

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

BAYER CROPSCIENCE LP, MONSANTO COMPANY, and INARI
AGRICULTURE, INC.,¹
Petitioner

v.

CORTEVA AGRISCIENCE LLC,
Patent Owner.

IPR2023-01036 (Patent 10,947,555 B2)
IPR2023-01037 (Patent 11,149,283 B2)
IPR2023-01038 (Patent 11,299,745 B2)

Record of Oral Hearing
Held: September 24, 2024

Before MICHAEL J. FITZPATRICK, ROBERT A. POLLOCK, and
TIMOTHY G. MAJORS, *Administrative Patent Judges*.

¹ The Board joined Inari Agriculture, Inc. as a party (Petitioner) to these proceedings via a Motion for Joinder in IPR2024-00179, IPR2024-00180, and IPR2024-00181.

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The above-entitled matter came on for hearing on Tuesday, September 24, 2024, commencing at 11:00 a.m., at the U.S. Patent and Trademark Office, 600 Dulany Street, Alexandria, Virginia.

1 PROCEEDINGS

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3 COURTROOM BAILIFF: All rise.

4 JUDGE POLLOCK: Good morning, please have a seat. Be with you
5 in a minute. Sorry, we're having a little technical difficulty. I'll be with you
6 in a second.

7 [Discussion of technical issues and brief recess]

8 JUDGE POLLOCK: Very good. All right. Good morning. I'm
9 Judge Pollock. With me are Judges Fitzpatrick by audio and Judge Majors
10 by video. Thank you for your forbearance as we work through some
11 technical difficulties.

12 This is the final oral hearing in three related inter partes review
13 proceedings. These proceedings are Case IPR 2023-01036, 01037, and
14 01038. Petitioners are Bayer CropScience, LP, Monsanto Company and
15 INARI Agriculture, Inc. joined as a party in this proceeding.

16 Patent Owner is CORTEVA Agriscience LLC. The court reporter is
17 present. The Board will issue a single transcript for the three cases which
18 will be made part of the record in due course. Counsel for Petitioner, would
19 you kindly identify who is present for Petitioner and who will be speaking?

20 MR. GROSSMAN: Good morning, Your Honors. Dov Grossman on
21 behalf of Petitioners, Bayer and Monsanto of Williams & Connolly. With
22 me today are my colleagues from Williams & Connolly, Ben Picozzi.

23 MR. PICOZZI: Good morning, Your Honors.

24 MR. GROSSMAN: Alex Zoland.

25 MR. ZOLAND: Good morning, Your Honors.

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1 MR. GROSSMAN: And Min Jong Yung.

2 MS. MIN JON YUNG: Good morning, Your Honors.

3 MR. GROSSMAN: And also with me today is my son, Jonas
4 Grossman as an observer.

5 JUDGE POLLOCK: Counsel for Patent Owner, would you kindly
6 identify who is present for Patent Owner and who will be speaking today?

7 MR. DeROO: Yes, thank you, Your Honor. My name is Pier DeRoo
8 from Finnegan. I am joined by Yieyie Yang, Mark Lambert, Lee McClellan
9 all from Finnegan. And also joining via remote audio link I believe are
10 Sendell Devitis, Jim Gorsche, and then Thomas Warnock from Corteva.

11 JUDGE POLLOCK: Welcome all. As set forth in our August 29th,
12 2024 Order, each side has 60 minutes to present its argument for the related
13 proceedings. My colleagues and I will do our best to keep track of the time,
14 but we suggest the parties do the same.

15 Petitioner will present its arguments first as it bears the burden of
16 showing the patentability of the challenged claims. Counsel for Petitioner,
17 would you like to reserve any time for rebuttal?

18 MR. GROSSMAN: Yes, Your Honor, 15 minutes. And I should add
19 for completeness, on the line I believe from Bayer CropScience and
20 Monsanto are Jamie Davis, Elizabeth Haselhorst and David Schramm all in-
21 house counsel.

22 JUDGE POLLOCK: Very good. All right. Counsel for Patent
23 Owner, would you like to reserve any of your time?

24 MR. DeROO: Yes, ten minutes please. And if I may address one
25 other issue. Patent Owner had made a request for some concerns about

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1 confidentiality. They just relate to two of the slides in Petitioner's deck.
2 Looking at the courtroom today, it doesn't look like there are any third
3 parties here so I don't think we need to seal anything for what's happening in
4 person here.

5 JUDGE POLLOCK: Oh, okay. I was not aware that you had made a
6 request.

7 MR. DeROO: Okay.

8 JUDGE POLLOCK: My apologies. That was, that's on file?

9 MR. DeROO: That's on file, yes.

10 JUDGE POLLOCK: Okay.

11 MR. DeROO: And my understanding is that the parties only
12 distributed an audio link to the folks who are covered under the Protective
13 Order. I suppose if it's possible that other third parties could access that link,
14 maybe we just mute the link for the couple of minutes that counsel is
15 addressing those two slides.

16 If the distribution is limited to who we provided it to, then that's
17 probably unnecessary. I just wanted to flag that for Your Honors.

18 JUDGE POLLOCK: All right. Gregory, could we confirm that
19 there's no video link to the slides?

20 PARTICIPANT: I didn't hear you.

21 JUDGE POLLOCK: Is there a video link to the slides to the public
22 line?

23 JUDGE FITZPATRICK: Are we live?

24 PARTICIPANT: There is not.

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1 JUDGE POLLOCK: All right. Well we will hope that the parties can
2 present their arguments regarding any confidential matters in more general
3 terms.

4 MR. DeROO: Yes.

5 JUDGE POLLOCK: And direct the panels to the relevant papers.

6 Apparently there's no video link if you have the slides up.

7 MR. DeROO: Okay. Thank you, Your Honor.

8 JUDGE POLLOCK: To the extent that there's any question about that
9 you need to present confidential material orally, let's see if we can save that
10 for the end. And close the lines. All right?

11 MR. DeROO: Thank you.

12 JUDGE POLLOCK: All right so we have access to the entire record
13 including the demonstratives. When referring to each demonstrative, paper
14 or exhibit, please do so by slide and page number so the record is clear and
15 pause a few seconds to allow us time to find it electronically please.

16 Let's see, our expectation is that counsel for the opposing party will
17 not interrupt the other party's presentation. Any objections may be lodged
18 when it's your turn to speak or at the end of all arguments. To the extent you
19 are arguing any issue that is specific to one of the three cases, please use
20 your best efforts to point that out to the panels so that we have a clear
21 transcript for later.

22 All right, Petitioner, we put 60 minutes on the clock. You've asked to
23 reserve 15, but we're going to let that run. You may stop when you're ready
24 and whatever is left will go on the clock.

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1 MR. GROSSMAN: Thank you and before I begin, would His Honor
2 like a hard copy of Petitioner's demonstratives?

3 JUDGE POLLOCK: Thank you, but no.

4 MR. GROSSMAN: Good morning. And may it please the Board, on
5 behalf of the Petitioners, we respectfully request that the court, the Board
6 cancel all claims of the three patents challenged in these three proceedings.

7 So in terms of the discussion today, I'm going to focus on Grounds IA
8 and IB and in particular the priority date question. And in focusing on that, I
9 am going to focus on the question of Common Structural Features.

10 I note all of this because No. 1, Corteva does not challenge that if the
11 claims are not entitled to a date earlier than October 2016, then they are
12 anticipated and obvious. And there's also, in my opinion, no real meaningful
13 dispute that there aren't representative species here given that there are only
14 three species with approximately 99 to 100 percent identity in a claim that
15 requires as little as 85 percent identity.

16 And in terms of that issue, I'd like to focus on one overall point that I
17 think is a theme here. The enzymes at issue are part of this overall family of
18 alpha-ketoglutarate dependent dioxygenases. I will refer to that mouthful
19 just as Alpha KGs.

20 And those enzymes as the record show, enzymes within that family
21 can act on a variety of different substrates. But the claim requires activity on
22 two particular categories of substrates. And the patent notes that one of
23 those substrates in particular RFOPS, that activity is totally new.

24 So to have written description support for these claims, the
25 specification needed to identify what structural features provide for that, for

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1 the activity on those claimed substrates, it failed to do so and that's why
2 there's no written description. And quite frankly, you don't need to take my
3 word for it.

4 We'll look at the Chekan Exhibit, Exhibit 1019 which was authored by
5 the lead inventor, their expert in this proceeding and Dr. Nair, their
6 prosecution declarant from 2019 and that admits that the structure function
7 relationships required by the enzymatic activity in these claims was not
8 known until 2019 which was long after the 2004 and 2005 provisional or
9 priority applications were filed.

10 So these are 555 Patents Claims 1 and 2. I will focus on the 555
11 Patent for purposes of the discussion, but the same analysis applies to the
12 other two in this proceeding, the 283 and the 745. And --

13 JUDGE FITZPATRICK: Counsel?

14 MR. GROSSMAN: Yes.

15 JUDGE FITZPATRICK: I cannot see, this is Judge Fitzpatrick.
16 Again, I apologize. I'm not on video. I can't, if you're gesturing to a slide, I
17 can't -- I have it. I have a copy in front of me. But I just need you to tell me
18 which slide.

19 MR. GROSSMAN: I apologize, Your Honor. It's Slide 3.

20 JUDGE FITZPATRICK: Thank you.

21 MR. GROSSMAN: There are a number of different structural and
22 functional issues here. I will just note the following: if Corteva loses on any
23 of these, there is no written description. And I will also note with respect to
24 Claim 2, this section, this limitation highlighted in green, (X)₂₈₂₋₂₈₄R, which

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1 we've also been calling the R285 limitation, that's the only claim of the
2 patents that Corteva has argued separately.

3 There's no support for that limitation either for purposes of Claim 2.
4 But the fact that there's no support for that is yet another reason why Claim 1
5 fails because that residue as Corteva acknowledged during prosecution is
6 critical to the enzymatic activity required by the claims. So I'm now on
7 Slide 4.

8 And let's first turn to the issue of the AAD-1 motif. The priority
9 applications do not talk at all about an AAD-1 motif. The only motif that is
10 discussed is this motif at the bottom of the top panel here, this HX(D/E)
11 motif which is this generic prior art Alpha KG motif that is much broader
12 than the AAD-1 motif encompasses a lots of different activity and lots of
13 different substrates.

14 And the only reason that motif is even mentioned here is that it is a
15 statement that the genes in the patent that are disclosed in the patent are part
16 of this overall family that has this broader activity. That is the limitation of
17 the discussion of any type of motif that they've claimed here which is not a
18 discussion of this sub-genus AAD-1 motif that they have tried to claim in
19 these patents.

20 The first that motif, that AAD-1 motif was added was to the claims in
21 2016 and then the specification was amended in 2019 to try to provide this
22 mapping explanation which is effectively the same argument Corteva makes
23 here as to why the claim is supported.

24 But as the Institution decision correctly recognized and I'm now on
25 Slide 5, that mapping argument only confirms that SEQ ID No. 9 which is

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1 sort of what that generic motif is mapped onto, is part of this overall family
2 that it has residues that fall within this generic broad prior art motif.

3 And the institution decision also correctly observed that this mapping
4 argument raises potential obviousness issues. And I think that observation
5 in the institution decision was critical because every single one of Corteva's
6 written description arguments in this case is truly in the nature of an
7 obviousness argument, not a written description argument.

8 For every single limitation, they rely on information outside the
9 specification. And so every time you hear Corteva talk about the Schleinitz
10 reference or the Minshull reference or the other Prior Art it is an admission
11 by Corteva that the specification itself is insufficient to support these claims.

12 And I will add that it is true that written description is from the
13 perspective of the POSA, but it is from the perspective of the POSA in terms
14 of what the inventor possessed in terms of what the inventor invented.

15 It's not some generic understanding of the POSA about general
16 approaches to modifying enzymes or general tricks of the trade or
17 understandings in this field. But that is what Corteva's arguments are really
18 premised on.

19 Not what the POSA would understand the inventor had actually
20 invented. And one example of that, you will see throughout Corteva's slides
21 a whole series of titles entitled AAD-1 motif active site. There's nothing in
22 the patent that talks about an AAD-1 motif active site.

23 Again, the motif that's discussed is what we saw back on Slide 4. It's
24 this broad, generic prior art motif. And that is what is referred to as
25 comprising the active site. There's nothing here in these priority applications

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1 that show that the inventors had made the necessary selections from that
2 motif to describe a new sub-genus which is what they're claiming and that
3 should not be changed.

4 That discussion is not in the patent anywhere. And it's not in the
5 priority applications anywhere either. So what does Corteva do? I'm now
6 on Slide 6, this is the Rivera case. And the Federal Circuit has said
7 consistent with what I was just saying that written description needs to come
8 from the specification.

9 While you can look at the prior art as to what would be well-known
10 by the POSA, for example, if there's a sequence referenced in the
11 specification, if that sequence was well-known in the prior art, the sequence
12 itself doesn't need to be laid out in the spec.

13 The POSA could rely on that, but you can't use the prior art to teach
14 limitations that are missing from the specification. But that's precisely what
15 Corteva does with respect to the AAD-1 motif. The priority applications
16 were filed a year apart in 2004 and 2005 and they are for purposes of this
17 limitation materially identical.

18 There's no disagreement on that. What Corteva then argued is the
19 Schleinitz reference is now prior art. That was published during this priority
20 year and they try to rely on that really for gap filling, but more generally to
21 try to support their written description argument.

22 But the problem with that argument is the only way Schleinitz can be
23 prior art is if the AAD-1 motif is not described in the provisional. And if it's
24 not described in the provisional and the PCT's material identical it's not in
25 the PCT either.

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1 And I will add the following: Schleinitz is published by a third party
2 so the notion that the POSA would read the provisional, not think the
3 inventor's had possession, but then during the priority year, read a
4 publication by somebody else and then suddenly think the inventors had
5 invented it when they re-read it in 2005, that argument fails. That argument
6 fails.

7 And as for Schleinitz on the substance, Schleinitz doesn't disclose the
8 AAD-1 motif either. All Schleinitz talks about is this generic prior art motif.
9 And it says that it is present in these various different enzymes that are
10 looked at here. Schleinitz doesn't disclose an AAD-1 motif. An AAD-1
11 here is referred to as RdpA. That's how it's referred to in the prior art.

12 JUDGE POLLOCK: And for Judge Fitzpatrick's benefit, we're on
13 Slide 9.

14 MR. GROSSMAN: Oh, I apologize. Thank you, Your Honor. And I
15 apologize, Judge Fitzpatrick. We are on Slide 9. There's no RdpA motif
16 discussed here. There's no SdpA motif. The only motif is this generic prior
17 art motif. And how is it given relevance?

18 Corteva focuses on whether it's described as functionally important. It
19 is functionally important for generic dioxygenase activity, but it doesn't tell
20 you about the substrates that it's acting on because all of these enzymes here
21 act on different substrates.

22 And what Schleinitz says, if you look at the middle panel is it says the
23 presence of that motif indicates that TfdA is related to these other enzymes
24 in this overall family which is what the patent says. It's only using the motif

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1 to show that they're part of a generic family, not to teach a sub-genus and not
2 to teach activity on particular substrates.

3 That is different structural features. Finally, and I'm now on Slide 10,
4 just to address one argument that Corteva raised in its Surreply, Corteva said
5 well how, the PCT was ultimately published as the Corteva 437 application
6 and that's what we use for our anticipation and obviousness analysis.

7 And they say well if that doesn't disclose the AAD-1 motif, how can it
8 anticipate these later claims that do claim the AAD-1 motif? And the
9 answer is very simple. This is in the nature of species genus anticipation.

10 We talk about SEQ IDs 9 and 10 and we say that those are covered by
11 the later claims. So the earlier publication discloses embodiments that later
12 anticipate the broad genus that's in the challenge patents.

13 But it doesn't disclose the AAD-1 motif and we talk about the Eli
14 Lilly case in all three of our Petitions and the relevant citations to this are at
15 the bottom of this slide, Slide 10. So unless there are any questions on that,
16 I'm going to move to a new topic which is the Claimed Activity. And we're
17 now on Slide 11 and at the top we have the 555 Patent.

18 And the 555 Patent talks about this AAD-1 protein having
19 aryloxyalkanoate dioxygenase activity on, again, these two classes, phenoxy
20 auxin herbicides and RFOPS. And as I mentioned earlier, the RFOPS is
21 what distinguishes this invention because it was already known in the prior
22 art that RdpA SEQ ID No. 9 AAD-1 was active on phenoxy auxin
23 herbicides.

24 That's in Schleinitz, for example. And the Institution decision
25 correctly observed there doesn't seem to be any structural support for why

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1 these are active on RFOPS. And I'm now on Slide 12. And I think the issue
2 here, again, is what I said earlier. The question is what makes these
3 enzymes?

4 What structural features, what correlation is between the structural
5 features of these enzymes that gives them the activity on the substrates in the
6 claim. Because that is, again, we see aryloxyalkanoate dioxygenase activity.
7 The patent describes aryloxyalkanoate dioxygenase activity as activity on
8 these phenoxy auxin herbicides and RFOPS.

9 So I'm now on Slide 12 again. I think there's been a lot of discussion
10 about Ajinomoto in the papers. I think the Board was spot on with
11 *Ajinomoto* and why it doesn't help the Patent Owner here. But I think the
12 discussion about *Ajinomoto* and *PureCircle* further flushes out this point
13 which is you do need a -- you don't need perfect correspondence.

14 That's what the correlation language is contrasted against. But it can't
15 be that the structure function relationship as unknown. And again, with
16 respect to the activity on these substrates, why there's activity on these
17 substrates, that was unknown.

18 And I'm now on Slide 13. This is just looking, again, at the evidence
19 that is discussed in the Patent to distinguish the invention. It talks about that
20 the enzymes are capable of degrading 2,4-D and AOPP. That's another way
21 of saying FOP herbicides and in an enantiospecific manner.

22 And no other enzyme had been reported to do that. And then it also
23 says unlike all the TfdA homologues to date, AAD-1 is able to degrade the
24 R-enantiomers. Again, so the question is what is providing for this activity
25 because this is different from what had come before?

1 JUDGE MAJORS: Mr. Grossman, this is Judge Majors. I have a
2 question.

3 MR. GROSSMAN: Yes.

4 JUDGE MAJORS: Can you hear me?

5 MR. GROSSMAN: Yes, I can hear you.

6 JUDGE MAJORS: Is it Petitioner's position, however, that Patent
7 Owner needed to describe in their specification each of the particular
8 residues that is responsible or perhaps not responsible for the selectivity of
9 the specific stereoisomer or in other words do they have to go in and say,
10 you know, it's this residue that we've seen at this position that's allowing for
11 the enzymes to select for the R-enantiomer or would a more generic
12 description have been sufficient?

13 MR. GROSSMAN: I think for present purposes, Your Honor, there is
14 no description of any of those residues whatsoever. So for purposes of
15 resolving this case, whether the answer is it needs to be generic or it needs to
16 be every single one doesn't matter.

17 Because there's no evidence of any of those structural features being
18 identified. I suppose if it were a question of how many need to be identified,
19 the question is well, which ones were identified and how many of them and
20 that would need to be looked at the fact-specific situation and whether that,
21 those particular identifications constitute the correlation, but it wasn't
22 perfect. But here there's none of that.

23 JUDGE MAJORS: So if I gave you a hypothetical, along the lines of
24 saying let's imagine that the specification disclosed expressly that there was
25 this active site that had four residues, what those residues are and how

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1 they're interacting with the substrate, even if there were some other residues
2 unknown at the time that might have explained why the enzyme is selecting
3 for a specific enantiomer, at least in that context, perhaps that would be
4 sufficient without each and every one of the, hundreds of amino acids that
5 have been mutated and figured out what indication such a mutation might
6 have on the overall function?

7 MR. GROSSMAN: I think the answer is it would have to really be
8 evaluated in context. I don't mean to not try to answer the question more
9 directly, but I think it really depends on what residues were shown to be
10 involved in the binding, how they were described and whether that was
11 enough so that the POSA had understood that there was a sufficient
12 correlation between the function they were claiming and the structures they
13 had identified

14 Here, this is a much easier case because they don't identify any and
15 that's actually, if I may, Your Honor, if I've sufficiently answered your
16 question --.

17 JUDGE MAJORS: Yes, I was sort of forecasting or I'll just tell you
18 where I'm going with this because I think the evidence here is at least at the
19 time of the priority applications, no one really knew why these enzymes or
20 the class of enzymes was able to select for specific enantiomers or not.

21 That was something that was still being explored. And Patent Owner,
22 however, in their trial papers comes back and they say well it was known
23 that there are these active site residues for the phenoxy auxins at least and
24 we determined according to the specification, Patent Owner says, that the
25 active site is behaving in the same way against the FOPS.

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1 And I would like, maybe this is in your presentation today, but I
2 would like to dive into that issue and why that is, why that argument has
3 merit or not.

4 MR. GROSSMAN: Sure and here's the reason why. If I understand
5 that issue, that issue is simply does the enzyme have dioxygenase activity?
6 All of their discussion about oh, these enzymes work by acting, you know,
7 with these residues that are within the generic prior art motif and acts with
8 alpha-ketoglutarate and iron. That's just a dioxygenase reaction.

9 That reaction was already known in the prior art that was how RdpA
10 worked. The question that wasn't known was how does it act on these
11 different substrates such that they can have a claim here with 85 percent
12 identify and be able to say I've now identified that because I'm informing to
13 you the residues that need to be maintained and the residues that don't need
14 to be maintained.

15 Otherwise, it's just a guess. It's just saying, yes, we've identified
16 residues that are involved in alpha-ketoglutarate generic or generic
17 dioxygenase activity. And that's all you need. But their claims require,
18 again, the specific activity on the substrates so you have to know how these
19 enzymes are binding the substrates and differentiating them.

20 For example, from other substrates including activity that is particular
21 to S enantiomers because we know there are substrates within this broader
22 class of Alpha KGs that are specific to the S substrate. Is that about --

23 JUDGE MAJORS: I do.

24 MR. GROSSMAN: Okay. So and I think Chekan, I'm now on Slide
25 No. 14. I think this actually just proves the point. This article again, Exhibit

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1 1019, authored by the lead inventor, Dr. Wright, their expert in this
2 proceeding, Dr. Bollinger, and their prosecution declarant, Dr. Nair, talks
3 about the molecular basis for the enantioselective herbicide degradation of
4 aryloxy dioxygenases in transgenic plants.

5 That's exactly, again, what they're claiming here. And this article says
6 there's an insufficient knowledge base to distinguish bona fide AADs from
7 other enzymes in this class. And then they go on to say and now I'm on
8 Slide 15, they reiterate that insights into the structure function relationships
9 within this family have been lacking.

10 And then they go on to say with regard to FOPS in particular, they
11 talk about the additional aryl ring of FOPS being accommodated by the
12 solvent-exposed tunnel and they've identified several different residues here.

13 And that is important because as Corteva pointed out in its
14 obviousness case, the POSA wouldn't understand, FOPS are bigger. Right?
15 They have an additional aryl ring. The POSA wouldn't understand
16 structurally why, how FOPS could be accommodated by the same enzyme
17 that has this dioxygenase reaction on the smaller, on the smaller phenoxy
18 auxins.

19 And so this is the first time that was ever disclosed. And so I think
20 going back to your question, Judge Majors, this is the type of information
21 that the patent would need to have because just saying, yes, well we found
22 that for SEQ ID No. 9 and for these three sequences, we found, yes, they all
23 work on both FOPS and phenoxy auxins.

24 But what structural features are allowing it to act on the RFOPS?

25 That was not known and according to Corteva, it would have been a

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1 question of the POSA it's not described in the patent. It wasn't described
2 until years later.

3 And so when the POSA is looking at a claim with 85 percent identity,
4 there's no indication to the POSA. Had they done any work to identify what
5 structural features provide for this activity on this particular substrate that
6 had never been shown before in the prior art as opposed to rewarding the
7 inventors for a guess.

8 But yes, maybe if get to 85 percent it will work on these other
9 enzymes. And, oh, by the way I'll add and I'll be getting to this later, but
10 even for the substrates they identify in the patent, the other problem one
11 can't forget is the R285 position because Corteva acknowledged that was
12 critical for activity.

13 They don't get any activity on FOPS without it. But that's not
14 disclosed anywhere in the specification and that's a critical residue. Even
15 putting aside any question about the aryl ring, you still need that R for the
16 dioxygenase reaction to run and presumably that's why in 2016 when
17 Corteva had the additional knowledge, they put that in as a specific claim for
18 Claim 2 because they knew it and that was the data they were submitting to
19 the Patent Office.

20 So just to go through another few slides very briefly on this,
21 Schleinitz says this reiterates the same point. It talks about, this is on Slide
22 16, site-specific mutagenesis studies are needed to reveal the molecular basis
23 of the substrate specificity and stereospecificity of RdpA and SdpA.

24 In the prior art, it didn't, it was not known how RdpA was able to act
25 on phenoxy auxins. Similarly, I am now on Slide 17. This is Müller.

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1 Müller which is post priority, it's 2006, but again, it says essentially nothing
2 is known about the phenoxypropanoic acid-binding sites, that's the phenoxy
3 auxin binding sites, of these proteins.

4 Especially with regard to the structural basis of the enantiospecificity.
5 So again, this was an open question until 2019. And reinforces that they
6 didn't have possession for the type of claim that they're seeking here.

7 If they had sought a claim that was just for SEQ ID No. 9 on RFOPS,
8 that's one thing, but to say well now I'm going to make as many as 44
9 changes and that's still going to have the activity that's required by the claim,
10 how would any, why would the POSA ever think that they possessed that
11 when they did no work, no variation to show that?

12 And, again, there's additional evidence here that shows, in fact, they
13 didn't possess it. I will skip ahead unless there's any further questions on the
14 activity issue. I will skip ahead to Slide 21 which is the 85 percent identity
15 limitation.

16 What we have here is testimony from Dr. Hausinger. This was all
17 acknowledged in the Institution decision, but the rough lower estimate of
18 sequences covered by their claims is 20 to the 44th (20^{44}) power. Corteva
19 never challenges that number.

20 There's only three examples here of 99 to 100 percent identity. So
21 how could those show, how could we know that there are common structural
22 features here? The structural features here that are needed to provide for the
23 claimed activity on these particular substrates, that again, goes back to your
24 question, Judge Majors, about how, where is the structure function

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1 correlation for what they've actually claimed as opposed to just saying yes,
2 these, I believe that SEQ ID 9 can effectuate a dioxygenase reaction.

3 And the POSA would not have known and could not have predicted
4 within such a large genus which sequences would have the activity and
5 which wouldn't because, again, there's no discussion of the residues that are
6 allowing for the binding and the activity on these particular substrates.

7 So the Institution just after the Patent Owner argued pre-Institution,
8 while it's argued that there's a universal principle that if you have at least 85
9 percent identity, then the POSA would expect the same activity.

10 And the Board is, of course, well aware asked for further briefing on
11 this issue from Patent Owner, but did say just be aware there is record
12 evidence here in Exhibit 1041 the Saari 1999 reference that there was a
13 TfdA-like protein, this *A. denitrificans* protein that had R stereoactivity and
14 at 86 and 95 percent amino acid identity to a sequence that had (S)-specific
15 stereo activity for it.

16 So it's another example here about when you're dealing with the
17 generic motif that could have R activity and could have S activity, well what
18 are the structural features that are providing for that especially when you're
19 going down to as little as 85 percent identity?

20 So I'm now on Slide 23 and Corteva's position was yes, the POSA
21 would routinely predict function based on sequence identity. This was a
22 universal principle. But the problem with this argument and I'm now on
23 Slide 24, is the Federal Circuit *Boston Scientific* case.

24 While one can rely on well-known information for purposes of the
25 written description test, not for gap filling, but for what the POSA would

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1 understand, that only goes so far because it can't be well-known information
2 if it's contradicted by the specification.

3 That cannot be relied on for purposes of written description because,
4 of course, it's the specification that governs. And I'm now on Slide 25. The
5 patent directly contradicts their argument because the patent explains it's not
6 just, you can't just rely on sequence percentage sequence identity for
7 predicting function.

8 The nature of these, of the modification matters. And of course, it
9 matters. I mean, even Corteva and its expert accept that, of course, the type
10 of modification matters. And the specification talks about how sometimes
11 conservatives amino acid substitutions work, will have the claimed activity
12 and sometimes they won't. And sometimes nonconservative substitutions
13 will have the claim activity and sometimes they won't. But it doesn't say
14 where or what types of modifications.

15 That's all its saying, but that's inconsistent with the idea that no matter
16 what modification you're making, as long as you've got 85 percent identity,
17 you can expect the same activity. So what does Corteva do?

18 They rely on a couple of different parts of the specification. I'll go
19 through these relatively briefly. First of all and I'm now on Slide 26, they
20 try to rely on this language in the lower corner of, lower left-hand corner of
21 Example 1 where they talk about only sequences with high homology would
22 be expected to retain similar properties.

23 Of course, the Board noted does that apply to RdpA? Because this
24 example is about TfdA and, but so that is one problem. Corteva has not

1 demonstrated that with regard to RdpA and I'll get more into that in a
2 moment, but the other problem is this example is about 2,4-D activity.

3 This is about TfdA activity on 2,4-D which is achiral. And of course,
4 the claim on its face talks about activity on RFOPS. And when it talks about
5 phenoxy auxin herbicides, you can have an achiral phenoxy auxin herbicide
6 like 2,4-D, but the S enantiomers are not herbicidally active.

7 It's the R enantiomers of phenoxy auxins that are herbicidally active.
8 So this, like the issue that the Board flagged, was Saari 1999. This doesn't
9 tell you whether it's going to have this activity on the R enantiomer as
10 specified in the column. Now for Saari itself and I'm now on Slide --

11 JUDGE POLLOCK: Counsel, it's correct though that at least Claim 1
12 doesn't require activity on only the R enantiomer.

13 MR. GROSSMAN: So I will, on that topic, which is something that
14 Corteva raised in its Surreply, that argument, in my opinion, is both untimely
15 and waived and I can get into that, but on the substance the Board doesn't
16 need to determine whether the claim requires activity on the R enantiomer
17 only or not.

18 Because the claim requires activity on the R enantiomers and there is,
19 sorry, in here there's no difference between whether that activity is just on
20 the R enantiomer or only on the R enantiomers. The entire claim is based on
21 RdpA.

22 RdpA is stereospecific. So in order to provide any level, just going
23 back to the comment from Judge Majors earlier, to provide any indication
24 about activity on R enantiomers, there need to be some identification of the
25 structural features in RdpA that give it that R enantiomer specificity.

1 There isn't any of that. And all of the examples here -- I'm just going
2 back to, I'm going to go back to Slide 20, as an example. Just as one
3 example, looking at the Nair Declaration which is the bottom panel here --

4 PARTICIPANT: What slide is this please?

5 MR. GROSSMAN: Oh, Slide 20. It talks about AAD-1 being (R)-
6 specific and it talks about AAD-1 variants being (R)-specific so all of the
7 evidence here is (R) enantiomer specific. So it doesn't matter to the written
8 description question.

9 It's not as if there's, if the claim requires only some level of activity,
10 there's written description, but not if the claim requires (R)-specific activity
11 or vice versa. Like all of the evidence here is just about the (R)-specific
12 activity and therefore, the claim is unsupported.

13 And I will just add to that. Corteva doesn't even argue that the claim
14 requires that this requires any identification of any residues for (R) activity
15 as I believe Judge Majors questions were directed to. Under their theory, all
16 you need is the AAD-1 motif and 85 percent identity.

17 And then you expect the same activity as RdpA. Now, that is
18 substantively wrong. But RdpA, of course, has an enantio-selective activity
19 so this is just one. If you're expecting the same activity, even their argument
20 is well then you're expecting it to be (R)-enantio specific so this is one giant
21 red herring. Have I sufficient addressed Your Honor's point?

22 JUDGE POLLOCK: Please go ahead.

23 MR. GROSSMAN: I am happy if the Board would like to address the
24 untimeliness and waiver issue, but now or rebuttal I will leave it to the

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1 Board. So going back to Slide 27, I'm now dealing with -- this is Saari 1999,
2 Exhibit 1041 that we were just talking about.

3 Now Corteva makes it, has a few criticisms of this reference. First
4 they say well, Saari, never really said that *A. denitrificans* had opposite
5 stereospecificity that (R)-stereospecificity as opposed to (S)-
6 stereospecificity, but that's specified right here in the abstract.

7 They also criticize Dr. Hausinger for using crude cells as opposed to
8 purified protein. But as Dr. Hausinger explained and he explained this in
9 paragraphs 52 to 54 of his Reply Declaration Exhibit 1070, that's cited here
10 at the bottom of the Demonstrative, that they performed additional tests such
11 as chiral HPLC to show that there was different activity from this *A.*
12 *denitrificans* of protein.

13 Corteva also points to what they call a contemporaneous criticism of
14 Dr. Hausinger or Saari, 1999 in Schleinitz, but all that, all that, all Schleinitz
15 really says is there are additional experiments that Saari could have done to
16 further confirm the data in it such as gene sequencing or amino acid
17 sequencing or something like that.

18 It doesn't say that Saari is wrong and it doesn't present different
19 contrary data. Okay, so I'm now on Slide 28. So what Corteva also does is
20 they make this argument about Tian and these various other references to try
21 to show that it was this general principle that one would expect 85 percent, if
22 you have 85 percent identity to expect the same activity.

23 We addressed a lot of this in our briefing, but just generally to
24 reinforce the point, none of that literature is in the specification. Corteva
25 tries to connect it to this discussion in Column 37 on Slide 28, but this

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1 discussion doesn't articulate the principle that Corteva says you have from
2 Tian which is if you have at least 60 percent identity, then you have a 90
3 percent chance of the same activity.

4 Because this has a lot of different numbers here any of which could be
5 the upper or lower limits. So this is not talking about Tian. But even more
6 fundamentally, and I'm now on Slide 29, the information in Tian is about
7 naturally occurring proteins.

8 It's not about artificial variance. And I'm now on Slide 31. This is
9 clear enough from Dr. Bollinger's Declaration because naturally occurring
10 proteins are subject to natural selection. There's a selection bias that allows
11 ones with the activities to survive even if there's a lot of changes.

12 That information is not, there is no selection bias for natural selection
13 applicable to naturally occurring proteins, to artificial variance. And
14 Corteva doesn't even really fight that. What they do is they try to rely on
15 Minshull reference. I'm now on Slide 32 from 2005.

16 This is, again, another example of a reference published during the
17 priority year that they deemed to be prior art that's by a third party so how
18 could this really change the POSA's understanding of what was in the
19 priority application when then reading the PCT published a few days later?

20 But Minshull, importantly, does not say that this Tian principle of if
21 you have at least 60 percent identity, you'll have 90 percent chance of the
22 same function. Minshull does not say that applies with respect to artificial
23 variance. Minshull says prediction of protein function from sequence and
24 structure is a difficult problem.

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1 And there still needs to be testing. And I'm now on Slide 33. Corteva
2 tries to suggest in its Surreply that actually Minshull is suggesting you don't
3 need testing, that you still need prediction based on Dr. Hausinger's
4 testimony that there needs to be screened for activity.

5 And then they site this portion of Minshull saying oh, well if you use
6 sequence activity relationships, you won't need to do high-throughput
7 screening, dot, dot, dot. But, dot, dot, dot is and allow them to directly
8 measure the protein properties they really care about, i.e., you still have to
9 test the artificial variant to see if it has the properties that you think it's
10 supposed to have in terms of the tactic.

11 That's on Slide 33. Very generally on Slides 34 and 35, maybe I
12 should just save this to the very end if that -- I can --

13 JUDGE POLLOCK: I'm sorry, just?

14 MR. GROSSMAN: This is a confidential slide, 34 and 35.

15 JUDGE POLLOCK: Can you talk about it generally?

16 MR. GROSSMAN: Sure. What this slide shows, this is of course
17 internal data. We talk about this in our briefing. This is internal data from
18 Corteva in 2019 that was not submitted to the Patent Office and it deals with
19 a different variation than the one they actually submitted as one can actually
20 see at the top of the slide.

21 And of course, the results show that there was no activity because of
22 these issues with solubility and purified protein. And this I think is a good
23 example of the lack of possession that even in 2019 this is the data, these are
24 the results this Corteva scientist got when trying to produce other variations
25 within the claim.

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1 And as we explain in our briefing, they had to look at other
2 information in order to try to make variants that did have the claimed
3 activity. But I will add Corteva tries to say oh, well there's all these other
4 things that one could do to affect solubility that Dr. Hausinger talked about,
5 but that's all, in my view, hindsight coulda, woulda, shoulda.

6 Because if that were for so easy then Corteva would have done that
7 and then provided the soluble information to the Patent Office. I'm now on
8 Slide 35. This is in part confidential and part nonconfidential. I'm now
9 moving to a different topic.

10 I'm now moving to the R285 point. The R285 limitation as the Board
11 correctly observed is not in the specification. It's not even part of the
12 generic prior art motif. That reason it fails as well and I will just note
13 talking about the bottom half of this and I will, again, describe this in
14 generalities because it's from 2018.

15 And by the way, this document in the prior internal Corteva document
16 we looked at were voluntarily produced by Corteva in this proceeding. And
17 they offered no contrary characterization to the characterizations that I'm
18 giving here.

19 But if you see in the upper right-hand corner of the bottom panel, the
20 highlighted information, that is an admission that what I was just saying
21 about the specification is, in fact, the case. And I also think if you look at
22 the highlighting on the top there and it talks about the proposed motif, that is
23 the AAD-1 motif.

1 And then if you look at the upper left-hand corner, the information in
2 quotations, we have described that again as a Tacet admission that this was
3 not conceived of, not thought of as of the relevant dates.

4 And Corteva has never challenged that characterization of the
5 evidence here. So now I'm on Slide 36. Again on R285 and, again, R285 is
6 critical for the activity. Corteva submitted data showing that if you don't
7 have R285, you get no activity. That goes to show that this is a critical
8 residue that Corteva didn't have.

9 It reinforces the lack of possession of the genus that is needed here for
10 purposes, a reinforced lack of possession of common structural features to
11 support the very broad genus that they have claimed.

12 JUDGE MAJORS: Mr. Grossman, do we, is there evidence of record
13 that the Arginine is critical in that location? I would recognize that's what's
14 said here on the slide. But this is a substitution I think what is it, alanine? Is
15 there any record evidence to say if he switched Arginine to another amino
16 acid in the common type or whatever the charge decides whether the protein
17 would be functional or not?

18 MR. GROSSMAN: I don't know that there's any further record
19 evidence of other substitutions at that position, but I think for purposes of
20 whether Corteva had possession, their admission that having the arginine
21 there is critical for the activity is sufficient because, again, the summary here
22 is demonstrating that these amino acids are critical for maintaining the
23 claimed function.

1 It wasn't limited to the specific substitution here for purposes of
2 proving their point. And finally, on Slide 37, Corteva again tries to gap-fill.
3 You'll see they're using prior art to try to get at the R285 limitation.

4 They can't do that under the Rivera case as I mentioned. I'll also say
5 that what they omit from their slides is this information here about black
6 arrows indicating 2,4-D binding residues in TfdA. There's no discussion
7 about whether this Arginine at 285, and there's some discussion of that in the
8 prior art, had any role in binding an RdpA. That wasn't determined until
9 later.

10 And so it can't be, they can't gap-fill and it's clearly not well known
11 that Arginine had any role in the claimed activity as part of the claims here.
12 Corteva, you may see they tried to say that there's some sort of a
13 contradiction between Dr. Hausinger's testimony about what he's saying in
14 this proceeding on that question and what he's said in the Müller article from
15 2006 Exhibit 1035.

16 I'll just note that there's no inconsistency because one is talking about
17 2004 and one is talking about 2006 when there's additional information on it.
18 I'll also just preview then you'll see their Slides 14 and 15 which have a
19 bunch of colored lines and circles suggesting that Dr. Hausinger somehow
20 admitted that Schleinitz disclosed the AAD-1 motif.

21 They can't gap-fill anyway, but as Dr. Hausinger explained, he was
22 talking about the generic prior art motif. There's no discussion in this
23 testimony that said that he's talking about any disclosure of an AAD-1 motif.
24 And that's explained in detail in paragraph 27 of his Reply Declaration,
25 Exhibit 1007.

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1 Finally, just very briefly on obviousness and we'll largely rest on our
2 papers on this, but there was a motivation based on the Saari references to
3 create a Transgenic plant that expressed RdpA. There's a reasonable
4 expectation of success for that. It was done with TfdA and cotton and in
5 fact, the patent admits that those procedures are well known.

6 And if one made that plant cell and that plant cell expressed RdpA,
7 that would inherently have the activities required by the claim because those
8 are inherent properties of RdpA. Corteva's argument largely is that you can't
9 have inherency when you have a biological system, but that's not so.

10 Unless there are any further questions from Your Honors, I'll reserve
11 the rest of my time.

12 JUDGE POLLOCK: Thank you very much. Mr. DeRoo, you had
13 reserved ten minutes, but we put the full 60 minutes on the clock so you're
14 welcome to stop whenever you would like.

15 MR. DeROO: Okay, thank you. Just getting hooked up to the slides
16 here, so.

17 JUDGE POLLOCK: Please take your time.

18 MR. DeROO: All right, may I begin? Thank you, Your Honors. Yie,
19 could you start with Slide 2 please. And we'll begin with the 555 Patent and
20 the work detailed in this patent was a pioneering invention bringing
21 significant crop protection solutions to American farmers and agriculture.

22 And this was recognized by Bayer's own scientists shown on Slide 50
23 who discuss the related publication that Corteva inventor, Dr. Terry Wright
24 and colleagues. And the problem in the industry was that the broadly used

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1 herbicide roundup, that is Bayer's product, had resulted in significant
2 development of Roundup resistant weeds.

3 And here the AAD enzymes and genes implemented in crops confers
4 protection against phenoxy auxins which are different herbicides than
5 Roundup and they're active against broadleaf weeds and also activity against
6 FOPS which are herbicides against grassy weeds so you get broad spectrum
7 weed control and crop protection with the invention of these patents.

8 Back to Slide 2 please. Shown here on Slide 2 is Claim 1 of the 555
9 Patent. We've highlighted the terms that are primarily at issue. There has
10 been no dispute from Bayer about the transgenic plant cell aspects of the
11 claims.

12 In yellow we have the claimed function which I'll be referring to
13 throughout the argument today. It's aryloxyalkanoate dioxygenase activity
14 wherein said activity enzymatically degrades a phenoxy auxin herbicide and
15 an (R) FOP herbicide. So the function we're focused on here is an oxidative
16 degradation reaction.

17 Then we have two structural features in the claims. They're
18 highlighted in green. And they make this case a bit different than most
19 written description or priority challenges which usually involve purely
20 functional claims.

21 So the two structural limitations in these claims are at least 85 percent
22 sequence identity to SEQ ID 9 and the AAD-1 motif. Slide 3 please. So
23 turning to Ground I, Bayer has contended that Corteva purportedly conceded
24 its 2004 priority date.

1 That's not the case. In the parameters of this proceeding were set for
2 the in the Institution decision shown on the screen here. To prevail, Bayer
3 still has to prove its case as of the 2005 priority date. As the Board made
4 clear in the last sentence from the ID shown on the screen. Slide 11 please.

5 Well first, as my counterpart noted, there are several aspects of this
6 case and I'd like to try to address them in a logical discreet fashion so let me
7 roadmap this just a minute and, Judge Majors, I will get to the some of the
8 issues that you asked about fairly early on here.

9 But I have just a little bit more background to provide. Then I would
10 like to address their arguments about literal disclosure of the motif then
11 structure function correlation for the motif including for the FOP substrates
12 that Judge Majors asked about.

13 Then I would like to address their (R) and enantio-specificity
14 arguments, 85 percent sequence identity and then Claim 2. And I have a few
15 notes on Ground II as well. If you have questions along the way, please
16 don't be shy about interrupting.

17 So we're on Slide 11. And I'd like to begin with the genus at a high
18 level here. So shown here are four enzymes RdpA which is wild type AAD-
19 1 is on the right-hand side and towards the left-hand side are RdpA's three
20 closest relatives, relative enzymes, TauD, TfdA, and SdpA.

21 None of these relatives are within the scope of the claims. They don't
22 have the same motif, the same active site motif as AAD-1. They are also
23 nowhere close to 85 percent sequence identity. And down to 35 percent
24 identity is how far you really had to go to get a different enzyme function
25 like with TauD which acts on taurine.

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1 Now we're standing here today after a full IPR trial and the closest
2 enzyme that catalyzes a different reaction than RdpA is still TauD. There's
3 been really no showing of any functional variation within 85 percent.

4 And in its Reply, Bayer asserted that they've made thousands of RdpA
5 variants. That's Exhibit 1070 at paragraph 64. And that raises some
6 questions. We've heard an argument that the AAD-1 motif is not correlated
7 to the claimed dual herbicide degrading activity.

8 So where are all of these Bayer variants that purportedly have the
9 claimed herbicide degrading activity but lack the motif or have a different
10 motif? And for that matter, where are all the enzymes that purportedly have
11 different functions or no function within this supposedly diverse genus.

12 There's been no such evidence in these proceedings. And what about
13 Corteva's variants? Out of the ones that Corteva scientists made that pertain
14 to AAD-1 motif, Petitioners argued on their Slide 34 that a grand total of
15 three had insolubility issues.

16 So we had thousands of variants that were made with no showing of
17 any functional diversity by Bayer and those enzymes were going down into
18 the 80 percent range, 89 potentially a little bit lower and a mere 3 that were
19 not tested in vitro for function because they weren't solubilized beforehand.

20 So the notion that there's a vast amount of diversity within the bounds
21 of the claims is really just speculation and unsupported say so from Dr.
22 Hausinger. That was his original position, Exhibit 1054 in paragraph 76 and
23 has not held up over the course of a full IPR trial.

24 Also, challengers in cases like these often hold up an embodiment like
25 an accused product to establish that product, their protein is entirely unlike

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1 other proteins within the scope of the claims. That was a fact pattern of
2 *AbbVie v. Janssen* that Bayer relied on in its Petition where the challenger
3 pointed to its Stelara antibody, Stelara the one you see in TV commercials.

4 They pointed to it as having completely different structural features
5 than the antibodies disclosed in an asserted patent, but Bayer has not --

6 JUDGE FITZPATRICK: Counsel --

7 MR. DeROO: -- been able --

8 JUDGE FITZPATRICK: Counsel --

9 MR. DeROO: Yes.

10 JUDGE FITZPATRICK: -- was that a District Court case?

11 MR. DeROO: No, it was the Federal Circuit, *AbbVie v. Janssen* --

12 JUDGE FITZPATRICK: Well, was that an appeal of a district court
13 case, you know, with patent infringement?

14 MR. DeROO: I believe --

15 JUDGE FITZPATRICK: You know what, we wouldn't have an
16 accused product here so the absence of it doesn't really speak to me.

17 MR. DeROO: Well, there's no accused product here, but there has
18 been a co-pending district court litigation. It's been stayed and, of course,
19 that evidence is available to Bayer. They could take their accused product
20 and try to hold it up as providing, as illustrating some unique feature within
21 the scope of the claims.

22 They haven't done that, they can't do that because there's no proof of
23 any significantly different enzymes within the tight scope of the claims here.
24 And as we showed in the Patent Owner Response, Bayer's AAD-1 variants
25 sequence is uniformly retained the AAD-1 motif and were confirmed to have

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1 the dual herbicide degrading activity. So let's turn now to the motif on Slide
2 12 please.

3 So this is the same paragraph of the specification that Bayer showed
4 earlier where they omitted any mention of the disclosure that the active site
5 of enzymes like AAD-1 is marked by its motif. I believe there's no dispute
6 that each a-ketoglutarate-dependent dioxygenases has its own specific motif
7 within the broad ranges of the consensus motif. Slide 13 please.

8 JUDGE POLLOCK: As far as each enzyme having a specific motif,
9 would you address why the finding that R-285 seems to be a critical for
10 function isn't fatal to --

11 MR. DeROO: Yes.

12 JUDGE POLLOCK: -- sufficiency of disclosure.

13 MR. DeROO: Yes, absolutely. And I will be going through some
14 slides on Ajinomoto in just a moment here. But the law doesn't require
15 disclosure of all potential residues that are important to function and I think
16 the issue, when I get to Claim 2, it's really distilled down to a question of
17 whether it is a permissible use of the knowledge of a skilled artisan to
18 inform what's in the specification.

19 That's the part they didn't highlight on their Rivera case slide or
20 whether it is gap filling. But under the appropriate legal standard, there is no
21 requirement that every single possible residue important to function needs to
22 be separately highlighted and disclosed.

23 So we are on Slide 13. And as shown in the lower box, Dr. Bollinger
24 testified that as of 2004-2005, RdpA's primary amino acid sequence alone
25 was sufficient for a skilled artisan to recognize the RdpA (AAD-1) motif.

1 And that primary sequence is, of course, disclosed in the specification
2 as SEQ ID No. 9. And Dr. Bollinger's testimony on the screen here is not
3 disputed. Dr. Hausinger did not disagree in his Reply Declaration.

4 And Dr. Bollinger's testimony that a skilled artisan would recognize
5 RdpA's unique motif from its primary sequence alone was also supported by
6 Schleinitz. And that's shown on the screen here. It published in 2004 and
7 we've made no modifications to the image here.

8 It individually highlighted each of the five motif residues in RdpA
9 sequence and three other enzyme sequences and showed their different
10 residue numbering. So Schleinitz confirms that skilled artisans would have
11 recognized the specific motif and RdpA from its primary sequence just as
12 Dr. Bollinger testified.

13 And Schleinitz is further evidence that as of the 2005 PCT filing date,
14 a skilled artisan would have come to the specification already knowing
15 where the specific RdpA motif residues were located.

16 And on Slide 8 please, that is important, that knowledge of a skilled
17 artisan is important because it is the lens through which a written description
18 analysis is carried out. And then we've quoted from the Board's decision in
19 *Ossia* as well as the en banc *Ariad* decision.

20 And here our skilled artisan has a strong background. This is not a
21 trivial level of skill, it's a Ph.D. three to five years of experience in
22 enzymology and familiarity with the various literature here. And Dr.
23 Hausinger has not disputed that.

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1 And so going back to Slide 13 please, regarding the AAD-1 motif,
2 there's no gap filling as Bayer has argued. RdpA has just one set of motif
3 residues. That's not disputed. There's no selections to be made.

4 It's also undisputed that a skilled artisan would have recognized that
5 specific set of motif residues in SEQ ID 9, the primary sequence of RdpA.
6 And, in fact, the location of those five residues had already been published
7 by the 2005 PCT filing date in the Schleinitz sequence alignment. If I could
8 go to Slide 14 please.

9 This is Dr. Hausinger's testimony. And we asked him during his
10 deposition about all five of those motif residues marked in black and
11 Schleinitz's sequence alignment. We've heard from counsel that Dr.
12 Hausinger was purportedly only talking about a consensus motif, but we
13 know the consensus motif is variable.

14 You can have wide ranges of positions for each individual residue.
15 That's not what these questions are about. It is the first residue, first motif
16 residue shaded in black is a histidine at position 111. That's not variable.
17 That's at position 111.

18 And he agreed, correct. We confirmed that the second motif residue
19 is in aspartate position at 113. He agreed. And there's one residue in
20 between them. It's a spacer at 112. He agreed. Third motif residue is a
21 threonine at position 138. He said, yes. And so on and so forth.

22 We confirmed every single residue, every single specific spacer of the
23 AAD-1 motif as published in Schleinitz. I would like to now address some
24 of the function structure function correlation for the motif. This would go to

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1 some of the issues you raised, Judge Pollock. If we could begin with some
2 legal principles on Slide 4.

3 JUDGE POLLOCK: Can you, let me make sure I have this here. So
4 the histidine, aspartate, all of these residues that were lined up in black, if
5 you match those, you -- these are specific for an a-ketoglutarate-dependent
6 dioxygenases generically?

7 And to get to the specific function that you're claiming, you also have
8 to reach into the 85 percent identity with SEQ ID 9. Right?

9 MR. DeROO: So if we could briefly go to Slide 19, so the motif
10 residue is at 111, 113 and so on and so forth, those aren't for a-ketoglutarate
11 dioxygenase generally. As the full file record now shows and we've
12 highlighted the different motifs and motif spacings here for RdpA and its
13 closest enzyme relatives, the AAD-1 motif is unique to AAD-1 enzymes.

14 Bayer hasn't identified any enzyme other than the party's own AAD-1
15 variants that have the activity. Guess what? They still have the specific
16 AAD-1 motif. There's been no showing whatsoever of any other enzyme
17 does any other function and still has the AAD-1 motif.

18 And, of course, there's no evidence of any other enzyme having the
19 AAD-1 motif also having at least 85 percent sequence identity to SEQ ID 9
20 and performing some different function. So there hasn't been a showing of
21 functional diversity within its genus.

22 JUDGE MAJORS: Mr. DeRoo, if I could interrupt you for a moment.

23 MR. DeROO: Sure.

24 JUDGE MAJORS: For my part, I guess my thinking at the DI stage
25 though was particularly I think in the context of the mapping argument as it

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1 was phrased at the time. This idea of you take the known consensus
2 sequence as in Hogan or other references and as described in Column 18 of
3 the specification and you look at that and use SEQ ID No. 9 and as the
4 argument goes, there's only one fit or one way to map that consensus
5 sequence on the SEQ ID No. 9.

6 But as we explained in the DI, that seemed to indicate okay, well we
7 know that this enzyme RdpA falls under the, you can conclude from that it
8 falls under the Alpha KGD family. It has the motif from which you can find
9 the consensus motif represented in the amino acid sequence.

10 But the question then in my head is okay, but where is there the
11 disclosure that those motif residues in that pattern having not just activity
12 against 2,4-D and other phenoxy auxins but against RFOPS? Because if you
13 look at Schleinitz, you look at these other references that you want to show
14 us and say well it was already known that the Alpha KGD consensus
15 sequence is in RdpA.

16 None of those prior references describe those residues or that the
17 sequence has any activity relative to FOPS as I understand the record.

18 MR. DeROO: Could we go to Slide 16 please. And so I'm going to
19 take this in two pieces, Your Honor. And so here, as Dr. Bollinger testified
20 at the bottom of the slide, a course of active-site is related to the activity or
21 function of an enzyme.

22 That's where the enzymatically catalyzed reaction is taking place to
23 which Bollinger confirmed too which mentions stating that changes at key
24 active site residues are generally deleterious. That's because they're
25 correlated to function.

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1 But if we look at the top box on the slide and this is what you're
2 referring to I believe with Schleinitz, let's look at where it leaves off. It
3 confirms there is a functionally important motif. It's present in RdpA and
4 then below the initial highlighting, you see it calls out the specific locations
5 for the motif residues in TfdA and then confirms that each of those five
6 motif residues are conserved in RdpA and which ones are those?

7 They are the ones shown in black and the sequence alignment that we
8 saw on Slide 13 is providing the more specific RdpA motif and so here we
9 are just before the 2004 or 2005 filing date. We know that RdpA just
10 degrades phenoxy auxins, the specification has told us that the motif
11 residues mark the active site.

12 Schleinitz tells us that the motif is functionally important. You can't
13 do the claim function without them. Now what about the FOPS? If we
14 could go to Slide 18 please. Sorry, 17 please. The specification discloses
15 the inventor's further investigations into AAD-1 functionality.

16 And it reports that AAD-1 enzymatically degrades -- and remember
17 that's our claimed function here, what we highlighted in yellow on Slide 2.
18 It enzymatically degrades FOP herbicides in a similar way as phenoxy
19 auxins and in the same active site

20 And so as we've shown in the top box, this example begins with
21 explaining the role of the active site and coordinating the necessary reactants
22 like a-ketoglutarate, iron, et cetera. And then discloses how the inventors set
23 up an experiment to see if FOP herbicides like haloxyfop or diclofop are
24 degraded in a similar way under the same conditions as the phenoxy auxin
25 2,4-D.

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1 And on Slide 19, their results showed that both classes of herbicides
2 are indeed degraded in the same way. I'm sorry, Slide 18. I'm one ahead.
3 And they diagrammed the antiemetic reaction here in Figures 1 and 4 on
4 both phenoxy auxin and FOP herbicides.

5 And we asked Dr. Hausinger and he confirmed during cross-exam to
6 really get this enzymatic reaction to run, you need alpha-ketoglutarate as
7 well as ferrous iron and oxygen. And what coordinates all of these reactants
8 together?

9 It's the active site motif, it's the 81 motif and that's why it's
10 functionally important. And I do want to circle back to the legal standards
11 here because Judge Pollock asked about that earlier. Because we haven't
12 heard much from Bayer about the legal standards so let's go to Slide 4
13 please.

14 So the case law has been quite clear the court should apply a
15 reasonableness standard for a written description. And at the top, *Ariad*
16 requires that a specification reasonably convey possession. *AbbVie* notes
17 that one way to satisfy written description is a reasonable structure-function
18 correlation.

19 If you could go to Slide 5 please. And we have the *Ajinomoto* case
20 which is also important. And it found adequate description of a more potent
21 promoter term applying a common structure analysis based on a consensus
22 sequence, but let's note what's not in the *Ajinomoto* claim here.

23 There's no sequence identity limitation, there's no motif, there's no
24 consensus sequence limitation. So you don't actually have to have the
25 common structure in your claims to satisfy the written description

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1 requirement. But of course, in this case, we do have those two features in
2 the claims.

3 On Slide 6, there's some further principles that I think we should glean
4 from the *Ajinomoto* case. And it provided useful guidance on what the legal
5 standard for a reasonable structure function correlation means.

6 And so one argument that the court rejected from the challenger was
7 that a promoter closer to the consensus sequence will not always be stronger
8 than one farther away from that sequence. In other words, there can be
9 exceptions under this legal standard. That's okay.

10 And there can also be other parts of the sequence that are important to
11 function beyond the motif or the consensus sequence. That's okay too. We
12 don't need a common structure to be solely determinative or responsible for
13 a claimed function.

14 And those are the points we detailed in our Patent Owner response.
15 And so, Judge Majors, you are absolutely right that you don't need sort of a
16 perfect description of every single residue potentially important to function.

17 Another rejected argument was that similarity to the consensus
18 sequence is still not enough to predict the strength of a promoter from a
19 given sequence. So again, there doesn't have to be -- I'm sorry?

20 JUDGE MAJORS: Go ahead, finish your point, Mr. DeRoo.

21 MR. DeROO: So again, there doesn't need to be absolute
22 predictability and it's okay if there are exceptions in other parts of the
23 sequence that are also important to function.

24 JUDGE MAJORS: What do you make, however, of the distinction
25 that we raised at the DI stage that in *Ajinomoto* the written description

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1 argument was concerning the correspondence between a nucleotide
2 sequence and more potent promoter?

3 And the court looked at that and said well this is really well-tread
4 ground and there are some examples, several examples, in the specification
5 that talk about that. In contrast, one might say to the specification of your
6 client's patent where if there is a disclosure of a structure correlating to
7 function for a FOP degradation, the only place that comes up, at least the
8 first place that comes up, is in the patent specification itself.

9 So we don't have the luxury of going and looking at a bunch of prior
10 art to say, you know, this is just kind of well-known, you know, nucleotide
11 sequencing and why are we fighting about this? We're talking about a
12 specific function that your client who, on this record, is the first one to
13 describe in the art.

14 So that's something that I'm still grappling with in my head in terms of
15 the applicability of what happened in *Ajinomoto*.

16 MR. DeROO: Yes. Yes, thank you, Your Honor. Two responses
17 there. One is that the description in the patent as I showed kind of in
18 columns 49 and 50 where they extended the observation that FOPS are
19 degraded in the same way as the phenoxy auxins.

20 There was knowledge in the art about how the phenoxy auxins were
21 being degraded. And they've confirmed that it's the same active site in the
22 same way degrading the FOPS. And also, in *Ajinomoto*, the patentee there
23 was pretty fortunate that there was more information in the literature about
24 more potent promoters because they claimed a lot more.

1 As I showed on a previous slide, they had no sequence limitations in
2 their claims. They were even claiming promoters within the Valero scope of
3 the claims. They didn't have this consensus sequence at all.

4 And the genus here in the claims is much tighter. It requires having
5 the same active site. It requires having highly identical sequences within at
6 least 85 percent sequence identity. And so you don't need as much pre-
7 existing knowledge because what we're arguing is a common structure
8 correlated to function as co-extensive with the scope of the claims here.

9 And then finally, back to Slide 6 please. The third rejected argument
10 was that the strongest promoters do not necessarily adhere to the consensus
11 sequence. I thought this was another interesting lesson to take away.

12 Because it's okay if you can achieve the same or stronger function
13 without necessarily having the common structure at all in this particular
14 case. And that's because on Slide 7 the emphasis is that it is a reasonable
15 correlation standard. It's not a responsible for standard.

16 It's not a causation standard. As in discussing *Ariad*, Ajinomoto said
17 we have spoken more modestly of a correlation between structure and
18 function. So if there's a general relationship, that's enough.

19 In the lower box on the slide, what the court affirmed in *Ajinomoto* is
20 the ITC's upholding of validity over a written description challenge and as
21 the commission there stated, respondents do not show that the consensus
22 sequence is unrelated to promoter strength. And that's essentially the burden
23 that Bayer has here.

24 It has to disassociate the AAD-1 motif from the claimed function
25 which isn't easy to do when we're talking about the active site of these

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1 enzymes and they've steadfastly maintained the AAD-1 motif in their own
2 variants. I believe, so if we could go to Slide 19 please.

3 And I'll briefly touch on this one again. As the full trial record has
4 shown, AAD-1 motif is unique to AAD-1 enzymes hasn't been shown to be
5 present and any other enzymes of different function. Slide 20 please. And
6 here we have more undisputed testimony from Dr. Bollinger on this slide.

7 The contours of an individual Alpha KG dioxygenases active site is
8 defined by the spacing and residues of its own specific motif. And again, on
9 a full trial record, no enzymes other than AAD enzymes have been shown to
10 have the AAD-1 motif.

11 It's a unique structural feature that's directly involved in the claimed
12 herbicide degradation function. Very easy to determine if you're inside or
13 outside of the claim based on that structural feature and the law doesn't
14 require anything more than that.

15 And on Slide 21, I do want to point out Bayer's variants. They claim
16 to have made thousands of these, but again, they haven't identified a single
17 one that has the claim function, but lacks the AAD-1 motif. And from what
18 they've published, the AAD-1 motif is uniformly retained in their variants.

19 And that's because the motif, it's a functionally important motif.
20 That's the point of it. So I'd like to now address Bayer's arguments about
21 enantiospecificity on Slide 29 please. And the first problem with this
22 argument and I think it's pretty incorrect to say that this is some kind of
23 waived argument when the first, when the second declaration comes in from
24 Dr. Hausinger.

1 And he barely talks about the claim language. All he's referring to 50,
2 60 times is enantioselectivity or enantiospecificity. That's what he's talking
3 about in his Reply Declaration. But the first problem is we have to note that
4 there isn't a term that says (R)-enantioselective or (R)-enantiospecific in the
5 claims.

6 And as shown on the screen here, it's something that Dr. Hausinger is
7 apparently reading from the specification into the claims and it's fairly
8 extreme in suggesting that the claimed enzymes are only acting on R
9 enantiomers which we know can't be correct.

10 2,4-D is achiral for example. But the point here is even if you loosen
11 up the sterics or the specificity, so that some amount of (S)-enantiomers get
12 in, they can enter into the active site, Bayer's provided no evidence that
13 means you've completely lost your (R)-enantiomer activity on the RFOPS or
14 on the (R) phenoxy auxins.

15 There's been no showing of that. If we could go to, actually, pull up
16 Bayer's Slide 15 please. If we can't do it then I can just talk through it. But I
17 would like to respond to Bayer's enantiospecificity arguments about the
18 Chekan paper. I'm on their Slide 15.

19 I think you can just pull up our slides again. In this slide from Bayer,
20 it is mostly talking about steric blocking, but there's also an omission in their
21 highlighting that I'd like to point out. In the lower box between the two
22 highlighted sentences, there's confirmation that both (R)-diclofop and (R)-
23 cyhalofop bind at the AAD-1 active site in a manner similar to that of the
24 phenoxy auxins.

1 And that closely parallels what we saw in the specification. Columns
2 49 and 50 confirming that AAD-1 coordinates the same degradation reaction
3 in the same active site for FOP purpose signs as it does for phenoxy auxins.

4 That it is showing up again here with a report of a crystal structure
5 only further confirms that there's adequate correlation between the active site
6 and its motif and the claimed function. But now let's look at what Bayer did
7 highlight on their slide.

8 It talks about a solvent-exposed tunnel comprised of a handful of
9 amino acids. But then it goes on to say well if there are only limited
10 interactions between those residues and the AOPP also known as FOP
11 herbicides, so these residues are just out of the way and the shifting away of
12 the tunnel in one direction suggests that the (S)-enantiomers won't fit in
13 there.

14 But that's steric blocking of an unclaimed enantiomer. Those residues
15 are not participating in the claimed degradation reaction, the claimed
16 function in the same way as the motif residues. I'd also like to briefly
17 address Bayer's Slide 14 and yes, an inventor, Dr. Terry Wright is listed as
18 an author, Satish Nair, Dr. Marty Bollinger.

19 Yet Bayer stayed far away from this paper during their short one-hour
20 deposition of Dr. Bollinger. And that's because they're going out on a limb
21 with this language about little being known in an insufficient knowledge
22 base. So I'd like to refer to Exhibit 1019 please. And I believe it's on Page
23 13300.

24 But as the Chekan paper actually states and this is under the results
25 and discussion header on that page. The investigators were seeking to locate

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1 other AAD enzymes and noted that homology searching is difficult because
2 it gives an example in the middle of the paragraph.

3 Sequence identity as between related enzymes in this family are low.
4 Just 30 percent between TauD and TfdA, just 28 percent between AAD-1
5 and TfdA. That's down in our twilight zone region of sequence identity.
6 And that's why they needed a different approach.

7 To try and find other enzymes that could be part of this family. And
8 none of this relates in any way to making high sequence identity AAD-1
9 variants. As Dr. Bollinger explained without rebuttal and without cross-
10 examination at paragraphs 119 to 121 of his Declaration.

11 And so, further down the paragraph in Chekan, the author has
12 described how they look for AAD family members based on co-localization
13 with other related genes. And they publish the list of candidate genes in the
14 appendix to the paper and that is Exhibit 1020.

15 It's the appendix and that Table 1 is on Page 17. Guess what? It's a
16 listing of protein IDs from a database and the natural organism they came
17 from. It has nothing to do with making AAD-1 variants. So as Dr.
18 Bollinger clearly explained in his Declaration, again that's Exhibit 2015,
19 paragraphs 119 to 121 without rebuttal from Dr. Hausinger, nothing about
20 Chekan relates to making high identity variants based on SEQ ID 9.

21 Yie, can we pull up Slide 10 please? So I would now like to address
22 85 percent sequence identity as shown here in the highlighting, the
23 specification describes the invention as including variant proteins, having
24 the same or similar activity of the exemplified proteins as noted in the
25 Institution decision.

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1 There's no dispute that the exemplified proteins referred to here are
2 the AAD-1 variants in the specification. And it says that the amino acid
3 identity will typically, not always, and remember that exceptions are okay
4 under our legal standard, but they will typically be at least 60 percent
5 identical and 85 percent identity is listed right there.

6 And that's sufficient disclosure under *Schnitzer v. Etzel*. So we have
7 two structural features now that need to be considered together in tandem.
8 We have a tight genus of at least 85 percent variance with the same
9 maintained AAD-1 active site and there's been no showing of functional
10 diversity within those bounds.

11 And again, at most, Bayer has pointed to a few AAD-1 variants that
12 had solubility issues in vitro and therefore weren't tested. But that doesn't
13 mean they were necessarily inactive. If we could go to Slide 43 please.

14 So Dr. Hausinger's testimony that insolubility means lack of function
15 contradicts what skilled artisans knew, contradicts what he did in his own
16 lab at Michigan State. So first off, enzymes typically exist outside or I'm
17 sorry, typically exist in cells not in vitro and in purified form.

18 So you're working with enzymes outside their normal environment.
19 And when I asked him during cross-examination, he said there's always
20 more you can do to improve solubility. So you can run the assay that you're
21 intending. And that includes things like just tweaking temperature, pH.

22 The one that I thought was interesting and wanted to include on this
23 slide is maltose binding protein which he confirmed is widely used. You
24 fuse it and it solves your solubility issue. But in his own Declaration, he
25 instead said that a POSA would understand that there's just no activity.

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1 Here with these three variants, the functional assay just wasn't wrong.
2 And that's where things left off. Again, there's thousands of variants from
3 Bayer on the other hand where there's been no showing of any functional
4 variation or difficulties.

5 And back to Slide 10 please. Another area where Dr. Hausinger has
6 ignored the level of skill in the art is his superficial position that one would
7 ignore or discount these disclosures on the basis that 85 percent sequence
8 identity treats all amino acid substitutions the same.

9 Of course, exercising some reasonable ordinary skill when making
10 substitutions it matters. And here to stay within the scope of the claims, all
11 your skilled artisan has to do is not totally destroy the claimed function. If
12 we could go to Slide 22.

13 As Dr. Bollinger testified, principles for maintaining function were
14 very well known and they're all common sense based. Number one, stay at
15 high sequence identity. You don't have to try to do something difficult, go
16 down to 20 percent, keep it high.

17 Number two, maintain your active site motif. We know that these are
18 essential residues. Number three, sequence alignments with related proteins
19 which were available in the art can provide guidance about which residues
20 are better to substitute than others.

21 And this is so well known that people even designed computer
22 programs to do this for you. And then Number four, the types of
23 substitutions. These are 100 percent common sense based. You don't want
24 to insert a ton of huge bulky amino acid residues that could block up your
25 enzyme.

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1 You also don't want to be flipping charges so that you have a situation
2 where two residues are attracting and now you're making them repel. And
3 so you take a little bit more care when you're dealing with those types of
4 situations. But Dr. Hausinger disputed none of these principles.

5 He's just kind of stuck his head in the sand and refused to apply them
6 instead assuming that all substitutions have to be treated as the same. And
7 that's just giving very little credence to how a skilled artisan would
8 understand this subject matter. And on Slide --

9 JUDGE POLLOCK: Mr. DeRoo, --

10 MR. DeROO: Yes.

11 JUDGE POLLOCK: -- your claims say nothing about conservative
12 substitutions. It's just a straight 85 percent identity. How do you square
13 that?

14 MR. DeROO: Well because we're allowed to leave something for a
15 person of ordinary skill in the art. Eight-five percent, there's been no
16 showing of really any functional diversity within 85 percent, but a skilled
17 artisan is allowed to use his or her knowledge in making enzymes that would
18 fall within that range and it's not exactly a mystery as to how to maintain
19 enzymatic function.

20 And again, going back to the legal principle, one doesn't have to go
21 through and map out with specificity every single possible residue, change
22 this one, don't change this one and provide a list for every possible
23 substitution.

24 We see it from Ajinomoto that just a consensus sequence is often
25 enough. And on the next slide, Slide 23, LifeScan expressed doubt at

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1 Institution about a written description challenge based on the motif of just
2 six amino acids within an enzyme sequence containing 593 amino acids.

3 And this is a case where the Board recognized structure function
4 correlation and the use of ordinary skill in making enzymes and in this case,
5 the Petitioner's expert, Dr. Cass was a lot more candid than Dr. Hausinger
6 and the Board credited this expert's acknowledgment that a skilled artisan
7 could locate a given sequence with some alterations from the base sequence
8 and make a fair guess about whether it would have a qualitatively similar
9 behavior.

10 That's something that Dr. Hausinger refuses to acknowledge. It's
11 something that Dr. Bollinger absolutely thinks is the case for people of
12 ordinary skill. But LifeScan here I believe is the only case of record that
13 involved claims reciting enzymes with a sequence identity limitation and a
14 motif limitation which is precisely what we have here in these IPRs. And
15 it's supportive of Corteva's position.

16 JUDGE MAJORS: That was, is that a DI?

17 MR. DeROO: Yes. Yes, it is a DI.

18 JUDGE MAJORS: Do you recall did they institute that case? Do you
19 recall?

20 MR. DeROO: Yes. Yes, they did on one claim because that motif of
21 six amino acids was not recited in the claims. Here we do have it in the
22 claims. And so it was narrowly instituted on one enablement ground.

23 Certainly not on written description. That was the reasoning. I would
24 like to briefly address on Slide 31 please of the Saari paper which is I think

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1 it's just a little bit of a sideshow here because it is rare to find two enzymes
2 having different function at very high sequence identities.

3 That's why the discussion in Saari was as cautious as it was and
4 counsel pointed to a discussion of the *A. denitrificans* bacterium. I don't
5 think anyone has disputing that the bacterium has this activity on the (R)-
6 enantiomers.

7 But didn't attribute that activity to a specific enzyme that was
8 expressed on Slide 33 very briefly. Bayer hasn't been able to find any
9 citation to Saari 1999 as disclosed in what Dr. Hausinger now claims it does.
10 It observed an activity and it used amplification, a probe to just find a
11 sequence that's somewhere close to TfdA.

12 In short, nobody was giving Saari 1999 the credence that Dr.
13 Hausinger now says it does. And if I could tie this up on Slide 36, whatever
14 Bayer's criticisms are about the many sequence function relationship studies
15 in the field, there is no dispute that at the very least they address natural
16 enzymes like the Denitrificans enzymes from Saari 1999.

17 And this slide shows the results of several different studies all in one
18 slide. Devos, Todd, Wilson, Rost, these are all of record. And the
19 consensus was that high sequence identity. It is almost universal to have the
20 same function.

21 It's not 100 percent, there are exceptions. And remember that
22 exceptions are still okay under our legal standard, but they're rare. And if
23 we go back to Slide 11 please, there's been no evidence after a full IPR trial
24 the AAD-1 RdpA is one of those exceptions. It's counter-part enzyme SdpA
25 is all the way down at 30 percent identity.

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1 And despite all the variants made by both parties, there's no evidence
2 that one can completely change the specificity or function or RdpA to
3 destroy the claimed function within 85 percent. And so with no diversity, it
4 is incorrect.

5 The argument that we've somehow conceded representative species,
6 this identic makes clear we cited it at least in the Surreply. The disclosed
7 AAD-1 variance, AAD-1, V2, V3, absolutely are representative if you have
8 a tight genus without much variation in it.

9 Slide 27 please. I'd like to address Claim 2. And here I think the
10 issue is kind of crystalized for the Board and it's fairly straightforward. With
11 this additional Arginine, does it require importing a limitation from outside
12 the specification which is Bayer's position?

13 Or is it a permissible use under *Rivera* of a skilled artisan's knowledge
14 to have informed the role of the Arginine? And that Arginine is quite
15 literally disclosed as part of SEQ ID No. 9. And we submit that it's the latter
16 here because the role of that Arginine was well established by 2004-2005.

17 Elkins confirmed its role in the related enzyme TauD. Hotopp further
18 extended it to TfdA. And Schleinitz even notes the importance of that
19 Arginine in RdpA. It's not just showing up in the figure here. It actually
20 says in the text, a homolog for that Arg278 was present only in RdpA, not
21 SdpA.

22 And we submit and we briefed this issue. Claim 2, whatever the
23 outcome should have no effect on written description for Claim 1 because
24 remember, under our legal standard, it is okay if other amino acid residues
25 beyond a consensus sequence or motif are important for activity.

1 And that's not a problem as *Ajinomoto* illustrated. If we could go to
2 Slide 28 please. Regarding the Claim 2 motif, Dr. Hausinger is again taking
3 inconsistent positions. Says there is no known role for R285 in his
4 Declaration, but in his own research, he is citing Elkins.

5 He's citing the same prior art literature that Dr. Bollinger cited in
6 predicting such a role for Arginine 285. If we could go to Slide 45 please.
7 This is Grounds IIA/IIB to wrap up these grounds were weak in the Petition
8 as the DI recognized. They've been rebutted by Dr. Bollinger and then Dr.
9 Hausinger essentially ignored them in his Reply Declaration.

10 He had just one paragraph on them, submitted no additional evidence,
11 no new reasoning about obviousness. So in Slide 48, for example, the
12 deficiencies the Board previously found regarding reasonable expectation
13 have not been cured.

14 Remember, we have to do this analysis before we have the benefit of
15 the disclosures of the specification, but the Petitioner's argument that a
16 POSA would have expected RdpA to degrade phenoxy auxins and RFOPS
17 to be the same mechanism as the Slide, I'm sorry, Slide 46 please.

18 The Board found that it lacks sufficient explanation and its wanting
19 for persuasive evidentiary support and it looks like hindsight in our
20 Response we pointed out Dr. Hausinger's concession that the prior art did
21 not report any testing of RdpA and FOPS.

22 And Dr. Bollinger testified that the structural differences between
23 these two classes of herbicides is sufficiently different that they have entirely
24 different chemical properties. These are significant differences. And what
25 were Bayer's responses to these arguments?

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1 They had none. On Slide 48, what this means is it leaves Bayer only
2 with its inherency position. But as the DI noted, the inherency theory was
3 entirely threadbare. It was just one sentence and that's not enough because
4 inherency requires a lot of proof.

5 It requires essentially absolute certainty that something is present or
6 will occur because possibilities and probabilities are not enough. That's
7 what the Federal Circuit tells us in *Millenium* and in *Honeywell*.

8 And the Petition just had a single sentence on inherency. It is too
9 threadbare on a full record, Dr. Hausinger hasn't come back to address it.
10 There's no further evidence submitted with their Reply Brief. And on Slide
11 47 please, what Bayer's inherency argument really does is try to excuse their
12 lack of prior art disclosure.

13 And what that does is just run afoul of the issue in *Honeywell* where
14 the court held that the Board in dismissing properties of the claimed
15 invention is merely inherent. Without further consideration as to
16 unpredictability and unexpectedness, here it is a matter of law.

17 And note that the discussion is not in the context of unexpectedness
18 for like unexpected results, objective indicia. Those aspects were addressed
19 in a different part of the decision. This is a lot closer to a reasonable
20 expectation of success type of analysis.

21 If we could turn to objective indicia on Slide 50 please. We
22 previously saw the praise and discussion from Petitioner's own scientists on
23 Slide 51. There is compelling evidence of unexpected results.

24 Unprecedented activity of degrading two different classes of
25 herbicides advantageously providing broad spectrum weed control as I

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1 discussed in the beginning. Closest prior art no matter which one you pick
2 doesn't disclose that activity.

3 And these are the quintessential types of facts that strongly support
4 non-obviousness as held in *Albrecht*. So sort of to tie up Grounds IIA and
5 IIB should fail, submit that these grounds really come down to ground, these
6 IPRs come down to Ground I and Bayer hasn't proven its case. If we could
7 go back to Slide 11 please.

8 Again, there's no proof of any functional diversity with an 85 percent
9 identity of SEQ ID 9. And there's no proof that the AAD-1 motif lacks
10 correlation to the claimed function. There's no dispute that skilled artisans
11 knew the AAD-1 motif from SEQ ID 9 itself and there's no dispute that
12 AAD-1 motif is unique to AAD-1 enzymes.

13 That's function correlated structure and that should be sufficient to
14 defeat their priority challenge in Ground I. So unless there are questions, I'll
15 reserve the balance of my time.

16 JUDGE MAJORS: Thank you. There's nothing from me at this time.

17 MR. GROSSMAN: If we can start with our Slide 11 and look at
18 Claim 1. So focusing first on the AAD-1 protein, or the AAD-1 motif
19 question, it's not in the specification. All of Mr. DeRoo's arguments for how
20 it would be obvious to the POSA, the POSA looking at SEQ ID No. 9 would
21 see these residues.

22 That's just the mapping argument. There's no actual description that
23 anyone actually thought of that in the specification. Again, the only motif is
24 the generic prior art motif. Under their theory, every time every single one

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1 of these enzymes TfdA, SdpA, TauD has its own motif based on where you
2 find the residues from the generic prior art motif.

3 But there's nothing in the record, let alone Schleinitz that ever
4 describes such a motif let alone an RdpA motif which is what they really
5 need. Second of all, I want to again emphasize the language of the claim.
6 The protein has to exhibit arlyoxyalkanoate dioxygenase activity where it
7 degrades a phenoxy auxin herbicide and an RFOP.

8 The question here is not how, what are the residues involved in this
9 generic dioxygenase activity, what are the residues that give it the activity on
10 these substrates because again, that's what makes this new and distinguishes
11 it from everything else in the field.

12 And there's nothing in the specification that says that either. The only
13 way they can try to get to written description here is to try to read out
14 arlyoxyalkanoate dioxygenase, again, the title of Chekan from the claim and
15 then read out the substrates from the claim. You can't get written description
16 by lowering the bar and reading out what the activity is on.

17 And a similar incident occurs with their arguments about what we
18 needed to prove to show lack of priority. It is our burden to show lack of
19 priority. But there's no priority when there's no description in the
20 specification of a structure correlated to function.

21 The suggestion that we somehow had to come forward with all
22 manner of different enzymes showing that they're guessing in these claims
23 that these variants would have this activity was wrong is not what we have
24 to show.

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1 What we have to show is they haven't described in the specification
2 the structural features they need to for the claimed activity and that is proven
3 by Chekan. If we go back to Slide 15, sorry, can we get to Slide 15?

4 Mr. DeRoo focused on this language about that both FOP, the FOPS
5 bind in the manner of similar to phenoxy auxins, but then it goes on to say
6 the additional aryl ring is accommodated by the solvent exposed tunnel that
7 does interact for whatever Mr. DeRoo's comments are, does interact with the
8 aryl of the FOP ring.

9 That's how you get the binding to that substrate or at least the activity
10 on the substrate because that tunnel needs to be there to accommodate the
11 substrate. That information wasn't known until 2019 and it certainly wasn't
12 in the specification.

13 That right there among the other evidence, even if they did somehow
14 have support for the AAD-1 protein shows that they're not providing the
15 common structural features necessary to show activity on this brand new
16 class of substrates.

17 I will also note that while Mr. DeRoo focuses on *LifeScan*, I would
18 like to remind the Board of the decision in *Porro* which *LifeScan* discusses.
19 And *Porro* was the only decision of the PTAB informative, precedential or
20 otherwise that deals with written description in the case of having a few
21 species and then trying to claim a genus.

22 And what *Porro* says is the specification does not provide guidance in
23 rejecting written description. What structural features are responsible for the
24 enzymatic activity? Nor does it describe what amino acid changes can be

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1 made in the wild-type sequence without affecting the enzymatic activity of
2 the protein.

3 That is what their specification needs to describe and it doesn't. And
4 going back to your question, Judge Majors, about other changes to R285, the
5 specification doesn't tell you what changes you can make to R285.

6 It leaves it open, sometimes conservative, sometimes non-
7 conservative. It doesn't specify the changes that can be made. And while
8 Corteva tries to suggest that this is a pre-*Ariad* decision, well it's still the
9 only informative decision of the Board and I see it as consistent with *Ariad*.

10 *Ariad* says you need a correlation between the structure and the
11 function. And what *Porro* was saying is, yes, this is what, this is what is
12 meant by that. It doesn't need to be perfect, do you still need to talk about
13 the residues responsible for the activity and you still need to talk about the
14 changes that can be made to preserve the activity going to your earlier
15 question, Judge Pollock, on that issue.

16 On this question about the record evidence and changes that can be
17 made, well we already know that there are changes that can be made that
18 don't have the claimed activity. We know about the changes to R285. We
19 know about the sequences that they made, sequences 10 to 12 that don't have
20 the claimed activity.

21 They are pointing to the work that, when they talk about Bayer
22 making thousands of sequences, what they're talking about is Bayer made
23 thousands of sequences. None of that information is of record. I don't
24 personally know what those changes were, but I know over the course of
25 years, they made thousands of changes, or thousands of different sequences

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1 because certainly the type of information that's provided by this patent even
2 if that were in front of him was not sufficient to tell them what they needed
3 for activity.

4 And let's be clear, what happened here, they did their research, they
5 published some of those sequences and then six months later Corteva copied
6 it and put down their claim with 85 percent sequence identity. That's how
7 they came up with the idea for AAD-1 motif and 85 percent sequence
8 identity.

9 Not when they filed their applications in 2004 and 2005, but when
10 they decided to copy Bayer's invention years later. That's where these
11 claims came from and that's why the written description requirement is so
12 important here to prevent parties like Corteva from doing exactly what
13 they're trying to do here.

14 Which is see someone else who put in the work to figure out what's
15 necessary and then try to copy if afterwards and say no, no, no, we have
16 thought of this all along despite any absence of a discussion in their original
17 priority documents.

18 On this question of enantiospecificity and waiver, I will just note the
19 following: we talk about, for example, in our Institution decision at Page 28
20 to 29 about enantiospecificity in the claims. Dr. Hausinger also talked about
21 that in his Declaration.

22 The Institution decision observes this enantiospecificity and
23 enantioselectivity stereospecificity discussion in multiple places, Pages 28 to
24 Page 30, Page 42. Corteva never discussed this issue until the last round.

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1 They were clearly on notice that this was an issue and they never brought it
2 up. And do we know how that's the case?

3 In paper number nine from the 1036 proceeding, their pre-Institution
4 Surreply, Pages 2 to 3, they talk about whether the claims require
5 enantiospecificity. And all they say is well, yes, the claims also act on 2,4-
6 D.

7 Well there's no dispute here the claims act on 2,4-D. But they never
8 quibbled about this issue. The Institution decision comes along. It says on
9 Page 70, if you don't raise it in your Patent Owner Response, it's waived.
10 They didn't raise this issue in their Patent Owner Response.

11 They decided to wait to the last round to try to come up with
12 something because their other arguments which, by the way, this is now like
13 we saw their arguments during prosecution, we saw their arguments -- sorry,
14 did we lose the other Judges?

15 JUDGE POLLOCK: Let's --

16 MR. GROSSMAN: Can we pause the time maybe?

17 JUDGE FITZPATRICK: I'm here.

18 JUDGE POLLOCK: Let's take a break.

19 JUDGE FITZPATRICK: Judge Fitzpatrick is here, let's --

20 TECHNICAL STAFF: All right. We've got audio.

21 TECHNICAL STAFF: Stand by for Judge Majors.

22 JUDGE POLLOCK: Mr. Grossman, you're welcome to take a seat
23 while we figure out what's going on.

24 MR. GROSSMAN: Thank you.

25 (Recess)

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1 JUDGE MAJORS: When it dropped, you were talking about that
2 Bayer had made numerous sequences and it was their work that discovered
3 that degree of diversity if that helps kind of re-orient you.

4 MR. GROSSMAN: Yes, thank you. Thank you.

5 JUDGE POLLOCK: Mr. Grossman, we'll put seven minutes back on
6 the clock and I do apologize to everyone for these unprecedented difficulties
7 in our communication system, but --

8 MR. GROSSMAN: Understood. It happens all the time with these
9 types of calls so no apology necessary.

10 JUDGE POLLOCK: Go ahead.

11 MR. GROSSMAN: Okay. So again, there's the -- I was just, I don't
12 know if His Honor heard the issue I was raising about the waiver argument.
13 Judge Majors, was that, were you on for that?

14 JUDGE MAJORS: Yes.

15 MR. GROSSMAN: Yes.

16 JUDGE MAJORS: Briefly you had said it was raised in the Petition
17 and the DI so I'm --

18 MR. GROSSMAN: Right.

19 JUDGE MAJORS: -- sorry.

20 MR. GROSSMAN: Yes.

21 JUDGE MAJORS: That's where I -- when I fell off.

22 MR. GROSSMAN: Right. So it was raised in the DI so it's, they
23 didn't include it in the Patent Owner Response. It's untimely under 37 CFR
24 42.23(b) so the Board need not even consider the argument, but again as I

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1 mentioned earlier, it ultimately doesn't matter because whether the claim
2 requires enantiospecific or not, there's no written description support.

3 I'd like to then go to a few of Patent Owner's slides. If we can go to
4 Slide 22 of the Patent Owner's slides. To me this is the quintessential
5 example of how all of their arguments are in the nature of obviousness.
6 None of this is in the patent.

7 None of this is in the patent. The only thing the patent talks about
8 making changes is sometimes you have a conservative substitution and it
9 works and sometimes you have a nonconservative substitution that works.

10 There's nothing about maintaining the active site motif, retaining
11 highly conservative across related enzymes. That can't be the case because
12 nothing else is active on RFOP so how do you even do that? Maintain
13 charge distribution steric bulk, that's not in the patent either.

14 This is why all of their arguments about this is what a POSA would do
15 and this is what a POSA wouldn't do, this is a research project that's
16 nowhere in the patent. That's obviousness. That's not written description.

17 Let's also now look at Corteva's Slide No. 27. Corteva focused on this
18 language -- again, all of their arguments about the arginine at 285 being in
19 SEQ ID No. 9, well that was rejected in the Institution decision. I mean it's
20 just one of hundreds of amino acids in the SEQ ID No. 9.

21 There's no reason to focus on it. And again, there's no description of
22 it. It's not what might be obvious to the POSA reading the literature, it's
23 what's described as part of the invention, part of the structure correlation,
24 function correlation in the priority documents.

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1 That's not here. But this statement that they focus on from Schleinitz
2 about a homolog from arginine 278 being present in RdpA, that's just
3 comparing it saying as opposed to SdpA. That's the whole discussion about
4 where there was some residues that were in TfdA and also in RdpA.

5 But that ignores the description of this figure, of the alignment which
6 I explained in my opening discussion that it says that residue in TfdA was
7 and TfdA was active for 2,4-D binding. There's nothing that talks about that
8 arginine being well known for RdpA.

9 So even if you could gap fill, Schleinitz still doesn't give you what
10 you need. If we can go then to Corteva's Slide 43, I just want to very briefly
11 touch on that slide. This is, again, where Mr. DeRoo was talking about
12 solubility and their ways to deal with solubility.

13 If it were so simple, wouldn't Corteva have taken those residues, the
14 sequence 10 to 19 or 10 to 12, made the soluble and submitted them? We
15 know that they had to deal with solubility issues for some of sequences No.
16 1 through 9 that they did submit to the Patent Office.

17 That's commented on, in the submission about why some of the
18 activities vary. Again, this is all hindsight, coulda, woulda, shoulda. And
19 here is record evidence that when Corteva went to try to make variants with
20 85 percent sequence identity and the AAD-1 motif, they couldn't.

21 In 2018, 2019 that right there is indication of whether or not they
22 actually had possession of what they're now claiming all the way back in
23 2004 and 2005. I'd also like to just very, very briefly go to Corteva's Slide, I
24 think it's 7, no, it's oh, Slide No. 19 where Mr. DeRoo talked about this
25 different spacing and all of these things that the POSA would understand.

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1 None of this information is in the Patent. And by the way, this isn't
2 even what Chekan said. Chekan doesn't say the spacing is relevant. Chekan
3 doesn't say all you need is this a-ketoglutarate dioxygenases motif residues
4 to have the activity.

5 It talks about, for example, on FOPS how you need these solvent
6 exposed tunnel residues. It also talks about the differences between why
7 AAD-2 is (S)-specific and AAD-1 is (R)-specific. That's what Chekan is
8 doing.

9 The title tells you this is about the very activity that's at issue in these
10 claims and it is a rare case here where you have an admission from the
11 inventors that this information was not known until 2019. And it's a rare
12 case where you have internal documents saying that this one residue that we
13 know is critical for the activity R-285 is not part of the specification.

14 I mean, these are clear admissions from them. They tried to shift it to
15 us to say oh, we need to come up with all these examples to show it doesn't
16 work. All we need to show is that it's not described in their specifications
17 that the POSA wouldn't think they had possession of it and they don't.

18 And I'd lastly like to note there are a number of different attacks that
19 Corteva tries to make on Dr. Hausinger's credibility here. I will just say the
20 following: All you really need to do is to look at no further than Dr.
21 Bollinger's deposition testimony. That's Exhibit 1072, Pages 40 to 41 where
22 he testified that Dr. Hausinger is a good scientist and a good person.

23 That is from their expert talking about our expert's scientific work and
24 his character. Unless there are other further questions from the Board, I
25 have nothing further.

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1 JUDGE POLLOCK: Judge Majors?

2 JUDGE MAJORS: Nothing from me. Thank you.

3 JUDGE POLLOCK: Judge Fitzpatrick?

4 JUDGE FITZPATRICK: No, thank you.

5 JUDGE POLLOCK: Thank you very much. You have 9 minutes.

6 MR. DeROO: All right. Thank you, Your Honors. Of course,
7 Corteva does not make any bones about Dr. Hausinger's academic research.
8 He's worked in his own lab. It's his testimony contrary to that in this case
9 that we've taken issue with.

10 But just at a high level. We've heard no dispute and Bayer has
11 identified at least no contrary evidence that there is just one active site motif
12 in SEQ ID 9. And that a skilled artisan would, in fact, recognize that motif
13 from the primary sequence alone in SEQ ID 9.

14 That's description. There's also no dispute that a person of skill would
15 come to the 2005 PCT application with knowledge, pre-existing knowledge
16 of where those motif residues were located in that sequence. And there's no
17 dispute that the RdpA AAD-1 motif is functionally important for its activity
18 on phenoxy auxins.

19 And then there was no argument against the inventors who then
20 showed in the specification that the same active site coordinates the
21 degradation of the RFOPS. And there's this question about what --

22 JUDGE POLLOCK: Mr. DeRoo, what would the POSA know that
23 the precise spacing as important looking at the specifications?

24 MR. DeROO: Yes, well that's I believe what we showed on Slide 19.
25 You have different enzymes across the family and you have these

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1 enormously variable spacers like the fourth spacer can be anywhere from
2 114 to 183 amino acids.

3 So in this family of enzymes, you're going to have individual motifs
4 that set the contours for an active site. Dr. Bollinger has been studying and
5 getting funded to research these enzymes for 20 plus years and that is
6 absolutely contributing to substrate specificity because you're going to have
7 differently sized and different-- I'm sorry, what were his words?

8 Yes, binding pockets of different sizes and different configurations for
9 catalyzing a diversity of reaction. So it is a diverse family of enzymes. But
10 within the claims it's very precise. It is a single active site motif and you
11 can't vary the spacing of it.

12 And you can't make too many changes within the overall sequence
13 identity and stay within 85 percent. And so we heard an argument about
14 well what distinguishes RdpA from other enzymes in the family?

15 This motif, the AAD-1 motif is an easy answer to that because as
16 shown on our Slide 19, we've had a full trial now. Bayer's had every
17 opportunity to see if they could find another enzyme somewhere that has an
18 AAD-1 motif and does some other function.

19 And they've never been able to find one. Regarding this mapping
20 argument, I mean even Dr. Hausinger testified in his paragraph 95, mapping
21 the generic consensus of the KG motif onto RdpA only confirms what the
22 prior art already taught and that's just consistent with Dr. Bollinger's
23 testimony.

24 A skilled artisan knew where the motif residues were in SEQ ID No.
25 9. We also heard a few arguments that I think really missed the forest for

1 the trees. With Chekan, there's a -- we've again heard about a solvent
2 exposed tunnel.

3 I don't think there's any dispute that those particular residues with that
4 vast weak Van der Waals interactions come nowhere close to the direct
5 involvement of the active site motif that coordinates all of the required
6 reactants to perform the claimed degradation reaction function.

7 And then again, there's no response to Dr. Bollinger's testimony.
8 There's nothing in the Reply Declaration, nothing in cross-exam and now
9 nothing on rebuttal that Chekan has anything to do with making AAD-1 high
10 sequence identity variance.

11 And turning to Bayer sequences, again, kind of missing the forest for
12 the trees, they're continuing to make a big deal holding up these three
13 insoluble variants or maybe it's nine. Corteva provided those for
14 consideration in this case. Bayer made kind of a big deal about them in the
15 district court action.

16 We provided them for consideration by both parties' experts and the
17 Board here. Bayer didn't provide any of their variants in this case. They
18 purport to have made thousands and to be clear, they made a bunch of them
19 including at least 1,200 of them using very basic techniques like alanine
20 scanning and recombination, this is in paragraph 66 of Exhibit 1017 cited by
21 Dr. Hausinger.

22 They didn't have a crystal structure when they were doing this. But
23 they withheld all of those variants from Dr. Hausinger and Dr. Hausinger
24 shows up giving an opinion that well there's this massively diverse genus
25 within the scope of the claims.

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1 But as we showed on our Slide 11, sort of the green sequence identity
2 slide, there's been no showing of any functional variation with an 85 percent
3 identity. With the case law and then *ex parte Porro*, indeed it is pre-Ariad
4 and pre-Ajinomoto.

5 That case involved no motif claims and I think it's a pretty big stretch
6 to pull reasonable correlation. And you saw the, some of the teachings or
7 takeaways from the Ajinomoto case on our Slides 4, 5, 6, 7 and conclude
8 that you need a feature that is "responsible for" the claimed activity.

9 The law doesn't go that far. We have the en banc area decision saying
10 it's more modest correlation. And then we heard some criticisms of Dr.
11 Bollinger's testimony of what a skilled artisan would have brought to the
12 table back in 2004, 2005 such as knowing how to make variants. It's not the
13 responsibility of a patent owner to provide a basic enzymology text book in
14 every specification.

15 POSAs get to use ordinary skill. They're allowed to use the
16 techniques available to them and nothing about those techniques is
17 particularly controversial. I think that's why Dr. Hausinger never disputed
18 them.

19 He took a head in the sand approach of there must be 10^{44} variants
20 and basically just assuming that you would randomly change any residue to
21 anything else and I think that's giving our person of ordinary skill too little
22 credit.

23 So again, to just kind of wrap up, we didn't hear anything about the
24 second set of grounds so these IPRs should come down to the first ground.

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1 Bayer hasn't proven its case. And the AAD-1 motif meets 85 percent
2 sequence identity within those bounds.

3 There's no functional variation and more than ample correlation to the
4 claimed function. So unless Your Honors have further questions, I thank
5 you for your attention and yield the balance of my time.

6 JUDGE POLLOCK: Judge Fitzpatrick? Questions?

7 JUDGE FITZPATRICK: No questions from me. Thank you.

8 JUDGE POLLOCK: Okay. Thank you.

9 JUDGE MAJORS: No, thank you, counsel.

10 MR. DeROO: Thank you.

11 JUDGE POLLOCK: I thank the parties for your attendance and
12 excellent presentations today. These matters are submitted to the panel for
13 determination and preparation of final written decision. If counsel could
14 kindly stay behind after we adjourn in case the Court Reporter has any
15 questions or requires clarification. And with that, we are adjourned.

16 (Whereupon, the proceedings at 1:20 p.m. were concluded.)

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