

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

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

v.

CORTEVA AGRISCIENCE LLC,
Patent Owner.

Case Nos. IPR2023-01036, IPR2023-01037,
and IPR2023-01038
Patent Nos. 10,947,555, 11,149,283
and 11,299,745

Thursday, April 4, 2024

9:01 a.m. (EDT)

Remote Deposition of ROBERT P. HAUSINGER, PhD

STENOGRAPHICALLY REPORTED BY:

Deanna J. Dean, RDR, CRR

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Thursday, April 4, 2024
9:01 a.m. EDT

Remote deposition of ROBERT P. HAUSINGER,
PhD, held via Zoom videoconference, before
Deanna J. Dean, a Registered Diplomate Reporter,
Certified Realtime Reporter, and licensed court
reporter of the state of New Hampshire.

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I N D E X

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E X H I B I T S

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Exhibit 1001	US Patent No. 10,947,555	56
Exhibit 1019	Chekan 2019 Publication	44
Exhibit 1021	W02005107437 (Corteva '437)	36
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Exhibit 1043	US Patent No. 6,153,401	62
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1 P R O C E E D I N G S

2 THE REPORTER: My name is Deanna Dean. I
3 am a New Hampshire licensed stenographic court
4 reporter.

5 At this time, do all parties agree to
6 waive any objection, now or in the future, to me
7 swearing in the witness remotely?

8 ATTORNEY GROSSMAN: We agree.

9 ATTORNEY DEROO: All good.

10 ROBERT P. HAUSINGER, PhD,
11 a witness called for examination, having been first
12 duly sworn according to law, was deposed and
13 testified as follows:

14 EXAMINATION

15 BY ATTORNEY DeROO:

16 Q. Good morning, Dr. Hausinger. I'm Pier
17 DeRoo with the law firm of Finnegan representing
18 Corteva. I believe I'll be joined by Mark Lampert,
19 who is also with Finnegan, a little later this
20 morning.

21 Do you understand that you are testifying
22 today in IPR proceedings before the US Patent and
23 Trademark Office involving three Corteva patents?

24 A. Yes.

25 Q. And those are the '555, the '283, and the

1 '745 patents. Correct?

2 **A. That is correct.**

3 Q. And for the record, the corresponding case
4 numbers are IPR2023-01036, 01037, and 01038.

5 Does that sound right?

6 **A. I'll take your word for that.**

7 Q. Okay. So today's deposition is being held
8 remotely, and we just heard some instructions about
9 how to handle exhibits as they are called up
10 electronically.

11 To the extent that you prefer to look at
12 hard copy documents, we sent a box to your address.
13 Did you receive it?

14 **A. Yes, I did.**

15 Q. And have you opened that box, or is it
16 still sealed?

17 **A. It is still sealed.**

18 Q. Thank you.

19 Do you understand that your testimony
20 today will be transcribed and made public in these
21 proceedings?

22 **A. Yes, I understand that.**

23 Q. And you understand that your answers today
24 are under oath?

25 **A. Yes, I understand that, too.**

1 Q. And you understand that is the same oath
2 that would apply in a courtroom before a judge?

3 A. **Correct.**

4 Q. Is there any reason you cannot provide
5 full and truthful testimony today?

6 A. **No.**

7 Q. Have you been deposed before?

8 A. **Yes, I have. Once.**

9 Q. Just once? Then you're probably familiar
10 with the process. I would ask that we just try to
11 help out the court reporter by giving audible
12 answers instead of shakes and nods of the head, and
13 not talking over each other today.

14 Is that acceptable?

15 A. **That sounds very reasonable, yes.**

16 Q. And this is not meant to be an endurance
17 contest. We can plan to take breaks approximately
18 every hour or so. If you need a break at a
19 different time, please just let me know. And I
20 would just ask if that if there is a question
21 pending, that you answer it before we go on a
22 break.

23 Is that fair?

24 A. **That's very reasonable, yes.**

25 Q. Dr. Hausinger, would you open the box that

1 we had shipped over to you. And if we could pull
2 up the document previously marked by Bayer as
3 Exhibit 1054, please.

4 **A. Exhibit 1054.**

5 Q. Dr. Hausinger, this is your declaration
6 concerning the '555, '283, and '745 patents.
7 Correct?

8 **A. That is correct.**

9 ATTORNEY DEROO: Nan and Deanna, I just
10 don't see the exhibit in the share folder quite
11 yet.

12 NAN MARSHALL: Can we go off the record
13 for a second?

14 THE REPORTER: Off the record at 9:05 a.m.
15 (Recess taken from 9:05 a.m.
16 to 9:08 a.m.)

17 THE REPORTER: Back on the record at
18 9:08 a.m.

19 BY ATTORNEY DEROO:

20 Q. Dr. Hausinger, at the back of your
21 declaration, you have an Appendix A, which is a
22 table of exhibits. Correct?

23 **A. Yes, I do.**

24 Q. Are these exhibits that you considered in
25 preparing your declaration?

1 **A. These are the files, the documents that I**
2 **considered while preparing this, yes.**

3 Q. And is it an accurate and complete list of
4 materials that you considered?

5 **A. I would say yes.**

6 Q. Were these materials provided to you by
7 counsel, or did you search for and select them
8 yourself?

9 **A. A combination. I had a number of**
10 **different articles already in my possession, and**
11 **then some of the different patents and so forth**
12 **were provided to me.**

13 Q. Did you review your declaration,
14 Dr. Hausinger, before you signed it?

15 **A. Yes, I did.**

16 Q. Would you turn the signature page that's
17 on page 239.

18 **A. Yes, I'm there.**

19 Q. And is that your signature?

20 **A. Yes, it is.**

21 Q. And when you signed your declaration, did
22 you believe it was complete and accurate?

23 **A. Yes, I did.**

24 Q. And sitting here today, is there anything
25 in your declaration that you believe requires any

1 correction?

2 **A. Not that I can think of, no.**

3 Q. What did you do to prepare for your
4 deposition today?

5 **A. To prepare for the deposition today, I met**
6 **with counsel virtually. We had half a dozen**
7 **meetings or so, each an hour or hour and a half**
8 **long, and discussed what would happen here;**
9 **basically did some practicing; and then I scanned**
10 **through the declaration a few times.**

11 Q. When is the last time you read your
12 declaration?

13 **A. I was looking at it yesterday. Again,**
14 **more in a scanning mode, not a complete reading**
15 **mode.**

16 Q. And when you say you met with counsel, is
17 that with Mr. Grossman?

18 **A. With Mr. Grossman, with Ms. Ryan, and with**
19 **Mr. Picozzi.**

20 Q. And did you meet with anyone else to
21 prepare for your deposition?

22 **A. No, I did not.**

23 Q. In preparing for your deposition, did you
24 review any of the documents cited in your
25 declaration?

1 **A. Yes. I reviewed a few documents that**
2 **were --**

3 ATTORNEY GROSSMAN: And Dr. Hausinger,
4 I'd -- just to jump in there, I'll let the
5 witness answer yes or no to that question.

6 **A. Yes.**

7 Q. Did you review any documents in preparing
8 for your deposition that were not cited in your
9 declaration?

10 **A. No.**

11 Q. In your box of documents, would you please
12 retrieve the document previously marked by Bayer as
13 Exhibit 1023.

14 **A. Got it.**

15 Q. This is the Elkins 2002 publication you
16 cited in your declaration. Correct?

17 **A. That is correct.**

18 Q. And you are a listed author on this
19 publication?

20 **A. Yes, I am.**

21 Q. And the Elkins publication reports an
22 X-ray crystal structure of TauD. Correct?

23 **A. Along with some analysis of the TfdA**
24 **protein, yes.**

25 **(Clarification by the reporter.)**

1 Q. I'll put some spellings in the chat if
2 they're helpful.

3 On the first page of Elkins, do you see
4 the Scheme 1 box?

5 A. I do see Scheme 1.

6 Q. And about five lines below, do you see a
7 sentence beginning "Sequence analyses"?

8 A. I do see the sentence, yes.

9 Q. And it states that sequence analyses
10 indicate that TauD is closely related to several
11 members (referred to as group II) of the alpha-KG
12 dioxygenase family. Correct?

13 A. That is what it says.

14 Q. And the next sentence provides a list of
15 those closely related enzymes. Correct?

16 A. It includes TauD, YSD, TfdA, AtsK --
17 (Clarification by the reporter.)

18 A. TauD, YSD, TfdA, AtsK, clavamate
19 synthase, gamma-butyrobetaine hydroxylase.

20 Q. The identification of those
21 closely-related enzymes to TauD was based on
22 identifying a motif in their amino acid sequences.
23 Correct?

24 ATTORNEY GROSSMAN: Objection to the form
25 of the question.

1 **A. I indicate that there is a motif in the**
2 **sentence that lists these enzymes: the HX (D/E),**
3 **then X 23-26, and then (T/S), and then X from**
4 **114-183, and then a His, and then an X 10-13 in the**
5 **arginine motif. That is present in all of these**
6 **enzymes.**

7 Q. Was the sequence analysis used to identify
8 these enzymes, did that involve identification of
9 the motif in their sequences?

10 ATTORNEY GROSSMAN: Objection to the form
11 of the question.

12 **A. So I'm not quite clear what you're asking.**
13 **Could you rephrase that?**

14 Q. Yes.

15 The previous sentence stated that sequence
16 analyses indicate that TauD is closely related to
17 several members of the alpha-KG-dioxygenase family,
18 and then it says a motif was found in those
19 enzymes.

20 So my question is whether the sequence
21 analyses involved identifying the motif in the
22 sequences of those enzymes that are listed.

23 ATTORNEY GROSSMAN: Objection to the form
24 of the question.

25 **A. The sequence comparisons, such as in**

1 **Figure 5 shown in the paper, try to align the**
2 **sequences and identify regions of identity. And so**
3 **that helped to identify these particular residues**
4 **that are in the motif.**

5 Q. And Figure 5 of Elkins on page 5190
6 contains a sequence alignment of those 10 enzymes.
7 Is that correct?

8 A. That is correct. This is not the first
9 sequence alignment of proteins. There have been in
10 prior publications other alignments. This --

11 Q. And in -- oh, sorry. Go ahead.

12 A. This one makes use of the crystal
13 structure to gain additional insight into the
14 sequence comparisons.

15 Q. And what additional insights are provided
16 by the sequence alignment?

17 A. In this particular case, TauD, we have the
18 crystal structure and so we knew what some of the
19 roles of the residues were doing. You could see
20 that three of these residues were coordinating the
21 metal center. We could see what was interacting
22 with the substrate, the alpha-ketoglutarate. And
23 we could see what was interacting with the
24 substrate -- the taurine, in this case -- and so
25 that we could infer some of the function for the

1 **other enzymes as well.**

2 Q. In Figure 5 above the sequence alignments,
3 there are indications of beta strands and alpha
4 helices. Is that correct?

5 A. **Those are derived from the crystal**
6 **structure of TauD. Correct, yes.**

7 Q. So those show the amino acid residues in
8 TauD that form those particular secondary
9 structures?

10 A. **That is correct, yes.**

11 Q. And then those are correlated to the
12 sequences of the other nine enzymes that are
13 aligned here?

14 ATTORNEY GROSSMAN: Objection to the form
15 of the question.

16 A. **The sequences are aligned, and so one**
17 **doesn't know for sure whether the secondary**
18 **structure is retained in the other sequences.**

19 Q. Dr. Hausinger, the black triangles -- I
20 believe there are five of them -- at the bottom of
21 the alignment mark the locations of the alpha-KG
22 motif residues in the sequences of these 10
23 enzymes. Correct?

24 A. **The black triangles indicate residues that**
25 **interact with alpha-ketoglutarate or with the -- or**

1 they indicate coordinating, metal-coordinating
2 residues.

3 Q. And those were -- those are the residues
4 in the motif that you looked at on the first page?

5 A. Well, the motif has more. The motif also
6 indicates -- let's see here.

7 Oh, okay. That is right. Yes, the --
8 those residues are the same as the residues in the
9 motif.

10 Q. Just so the record is clear, motif
11 residues in the alignment in Figure 5 of Elkins are
12 marked with the five black triangles below the
13 alignment. Correct?

14 ATTORNEY GROSSMAN: Objection to the form
15 of the question.

16 A. The residues marked with the triangles in
17 Figure 5 indicate the residues in TauD that match
18 the motif.

19 Q. It appears that there is also black
20 shading for many of those residues marked with the
21 triangle. What does the shading mean?

22 A. I'm taking a moment to look at this,
23 because it's been a lot of years since I've looked
24 at this.

25 So the black shading, I believe, indicates

1 highly conserved residues, sequences that are
2 essentially identical in all cases. So they're not
3 identical in all cases but in most.

4 Q. If the residues are identical in all or
5 most cases, did that indicate that they are
6 important for structure or function of the enzyme?

7 ATTORNEY GROSSMAN: Objection to the form
8 of the question.

9 A. It provides a hint that the residues may
10 be functioning in the same manner in other
11 sequences, but there's no guarantee of that.

12 Q. Four lines down in the sequence alignment,
13 there's a sequence for TfdA. Correct?

14 A. TfdA is listed as the fourth sequence,
15 yes.

16 Q. And looking at the TfdA sequence, can you
17 confirm for me that the first motif residue is a
18 histidine at position 114?

19 A. It's a little hard to tell that it's
20 position 114. The closest number is 135, so one
21 has to count back. Five, four, three, four, two,
22 one. 130. Nine, eight, seven, six, five, four,
23 three, two, one. 120. Nine, eight, seven, six,
24 five, four -- looks like 114.

25 Q. And the second motif residue is an

1 aspartate at position 116 in TfdA. Correct?

2 **A. That is correct.**

3 Q. And TfdA, the third motif residue is a
4 threonine at position 141?

5 **A. That is correct. Threonine 141.**

6 Q. And TfdA, the fourth motif residue is a
7 histidine at position 263?

8 **A. Histidine 163 is correct.**

9 Q. 263. Correct?

10 **A. Yes.**

11 Q. And TfdA, the fifth motif residue is an
12 arginine at position 274?

13 **A. Arginine at 274 is correct.**

14 Q. What relationship do the five motif
15 residues have to the enzyme's function?

16 ATTORNEY GROSSMAN: Objection to the form
17 of the question.

18 **A. The residues are important for the**
19 **function of the protein as an**
20 **alpha-ketoglutarate-dependent dioxygenase. These**
21 **residues do not define what the substrate of the**
22 **enzyme is. These different enzymes have very, very**
23 **different substrates. But three of these residues**
24 **coordinate the metal center. The other residues**
25 **interact with binding the alpha-ketoglutarate.**

1 Q. In TfdA there's an additional conserved
2 arginine residue at position 278, and it's marked
3 by a gray triangle at the bottom of the alignment.
4 Correct?

5 ATTORNEY GROSSMAN: Objection to the form
6 of the question.

7 A. So there is an arginine at 278. It is not
8 conserved in all of the enzymes. It's not
9 conserved in the gamma-butyrobetaine acid enzyme
10 and in syrB --

11 (Clarification by the reporter.)

12 A. It's not conserved in the
13 gamma-butyrobetaine hydroxylase and in syrB.

14 Q. My question was a -- let me focus just on
15 TauD and TfdA.

16 The arginine at position 278 and TfdA is
17 conserved in TauD. Correct?

18 ATTORNEY GROSSMAN: Objection to the form
19 of the question.

20 A. It happens that both of those enzymes have
21 an arginine in there, yes.

22 Q. And feel free to refer to the legend for
23 Figure 5 towards the bottom.

24 But that arginine at 278 is a ligand that
25 binds with the primary substrate, which is taurine,

1 for TauD. Correct?

2 A. Okay. So I want to double-check your
3 question.

4 You're saying that in TauD, the arginine,
5 which is arginine 270 -- is that right? -- is
6 binding the taurine. Is that what you said?

7 Q. I believe so.

8 A. So if one goes to Figure 4 in this same
9 paper, Elkins, et al., then one can see that
10 arginine 270 is, in fact, forming bonds to the --
11 let's see here.

12 Yeah, so it does look like it is, in fact,
13 forming bonds to the substrate taurine.

14 Q. On the same page, 5189 of Elkins, in the
15 left-hand column, about five lines down, you see
16 that it says, "Arg 270 is partially conserved
17 across a range of the group II dioxygenases (Figure
18 5) presumably to act as a counterion to the
19 substrate anion." Correct?

20 A. That is what the text states.

21 Q. And that arginine is conserved in TfdA.
22 Correct?

23 A. There is an arginine in a comparable
24 position. Whether it serves the same function, one
25 can't know. It really will depend on the specific

1 **situation.**

2 Q. Let's turn to the TfdA model in Elkins.

3 Did your group create a complete
4 structural model of TfdA, or was it a partial model
5 of TfdA?

6 **A. We had a complete model of TfdA.**

7 Q. Could you turn to page 5187.

8 In the left-hand column, do you see
9 there's a header "Modeling Methods"?

10 **A. I do see that.**

11 Q. About 11 lines down, there's a sentence
12 that refers to residues 86-110 which contained a
13 knot.

14 Do you see that?

15 **A. I do see the reference to the knot, yes.**

16 Q. And a few lines further down, it states,
17 "No model is convincingly superior to the others,
18 and since this region of TfdA contains a 16 amino
19 acid insertion when compared to TauD, residues
20 86-111 were omitted from the model." Correct?

21 **A. So, yes, we did have a complete model or**
22 **several complete models; but because there was a**
23 **lack of confidence in this particular region -- we**
24 **did not include those residues in the model that**
25 **was deposited.**

1 Q. Would you please retrieve from the box the
2 document previously marked by Bayer as Exhibit
3 1042.

4 A. **So that's the Schleinitz, et al., in 2004.**

5 Q. Would you please turn to page 5360, and
6 let me know when you're there.

7 A. **I am there.**

8 Q. And do you see Figure 2 in the upper
9 right-hand corner?

10 A. **Yes, I do see Figure 2.**

11 Q. And Figure 2 of Schleinitz is a multiple
12 sequence of alignment of RdpA, TauD, TfdA, and
13 SdpA. Correct?

14 A. **That is what it shows.**

15 Q. And if you recall, we just went through
16 the TfdA sequence in Elkins to identify the
17 positions of TfdA's motif residues. Correct?

18 A. **That is correct, yes.**

19 Q. And to orient you to the next few
20 questions, I'd like to confirm that those five TfdA
21 motif residues are the same ones shaded in black in
22 Figure 2 of Schleinitz.

23 And to assist, I did include a blow-up of
24 Figure 2 in the box if you would like to refer to
25 that. It's Exhibit 2042.

1 Do you have Exhibit 2042?

2 A. I do. And I'm comparing --

3 Q. Yeah.

4 A. -- that Figure 2, Schleinitz 2, to Figure
5 5 from Elkins and just double-checking that the
6 highlighted -- the residues shown with a black
7 background are the same.

8 And, yes, they seem to be the same.

9 Q. Looking at the TfdA sequence in Figure 2,
10 the first motif residue, histidine position 114?

11 A. TfdA. 138, seven, six, five, four, three,
12 two, one. 130. Nine, eight, seven, six, five,
13 four, three, two, one. 120. Nine, eight, seven,
14 six, five, four.

15 114, correct.

16 Q. TfdA, the second motif residue is an
17 aspartate at position 116?

18 A. That is correct.

19 Q. And TfdA, the third motif residue is a
20 threonine at position 141?

21 A. Threonine at 141 is correct.

22 Q. And TfdA, the fourth motif residue is a
23 histidine at position 263?

24 A. Histidine 263 in TfdA, correct.

25 Q. TfdA, the fifth motif residue is an

1 arginine at position 274?

2 **A. Arginine 274 is correct for TfdA.**

3 Q. And TfdA, there's a conserved arginine
4 residue at position 278 marked with an arrow at the
5 bottom of the sequence alignment. Correct?

6 ATTORNEY GROSSMAN: Objection to the form
7 of the question.

8 **A. There is an arginine and TfdA that happens**
9 **to be conserved in this alignment with RdpA and**
10 **TauD.**

11 Q. In the legend for Figure 2, that arginine
12 is indicated to be a 2,4-D binding residue.
13 Correct?

14 ATTORNEY GROSSMAN: Objection to the form
15 of the question.

16 **A. So it says, "Black arrows indicate 2,4-D**
17 **binding residues in TfdA," and that it includes the**
18 **arginine 278.**

19 Q. Let's now look at the RdpA sequence in
20 Schleinitz's Figure 2.

21 The first motif residue shaded in black is
22 a histidine at position 111. Correct?

23 **A. RdpA has a histidine at 111, correct.**

24 Q. And RdpA, the second motif residue is an
25 aspartate at position 113. Correct?

1 **A. RdpA does have an aspartate at position**
2 **113.**

3 Q. The histidine at position 111 and the
4 aspartate at position 113 are separated by one
5 amino acid at position 112. Correct?

6 **A. There is a threonine at position 112 in**
7 **RdpA.**

8 Q. In RdpA, the third motif residue
9 highlighted in black is a threonine at position
10 138. Correct?

11 **A. RdpA does have a threonine highlighted in**
12 **black at position 138, yes.**

13 Q. The second motif residue at position 113
14 and the third motif residue at position 138 are
15 separated by residues 114-137. Correct?

16 **A. That's how the math works, yes.**

17 Q. In RdpA, the fourth motif residue is a
18 histidine at position 270. Correct?

19 **A. There is a histidine at 27 -- residue 270**
20 **in RdpA, yes.**

21 Q. And it's separated from the third motif
22 residue by residues 139-269. Correct?

23 **A. That is how it works out, yes.**

24 Q. In RdpA, the fifth residue highlighted in
25 black is an arginine at position 281. Correct?

1 **A. RdpA does have an arginine at 281,**
2 **correct.**

3 Q. And it's separated from the fourth motif
4 residue at position 270 by residues 271-280.
5 Correct?

6 **A. Those residues do separate the two**
7 **conserved residues, yes.**

8 Q. In RdpA, there's an additional arginine
9 residue shaded in gray at position 285, again
10 marked with the arrow at the bottom of the sequence
11 alignment. Correct?

12 **A. Well, it says in the legend that the black**
13 **arrows indicate 2,4-D binding residues in TfdA, so**
14 **it doesn't necessarily apply to the RdpA.**

15 Q. In Elkins we saw that the arginine was at
16 position 270 of TauD and was disposed to bind to
17 taurine. Correct?

18 ATTORNEY GROSSMAN: Objection to the form
19 of the question.

20 **A. That arginine 270 was involved in**
21 **coordinating taurine in TauD.**

22 Q. In Schleinitz here, it states that the
23 arginine is involved in binding 2,4-D. Correct?

24 ATTORNEY GROSSMAN: Objection to the form
25 of the question.

1 **A. The legend states that it's involved in**
2 **binding 2,4-D, yes.**

3 Q. And taurine is a primary substrate of
4 TauD. Correct?

5 **A. Taurine is a substrate of TauD.**

6 Q. 2,4-D is a substrate of TfdA. Correct?

7 **A. 2,4-D is a substrate of TfdA, yes.**

8 Q. 2,4-D is a substrate of RdpA as well.
9 Correct?

10 **A. 2,4-D is used as a substrate by RdpA, yes.**

11 Q. Would you please turn in the Schleinitz
12 2004 article to page 5362. And if you kind of
13 rotate the page, you will see Table 3 titled
14 "Localization and predicted function of ORFs in the
15 genomic region of strain MCI1 containing RdpA and
16 SdpA."

17 **A. I do see Table 3.**

18 Q. ORFs is an acronym for "open reading
19 frames." Is that correct?

20 **A. ORF is an acronym for "open reading**
21 **frames."**

22 Q. And regarding the predicted function of
23 the ORFs, do you see a column of proteins labeled
24 "Function of Closest Match"?

25 **A. Yes, I see that column labeled "Function**

1 of Closest Match."

2 Q. For the prediction, or predicted function,
3 how was the function of these proteins predicted?

4 A. I have not read this paper for a long time
5 in that sort of detail. I don't know what program
6 they used to do their predictions. We can look at
7 the methods and perhaps sort that out, but I'm not
8 sure you want to take the time to deal with that
9 now.

10 Q. Please take the time that you need.

11 A. Okay. So you want to know how they did
12 their predictions.

13 Q. The column does say "Function of Closest
14 Match." I'm wondering what -- how you determine a
15 closest match, if that helps.

16 A. On page 5359, the text states that the
17 programs called BLASTn and BLASTx. So BLASTn and
18 BLASTx programs were used to search for similar
19 sequences in nucleotide and protein sequence
20 databases. And then the sequences were aligned
21 using programs CLUSTAL W or MultAlign.

22 Q. When Figure 3 refers to the closest match,
23 that would be the sequence that has the highest
24 sequence identity to the one that was used in the
25 Blast search?

1 A. I think you meant Table 3. And I presume
2 that is -- that they identify the closest match.
3 But this is not my work. I can't say for certain.

4 Q. And two columns over, you see it provides
5 values for amino -- percentage amino acid identity?

6 A. I do see that column, yes.

7 Q. And in this column, there's a fairly wide
8 range of sequence identities from 35 percent up to
9 99 percent identity. Correct?

10 ATTORNEY GROSSMAN: Objection to the form
11 of the question.

12 A. The column does contain numbers ranging
13 from 35 to 99.

14 Q. Would two enzymes having 99 percent
15 sequence identity be more likely to have the same
16 function than two enzymes having 35 percent
17 sequence identity?

18 A. Well, it depends. The differences could
19 have a very great function -- very great impact on
20 what the function of the enzymes are. For example,
21 one residue change could abolish enzyme activity.

22 So, in general terms, I think one has to
23 look at the specific cases instead of talking in
24 very generalities -- in generalities.

25 Q. And understanding that there can be

1 exceptions, do you have any view on what two
2 enzymes having 99 percent sequence identity would
3 be more likely to have the same function than two
4 enzymes having 35 percent sequence identity?

5 ATTORNEY GROSSMAN: Objection to the form
6 of the question.

7 A. If you have two sequences that are being
8 considered in terms of function, I think you want
9 to test the function and not just look at the
10 sequences. Because sequences that are available in
11 databases in many cases may encode cryptic enzymes.
12 They don't actually have any activity. They are
13 left over from evolutionary events. You have to
14 actually test the activity in order to see if it
15 has the activity of interest.

16 Q. So, in your view, skilled artisans did not
17 make any predictions of enzyme function based on
18 sequence comparisons to other enzymes?

19 ATTORNEY GROSSMAN: Objection to the form
20 of the question.

21 A. A POSA would want to see experimental data
22 to show what the function is, and not just base it
23 on sequence comparisons.

24 Q. As a scientist, you'd prefer to see actual
25 data rather than expectations or predictions. Is

1 that fair?

2 ATTORNEY GROSSMAN: Objection to the form
3 of the question.

4 A. I think one wants to obtain experimental
5 evidence in order to test whether a particular
6 sequence encodes an enzyme's particular function,
7 not just a mere analysis on the sequence itself.
8 You can raise the hypothesis, but you have to
9 obtain results.

10 Q. We've been going -- I'm about to shift
11 gears. Is it a good time for a break or would you
12 like to keep going?

13 A. Now would be a great time for a break,
14 yeah.

15 Q. Okay.

16 THE REPORTER: Off the record at 9:56.

17 (Recess taken from 9:56 a.m.
18 to 10:11 a.m.)

19 BY ATTORNEY DEROO:

20 Q. Welcome back, Dr. Hausinger.

21 A. Thank you.

22 Q. During the break, did you discuss the
23 substance of your testimony with counsel or anyone
24 else?

25 A. No, I did not.

1 Q. Will you please return to your
2 declaration, Exhibit 1054.

3 A. Got it.

4 Q. And would you please turn to paragraph 48.

5 A. Okay. I'm there.

6 Q. A few lines down, you stated that TfdA
7 initiates the degradation of 2,4-D by cleaving it
8 into phenol and a carboxylic acid. Molecular
9 oxygen (O₂), the cosubstrate alpha-KG, and Fe²⁺ are
10 necessary for this reaction to take place.
11 Correct?

12 A. That is what it says.

13 Q. What is the role of alpha-KG in this
14 oxidation reaction?

15 A. The alpha-ketoglutarate is what really
16 drives the reaction. It's providing the electrons
17 as it undergoes this oxidative decarboxylation
18 reaction. And it generates a very active iron
19 species called a ferryl species, an iron IV oxo
20 species, that is able to catalyze the hydroxylation
21 reaction.

22 Q. What is the role of oxygen, O₂, in this
23 oxidation reaction?

24 A. It participates in -- it's necessary in
25 order to form this ferryl species, this iron IV oxo

1 species. And it's providing the two oxygen atoms,
2 one of which ends up in the glyoxylate product.
3 But it's the oxygen that inserts into the 2,4-D.
4 It's the hydroxyl group in brackets in the scheme
5 that's shown there for the 2,4-D reaction. The
6 other oxygen atom of O2 ends up in succinate.

7 Q. And so one oxygen is incorporated into the
8 alpha-KG substrate, and one oxygen is incorporated
9 into the primary substrate?

10 A. That is one way to say it, yes.

11 Q. And in paragraph 48, you stated that these
12 three items -- the oxygen, the alpha-KG, and the
13 Fe²⁺ -- are necessary for this reaction to take
14 place.

15 Would the reaction occur if you just have
16 a primary substrate by itself without the alpha-KG?

17 ATTORNEY GROSSMAN: Objection to the form
18 of the question.

19 A. Without the alpha-ketoglutarate, the
20 reaction does not occur in this enzyme.

21 Q. In an alpha-KG enzyme, do the primary
22 substrate and the alpha-KG substrate need to be in
23 any kind of alignment for the oxygen to be
24 incorporated into both of their structures?

25 ATTORNEY GROSSMAN: Objection to the form

1 of the question.

2 A. The alpha-ketoglutarate has a particular
3 structural requirement for how it coordinates the
4 iron atom. So there's a connection between the
5 alpha-ketoglutarate and iron, and then oxygen binds
6 to the iron and generates this ferryl species,
7 which then reacts with the substrate 2,4-D in this
8 case.

9 In some enzymes in this class of enzymes,
10 it's been suggested that the reaction with what can
11 be referred to as the primary substrate is a
12 secondary step, that it's not necessarily to
13 have -- it's not necessary to have the
14 alpha-ketoglutarate still be in the neighborhood;
15 that one can generate the ferryl species. And then
16 a second reaction using this intermediate is used
17 to do the hydroxylation or whatever chemistry
18 occurs.

19 Q. If the alpha-KG, for example, is bound
20 incorrectly or out of alignment, would that prevent
21 it from coordinating the Fe²⁺ as required to
22 initiate the reaction?

23 A. The alpha-ketoglutarate, I know of one
24 enzyme in this family where the alpha-ketoglutarate
25 is, in fact, bound incorrectly until another

1 **compound binds nearby, and that allows the**
2 **alpha-ketoglutarate to form a chelate structure,**
3 **which is necessary for the reaction to occur.**

4 Q. What enzyme is that?

5 A. **That's called the ethylene-forming enzyme.**

6 Q. Are any other alpha-KG-dependent
7 dioxxygenases that can catalyze the oxidation
8 degradation reaction if alpha-ketoglutarate is
9 bound incorrectly or out of alignment?

10 ATTORNEY GROSSMAN: Objection to the form
11 of the question.

12 Q. To your knowledge.

13 A. **To my knowledge, one requires the correct**
14 **coordination of alpha-ketoglutarate in order for**
15 **these enzymes to function. Even in the case of the**
16 **ethylene-forming enzyme, it does get to that stage**
17 **when the other compound is present.**

18 Q. So when the oxidation reaction occurs, a
19 phenol is produced from the primary substrate.
20 Correct?

21 A. **In the case of 2,4-D, a phenol is the**
22 **product, yes.**

23 Q. Okay. And a phenol is produced from
24 degradation of 2,4-D by AAD-1. Correct?

25 A. **I actually don't like the term "AAD-1."**

1 **But RdpA does produce a phenol as well.**

2 Q. A phenol is also produced from degradation
3 of fop herbicides by RdpA or AAD-1. Correct?

4 ATTORNEY GROSSMAN: Objection to the form
5 of the question.

6 A. **The fop herbicides are basically just an**
7 **extension of the phenoxy propionic acid herbicides,**
8 **and they have the same substructure. And so, yes,**
9 **obviously, they also then have a phenol as a**
10 **product.**

11 Q. Both 2,4-D and fops are primary substrates
12 for AAD-1 or RdpA, whichever term you prefer?

13 A. **I'm not sure that "primary substrate" is**
14 **actually a good term to use. But if one is saying**
15 **what is the substrate for the enzyme other than**
16 **oxygen, other than alpha-ketoglutarate, then, yes,**
17 **that is the other substrate that's necessary.**

18 Q. Can you please turn to Exhibit 1021 in the
19 box.

20 A. **Okay. I have Exhibit 1021. That's the**
21 **'437 patent.**

22 Q. This is the Corteva '437 publication you
23 relied on in your declaration?

24 A. **Correct.**

25 Q. Would you please turn to Figure 1, which

1 is much closer to the back of the document.

2 Just let me know when you're there.

3 **A. I'm there.**

4 Q. On the left side of Figure 1, it shows a
5 substrate, oxygen and alpha-ketoglutarate.

6 Correct?

7 **A. That is correct.**

8 Q. And the degradation of the first substrate
9 as shown at the top of Figure 1, and below it is
10 the degradation of the alpha-KG substrate.

11 Correct?

12 **A. That is what the figure shows, yes.**

13 Q. And whether with AAD-1 or TfdA, is this
14 oxidation reaction known to occur in nature without
15 the presence of an alpha-KG-dependent oxygenase?

16 ATTORNEY GROSSMAN: Objection to the form
17 of the question.

18 **A. So there are other types of oxygenases
19 that do not use alpha-ketoglutarate. There's a
20 large breadth of these different enzymes that act
21 on different substrates. I don't know offhand if
22 in nature there is an oxygenase that happens to act
23 on something like 2,4-D that decomposes it by a
24 different mechanism not using alpha-ketoglutarate.**

25 Q. Let me rephrase the question a little bit.

1 Do alpha-ketoglutarate, oxygen, and a
2 substrate -- for example, 2,4-D -- come together in
3 nature and undergo this reaction without enzyme
4 assistance or catalysis?

5 ATTORNEY GROSSMAN: Same objection.

6 **A. One requires an enzyme in order for these**
7 **components to react and decompose the herbicide.**

8 Q. These enzymes improve the rate of
9 catalysis for this oxidation reaction by
10 essentially infinity compared to what occurs in
11 nature. Is that correct?

12 ATTORNEY GROSSMAN: Objection to the form
13 of the question.

14 **A. They greatly improve the rate of**
15 **degradation, yes. I mean, these components will be**
16 **decomposed without the enzyme if they're in fire,**
17 **for example, in nature.**

18 Q. Let's hope that we don't have to resort to
19 that.

20 Dr. Hausinger, Corteva '437 was one of the
21 original patent applications that led to the three
22 Corteva patents in these proceedings. Correct?

23 **A. That is correct.**

24 Q. It's a priority application to the '555,
25 '283, and '745 patents?

1 **A. I believe that's how things work, yeah.**

2 Q. Would you turn to page -- I'm sorry --
3 paragraph 60 of your declaration.

4 **A. Okay. I'm there.**

5 Q. Here you have a header stating that the
6 challenged claims are not entitled to a priority
7 date earlier than October 7, 2016. Correct?

8 **A. That is what the header says.**

9 Q. Is that the later filing date of the
10 application for the '555 patent?

11 **A. Yes, I believe that is correct.**

12 Q. Your next header is before paragraph 63.
13 You state, "The original specification did not
14 disclose the claimed AAD-1 motifs."

15 Do you see that?

16 **A. That is what I have written in my**
17 **declaration, yes.**

18 Q. I would like to know if that's still your
19 opinion. Does Corteva '437 disclose the AAD-1
20 motifs to a person skilled in the art?

21 ATTORNEY GROSSMAN: Objection to the form
22 of the question.

23 **A. So my recollection is that in the '437**
24 **patent publication, the motif is not listed.**

25 Q. Would a person of ordinary skill

1 understand the AAD-1 motif to be disclosed anywhere
2 in Corteva '437?

3 **A. I don't believe so, no.**

4 Q. In your box of documents -- would you
5 please retrieve Exhibit 1035.

6 **A. I have it. This is Müller, et al., from**
7 **2006.**

8 Q. You were one of the authors of Müller
9 2006. Correct?

10 **A. Correct.**

11 Q. Would you please turn to page 1362 of
12 Müller 2006.

13 **A. Okay.**

14 Q. Here you have a section titled "Residues
15 determining enantiospecificity in RdpA and SdpA."
16 Correct?

17 **A. That is the subsection that's listed as.**

18 Q. RdpA is (R)-specific. Is that right?

19 **A. Correct.**

20 Q. SdpA is (S)-specific?

21 **A. Correct.**

22 Q. About six lines down, you identify
23 particular residues in RdpA that could hinder
24 binding of (S)-mecoprop.

25 Do you see that?

1 **A. I do see that.**

2 Q. The residues listed are leucine 83,
3 glutamine 93, isoleucine 95, isoleucine 106,
4 phenylalanine 171, and arginine 285. Correct?

5 **A. That is what it says.**

6 Q. How does hindering the binding of an
7 (S)-enantiomer like (S)-mecoprop help to explain
8 why RdpA has greater specificity for
9 (R)-enantiomers?

10 **A. Yes. The enzyme is present in the**
11 **solution that has both enantiomers, and some of**
12 **these residues prevent the (S)-enantiomer from**
13 **binding. Then the enzyme is able to function,**
14 **assuming it can bind properly the (R)-enantiomer.**

15 Q. The next paragraph refers to site-directed
16 variants of RdpA and SdpA.

17 Do you see that?

18 **A. Yes, I do.**

19 Q. And it states that they were purified.
20 Why was the purification done?

21 **A. I'm trying to think. It's been a while.**
22 **When one expresses these enzymes in a**
23 **heterologous host like E. coli, the proteins have**
24 **the activity, but it's easier to do the assay when**
25 **you're purifying the proteins and doing the assay**

1 on the purified proteins.

2 Q. Does it also ensure that you can attribute
3 the right activity to the right protein if you
4 purify them beforehand?

5 A. Yes, that is true. But there should not
6 be any activity unless these proteins are there.

7 Q. Why is it easier to see the assay with the
8 purified protein instead of an extract from a
9 heterologous host, I think you said?

10 A. The assay, one -- there are different
11 types of assays. One assay is to look for the
12 production of phenol. And if one has just crude
13 cell extracts, that assay testing for release of
14 enol can be compromised to some extent. So having
15 the purified enzyme, you don't have any interfering
16 substances that can give you false readings.

17 Q. Sorry. Could you explain just a little
18 bit more about what you mean, that the assay would
19 be compromised and give a false reading?

20 ATTORNEY GROSSMAN: Objection to the form
21 of the question.

22 A. I'm thinking here.

23 If we go to the method section, it talks
24 about assays and it talks about using a continuous
25 enzyme assay, and it doesn't give the details. It

1 just refers to another citation in 2004.

2 But this assay, if I recall correctly, is
3 a colorimetric reagent that reacts with phenol to
4 give a color. And so if you have crude cell
5 extracts, you can have a situation where there may
6 be pigments present. You can have other compounds
7 in that solution of metabolites in the cell that
8 can react with reagents, and can give you a meaning
9 that is inconsistent with what the enzyme is
10 showing you. So by purifying the enzyme, you can
11 get authentic rates of reactivity of phenol
12 release.

13 Q. The next paragraph states that among the
14 RdpA variants were several that showed evidence of
15 inhibition by the (S)-enantiomer.

16 Do you see that?

17 A. That is shown here, yes.

18 Q. Does that mean that some of the
19 site-directed mutations in those RdpA variants
20 reduced steric hindrance to (S)-mecoprop binding in
21 RdpA?

22 ATTORNEY GROSSMAN: Objection to the form
23 of the question.

24 A. So it means that substituting one or a
25 small number -- I think two residues -- can change

1 the specificity so that the (S)-enantiomer is not
2 precluded from binding to the active site in the
3 same manner, and it reduces the activity toward the
4 (R)-enantiomer.

5 Q. Will you please turn back to your
6 declaration.

7 A. Okay.

8 Q. If you can go to paragraph 106, please.

9 A. Got it.

10 Q. Here you refer to a 2019 paper indicating
11 that other features are relevant to the
12 (R)-enantioselective activity.

13 Do you see that?

14 A. Yes, I see that.

15 Q. Is that the Chekan 2019 paper I believe
16 you're referring to there?

17 A. Yes. That is Exhibit 1019.

18 Q. Would you please retrieve Exhibit 1019.
19 Let me know when you have it.

20 A. Got it.

21 Q. This is the paper that you're referring to
22 in paragraph 106?

23 A. That is correct.

24 Q. Towards the bottom of your paragraph 106,
25 on page 61, you cite an about-20-residue insertion.

1 Do you see that?

2 **A. I point out that the paper states that**
3 **there is a 20-residue insertion, yes.**

4 Q. And it states that it likely results in
5 the change in substrate specificity. Correct?

6 **A. That is what is claimed in the paper.**

7 Q. And this about-20-residue insertion is an
8 AAD-2. Correct?

9 **A. That is what I wrote in the declaration,**
10 **yes.**

11 Q. Does AAD-2 have greater (R)-specificity or
12 (S)-specificity?

13 **A. AAD-2 is specific for the (S)-enantiomer.**

14 Q. The change in substrate specificity
15 referred to or quoted in your declaration means
16 from (R)- to (S)-stereospecificity, then. Correct?

17 ATTORNEY GROSSMAN: Objection to the form
18 of the question.

19 **A. The authors in the Chekan paper were**
20 **making the claim that this insertion was**
21 **responsible for the change in specificity. And as**
22 **I point out in my declaration, I do not believe**
23 **that is accurate.**

24 Q. If you could turn in the Chekan paper to
25 page 1303.

1 **A. Okay. I'm on 13303.**

2 Q. And the bottom paragraph on the left-hand
3 column. Let me know when you're there.

4 **A. Ready.**

5 Q. It says, "A second distinguishing
6 structural feature of AAD-2 is its shorter
7 substrate-capping loop, in the region including
8 serine 183 through aspartate 193." Correct?

9 **A. That is what it says.**

10 Q. And we can look at a sequence alignment if
11 you wish. But those residues in the region of
12 serine 183 to aspartate 193 are within the span
13 encompassed by the alpha-KG motif. Correct?

14 ATTORNEY GROSSMAN: Objection to the form
15 of the question.

16 **A. So your question is asking whether these**
17 **residues are involved in aligning**
18 **alpha-ketoglutarate. Is that correct?**

19 Q. What I am asking is whether these residues
20 are inside the overall span of residues included in
21 the alpha-ketoglutarate motif.

22 ATTORNEY GROSSMAN: Same objection.

23 **A. And when you say alpha-ketoglutarate**
24 **motif, I'm not sure what you're referring to there.**

25 Q. You recall that earlier today we walked

1 through Elkins 2002, for example, and looked at the
2 alpha-KG family motif residues that appeared in 10
3 different enzyme sequences. Correct?

4 A. Yes. But we did not refer to anything as
5 an alpha-KG motif, unless you mean the five
6 residues -- the histidine, aspartic acid, another
7 histidine, and two arginines, and the three inner
8 serines -- if that's what you mean by the alpha-KG
9 motif, that's a broad -- very broad sort of group
10 of residues that are not necessary for function of
11 an alpha-ketoglutarate dioxygenase that has nothing
12 to do with enantiospecificity.

13 Q. I am just asking about the location of
14 these residues. Are they inside or outside of the
15 motif region?

16 A. It's an unusual way to frame it, because
17 the structure is three dimensions, and here, this
18 is talking about crystal structures. And you have
19 residues that may be at the active site, may be
20 critical for catalysis, and you can't talk in terms
21 of the linear sequence.

22 Q. Let's turn back to your paragraph 106.

23 A. Okay.

24 Q. About halfway down the paragraph, you
25 refer to a solvent exposed tunnel from the Chekan

1 paper. Correct?

2 **A. I was quoting Chekan, and, yes, I quoted a**
3 **solvent exposed tunnel.**

4 Q. And you state that the paper Chekan 2019
5 points to a number of residues: specifically,
6 arginine 104, aspartate 108, aspartate 109, as well
7 as residues Asn90 and cysteine 112?

8 **A. That's what I quoted from them, yes.**

9 Q. I don't think we're looking at the
10 right -- let's go straight to Chekan a minute,
11 please.

12 **A. Okay.**

13 Q. And on page 13302, please.

14 **A. I'm there.**

15 Q. And it says a few lines above Figure 4, "A
16 solvent exposed tunnel comprising arginine 104,
17 aspartate 108, aspartate 109, valine 170,
18 phenylalanine 182, and valine 220." Correct?

19 **A. You are quoting correctly.**

20 Q. In your paragraph 106, in the sentence
21 bridging pages 61 and 62, I believe you indicated
22 that only the first three residues here are located
23 outside the consensus motif. Correct?

24 **A. In my declaration, I say none of the**
25 **residues identified in these statements is**

1 discussed in the original application as specified
2 by the consensus motif. And then I list Arg104,
3 Asp108, Asp109, and ~20-residues in AAD-2 are
4 located outside the consensus motif.

5 And the next sentence, I think, is
6 important. I say, "Thus, the 2019 paper is
7 consistent with what the POA would have understood
8 in 2004: the consensus motif does not describe the
9 residues important to the distinctive
10 (R)-enantiospecificity of RdpA."

11 Q. Dr. Hausinger, does that mean that you do
12 believe the discussion of the solvent exposed
13 tunnel in the Chekan paper?

14 A. There is access to the active site by what
15 you may refer to as the tunnel, and it is solvent
16 exposed. And what's important is that the
17 phenoxypropionic acid, the terminal portion of it,
18 the portion distant from the carboxylic acid, is
19 pointing out into the solvent. And so that one can
20 readily understand why fops are degraded, because
21 that would be where the additional material is, the
22 additional chemical components. They're out in the
23 solvent exposed area.

24 So, again, the same substructure of the
25 two different chemicals are being decomposed at the

1 **active site buried in the protein.**

2 Q. Would you please turn to page, the next
3 page, 13303.

4 A. **Yes.**

5 Q. It discloses that there is a lack of
6 significant interactions in the tunnel -- between
7 residues in the tunnel and the AOPP herbicides.
8 Correct?

9 A. **That is what it says, yes.**

10 Q. Would you please retrieve Exhibit 1055
11 from the box.

12 A. **1055 is my curriculum vitae.**

13 Q. Is Exhibit 1055 your standard CV, or was
14 it specially tailored in any way for this
15 proceeding?

16 A. **There was nothing specially tailored for**
17 **it. It's my standard CV.**

18 Q. You obtained your bachelor's degree in
19 chemistry and biochemistry from University of
20 Wisconsin. Correct?

21 A. **Yes.**

22 Q. You also obtained a PhD in biochemistry
23 from the University of Minnesota in 1982. Correct?

24 A. **Yes.**

25 Q. You did a postdoc at MIT?

1 **A. I did a postdoc at MIT, yes.**

2 Q. During your time at Wisconsin, Minnesota,
3 and MIT, did you ever make a transgenic plant?

4 **A. That was not any part of my experimental**
5 **studies during those times, no.**

6 Q. After your postdoc, you spent your entire
7 career at Michigan State. Correct?

8 **A. Correct.**

9 Q. Your positions have been in the department
10 of biochemistry and molecular biology. Correct?

11 **A. That is one department, yes.**

12 Q. Are there others?

13 **A. Yes. My main appointment is actually in**
14 **what is now called Microbiology, Genetics, and**
15 **Immunology. The name has just changed a couple**
16 **months ago.**

17 Q. Any others?

18 **A. I'm part of various programs, the Cell and**
19 **Molecular Biology program on campus.**

20 Q. And what are those?

21 **A. Pardon?**

22 Q. And what are those programs?

23 **A. These are graduate study programs, so**
24 **providing access to graduate students, and serving**
25 **on committees for -- guidance committees for**

1 **graduate students.**

2 Q. Have you ever performed
3 Agrobacterium-mediated transformation to create a
4 transgenic plant?

5 A. That's not something I've done myself, but
6 I am familiar with the technique. After all,
7 Michigan State University is one of the premier
8 institutions when it comes to plant biology, the
9 methods that have been developed here. We have the
10 Department of Energy Plant Research Laboratory
11 here. I've served on guidance committees for
12 graduate students who have done such studies. We
13 have seminar speakers routinely come through that
14 talk about these sorts of methods. And so they are
15 methods that I am quite familiar with.

16 Q. I grew up outside Detroit, so I'm very
17 familiar with MSU's standing here.

18 I would like to focus just on your
19 personal experience. Your counsel is free to ask
20 you whatever questions they like at the end of the
21 deposition.

22 But just so we're clear, you have not
23 personally performed any Agrobacterium-mediated
24 transformation. Correct?

25 A. I have not done those experiments myself,

1 **no.**

2 Q. Have you ever used particle bombardment
3 transformation to create a transgenic plant?

4 **A. I have not done those experiments myself.**

5 Q. Have you performed whiskers-mediated
6 transformation to create a transgenic plant?

7 **A. I have not done that experiment as well.**

8 Q. Have you used any other method of genetic
9 transformation to create a transgenic plant, that I
10 haven't mentioned yet?

11 **A. I have done a lot of work with bacterial**
12 **transformation but not with plants.**

13 Q. Do you hold yourself out as an expert in
14 the science of weed control?

15 **A. I am very knowledgeable about herbicide**
16 **degradation, the biochemistry of that, and part of**
17 **that in our studies with 2,4-D metabolism. I read**
18 **a lot of literature about transformation of plants**
19 **with the TfdA gene, so I'm quite familiar with**
20 **that. And so I think I have the appropriate**
21 **experience to be able to evaluate and understand**
22 **what's discussed in the patents and the history of**
23 **the various documents associated with it.**

24 Q. TfdA was of interest for the potential to
25 create herbicide resistance in plants. Correct?

1 **A. TfdA was one of the, I think, earlier**
2 **examples of transforming a plant with a bacterial**
3 **enzyme in order to provide resistance to an**
4 **herbicide.**

5 Q. The question has been not about herbicide
6 resistance, but weed control. So I'm asking if you
7 hold yourself out as an expert in the science of
8 weed control.

9 ATTORNEY GROSSMAN: Objection to the form
10 of the question.

11 **A. Only so much as one way to control weeds**
12 **is making use of herbicides and herbicide**
13 **resistance.**

14 Q. Do you have any expertise in
15 glyphosate-resistant weeds?

16 **A. I have no direct experience with that.**

17 Q. Do you have any expertise in the problems
18 that glyphosate-resistant weeds have caused in
19 agriculture?

20 ATTORNEY GROSSMAN: Objection to the form
21 of the question.

22 **A. Glyphosate -- only from reading what I see**
23 **in the press, the issues that have been discussed**
24 **there.**

25 Q. Do you hold yourself out as an expert in

1 modes of herbicide action in plants?

2 **A. I'm quite familiar with some of the**
3 **herbicide modes of action. So, for example, the --**
4 **how TfdA -- I'm sorry -- how 2,4-D affects plants.**
5 **And I know that some of the fops act on acetyl-CoA**
6 **carboxylase as its mode of action.**

7 Q. Do you have any expertise in selecting
8 herbicides for pre-emergent use versus
9 post-emergent use on crops?

10 **A. That sort of detail is not something that**
11 **I have expertise on. I just have a general**
12 **familiarity with the topic.**

13 Q. Do you have any expertise in selecting
14 particular herbicides for use on particular crops?

15 ATTORNEY GROSSMAN: Objection to the form
16 of the question.

17 **A. In general, I have only familiarity with**
18 **various herbicides being useful on various types of**
19 **crops.**

20 Q. You don't hold yourself out as having
21 expertise in selecting particular herbicides for --

22 **A. I think I answered that. I have**
23 **familiarity that is separate from being expert in**
24 **the area.**

25 Q. Do you have any expertise in selecting

1 particular herbicides for use under particular
2 agronomic conditions?

3 ATTORNEY GROSSMAN: Objection to the form
4 of the question.

5 A. It's basically the same answer, that I
6 don't have direct expertise in this area, but I
7 have wide-ranging expert knowledge and familiarity
8 of use of various herbicides under various
9 conditions.

10 Q. In your laboratory, have you conducted any
11 experiments evaluating transgenic plants, for
12 example, for herbicide resistance?

13 A. Our focus in the laboratory has been
14 focused on the biochemistry of the enzymes that
15 were degrading herbicides. We did not directly
16 work with transgenic plants in our lab.

17 Q. Would you please pull up the '555 patent,
18 which should be Exhibit 1001 in your box.

19 A. Got it.

20 Q. Please turn towards the back. I'd like to
21 look at Claim 6, please.

22 A. I see Claim 6.

23 Q. Do you see where Claim 6 says "wherein
24 expression of said polynucleotide renders said
25 plant tolerant to an aryloxyalkanoate herbicide"?

1 **A. Claim 6 does say "a transgenic plant**
2 **comprising a plurality of the plant cells of Claim**
3 **1, wherein expression of said polynucleotide**
4 **renders said plant tolerant to an aryloxyalkanoate**
5 **herbicide."**

6 Q. Have you ever conducted research to
7 determine what expression levels are necessary to
8 render a transgenic plant tolerant to any
9 herbicide?

10 **A. I have not directly done those sorts of**
11 **experiments, but I've heard a lot of seminars.**
12 **I've heard a lot of students talk about their work.**
13 **When I was a panel manager at USDA, I heard -- I**
14 **read about grant proposals, and so I'm familiar**
15 **with analysis such as that.**

16 Q. Analysis of obtaining sufficient
17 expression to produce herbicide tolerance in
18 plants?

19 ATTORNEY GROSSMAN: Objection to the form
20 of the question.

21 **A. More generally looking at what expression**
22 **levels are present under different conditions, not**
23 **necessarily just restricted to herbicide tolerance.**

24 Q. How can different conditions affect
25 expression levels?

1 ATTORNEY GROSSMAN: Same objection.

2 A. The expression of genes in plants is
3 dependent on drought status, temperature, light. A
4 lot of different environmental conditions will
5 affect expression.

6 Q. Can those conditions both increase or
7 decrease expression levels?

8 A. Different environmental conditions will
9 lead to increases, and other environmental
10 conditions will lead to decreases in transcription.

11 Q. And under certain conditions, would
12 expression levels -- or would -- sorry. I'll start
13 again.

14 Under different conditions, can that
15 affect whether active enzyme is expressed in a
16 plant?

17 A. Whether an enzyme is active in a plant
18 when the enzyme is encoded by transgenic means will
19 depend on the transcription level, but it will also
20 depend on other factors such as proper folding of
21 the protein, insertion of appropriate cofactors,
22 and so forth.

23 Q. Can the choice of which transgene to use
24 in a plant affect expression levels?

25 A. Can the choice of which gene? Yes, of

1 **course.**

2 Q. Can the choice of which promoters to use
3 with a gene affect its expression levels?

4 **A. Yes, the promoters will affect**
5 **transcription and transgenes.**

6 Q. If we were thinking back to 2004 or 2005
7 before the applications leading to the patents in
8 these proceedings were published, if one chose the
9 wrong promoter to use with a gene, could that
10 affect whether a transgenic plant would express
11 active protein?

12 **A. There was already a large literature on**
13 **use of promoters for optimal expression in plants**
14 **at that time, back in 2004 and earlier.**

15 Q. So if one chose the wrong promoter to use
16 with a gene, would that affect whether the
17 transgenic plant would express active protein?

18 **A. That would reduce the amount of transgenic**
19 **protein.**

20 Q. Do you have any experience using the
21 pMCJC1007 promoter with transgenic plants?

22 **A. No.**

23 Q. Do you have any experience using the
24 pMLJC1005 promoter with transgenic plants?

25 **A. These promoters, I have likely encountered**

1 in my readings, but I don't recall any specific
2 time or any specific use. And I have not used them
3 myself.

4 Q. Could you please pull Exhibit 1043 out of
5 the box.

6 ATTORNEY GROSSMAN: I was actually going
7 to say, Pier, we've been going for about an
8 hour. Can we maybe --

9 ATTORNEY DER00: Yeah, we can take a
10 break.

11 THE WITNESS: Okay.

12 ATTORNEY DER00: Another 10 or so minutes?

13 ATTORNEY GROSSMAN: Sounds good.

14 ATTORNEY DER00: Okay.

15 THE REPORTER: Off the record at
16 11:07 a.m.

17 (Recess taken from 11:07 a.m.
18 to 11:20 a.m.)

19 THE REPORTER: Back on the record at
20 11:20 a.m.

21 BY ATTORNEY DER00:

22 Q. Welcome back, Dr. Hausinger.
23 Did you discuss the substance of your
24 testimony with counsel during the break?

25 A. No.

1 Q. Could you please retrieve Exhibit 2001
2 from the box, please.

3 A. Okay. 2001. Fukumori and Hausinger from
4 1993. Brings back some memories.

5 Q. And you are an author on this paper.
6 Correct?

7 A. That is correct.

8 Q. The enzyme referenced in the title is
9 TfdA. Correct?

10 A. Yes, it is TfdA.

11 Q. And halfway down the abstract, it states
12 that ferrous ion is absolutely required for
13 activity.

14 Do you see that?

15 A. I do see that, yes.

16 Q. Do you know if ferrous ion is similarly
17 required for RdpA activity?

18 A. Ferrous ion is required for RdpA activity,
19 yes.

20 Q. And a couple sentences later, your article
21 states that the enzyme -- it's TfdA -- exhibits
22 maximum activity at pH 6.5 to 7. However, it is
23 stable over a pH range of 6.5 to 11. Correct?

24 A. That's what we said, yes.

25 Q. Does RdpA's activity -- I'm sorry --

1 RdpA's stability also vary by pH?

2 **A. I don't recall results of such**
3 **experiments. I'm sure that there is an effective**
4 **pH on activity of RdpA.**

5 Q. Do you know roughly what pH is the optimum
6 for RdpA activity?

7 **A. Again, I don't recall the specifics of it.**
8 **I would assume that it is likely to be most active**
9 **around neutral pH.**

10 Q. Okay. Before the break, you retrieved the
11 Exhibit 1043. Would you pull that up, please.

12 Is this the Streber patent that you relied
13 upon in your declaration?

14 **A. I'm looking at -- I have a message from**
15 **Windows Security. I don't know what this is all**
16 **about.**

17 **Yes, this is the exhibit that I used when**
18 **preparing the declaration.**

19 Q. On the first page, there's an abstract in
20 the lower right?

21 **A. Correct.**

22 Q. It refers to a TfdA chain.

23 Do you see that?

24 **A. Yes, I do.**

25 Q. To your knowledge, were any

1 TfdA-transformed crops ever commercialized by
2 2004-2005?

3 A. I'm sorry. I don't remember the timing.
4 I think -- yeah, I just don't remember the timing
5 of that.

6 Q. Do you know if any TfdA-transformed crops
7 were ever launched commercially?

8 A. I do not recall at this point.

9 Q. To your knowledge, were there any other
10 crops transformed to express any other
11 alpha-KG-dependent dioxygenase that had been
12 commercialized by 2004-2005?

13 A. I only know that there were multiple crops
14 that had been transformed to express TfdA. I know
15 that other crops have been transformed to express a
16 large range of different genes, but I don't
17 remember about any that were specifically for
18 herbicide tolerance.

19 Q. Among the genes that have been used in
20 transgenic plants, the only alpha-KG-dependent
21 dioxygenase having been used, to your knowledge,
22 was TfdA?

23 ATTORNEY GROSSMAN: Objection to the form
24 of the question.

25 A. That is the only -- TfdA is the only one

1 **that I can recall.**

2 Q. Can you identify any particular weeds ever
3 controlled using (R)-mecoprop in 2004-2005?

4 A. **In general, it was broadleaf weeds that**
5 **were controlled.**

6 Q. As of 2004-2005, do you know what crops
7 (R)-mecoprop was used with?

8 A. **So the mecoprop was used with monocots,**
9 **but I don't recall what range of different plants,**
10 **different crops were used.**

11 Q. Monocots include crops like wheat, corn,
12 and barley?

13 A. **That is correct.**

14 Q. Can you identify any particular weeds that
15 were controlled using (R)-dichlorprop in 2004-2005?

16 A. **To my recollection, it was the same group**
17 **of plants as the mecoprop.**

18 Q. Broadleaf weeds?

19 A. **Broadleaf, yeah.**

20 Q. As of 2004-2005, what crops was
21 (R)-dichlorprop used with?

22 A. **Any -- and I think according to my**
23 **recollection, the same as the mecoprop. The**
24 **monocots, various types.**

25 Q. Was it all monocots or some monocots? Do

1 you know any specifically?

2 **A. My recollection is faulty there. I don't**
3 **recall.**

4 Q. Can we turn back to your declaration,
5 please.

6 **A. Okay.**

7 Q. Let's go to paragraph 27.

8 **A. I'm there.**

9 Q. Here you produce independent Claim 1 of
10 the '555 patent. Correct?

11 **A. That is correct. That's what the**
12 **declaration shows.**

13 Q. Do you hold yourself out as an expert in
14 the legal interpretation of patent claims?

15 **A. No, I do not.**

16 Q. Do you provide any opinion on the proper
17 legal interpretation of the '555 patent claims?

18 **A. I just accept that what is written is what**
19 **is meant, so a common understanding is my**
20 **understanding.**

21 Q. What is the activity of AAD-1 proteins
22 that Claim 1 requires?

23 **A. Claim 1 states that an AAD-1 protein**
24 **exhibits aryloxyalkanoate dioxygenase activity**
25 **which is able to degrade a phenoxy auxin herbicide**

1 **and an aryloxyphenoxypropionate herbicide.**

2 Q. Is any other type of activity required?

3 **A. Other activity is not required.**

4 Q. Do you hold yourself out as an expert with
5 respect to the written description requirement?

6 ATTORNEY GROSSMAN: Objection to the form
7 of the question.

8 **A. I have common understanding when I read**
9 **the written descriptions.**

10 Q. Would you turn to paragraph 31 of your
11 declaration, please.

12 **A. Okay.**

13 Q. You stated in the last sentence "... a
14 sufficient written description requires the
15 disclosure that either a representative number of
16 species falling within the scope of the claimed
17 genus, or structural features that the members of
18 the genus have in common, so that a POSA can
19 'visualize or recognize' the members of the genus."
20 Correct?

21 **A. That's what I state in the declaration.**

22 Q. Is that your own personal understanding,
23 or is that a standard that was provided to you by
24 counsel?

25 **A. That was after discussion with counsel.**

1 Q. Let's please turn to paragraph 109. I'm
2 looking at the bottom of page 65, at the paragraph.

3 A. Okay.

4 Q. At the bottom, you have a sentence that
5 says, "These findings provide yet another reason
6 that the POSA would not have believed that the
7 length of the 131-amino acid region in RdpA was
8 determinative of its enantioselectivity."

9 Did I read that correctly?

10 A. That is what it states.

11 Q. Is it your understanding that written
12 description requires disclosure of residues
13 determinative of enantioselectivity?

14 A. In a particular case like this where one
15 is focused on an enzyme that has the capability of
16 degrading one specific enantiomer, then one has to
17 be able to understand how it's able to decompose
18 that enantiomer that was not identified in the
19 specifications here. They list the motif that we
20 discussed at length earlier, but that motif was not
21 really -- was not at all involved in identifying
22 whether the enzyme was (R)-specific or
23 (S)-specific.

24 Q. So it's your understanding in this case
25 that there has to be an identification of residues

1 that determine enantiospecificity to satisfy the
2 written description requirement?

3 **A. My view is that a POSA would require that**
4 **the specifications include sufficient information**
5 **that you can identify sequences that retain the**
6 **function specifically for the (R)-enantiomer. So**
7 **it could be something like reading a homology model**
8 **and docking in a substrate so that you can**
9 **visualize what residues are likely involved in**
10 **that -- which was not done -- or it could be**
11 **obtaining a crystal structure of the enzyme with**
12 **the substrate gone -- which was not done in 2004;**
13 **it was done 15 years later -- or another type of**
14 **situation where you clearly identify what is the**
15 **basis of the enantiospecificity.**

16 **Q. Is it enough for written description, in**
17 **your view, if there is disclosure of residues that**
18 **only have a correlation rather than are**
19 **determinative of the enzymatic activity required by**
20 **the claims?**

21 ATTORNEY GROSSMAN: Objection to the form
22 of the question.

23 **A. I think I just answered that, that I think**
24 **one needs to identify which residues are critical.**
25 **Just the sequence alone is insufficient.**

1 An example is in the Saari 1999 paper that
2 is in this paragraph 109, where two sequences that
3 are 86 percent identical have opposite
4 enantiospecificities. The TfdA and another one,
5 another protein, RASC, are specific for the
6 (S)-enantiomer, but the corresponding sequence from
7 alcaligenes denitrificans is specific for the
8 (R)-enantiomer. And yet if you look at the
9 sequence, one incorrectly assumed that they would
10 have the same function and they do not.

11 Q. Would you please turn to paragraph 108.

12 A. Okay.

13 Q. At the bottom of the page, you state that
14 the POSA would not have understood the variables in
15 the alpha-KG consensus motif, or any motif derived
16 from it, to be responsible for giving RdpA its
17 distinctive (R)-enantioselective activity.

18 Did I read that correctly?

19 A. That is correct, yes.

20 Q. Here you use the words "responsible for"
21 instead of "determinative."

22 Is there a difference, in your view?

23 ATTORNEY GROSSMAN: Objection to the form
24 of the question.

25 A. I think you can use either construction.

1 **But these -- the alpha-KG motif is not dictating**
2 **which substrate is utilized by the enzyme.**

3 Q. Let me try to share a file a minute.

4 I don't have a paper copy of this one,
5 Dr. Hausinger, but I've moved it to the marked
6 exhibits folder if you have that tab open. And we
7 can pause if anyone is having difficulty retrieving
8 this.

9 A. **And which exhibit is it that you're --**

10 Q. 2043.

11 A. **Okay.**

12 ATTORNEY GROSSMAN: Can you just give me
13 one second here? I'm still trying to get this
14 up.

15 ATTORNEY DEROO: Yeah. Yeah, of course.

16 ATTORNEY GROSSMAN: Okay. Yeah, I got it.
17 Sorry.

18 Q. Dr. Hausinger, this is an article listing
19 you as an author, titled "Thiol reactivity of the
20 nitrogenase Fe-protein from Azotobacter
21 vinelandii."

22 Did I pronounce that correctly?

23 A. **Close enough.**

24 ATTORNEY GROSSMAN: Sorry. I'm just going
25 to object to this exhibit on authenticity,

1 hearsay, and relevance grounds.

2 Q. And your article here, Exhibit 2043, was
3 published in the Journal of Biological Chemistry in
4 1983. Correct?

5 **A. That is correct.**

6 Q. Below the abstract, it states that
7 biological reduction of dinitrogen to ammonia is
8 catalyzed by a complex of two enzymes, the
9 MoFe-protein and the Fe-protein. Correct?

10 **A. Correct.**

11 Q. Is the first one a molybdenum-iron
12 protein?

13 **A. Yes, it is a molybdenum-iron protein.**

14 Q. And the second is an iron protein.
15 Correct?

16 **A. Yes. It has a 4 iron, 4 sulfur cluster.**

17 Q. In the next paragraph, you see that it
18 indicates that the amino acid sequence of the iron
19 protein, the Fe-protein from five different species
20 has been determined?

21 **A. That is what it states.**

22 Q. And on the next page -- it's page 13487 of
23 Exhibit 2043 -- do you see the Table 1 at the top?

24 **A. I see the Table 1.**

25 Q. And it show -- or it lists the source, the

1 five sources of the Fe-proteins from different
2 species?

3 **A. That is what it shows, yes.**

4 Q. The total number of amino acid residues in
5 these proteins range from 273 to 299. Is that
6 correct?

7 **A. That is what the table shows.**

8 Q. You can turn back to the first page where
9 we were. It states that these sequences are about
10 60 percent identical.

11 Do you see that?

12 **A. I do see that.**

13 Q. Was it surprising to you to see that
14 proteins having 60 percent identity had the same
15 function?

16 ATTORNEY GROSSMAN: Objection to the form
17 of the question.

18 **A. I was not surprised that these enzymes had
19 this level of sequence identity.**

20 ATTORNEY DER00: Why don't we take a short
21 break. I'll see if I can wrap things up and
22 maybe let everyone have a longer lunch.

23 ATTORNEY GROSSMAN: How long do you want?

24 ATTORNEY DER00: Can I just have
25 10 minutes, please?

1 ATTORNEY GROSSMAN: Sure.

2 THE REPORTER: Off the record at 11:44.

3 (Recess taken from 11:44 a.m.
4 to 11:53 a.m.)

5 THE REPORTER: On the record at 11:53 a.m.

6 BY ATTORNEY DEROO:

7 Q. Dr. Hausinger, did you discuss the
8 substance of your testimony with counsel during the
9 break?

10 A. No.

11 Q. Okay. I don't have any further questions
12 for you at this time.

13 ATTORNEY GROSSMAN: Okay. Why don't we go
14 off the record and see if I have any redirect.

15 In the meantime, Deanna, I'll reserve
16 signature.

17 Okay. We'll jump off for a short break.

18 THE REPORTER: Off the record at
19 11:54 a.m.

20 (Recess taken from 11:54 a.m.
21 to 12:03 p.m.)

22 THE REPORTER: Back on the record at
23 12:03 p.m.

24 ATTORNEY GROSSMAN: Thank you, Dr.
25 Hausinger. I don't have any questions.

1 THE WITNESS: Am I excused? Do I leave
2 now?

3 ATTORNEY DER00: You are free to go.

4 ATTORNEY GROSSMAN: You're free to go,
5 yes.

6 Thank you, Dr. Hausinger.

7 ATTORNEY DER00: Deanna, can you confirm
8 what order we placed on the transcript? It's
9 probably fairly expedited.

10 THE REPORTER: I believe I have 2-day, so
11 you'd get it Monday.

12 ATTORNEY DER00: Okay. That sounds
13 perfect.

14 Can you send us a rough draft today?

15 THE REPORTER: Yeah.

16 ATTORNEY DER00: Okay.

17 ATTORNEY GROSSMAN: Yeah. If we could get
18 a rough, too.

19 THE REPORTER: Sure.

20 ATTORNEY GROSSMAN: Thank you.

21 ATTORNEY DER00: Okay.

22 Thanks, everyone.

23 (Witness excused and deposition concluded
24 at 12:04 p.m.)
25

1 WITNESS CERTIFICATION and ERRATA SHEET

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19 Date: _____

20 ROBERT P. HAUSINGER, PhD

21 Subscribed and sworn to before me this _____

22 day of _____, 20____.

24 _____
25 Notary Public/Justice of the Peace

CERTIFICATE OF REPORTER

I, Deanna J. Dean, Registered Diplomat Reporter, Certified Realtime Reporter, and New Hampshire licensed court reporter #87, the officer before whom the proceedings were taken, do hereby certify that the foregoing transcript is a true and accurate record of these proceedings; that said proceedings were taken in Stenotype note by me on Thursday, April 4, 2024, commencing at 9:01 a.m. and ending at 12:04 p.m.

I further certify that present on behalf of Party Bayer CropScience LP were Dov P. Grossman of Williams & Connolly LLP and on behalf of Party Corteva Agriscience LLC Pier D. DeRoo of Finnegan, Henderson, Farabow, Garrett & Dunner LLP.

I further certify that I am not related to, nor associated with any of the parties or their attorneys, nor do I have any disqualifying interest, personal or financial, in the actions within.

Dated this 7th day of April, 2024, at Hillsborough County in the State of New Hampshire.

Deanna J. Dean



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