not.
Q. But it's linked?
A. It's linked.
Q. So pellagra reflects an NAD deficiency, correct?
A. I think so, yes.
Q. And do you agree that the Goldberger and Tanner article concluded that buttermilk prevents pellagra?
A. Yes. I looked at a paper and see

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their evidence in humans, yes, prevents pellagra.
Q. And do you agree that black tongue reflects a deficiency in NAD as well?
A. Just from reading. I even know less about the chemistry of NAD in dogs.
Q. But based on your reading of the literature, that's your understanding, correct?
A. Yes.
Q. And do you agree Goldberger concluded that skim milk contains the quote/unquote black tongue preventative?
A. Yes, that's his statement.
Q. And that's because there's something in the milk that increased NAD biosynthesis, right?
A. That's the hypothesis. They may be working through another mechanism, but at least that's one of the hypothesis accepted by people and by reading the paper, I agree with that as well.
Q. And do you also agree with the hypothesis that the buttermilk that was used in the Goldberger and Tanner article prevented pellagra because something in that buttermilk

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increased NAD+ biosynthesis?
A. Very likely that's the mechanism, yes.
MR. YOUNKIN: I have no further questions.
MR. ABRAMIC: I have no questions.
(Whereupon the deposition concluded at 11:21 a.m.)

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CERTIFICATE OF DEPONENT

I hereby certify that I have read the foregoing pages of my deposition testimony in this proceeding, and with the exception of changes and/or corrections, if any, find them to be a true and correct transcription thereof.

_____
Deponent

_____
Date

NOTARY PUBLIC
Subscribed and sworn to before me this _____ day of _____, 20___.

_____
Notary Republic

My Commission Expires:_____

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ERRATA SHEET

PAGE -- LINE -- CORRECTION/REASON

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ERRATA SHEET

PAGE -- LINE -- CORRECTION/REASON

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Page 89

ERRATA SHEET

PAGE -- LINE -- CORRECTION/REASON

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C E R T I F I C A T E

COMMONWEALTH OF MASSACHUSETTS
SUFFOLK, SS.

I, Michael O'Connor, Registered Merit Reporter/Certified Realtime Reporter, and Notary Public in and for the Commonwealth of Massachusetts, do hereby certify:

That ZHAOHUI SUNNY ZHOU, Ph.D., the witness whose testimony is hereinbefore set forth, was duly sworn by me and that such testimony is a true and accurate record of my stenotype notes taken in the foregoing matter to the best of my knowledge, skill and ability.

IN WITNESS WHEREOF, I have hereunto set my hand and Notarial Seal this 2nd day of August 2018.

_____

MICHAEL O'CONNOR, RMR, CRR, CRC
Notary Public

My Commission expires: November 22, 2022

CERTIFICATE OF DEPONENT

I hereby certify that I have read the foregoing pages of my deposition testimony in this proceeding, and with the exception of changes and/or corrections, if any, find them to be a true and correct transcription thereof.

Deponent

20 August 2018

Date

NOTARY PUBLIC

Subscribed and sworn to before me this _____ day of _____, 20___.

_____

Notary Republic

My Commission Expires:_____

ERRATA SHEET

PAGE	LINE	CORRECTION/REASON	
9	22	change "invite minutes" to "in vitamins"	transcription error
21	25	change "law, a" to "law, in a"	transcription error
26	18	change "fact" to "effects"	transcription error
55	12	change "bioavailable" to "bioavailability"	transcription error
57	25	change "don't" to "do"	transcription error
62	25	change "whether they ever studied" to "what they studied was"	transcription error