

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

-----X
NOVARTIS PHARMACEUTICALS CORPORATION, :
Petitioner, : Case IPR 2023-01346
v. : U.S. Patent No. 10,633,344
REGENTS OF THE UNIVERSITY OF MICHIGAN :
and UNIVERSITY OF SOUTH FLORIDA, :
Patent Owners. :
-----X

DEPOSITION OF
LEAH APPEL, Ph.D.
May 8, 2024
9:05 a.m. EDT
4 Times Square
New York, New York

REPORTED BY: MARIE FOLEY, RMR CRR

DIGITAL EVIDENCE GROUP
1730 M Street, NW, Suite 812
Washington, D.C. 20036
(202) 232-0646

1 Deposition of LEAH APPEL, Ph.D.,
2 held at 151 West 42nd Street, New York,
3 New York, commencing at 9:00 a.m. EDT, on
4 the above date, before Marie Foley, a
5 Registered Merit Reporter, Certified
6 Realtime Reporter and Notary Public.

7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

1 A P P E A R A N C E S:

2

3 ON BEHALF OF PLAINTIFF:

4 VENABLE, LLP

5 BY: CHRISTINA SCHWARZ, ESQUIRE

6 ALEXIS M. McJOYNT, ESQUIRE

7 151 West 42nd Street, 49th Floor

8 New York, New York 10036

9 PHONE: 212.307.5500

10 EMAIL: Cschwarz@venable.com

11

12

13 ON BEHALF OF DEFENDANT:

14 FISH & RICHARDSON P.C.

15 BY: TAYLOR CALDWELL BURGNER, ESQUIRE

16 MICHAEL J. KANE, ESQUIRE

17 1000 Maine Avenue SW, Suite 1000

18 Washington, D.C. 20024

19 PHONE: 202.783.5070

20 EMAIL: Burgener@fr.com

21

22 ALSO PRESENT:

23 Brian Robinson, Novartis

24

25

1	TRANSCRIPT INDEX	
2		PAGE
3	EXAMINATION OF LEAH APPEL, Ph.D.:	
4	BY: MS. BURGNER.....	5
5	BY: MS. SCHWARZ.....	94
6	BY: MS. BURGNER.....	98

7			
8			
9	E X H I B I T S		
10	NO.	DESCRIPTION	PAGE
11	Novartis	Declaration of Leah Appel,	15
12	Exhibit 1003	Ph.D. In Support of Petition	
13		For Inter Partes Review	

14

15 (REPORTER'S NOTE: All quotations from

16 exhibits are reflected in the manner

17 in which they were read into the

18 record and do not necessarily denote

19 an exact quote from the document.)

1 - - -

2 9:05 a.m.

3 New York, New York

4 - - -

5 THE STENOGRAPHER: Doctor, if I
6 could ask you to raise your right
7 hand, please.

8 Do you swear or affirm the
9 testimony you give will be the truth,
10 the whole truth, and nothing but the
11 truth today?

12 THE WITNESS: I do.

13 THE STENOGRAPHER: Thank you.

14 - - -

15 LEAH APPEL, Ph.D., the Witness herein,
16 having been first duly sworn by a
17 Notary Public in and of the State of
18 New York, was examined and testified
19 as follows:

20 EXAMINATION BY

21 MS. BURGNER:

22 Q. Dr. Appel, can you please state
23 your full name and address for the record?

24 A. Sure. Leah Appel, 4042
25

1 Northwest Northcliff, Bend, Oregon 97703.

2 Q. Have you been deposed before?

3 A. Yes.

4 Q. How many times?

5 A. I don't recall exactly. Some
6 number like 15 to 20.

7 Q. Given the number, what range of
8 time were those depositions taken? Since
9 when, for example?

10 A. I'm sorry, I don't quite
11 understand what you're asking.

12 Q. When was your first deposition?

13 A. Approximately 2016, '17,
14 something like that.

15 Q. And when was your last
16 deposition besides this one?

17 A. Last week.

18 Q. Frequency being of those
19 depositions, how many per year, let's say?

20 A. Gosh. I wouldn't even want to
21 venture a guess. I really wouldn't.

22 Q. Generally scattered throughout
23 that time frame then?

24 A. I would say it's been scattered.
25

1 Q. Okay.

2 Were each of those depositions
3 related to patent litigations?

4 A. Everything except for one.

5 Q. What was that deposition related
6 to?

7 A. It was I think an -- called an
8 arbitration, so it was a disagreement
9 between two companies with regard to their
10 business relationship and contract and...

11 Q. Was that related to patent
12 licensing in any way, or was that separate
13 from any type of patent?

14 A. No patent. It was about
15 know-how.

16 Q. For those that were related to
17 patents, what was your role in those
18 litigations?

19 A. As an expert.

20 Q. You served as an expert witness?

21 A. Correct.

22 Q. Was it related to claim
23 construction?

24 A. I have done that. Sometimes
25

1 I've -- you know, that's part of it and
2 sometimes it isn't.

3 Q. How many of the 15 to 20 would
4 you say were related to claim
5 construction?

6 A. No idea.

7 Q. Can't estimate?

8 A. I don't want to guess, yeah.

9 Q. Okay.

10 And was your testimony in those
11 15 to 20 depositions, or I'll say 15 to
12 19, related to invalidity?

13 A. I have testified related to
14 invalidity in some of them.

15 Q. Can you provide an estimation of
16 how many of those were related to
17 invalidity?

18 A. No.

19 Q. I'm going to ask the same
20 question with respect to infringement.

21 How many of the 15 to 19 were
22 infringement based?

23 A. Some of them. No idea how many.

24 Q. Did you issue reports in any of
25

1 the cases where you provided deposition?

2 A. To my recollection, I think all
3 of them, but to the best of my
4 recollection.

5 Q. And are you able to identify of
6 the reports you provided, which related to
7 invalidity or infringement?

8 A. Sitting here today?

9 Q. Yeah.

10 A. No. I'd need to go back and
11 review them.

12 Q. Of those 15 to 19 litigations,
13 were any related to co-crystals?

14 MS. SCHWARZ: Objection to form.

15 A. Not that I recall.

16 Q. Were any of the 15 to 20
17 depositions related to pharmaceutical
18 formulations of co-crystals?

19 MS. SCHWARZ: Objection to form.

20 A. Not that I recall.

21 Q. All right. So now I'm just
22 going to go through, and I know you've
23 done this before given that you've done 15
24 to 20 depositions, but some of the
25

1 admonitions are, kind of, rudimentary
2 walk-through of the rules and regulations
3 of the deposition.

4 Do you understand that you are
5 under oath today?

6 A. I do.

7 Q. And your answers must be
8 truthful, accurate, and complete, just as
9 if you were testifying before a judge.
10 You understand that, right?

11 A. I do.

12 Q. Any reason, medical or
13 otherwise, that would prevent you from
14 giving complete and accurate testimony
15 today?

16 A. None that I'm aware of.

17 Q. If that changes, will you please
18 let me know?

19 A. Yes.

20 Q. Thank you.

21 If at any point during today's
22 deposition I ask a question that is
23 unclear to you, will you please let me
24 know?

25

1 A. Absolutely.

2 Q. If you answer my question, I'm
3 going to assume you understood the
4 question.

5 Is that fair?

6 A. That's fair.

7 Q. And if at any point during the
8 deposition you need to clarify anything,
9 please let me know. We can do that on the
10 record.

11 A. Okay.

12 Q. If you need to take a break, I
13 just ask, and there's a pending question,
14 I would just ask that you answer the
15 question first, and then we can take a
16 break thereafter.

17 Is that fair?

18 A. Yes.

19 MS. BURGNER: For the room, we
20 might need to take more frequent
21 breaks because I'm six months
22 pregnant. So I'm just letting
23 everybody know. It's not intentional
24 or strategic or anything like that.

25

1 Q. So, we need to speak as clearly
2 as possible, or we are going to try to
3 speak as clearly as possible and try to
4 avoid talking over each other for the
5 court reporter's sake.

6 Do you understand that?

7 A. Yes.

8 Q. And do you understand that you
9 need to provide a verbal response and not
10 just gesture yes or no or by nodding your
11 head or shaking your head? You understand
12 that, right?

13 A. Yes.

14 Q. Your attorney may object to my
15 questions throughout the deposition, but
16 unless your attorney instructs you not to
17 answer, you're required to answer.

18 Do you understand that?

19 A. I do.

20 Q. Did you bring anything with you
21 to the deposition today, any documents?

22 A. No.

23 Q. So, do you understand that
24 you're here to testify on behalf of
25

1 Novartis related to two IPR proceedings,
2 one with the number ending in '1346 and
3 one with the number ending in '1347?

4 A. I don't recall the exact
5 numbers.

6 I certainly know that I'm here
7 on behalf of Novartis for two IPR
8 proceedings.

9 Q. And each of those -- and in each
10 of those proceedings, you provided a
11 declaration, correct?

12 A. That's correct.

13 Q. Do you have any understanding of
14 the differences between the two
15 proceedings?

16 A. I'm not a -- an attorney.

17 Q. Sure.

18 A. But as a layperson, I do
19 understand they pertain -- that they're
20 different.

21 Q. What do you understand the
22 differences to be?

23 A. Specific claims that are being
24 discussed in -- in each one, they're
25

1 different.

2 Q. Do you know which claims are
3 being discussed in either?

4 A. You know, I -- I didn't memorize
5 them. I have an idea, but I didn't
6 memorize what claim number.

7 Q. Okay.

8 Do you understand how the claims
9 may be different substantively? You said
10 you had an idea, so I guess my question is
11 what's that idea of the differences
12 between the two claims?

13 MS. SCHWARZ: Objection to form.

14 A. Yeah, I mean, they're --
15 they're -- they're distinct claims that
16 certainly share some -- some parts of
17 them. But beyond that, no.

18 Q. So, in each of the declarations
19 you provided, your statements cover the
20 same section of the claim language. Is
21 that correct?

22 A. Could you clarify what you mean
23 by that, please?

24 Q. Sure.

25

1 MS. BURGNER: It might actually
2 be better if I just introduce into the
3 record one of your declarations so we
4 can walk through it.

5 This has been previously marked
6 as Novartis Exhibit 1003.

7 (Novartis Exhibit 1003,
8 Declaration of Leah Appel, Ph.D. In
9 Support of Petition For Inter Partes
10 Review, was marked for identification,
11 as of this date.)

12 BY MS. BURGNER:

13 Q. So, if we can turn to -- I
14 should say, Dr. Appel, do you recognize
15 this document?

16 A. I do.

17 Q. What is it?

18 A. This is one of the declarations
19 I prepared for this case.

20 Q. You see down here in the bottom
21 right corner of the first page it says
22 IPR 2023-01346.

23 Correct?

24 A. Yes.

25

1 Q. And your signature is on page
2 42, the last page?

3 A. Yes.

4 Q. Dated August 24th, 2023?

5 A. Yes.

6 Q. How much time did you spend
7 preparing this declaration?

8 A. I don't recall.

9 Q. Can you give, like, an estimate?

10 A. No.

11 Q. When was the declaration
12 prepared?

13 A. Last summer.

14 Q. How was the declaration
15 prepared?

16 A. Certainly it was a joint effort
17 between counsel and myself, meetings, and,
18 you know, each of us reviewing things and
19 writing things and putting it together.

20 Q. Did you talk to anyone else when
21 working on the declaration outside of your
22 attorney team?

23 A. No.

24 Q. No other experts?

25

1 A. No.

2 Q. No other people in industry?

3 A. No.

4 Q. Okay.

5 If we can turn to paragraph 26,

6 which I believe is on page 13.

7 A. Yes, I'm there.

8 Q. Okay. The highlighted section
9 that states: A pharmaceutical composition
10 comprising of a pharmaceutically
11 acceptable carrier in a therapeutically
12 effective amount of a co-crystal.

13 What was the purpose of
14 highlighting that section?

15 A. That's really the focus of my
16 analysis. There's a lot of other things
17 in the claims that I was not asked to
18 opine on.

19 Q. And if you recall, in your other
20 declaration for the '1347 IPR, was your
21 analysis similarly limited to this
22 language in claim 10?

23 MS. SCHWARZ: Objection to form;
24 mischaracterizes the witness's

25

1 testimony.

2 BY MS. BURGNER:

3 Q. And if it is helpful, I can give
4 you the other declaration as well.

5 A. I don't need that right this
6 second, but of course I would like it at
7 some point.

8 So, the -- the specific
9 language, you know, in -- that we are
10 looking at here in paragraph 26 under
11 claim 10 "A pharmaceutical composition
12 comprising of pharmaceutically acceptable
13 carrier in a therapeutically effective
14 amount of a co-crystal," the language
15 that's used in the other three dependent
16 claims is on page 14 under paragraph 27,
17 and in each case, the highlighted section
18 of claims 11, 16 and 18 start with "The
19 pharmaceutical composition of claim 10."
20 And that's identical for -- for each of
21 those.

22 So hopefully that clarifies for
23 you my focus.

24 Q. Would it be fair to say that the
25

1 highlighted portions of the claim language
2 that you've included in paragraphs 26 and
3 27 are the focus of your analyses in
4 either declaration?

5 MS. SCHWARZ: Objection to form.

6 A. Those are the -- that -- that is
7 what I was asked to consider and analyze
8 in preparing my declaration.

9 Q. All right. If we can move to
10 paragraph 31 which is on page 16.

11 A. Okay.

12 Q. It references the two -- sorry.
13 Taking a step back from paragraph 31.

14 The two declarations that we've
15 been discussing, much of the two
16 declarations are identical. Is that
17 correct?

18 A. There are many sections that are
19 the same.

20 Q. Would it be fair to say that the
21 testimony that you provide today when
22 speaking about the opinions provided in
23 one of your declarations would also apply
24 to the opinions provided in the other
25

1 declaration?

2 MS. SCHWARZ: Objection to form.

3 A. That's probably generally true,
4 but probably also dependent on the
5 question, so.

6 Q. That's fair. My purpose there
7 being given the overlap of the two
8 declarations, trying to find a way to,
9 kind of, limit ourselves to one and then
10 move to the other if possible.

11 A. I like that idea.

12 Q. Yeah, from an efficiency
13 perspective.

14 Okay. When were you first
15 retained by Novartis? It doesn't have to
16 be a specific date. Ballpark is fine.

17 A. Early last summer, I think.

18 Q. Was it limited to the IPR
19 proceedings, or also for the litigation,
20 or both?

21 A. This -- I -- I've only worked on
22 the IPR proceedings.

23 Q. Okay. Just a few more
24 formalities, if you will.

25

1 Going back to paragraph 19,
2 Section 4 titled "Materials Reviewed" on
3 page 9.

4 A. I see that.

5 Q. In preparing your declaration,
6 I'd just like to confirm the scope of what
7 you've reviewed.

8 So, you reviewed the '344 patent
9 which is the patent at issue here,
10 correct?

11 A. That's correct.

12 Q. The file history for the '344
13 patent?

14 A. That's correct.

15 Q. The file history of U.S.
16 Application number ending in '956?

17 A. That's correct.

18 Q. And any exhibits or references
19 you cited in your declaration I'm assuming
20 you reviewed, correct?

21 A. That's correct.

22 Q. Okay. Don't need to walk
23 through all of them.

24 Is there anything else that
25

1 you'd like to include as something you
2 reviewed in preparing your declaration?

3 A. Not that I recall at this time.

4 Q. Would the same scope of
5 documents apply for the materials that you
6 reviewed for your declaration in the '1347
7 IPR?

8 A. Yes.

9 Q. Okay. Going back one step
10 further to page 6, paragraph 7 of your
11 declaration.

12 So, I'd like to just get to know
13 you a little bit better from your work
14 experience at this stage. So, if we just
15 walk through from earliest to most recent,
16 your different work experiences.

17 So, the first I see that you
18 mention, if that's correct, is INTERx
19 Research Corporation in 1988. Is that
20 correct?

21 A. It is.

22 Q. What was your position at INTERx
23 Research Corporation?

24 A. I think I started as a senior
25

1 research chemist and ended as a research
2 fellow, I think was the terminology they
3 used.

4 Q. And what did you do as a senior
5 research chemist?

6 A. Basically formulated drugs and
7 worked on drug delivery systems, that is
8 platforms. So not necessarily with a
9 specific API in mind, but let's say a
10 controlled release platform that could be
11 used for a wide range of actives.

12 Q. This may be a very rudimentary
13 question, but can you explain what
14 formulating drugs means?

15 A. Sure.

16 The way I use that term, it
17 means basically taking an active
18 pharmaceutical ingredient, an API, an
19 active, those are all synonymous in this
20 scenario, taking that and formulating into
21 a dosage form. And so the dosage form,
22 I -- we're talking about oral dosage forms
23 and, you know, there are other kinds of
24 dosage forms, but for this example I'm
25

1 going to just talk about dosage forms and
2 solid dosage forms which are most often
3 tablets and capsules. So basically taking
4 that pharmaceutical ingredient and
5 creating a dosage form out of it. So the
6 dosage form is not pure drug, contains
7 other things. Let's say it's an immediate
8 release dosage form. It may have filler
9 or carrier, it may have disintegrant, it
10 may have binder, it may have lube, other
11 things, and those are called excipients.

12 And then so there's what the
13 ingredients are, that's part of it. And
14 then honestly, similar to a recipe, it's a
15 list of ingredients and amounts.

16 And then there's -- then there's
17 the process, how do you make that. Do you
18 make it with -- do you granulate it and
19 then press it into a tablet, or do you
20 just mix it and then compress it? What --
21 what do you do? So it's a process.

22 So I would, in summary, say that
23 formulation is taking that active
24 pharmaceutical product and turning it into
25

1 a dosage form, including what the
2 ingredients are and the process that you
3 used to -- to make it.

4 Q. That's all very helpful. Thank
5 you. There's a few things to unpack there
6 that I, kind of, wanted to follow up on.

7 In working to formulate the
8 dosage forms, or in working to create the
9 dosage forms as part of your formulation
10 process, are you typically given an API to
11 work with and then you start developing
12 the process from there, or do you get
13 involved earlier?

14 A. I would say, yeah, typically I
15 am not involved in, you know, activities
16 like synthesizing the API or something
17 like that. I may be in meetings, you
18 know, team meetings that they talk about
19 that, but -- but that's not my area of
20 expertise.

21 Q. Okay. I may have a few more
22 follow-up questions later on, but I don't
23 want to get off track of also making sure
24 I understand what you did.

25

1 So that was as a senior research
2 chemist.

3 How if at all did your position
4 or role change at INTERx when you became a
5 research fellow?

6 A. I think I got direct reports.
7 So I had some managerial responsibilities,
8 but technically very similar.

9 Q. Then in paragraph 7 again it
10 moves from 1995 to 1996 you were a project
11 leader at Sarcos Research Corporation,
12 correct?

13 A. True.

14 Q. And what did you do in that
15 role?

16 A. Looked for another job.

17 It was -- so, that was INTERx
18 was closed and so I -- Merck shut that --
19 that unit down, and so I found a job, and
20 they -- they worked on miniaturized pumps,
21 so microelectrical mechanical systems.
22 Some pretty cool stuff that you can do
23 broad range. So they did robotics. They
24 made Disney robots and stuff like that,
25

1 but in the area of drug delivery, we were
2 looking at using miniaturized pumps for
3 drug delivery. So kind of a cool idea,
4 but a bit outside my interest and
5 technical capabilities and a very
6 different kind of company that I quickly
7 figured out I didn't want to stay at, so
8 then I left.

9 Q. Consistent with the 1995 to 1996
10 stint.

11 A. Correct.

12 Q. Fair enough. We've all been
13 there.

14 So then from 1996 to 2006 you
15 worked as the director of controlled
16 research at Bend Research. Is that right?

17 A. Yes, except for there's a typo
18 there. Sorry.

19 Q. Sure, no problem.

20 A. I just noticed it.

21 Controlled release, not
22 research, at Bend Research.

23 Q. Got it.

24 And what was your role as the
25

1 director of controlled release at Bend
2 Research?

3 A. Bend Research at the time was a
4 small company, 50 people, and your title
5 didn't necessarily reflect exactly what
6 you did. So you did a lot of things.

7 But basically they, at the time,
8 were working in the -- in the pharma
9 industry almost exclusively for Pfizer,
10 and they were a contract research and
11 development lab. And so really what we
12 got there was our problem statements and
13 areas of focus for technologies to develop
14 from Pfizer. It was very much a -- a
15 collaborative effort. And we developed
16 technologies and advanced candidates with
17 those technologies to, you know, first
18 early -- early studies, you know, animal
19 studies, early formulation development for
20 clinical studies, and then on through to
21 commercialization.

22 Q. What do you mean by "advanced
23 candidates"?

24 A. So, a candidate might advance
25

1 from phase 1 to phase 2 or phase 2 to
2 phase 3. So getting further along in the
3 development process, closer to a
4 commercial dosage form.

5 Q. I see.

6 So would a candidate be
7 considered synonymous with, like, an API,
8 for example? Or could it be?

9 A. That's generally not how the
10 language is used.

11 Q. Okay.

12 A. Most companies, including
13 Pfizer, but most -- and Merck, they make
14 thousands, tens of thousands of compounds,
15 and not all of those become candidates.
16 So they sort through those and make
17 sure -- they decide on what they want to
18 advance, and there's actually, kind of, a
19 formal candidate nomination process
20 usually in most of these companies where,
21 you know, they're justifying why this one
22 out of all these other ones is the one
23 they would like to name a candidate and
24 then it goes on to development.

25

1 So no, I wouldn't say all of the
2 APIs are can -- turn into candidates.

3 Q. Would all of the candidates be
4 considered APIs? May not be the reverse,
5 but would all the candidates be considered
6 APIs?

7 A. That sounds right to me,
8 thinking about it as the -- at this
9 moment.

10 Q. Okay.

11 And were you involved at all in
12 your role at Bend Research in proposing
13 which API should become candidates?

14 A. No.

15 Q. Just to make sure I understood
16 the full scope of your work at Bend
17 Research, your role was to do early
18 formulation development, at least in part
19 for any candidate or just the advanced
20 candidates?

21 A. So, would start with candidates
22 that hadn't been in, you know, hadn't been
23 really in a real dosage form. Maybe
24 they'd been tried in, you know, rats and
25

1 in solution, but certainly hadn't been in
2 an oral solid dosage form, like a tablet
3 or a capsule in, you know, things like
4 dogs or monkeys, something larger than a
5 rat and something that you could give a
6 solid dosage form to, and -- and certainly
7 not in man.

8 So really from that point that
9 the first time you'd want to make a dosage
10 form to test those kinds of things through
11 advancing drugs to commercialization. So
12 I would say all stages of development from
13 early stage to late stage in commercial.

14 Q. Okay.

15 Then you moved, based on
16 paragraph 7, you left Bend Research and
17 founded Green Ridge Consulting. Is that
18 right?

19 A. Yes.

20 Q. And are you the CEO of Green
21 Ridge Consulting?

22 A. My title is managing partner.

23 Q. What do you do in that role?

24 A. So, Green Ridge Consulting
25

1 provides -- really we loan our formulation
2 and development expertise to other
3 companies and help them develop their
4 drugs.

5 So a typical kind of thing we
6 would do is somebody would say hey, we
7 have this API and we want to develop a --
8 a dosage form for oral delivery. We're,
9 you know, early phase 1 or something
10 early. We want to get to the clinic
11 really quickly and, you know, this is the
12 dose that we are looking at. Something
13 like that. And so we would recommend what
14 kinds of dosage forms, where they might do
15 that work. Most of this work for the
16 small guys is done at contract
17 organizations. Or they might have
18 something -- they might have a dosage form
19 already that's in phase 1 or phase 2, but
20 it's not ready for commercialization. So
21 it hasn't been scaled up. Maybe there's
22 some issues. Maybe it sticks to the
23 tablet punches a little bit and, you know,
24 so that's a manufacturing issue. Or maybe
25

1 they have to keep it in the refrigerator
2 because it's not chemically stable enough
3 to be a commercial product, but they can
4 do this for clinical studies. So it has
5 some issue or issues that need to be
6 addressed.

7 And then another type of client
8 we help are large pharma, and a lot of
9 times those guys are just looking for an
10 outside perspective of hey, this is what
11 we're doing, are we missing something.
12 They use us differently than small pharma
13 does.

14 But those are the kinds of
15 things we consult on.

16 Q. Okay.

17 So, say a client comes to you
18 with a specific API and they'd like to
19 formulate a dosage form for that API.

20 How would you go about helping
21 your clients do that? Like what are the
22 steps you would take?

23 MS. SCHWARZ: Objection to form.

24 A. So, first you need to understand
25

1 their specific goals. So are they the
2 client that just is trying to get this
3 into man and get a read as fast as
4 possible. And so we want a -- we would
5 call it a fit-for-purpose dosage form. So
6 we don't care if it's got long-term
7 stability like we would care if it had to
8 be a commercial product. And we don't
9 care if you can scale it up to make, you
10 know, hundreds of kilos batch size. We
11 just -- what they care about the most is
12 is how fast can we get this to the clinic,
13 and often, you know, they also care about
14 money. Often they care about -- they only
15 have a limited amount of the material, of
16 the API. So it's constrained in -- it
17 could be constrained in a number of
18 different ways.

19 So it's understanding what do
20 you want. Do you want, you know,
21 something that if the clinical result is
22 positive, we have some hope of being able
23 to use this in later stage with some maybe
24 some modifications, maybe not, but what
25

1 level of work do you want to go into this
2 dosage form so that, you know, what do you
3 need to know about it. Is six months
4 stability good enough, is three months
5 stability good enough, or do you need
6 more. That kind of thing.

7 So understanding that, and then
8 understanding -- so that's, kind of, the
9 goal. And then understanding from a
10 technical perspective the properties, the
11 physicochemical properties of the drug.
12 So this often if they don't already have
13 this, you would perform something called
14 preformulation, and so that's where you
15 measure things like the -- and I am really
16 speaking about oral dosage forms
17 throughout.

18 Q. Okay.

19 A. That's my primary experience
20 and -- and I think relevant here.

21 So, for oral medications drugs,
22 it's important to understand their
23 solubility is a function of pH because in
24 the GI track they experience different pH
25

1 levels, so, and that can impact all sorts
2 of things. It can impact stability; it
3 can impact absorption. So measuring
4 things like pH, what we call the pH
5 solubility profile of the API.

6 Understanding how hydrophilic or
7 lipophilic it is, you know, a measurement
8 called LogP where what -- at what pH is it
9 ionized, things like pKa's.

10 Those are just some examples,
11 but we would determine what the relevant
12 physicochemical properties are.

13 Q. Of the API that is?

14 A. Of -- just of the pure API.

15 So it --

16 Q. Sorry, go ahead.

17 A. Do you want to ask a question?

18 Q. No. You were probably on the
19 same path that I was, so I'll let you
20 finish, and then I'll ask you any
21 follow-up questions afterwards.

22 A. So now we have what's the goal,
23 and we have some knowledge about our
24 molecules. So now we can think about what
25

1 are our options. This is a highly soluble
2 molecule, so maybe we could just put API
3 in a capsule and that will work and, you
4 know, life will be good.

5 Or it's a poorly soluble
6 compound. Boy, if we did that, it's just
7 not even going to dissolve. Maybe we'll
8 need to grind it up and make it a smaller
9 particle size. Maybe we'll need to add a
10 solubilizer to help it go into solution.
11 Maybe we'll need to make an amorphous --
12 an amorphous-based technology to give it a
13 higher energy form.

14 So there's all sorts of
15 different things you might consider
16 depending on these physicochemical
17 properties and what you're trying to make.
18 But at this point, you decide, you know,
19 these are our options, and kind of
20 depending on the company, some people want
21 to pursue a primary approach and a back-up
22 approach. Some people just want to pursue
23 one approach, that's all they can afford
24 or have API to do. And then you -- once
25

1 you've chosen the specific, then you start
2 to do the work towards formulation.

3 So, I'll be quiet and see what
4 about that you want to know.

5 Q. So what we just discussed, the
6 goal and the knowledge of the molecule
7 with respect to the physicochemical
8 properties, all of that would be part of
9 the preformulation stage?

10 MS. SCHWARZ: Objection to form.

11 A. So, the second part of that is
12 preformulation.

13 Q. Okay.

14 A. The goal is really, I don't
15 know, the strategy, you know, the project
16 strategy. I wouldn't call that a specific
17 name.

18 Q. Okay. That's fine.

19 You mentioned earlier
20 excipients, which you, I believe, stated
21 could be also characterized as a diluent
22 or a carrier, correct?

23 A. So, excipients is a broad class
24 of materials that are considered

25

1 non-actives.

2 Q. Okay.

3 A. That we can use in our dosage
4 form. For example -- and diluent carriers
5 are one broad classification of
6 excipients, but there's many others.

7 So excipients is the large
8 group, and diluent carriers are a small --
9 small group underneath that.

10 Q. Understood. Thank you for the
11 clarification.

12 For the purposes of our
13 discussion, I'm going to characterize the
14 stage we just discussed earlier about
15 analyzing the physicochemical properties
16 of the API as the knowledge step.

17 Is that fine with you?

18 A. Sure. I mean, I think about it
19 as preformulation, but...

20 Q. Preformulation, I'll go with
21 that.

22 So, once you've completed
23 preformulation, if an excipient is
24 necessary for the goal of the project, how
25

1 would you go about deciding which
2 excipient to use?

3 MS. SCHWARZ: Objection to form.

4 A. So, you know what you're trying
5 to make. Let's say -- let's say we know
6 we want to make a tablet. I don't know of
7 a tablet that's made of pure API. Maybe
8 there is one, but it's not common.

9 So, and let's say that we
10 understand that this drug from our
11 preformulation work may have stability
12 issues if water's involved, and let's say
13 we're dosing it at a very small dose, so,
14 you know, one milligram. So, all of those
15 factors would say, well, you probably
16 don't want a wet granulate because that
17 would expose it to water. You want to
18 make sure -- one issue that is really
19 important to us and to places like the FDA
20 is that the right amount of drug is in
21 every dosage form. And so when you're
22 making a tablet that contains a really
23 small amount, that's a harder problem to
24 make sure that every dosage form has one
25

1 milligram is a lot harder than to make
2 sure every dosage form has a hundred
3 milligrams. There's just very little room
4 for error and your mixing has to be
5 really, really, really good. And we can
6 probably all relate to that from cooking
7 and making sure everything is well mixed.

8 So, when you need to make sure
9 things are well mixed, there's a number of
10 different ways to do it, but often we
11 granulate and it's a combination of mixing
12 and making granules.

13 Well, we don't want a wet
14 granulate potentially in my hypothetical
15 because we've got stability problems. So
16 we're thinking okay, we might want a dry
17 granulate. So what I've done now is I
18 said I'm going to make an immediate
19 release tablet, it's dry granulation, it's
20 low dose. And so I've started to form a
21 little bit about what this tablet has to
22 do, so. And so this is going to inform my
23 selection of excipient types. So it's low
24 dose, so the majority of the tablet is

25

1 going to be made up of a carrier or a
2 diluent or a filler. Those terms are used
3 fairly synonymously in this area. And I'm
4 going to need a dry -- a compound that
5 functions as a binder to hold these -- so,
6 granulates are really just bigger
7 particles with the smaller powder stuck in
8 it into a granule. And so I'm going to
9 need something that functions as a dry
10 binder so it works well. I don't need a
11 wet glue; I need a dry binder. So that
12 helps inform what kind of binder I need.

13 I'm making a -- an immediate
14 release tablet, and so that means I want
15 it to fall apart quickly, so I want a
16 disintegrant in there. I'm making a
17 tablet on a tablet press and the tooling
18 is metal, and we always put a lubricant,
19 the most common one is magnesium stearate,
20 at a small level. So right there I've,
21 kind of, defined in my simple example, you
22 know, several classes of excipients that I
23 care about.

24 So now that I know that, the
25

1 typical thing that's done next is
2 excipient compatibility; so are the
3 excipients compatible physically and
4 chemically with my drug? And there's a
5 number of different ways to do that. And
6 different organizations do things
7 differently, but one way is we do binary
8 mixtures, so API and excipient.

9 So let's say microcrystalline
10 cellulose, which is a commonly used
11 diluent or filler, or lactose, those are
12 both very commonly used. So let's just
13 say I think, well, you know, I'm probably
14 going to use at least one of those. I'm
15 going to make binary mixtures of drug and
16 MCC, mix it up real well, and put it in an
17 oven or something to accelerate how fast
18 we might see either a physical or a
19 chemical change. So we don't really want
20 to wait around for two years at ambient
21 temperature to see what happens. So we
22 put things in ovens and give them humidity
23 challenges because these tend to be
24 harsher treatments. So I want to have a
25

1 choice of -- of -- of carriers, so I might
2 want to put up several of these in each
3 category. So I've got three or four
4 different fillers maybe. And then I do
5 the same thing, I won't go through it ad
6 nauseam, with my binders, with my
7 disintegrants. And you pull those and you
8 look for drug degradation for chemical
9 stability and any physical changes, did
10 the drug deliquesce, you know, turn into a
11 puddle. Hard to formulate when you're
12 trying to make a solid oral dosage form
13 when something's a liquid.

14 Q. Sure.

15 A. Was there a form change. Did it
16 change -- that could be it changed from
17 crystallin to a different crystal form.
18 It could be amorphous. It could be -- so
19 anyway, some physical change, or both.
20 And so we look at that, and that helps
21 inform our -- and that's one way to do
22 excipient compatibility. Other people
23 just make formulations of different
24 flavors and -- and bake that. And there's
25

1 pros and cons, and I don't think we need
2 to go into all that.

3 But suffice it to say once
4 you've done this, you have a better idea
5 of which excipients will work with your
6 compound.

7 Q. Okay.

8 You mentioned that -- let me
9 take a step back.

10 How do you determine which
11 exemplary excipients you use in order to
12 do the compatibility testing?

13 MS. SCHWARZ: Objection to form.

14 A. So, you -- I, kind of, took you
15 through the example of we're making an
16 immediate release tablet, and so I told
17 you, okay, that's how we -- that informs
18 which categories I need, and then within
19 those, that -- that helps you also inform
20 which of those might -- might work.

21 We also have -- I would say
22 there's some of these excipients, mag
23 stearate as a lube is a really good
24 example. There's a couple other lubes we
25

1 use, but really only if there's an issue
2 with mag stearate, but I would say mag
3 stearate is in 90 percent of the data
4 formulations out there.

5 Q. Okay.

6 So it seems like you have, would
7 it be fair to say that you have, kind of,
8 your baseline set that you would use in
9 order to do the compatibility testing
10 under each of the categories that you
11 mentioned earlier?

12 MS. SCHWARZ: Objection to form.

13 A. So, this is where I don't think
14 everyone's going to have the exact same
15 set. There's going to be some
16 commonalities.

17 Q. Okay.

18 A. I think everyone would consider
19 mag stearate, you know, for example, as
20 the lube. So there's going to be some
21 commonalities. And then there's just --
22 and in some cases, there's really only
23 three to five disintegrants, say, that
24 people use. So it's easy to screen them

25

1 all, or most of them.

2 So depending on which category,
3 I would say there's definitely some --
4 some go-tos as you start to get to
5 something like I need to add a
6 solubilizer. Well, that's very specific
7 to your molecule, and is that an acid
8 because it's more soluble in acid? Is it
9 a base because it's more soluble there?
10 Or is it a lipid because it needs that?
11 You know, so then you're starting to get
12 into a much wider range.

13 But in the basic example that I
14 gave you with a -- I would say, you know,
15 there's a hand -- five to ten excipients
16 in each category that are common -- very
17 commonly used.

18 Q. Okay.

19 Is it fair to assume that
20 carriers are considered a category in the
21 list of categories that you provided
22 earlier that you do excipient
23 compatibility with?

24 A. Yeah, car --

25

1 MS. SCHWARZ: Objection to form.

2 A. Yeah, carrier, diluent, filler,
3 whatever you call it.

4 Q. Is there a resource that you use
5 that provides a listing of approved
6 diluents or carriers --

7 A. Yes.

8 Q. -- to be used as excipients?
9 Yes.

10 What is that resource?

11 A. Handbook of Pharmaceutical
12 Excipients.

13 Q. I'm going to take a step back.
14 It helps me to understand if I can
15 communicate it to you. Then we can
16 confirm, and hopefully my understanding is
17 correct.

18 So, in my hypothetical when I
19 said the client would come to you with a
20 specific API and ask you to assist them in
21 formulating the composition for that API,
22 the general steps taken would be to
23 identify the goals of the project. That
24 would be the first step, correct?

25

1 A. You know, every -- every program
2 goes a little bit differently. But yes, I
3 think it's important to understand the
4 goal. And so, yeah, that's a reasonable
5 first step.

6 Q. Okay.

7 And then generally the next step
8 would be to take a look at the
9 physicochemical properties of the drug or
10 the API which we've labeled as the
11 preformulation stage. Is that correct?

12 MS. SCHWARZ: Objection to form.

13 A. It -- you would want -- need to
14 do that work unless it had already been
15 done for some reason, yes.

16 Q. Sure.

17 And then based on your
18 understanding from the preformulation
19 stage of the specific physicochemical
20 properties of the API, you would then
21 determine or conduct some sort of
22 excipient compatibility testing to
23 determine which excipients would be --
24 would meet the goals of the specific

25

1 project. Is that fair?

2 MS. SCHWARZ: Objection to the
3 form.

4 A. I think you left out a step.

5 Q. Okay.

6 What's the step I left out?

7 A. It was really once you have the
8 goal and the physicochemical properties of
9 the drug, then it's what are my options.

10 Q. Okay.

11 A. For -- for -- you know, so now
12 you're designing I'm going to make an
13 immediate release tablet with dry
14 granulation, and so that helps inform what
15 kinds of excipients you need.

16 Q. And that would be the options
17 you mentioned would be the dosage form
18 options?

19 A. Yeah, what -- what's my dosage
20 form options? Am I going to granulate?
21 Helps put some definition to my process as
22 well and what I'm trying to make and I'm
23 considering the dose I'm trying to
24 deliver. All those factors.

25

1 Q. Okay.

2 A. Because you don't know how to
3 pick your excipients until you know what
4 kind of dosage form you're trying to make.

5 Q. Understood. Thank you for the
6 clarification.

7 So after you've determined which
8 option you've picked of the different
9 types of dosage forms and the various
10 considerations you just mentioned, you
11 would then move on to excipient
12 compatibility testing?

13 MS. SCHWARZ: Objection to the
14 form.

15 A. That's how it's commonly done.

16 Q. In determining which excipients
17 to use in the compatibility testing, you
18 would reference the Handbook of
19 Pharmaceutical Excipients. Is that fair?

20 MS. SCHWARZ: Objection to form.

21 A. That is a reference you can use
22 if you need to.

23 I think a formulator who's been
24 doing this also has their experience and
25

1 knowledge, so probably isn't always
2 running to the Handbook of Pharmaceutical
3 Excipients.

4 Q. Fair.

5 Would it be fair to say that at
6 each stage of this formulation process,
7 stages 1, 2, 3 and 4, we've discussed four
8 stages at least, the choices for
9 excipients to be used for a specific API
10 would narrow at each stage?

11 MS. SCHWARZ: Objection to form.

12 A. I don't really see it that way.

13 Q. Why not?

14 A. So at -- certainly there is some
15 narrowing at places. But for example, at
16 the excipient compatibility stage you're
17 going big, right, and you're -- you're --
18 you're looking at that.

19 You're also further down that we
20 haven't talked about, part of the reason
21 you're going big initially is not
22 everything works out as planned, and so
23 maybe something looked pretty good
24 initially, but it doesn't. So now you
25

1 have some options to go back to. So you
2 have to blow it back up again and look at
3 other things, and maybe one change
4 precipitates the need for another change.

5 So I guess I don't necessarily
6 look at it as a process of narrowing. I
7 do look at it as a process of better
8 definition of options for your dosage
9 form, but pretty frequently we're in an
10 iterative loop and sometimes you go back
11 to excipient compatibility if, you know,
12 things are problematic. So I don't
13 completely look at it as this linear
14 marching-down-a-funnel process.

15 Q. You said that at the excipient
16 compatibility stage you may go big. Is
17 that right?

18 A. Yeah.

19 Q. How big is big?

20 MS. SCHWARZ: Objection to form.

21 A. I've seen people screen 20 to 50
22 excipients, you know, on the high end.

23 Q. What's the typical number of
24 excipients used for screening?

25

1 MS. SCHWARZ: Objection to form.

2 A. If I had to hazard a guess, I've
3 never counted them, I would say some
4 number between 10 and 20 is pretty common.

5 Q. So, going back to my question
6 about narrowing. I appreciate what you
7 said. Thank you.

8 Would it be fair to say that
9 step 2, the preformulation stage when
10 we're understanding the physicochemical
11 properties of the API, that stage would
12 then inform which options you would choose
13 at stage 3 which are the dosage form
14 option stage?

15 A. Some of those, but also some of
16 it comes from and what's the dose, for
17 example.

18 Q. Sure.

19 A. So, and, you know, what kind of
20 dosage form are we trying to achieve? Is
21 this something that's ready for prime
22 time, or are we just going to, kind of,
23 make a few?

24 So, I -- I really think it's
25

1 the, as I stated before, it's the
2 combination of knowing what it is you're
3 trying to make and the physicochemical
4 properties of the drug.

5 Q. But would it be fair to say that
6 there would be certain dosage options or
7 forms that you would not use based on the
8 results of your preformulation stage
9 analysis?

10 MS. SCHWARZ: Objection to form.

11 A. I'm sorry, could you -- could
12 you say that again?

13 Q. Yeah.

14 So we were discussing that
15 there's various different types of dosage
16 form options, right?

17 A. Yes.

18 Q. And if you understood the
19 physicochemical properties of a specific
20 API that you were working with and then
21 you went to go look at the different
22 dosage form options, the full scope, are
23 there any that, based on the
24 physicochemical properties, are there any
25

1 that you would not use? Would you cancel
2 some out, I guess I should say?

3 MS. SCHWARZ: Objection to form.

4 A. In that hypothetical, the answer
5 is it depends what the results are. It
6 may look -- you know, maybe everything's
7 an option.

8 Q. Okay.

9 A. You know, it has no water
10 sensitivity. It's not super low dose,
11 doesn't have any solubility issues.
12 What -- whatever it is. Boy, we could
13 make this from a wide range of different
14 options.

15 Q. But in your example, if there
16 are solubility issues, that would remove
17 certain dosage form options from the
18 listing of possibilities for that specific
19 API, right?

20 MS. SCHWARZ: Objection to form.

21 A. So, it may remove some, but it
22 probably adds others.

23 So, I would say more complex
24 technologies that you're not thinking
25

1 about at first blush, but if you determine
2 that you have an extreme solubility
3 problem, you may need to look at more
4 advanced technologies that, you know,
5 you're not going to do unless you have to.
6 So originally you don't really have these
7 on the table until you really see a need,
8 and then you might go deep into that. So
9 you may add a whole host of things that
10 you weren't thinking about before.

11 Q. Okay.

12 So would it be fair to say that
13 the properties of the API would dictate
14 which dosage form you may move forward
15 with of all of the options?

16 MS. SCHWARZ: Objection to form.

17 A. I feel like I've answered this
18 already, and it's a combination of the
19 properties of the API and what you're
20 trying to make inform what might be your
21 options.

22 And then, you know, there's a
23 whole host of considerations in choosing
24 which of those you go forward with. Do I
25

1 have access to that equipment?

2 Q. Right.

3 A. Can I make it at that scale? Do
4 I have enough API to run both? Blah,
5 blah, blah.

6 So there's all sorts of
7 considerations in picking out which your
8 dosage form option or options that you
9 actually pursue.

10 Q. The physicochemical properties
11 of the API would be one of them, right?

12 A. That's fair.

13 MS. SCHWARZ: Would this be a
14 good time to take a break?

15 MS. BURGNER: Sure.

16 (Recess taken.)

17 BY MS. BURGNER:

18 Q. Two quick follow-up questions to
19 what we were discussing early, Dr. Appel.

20 You mentioned the Handbook of
21 Pharmaceutical Excipients. That
22 existed -- did you use the Handbook of
23 Pharmaceutical Excipients when you were
24 at -- when you were a senior research

25

1 chemist back in 1999?

2 A. Probably, but I don't recall.

3 Q. Was it available then?

4 A. I don't know when the first
5 edition was.

6 Q. Have you used it throughout the
7 course of your career?

8 A. Yes.

9 Q. Are there any regulations about
10 what can be used as an excipient in a
11 pharmaceutical composition?

12 MS. SCHWARZ: Objection to form;
13 outside the scope of the expert's
14 declarations.

15 A. So, you just asked a really
16 broad question. So what should I assume
17 about that pharmaceutical composition?
18 What -- what's it -- yeah.

19 Q. Maybe take hopefully a more
20 efficient approach.

21 The Handbook of Pharmaceutical
22 Excipients, is that just a listing of
23 FDA-approved pharmaceutical excipients as
24 of the publication of that edition?

25

1 A. It's not quite like that. It's
2 not just FDA. There's a number of -- you
3 know, there's EU regulatory bodies and
4 Japanese.

5 So each -- each excipient has a
6 monograph, and it tells you which
7 pharmacopeias accept it, or if it's USP or
8 JP or EU.

9 So, but generally it is a
10 compilation of excipients that are okay to
11 use dosage forms for -- by some regulatory
12 body, including -- I mean, it -- it's
13 really -- I don't exactly know how it
14 works with FDA and USP and, you know, who
15 exactly does what, but that they're okay
16 to use in human dosage forms.

17 Q. What does USP mean?

18 A. US Pharmacopeia.

19 Q. And is that a regulatory body
20 that determines what's okay to use in
21 U.S., dosage forms used in the U.S.?

22 MS. SCHWARZ: Objection to form.

23 A. I don't know if it's considered
24 a regulatory body. It's certainly an

25

1 organization.

2 Q. So what's their purpose?

3 MS. SCHWARZ: Objection to form;
4 outside the scope of the expert's
5 declarations.

6 A. I don't know their purpose.

7 Q. Do you know how US Pharmacopeia
8 differs at all from the FDA?

9 MS. SCHWARZ: Same objections.

10 A. The FDA is -- is a regulatory
11 body.

12 USP does things like tell you
13 how to run your dissolution tests and have
14 methods. And, you know, they're certainly
15 both used in the industry, but
16 differently, and I don't -- I'm not an
17 expert on the difference between the USP
18 and the FDA and all those things. There's
19 kind of a regulatory component here.

20 Q. So the Handbook of
21 Pharmaceutical Excipients, is it fair to
22 say that that includes excipients that are
23 approved and not approved of by the FDA?

24 MS. SCHWARZ: Objection to form.

25

1 BY MS. BURGNER:

2 Q. Let me ask that differently.

3 Would the Handbook of

4 Pharmaceutical Excipients include

5 excipients that are not approved by the

6 FDA for use in the United States?

7 A. I don't know.

8 MS. SCHWARZ: Objection to form;

9 outside the scope of the expert's

10 declarations.

11 BY MS. BURGNER:

12 Q. So I guess looking beyond the

13 Handbook of Pharmaceutical Excipients, how

14 would you know in developing a formulation

15 for a client which excipients would be

16 permitted for use in the United States or

17 not?

18 MS. SCHWARZ: Objection to form;

19 outside the scope of the expert's

20 declarations.

21 A. So, outside of the excipient

22 handbook, which will tell you if there's a

23 USP version of it, in which case you know

24 you can use it.

25

1 Q. Okay.

2 A. But also the FDA has an inactive
3 ingredients database that you can use
4 that's updated.

5 There's probably other sources
6 as well.

7 Q. Any that you can think of, any
8 of those other sources that you can think
9 of off the top of your head?

10 A. Not right now.

11 Q. So, in our earlier discussion we
12 discussed excipient compatibility testing,
13 correct?

14 A. Yes.

15 Q. Are there any other types of
16 testing that you would do to determine
17 which excipients you would use in a
18 specific formulation?

19 MS. SCHWARZ: Objection to form.

20 A. There may be.

21 Q. What are those types of
22 testings?

23 A. Depends on the dosage form
24 you're trying to make.

25

1 Q. Okay. We were discussing oral
2 solid dosage forms.

3 What types of additional testing
4 would you do in that instance?

5 A. It's still a very broad
6 category, and there's lots of different
7 kinds and lots of different behaviors you
8 might want to determine, so.

9 Q. Could you just give me maybe one
10 or two examples of the types of tests?

11 A. You might want to understand if
12 both the API and a particular excipient go
13 into solution in the same solvent. So
14 they're both acetone soluble or something
15 like that.

16 Q. Generally how long would it take
17 for you to determine the final formulation
18 for a specific API?

19 MS. SCHWARZ: Objection to form.

20 A. What do you mean by "final"?

21 Q. Commercial.

22 A. And where are you starting?

23 Q. If you were given, let's say
24 we're still in the hypothetical that I
25

1 gave before where you were given a
2 specific API and your client said, We'd
3 like to create an oral solid dosage form
4 for this, please proceed.

5 How long would it take from that
6 stage?

7 A. So --

8 MS. SCHWARZ: Objection to form.

9 A. -- really hard question with a
10 wide range depending on the program.

11 Q. What's the range, in your
12 experience?

13 A. Is this an NCE?

14 Q. What does NCE mean?

15 A. New chemical entity.

16 Q. Let's assume that it is.

17 A. So that means it's not on the
18 market already in some other form.

19 Q. Correct.

20 A. So that's going to take longer,
21 often, than something that's already on
22 the market in another -- in a form.

23 It really depends on the
24 clinical program 'cause it advances along
25

1 with the clinical program. Maybe, highly
2 variable, maybe five to ten years.

3 Q. What about for a product that is
4 not an NCE?

5 A. Well, at the extreme we could
6 look at the generics, and they go pretty
7 fast. I've never formulated for a
8 generic, so I didn't know the exact, but I
9 think it's something like a year to two
10 years.

11 Q. Okay. I just have a few
12 questions about some specific paragraphs
13 in your declaration. So if you can take a
14 look at that again, that would be great.

15 If we could flip to paragraph 8,
16 which in theory is the next paragraph that
17 we're discussing.

18 Here starting on the second line
19 you say that, or starting at the top: My
20 areas of expertise include development and
21 application of drug delivery technology,
22 including formulation and process
23 development for oral solid dosage forms.

24 Is that correct?

25

1 A. That's what it says.

2 Q. Curious what is the difference,
3 in your opinion, between formulation and
4 process development?

5 A. To me the formulation is the
6 ingredients and the amounts of those
7 ingredients in a particular dosage form.
8 So it's defining that.

9 And the process is the process
10 used to make that, so the specific pieces
11 of equipment and their settings, how long
12 do you mix for, that kind of thing.

13 Q. Okay. If we can flip to
14 paragraph 21.

15 Are you there?

16 A. Yes.

17 Q. Okay. Starting on the fourth
18 line down of paragraph 21, the declaration
19 states: The '334 patent cites Remington's
20 as an example of a source describing
21 formulations that were well-known and
22 readily available to those in the art.

23 Is that correct?

24 A. That's what it says.

25

1 Q. Then it goes on to say that:
2 Remington's was and still is an
3 authoritative and well-known reference on
4 the science and practice of pharmacy,
5 including pharmaceutical information and
6 manufacturing.

7 Correct?

8 A. I think -- what I heard you just
9 say was "pharmaceutical information and
10 manufacturing."

11 What it says is "pharmaceutical
12 formulation and manufacturing."

13 Q. With that correction, that's an
14 accurate -- I'll just re-read it.

15 It states: Remington's was and
16 still is an authoritative and well-known
17 reference on the science and practice of
18 pharmacy, including pharmaceutical
19 formulation and manufacturing.

20 Correct?

21 A. Correct.

22 Q. And then you go on to reference
23 both the 1995 version of Remington's and
24 the 2012 version of Remington's, correct?

25

1 A. Correct.

2 Q. And on to the next page you say
3 that -- would it be fair to say that your
4 understanding is that what's disclosed in
5 Remington's 2012 includes the --
6 essentially the same disclosure as
7 Remington's 1995?

8 MS. SCHWARZ: Objection to form;
9 mischaracterizes the document.

10 A. Yeah, I mean, the words say what
11 they say.

12 Remington's 2012 includes
13 essentially the same disclosure as
14 Remington's 1995. They make some updates
15 and things. But it's essentially the same
16 disclosure.

17 Q. Okay. Thank you for the
18 clarification.

19 So, when you state that
20 Remington's is an example of a source
21 describing formulations, is that different
22 than what's included in the Handbook of
23 Pharmaceutical Excipients we discussed
24 earlier?

25

1 A. Yes.

2 Q. How so?

3 A. Remington's is more like a
4 textbook with sections talking about
5 various subject matter.

6 The Handbook of Pharmaceutical
7 Excipients consists of a section on each
8 excipient and some data on that excipient,
9 who makes it, what its particle size is,
10 those kinds of things, some technical
11 descriptors.

12 So they're quite different.

13 Q. Do you ever reference
14 Remington's when assisting clients to
15 formulate or develop pharmaceutical
16 compositions?

17 A. I think I have, but I don't
18 recall specifics.

19 Q. How would one use Remington's to
20 inform or assist with developing a
21 specific pharmaceutical formulation?

22 MS. SCHWARZ: Objection to form.

23 A. Remington's is a general
24 reference that talks about specific types
25

1 of dosage forms and specific processes,
2 let's say the discussion about wet versus
3 dry granulation, something like that. So
4 it's a nice general overview of -- of
5 potential options, for example, for
6 processes.

7 Q. Would it be helpful to
8 identify --

9 MS. BURGNER: I should take a
10 step back.

11 Q. Would Remington's be helpful in
12 identifying excipients to use when
13 determining a specific formulation?

14 MS. SCHWARZ: Objection to form.

15 A. It certainly has -- has
16 excipients that it talks about. I
17 wouldn't -- it's not encyclopedic in the
18 way the Handbook of Pharmaceutical
19 Excipients is, but it has -- it talks
20 about a number of excipients and that are
21 useful.

22 Q. Does it talk about when you
23 would pick a specific excipient versus
24 another excipient?

25

1 MS. SCHWARZ: Objection to form.

2 A. I don't recall.

3 Q. Okay. If you can flip to
4 paragraph 36.

5 Are you there?

6 A. Yes.

7 Q. Do you see in paragraph 36 where
8 it states: The same formulation
9 strategies, technologies, and processes
10 would have been considered and used for
11 APIs not in a co-crystal as would be used
12 for different types of multiple component
13 co-crystals?

14 A. I see that.

15 Q. What are the formulation
16 strategies you mentioned here?

17 A. It's meant to be general.
18 You -- you'd consider the same things.
19 It's meant to be general.

20 Q. Right. But what do you mean by
21 "formulation strategies" as used in this
22 sentence?

23 A. Oh, okay.

24 So let's say that, go back to
25

1 the example where the API has sensitivity
2 to water for some reason; either
3 physically or chemically it causes
4 something negative to happen. So you
5 would use the same kinds of formulation
6 strategies around -- with a
7 multiple-component crystal than you would
8 with an API that's not a co-crystal to
9 mitigate that risk.

10 Q. I understand that. I guess I'm
11 trying to take one step back of what you
12 mean by formulation strategy.

13 Like what falls under the scope
14 of a formulation strategy as used in this
15 sentence?

16 A. It's broad and encompasses
17 really what strategy would you use to
18 formulate a particular active given the
19 goals of the project and the properties of
20 the API.

21 Q. Are those the same types of
22 strategies we discussed earlier with that
23 four-step process?

24 MS. SCHWARZ: Objection to form.

25

1 A. I don't remember the number of
2 steps, but when we went -- when we talked
3 about it before, we were talking about
4 starting a project with a goal, getting
5 some data on the molecule and then
6 figuring out what different formulations
7 you could do and then getting started, and
8 I think the first step we talked about was
9 excipient compatibility.

10 So if that's what you mean by
11 four, yeah, I think that's, you know, the
12 beginning of -- of that would -- would
13 mirror, or those would be the -- would be
14 very similar with a co-crystal or a
15 multi-component crystal as an API that is
16 not in a co-crystal.

17 Q. Are there any ways that those
18 processes would be dissimilar if there was
19 a co-crystal or multiple-component crystal
20 of an API or if the API was not in a
21 co-crystal?

22 MS. SCHWARZ: Objection to form.

23 A. Not that I can think of as we
24 sit here.

25

1 Q. The next sentence in paragraph
2 36 states: The formulator considers the
3 specific physicochemical properties of the
4 API and other factors to inform the
5 selection of a dosage form type, the
6 excipients used and the processes used to
7 make the dosage form.

8 Correct?

9 A. That's what it says.

10 Q. I think we discussed earlier
11 looking at the physicochemical properties
12 as part of the preformulation process. Is
13 that right?

14 A. So, you look at the specific
15 physicochemical properties of the API.
16 You determine them if they're not already
17 known in a process call -- in a stage of
18 development called preformulation.

19 Q. Okay.

20 What are the physicochemical
21 properties that you determine in
22 preformulation?

23 MS. SCHWARZ: Objection to form.

24 A. I think I've already answered
25

1 this. I gave examples of things like pH
2 solubility profile, LogP, pKa, melting
3 point, glass transition temperature,
4 particle size, distribution, and many
5 others. So those are just examples, and
6 they may differ depending on what you're
7 thinking about making.

8 Q. Okay.

9 And what are the other factors
10 that you mentioned beyond the
11 physicochemical properties that would
12 inform the selection?

13 A. The goals of the project, the
14 dose, what -- what kind of -- do you want
15 controlled release, do you want immediate
16 release, do you want delayed release.
17 Those kinds of things.

18 Q. Okay, that's helpful. Thank
19 you.

20 At the very end it states, the
21 last sentence of paragraph 36 it states:
22 It would have been the skill of the
23 ordinary formulator to select an
24 appropriate strategy depending on such
25

1 properties.

2 Is that right?

3 A. That's what it says.

4 Q. Would the appropriate strategy
5 for the API change if the API was in
6 co-crystal form?

7 MS. SCHWARZ: Objection to form.

8 A. Not -- not that I can see.

9 Q. Okay.

10 If we can turn to paragraph 42,
11 and it will be just before paragraph 43.
12 So we're on page 22 of your declaration.

13 A. Okay.

14 Q. The last sentence states: The
15 Hickey investigators concluded that it
16 seems reasonable to assert that co-crystal
17 approaches should be considered routinely
18 as part of a broader set of form and
19 formulation explorations to strive for the
20 best possible drug products.

21 Correct?

22 A. That's what it says.

23 Q. Do you know what the co-crystal
24 approaches are as referenced here?

25

1 MS. SCHWARZ: Objection to form.

2 A. I would want to go back and look
3 at the Hickey reference to make sure that,
4 you know, I understand exactly where this
5 comes in.

6 Q. And that you would also want to
7 look at Hickey, I'm assuming, to determine
8 what the broader set of form and
9 formulation explorations would be?

10 A. I think that's fair.

11 Q. If we could look at paragraph
12 51.

13 A. I'm there.

14 Q. And it states: A POSA would
15 know the types and identities of
16 well-known formulation methods for making
17 pharmaceutical compositions which would
18 have been used to prepare pharmaceutical
19 composition comprising a multiple-component
20 crystal that included a drug substance in
21 a pharmaceutically accepted carrier.

22 Correct?

23 A. That's what it says.

24 Q. What are the well-known
25

1 formulation methods used to prepare a
2 pharmaceutical composition you mention
3 here?

4 A. What I'd like to do is look at
5 the patent, 'cause it's really the patent
6 that brings in this, and see what it -- it
7 says there.

8 Q. Is there any --

9 A. And so, there are references
10 here to the patent. There are references
11 to Remington's, to some specific sections,
12 and, you know, I don't recall what --
13 which exact methodologies are taught in
14 which exact reference. So I just wouldn't
15 mind seeing the references to answer that.

16 Q. So sitting here today, you can't
17 list any of the well-known formulation
18 methods without referencing the patent or
19 Remington's 2012. Is that correct?

20 MS. SCHWARZ: Objection to form;
21 mischaracterizes the witness's
22 testimony.

23 A. I didn't say can't.

24 I would say I prefer to look at

25

1 the references.

2 Q. Are there any that you can list
3 right now without looking at the
4 references?

5 A. None that I choose to do so
6 with.

7 Q. Would a POSA, in your opinion,
8 look at anything else beyond the patent or
9 Remington's 2012 in determining a
10 formulation method for a particular API?

11 MS. SCHWARZ: Objection to form.

12 A. You say "look at anything else."
13 Are -- are you --

14 Q. Reference.

15 A. Can you tell me what you mean by
16 that?

17 Q. Reference.

18 MS. SCHWARZ: Objection to form.

19 A. They might. There's other texts
20 that cover the same kinds of things that
21 Remington's does.

22 Q. What are the other texts?

23 A. I'm not recalling names right
24 now, but there's more than one textbook on
25

1 the subject.

2 Q. Taking kind of a broader step
3 back.

4 Would any of the opinions that
5 we've discussed today or that you've
6 provided today change if considered in the
7 context of 2002 or 2003 rather than 2014?

8 MS. SCHWARZ: Objection to form;
9 outside the scope of the expert's
10 declarations.

11 A. That's not something I was asked
12 to consider. I'm not comfortable just
13 opining on that without thinking about it
14 more.

15 Q. Would you have taken the same
16 strategies and approaches that we've
17 discussed today with respect to
18 formulation in 2002 and 2003 as you would
19 in 2014?

20 MS. SCHWARZ: Same objections.

21 A. That's not something that I've
22 considered, and I'm not comfortable just
23 opining on the spot on that.

24 Q. Have your approaches to
25

1 formulation changed from when you worked
2 as the director of controlled release at
3 Bend Research to now?

4 MS. SCHWARZ: Objection to form.

5 A. I'm sorry, have my approaches?
6 I'm sorry, what -- has what changed?

7 Q. The steps that we had discussed
8 earlier about formulation. If a client
9 comes to you and asks you to formulate --

10 MS. BURGENER: Let me take a
11 step back.

12 Q. If a client asked you in 2002 to
13 formulate a drug using a specific API,
14 would the steps you have taken to do that
15 then be the steps you would have taken to
16 do that now?

17 MS. SCHWARZ: Objection to form.

18 A. Not in any significant way that
19 I can think of sitting here right now.

20 Q. They haven't changed?

21 A. They have not changed.

22 Q. If you could turn to paragraph
23 14 of the declaration. Let me know when
24 you're there.

25

1 A. I am there.

2 Q. Here you state that you
3 understand that obviousness is analyzed
4 from the perspective of a POSA as of the
5 date of the invention, correct?

6 A. I see that, yes.

7 Q. And in parentheses after
8 "invention" it says here "2014."
9 Correct?

10 A. Correct.

11 Q. Is it fair to assume you
12 understand the date of the invention of
13 the '344 patent to have a priority date of
14 2014?

15 A. That's my understanding.

16 MS. SCHWARZ: Objection to form.

17 THE WITNESS: Sorry.

18 A. That's my understanding.

19 Q. Why is that your understanding?

20 MS. SCHWARZ: Objection to form;
21 calls for a legal conclusion.

22 A. So, if we go to paragraph 3 and
23 I think that's the second sentence: I
24 have been asked to perform my analysis as
25

1 of February 13, 2014 from the perspective
2 of an ordinary formulator.

3 So because -- and that --
4 there's a footnote there, footnote 1 that
5 says I understand from petitioner's
6 counsel that February 13th, 2014 is the
7 filing date of the U.S. patent, the '862
8 application that issued at the '344
9 patent.

10 So I think that summarizes.

11 Q. So you didn't do any independent
12 analysis to confirm that date, correct?

13 A. That's correct.

14 Q. If we can -- sorry, I know I'm
15 making you traverse your declaration quite
16 heavily, but if we can flip to paragraph
17 30. Let me know when you're there. And
18 it will be the portion that's on page 16.

19 A. Okay, I'm there.

20 Q. At the bottom of the paragraph
21 it says: As of 2014, I had at least
22 ordinary experience in formulation of oral
23 solid dosage form pharmaceutical
24 compositions (i.e. at least the experience
25

1 of someone with whom the POSA would
2 consult and the formulator POSA.)

3 Is that correct?

4 A. That's what it says.

5 Q. Do you agree with that
6 statement?

7 A. Yes.

8 Q. Would the same have been true in
9 2002?

10 MS. SCHWARZ: Objection to form.

11 A. Yes.

12 Q. And also in 2003, I'm assuming?

13 A. Yes.

14 MS. BURGNER: Okay.

15 I think we can take a break, ten
16 minutes or so.

17 (Recess taken.)

18 BY MS. BURGNER:

19 Q. Dr. Appel, when choosing an
20 excipient, you would limit your choices to
21 those that are approved by the FDA,
22 correct?

23 MS. SCHWARZ: Objection to form;
24 lack of foundation.

25

1 A. When choosing an excipient for
2 what?

3 Q. So, in our hypothetical that we
4 discussed earlier, if you were given an
5 API and you were trying to determine the
6 correct formulation for the API, given the
7 goals of the project, when choosing
8 excipients to do compatibility testing for
9 for that API, you would limit the
10 excipients to those that are approved by
11 the FDA, correct?

12 MS. SCHWARZ: Same objections.

13 A. Generally I would choose
14 excipients that are deemed acceptable for
15 use in humans in pharmaceutical
16 formulations.

17 There may be exceptions to that.
18 We may be looking at new excipients that
19 aren't quite approved yet but have some
20 advantage so.

21 But generally that's correct.

22 Q. Okay.

23 If we could turn to paragraph 8
24 of your declaration, it's the last
25

1 sentence on page 7.

2 A. I'm confused. Paragraph 8, the
3 last sentence of --

4 Q. Should be on page 7.

5 A. Okay, got it. Thank you.

6 Q. Let me know when you're there.

7 A. I am.

8 Q. Okay.

9 The last sentence states: I am
10 familiar with formulating multiple
11 component crystals as defined in paragraph
12 20 below into pharmaceutical compositions.

13 Correct?

14 A. Correct.

15 Q. What is your experience with
16 formulating multiple component crystals
17 into pharmaceutical compositions?

18 A. I've formulated -- I've
19 formulated them into pharmaceutical dosage
20 forms. I've worked on programs where that
21 was part of the program.

22 Q. Where the API was a multiple
23 component crystal?

24 A. As defined in paragraph 20
25

1 below, yes.

2 Q. Are you able to estimate how
3 many times you've done that over the
4 course of your career?

5 A. That would be difficult. I've
6 formulated literally hundreds of
7 molecules.

8 Q. All of which were multiple
9 component crystals as defined in paragraph
10 20, or just a subset?

11 A. Just a subset.

12 Q. As an estimate, what portion of
13 the hundreds of molecules that you've
14 formulated would have been multiple
15 component crystals?

16 A. I wouldn't want to venture a
17 guess.

18 Q. More than half?

19 A. You know, I formulated molecules
20 starting in 1988. I don't -- I mean, I
21 just don't remember all these, so I really
22 don't want to guess.

23 Q. Okay.

24 Let's flip two pages, I believe,
25

1 to paragraph 18.

2 A. Okay.

3 Q. Second to the last line of that
4 paragraph you reference "additional
5 hurdles associated with formulating a
6 commercially viable pharmaceutical
7 product."

8 Is that correct?

9 A. That's what it says.

10 Q. What are those additional
11 hurdles?

12 A. So, we talked about early phase
13 development, and maybe you're just trying
14 to get a read on a really simple
15 formulation, so you don't care about
16 long-term stability or good
17 manufacturability, whether you could scale
18 it up, that kind of thing. So those would
19 be the additional hurdles, those kinds of
20 things.

21 Q. Okay.

22 A. And there's many others too, but
23 those are two examples.

24 Q. If we could revisit paragraph 51

25

1 of your declaration.

2 A. Okay. I'm at the bottom on page
3 25.

4 Q. Right.

5 You've testified today that you
6 believe you are a POSA as of 2014,
7 correct?

8 A. That -- that's correct.

9 Q. And you state in paragraph 51
10 that: A POSA would know the types and
11 identities of well-known formulation
12 methods for making pharmaceutical
13 compositions.

14 Correct?

15 A. I'm just reading the rest of the
16 sentence --

17 Q. Sure.

18 A. -- for context.

19 Yes, that's what I state.

20 Q. So as a POSA, are you able to
21 identify any of the well-known formulation
22 methods you reference here today?

23 A. I certainly am able to. I
24 think, you know, before what I was trying
25

1 to do here is look at specifically what
2 Remington's taught. I guess that's what's
3 referenced here.

4 Q. Outside of what Remington's
5 teaches, however, just in your knowledge
6 as a POSA, what are the well-known
7 formulation methods?

8 A. Some -- so, two commonly used
9 oral solid dosage forms are capsules and
10 tablets. Commonly used processes to get
11 there include direct compression, various
12 types of granulation, both wet and dry,
13 compression, for example.

14 Q. Any other formulation methods?

15 A. There are other ones, but, you
16 know, generally at a high level for making
17 those, that covers a good part of them.

18 Q. And would the same well-known
19 formulation methods have applied in 2014
20 as in 2002 and 2003?

21 MS. SCHWARZ: Objection to form;
22 outside the scope of the expert's
23 declarations.

24 A. The ones I just listed existed
25

1 in, I'm sorry, what year?

2 Q. 2002 to 2003.

3 A. In that time frame.

4 Q. Dr. Appel, are you aware of
5 other declarations submitted by other
6 experts in these IPRs?

7 A. I assume that somebody else is
8 opining on some of the things I'm not, but
9 I'm not -- any more than that, I'm not
10 aware.

11 Q. So, assuming your assumption is
12 correct, have you read the report -- have
13 you read a report or talked to any other
14 expert related to that declaration?

15 A. I have not read any other
16 declarations other than my own.

17 Q. Dr. Appel, throughout your
18 declaration you state that you assumed
19 that certain co-crystals, or that certain
20 molecules were co-crystals, specifically
21 those discussed in Almarsson and Hickey.

22 Is that correct?

23 A. Is there somewhere you want to
24 point me to in my report? And I just want
25

1 to understand the context.

2 Q. Paragraph 39, for example. Let
3 me know when you're there.

4 A. I'm here.

5 Q. At the top it says. Coumadin,
6 which I have been asked to assume is a
7 co-crystal of warfarin sodium.

8 Do you see that?

9 A. I do.

10 Q. Did you do any independent
11 analysis to determine whether Coumadin is
12 a co-crystal of warfarin sodium?

13 A. No.

14 Q. If you go down to paragraph 40,
15 a similar sentence there says, apologies
16 for my pronunciation but: Vibramycin
17 Hyclate, which I have been asked to assume
18 is a co-crystal of doxycycline hyclate.

19 Do you see that?

20 A. I do.

21 Q. Did you do any independent
22 analysis to determine whether Vibramycin
23 Hyclate is a co-crystal of doxycycline
24 hyclate?

25

1 A. I did not.

2 Q. Would the same answer apply for
3 the Amoxil discussed in paragraph 41 of
4 your declaration?

5 A. Yes.

6 Q. During the breaks today, did you
7 talk about the substance of your testimony
8 with counsel?

9 A. No.

10 MS. BURGENER: All right.

11 Counsel, I think I'm all set.

12 MS. SCHWARZ: Can we go off the
13 record, and we'll see if we have any
14 redirect?

15 MS. BURGENER: Sure.

16 (Recess taken.)

17 EXAMINATION BY

18 MS. SCHWARZ:

19 Q. Dr. Appel, you were asked
20 earlier about paragraph 14 of
21 Exhibit 1003.

22 A. Yes.

23 Q. And in connection with this
24 discussion which references the date 2014,
25

1 you were also asked about paragraph 3 of
2 your declaration and footnote 1.

3 A. Yes.

4 Q. Did you do any analysis of
5 whether the subject matter of any claims
6 of the '344 patent have written
7 description or enablement support in the
8 '862 application filed in February 2014?

9 A. I did not.

10 Q. You were also asked earlier
11 about excipient compatibility testing.

12 Do you recall that?

13 A. Yes.

14 Q. What is the purpose of excipient
15 compatibility testing?

16 A. It's really a risk mitigation
17 step to try to rule out excipients that
18 may cause a -- an issue with that API so
19 you don't find out two or three months
20 down the road that, oops, I shouldn't have
21 chosen that.

22 Q. When you say "an issue with that
23 API," what do you mean by that?

24 A. Stability. For example, the
25

1 chemical stability of the API may be
2 adversely affected by that excipient.

3 Q. If you're preparing a solid oral
4 dosage formulation that will not be
5 stored, is excipient compatibility testing
6 required?

7 A. No, it's definitely not
8 required. There's for -- yeah, no.

9 Q. For a solid oral dosage
10 formulation that will be used in animals,
11 is excipient compatibility testing
12 required?

13 A. No.

14 Q. For a solid oral dosage
15 formulation that's going to be used in
16 animals, is preformulation testing
17 required?

18 A. No.

19 Q. Are there instances where you're
20 preparing a solid oral dosage formulation
21 for use in humans and excipient
22 compatibility testing is not required?

23 A. Like I said, it's a -- it's a
24 risk mitigation strategy, and you may be
25 willing to accept the risk if, for

1 example, you're not going to store the
2 material for very long, you're going to
3 make this there's something called
4 extemporaneous prep where the clinical
5 site is essentially co-housed with the
6 formulation lab. So they make things,
7 like a compounding pharmacy kind of thing
8 and dosage forms and then go right next
9 store and dose them to a person, and in
10 that case, there's essentially no storage
11 of it. So there is certainly no -- no
12 requirement for excipient compatibility.

13 Q. If you were pursuing a solid
14 oral dosage form for use in animals, do
15 you need to use FDA-approved excipients in
16 that situation?

17 A. No.

18 MS. SCHWARZ: Thank you, Dr.
19 Appel. I don't have any further
20 questions.

21 MS. BURGNER: Just give me five
22 minutes for us to decide if there's
23 anything else.

24 MS. SCHWARZ: Sure.

25 (Recess taken.)

1 FURTHER EXAMINATION

2 BY MS. BURGNER:

3 Q. Dr. Appel, if we can turn to
4 paragraph 36 of your declaration.

5 A. Yes.

6 Q. I'm at the bottom of page 18.

7 A. Okay.

8 Q. It states: The formulator
9 considers the specific physical chemical
10 properties of the API and other factors to
11 inform the selection of a dosage form
12 type, the excipients to use, and the
13 processes used to make the dosage form.

14 Correct?

15 A. That's correct.

16 Q. Is that still your testimony
17 today?

18 A. Yeah, that -- that's the common
19 practice.

20 MS. BURGNER: Okay. That's it
21 for me.

22 MS. SCHWARZ: Nothing further
23 from us. Thank you.

24 (Deposition adjourned at
25 approximately 12:00 p.m. EDT)

1 C E R T I F I C A T E

2 I, MARIE FOLEY, Registered Merit
3 Reporter, Certified Realtime Reporter, and
4 Notary Public for the State of New York,
do hereby certify that prior to the
5 commencement of the examination,
LEAH APPEL, PH.D., was duly sworn by me to
6 testify to the truth, the whole truth and
nothing but the truth.

7 I DO FURTHER CERTIFY that the foregoing
is a verbatim transcript of the testimony
8 as taken stenographically by me at the time,
place and on the date hereinbefore set forth,
9 to the best of my ability.

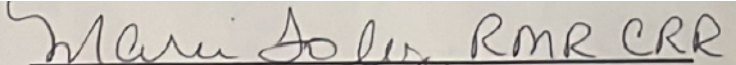
10 I DO FURTHER CERTIFY that I am neither
11 a relative nor employee nor attorney nor
12 counsel of any of the parties to this action,
13 and that I am neither a relative nor employee
14 of such attorney or counsel, and that I am
15 not financially interested in the action.

16

17

18

19

20  RMR CRR

21 COURT REPORTER

22 Registered Merit Reporter

23 Certified Realtime Reporter

24 Notary Public

25 Dated: May 14, 2024

1 Leah Appel, Ph.D., c/o

2 VENABLE, LLP

3 151 West 42nd Street, 49th Floor

4 New York, New York 10036

5

6 Case: Novartis Pharmaceuticals Corporation v. Regents of the University of
Michigan et al.

7 Date of deposition: May 8, 2024

8 Deponent: Leah Appel, Ph.D.

9

10 Please be advised that the transcript in the above
11 referenced matter is now complete and ready for signature.

12 The deponent may come to this office to sign the transcript,
13 a copy may be purchased for the witness to review and sign,
14 or the deponent and/or counsel may waive the option of
15 signing. Please advise us of the option selected.

16 Please forward the errata sheet and the original signed
17 signature page to counsel noticing the deposition, noting the
18 applicable time period allowed for such by the governing
19 Rules of Procedure. If you have any questions, please do
20 not hesitate to call our office at (202)-232-0646.

21

Sincerely,

22 Digital Evidence Group

23 Copyright 2024 Digital Evidence Group

24 Copying is forbidden, including electronically, absent

25 express written consent.

1 Digital Evidence Group, L.L.C.

2 1730 M Street, NW, Suite 812

3 Washington, D.C. 20036

4 (202) 232-0646

5

6 SIGNATURE PAGE

7 Case: Novartis Pharmaceuticals Corporation v. Regents of the University of
Michigan et al.

8 Witness Name: Leah Appel, Ph.D.

9 Deposition Date: May 8, 2024

10

11 I do hereby acknowledge that I have read
12 and examined the foregoing pages
13 of the transcript of my deposition and that:

14

15 (Check appropriate box):

() The same is a true, correct and
16 complete transcription of the answers given by
me to the questions therein recorded.

17 () Except for the changes noted in the
attached Errata Sheet, the same is a true,
18 correct and complete transcription of the
answers given by me to the questions therein
19 recorded.

20

DATE

WITNESS SIGNATURE

21

22

23

24

DATE

NOTARY

25

1 Digital Evidence Group, LLC
2 1730 M Street, NW, Suite 812
3 Washington, D.C. 20036
4 (202)232-0646
5

6 ERRATA SHEET
7

8 Case: Novartis Pharmaceuticals Corporation v. Regents of the University of
Michigan et al.

9 Witness Name: Leah Appel, Ph.D.

10 Deposition Date: May 8, 2024

11 Page No. Line No. Change
12
13
14
15
16
17
18
19
20
21
22
23

24 _____
25 Signature Date

A				
a.m 1:16 2:3 5:2	affirm 5:8	40:7 43:8 48:20	area 25:19 27:1	back-up 37:21
ability 99:9	afford 37:23	48:21 49:10,20	42:3	bake 44:24
able 9:5 34:22	agree 85:5	52:9 54:11	areas 28:13 66:20	Ballpark 20:16
88:2 90:20,23	ahead 36:16	55:20 56:19	art 67:22	base 47:9
absent 100:24	al 100:6 101:7	57:13,19 58:4	asked 17:17 19:7	based 8:22 31:15
Absolutely 11:1	102:8	58:11 64:12,18	59:15 81:11	49:17 55:7,23
absorption 36:3	ALEXIS 3:6	65:2 73:1,8,20	82:12 83:24	baseline 46:8
accelerate 43:17	allowed 100:18	74:15,20,20	93:6,17 94:19	basic 47:13
accept 60:7 96:25	Almarsson 92:21	75:4,15 77:5,5	95:1,10	basically 23:6,17
acceptable 17:11	ambient 43:20	80:10 82:13	asking 6:11	24:3 28:7
18:12 86:14	amorphous 37:11	86:5,6,9 87:22	asks 82:9	batch 34:10
accepted 78:21	44:18	95:18,23 96:1	assert 77:16	beginning 74:12
access 58:1	amorphous-ba...	98:10	assist 48:20 70:20	behalf 3:3,13
accurate 10:8,14	37:12	APIs 30:2,4,6	assisting 70:14	12:24 13:7
68:14	amount 17:12	72:11	associated 89:5	behaviors 64:7
acetone 64:14	18:14 34:15	apologies 93:15	assume 11:3	believe 17:6
achieve 54:20	40:20,23	APPEAL 1:2	47:19 59:16	38:20 88:24
acid 47:7,8	amounts 24:15	Appel 1:14 2:1	65:16 83:11	90:6
acknowledge	67:6	4:3,11 5:15,22	92:7 93:6,17	Bend 6:1 27:16
101:11	Amoxil 94:3	5:24 15:8,14	assumed 92:18	27:22 28:1,3
action 99:12,15	analyses 19:3	58:19 85:19	assuming 21:19	30:12,16 31:16
active 23:17,19	analysis 17:16,21	92:4,17 94:19	78:7 85:12	82:3
24:23 73:18	55:9 83:24	97:19 98:3 99:5	92:11	best 9:3 77:20
actives 23:11	84:12 93:11,22	100:1,8 101:8	assumption	99:9
activities 25:15	95:4	102:9	92:11	better 15:2 22:13
ad 44:5	analyze 19:7	applicable	attached 101:17	45:4 53:7
add 37:9 47:5	analyzed 83:3	100:18	attorney 12:14	beyond 14:17
57:9	analyzing 39:15	application 21:16	12:16 13:16	62:12 76:10
additional 64:3	and/or 100:14	66:21 84:8 95:8	16:22 99:11,14	80:8
89:4,10,19	animal 28:18	applied 91:19	August 16:4	big 52:17,21
address 5:23	animals 96:10,16	apply 19:23 22:5	authoritative	53:16,19,19
addressed 33:6	97:14	94:2	68:3,16	bigger 42:6
adds 56:22	answer 11:2,14	appreciate 54:6	available 59:3	binary 43:7,15
adjourned 98:24	12:17,17 56:4	approach 37:21	67:22	binder 24:10
admonitions 10:1	79:15 94:2	37:22,23 59:20	Avenue 3:17	42:5,10,11,12
advance 28:24	answered 57:17	approaches	avoid 12:4	binders 44:6
29:18	75:24	77:17,24 81:16	aware 10:16 92:4	bit 22:13 27:4
advanced 28:16	answers 10:7	81:24 82:5	92:10	32:23 41:21
28:22 30:19	101:16,18	appropriate		49:2
57:4	anyway 44:19	76:24 77:4		blah 58:4,5,5
advances 65:24	apart 42:15	101:15	B	blow 53:2
advancing 31:11	API 23:9,18	approved 48:5	B 4:9	blush 57:1
advantage 86:20	25:10,16 29:7	61:23,23 62:5	back 9:10 19:13	BOARD 1:2
adversely 96:2	30:13 32:7	85:21 86:10,19	21:1 22:9 45:9	bodies 60:3
advise 100:15	33:18,19 34:16	approximately	48:13 53:1,2,10	body 60:12,19,24
advised 100:10	36:5,13,14 37:2	6:13 98:25	54:5 59:1 71:10	61:11
	37:24 39:16	arbitration 7:8	72:24 73:11	bottom 15:20
			78:2 81:3 82:11	

84:20 90:2 98:6 box 101:15 Boy 37:6 56:12 break 11:12,16 58:14 85:15 breaks 11:21 94:6 Brian 3:23 bring 12:20 brings 79:6 broad 26:23 38:23 39:5 59:16 64:5 73:16 broader 77:18 78:8 81:2 BURGNER 3:15 4:4,6 5:21 11:19 15:1,12 18:2 58:15,17 62:1,11 71:9 82:10 85:14,18 94:10,15 97:21 98:2,20 Burgener@fr.c... 3:20 business 7:10	30:21 capabilities 27:5 capsule 31:3 37:3 capsules 24:3 91:9 car 47:24 care 34:6,7,9,11 34:13,14 42:23 89:15 career 59:7 88:4 carrier 17:11 18:13 24:9 38:22 42:1 48:2 78:21 carriers 39:4,8 44:1 47:20 48:6 case 1:5 15:19 18:17 62:23 97:10 100:6 101:7 102:8 cases 9:1 46:22 categories 45:18 46:10 47:21 category 44:3 47:2,16,20 64:6 cause 65:24 79:5 95:18 causes 73:3 cellulose 43:10 CEO 31:20 certain 55:6 56:17 92:19,19 certainly 13:6 14:16 16:16 31:1,6 52:14 60:24 61:14 71:15 90:23 97:11 Certified 2:5 99:3 99:23 certify 99:4,7,10 challenges 43:23 change 26:4 43:19 44:15,16 44:19 53:3,4 77:5 81:6 102:11	changed 44:16 82:1,6,20,21 changes 10:17 44:9 101:17 characterize 39:13 characterized 38:21 Check 101:15 chemical 43:19 44:8 65:15 96:1 98:9 chemically 33:2 43:4 73:3 chemist 23:1,5 26:2 59:1 choice 44:1 choices 52:8 85:20 choose 54:12 80:5 86:13 choosing 57:23 85:19 86:1,7 chosen 38:1 95:21 CHRISTINA 3:5 cited 21:19 cites 67:19 claim 7:22 8:4 14:6,20 17:22 18:11,19 19:1 claims 13:23 14:2 14:8,12,15 17:17 18:16,18 95:5 clarification 39:11 51:6 69:18 clarifies 18:22 clarify 11:8 14:22 class 38:23 classes 42:22 classification 39:5 clearly 12:1,3 client 33:7,17 34:2 48:19	62:15 65:2 82:8 82:12 clients 33:21 70:14 clinic 32:10 34:12 clinical 28:20 33:4 34:21 65:24 66:1 97:4 closed 26:18 closer 29:3 co-crystal 17:12 18:14 72:11 73:8 74:14,16 74:19,21 77:6 77:16,23 93:7 93:12,18,23 co-crystals 9:13 9:18 72:13 92:19,20 co-housed 97:5 collaborative 28:15 combination 41:11 55:2 57:18 come 48:19 100:12 comes 33:17 54:16 78:5 82:9 comfortable 81:12,22 commencement 99:5 commencing 2:3 commercial 29:4 31:13 33:3 34:8 64:21 commercializat... 28:21 31:11 32:20 commercially 89:6 common 40:8 42:19 47:16 54:4 98:18 commonalities 46:16,21	commonly 43:10 43:12 47:17 51:15 91:8,10 communicate 48:15 companies 7:9 29:12,20 32:3 company 27:6 28:4 37:20 compatibility 43:2 44:22 45:12 46:9 47:23 49:22 51:12,17 52:16 53:11,16 63:12 74:9 86:8 95:11 95:15 96:5,11 96:22 97:12 compatible 43:3 compilation 60:10 complete 10:8,14 100:11 101:16 101:18 completed 39:22 completely 53:13 complex 56:23 component 61:19 72:12 87:11,16 87:23 88:9,15 composition 17:9 18:11,19 48:21 59:11,17 78:19 79:2 compositions 70:16 78:17 84:24 87:12,17 90:13 compound 37:6 42:4 45:6 compounding 97:7 compounds 29:14 compress 24:20 compression 91:11,13
C C 3:1 99:1,1 c/o 100:1 CALDWELL 3:15 call 34:5 36:4 38:16 48:3 75:17 100:20 called 7:7 24:11 35:13 36:8 75:18 97:3 calls 83:21 cancel 56:1 candidate 28:24 29:6,19,23 30:19 candidates 28:16 28:23 29:15 30:2,3,5,13,20				

comprising 17:10 18:12 78:19	copy 100:13 Copying 100:24 Copyright 100:23 corner 15:21 Corporation 1:4 22:19,23 26:11 100:6 101:7 102:8 correct 7:21 13:11,12 14:21 15:23 19:17 21:10,11,14,17 21:20,21 22:18 22:20 26:12 27:11 38:22 48:17,24 49:11 63:13 65:19 66:24 67:23 68:7,20,21,24 69:1 75:8 77:21 78:22 79:19 83:5,9,10 84:12 84:13 85:3,22 86:6,11,21 87:13,14 89:8 90:7,8,14 92:12 92:22 98:14,15 101:15,18 correction 68:13 Coumadin 93:5 93:11 counsel 16:17 84:6 94:8,11 99:12,14 100:14,17 counted 54:3 couple 45:24 course 18:6 59:7 88:4 court 12:5 99:21 cover 14:19 80:20 covers 91:17 create 25:8 65:3 creating 24:5 CRR 1:21 crystal 44:17	73:7 74:15,19 78:20 87:23 crystallin 44:17 crystals 87:11,16 88:9,15 Cschwarz@ve... 3:10 Curious 67:2	defined 42:21 87:11,24 88:9 defining 67:8 definitely 47:3 96:7 definition 50:21 53:8 degradation 44:8 delayed 76:16 deliquesce 44:10 deliver 50:24 delivery 23:7 27:1,3 32:8 66:21 denote 4:18 dependent 18:15 20:4 depending 37:16 37:20 47:2 65:10 76:6,24 depends 56:5 63:23 65:23 deponent 100:8 100:12,14 deposed 6:2 deposition 1:13 2:1 6:12,16 7:5 9:1 10:3,22 11:8 12:15,21 98:24 100:7,17 101:9,13 102:10 depositions 6:8 6:19 7:2 8:11 9:17,24 describing 67:20 69:21 description 4:10 95:7 descriptors 70:11 designing 50:12 determine 36:11 45:10 49:21,23 57:1 63:16 64:8 64:17 75:16,21 78:7 86:5 93:11 93:22	determined 51:7 determines 60:20 determining 51:16 71:13 80:9 develop 28:13 32:3,7 70:15 developed 28:15 developing 25:11 62:14 70:20 development 28:11,19 29:3 29:24 30:18 31:12 32:2 66:20,23 67:4 75:18 89:13 dictate 57:13 differ 76:6 difference 61:17 67:2 differences 13:14 13:22 14:11 different 13:20 14:1,9 22:16 27:6 34:18 35:24 37:15 41:10 43:5,6 44:4,17,23 51:8 55:15,21 56:13 64:6,7 69:21 70:12 72:12 74:6 differently 33:12 43:7 49:2 61:16 62:2 differs 61:8 difficult 88:5 Digital 1:23 100:22,23 101:1 102:1 diluent 38:21 39:4,8 42:2 43:11 48:2 diluents 48:6 direct 26:6 91:11 director 27:15 28:1 82:2
--	--	--	--	--

disagreement 7:8	56:17 57:14	31:13 32:9,10	100:22,23	62:4,5,13,15
disclosed 69:4	58:8 60:11,16	58:19 89:12	101:1 102:1	63:17 69:23
disclosure 69:6	60:21 63:23	easy 46:24	exact 4:19 13:4	70:7 71:12,16
69:13,16	64:2 65:3 66:23	edition 59:5,24	46:14 66:8	71:19,20 75:6
discussed 13:24	67:7 71:1 75:5	EDT 1:16 2:3	79:13,14	86:8,10,14,18
14:3 38:5 39:14	75:7 84:23	98:25	exactly 6:5 28:5	95:17 97:15
52:7 63:12	87:19 91:9 96:4	effective 17:12	60:13,15 78:4	98:12
69:23 73:22	96:9,14,20 97:8	18:13	examination 4:3	exclusively 28:9
75:10 81:5,17	97:14 98:11,13	efficiency 20:12	5:20 94:17 98:1	exemplary 45:11
82:7 86:4 92:21	dose 32:12 40:13	efficient 59:20	99:5	Exhibit 4:12 15:6
94:3	41:20,24 50:23	effort 16:16	examined 5:18	15:7 94:21
discussing 19:15	54:16 56:10	28:15	101:12	exhibits 4:16
55:14 58:19	76:14 97:9	either 14:3 19:4	example 6:9	21:18
64:1 66:17	dosing 40:13	43:18 73:2	23:24 29:8 39:4	existed 58:22
discussion 39:13	doxycycline 93:18	electronically	42:21 45:15,24	91:24
63:11 71:2	93:23	100:24	46:19 47:13	experience 22:14
94:24	Dr 5:22 15:14	EMAIL 3:10,20	52:15 54:17	35:19,24 51:24
disintegrant 24:9	58:19 85:19	employee 99:11	56:15 67:20	65:12 84:22,24
42:16	92:4,17 94:19	99:13	69:20 71:5 73:1	87:15
disintegrants	97:18 98:3	enablement 95:7	91:13 93:2	experiences
44:7 46:23	drug 23:7 24:6	encompasses	95:24 97:1	22:16
Disney 26:24	27:1,3 35:11	73:16	examples 36:10	expert 7:19,20
dissimilar 74:18	40:10,20 43:4	encyclopedia	64:10 76:1,5	61:17 92:14
dissolution 61:13	43:15 44:8,10	71:17	89:23	expert's 59:13
dissolve 37:7	49:9 50:9 55:4	ended 23:1	exceptions 86:17	61:4 62:9,19
distinct 14:15	66:21 77:20	energy 37:13	excipient 39:23	81:9 91:22
distribution 76:4	78:20 82:13	entity 65:15	40:2 41:23 43:2	expertise 25:20
Doctor 5:5	drugs 23:6,14	equipment 58:1	43:8 44:22	32:2 66:20
document 4:19	31:11 32:4	67:11	47:22 49:22	experts 16:24
15:15 69:9	35:21	errata 100:16	51:11 52:16	92:6
documents 12:21	dry 41:16,19 42:4	101:17 102:6	53:11,15 59:10	explain 23:13
22:5	42:9,11 50:13	error 41:4	60:5 62:21	explorations
dogs 31:4	71:3 91:12	ESQUIRE 3:5,6	63:12 64:12	77:19 78:9
doing 33:11	duly 5:16 99:5	3:15,16	70:8,8 71:23,24	expose 40:17
51:24		essentially 69:6	74:9 85:20 86:1	express 100:25
dosage 23:21,21		69:13,15 97:5	95:11,14 96:2,5	extemporaneous
23:22,24 24:1,2	E	97:10	96:11,21 97:12	97:4
24:5,6,8 25:1,8	E 3:1,1 4:9 99:1,1	estimate 8:7 16:9	excipients 24:11	extreme 57:2
25:9 29:4 30:23	earlier 25:13	88:2,12	38:20,23 39:6,7	66:5
31:2,6,9 32:8	38:19 39:14	estimation 8:15	42:22 43:3 45:5	
32:14,18 33:19	46:11 47:22	et 100:6 101:7	45:11,22 47:15	F
34:5 35:2,16	63:11 69:24	102:8	48:8,12 49:23	F 99:1
39:3 40:21,24	73:22 75:10	EU 60:3,8	50:15 51:3,16	factors 40:15
41:2 44:12	82:8 86:4 94:20	everybody 11:23	51:19 52:3,9	50:24 75:4 76:9
50:17,19 51:4,9	95:10	everyone's 46:14	53:22,24 58:21	98:10
53:8 54:13,20	earliest 22:15	everything's 56:6	58:23 59:22,23	fair 11:5,6,17
55:6,15,22	early 20:17 28:18	Evidence 1:23	60:10 61:21,22	18:24 19:20
	28:18,19 30:17			

20:6 27:12 46:7 47:19 50:1 51:19 52:4,5 54:8 55:5 57:12 58:12 61:21 69:3 78:10 83:11 fairly 42:3 fall 42:15 falls 73:13 familiar 87:10 fast 34:3,12 43:17 66:7 FDA 40:19 60:2 60:14 61:8,10 61:18,23 62:6 63:2 85:21 86:11 FDA-approved 59:23 97:15 February 84:1,6 95:8 feel 57:17 fellow 23:2 26:5 figured 27:7 figuring 74:6 file 21:12,15 filed 95:8 filing 84:7 filler 24:8 42:2 43:11 48:2 fillers 44:4 final 64:17,20 financially 99:15 find 20:8 95:19 fine 20:16 38:18 39:17 finish 36:20 first 5:16 6:12 11:15 15:21 20:14 22:17 28:17 31:9 33:24 48:24 49:5 57:1 59:4 74:8 FISH 3:14 fit-for-purpose	34:5 five 46:23 47:15 66:2 97:21 flavors 44:24 flip 66:15 67:13 72:3 84:16 88:24 Floor 3:7 100:3 FLORIDA 1:8 focus 17:15 18:23 19:3 28:13 Foley 1:21 2:4 99:2 follow 25:6 follow-up 25:22 36:21 58:18 follows 5:19 footnote 84:4,4 95:2 forbidden 100:24 foregoing 99:7 101:12 form 9:14,19 14:13 17:23 19:5 20:2 23:21 23:21 24:5,6,8 25:1 29:4 30:23 31:2,6,10 32:8 32:18 33:19,23 34:5 35:2 37:13 38:10 39:4 40:3 40:21,24 41:2 41:20 44:12,15 44:17 45:13 46:12 48:1 49:12 50:3,17 50:20 51:4,14 51:20 52:11 53:9,20 54:1,13 54:20 55:10,16 55:22 56:3,17 56:20 57:14,16 58:8 59:12 60:22 61:3,24 62:8,18 63:19 63:23 64:19 65:3,8,18,22	67:7 69:8 70:22 71:14 72:1 73:24 74:22 75:5,7,23 77:6 77:7,18 78:1,8 79:20 80:11,18 81:8 82:4,17 83:16,20 84:23 85:10,23 91:21 97:14 98:11,13 formal 29:19 formalities 20:24 forms 23:22,24 24:1,2 25:8,9 32:14 35:16 51:9 55:7 60:11 60:16,21 64:2 66:23 71:1 87:20 91:9 97:8 formulate 25:7 33:19 44:11 70:15 73:18 82:9,13 formulated 23:6 66:7 87:18,19 88:6,14,19 formulating 23:14,20 48:21 87:10,16 89:5 formulation 24:23 25:9 28:19 30:18 32:1 38:2 52:6 62:14 63:18 64:17 66:22 67:3,5 68:12,19 70:21 71:13 72:8,15,21 73:5 73:12,14 77:19 78:9,16 79:1,17 80:10 81:18 82:1,8 84:22 86:6 89:15 90:11,21 91:7 91:14,19 96:4 96:10,15,20 97:6	formulations 9:18 44:23 46:4 67:21 69:21 74:6 86:16 formulator 51:23 75:2 76:23 84:2 85:2 98:8 forth 99:8 forward 57:14,24 100:16 found 26:19 foundation 85:24 founded 31:17 four 44:3 52:7 74:11 four-step 73:23 fourth 67:17 frame 6:23 92:3 Frequency 6:18 frequent 11:20 frequently 53:9 full 5:23 30:16 55:22 function 35:23 functions 42:5,9 further 22:10 29:2 52:19 97:19 98:1,22 99:7,10	97:21 given 6:7 9:23 20:7 25:10 64:23 65:1 73:18 86:4,6 101:16,18 giving 10:14 glass 76:3 glue 42:11 go 9:10,22 33:20 35:1 36:16 37:10 39:20 40:1 44:5 45:2 53:1,10,16 55:21 57:8,24 64:12 66:6 68:22 72:24 78:2 83:22 93:14 94:12 97:8 go-tos 47:4 goal 35:9 36:22 38:6,14 39:24 49:4 50:8 74:4 goals 34:1 48:23 49:24 73:19 76:13 86:7 goes 29:24 49:2 68:1 going 8:19 9:22 11:3 12:2 21:1 22:9 24:1 37:7 39:13 41:18,22 42:1,4,8 43:14 43:15 46:14,15 46:20 48:13 50:12,20 52:17 52:21 54:5,22 57:5 65:20 96:15 97:1,2 good 35:4,5 37:4 41:5 45:23 52:23 58:14 89:16 91:17 Gosh 6:20 governing 100:18 granulate 24:18
--	--	--	---	--

40:16 41:11,14 41:17 50:20 granulates 42:6 granulation 41:19 50:14 71:3 91:12 granule 42:8 granules 41:12 great 66:14 Green 31:17,20 31:24 grind 37:8 group 1:23 39:8,9 100:22,23 101:1 102:1 guess 6:21 8:8 14:10 53:5 54:2 56:2 62:12 73:10 88:17,22 91:2 guys 32:16 33:9	71:7,11 76:18 helping 33:20 helps 42:12 44:20 45:19 48:14 50:14,21 hereinbefore 99:8 hesitate 100:20 hey 32:6 33:10 Hickey 77:15 78:3,7 92:21 high 53:22 91:16 higher 37:13 highlighted 17:8 18:17 19:1 highlighting 17:14 highly 37:1 66:1 history 21:12,15 hold 42:5 honestly 24:14 hope 34:22 hopefully 18:22 48:16 59:19 host 57:9,23 human 60:16 humans 86:15 96:21 humidity 43:22 hundred 41:2 hundreds 34:10 88:6,13 hurdles 89:5,11 89:19 hyclate 93:17,18 93:23,24 hydrophilic 36:6 hypothetical 41:14 48:18 56:4 64:24 86:3	19:16 identification 15:10 identify 9:5 48:23 71:8 90:21 identifying 71:12 identities 78:15 90:11 immediate 24:7 41:18 42:13 45:16 50:13 76:15 impact 36:1,2,3 important 35:22 40:19 49:3 inactive 63:2 include 22:1 62:4 66:20 91:11 included 19:2 69:22 78:20 includes 61:22 69:5,12 including 25:1 29:12 60:12 66:22 68:5,18 100:24 independent 84:11 93:10,21 INDEX 4:1 industry 17:2 28:9 61:15 inform 41:22 42:12 44:21 45:19 50:14 54:12 57:20 70:20 75:4 76:12 98:11 information 68:5 68:9 informs 45:17 infringement 8:20,22 9:7 ingredient 23:18 24:4 ingredients 24:13 24:15 25:2 63:3 67:6,7	initially 52:21,24 instance 64:4 instances 96:19 instructs 12:16 intentional 11:23 Inter 4:13 15:9 interest 27:4 interested 99:15 INTERx 22:18 22:22 26:4,17 introduce 15:2 invalidity 8:12,14 8:17 9:7 invention 83:5,8 83:12 investigators 77:15 involved 25:13 25:15 30:11 40:12 ionized 36:9 IPR 1:5 13:1,7 15:22 17:20 20:18,22 22:7 IPRs 92:6 issue 8:24 21:9 32:24 33:5 40:18 46:1 95:18,22 issued 84:8 issues 32:22 33:5 40:12 56:11,16 iterative 53:10	kind 10:1 20:9 25:6 27:3,6 29:18 32:5 35:6 35:8 37:19 42:12,21 45:14 46:7 51:4 54:19 54:22 61:19 67:12 76:14 81:2 89:18 97:7 kinds 23:23 31:10 32:14 33:14 50:15 64:7 70:10 73:5 76:17 80:20 89:19 know 8:1 9:22 10:18,24 11:9 11:23 13:6 14:2 14:4 16:18 18:9 22:12 23:23 25:15,18 28:17 28:18 29:21 30:22,24 31:3 32:9,11,23 34:10,13,20 35:2,3 36:7 37:4,18 38:4,15 38:15 40:4,5,6 40:14 42:22,24 43:13 44:10 46:19 47:11,14 49:1 50:11 51:2 51:3 53:11,22 54:19 56:6,9 57:4,22 59:4 60:3,13,14,23 61:6,7,14 62:7 62:14,23 66:8 74:11 77:23 78:4,15 79:12 82:23 84:14,17 87:6 88:19 90:10,24 91:16 93:3 know-how 7:15 knowing 55:2 knowledge 36:23
H H 4:9 half 88:18 hand 5:7 47:15 handbook 48:11 51:18 52:2 58:20,22 59:21 61:20 62:3,13 62:22 69:22 70:6 71:18 happen 73:4 happens 43:21 hard 44:11 65:9 harder 40:23 41:1 harsher 43:24 hazard 54:2 head 12:11,11 63:9 heard 68:8 heavily 84:16 held 2:2 help 32:3 33:8 37:10 helpful 18:3 25:4	I i.e 84:24 idea 8:6,23 14:5 14:10,11 20:11 27:3 45:4 identical 18:20		J J 3:16 Japanese 60:4 job 26:16,19 joint 16:16 JP 60:8 judge 10:9 justifying 29:21	
			K KANE 3:16 keep 33:1 kilos 34:10	

38:6 39:16 52:1 91:5 known 75:17	liquid 44:13 list 24:15 47:21 79:17 80:2 listed 91:24 listing 48:5 56:18 59:22 literally 88:6 litigation 20:19 litigations 7:3,18 9:12 little 22:13 32:23 41:3,21 49:2 LLC 102:1 LLP 3:4 100:2 loan 32:1 LogP 36:8 76:2 long 64:16 65:5 67:11 97:2 long-term 34:6 89:16 longer 65:20 look 44:8,20 49:8 53:2,6,7,13 55:21 56:6 57:3 66:6,14 75:14 78:2,7,11 79:4 79:24 80:8,12 91:1 looked 26:16 52:23 looking 18:10 27:2 32:12 33:9 52:18 62:12 75:11 80:3 86:18 loop 53:10 lot 17:16 28:6 33:8 41:1 lots 64:6,7 low 41:20,23 56:10 lube 24:10 45:23 46:20 lubes 45:24 lubricant 42:18	M 1:24 3:6 101:2 102:2 mag 45:22 46:2,2 46:19 magnesium 42:19 Maine 3:17 majority 41:24 making 25:23 40:22 41:7,12 42:13,16 45:15 76:7 78:16 84:15 90:12 91:16 man 31:7 34:3 managerial 26:7 managing 31:22 manner 4:16 manufacturabi... 89:17 manufacturing 32:24 68:6,10 68:12,19 marching-dow... 53:14 Marie 1:21 2:4 99:2 marked 15:5,10 market 65:18,22 material 34:15 97:2 materials 21:2 22:5 38:24 matter 70:5 95:5 100:11 MCC 43:16 McJOYNT 3:6 mean 14:14,22 28:22 39:18 60:12,17 64:20 65:14 69:10 72:20 73:12 74:10 80:15 88:20 95:23 means 23:14,17 42:14 65:17 meant 72:17,19	measure 35:15 measurement 36:7 measuring 36:3 mechanical 26:21 medical 10:12 medications 35:21 meet 49:24 meetings 16:17 25:17,18 melting 76:2 memorize 14:4,6 mention 22:18 79:2 mentioned 38:19 45:8 46:11 50:17 51:10 58:20 72:16 76:10 Merck 26:18 29:13 Merit 2:5 99:2,22 metal 42:18 method 80:10 methodologies 79:13 methods 61:14 78:16 79:1,18 90:12,22 91:7 91:14,19 MICHAEL 3:16 Michigan 1:7 100:6 101:7 102:8 microcrystalline 43:9 microelectrical 26:21 milligram 40:14 41:1 milligrams 41:3 mind 23:9 79:15 miniaturized 26:20 27:2 minutes 85:16 97:22	mirror 74:13 mischaracterizes 17:24 69:9 79:21 missing 33:11 mitigate 73:9 mitigation 95:16 96:24 mix 24:20 43:16 67:12 mixed 41:7,9 mixing 41:4,11 mixtures 43:8,15 modifications 34:24 molecule 37:2 38:6 47:7 74:5 molecules 36:24 88:7,13,19 92:20 moment 30:9 money 34:14 monkeys 31:4 monograph 60:6 months 11:21 35:3,4 95:19 move 19:9 20:10 51:11 57:14 moved 31:15 moves 26:10 multi-compone... 74:15 multiple 72:12 87:10,16,22 88:8,14 multiple-comp... 73:7 74:19 78:19
L	M			N
L.L.C 101:1 lab 28:11 97:6 labeled 49:10 lack 85:24 lactose 43:11 language 14:20 17:22 18:9,14 19:1 29:10 large 33:8 39:7 larger 31:4 late 31:13 layperson 13:18 leader 26:11 Leah 1:14 2:1 4:3 4:11 5:15,24 15:8 99:5 100:1 100:8 101:8 102:9 left 27:8 31:16 50:4,6 legal 83:21 let's 6:19 23:9 24:7 40:5,5,9 40:12 43:9,12 64:23 65:16 71:2 72:24 88:24 letting 11:22 level 35:1 42:20 91:16 levels 36:1 licensing 7:12 life 37:4 limit 20:9 85:20 86:9 limited 17:21 20:18 34:15 line 66:18 67:18 89:3 102:11 linear 53:13 lipid 47:10 lipophilic 36:7				N 3:1 name 5:23 29:23 38:17 101:8 102:9 names 80:23 narrow 52:10 narrowing 52:15

53:6 54:6 nauseam 44:6 NCE 65:13,14 66:4 necessarily 4:18 23:8 28:5 53:5 necessary 39:24 need 9:10 11:8,12 11:20 12:1,9 18:5 21:22 33:5 33:24 35:3,5 37:8,9,11 41:8 42:4,9,10,11,12 45:1,18 47:5 49:13 50:15 51:22 53:4 57:3 57:7 97:15 needs 47:10 negative 73:4 neither 99:10,13 never 54:3 66:7 new 1:18,18 2:2,3 3:8,8 5:3,3,18 65:15 86:18 99:4 100:4,4 nice 71:4 nodding 12:10 nomination 29:19 non-actives 39:1 Northcliff 6:1 Northwest 6:1 Notary 2:6 5:17 99:4,24 101:25 NOTE 4:15 noted 101:17 noticed 27:20 noticing 100:17 noting 100:17 Novartis 1:4 3:23 4:11 13:1,7 15:6,7 20:15 100:6 101:7 102:8 number 6:6,7 13:2,3 14:6 21:16 34:17	41:9 43:5 53:23 54:4 60:2 71:20 74:1 numbers 13:5 NW 1:24 101:2 102:2 O oath 10:5 object 12:14 Objection 9:14 9:19 14:13 17:23 19:5 20:2 33:23 38:10 40:3 45:13 46:12 48:1 49:12 50:2 51:13,20 52:11 53:20 54:1 55:10 56:3,20 57:16 59:12 60:22 61:3,24 62:8,18 63:19 64:19 65:8 69:8 70:22 71:14 72:1 73:24 74:22 75:23 77:7 78:1 79:20 80:11,18 81:8 82:4,17 83:16 83:20 85:10,23 91:21 objections 61:9 81:20 86:12 obviousness 83:3 office 1:1 100:12 100:20 Oh 72:23 okay 7:1 8:9 11:11 14:7 17:4 17:8 19:11 20:14,23 21:22 22:9 25:21 29:11 30:10 31:14 33:16 35:18 38:13,18 39:2 41:16 45:7	45:17 46:5,17 47:18 49:6 50:5 50:10 51:1 56:8 57:11 60:10,15 60:20 63:1 64:1 66:11 67:13,17 69:17 72:3,23 75:19 76:8,18 77:9,13 84:19 85:14 86:22 87:5,8 88:23 89:2,21 90:2 98:7,20 once 37:24 39:22 45:3 50:7 ones 29:22 91:15 91:24 oops 95:20 opine 17:18 opining 81:13,23 92:8 opinion 67:3 80:7 opinions 19:22 19:24 81:4 option 51:8 54:14 56:7 58:8 100:14,15 options 37:1,19 50:9,16,18,20 53:1,8 54:12 55:6,16,22 56:14,17 57:15 57:21 58:8 71:5 oral 23:22 31:2 32:8 35:16,21 44:12 64:1 65:3 66:23 84:22 91:9 96:3,9,14 96:20 97:14 order 45:11 46:9 ordinary 76:23 84:2,22 Oregon 6:1 organization 61:1 organizations 32:17 43:6	original 100:16 originally 57:6 outside 16:21 27:4 33:10 59:13 61:4 62:9 62:19,21 81:9 91:4,22 oven 43:17 ovens 43:22 overlap 20:7 overview 71:4 Owners 1:9 P P 3:1,1 P.C 3:14 p.m 98:25 page 4:2,10 15:21 16:1,2 17:6 18:16 19:10 21:3 22:10 69:2 77:12 84:18 87:1,4 90:2 98:6 100:17 101:6 102:11 pages 88:24 101:12 paragraph 17:5 18:10,16 19:10 19:13 21:1 22:10 26:9 31:16 66:15,16 67:14,18 72:4,7 75:1 76:21 77:10,11 78:11 82:22 83:22 84:16,20 86:23 87:2,11,24 88:9 89:1,4,24 90:9 93:2,14 94:3,20 95:1 98:4 paragraphs 19:2 66:12 parentheses 83:7 part 8:1 24:13 25:9 30:18 38:8 38:11 52:20	75:12 77:18 87:21 91:17 Partes 4:13 15:9 particle 37:9 70:9 76:4 particles 42:7 particular 64:12 67:7 73:18 80:10 parties 99:12 partner 31:22 parts 14:16 patent 1:1,2,6,9 7:3,11,13,14 21:8,9,13 67:19 79:5,5,10,18 80:8 83:13 84:7 84:9 95:6 patents 7:17 path 36:19 pending 11:13 people 17:2 28:4 37:20,22 44:22 46:24 53:21 percent 46:3 perform 35:13 83:24 period 100:18 permitted 62:16 person 97:9 perspective 20:13 33:10 35:10 83:4 84:1 pertain 13:19 Petition 4:12 15:9 Petitioner 1:5 petitioner's 84:5 Pfizer 28:9,14 29:13 pH 35:23,24 36:4 36:4,8 76:1 Ph.D 1:14 2:1 4:3 4:12 5:15 15:8 99:5 100:1,8 101:8 102:9 pharma 28:8
--	--	--	---	--

33:8,12 pharmaceutical 9:17 17:9 18:11 18:19 23:18 24:4,24 48:11 51:19 52:2 58:21,23 59:11 59:17,21,23 61:21 62:4,13 68:5,9,11,18 69:23 70:6,15 70:21 71:18 78:17,18 79:2 84:23 86:15 87:12,17,19 89:6 90:12 pharmaceutica... 17:10 18:12 78:21 Pharmaceuticals 1:4 100:6 101:7 102:8 Pharmacopeia 60:18 61:7 pharmacopeias 60:7 pharmacy 68:4 68:18 97:7 phase 29:1,1,1,2 32:9,19,19 89:12 PHONE 3:9,19 physical 43:18 44:9,19 98:9 physically 43:3 73:3 physicochemical 35:11 36:12 37:16 38:7 39:15 49:9,19 50:8 54:10 55:3 55:19,24 58:10 75:3,11,15,20 76:11 pick 51:3 71:23 picked 51:8 picking 58:7	pieces 67:10 pKa 76:2 pKa's 36:9 place 99:8 places 40:19 52:15 PLAINTIFF 3:3 planned 52:22 platform 23:10 platforms 23:8 please 5:7,22 10:17,23 11:9 14:23 65:4 100:10,15,16,19 point 10:21 11:7 18:7 31:8 37:18 76:3 92:24 poorly 37:5 portion 84:18 88:12 portions 19:1 POSA 78:14 80:7 83:4 85:1,2 90:6,10,20 91:6 position 22:22 26:3 positive 34:22 possibilities 56:18 possible 12:2,3 20:10 34:4 77:20 potential 71:5 potentially 41:14 powder 42:7 practice 68:4,17 98:19 precipitates 53:4 prefer 79:24 preformulation 35:14 38:9,12 39:19,20,23 40:11 49:11,18 54:9 55:8 75:12 75:18,22 96:16 pregnant 11:22 prep 97:4	prepare 78:18 79:1 prepared 15:19 16:12,15 preparing 16:7 19:8 21:5 22:2 96:3,20 PRESENT 3:22 press 24:19 42:17 pretty 26:22 52:23 53:9 54:4 66:6 prevent 10:13 previously 15:5 primary 35:19 37:21 prime 54:21 prior 99:4 priority 83:13 probably 20:3,4 36:18 40:15 41:6 43:13 52:1 56:22 59:2 63:5 problem 27:19 28:12 40:23 57:3 problematic 53:12 problems 41:15 Procedure 100:19 proceed 65:4 proceedings 13:1 13:8,10,15 20:19,22 process 24:17,21 25:2,10,12 29:3 29:19 50:21 52:6 53:6,7,14 66:22 67:4,9,9 73:23 75:12,17 processes 71:1,6 72:9 74:18 75:6 91:10 98:13 product 24:24 33:3 34:8 66:3 89:7	products 77:20 profile 36:5 76:2 program 49:1 65:10,24 66:1 87:21 programs 87:20 project 26:10 38:15 39:24 48:23 50:1 73:19 74:4 76:13 86:7 pronunciation 93:16 properties 35:10 35:11 36:12 37:17 38:8 39:15 49:9,20 50:8 54:11 55:4 55:19,24 57:13 57:19 58:10 73:19 75:3,11 75:15,21 76:11 77:1 98:10 proposing 30:12 pros 45:1 provide 8:15 12:9 19:21 provided 9:1,6 13:10 14:19 19:22,24 47:21 81:6 provides 32:1 48:5 Public 2:6 5:17 99:4,24 publication 59:24 puddle 44:11 pull 44:7 pumps 26:20 27:2 punches 32:23 purchased 100:13 pure 24:6 36:14 40:7 purpose 17:13 20:6 61:2,6	95:14 purposes 39:12 pursue 37:21,22 58:9 pursuing 97:13 put 37:2 42:18 43:16,22 44:2 50:21 putting 16:19 Q question 8:20 10:22 11:2,4,13 11:15 14:10 20:5 23:13 36:17 54:5 59:16 65:9 questions 12:15 25:22 36:21 58:18 66:12 97:20 100:19 101:16,18 quick 58:18 quickly 27:6 32:11 42:15 quiet 38:3 quite 6:10 60:1 70:12 84:15 86:19 quotations 4:15 quote 4:19 R R 3:1 99:1 raise 5:6 range 6:7 23:11 26:23 47:12 56:13 65:10,11 rat 31:5 rats 30:24 re-read 68:14 read 4:17 34:3 89:14 92:12,13 92:15 101:11 readily 67:22 reading 90:15 ready 32:20
--	--	---	---	--

54:21 100:11 real 30:23 43:16 really 6:21 17:15 28:11 30:23 31:8 32:1,11 35:15 38:14 40:18,22 41:5,5 41:5 42:6 43:19 45:23 46:1,22 50:7 52:12 54:24 57:6,7 59:15 60:13 65:9,23 73:17 79:5 88:21 89:14 95:16 Realtime 2:6 99:3 99:23 reason 10:12 49:15 52:20 73:2 reasonable 49:4 77:16 recall 6:5 9:15,20 13:4 16:8 17:19 22:3 59:2 70:18 72:2 79:12 95:12 recalling 80:23 Recess 58:16 85:17 94:16 97:25 recipe 24:14 recognize 15:14 recollection 9:2,4 recommend 32:13 record 4:18 5:23 11:10 15:3 94:13 recorded 101:16 101:19 redirect 94:14 reference 51:18 51:21 68:3,17 68:22 70:13,24 78:3 79:14 80:14,17 89:4	90:22 referenced 77:24 91:3 100:11 references 19:12 21:18 79:9,10 79:15 80:1,4 94:24 referencing 79:18 reflect 28:5 reflected 4:16 refrigerator 33:1 regard 7:9 Regents 1:7 100:6 101:7 102:8 Registered 2:5 99:2,22 regulations 10:2 59:9 regulatory 60:3 60:11,19,24 61:10,19 relate 41:6 related 7:3,5,11 7:16,22 8:4,12 8:13,16 9:6,13 9:17 13:1 92:14 relationship 7:10 relative 99:11,13 release 23:10 24:8 27:21 28:1 41:19 42:14 45:16 50:13 76:15,16,16 82:2 relevant 35:20 36:11 remember 74:1 88:21 Remington's 67:19 68:2,15 68:23,24 69:5,7 69:12,14,20 70:3,14,19,23 71:11 79:11,19 80:9,21 91:2,4 remove 56:16,21	report 92:12,13 92:24 REPORTED 1:21 Reporter 2:5,6 99:3,3,21,22,23 reporter's 4:15 12:5 reports 8:24 9:6 26:6 required 12:17 96:6,8,12,17,22 requirement 97:12 research 22:19 22:23 23:1,1,5 26:1,5,11 27:16 27:16,22,22 28:2,3,10 30:12 30:17 31:16 58:24 82:3 resource 48:4,10 respect 8:20 38:7 81:17 response 12:9 responsibilities 26:7 rest 90:15 result 34:21 results 55:8 56:5 retained 20:15 reverse 30:4 review 4:13 9:11 15:10 100:13 reviewed 21:2,7,8 21:20 22:2,6 reviewing 16:18 revisit 89:24 RICHARDSON 3:14 Ridge 31:17,21 31:24 right 5:6 9:21 10:10 12:12 15:21 18:5 19:9 27:16 30:7 31:18 40:20	42:20 52:17 53:17 55:16 56:19 58:2,11 63:10 72:20 75:13 77:2 80:3 80:23 82:19 90:4 94:10 97:8 risk 73:9 95:16 96:24,25 RMR 1:21 road 95:20 Robinson 3:23 robotics 26:23 robots 26:24 role 7:17 26:4,15 27:24 30:12,17 31:23 room 11:19 41:3 routinely 77:17 rudimentary 10:1 23:12 rule 95:17 rules 10:2 100:19 run 58:4 61:13 running 52:2 S S 3:1 4:9 sake 12:5 Sarcos 26:11 says 15:21 67:1 67:24 68:11 75:9 77:3,22 78:23 79:7 83:8 84:5,21 85:4 89:9 93:5,15 scale 34:9 58:3 89:17 scaled 32:21 scattered 6:22,24 scenario 23:20 SCHWARZ 3:5 4:5 9:14,19 14:13 17:23 19:5 20:2 33:23 38:10 40:3 45:13 46:12	48:1 49:12 50:2 51:13,20 52:11 53:20 54:1 55:10 56:3,20 57:16 58:13 59:12 60:22 61:3,9,24 62:8 62:18 63:19 64:19 65:8 69:8 70:22 71:14 72:1 73:24 74:22 75:23 77:7 78:1 79:20 80:11,18 81:8 81:20 82:4,17 83:16,20 85:10 85:23 86:12 91:21 94:12,18 97:18,24 98:22 science 68:4,17 scope 21:6 22:4 30:16 55:22 59:13 61:4 62:9 62:19 73:13 81:9 91:22 screen 46:24 53:21 screening 53:24 second 18:6 38:11 66:18 83:23 89:3 section 14:20 17:8,14 18:17 21:2 70:7 sections 19:18 70:4 79:11 see 15:20 21:4 22:17 29:5 38:3 43:18,21 52:12 57:7 72:7,14 77:8 79:6 83:6 93:8,19 94:13 seeing 79:15 seen 53:21 select 76:23 selected 100:15 selection 41:23
--	--	--	---	---

75:5 76:12 98:11 senior 22:24 23:4 26:1 58:24 sensitivity 56:10 73:1 sentence 72:22 73:15 75:1 76:21 77:14 83:23 87:1,3,9 90:16 93:15 separate 7:12 served 7:20 set 46:8,15 77:18 78:8 94:11 99:8 settings 67:11 shaking 12:11 share 14:16 sheet 100:16 101:17 102:6 shut 26:18 sign 100:12,13 signature 16:1 100:11,17 101:6,20 102:25 signed 100:16 significant 82:18 signing 100:15 similar 24:14 26:8 74:14 93:15 similarly 17:21 simple 42:21 89:14 Sincerely 100:21 sit 74:24 site 97:5 sitting 9:8 79:16 82:19 situation 97:16 six 11:21 35:3 size 34:10 37:9 70:9 76:4 skill 76:22 small 28:4 32:16 33:12 39:8,9	40:13,23 42:20 smaller 37:8 42:7 sodium 93:7,12 solid 24:2 31:2,6 44:12 64:2 65:3 66:23 84:23 91:9 96:3,9,14 96:20 97:13 solubility 35:23 36:5 56:11,16 57:2 76:2 solubilizer 37:10 47:6 soluble 37:1,5 47:8,9 64:14 solution 31:1 37:10 64:13 solvent 64:13 somebody 32:6 92:7 something's 44:13 sorry 6:10 19:12 27:18 36:16 55:11 82:5,6 83:17 84:14 92:1 sort 29:16 49:21 sorts 36:1 37:14 58:6 sounds 30:7 source 67:20 69:20 sources 63:5,8 SOUTH 1:8 speak 12:1,3 speaking 19:22 35:16 specific 13:23 18:8 20:16 23:9 33:18 34:1 38:1 38:16 47:6 48:20 49:19,24 52:9 55:19 56:18 63:18 64:18 65:2 66:12 67:10	70:21,24 71:1 71:13,23 75:3 75:14 79:11 82:13 98:9 specifically 91:1 92:20 specifics 70:18 spend 16:6 spot 81:23 Square 1:17 stability 34:7 35:4,5 36:2 40:11 41:15 44:9 89:16 95:24 96:1 stable 33:2 stage 22:14 31:13 31:13 34:23 38:9 39:14 49:11,19 52:6 52:10,16 53:16 54:9,11,13,14 55:8 65:6 75:17 stages 31:12 52:7 52:8 start 18:18 25:11 30:21 38:1 47:4 started 22:24 41:20 74:7 starting 47:11 64:22 66:18,19 67:17 74:4 88:20 state 5:17,22 69:19 83:2 90:9 90:19 92:18 99:4 stated 38:20 55:1 statement 85:6 statements 14:19 28:12 states 1:1 17:9 62:6,16 67:19 68:15 72:8 75:2 76:20,21 77:14 78:14 87:9 98:8 stay 27:7	stearate 42:19 45:23 46:2,3,19 STENOGRAP... 5:5,13 stenographically 99:8 step 19:13 22:9 39:16 45:9 48:13,24 49:5,7 50:4,6 54:9 71:10 73:11 74:8 81:2 82:11 95:17 steps 33:22 48:22 74:2 82:7,14,15 sticks 32:22 stint 27:10 storage 97:10 store 97:1,9 stored 96:5 strategic 11:24 strategies 72:9,16 72:21 73:6,22 81:16 strategy 38:15,16 73:12,14,17 76:24 77:4 96:24 Street 1:24 2:2 3:7 100:3 101:2 102:2 strive 77:19 stuck 42:7 studies 28:18,19 28:20 33:4 stuff 26:22,24 subject 70:5 81:1 95:5 submitted 92:5 subset 88:10,11 substance 78:20 94:7 substantively 14:9 suffice 45:3 Suite 1:24 3:17 101:2 102:2	summarizes 84:10 summary 24:22 summer 16:13 20:17 super 56:10 support 4:12 15:9 95:7 sure 5:24 13:17 14:24 23:15 25:23 27:19 29:17 30:15 39:18 40:18,24 41:2,7,8 44:14 49:16 54:18 58:15 78:3 90:17 94:15 97:24 SW 3:17 swear 5:8 sworn 5:16 99:5 synonymous 23:19 29:7 synonymously 42:3 synthesizing 25:16 systems 23:7 26:21
T				
T 4:9 99:1,1				
table 57:7				
tablet 24:19 31:2 32:23 40:6,7,22 41:19,21,24 42:14,17,17 45:16 50:13				
tablets 24:3 91:10				
take 11:12,15,20 33:22 45:9 48:13 49:8 58:14 59:19 64:16 65:5,20 66:13 71:9 73:11 82:10				

85:15 taken 6:8 48:22 58:16 81:15 82:14,15 85:17 94:16 97:25 99:8 talk 16:20 24:1 25:18 71:22 94:7 talked 52:20 74:2 74:8 89:12 92:13 talking 12:4 23:22 70:4 74:3 talks 70:24 71:16 71:19 taught 79:13 91:2 TAYLOR 3:15 teaches 91:5 team 16:22 25:18 technical 27:5 35:10 70:10 technically 26:8 technologies 28:13,16,17 56:24 57:4 72:9 technology 37:12 66:21 tell 61:12 62:22 80:15 tells 60:6 temperature 43:21 76:3 ten 47:15 66:2 85:15 tend 43:23 tens 29:14 term 23:16 terminology 23:2 terms 42:2 test 31:10 testified 5:18 8:13 90:5 testify 12:24 99:6 testifying 10:9 testimony 5:9 8:10 10:14 18:1	19:21 79:22 94:7 98:16 99:7 testing 45:12 46:9 49:22 51:12,17 63:12 63:16 64:3 86:8 95:11,15 96:5 96:11,16,22 testings 63:22 tests 61:13 64:10 textbook 70:4 80:24 texts 80:19,22 Thank 5:13 10:20 25:4 39:10 51:5 54:7 69:17 76:18 87:5 97:18 98:23 theory 66:16 therapeutically 17:11 18:13 they'd 30:24 33:18 thing 32:5 35:6 43:1 44:5 67:12 89:18 97:7 things 16:18,19 17:16 24:7,11 25:5 28:6 31:3 31:10 33:15 35:15 36:2,4,9 37:15 41:9 43:6 43:22 53:3,12 57:9 61:12,18 69:15 70:10 72:18 76:1,17 80:20 89:20 92:8 97:6 think 7:7 9:2 20:17 22:24 23:2 26:6 35:20 36:24 39:18 43:13 45:1 46:13,18 49:3 50:4 51:23 54:24 63:7,8	66:9 68:8 70:17 74:8,11,23 75:10,24 78:10 82:19 83:23 84:10 85:15 90:24 94:11 thinking 30:8 41:16 56:24 57:10 76:7 81:13 thousands 29:14 29:14 three 18:15 35:4 44:3 46:23 95:19 time 6:8,23 16:6 22:3 28:3,7 31:9 54:22 58:14 92:3 99:8 100:18 times 1:17 6:4 33:9 88:3 title 28:4 31:22 titled 21:2 today 5:11 9:8 10:5,15 12:21 19:21 79:16 81:5,6,17 90:5 90:22 94:6 98:17 today's 10:21 told 45:16 tooling 42:17 top 63:9 66:19 93:5 track 25:23 35:24 TRADEMARK 1:1 transcript 4:1 99:7 100:10,12 101:13 transcription 101:16,18 transition 76:3 traverse 84:15 treatments 43:24 TRIAL 1:2	tried 30:24 true 20:3 26:13 85:8 101:15,17 truth 5:9,10,11 99:6,6,6 truthful 10:8 try 12:2,3 95:17 trying 20:8 34:2 37:17 40:4 44:12 50:22,23 51:4 54:20 55:3 57:20 63:24 73:11 86:5 89:13 90:24 turn 15:13 17:5 30:2 44:10 77:10 82:22 86:23 98:3 turning 24:24 two 7:9 13:1,7,14 14:12 19:12,14 19:15 20:7 43:20 58:18 64:10 66:9 88:24 89:23 91:8 95:19 type 7:13 33:7 75:5 98:12 types 41:23 51:9 55:15 63:15,21 64:3,10 70:24 72:12 73:21 78:15 90:10 91:12 typical 32:5 43:1 53:23 typically 25:10 25:14 typo 27:17	12:11,18,23 13:19,21 14:8 25:24 33:24 35:22 40:10 48:14 49:3 64:11 73:10 78:4 83:3,12 84:5 93:1 understanding 13:13 34:19 35:7,8,9 36:6 48:16 49:18 54:10 69:4 83:15,18,19 understood 11:3 30:15 39:10 51:5 55:18 unit 26:19 United 1:1 62:6 62:16 University 1:7,8 100:6 101:7 102:8 unpack 25:5 updated 63:4 updates 69:14 use 23:16 33:12 34:23 39:3 40:2 43:14 45:11 46:1,8,24 48:4 51:17,21 55:7 56:1 58:22 60:11,16,20 62:6,16,24 63:3 63:17 70:19 71:12 73:5,17 86:15 96:21 97:14,15 98:12 useful 71:21 USP 60:7,14,17 61:12,17 62:23 usually 29:20
U				
U.S 1:6 21:15 60:21,21 84:7 unclear 10:23 underneath 39:9 understand 6:11 10:4,10 12:6,8				
V				
v 1:6 100:6 101:7 102:8 variable 66:2				

various 51:9 55:15 70:5 91:11 VENABLE 3:4 100:2 venture 6:21 88:16 verbal 12:9 verbatim 99:7 version 62:23 68:23,24 versus 71:2,23 viable 89:6 Vibramycin 93:16,22	44:21 52:12 71:18 82:18 ways 34:18 41:10 43:5 74:17 we'll 37:7,9,11 94:13 we're 23:22 32:8 33:11 40:13 41:16 45:15 53:9 54:10 64:24 66:17 77:12 we've 19:14 27:12 41:15 49:10 52:7 81:5 81:16 week 6:17 well-known 67:21 68:3,16 78:16,24 79:17 90:11,21 91:6 91:18 went 55:21 74:2 weren't 57:10 West 2:2 3:7 100:3 wet 40:16 41:13 42:11 71:2 91:12 wide 23:11 56:13 65:10 wider 47:12 willing 96:25 witness 5:12,15 7:20 83:17 100:13 101:8 101:20 102:9 witness's 17:24 79:21 words 69:10 work 22:13,16 25:11 30:16 32:15,15 35:1 37:3 38:2 40:11 45:5,20 49:14 worked 20:21 23:7 26:20	27:15 82:1 87:20 working 16:21 25:7,8 28:8 55:20 works 42:10 52:22 60:14 wouldn't 6:20,21 30:1 38:16 71:17 79:14 88:16 writing 16:19 written 95:6 100:25 X X 1:3,10 4:9 Y yeah 8:8 9:9 14:14 20:12 25:14 47:24 48:2 49:4 50:19 53:18 55:13 59:18 69:10 74:11 96:8 98:18 year 6:19 66:9 92:1 years 43:20 66:2 66:10 York 1:18,18 2:2 2:3 3:8,8 5:3,3 5:18 99:4 100:4 100:4 Z 0 1 1 29:1 32:9,19 52:7 84:4 95:2 10 17:22 18:11,19 54:4 10,633,344 1:6 1000 3:17,17 1003 4:12 15:6,7	94:21 10036 3:8 100:4 11 18:18 12:00 98:25 13 17:6 84:1 1346 13:2 1347 13:3 17:20 22:6 13th 84:6 14 18:16 82:23 94:20 99:25 15 4:11 6:6 8:3,11 8:11,21 9:12,16 9:23 151 2:2 3:7 100:3 16 18:18 19:10 84:18 17 6:13 1730 1:24 101:2 102:2 18 18:18 89:1 98:6 19 8:12,21 9:12 21:1 1988 22:19 88:20 1995 26:10 27:9 68:23 69:7,14 1996 26:10 27:9 27:14 1999 59:1 2 2 29:1,1 32:19 52:7 54:9 20 6:6 8:3,11 9:16 9:24 53:21 54:4 87:12,24 88:10 2002 81:7,18 82:12 85:9 91:20 92:2 20024 3:18 2003 81:7,18 85:12 91:20 92:2 20036 1:24 101:3 102:3 2006 27:14	2012 68:24 69:5 69:12 79:19 80:9 2014 81:7,19 83:8 83:14 84:1,6,21 90:6 91:19 94:24 95:8 2016 6:13 202 1:25 101:4 202)-232-0646 100:20 202)232-0646 102:4 202.783.5070 3:19 2023 16:4 2023-01346 1:5 15:22 2024 1:15 99:25 100:7,23 101:9 102:10 21 67:14,18 212.307.5500 3:9 22 77:12 232-0646 1:25 101:4 24th 16:4 25 90:3 26 17:5 18:10 19:2 27 18:16 19:3 3 3 29:2 52:7 54:13 83:22 95:1 30 84:17 31 19:10,13 334 67:19 344 21:8,12 83:13 84:8 95:6 36 72:4,7 75:2 76:21 98:4 39 93:2 4 4 1:17 21:2 52:7 40 93:14
---	---	---	--	---

4042 5:24 41 94:3 42 16:2 77:10 42nd 2:2 3:7 100:3 43 77:11 49th 3:7 100:3 5 5 4:4 50 28:4 53:21 51 78:12 89:24 90:9 6 6 22:10 7 7 22:10 26:9 31:16 87:1,4 8 8 1:15 66:15 86:23 87:2 100:7 101:9 102:10 812 1:24 101:2 102:2 862 84:7 95:8 9 9 21:3 9:00 2:3 9:05 1:16 5:2 90 46:3 94 4:5 956 21:16 97703 6:1 98 4:6				
---	--	--	--	--

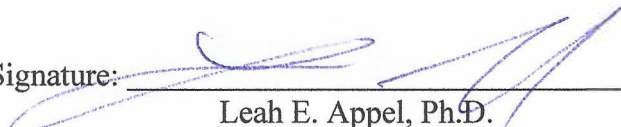
*Novartis Pharmaceuticals Corporation v.
Regents of the University of Michigan and University of South Florida
IPR Nos. 2023-01346, 2023-01347*

Errata to the Transcript of the May 8, 2024 Deposition of Leah E. Appel, Ph.D.

Page	Line	Change	To	Reason for Change
13	2	'1346	1346	Mistranscription
13	3	'1347	1347	Mistranscription
17	20	'1347	1347	Mistranscription
18	18	start	starts	Mistranscription
22	6	'1347	1347	Mistranscription
23	20	formulating into	formulating it into	Mistranscription
24	6	drug, contains	drug, it contains	Mistranscription
24	10	lube, other	lube, or other	Mistranscription
30	21	So, would	So, we would	Mistranscription
34	11	most is	most	Mistranscription
38	1	specific,	specifics,	Mistranscription
39	4	diluent carriers	diluents/carriers	Mistranscription
39	8	diluent carriers	diluents/carriers	Mistranscription
44	11	puddle. Hard	puddle. It is hard	Mistranscription
44	17	crystallin	crystalline	Mistranscription
44	17	crystal	crystalline	Mistranscription/Misspoke
47	15	hand	handful	Mistranscription/Misspoke
54	16	from and what's	from -- what's	Mistranscription
57	20	make inform	make that inform	Mistranscription/Misspoke
58	7	which your	which of your	Mistranscription
65	24	'cause	because	Mistranscription/Misspoke
66	8	didn't	don't	Mistranscription/Misspoke
66	8	exact,	exact time,	Mistranscription
67	21	well-known	"well known	Mistranscription
67	22	art.	art."	Mistranscription
73	7	than	that	Mistranscription
77	15	it	"[i]t	Mistranscription
77	20	products.	products."	Mistranscription
78	14	A POSA	"A POSA	Mistranscription
78	18	prepare pharmaceutical	prepare a pharmaceutical	Mistranscription
78	20	that included a drug substance	(that included a drug substance)	Mistranscription
78	21	carrier	carrier."	Mistranscription
79	5	'cause	because	Mistranscription/Misspoke
83	8	here "2014."	"here, 2014."	Mistranscription
84	8	application	application,	Mistranscription
84	8	at	as	Mistranscription

87	9	I am	"I am	Mistranscription
87	11-12	as defined in paragraph 20 below	(as defined in paragraph 20 below)	Mistranscription
87	12	compositions.	compositions."	Mistranscription
98	8	The formulator	"The formulator	Mistranscription
98	9	physical chemical	physicochemical	Mistranscription
98	13	form.	form."	Mistranscription

Date: 5/22/24

Signature: 
Leah E. Appel, Ph.D.