

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

NOVARTIS PHARMACEUTICAL CORPORATION,
Petitioner,

v.

REGENTS OF THE UNIVERSITY OF MICHIGAN
AND UNIVERSITY OF SOUTH FLORIDA,
Patent Owner.

IPR2023-01346
Patent 10,633,344 B2

Record of Oral Hearing
Held: January 8, 2025

Before JEFFREY N. FREDMAN, MICHAEL J. FITZPATRICK, and
SHERIDAN K. SNEDDEN, *Administrative Patent Judges*.

APPEARANCES:

ON BEHALF OF THE PETITIONER:

CHRISTINA SCHWARTZ, ESQ.
ERIN BELFIELD, ESQ.
Venable LLP
151 West 42nd Street
New York, New York 10036
(212) 307-5500

ON BEHALF OF THE PATENT OWNER:

MICHAEL J. KANE, ESQ.
TAYLOR BURGNER, ESQ.
Fish & Richardson P.C.
60 South 6th Street, Suite 3200
Minneapolis, Minnesota 55402
(612) 335-5070

The above-entitled matter came on for hearing on Wednesday, January 8, 2025, commencing at 1:00 p.m., at the U.S. Patent and Trademark Office, 600 Dulany Street, Alexandria, Virginia.

P R O C E E D I N G S

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(12:59 p.m.)

JUDGE SNEDDEN: Good afternoon. Please be seated. All right. This is the oral hearing in IPR2023-01346. I'm Judge Sneddon. With me on the Panel are Judges Fredman and Fitzpatrick. We will begin with appearances, starting with Petitioner. Please stand, introduce yourself and who you have with you today.

MS. SCHWARZ: Good morning, Your Honor. Christina Schwarz, on behalf of Petitioner Novartis. I'm here with my colleague, Erin Belfield. And we have Brian Robertson on behalf of Novartis, here with us.

JUDGE SNEDDEN: Welcome. Thank you.

MR. KANE: Good afternoon, Your Honor. Michael Kane from Fish & Richardson, on behalf of Patent Owners. And I have with me my associate, Taylor Burgener.

JUDGE SNEDDEN: Welcome. Thank you. Per our order granting, this oral hearing, each party will have 60 minutes of total time to present their arguments. We'll begin with Petitioner, who will open the hearing with its presentation. Patent Owner would then respond to Petitioner's arguments. Each side may reserve time for rebuttal.

We, the Judges, have electronic versions of your presentations today, your slide decks. I would take this opportunity to remind the parties to please speak the slide numbers as you proceed through your presentations today. And that's for both the benefit of the the record, and also for Judge Fitzpatrick, who is joining us remotely.

1 Okay. So, that is it. Ms. Schwarz, when you're ready, you can begin.
2 Will you be reserving time for rebuttal?

3 MS. SCHWARZ: Yes. Your Honor, may I please reserve 15
4 minutes of time for rebuttal?

5 JUDGE SNEDDEN: Yeah. Okay. When you're ready.

6 MS. SCHWARZ: Good afternoon, Your Honors. As shown on slide
7 2, the only remaining disputes in this IPR are whether the '956 application,
8 which was filed in March of 2003, provides written description and
9 enablement support for the challenged claims, claims 10, 11, and 18. It does
10 neither, let alone both.

11 Turning to slide 3. Put simply, the problem here with the challenge
12 claims is that the Patent Owners claimed too broadly. They made a few co-
13 crystals and then filed claims to a very broad genus of co-crystals without
14 describing the co-crystals in that genus or explaining how to make and use
15 them. And this is a problem because co-crystallization was unpredictable as
16 of March 2003. As the Petitioner's expert, Dr. Rogers, explained, citing to
17 documentary evidence that we'll look at today. As of 2003, it was not
18 possible to predict co-crystal formation at all, let alone across the full scope
19 of the claims.

20 Patent Owners responded to that testimony with the unsupported
21 testimony of Dr. Ward and attorney argument. They never explain in any
22 detail how a person of ordinary skill in the art would go about predicting co-
23 crystal formation, and they don't have a single example of anyone having
24 made such predictions.

25 JUDGE FREDMAN: They do, Counsel, they do point to this Etter
26 Rules. Can you explain that and discuss that a little bit?

1 MS. SCHWARZ: Yes, Your Honor, they do point to the Etter Rules.
2 We can look at those rules. We can look at those rules, which are on slide
3 19. And the Patent Owners have argued here in this IPR that knowledge of
4 hydrogen bond formation and knowledge of Etter's Rules would have
5 allowed the prediction of co-crystal formation. But that's not supported by
6 the evidence. First of all, Etter's Rules had been available for 13 years
7 before the '956 application was filed. Yet the Patent Owners themselves
8 acknowledged during prosecution that as of March 2003, when they filed
9 their application, co-crystals were not predictable. That's supported by some
10 additional prior art that we'll also look at today.

11 But even if we were to agree that Etter's Rules could be used, there
12 are at least two other problems with the Patent Owners' reliance on these
13 rules. First, as Dr. Rogers explained, these rules were not used in the art
14 prospectively to make predictions about co-crystal formation. They were
15 used to identify the location of hydrogen bonds in already formed co-
16 crystals. So, it's not surprising for this reason that the Patent Owners haven't
17 cited a single example of anyone using these rules prospectively to make
18 predictions about co-crystal formation. It's also not surprising that they
19 never explain in any detail how somebody would use those rules, providing
20 a specific example, rather than just simply saying, yes, these rules could be
21 used to make predictions.

22 JUDGE SNEDDEN: The claims do narrow the field of certain APIs
23 and other compounds to be used within the crystals, and those are
24 compounds that have certain functionalities. So, they did narrow the field to
25 three functionality or compounds having three functional groups on them.
26 So, could you speak to that in terms of the predictability there?

1 MS. SCHWARZ: Yes, sure. So, you are correct, Your Honor, that
2 the claims are narrowed in some respects because the API has to have one of
3 the three listed first chemical functionalities. But notwithstanding that,
4 there's no dispute here that the breadth of the claims is extremely broad.
5 Although the APIs have to have those three particular functional groups, and
6 we can look at specifically how API is defined in the specification, can go
7 back to slide 7. So, the patent here explains that the API can be any
8 biologically active moiety having a therapeutic effect on a human or animal
9 suffering from a given pathological condition when administered in a given
10 concentration or, sorry, in a -- yes, you're right, in a given concentration.

11 Now, there's no dispute that this is an extremely large genus, even
12 though there has to be one of the three specified first chemical
13 functionalities. Just considering APIs with carboxamide groups, a C double
14 bond O NH₂ group, there were over 50 carboxamide containing APIs in the
15 Merck Index alone as of March 2003. So, it's an extremely broad number of
16 APIs. There's no limit on the additional functional groups that the API can
17 have.

18 JUDGE FREDMAN: The claims actually already cover any APIs,
19 right? This is prospective to any API ever discovered, right?

20 MS. SCHWARZ: Your Honor, yes, the claims capture any API that
21 was known before March 2003 or even known after March 2003. So,
22 obviously the 50 APIs with a carboxamide group is a significant
23 underestimate of the potential number of APIs captured by the claim. But
24 it's not just the APIs that are broad here. Also, the co-formers are broad.

25 If we look on slide 8, co-formers are defined in the '344 Patent to be
26 other drug molecules, grass compounds, or approved food additives. And

1 there's no dispute here that there are no restrictions on the number or types
2 of functional groups that can be present in the co-former, provided they're
3 solid and have a second chemical functionality that interacts with the API.
4 It's undisputed here that there were thousands of potential co-formers as of
5 2003.

6 JUDGE FREDMAN: So, let me ask just one question. The claim
7 does talk about doing hydrogen bonding as the way that these interact. Is
8 that the only element that would be required to figure out crystallization, or
9 are there other component, other sort of, you know, structural interactions or
10 things that would be required to determine crystallization if you're trying to
11 predict it?

12 MS. SCHWARZ: So, Your Honor, I'm not sure I fully understand
13 your question, but let me try to answer it and you can --

14 JUDGE FREDMAN: I can simplify it a little bit. So, when we think
15 about crystallization with, say, proteins, which I'm a little more familiar
16 with, right. And we're talking about, you know, you want to crystallize a
17 protein and you maybe want to co-crystallize it with an active agent in the
18 active site, right. There are several factors at play, right? One of them is
19 going to be hydrogen bonding. Right? They are going to be presumptively
20 hydrogen bonded, but they're also, the exact orientations matter. The salts
21 can matter, lots of other things. The pH can matter. Right. Which affects
22 water, which affects crystallization. Right. So, there are lots of other factors
23 at play. Is the same thing true here or not?

24 MS. SCHWARZ: Yes, Your Honor. The same is absolutely true
25 here. We can look at -- there was testimony from Dr. Rogers who explained
26 all the different factors that go into co-crystallization.

1 JUDGE FREDMAN: Can you point to that --

2 MS. SCHWARZ: We need to look at --

3 JUDGE FREDMAN: -- where that is? Is that the declaration or is
4 that in the deposition?

5 MS. SCHWARZ: I believe these are addressed in Dr. Rogers's reply
6 at paragraph 21, but we can just --

7 JUDGE FREDMAN: Okay. That's fine.

8 MS. SCHWARZ: -- double check that for you --

9 JUDGE FREDMAN: Sure.

10 MS. SCHWARZ: -- and provide a site. Some of the things Dr.
11 Rogers talked about is that when doing a co-crystallization experiment you
12 need to look at the concentration of the API and the co-former, the
13 stoichiometries of the two relative to one another, the solvent, including the
14 solvent combinations that could be tested, the concentration of solvent, the
15 time, the temperature, the mixing speed. There's a whole host of different
16 factors that need to be considered when doing a co-crystallization
17 experiment.

18 And we have from the Patent Owners this quote at the top of slide 10,
19 which I think is particularly relevant here. This is the Patent Owners talking
20 about the state of the art as of March 2003. And here they say prior to the
21 present invention it was not understood even by leading scientists which
22 chemical factors would predetermine the formation of a drug co-crystal.
23 The aspects of different kinds of charges, functional groups, size and shape
24 in molecules and the relationships between them were heretofore not
25 understood in a manner that one could predictably, to almost a certainty,
26 predesign a co-crystal. In short, prior to this invention, co-crystals were like

1 polymorphs, solvates, and hydrates in that random trial and error was used to
2 isolate them.

3 This is consistent with admissions from the Patent Owners' expert
4 during parallel litigation where Dr. Childs, shown at the bottom of slide 10,
5 this is Exhibit 1020, said that it's not possible to predict whether any
6 particular hydrogen bonds would form between two components of a co-
7 crystal in advance of making it. So, even if you could predict co-crystal
8 formation, which we certainly disagree has been shown here, it's not
9 possible to predict which specific hydrogen bonds have been formed.

10 JUDGE FREDMAN: Well, that's not required by the claim, is it?
11 It's
12 just --

13 MS. SCHWARZ: It is. It is, Your Honor. If we go back to slide 6,
14 we have a depiction here. And this is actually one of the errors that Patent
15 Owners make several places in their papers in suggesting that any co-crystal
16 made up of the API and co-former would be sufficient. That's not correct.
17 The claim claims here require that the co-crystal is formed by a hydrogen
18 bond, not any type of bond. Right? There's obviously other types of non-
19 covalent interactions --

20 JUDGE FREDMAN: Sure.

21 MS. SCHWARZ: -- that could form a co-crystal.

22 JUDGE FREDMAN: Van der Waals forces.

23 MS. SCHWARZ: Correct. And secondly, the hydrogen bond has to
24 be formed between the first chemical functionality of the API and the co-
25 former. If the hydrogen bond is between a different part of the API and the
26 co-former, that co-crystal would fall outside the scope of the claims. So, it's

1 important not just to form co-crystals, but to form the specific co-crystals by
2 the claims here.

3 All right, so going back to the scope of the claims, we talked about
4 the breadth of the APIs, the breadth of the co-formers. And I want to make
5 one additional point here, which is on slide 9, which is that there's no dispute
6 that the claims here encompass co-crystals that are made up of at least one
7 API and at least one co-former. So, the claims here cover co-crystals
8 crystals made up of any stoichiometric ratio of APIs to co-formers.

9 Now, as I mentioned earlier, the Patent Owners have admitted that
10 the state of the art, right as of March 2003, when they filed their application,
11 co-crystals were not predictable as of that date. So, what I'd like to do now
12 is look at the portions of the '956 application that the Patent Owners have
13 relied on for written description and enablement support and show why
14 those don't change the state of the art. Those specific disclosures in the '956
15 application don't make co-crystals predictable.

16 And we have here on slide 14, the universe of portions of the '344
17 Patent, which is the same specification as the '956 application that the Patent
18 Owners have relied on in this IPR. If we look at numbers one and two, these
19 are the passages that we just looked at on slides 7 and 8. It's the definition of
20 API, definition of co-former in the patent. These say nothing about
21 predicting co-crystal formation.

22 The next thing the Patent Owners rely on, item number three is a
23 passage in column three of the patent, and we can put that up on slide 15.
24 So, here this passage lists six different active ingredients, and it states that
25 multiple component solids have been characterized by various techniques
26 and can exhibit properties that are the same as or different from the API

1 alone. Again, this passage says absolutely nothing about how to predict co-
2 crystal formation.

3 Turning now to slide 16, Patent Owners rely on the examples in the
4 '956 application. And Patent Owners haven't disputed that these examples
5 are not representative of the full scope of the claims. But we expect you'll
6 hear Patent Owners will argue that these examples illustrate the different
7 limitations of the claims, but that's not the right analysis. This isn't a
8 mechanical invention where you can take an API from one example and a
9 co-former from another example and expect they're going to form a co-
10 crystal.

11 But more importantly, these examples don't disclose all of the claim
12 limitations or reflect the broad scope of the claims. Patent Owners
13 themselves admit that at most nine of these examples fall within the scope of
14 claims 10 and 18, and only three fall within the scope of claim 11. And
15 those nine examples falling within the scope of claims 10 and 18 are very
16 limited. They reflect only three different active ingredients, and every one
17 of those active ingredients has a carboxamide first chemical functionality.
18 There are no examples with a carbonyl or amine, which are two of the three
19 recited first chemical functionalities in the asserted claims, claims 10 and 11.
20 None of these examples is a co-crystal with multiple APIs. None of these is
21 a co-crystal with multiple co-formers. And as a result, these limited
22 examples don't reflect the full scope of the claims here, which cover over 50
23 potential APIs. It's undisputed. At least 50 API, thousands of co-formers,
24 27 solvents, all of which can be combined in any stoichiometric ratio.

25 JUDGE FREDMAN: So, let me ask more on the enablement side, I
26 think really than on the description side. How do you respond to the

1 argument that while we do have high-throughput screening nowadays, we
2 could run, you know, drug companies routinely use million compound
3 libraries to screen for things; we could screen with any particular API that
4 we're interested in, a number, probably thousands if not millions of different
5 co-formers and then just test to see which ones actually work, run them
6 through a mass spec or whatever?

7 MS. SCHWARZ: Sure, I'd be happy to address high-throughput
8 screening. And it's Petitioner's position that high throughput scanning
9 doesn't change the result here at all.

10 JUDGE FREDMAN: For either enablement or description or for
11 both?

12 MS. SCHWARZ: It's unclear to us exactly how the Patent Owners
13 have relied on high-throughput screening. It seems they've only ever
14 discussed it with any expert support whatsoever in the context of
15 enablement.

16 JUDGE FREDMAN: Okay.

17 MS. SCHWARZ: We're not really sure how they would use it for
18 written description --

19 JUDGE FREDMAN: Okay.

20 MS. SCHWARZ: -- but I think it is mentioned.

21 JUDGE FREDMAN: That's what I'm asking, yeah.

22 MS. SCHWARZ: But the arguments here apply to both enablement
23 and written description. And there are really three reasons why the Patent
24 Owners' high-throughput screening arguments don't change the result here.
25 So, first, as shown on slide 40, there's no dispute that high-throughput
26 screening was not used for co-crystal screening as of March 2003. The art

1 that the Patent Owners have relied on, the prior art, relates to polymorph
2 screening. And according to Luu 2012, that's Exhibit 1077 at page 356, the
3 first paper that reported the use of high-throughput screening for co-crystals
4 was not available as of March 2003. It was published later.

5 And screening for polymorphs isn't the same as screening for co-
6 crystals. Polymorph screening involves looking at a known compound and
7 attempting to identify different crystalline forms of that single known
8 compound. In contrast, co-crystal screening involves taking two compounds
9 and making a brand new supramolecular complex. Neither the '956
10 application nor Patent Owners or their expert in this IPR have explained how
11 a person of ordinary skill would take their knowledge of polymorph
12 screening, which their expert admitted was only emerging as of 2003, and
13 apply that to co-crystallization screening.

14 Now, the second reason why --

15 JUDGE FREDMAN: I mean, I guess, the only other question I have
16 there though is, I mean, you say it's emerging and I guess this is
17 crystallization of essentially when we call them small molecules, again. I
18 mean in the context, and I don't know if this was mentioned in the
19 declaration, so I'm maybe stepping a bit outside of that, but there's no doubt
20 that in the context of protein crystals and protein co-crystals, where they
21 were, for example, trying to put in different heavy elements to make it more
22 visible to the X-ray or other types of co-crystallizations of proteins with their
23 targets, people did a lot of co-crystallization prior to 2003, I mean, where
24 they played with it.

1 MS. SCHWARZ: So, Your Honor, the Patent Owners here have
2 recognized that co-crystal screening for drug compounds was only emerging
3 as of 2003. So, that's their admission that that was the state of the art --

4 JUDGE FREDMAN: Okay.

5 MS. SCHWARZ: -- as of this time. But even to the extent it was
6 available and could have potentially been applied to co-crystallization, there
7 are a few issues here that don't allow high-throughput screening to overcome
8 the lack of undue experimentation that would be required. In particular, the
9 breadth of the claims being one important factor here.

10 JUDGE FREDMAN: Sure.

11 MS. SCHWARZ: We're not talking about screening one particular
12 co-crystal of one API and one co-former. There's no dispute that the genus
13 of potential co-crystals here is almost infinite and has limited -- unlimited
14 structural variation. Those are admissions here that the Patent Owners have
15 made. So, this is not a single screen. So, running screens across the entire
16 breadth of the claims requires considering factors as shown on the right of
17 slide 41. We mentioned some of these earlier, needing to consider the
18 amounts of the API and co-former, the relative concentrations of the two, the
19 stoichiometric amounts of the two, timing, temperature, mixing rates, all
20 sorts of different factors.

21 And again, the '956 application provides no guidance on how to
22 narrow this screening to accurately address and screen for co-crystals within
23 the scope of the claims. It doesn't mention high-throughput screening at all.
24 And this ties in somewhat to the third argument for why high-throughput
25 screening here doesn't mention provide enablement.

1 And that's because even if you could design and run high-throughput
2 screening experiments, they wouldn't tell the person of ordinary skill in the
3 art whether the products of that screen fall within the scope of the claims or
4 not. And that's because the techniques that were used in high-throughput
5 screening, like X-ray powder diffraction, won't tell you which specific
6 hydrogen bond are present in the product of any such co-crystal. So, this
7 comes back to Judge Fredman, one of the questions you asked earlier about
8 whether it's important where the hydrogen bond is. And it certainly is. And
9 that comes into play here with high-throughput screening.

10 To know whether the product of the high-throughput screen has the
11 hydrogen bonds within the scope of the claim, the person of ordinary skill in
12 the art has to do single crystal X-ray analysis for each product. That takes
13 time. And it's also necessary to have a co-crystal of sufficient quality and
14 size to do that single crystal X-ray analysis on. Now, Petitioner doesn't
15 dispute that the person of ordinary skill would have known how to do single
16 crystal X-ray analysis or how to grow a single crystal. But this would need
17 to be done manually for every product of the high-throughput screen that's
18 potentially a co-crystal. And this certainly contributes to an undue amount
19 of experimentation.

20 All right, I'd like to go back to one last point with respect to the
21 portions of the '344 Patent that the Patent Owners have relied on here in this
22 IPR for both written description and enablement support. And that's on slide
23 18 and it's figure 24 of the '344 Patent. Now, Patent Owners rely heavily on
24 this as part of their arguments to suggest that co-crystals were predictable as
25 of March 2003 once they filed their application. But at best this scheme sets
26 forth a research plan.

1 It's not specific to the challenge claims and it tells the skilled person
2 to evaluate, identify, and determine certain things without providing any
3 further guidance, even though the applicants admitted to the Patent Office
4 during prosecution that the prior art taught that co-crystallization was
5 unpredictable and it wasn't understood which chemical factors would
6 predetermine the formation of a drug co-crystal. There's nothing in this
7 figure or the '344 Patent generally to bridge the gap between identifying
8 functional groups that might potentially form a hydrogen bond with one
9 another and knowing which API and co-former combinations will actually
10 come together and form a co-crystal. The only way to know that is to make
11 and test different co-crystals.

12 Now, Patent Owners seem to acknowledge the deficiencies with the
13 '956 application because they pivot generally to relying on things outside the
14 specifications, such as the person of ordinary skill knowledge of hydrogen
15 bonding and Etter's Rules. Now, we talked already about how Etter's Rules
16 were typically used, as explained by Dr. Rogers, to identify the location of
17 hydrogen bonds in already formed co-crystals. But I also wanted to talk
18 about some of the limitations on Etter's Rules.

19 So, even if they were predictable or were used to predict co-crystals,
20 they have important limitations that are relevant here given the breadth of
21 the claims, and that's not disputed. As shown on slide 21, the Patent Owners
22 and Dr. Etter herself admit that the rules are most useful for systems with a
23 limited number of functional groups and without other competing forces.
24 These other competing forces include intermolecular interactions, sterics,
25 and geometry. And these undisputed limitations on Etter's Rules are
26 particularly relevant here because the challenge claims are not limited to

1 APIs and co-formers that lack other competing forces. As we discussed
2 earlier, they cover a very broad range of APIs and co-formers which can
3 have any shape and size and multiple different functional groups.

4 And here's an example that we included in our paper. There are three
5 APIs here, shown on slide 22. All of these were known as of March 2003
6 and each of these has multiple different functional groups, including the
7 functional groups that could be considered to be a carboxamide, carbonyl, or
8 amine. How would a person of ordinary skill go about applying Etter's
9 Rules to any of these APIs to determine if they would interact with a
10 particular co-former and if they did that it would have the right hydrogen
11 bond as required by the claims? The Patent Owners never explained how
12 this would be done.

13 JUDGE FREDMAN: So, were there docking programs back then or
14 did they not exist?

15 MS. SCHWARZ: I apologize. I missed --

16 JUDGE FREDMAN: Docking programs?

17 MS. SCHWARZ: Were there --

18 JUDGE FREDMAN: The computer programs that are used to dock
19 molecules with each other?

20 MS. SCHWARZ: I don't know the answer to that, Your Honor.

21 JUDGE FREDMAN: Don't know. Okay.

22 MS. SCHWARZ: I know there's some mention of some computer
23 modeling, but I think that its predictive value was very limited as of --

24 JUDGE FREDMAN: Right. Obviously, the Nobel Prize for
25 crystallization wasn't until a couple years ago. I don't know about for
26 smaller molecules. Yeah.

1 MS. SCHWARZ: All right. It's also undisputed that Etter's Rules
2 don't address certain embodiments captured by the claims. For example,
3 Etter's Rules don't address how you would predict co-crystals with more
4 than one API or more than one co-former, or co-crystals that also include
5 solvent, for example water. So, the API, the co-former, and also solvent,
6 and that's referred to as a co-crystal hydrate. And this is particularly relevant
7 because one of the inventors of the '344 Patent, Dr. Zaworotko, in 2010, a
8 paper, Exhibit 1078, admitted that even as of 2010, the structure and
9 composition of co-crystal hydrates remain largely unpredictable.

10 So, overall, Etter's Rules have exceptions. That's undisputed. They
11 don't address the full scope of the claims. That's undisputed. And Dr.
12 Rogers had explained that they're used retrospectively, not prospectively,
13 and we have no evidence of prospective application of those rules. So, for
14 all those reasons, Etter's Rules don't overcome the lack of predictability.

15 So, I'll turn now to written description, and this is on slide 24. Now,
16 as I've already discussed, the claims here cover an extremely broad genus of
17 co-crystals. That's not disputed. Written description support for a genus
18 claim requires evidence of representative species or common structural
19 features. The Patent Owner here --

20 JUDGE FREDMAN: So, the question, I guess, they obviously are
21 going to argue the common structural features are the three particular groups
22 that they're relying on.

23 MS. SCHWARZ: Their papers are not particularly clear as to what
24 exactly the Patent Owners are relying on in terms of the common structural
25 features. It may be the three groups. It may be the presence of a hydrogen
26 bond. Regardless of what it is, those are not common structural features.

1 JUDGE FREDMAN: In what way? They're structural features, and
2 they're required. I'm not sure how they're not common.

3 MS. SCHWARZ: Well, the first chemical functionality is a
4 structural feature. I agree with you, Your Honor. But the claims here
5 require more than having a molecule with that particular structural feature.
6 Importantly, the claims here include functional limitations, and that's
7 important. They require forming supramolecular synthons, and they require
8 forming co-crystals. The API and the co-former have to come together to
9 form synthons and form co-crystals.

10 Where claims include functional limitations, it's necessary to have
11 some sort of correlation in the specification linking any structural features
12 with that claimed function. And that's not present here. There are no
13 disclosures in the specification of structural features common to all APIs
14 other than the first chemical functionality. There's no common structural
15 features identified for the co-formers. And there's no correlation between
16 any structural feature and the claimed functions of forming supramolecular
17 synthons and forming co-crystals. Essentially, there's nothing in the '956
18 application that would allow someone reading it to look at the genus of
19 potential APIs and the genus of potential co-formers and know which co-
20 crystals within the scope of the claims can be formed from those APIs and
21 co-formers.

22 JUDGE FREDMAN: So, to preview my question to them a little bit,
23 essentially you're sort of saying this like Rochester, or maybe Ariad
24 (phonetic) if you prefer, where it's essentially kind of a reach through claim
25 we have in Rochester, right, it was -- well, in area was the I Kappa B NF
26 Kappa B lin , right? And we had NF Kappa B, and we were screening and

1 we're going get something that bound to it. And that wasn't enough because
2 knowing that we could get something, and that would be the argument
3 perhaps for enablement here, that you could maybe screen and get
4 something, but even knowing that isn't enough, necessarily, to satisfy written
5 description.

6 MS. SCHWARZ: Exactly, Your Honor. This is simply a research
7 plan. The patent, all that it does for the co-crystals beyond those in the
8 examples is tell the person of ordinary skill to test an API and a co-former,
9 put them together and see what happens. The law is clear. For example, in
10 Ariad, also the Pure Circle case that we cited in our papers, that a research
11 plan that requires extensive experimentation to implement in an
12 unpredictable field lacks adequate written description.

13 I'd like to talk briefly, turning to slide 25, about the prosecution
14 histories of two related family members that also claim priority to the same
15 '956 application, because these also support the lack of written description
16 here. I'm going to talk specifically about the '223 application and the
17 Almarsson Patent. And both of those include the same inventors as the '344
18 Patent. And in both cases the applicant for prosecuting claims of similar
19 scope to the '344 Patent claims, that's not disputed.

20 So, starting with the '223 application on slide 27. During prosecution
21 of the '223 application, the Examiner specifically rejected the pending
22 claims of that application, noting that they were broad and generic with
23 limitless possible structural variation and no correlation between structure
24 and function between the specific examples disclosed in the specification.
25 That's the 19 numbered examples.

1 Turning to slide 28 in the same Office action, the Examiner explained
2 that the specification did not include a sufficient variety of species to support
3 the broad genus claims. And while there was adequate written description
4 for the co-crystals in the examples that didn't support broader claims. This
5 application was subsequently abandoned. But the Examiner's reasoning here
6 in the '223 application applies equally to the challenged claims of the '344
7 Patent. The claims are broad and extend far beyond the scope of the
8 examples. And the Patent Owners here haven't disputed the applicability of
9 the Examiner's statements in these related prosecutions to the asserted
10 claims.

11 A second related prosecution involves the Almarsson Patent. And
12 here the applicants were trying to obtain claims to co-crystals made up of
13 specific APIs that were identified in the specification there along with any
14 co-crystal former. So, the '344 claims are actually broader than these claims
15 in that they're not limited to specifically identified APIs, they only need to
16 be APIs with certain chemical functionalities.

17 Now, during prosecution of the Almarsson application as shown on
18 slide 30, the Examiner rejected claim 1 that we just looked at, stating there
19 was written description for only the co-crystals that were actually made and
20 reported in the examples, not all co-crystals with the claimed APIs. In
21 response, the applicants canceled all of the pending claims here and sought
22 claims limited to the specific co-crystals that were made and disclosed in the
23 examples. Again, the Examiner's reasoning here during Almarsson applies
24 equally to the '344 Patent claims whose scope is even broader.

25 Now I'd like to address arguments that the Patent Owners have made
26 with respect to written description, and these are on slide 31. So, first, as

1 Judge Fredman mentioned earlier, one of the Patent Owners arguments on
2 common structural features is that there are some sort of common structural
3 features associated with the claimed co-crystals. And one of the things the
4 Patent Owners have argued is that they have similar structures based on
5 hydrogen bonding between the APIs and the co-formers, but starting with
6 the final product, starting with the already formed co-crystal that has been
7 made and analyzed, that's the wrong analysis. That's doing the analysis
8 backwards.

9 To show that the inventors had possession of the claimed invention
10 and not just a research plan, the person of ordinary skill has to look at the
11 disclosure in the specification. And here that specification doesn't tell the
12 person of ordinary skill which API and co-former combinations will form
13 the claimed co-crystals. That's because the applicants didn't know which
14 API and co-former combinations would produce the claimed co-crystals
15 beyond the ones they specifically made and tested.

16 Now, the second argument that the Patent Owners have made on
17 written description is that a person of ordinary skill could rely on their
18 knowledge of hydrogen bonding and Etter's Rules to predict which co-
19 crystals might form and that was common knowledge that didn't need to be
20 disclosed in the specification. Now, as a factual matter, this argument is
21 incorrect. As I've already explained, Etter Rules were subject to many
22 limitations and knowledge of hydrogen bonding is not the same as predicting
23 co-crystal formation. The Patent Owners here have no evidence that
24 knowledge of hydrogen bonding or Etter's work would enable or would
25 allow a person of ordinary skill to predict the full scope of claimed co-
26 crystals.

1 The art well after Etter's Rules were published made clear that
2 knowledge of hydrogen bonding and synthons did not make co-crystals
3 predictable. And I'd like to just go back to that for a minute because we
4 missed it earlier. All right. So, here is some art that was available as of
5 March 2003. We have two examples, and both of these make clear that even
6 though knowledge of hydrogen bonding was something that was available in
7 the field and knowledge of Etter's Rules was something that was known to
8 people of ordinary skill, had been known since 1990, co-crystals remained
9 unpredictable. Desiraju says, in Exhibit 1024, that even after identifying an
10 important intermolecular interaction, he's referring there to an interaction, a
11 hydrogen bonding interaction. Failure to predict a crystal structure can arise
12 because the same interaction can be used to make many different synthons.
13 The synthon concept tries to simplify what's essentially a very difficult
14 problem. But even with apparently straightforward synthons, things can go
15 wrong.

16 And similarly, Dunitz in Exhibit 1026 in a paper entitled "Are Crystal
17 Structures Predictable?" says, one can describe almost any observed crystal
18 structure in terms of hydrogen bond interactions. The trouble with this
19 approach is that its physical basis is shaky and its predictive capacity is poor.
20 Of course, inspired guessing may occasionally lead to a correct prediction
21 with any approach. So, here, this is the prior art confirming that even with
22 knowledge of hydrogen bonding principles and Etter's Rules, co-crystals
23 remained unpredictable.

24 Now, related to this, as shown on slide 32, during prosecution of the
25 '223 application, that's one of the two related applications that we looked at
26 earlier, the Patent Office previously considered and rejected the argument

1 that the Patent Owners are making now, which is that the '956 application
2 knowledge of hydrogen bonding allows for some sort of correlation between
3 structure and function. The Examiner there correctly noted that the whole
4 structure of each component of the co-crystal has to be taken into
5 consideration. So, it's not proper just to focus on hydrogen bonding between
6 two functional groups while ignoring the rest of the API in the co-former.

7 Now, as a legal matter, the Patent Owners' argument here on written
8 description relying on Etter's Rules and hydrogen bonding is also incorrect.
9 And despite their accusations, Novartis, Petitioner, hasn't required any
10 heightened standard with respect to requiring conventional and well-known
11 information be disclosed in the specification. Applying knowledge about
12 hydrogen bonding or Etter's Rules to predict co-crystal formation was not
13 known at all. They haven't presented evidence that that was known at all, let
14 alone that that was common general knowledge that did not need to be
15 disclosed. So, for that reason the slew of cases they've cited on this point are
16 not relevant.

17 All right, I will turn now to enablement, which we've already touched
18 on briefly. So, with respect to enablement, seven of the eight Wands factors
19 all support enablement and the remaining factor is neutral. So, the first
20 factor, breadth of the claims, plainly supports no- enablement. We've
21 already discussed this in detail. I won't go over it again, but it's undisputed
22 that this factor supports non-enablement.

23 Turning to slide 35, the next three factors are nature of the invention,
24 state of the art, and predictability of the art. These also support non-
25 enablement. The '344 Patent claims here relate to co-crystals. And as
26 shown on slide 36, Novartis has cited prior art references showing that co-

1 crystals were not predictable as of 2003 even though there was knowledge of
2 Etter's Rules and hydrogen bonding. For example, we have Desiraju saying
3 that it's difficult to predict supramolecular structures, in Exhibit 1024. We
4 have Dunitz saying the predictive capacity of using hydrogen bonds is poor.
5 And we have the Patent Owners' admission that the state of the art as of
6 March 2003 was that it was not understood which factors would
7 predetermine the formation of a drug co-crystal and that random trial and
8 error was required. So, all of these factors support non-enablement.

9 Turning to slide 38. The next factor is relative skill of those in the
10 art. Now, Petitioner doesn't dispute that the level of skill in the art here is
11 relatively high, but no amount of skill makes co-crystals predictable, so the
12 level of skill here doesn't favor enablement, and this factor is neutral. It's
13 also improper to do what the Patent Owners are attempting to do here, which
14 is to rely on the POSA skill as a substitute for an enabling disclosure.

15 Turning now to slide 39, the last three Wands factors also support
16 non-enablement, the presence or absence of working examples, the amount
17 of direction or guidance, and the quantity of experimentation. According to
18 the Patent Owners' expert, there are no more than nine working examples
19 that fall within the scope of the claims, claims 10 and 18, and only three
20 within the scope of claim 11. These examples are not representative of the
21 full scope of the claims. That's not disputed. They show only three different
22 APIs and only one first chemical functionality. There are no examples with
23 multiple APIs or multiple co-formers. And as we've already discussed,
24 there's nothing in the remainder of the specification that would allow one of
25 ordinary skill to make and use the full scope of claimed co-crystals without
26 undue experimentation. And without the ability to predict which API and

1 co-former combinations will form the claimed co-crystals, the person of
2 ordinary skill would need to conduct even more extensive trial and error
3 experimentation to practice the full scope of the very broad claims here. The
4 amount of work here is certainly undue. As I've already discussed the Patent
5 Owners' attempt to address this by relying on high-throughput screening.
6 But that doesn't change the result for the reasons I've explained.

7 So, because seven of the eight Wands factors support enablement and
8 one is neutral, there's ample support for a finding of non-enablement here.
9 Non-enablement is also supported by the prosecution history of the
10 Almarsson Patent, one of the related applications we've discussed already.
11 As shown on slide 44, the Examiner there explained that the state of the art
12 regarding the formation of different crystalline forms is unpredictable due to
13 the numerous different crystallization factors needing to be controlled to
14 provide different crystal states. The Examiner there also rejected arguments
15 that any experimentation was routine and that the specification provides a
16 reasonable amount of guidance with respect to the direction in which
17 experimentation should proceed. And that same analysis applies to the
18 challenge claims here.

19 So, for all these reasons, Petitioner respectfully requests that the
20 Board find the challenge claims unpatentable. Happy to answer any
21 questions Your Honors may have.

22 JUDGE SNEDDEN: Judge Fitzpatrick?

23 JUDGE FITZPATRICK: I'm sorry Ms. Schwarz, I was slow to
24 unmute myself. I had a question.

25 MS. SCHWARZ: Sure.

1 JUDGE FITZPATRICK: On slide 44, this admission, so to speak,
2 has made another patent application. Does, how does, you know, what does
3 Patent Owner say in response to this?

4 MS. SCHWARZ: In?

5 JUDGE FITZPATRICK: To the Examiner. What did they say?

6 MS. SCHWARZ: So, in this --

7 JUDGE FITZPATRICK: In other words, what happened after this?

8 MS. SCHWARZ: In this IPR, they've said nothing at all. During the
9 Almarsson prosecution, I can't remember if it's right after this rejection,
10 which I think it might have been, they canceled all of the pending claims and
11 sought claims that were limited to just the specific co-crystals that were
12 exemplified in the examples of the Almarsson specification and that issued
13 as the Almarsson Patent.

14 JUDGE FITZPATRICK: Thank you.

15 JUDGE FREDMAN: Since we're doing questions, let me ask one
16 more.

17 MS. SCHWARZ: Sure.

18 JUDGE FREDMAN: So, on the quantity of experimentation, you
19 have a statement, I know from your deck (phonetic) here that says it's an
20 undue quantity of experimentation. Does he describe that in any way or
21 does he really just say it's undue without giving, it would take skilled
22 researchers two years to do one molecule or whatever, that kind of thing?

23 MS. SCHWARZ: I think, Your Honor, it's the combination of all the
24 work here that is certainly undue. He does talk about the time required to do
25 certain things. We know that there are at least 50 APIs, thousands of co-
26 formers, 27 different potential solvents that were used --

1 JUDGE FREDMAN: Right. I mean, I hear that. I guess I just am
2 thinking that if I'm a big pharmaceutical company and I want to, you know,
3 (inaudible), let's say, and I want to spend, you know, a few hundred
4 thousand dollars and have a couple grad students do it, I mean that might not
5 actually take that much time. I'm not really going to challenge you on
6 predictability here, but in terms of the amount of time to do, you have one,
7 you know, three or four people who each, you know, work all day doing
8 this. It might not. I mean, do you have any evidence that it really would
9 take a lot of time?

10 MS. SCHWARZ: Well, I think Your Honor's question may assume
11 that high-throughput screening was available to do this type of
12 experimentation.

13 JUDGE FREDMAN: Even without high-throughput screening, just
14 people with pipette machine, you know, doing it the old way.

15 MS. SCHWARZ: For 50 APIs, thousands of potential co-formers in
16 any stoichiometric ratio, as well as the need to do single crystal, gross single
17 crystals, which Dr. Rogers explains could take anywhere from a few days or
18 a few hours to a few days and then to run single crystal analysis, which can
19 also be a time consuming process running the single crystal analysis.

20 JUDGE FREDMAN: Is there evidence though of all of this in the
21 record? And can you point to something for me where he says all this. You
22 can do that in rebuttal if you'd rather.

23 MS. SCHWARZ: Sure, I can, get --

24 JUDGE FREDMAN: Because I'm just thinking to myself, the lab
25 below me when I was in graduate school was a crystallization lab. And they
26 would have every cabinet full with those 96-well plates. And that was all

1 different proteins doing that. And it seemed like they had a bunch of people
2 doing it. And they could do a bunch of crystallization experiments in a
3 fairly short, I mean, months. It wasn't like days. But no, that's quantity.
4 That doesn't really help with all the other factors, but I'm just curious. Okay,
5 thanks.

6 MR. KANE: Excuse me, Your Honor, does this cable extend?

7 JUDGE SNEDDEN: Mr. Kane, will you be reserving any time for
8 rebuttal?

9 MR. KANE: Twenty minutes, Your Honor. We are ready, Your
10 Honor, whenever you are.

11 JUDGE SNEDDEN: We are ready.

12 MR. KANE: Good afternoon, Your Honors. Michael Kane,
13 appearing on behalf of Patent Owners. So, the '344 Patent is entitled to the
14 priority date of no later than the date of the U.S. Application 19/378,956,
15 which is March 3, 2003. The application provides more than adequate
16 written description support for the claims and also enables the claims.
17 Starting with some of the -- there was a lot of discussion about high-
18 throughput screening. I want to go right to that. If you look at Dr. Ward's
19 declaration, he starts high-throughput screening.

20 JUDGE FREDMAN: What exhibit is that?

21 MR. KANE: Excuse me, it is Exhibit 2014.

22 JUDGE FREDMAN: Okay.

23 MR. KANE: And I'm looking at paragraph 47, which starts on page
24 20. And there he starts to describe the fact that high-throughput screening,
25 what it is, and cites to, at the end of that paragraph, this Morissette prior art
26 reference 279, Exhibit 2011 at 279. He continues, in 48, to talk about this.

1 And he says at the next, in paragraph 48, high-throughput screening
2 techniques have been used in pharmaceutical context since at least
3 2002/2003. So, the relevant date. Most notably in the area of drug
4 discovery and citing again, this Morissette reference continues down a little
5 bit later in that paragraph, another reference, Peterson, that describes a series
6 of iterative high-throughput experiments for generation and identification of
7 acetaminophen polymorphs, excuse me, across thousands of crystallization
8 conditions.

9 JUDGE FREDMAN: Are those co-crystals?

10 MR. KANE: They're not co-crystals, but it's the same concept here,
11 Your Honor, of, they're changing the crystallization conditions and
12 generating polymorphs.

13 JUDGE FREDMAN: So, they're essentially randomly screening a
14 number of different conditions to see if they can get co-crystals?

15 MR. KANE: Right. But the point is they can do that very quickly
16 and they can do thousands very quickly.

17 JUDGE FREDMAN: Right.

18 MR. KANE: Continuing though, Your Honor.

19 JUDGE FREDMAN: So, you're speaking to enablement now?
20 That's where your focus is?

21 MR. KANE: I am. I am, generally. Although I think it plays into
22 written description.

23 JUDGE FREDMAN: I don't think this plays very well for written
24 description.

25 MR. KANE: Okay.

1 JUDGE FREDMAN: I think Rochester tells you that just screening
2 something that you don't know what it does, a COX-2 inhibitor is not,
3 Rochester is actually, after your priority date, even, says that's not good
4 enough.

5 MR. KANE: Yeah, and I don't think that's the written description
6 argument we're making. We're making really that the structural components
7 are in the claim.

8 JUDGE FREDMAN: Okay.

9 MR. KANE: But continuing on with this discussion to respond to
10 Petitioner's argument, paragraph 49, again, continues with the same
11 discussion of the same reference. And you'll see there that quoting from that
12 at page 275 it describes, and Dr. Ward opines, that these emerging strategies
13 are used for instance to identify polymorphs. Then he continues, dot, dot,
14 dot, however diverse salt forms co-crystals. Co-crystals, Your Honor,
15 hydrates and solvates are also to study in high-frequency crystallization
16 systems. So, in 2003, Morissette was teaching using high-frequency
17 screening for co-crystals.

18 JUDGE FREDMAN: Okay, so speaking to that now in terms of the
19 Etter's Rules and the predictability, I'm kind of interested in that as well.
20 When you talk about the Etter's Rules in your briefs, you seem to imply that
21 you could use that to predict what co-crystals would form. Can you give an
22 example where that was done prospectively?

23 MR. KANE: I can, Your Honor.

24 JUDGE FREDMAN: Okay.

25 MR. KANE: We've cited that in our sur-reply at page 4.

26 JUDGE FREDMAN: Can you point to an exhibit where it was used?

1 MR. KANE: Yes. So, we cite several exhibits in responding to Dr.
2 Rogers contention on that we cite to Aakeroy Exhibit 1025.

3 JUDGE FREDMAN: 1025.

4 MR. KANE: We quote a similar classification of three polymorphs
5 of two reveals that the expected intermolecular amino nitro hydrogen bond is
6 present. so, it's expected. So, they --

7 JUDGE FREDMAN: Does it say, though, that they design the
8 crystallization expecting that to form or simply that -- I mean, you're kind of
9 reading something into it a little bit, I think.

10 MR. KANE: Well, but the point being that they -- right. That they --
11 but according to the Petitioner, it's completely unpredictable. So, you
12 couldn't design it with the expectation that it would form any crystal. But
13 these --

14 JUDGE FREDMAN: I think it's going to depend, right, on the
15 situations. And so, I think that when you say you can predict it, there's lots
16 and lots of different molecules, some of which have multiple groups, some
17 of which have single groups. If you have a single groups, which I think is
18 the situation here, there's two groups that are interacting, right. Like on page
19 164 of the however you pronounce that guy's name reference, there's scheme
20 two. And it looks like there's basically in this case, it's always essentially
21 hydroxyls to carbonyls and amines to sort of free nitrogen or whatever you
22 want to call that. So, it's a little bit, it's a limited case.

23 MR. KANE: Well, but that's the whole thing is that kind of goes to
24 the point that I think that we think the Petitioner is overlooking, is that again,
25 these are persons of very high level of skill. They're going to design the

1 experiment. They're not just randomly picking co-formers and crystals and
2 solvents. Right? They are looking at the structure of the API.

3 JUDGE FREDMAN: Yeah, but you're claiming any of them. So,
4 your scope of your claim is very, very large. I mean, it's essentially the
5 entirety of chemical space with those three things in it.

6 MR. KANE: Well, there's --

7 JUDGE FREDMAN: Essentially.

8 MR. KANE: But only to the extent that it, first of all, there are
9 requirements that it has to form a homosynthon. It has to be able to then
10 form --

11 JUDGE FREDMAN: Right, but that functional recitation is
12 indeterminable in advance. Unless you can tell me how. You don't know
13 what's going to form a homosynthon. In other words, if I take a computer
14 and I generate compounds that fall within the scope of your claim, we could
15 easily generate hundreds of millions, hundreds of billions of them. It will be
16 no trouble at all. Right? And we don't know which of those are going to do
17 what, right?

18 MR. KANE: But I think the distinction here, Your Honor, is in some
19 of the other case law, like Amgen (phonetic) and Ariad and those types of
20 cases where again, we're not -- the difference here is those cases, for
21 instance, like the antibody cases in particular I'm most familiar with, there's
22 no structure. You're just looking at the result. You're saying, are we going
23 to bind and block at a particular site, right? And so, we can generate
24 millions of molecules. Some are going to bind and block, some are not. We
25 don't know without testing them. Here we have specific structure
26 requirements. You have to have these three first chemical entities. You've

1 got to have it form a homosynthon. You've got to be able to then
2 form the --

3 JUDGE FREDMAN: I mean, the antibodies all have to have amino
4 acids. So, I mean, you could easily say that they have at least as much
5 structure as you, in fact, more amino acids are certainly more structure than
6 the three compounds you've got.

7 MR. KANE: But here the structure is tied to the functionality. The
8 bond that's being formed is with the structural components.

9 JUDGE FREDMAN: it's --

10 MR. KANE: Certainly, antibodies have amino acids, but you don't
11 know which one of the amino acids. If you go to the Amgen case, for
12 instance, that's what they said. You don't know. You have to try them all
13 and find out. Or you can do conservative substitution, starting with one that
14 works and change it until you figure out which one is sort of the linchpin.
15 But that's not what we're talking about here. Unless you have these three
16 components, these three groups and their function -- and the bond has been
17 formed, hydrogen bond has been formed to form this co-crystal. It's not
18 within the scope of the claim.

19 JUDGE FREDMAN: I don't really say that's different than let's say
20 Ariad itself where we have a NF Kappa B. So, a fairly small molecule.
21 Right? Not tiny, but we're binding it to what is really a small molecule and
22 we just screen and that wasn't good enough.

23 MR. KANE: Right. Because there's no particular structure. You
24 don't know --

25 JUDGE FREDMAN: There is. There's a structure of NF Kappa B.
26 We know exactly the structure of NF Kappa B. I could draw it for you.

1 MR. KANE: But they didn't identify where the binding was. And
2 there could be other -- again, the antibody in those kind of cases, you don't
3 know where the binding has occurred.

4 JUDGE FREDMAN: NF Kappa B isn't an antibody, it's a growth
5 factor, but yeah.

6 MR. KANE: What?

7 JUDGE FREDMAN: It's a protein, I think, but not an antibody.

8 MR. KANE: Yeah. Right. But if you -- again, I guess I'm not as
9 familiar with the case as you are, Your Honor, but.

10 JUDGE FREDMAN: Sure.

11 MR. KANE: But if you know exactly what the structure is of both
12 pieces and you know exactly where the binding is, well then why do you
13 have to screen a million compounds?

14 JUDGE FREDMAN: Well, in your case you'd still need to know
15 which amounts to use to co-crystallize. You wouldn't even know still, even
16 with that.

17 MR. KANE: And that's where the high-throughput screening comes
18 in, Your Honor, and that's what Morissette teaches, is that a person of
19 ordinary
20 skill --

21 JUDGE FREDMAN: But we don't know where the bond is going to
22 be in advance.

23 MR. KANE: You don't, but that's the point is you're not -- that's why
24 you're screening. In this case --

25 JUDGE FREDMAN: But if you don't know where the bond is going
26 to be and you don't know what you're going to get. Yes, you could screen

1 for it. I'm not really challenging enablement as hard. I'm really focused on
2 description more.

3 MR. KANE: Right.

4 JUDGE FREDMAN: Though I think it is unpredictable. I think
5 there's some degree of unpredictability I would contend, but at least I think
6 that's supported by the evidence that Petitioners brought forward. But I
7 think that from a description standpoint it's really complicated.

8 MR. KANE: I'm sorry, I missed that, Your Honor.

9 JUDGE FREDMAN: It's really complicated from a description
10 standpoint. I mean, here to say that you've described something where I
11 don't know what I'm starting with other than three basic very functional
12 groups, very simple groups and I'm adding something to them. And then I'm
13 going to get a bond of a hydrogen bond and other things. There will be
14 steric issues as well, which is kind of the big issue with the antibody cases.
15 Right? Those --

16 MR. KANE: Yep.

17 JUDGE FREDMAN: -- because you are essentially operating under
18 steric concerns. And then I'm going to end up getting something and I don't
19 know what it is and you haven't told me how I can get it. You're not telling
20 me I can use a docking program. You haven't, at least, provided evidence
21 that I'm aware of that that was well known, that I can just run it on a
22 computer. So, you've actually got to do it.

23 MR. KANE: Right. You had to do it, Your Honor. And so, but
24 again, I think you're not giving full credit to the person of ordinary skill.
25 And the fact this is an API, it's been fully characterized. We understand the
26 structure, we know where the groups are, we know the solubility, we know

1 all those characteristics of that molecule and we can see which groups are
2 available for this. And it claims three specific groups for this hydrogen bond
3 formation. And then we can look at co-formers and understanding the types
4 of solubility, parameters, and things that are going to affect the performance
5 of the co-former. The person of ordinary skill is able to create the scenario
6 and --

7 JUDGE FREDMAN: But the person of ordinary skill, I mean, I
8 think to some extent you're almost saying they're, I mean, you know, as an
9 Examiner in 2003, we often got to meet with the clients, you know, when
10 they come in and argue their cases. And I mean they were PhD scientists
11 with years of experience. They weren't able to just do this stuff magically.

12 MR. KANE: Well, it takes work. But there's a lot of prior art, Your
13 Honor. They're making crystals, they're making co-crystals, and they're
14 saying that they getting the expected structures or that the rules, the bonds
15 are being formed in an expected way consistent with Etter. And they notice
16 and they, in references they'll say, you know, these nine followed and gave
17 us the expected structure; this one didn't; it gave us an unexpected structure
18 because there was some ambiguity. But, that's fine. Again, largely what the
19 Petitioner is trying to demand is that the person of ordinary skill, before
20 running the experiment, has to know what the result is. They have to know
21 the particular structure. And that's really the problem here because --

22 JUDGE FREDMAN: How are you certain that that isn't the law, that
23 that isn't required even?

24 MR. KANE: That you have to know the result from the experiment?

25 JUDGE FREDMAN: Well, that you have to know what you're going
26 to get, if you're claiming it.

1 MR. KANE: The --

2 JUDGE FREDMAN: Why is that wrong?

3 MR. KANE: Because it --

4 JUDGE FREDMAN: There's a case that's says you don't need to
5 know that, that you can get away with just saying, well, we're going to get
6 something, it's okay to get something? I'm just talking about --

7 MR. KANE: I'm not saying you're going to get something, I'm
8 saying you're going to get --

9 JUDGE FREDMAN: -- is there's a case on point for that?

10 MR. KANE: I think Ariad stands for that proposition.

11 JUDGE FREDMAN: Ariad says you don't. Ariad was a --

12 MR. KANE: It --

13 JUDGE FREDMAN: They did not find satisfaction in the written
14 description requirements.

15 MR. KANE: Right. But they --

16 JUDGE FREDMAN: That would go the other way. I don't think that
17 supports your position.

18 MR. KANE: But they said that you could satisfy written description
19 through structural features directed at --

20 JUDGE FREDMAN: If you have the structure in advance, that's
21 good enough. Sure.

22 MR. KANE: And we have the structure in advance. That's the
23 whole point.

24 JUDGE FREDMAN: You have the structure of three things, not of
25 the complex.

1 MR. KANE: Right. But we have the structure of the three that are
2 going to form one side of the hydrogen bond and then we're going to pick
3 co-formers that are complement, that have to be complementary to those
4 three to form the other side of the hydrogen bond.

5 JUDGE FREDMAN: Yeah, right.

6 MR. KANE: So, we have that structure. Persons of ordinary skill
7 are doing this. And again, it's really, it's very analogous, I think, or we
8 think, to the polymorph situation. Right? Again, again, that's why they do
9 all these polymorph analyses at the time where they were taking
10 acetaminophen, for instance, and doing thousands of different conditions and
11 getting all kinds of polymorphs. And even in drug development, as the
12 references show, they would, you know, they would get a drug, they would
13 get an API, they would then run a variety of conditions to get the most
14 robust crystalline form --

15 JUDGE FREDMAN: Mm-hmm?

16 MR. KANE: -- so that they could then have stability or solubility,
17 whatever the parameters were that they needed, and guarantee that in their
18 manufacturing process, that's what they got because they didn't want to have
19 variations. This is really no different. This is saying we have this API, we
20 can analyze what this API is, we can make informed decisions based on the
21 fact that we know how hydrogen bonding works, we know what Etter's
22 Rules are. We can look at the steric issues, and if there are steric issues, we
23 can account for that. Not all APIs are, even if they had these groups
24 necessarily would fall within --

25 JUDGE FREDMAN: But your expert said it's only 20 percent, right?

26 MR. KANE: That --

1 JUDGE FREDMAN: Compared to 74?

2 MR. KANE: That's not what he said. Our inventor did do an --

3 JUDGE FREDMAN: Dr. Ward said, in Exhibit 2014, said, I would
4 have viewed a 20 percent success rate in co-crystallizing as an acceptable
5 benchmark for success.

6 MR. KANE: Right.

7 JUDGE FREDMAN: Okay. So, that suggests that 20 percent is
8 good. And you know, I'll be honest, that's not, you know, passing grade in a
9 lot of places.

10 MR. KANE: Well, you have to look at that in context, Your Honor.
11 And what Dr. Ward actually says is you don't know about the other 80.
12 Right. They took 50 compounds or 50 co-formers, they got 10 co-crystals
13 formed, the other 40 didn't. But you don't know how the experiment was set
14 up. And in fact, if you look at the reference, again, I'll go to Dr. Ward,
15 paragraph 49 at the end of that paragraph. Right. Again, this is this
16 Morissette reference talking about high throughput.

17 JUDGE FREDMAN: I think it's a different reference, but yeah.

18 MR. KANE: I think it's actually the same reference, but.

19 JUDGE FREDMAN: No, I think you're talking about Exhibit 128,
20 which is, what is that one? Fleischman (phonetic). That's the reference that
21 did crystal engineering in 2003.

22 MR. KANE: Yeah, well, whichever reference it is, but you can see
23 the sentence there, Your Honor, high-throughput crystallization experiments
24 can yield hit rates ranging from tens of percents to nearly 100 percent
25 depending upon the type of experiment, and the process molds (phonetic)
26 you. So, again, just saying I ran this experiment, maybe they expected only

1 20 percent. That doesn't mean it was a bad result if they thought the other
2 40 co-formers were not likely to form.

3 JUDGE FREDMAN: Yeah. But the problem is that it's screening,
4 it's not resulting. I mean, you have Dr. Rogers who says, for example, in the
5 deposition, which I thought was interesting, there's no predictive capability
6 of crystallization. This is at page 22, I think, of the second deposition of Dr.
7 Rogers in Exhibit 2017. A lot of that's discussed in the papers, which go
8 into many factors that Dr. Etter doesn't consider and which she admits. And
9 Dr. Rogers really gives a very nice explanation here of why he thinks that it
10 is strongly unpredictable.

11 MR. KANE: Well, again, we've cited documents and we've quoted
12 the papers that talked about getting the expected results. So, he says it's
13 unpredictable. He says you can't predict.

14 JUDGE FREDMAN: He cites the papers too. This is not --

15 MR. KANE: Right.

16 JUDGE FREDMAN: -- an unsupported declaration.

17 MR. KANE: Well, okay, if you look at Dr. Rogers, and we've dealt
18 with that as well, Your Honor, at page 20 of the Patent Owner response.

19 JUDGE FREDMAN: Okay.

20 MR. KANE: If you look at Dr. Rogers declaration, paragraph 78, he
21 says a POSA would have understood the entire structure of the API and the
22 co-fomer must be taken into account in determining whether any particular,
23 particular, co-crystal will form. Right. And then next, even after identifying
24 the important molecular interactions, failure to predict a crystal structure can
25 arise because the interaction can be used to make many different synthons.
26 That's the point. You're going to make lots of, you're potentially going to

1 get multiple polymorphs, multiple synthons from an experiment. Our claims
2 don't care. Again, in these crystal engineering papers --

3 JUDGE FREDMAN: But when you're saying they don't care, that
4 kind of is the problem to me. You're saying, we don't know what we're
5 going to get; we're claiming anything that we get; we haven't described it,
6 we're claiming it.

7 MR. KANE: No, we have described it, Your Honor. I said --

8 JUDGE FREDMAN: You described it by saying we want it as a
9 functional thing.

10 MR. KANE: No, it's not a functional thing. It's because the structure
11 exists. When I say different synthons. So, if we get three polymorphs, that's
12 all, that's a success in our --

13 JUDGE FREDMAN: And what if they're, I mean, they're not all
14 going to necessarily have the right hydrogen bonding, right?

15 MR. KANE: They're what?

16 JUDGE FREDMAN: We've already established that the hydrogen
17 bond isn't necessarily the interaction point.

18 MR. KANE: I'm assuming that we've got three with the hydrogen
19 bond that meet --

20 JUDGE FREDMAN: Okay, so --

21 MR. KANE: -- the scope of the claims. Right. So, that's the point.

22 JUDGE FREDMAN: They have to be determined by crystallization.

23 MR. KANE: What?

24 JUDGE FREDMAN: We have to do X-ray analysis of the crystals.

25 MR. KANE: You would. To confirm it. But again, he's assuming
26 that, that -- but again, all of these as cited here, he's citing, you know, in the

1 next one, again, talking about Fleischman, the 2003 paper. Right. The
2 crystal packing tends to be less predictable, right, than other organics. They
3 often have multiple avenues for self-assembly and therefore are predisposed
4 to exhibit polymorphism.

5 JUDGE FREDMAN: Mm-hmm.

6 MR. KANE: Right. So, that's the point. They're going to make
7 these different polymorphs. All of which would fall within the scope of our
8 claim. Now, the crystal engineer may not be happy because he or she wants
9 to limit the number of polymorphs and identify the polymorph that's
10 desirable for a manufacturing process. But in terms of the scope of the
11 claim, and in terms of being within the scope of the claim, all of the
12 polymorphs are in the scope of the claim. And so, Dr. Rogers --

13 JUDGE FREDMAN: If --

14 MR. KANE: -- is requiring that --

15 JUDGE FREDMAN: You're also assuming they will all form, which
16 I don't know that is a guarantee either, because you have to have particular
17 conditions for crystallization.

18 MR. KANE: And that's why you do high-throughput screening and
19 you do as they did in the acetaminophen, thousands of different
20 crystallization schemes. Thousands. Because again, you have different
21 solvents, different temperatures, different concentrations. Yes. That's why
22 you do thousands. And that's what they did in acetaminophen. That's why
23 high-throughput screening enables these claims, because you can get there.
24 And that's what, again, it's a -- a person of ordinary skill is going to design
25 the experiment in view of all the pre-formulation work and the
26 characterization of the API and all of the, you know, characterization of the

1 co-formers and then come up with an informed experiment to put those two
2 together under various crystallization conditions with the expectation that
3 the Etter Rules are going to be filed and the hydrogen bonds are going to
4 form.

5 JUDGE FREDMAN: The expectation, not the prediction.

6 MR. KANE: Nothing's perfect, Your Honor. They predict based on
7 Etter's Rules.

8 JUDGE FREDMAN: So, this is --

9 MR. KANE: They expect.

10 JUDGE FREDMAN: When you're doing high-throughput screening,
11 you're not using Etter's Rules to predict. You can't say that, too.

12 MR. KANE: Well, you are. They are. That's --

13 JUDGE FREDMAN: How?

14 MR. KANE: Because they're, by picking the co-former and the --

15 JUDGE FREDMAN: But they don't know what they're going to get,
16 so they don't know where it's going to interact. Water is going to make a
17 difference. Right? I mean, when you try and crystallize things, the hydrates,
18 which your opposing counsel pointed out, have tremendous effects on these
19 crystals. Right? And so, it's clear that when you crystallize with water
20 present, for example, in the hydrate situation, the bonds could shift all over
21 the place. So, to argue that you can predict what the bond is going to be
22 when you're simply throwing a bunch of things together, screening 10,000 of
23 them and finding it, I think that that's a little bit of an overstatement. I think
24 it's a lot of an overstatement.

25 MR. KANE: Well, they -- that reference, what that reference points
26 out is, again, I would argue that reference actually supports our position.

1 They were able to form the hydrates. They didn't say it was hard to form the
2 11 hydrates that were analyzed. What they said was there was more
3 variability because of the water that affected in particular the thermal
4 stability of the resulting co-crystals.

5 JUDGE FREDMAN: Which says the temperature is another factor
6 you've got to play with.

7 MR. KANE: It is. That's part of the --

8 JUDGE FREDMAN: Yeah.

9 MR. KANE: -- crystallization scheme. But I think there they were
10 talking about more of the stability once it had been formed. But again, they
11 formed the 11 crystals, Your Honor, even with the hydrate. And they
12 analyzed those 11 crystals and pointed out, yes, that adding the hydrate in,
13 adding the water in does lead to more randomness and get different kind of
14 results. But they were -- and so even between the, in the crystals that they
15 formed, they saw different, much more variations.

16 JUDGE FREDMAN: So, they point to Etter's Rules in their paper?

17 MR. KANE: I don't know that they, I don't believe that I saw
18 that --

19 JUDGE FREDMAN: Okay.

20 MR. KANE: -- language in there. But again, it's, I don't think that
21 people necessarily point to Etter's Rules, you know, every day. They know
22 Etter's Rules. And Dr. Rogers admitted that at his deposition. And he
23 admitted, he said, you know, that it was important in 1990 when she wrote
24 them. It was important in the early 2000s when this patent was being filed.
25 It's important today. That's what he testified to.

26 JUDGE FREDMAN: Yeah.

1 MR. KANE: So, these persons of ordinary skill, they know that.
2 They know these hydrogen bonding, you know --

3 JUDGE FITZPATRICK: Mr. Kane.

4 MR. KANE: Yes.

5 JUDGE FITZPATRICK: Let me answer the question. It may be the
6 identical question may have misheard. I don't know what the subject of
7 what was in their last question, but I want to know whether the patent that's
8 being challenged, whether it mentions Etter's Rules, because I don't. I didn't
9 see that asserted in the briefs.

10 MR. KANE: It does not explicitly mention that, Your Honor. Judge
11 Fitzpatrick. It does not mention that.

12 JUDGE FITZPATRICK: Okay. okay. That's bothersome to me,
13 that I think undercuts of some of what you're arguing. But on written
14 description. But in the brief that you're opening or paper 19, you have a
15 section dedicated to the written description and it's basically pages 16
16 through 21 and it includes just two citations to patent, column three, lines 35
17 or 37, and figure 24. What am I missing there? It seems like your whole
18 written inscription argument, almost all, except for those two minor
19 citations, is all about the person of ordinary skill in the art.

20 MR. KANE: Well, I think that because the specification doesn't need
21 to disclose all of the detail and we cite the case law to that, that these
22 techniques were well known in the art and so they did not need to be
23 included in the specification, Your Honor.

24 JUDGE FITZPATRICK: It's almost like maybe this is a slight
25 exaggeration, but to accept your argument would almost, you would have to

1 say you didn't invent anything because you're basically saying the person or
2 ordinary skill in the art already possessed all this based on his skill.

3 MR. KANE: Well, they would understand. Again, what was
4 invented, I believe, Your Honor, was forming these types of co-crystals.
5 Again, these techniques were well known for forming single crystals
6 structures. They were well known in terms of evaluating polymorphs. What
7 was new here was using these well-known crystal engineering techniques for
8 forming co-crystals for pharmaceutical use. And that's what the inventors
9 discovered. And in fact, Your Honor, if you look at Exhibit 1028, which is
10 one of the references that Petitioner has cited and that Dr. Zaworotko is a
11 reference on. If you read the conclusion on page 7 of 11, the last thing he
12 says is simply put, we have applied new tricks to old procedures and
13 molecules. So, yeah, they took --

14 JUDGE FITZPATRICK: Mr. Kane, I'm sorry, I just need to catch up
15 on the citation. Do you say Exhibit 1028?

16 MR. KANE: 1028.

17 JUDGE FITZPATRICK: Okay. In page seven of that document.

18 MR. KANE: Yeah.

19 JUDGE FREDMAN: Should be 1034 of our record.

20 JUDGE FITZPATRICK: Thank you. Okay. It's supposed to be in
21 the conclusion section?

22 MR. KANE: Yes, the last sentence.

23 JUDGE FITZPATRICK: Thank you. Okay, thank you.

24 MR. KANE: At the bottom of the page there, simply put, we have
25 applied new tricks to old procedures and molecules. All right. So, these
26 were old procedures, and that's why they didn't need to disclose them. And

1 as I'm sure the Board knows, the law is that you don't need to disclose what
2 persons of ordinary skill knew. It's undisputed that Dr. Etter's Rules were
3 very important, Dr. Rogers, Dr. Ward, agree. They were important in the
4 90s. They're important today. So, you don't need to include those kinds of
5 discussions in this specification. It's really applying those laboratory
6 techniques to this new application.

7 JUDGE FREDMAN: But the thing is, you're sort of trying to rely
8 on, essentially, the Capon reasoning, right? Where the nucleic acid
9 sequences were all known. We're just picking out nucleic acid sequences,
10 and therefore we're allowed to then claim something using those nucleic acid
11 sequences. But this really isn't Capon because your case relies on molecules
12 that are not necessarily described in the prior art that you've encompassed.
13 Capon was limited to things that were in the prior art. You are not limited to
14 things that are in the prior art. You include molecules that have not yet been
15 discovered in the scope of your claim.

16 MR. KANE: I agree with that, Your Honor, but I think --

17 JUDGE FREDMAN: So, you don't get the benefit of Capon because
18 you're claiming things that are just not a prior art. You can't say, well, the
19 prior art knew this because it doesn't know the thing. It doesn't know the
20 molecule.

21 MR. KANE: It --

22 JUDGE FREDMAN: Maybe it doesn't know the co-former. Maybe
23 both of those were recently discovered and yet you're trying to claim them.

24 MR. KANE: We're trying to claim if they meet the limitations, if
25 they have those groups, and if those groups can form the homosynthon and
26 they do form the co-crystal. Yes.

1 JUDGE FREDMAN: Right. So, if one of a thousand out of the
2 billions of possible molecules meet it, you're trying to claim that thousand,
3 one of those thousand from the billions that might exist.

4 MR. KANE: Again, I don't know that that's the right analysis. I
5 don't think that is the right analysis.

6 JUDGE FREDMAN: Well, that's what you're doing. Whether you
7 want to acknowledge it, it's fine, you don't have to, but.

8 MR. KANE: I'm not sure how you get to billions of --

9 JUDGE FREDMAN: Of molecules?

10 MR. KANE: Yeah.

11 JUDGE FREDMAN: You can draw more than billions; you could
12 draw so many that I can't give you a number because it's probably the
13 number of molecules and some 10 to the 50th type number. But just in
14 terms of rearrange molecules, there's huge numbers of chemical space.
15 Right. That's why we can't simply compute these things.

16 MR. KANE: Well, that's true. You can draw all those molecules.
17 But the question is when a person of ordinary skill has a real molecule in
18 front of them and needs to form -- and the desire to form --

19 JUDGE FREDMAN: And that might be different if you're limiting it
20 to the 53 that had already been disclosed. That would be more like the cases
21 where the Examiners like to always use the salts that can be used for co-
22 crystallization with an active pharmaceutical agent. And the Examiner will
23 say, well, any of the known 53 salts, I think there's 53 that were in that case,
24 can be used. And so, it's obvious to pick one. Right. And the Federal
25 Circuit actually found, I think that was an even unexpected result, even
26 though it was a little bit better.

1 MR. KANE: Yeah, but again, the distinction here, Your Honor, is
2 you're focusing on the molecule in total rather than the groups. And I think
3 that what we're saying is --

4 JUDGE FREDMAN: I'm looking at the scope of your claim, I think,
5 is what I'm saying.

6 MR. KANE: Well, the scope of the claim is limited to the groups
7 and what the groups have to do. And if the groups don't do that, it's not
8 within the scope of my, of the claim. And so that's the difference.

9 JUDGE SNEDDEN: Let me try to understand the scope of the claim
10 within the conversation we were just having. If we look at the claim, the
11 claim recites, basically take a first API that has a carboxamide. And the idea
12 there is we'll use what is known in the art about the supramolecular synthon
13 formation and we'll add a co-former and then we're looking for something
14 that's complementary to that first API that contains the carboxamide. Now
15 the way we're going to figure out what's complementary is that we're going
16 to use high-throughput screening until we find something that forms a
17 crystal with that first API containing the carboxamide. Is that correct?

18 MR. KANE: No, Your Honor. I think --

19 JUDGE SNEDDEN: Okay.

20 MR. KANE: -- the co-formers will be, the co-formers will be
21 selected based on the structure of the API. So, it's not --

22 JUDGE SNEDDEN: How do you do that? Now, where -- now, that
23 means --

24 MR. KANE: That's based on --

25 JUDGE SNEDDEN: So, what is complementary to a common
26 carboxamide. And where is that described in the spec?

1 MR. KANE: Well, again, I think it's not described in the spec
2 directly because that's Etter's Rules. That's saying here are these known
3 groups here that are going to form these hydrogen bonds and there's a certain
4 hierarchy depending upon the energy levels, which are going to be preferred
5 --

6 JUDGE SNEDDEN: But Etter's Rules apply specifically to
7 carboxamides.

8 MR. KANE: I think it describes all of those kinds of groups. Yes.
9 And says, and describes that these are the bonds that will form. It's not --

10 JUDGE SNEDDEN: Yeah.

11 MR. KANE: And so, therefore, a person of ordinary skill can look at
12 that carboxamide and look at another group on a co-former and say is that
13 going to form? Is that likely to form a hydrogen bond? And if it's not, then
14 that co-former could be discarded and they're going to, again, the person of
15 ordinary skill is not in the business of trying every co-former to see which
16 ones work. They're going to make an informed guess based on their high
17 level of skill and the Etter Rules to pick co-formers that will, they do expect
18 to form these co-crystals.

19 JUDGE SNEDDEN: It seems based on that answer, the claims cover
20 a whole area of chemistry involving crystallization of compounds containing
21 carboxamides.

22 MR. KANE: Well, they don't -- they cover what they cover, Your
23 Honor. And they cover the specific application here. If you have, you
24 know, an API, you will analyze that. You will identify, then, co-formers
25 that would have complementary groups that would be expected to form
26 those bonds. You would look at potential issues for steric interference. You

1 would look at the solubility of the various co-formers and the API and
2 temperature stability --

3 JUDGE SNEDDEN: Yeah.

4 MR. KANE: -- and those kinds of things. And you --

5 JUDGE SNEDDEN: Would those co-formers have a -- sorry to
6 interrupt, but will those co-formers have a common structural feature?

7 MR. KANE: They will have the groups that are known to form these
8 hydrogen bonds just like the API has the groups that are known to form
9 them. So --

10 JUDGE SNEDDEN: What are those groups?

11 MR. KANE: I didn't mean to cut you off. I'm not sure if I did.

12 JUDGE SNEDDEN: I'm sorry. I'm sorry. No worries. I might be
13 cutting you off. Please.

14 MR. KANE: Okay, I was just going to say, so, I mean, persons of
15 ordinary skill understand when they see a carboxamide what groups are
16 likely to form.

17 JUDGE FREDMAN: Does the specification list them?

18 MR. KANE: What?

19 JUDGE FREDMAN: Does the specification list any of those
20 groups?

21 MR. KANE: No.

22 JUDGE FREDMAN: Okay.

23 MR. KANE: Because they don't need to. Because they know that --

24 JUDGE FREDMAN: Does the prior art, do you point to the prior art
25 where it lists them like a citation to a reference?

1 MR. KANE: I think it would be the Etter Rules, Your Honor. All
2 the four papers that --

3 JUDGE FREDMAN: Good. Quick question to go into Judge
4 Fitzpatrick's point. He talked about things that were in the spec. Is high-
5 throughput screening in the spec or are you sort of pulling that in from just
6 the general knowledge?

7 MR. KANE: General knowledge.

8 JUDGE FREDMAN: So, it's not in the specification?

9 MR. KANE: It's not directly listed, no.

10 JUDGE FREDMAN: Okay.

11 MR. KANE: And as Dr. Ward said at the time, you could actually
12 do, I think sort of what you were referring to, Judge Fredman, Dr. Ward, at
13 the time, would do, mentions that you could either do it sort of manually.
14 You could design the same experiment and get a bunch of grad students and
15 turn them loose on the lab --

16 JUDGE FREDMAN: Yeah.

17 MR. KANE: -- and they would just do them manually. Or you can
18 do the high-throughput screening. Obviously, high-throughput screening is
19 much more efficient and you can do a lot more screening --

20 JUDGE FREDMAN: Yeah.

21 MR. KANE: -- to identify, you know, try different crystallization
22 schemes to determine which is going to result in the most desirable co-
23 crystal. But either way can be done. So, no, it was not explicitly referenced.
24 These are, you know, Dr. Ward, though, lays out in the references we've
25 walked through, show that it was being used for co-crystal analysis at that
26 time.

1 JUDGE FREDMAN: There's one other thing I'm thinking about is
2 the just all the Van der Waals forces that are involved here when you're
3 trying to sort of interact hydrogen bonding in Van der Waals. They're both,
4 I mean, there's all sorts of other factors. As Dr. Rogers points out, there's so
5 many other factors at play into how this interaction goes, whether it's going
6 to crystallize. The Van der Waals forces usually are predominant in these.

7 MR. KANE: And Dr. Ward doesn't disagree with that. I mean, I
8 don't think there's any dispute about the science here, really. Dr. Ward is not
9 disputing that. Dr. Ward acknowledges these other forces that may create a
10 different kind of bond or create a bond that doesn't, a hydrogen bond, but not
11 the hydrogen bond that would have necessarily been expected because other
12 forces and maybe the geometry of the molecules are such that a different
13 type of hydrogen bond was formed than the experimenter might have
14 expected beforehand. And we've seen some of that. Right? Again, the
15 references described, 9 out of 10 gave the experiment expected bond, one
16 gave a different bond, it formed a bond, but it just wasn't what they
17 expected. Maybe because of these types of forces that impacted that
18 reaction.

19 JUDGE FREDMAN: Just to go to the number of examples in this
20 spec, how many would you say you have? You have 19 working examples.
21 How many different molecules does that represent?

22 MR. KANE: Well, I think there's 19. I don't recall exactly. We
23 pointed to nine examples that are within the scope of the claim.

24 JUDGE FREDMAN: How many co-formers?

25 MR. KANE: I don't know the details, Your Honor. I can look them
26 up.

1 JUDGE FREDMAN: I mean, you have a list here like, you know,
2 4,4 bipyridine. I mean, they're very particular co-formers.

3 MR. KANE: What?

4 JUDGE FREDMAN: Like, I mean, example one uses, for example,
5 4, 4 bipyridine. They're very particular co-formers.

6 MR. KANE: Right.

7 JUDGE FREDMAN: Okay. So, you don't want to address that.
8 Okay, thank you.

9 MR. KANE: But again, the claims are not directed to a specific co-
10 former or specific API. And as you well point out, there could be --

11 JUDGE FREDMAN: Okay.

12 MR. KANE: -- in the last 20 years, there have been new APIs and
13 very likely new co-formers. It's the claimed -- to practice this invention, if
14 you have that structural feature that results from the experiment, it's within
15 the scope of the claim.

16 JUDGE SNEDDEN: I think I'm still struggling with that scope of the
17 claim and I'm going to try again.

18 MR. KANE: Okay.

19 JUDGE SNEDDEN: Okay. And so --

20 MR. KANE: I'll try too, Your Honor.

21 JUDGE SNEDDEN: If we look at, so, we have a compound with the
22 first functional group, it's called a carboxamide. It's the most narrow claim,
23 claim 18. So, we have an API with a carboxamide. What we're going to do
24 now is we're going to find a co-former that's complementary to that. So, first
25 we need a compound with a carboxamide. And what you're saying is you
26 take a compound with a carboxamide and using what's known in the art, a

1 person would look at that and then they would know what co-formers will be
2 complementary to that carboxamide on that compound and then that's the
3 invention.

4 MR. KANE: Well, I think it's, they would know that --

5 JUDGE SNEDDEN: An embodiment of.

6 MR. KANE: It's what?

7 JUDGE SNEDDEN: That would be an embodiment of the invention.

8 MR. KANE: If they, again, they would start with the API with a
9 carboxamide. They would, again, full characterization of the API. So,
10 they've got more than just that. Right. They then look at the potential co-
11 formers that would be expected to form that hydrogen bond with that
12 carboxamide. They then look at the, again, the characterization of the co-
13 former, again, the solubility and other factors that play into this and what
14 solvent you're going to use and all of those kinds of things. And they would
15 then design, they would pick co-formers with that API with crystallization
16 conditions with the expectation that you're going to form that bond under
17 some set of conditions.

18 JUDGE SNEDDEN: And so, I understand. So, then. But that's all
19 based -- so, that relies a lot on what's already known in the art. So, the
20 contribution here, then, is just identifying carboxamide as a group to which
21 to form crystals around?

22 MR. KANE: I don't think that's the -- that's not the invention. No,
23 Your Honor.

24 JUDGE SNEDDEN: Help me with that too then, I guess.

25 MR. KANE: I think carboxamides were known. I think probably
26 single crystal carboxamides existed in the prior art. Again, even here in this

1 claim, it requires that the homosynthon could be formed. So, in other words,
2 the API can form, in our example, the API that has a carboxamide group
3 could form a synthon with itself. Some other group on that same API could
4 form a hydrogen bond with that carboxamide. Right. Again, that's just basic
5 chemistry. That's not a dispute. And that was being done before this. And
6 so, what the inventors did here though is again they discovered this, they
7 came up with this concept of let's take those, as they said, these old
8 molecules and these old techniques and apply them in a new way to these
9 co-crystals for pharmaceutical use so that we can improve the characteristics
10 of the crystal in the product. And so, that's what the invention is. It's not
11 carboxamides will form hydrogen bonds. That was known for decades, I'm
12 sure, before this.

13 So, that's, you know, that's why, but that's why there's not a
14 requirement to explain that. Right. They know that. But really the key is, I
15 think as Judge Fredman and all of you have been asking about is, well, how
16 do you design this experiment? And you do it just the way I've tried to
17 explain and like Dr. Ward explains is you look at all the characterizations of
18 the API, the co-formers, you can make an informed decision based on the
19 Etter Rules of how these are going to come together. And then you pick
20 solvents and crystallization conditions with the expectation that you're going
21 to get that bond. And it's not just shooting randomly in the dark. It's a very
22 focused approach that as shown in the prior art, persons of ordinary skill can
23 make these crystals. They don't have to do a billion to find out where the
24 crystals are. They can identify the characteristics based on the known
25 chemical interactions, hydrogen bonding rules and the Etter Rules that allow

1 them to create these experimental conditions, these crystallization conditions
2 and form co-crystals that meet the scope of the claims.

3 JUDGE SNEDDEN: We had a lot of questions, but I hope you were
4 able to get your arguments across.

5 MR. KANE: I'll reserve the rest of my time, Your Honor.

6 JUDGE SNEDDEN: Okay.

7 MR. KANE: Thank you.

8 JUDGE SNEDDEN: Ms. Schwarz, you have 15 minutes.

9 MS. SCHWARZ: Your Honors, we don't have any rebuttal. We rest
10 on our papers. Unless you have any questions. I do just want to provide a
11 cite that Judge Fredman asked for earlier with respect to the amount of work
12 required. Dr. Rogers discusses this in Exhibit 1072 at paragraphs 21 to 22,
13 51, and 56 of his declaration.

14 JUDGE FREDMAN: Say that again, where did you cite, where it
15 was, the paragraph numbers?

16 MS. SCHWARZ: So, Exhibit 1072, paragraphs 21 to 22, 51, and 56.

17 JUDGE FREDMAN: Okay.

18 MS. SCHWARZ: Again, I'm happy to answer any questions that you
19 may have, but otherwise we'll rest on our papers.

20 JUDGE SNEDDEN: Looks like no questions. Okay, Mr. Kane, 20
21 minutes.

22 MR. KANE: I've made my arguments, Your Honors. I will rest on
23 my papers, as well.

24 JUDGE SNEDDEN: Thank you very much. Okay. Well, that will
25 conclude our hearing today. I'd like to thank you both for your
26 presentations. The next step will be for us to complete the final written

1 decision and today we are adjourned. Thank you very much. If you
2 wouldn't mind, stick around just a little bit for the court reporter and see if
3 they have any issues with the spellings or any other questions with respect to
4 the transcript. That would be helpful. Thank you.
5 (Whereupon, the proceedings at 2:32 p.m. were concluded.)

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PETITIONER:

Nicholas Kallas
Christina Schwarz
Laura Fishwick
VENABLE LLP
nkallas@venable.com
cschwarz@venable.com
lfishwick@venable.com

PATENT OWNER:

Michael Kane
Ahmed Davis
Kelly Del Dotto
FISH & RICHARDSON P.C.
kane@fr.com
davis@fr.com
kad@fr.com