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 IPR2023-01036

Patent No. 10,947,555

Case IPR2023-01037

Patent No. 11,149,283

Case IPR2023-01038

Patent No. 11,299,745

** CONFIDENTIAL **

REMOTE VIDEOTAPED DEPOSITION OF

ROBERT P. HAUSINGER, PH.D.

August 1, 2024

8:01 a.m. EST

Reported by:
Janice M. Kocek, CSR, CLR
Job No. 55812

The videotaped deposition of ROBERT P. HAUSINGER, PH.D., via Zoom videoconferencing, called by the Patent Owner for examination, reported stenographically by Janice M. Kocek, License No. 084-002871, Certified Shorthand Reporter, Certified LiveNote Reporter, and Notary Public for the State of Illinois, commencing at the hour of 8:01 a.m. EST, on the 1st day of August, 2024.

* * *

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Exhibit 1021 WO 2005/1074347 A2
Exhibit 1025 Critical Review In...Biochemistry and Molecular Biology
Exhibit 1027 Site-directed Mutagenesis of 2,4-Dichlorophenoxyacetic Acid/a-Ketoglutarate Dioxygenase - Hogan, et al.
Exhibit 1035 Structural basis for the enantiospecificities of R- and S-specific phenoxypropionate/ a-ketoglutarate dioxygenases - Müller

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Exhibit 1042	Localization and Characterization of Two Novel Genes Encoding Stereospecific Dioxygenases Catalyzing 2(2,4-Dichlorophenoxy)propionate Cleavage in Delftia acidovorans MC1 - Schleinitz
Exhibit 1043	United States Patent 6,143,401
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Exhibit 1078	Site-directed Mutagenesis of Putative Substrate-binding Residues Reveals a Mechanism Controlling the Different Stereospecificities of Two Tropinone Reductases - Nakajima
Exhibit 1079	Structural and functional comparison of 15S- and 15R-specific cyclooxygenases from the coral Plexaura homomalla - Valmsen

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Exhibit 1080	On the Relationships of Substrate Orientation, Hydrogen Abstraction, and Product Stereochemistry in Single and Double Dioxygenations by Soybean Lipoxygenase-1 and Its Ala542Gly Mutant - Coffa
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Exhibit 2004	Sequencing COR-AAD-1-00585579-00585584
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DEPOSITION EXHIBITS REFERENCED

Exhibit 2065 Declaration of Robert P. Hausinger In Support of Plaintiff Bayer's Motion for Partial Summary Judgment of Infringement Infringement U.S. Patent No. 6,153,401 by Dow AgroSciences LLC

(Witness remotely sworn.)

ROBERT P. HAUSINGER, PH.D.,
called as a witness herein, having been first duly sworn, was examined and testified as follows:

EXAMINATION

BY MR. DeROO:

Q. Good morning, Dr. Hausinger. I'm Pier DeRoo with the law firm Finnegan representing Corteva. And I'm joined by Mark Lampert, who is also with Finnegan. 08:01

Do you understand that you are testifying today in IPR proceedings before the U.S. Patent and Trademark Office involving three Corteva patents? 08:01

A. Yes.

Q. And those are the '555, '283, and '745 patents?

A. That sounds right, yes.

Q. Today's deposition is being held remotely. So the way it will work is that when we have documents to look at, we can call them up electronically on the screen. But if you prefer to look at hard copy documents, we sent a box to your address. 08:01 08:02

Did you receive it?
A. I did.
Q. Have you opened the box or is it still sealed?
A. It's still sealed. 08:02
Q. Do you understand that your testimony today will be transcribed and made public in these proceedings?
A. Yes.
Q. And do you understand that your 08:02
answers today are under oath?
A. Yes.
Q. Is there any reason you cannot provide full and truthful testimony today?
A. No. 08:02
Q. Would you please go ahead and open the box that we sent you.
A. Okay.
Q. Would you please retrieve Exhibit 1070. 08:03
A. Okay. It's my declaration.
Q. And this is the second declaration you've submitted in these IPRs, correct?
A. Yes.
Q. And you reviewed your declaration 08:03

before you signed it?
A. I did, yes.
Q. Would you turn to page 57, please.
A. Okay.
Q. And this is your signature on page 57, correct? 08:03
A. (No audible response.)
Q. And this is your signature on page 57, correct?
A. I said correct. 08:04
Q. When you signed your declaration you believed it was complete and accurate?
A. Yes.
Q. And sitting here today, is there anything in your declaration that you believe requires correction? 08:04
A. No.
Q. About how many hours did you spend in preparing this declaration?
A. Roughly 20 to 25 hours. 08:04
Q. What did you do to prepare for your deposition today?
A. For preparing for today I had -- I had I think five virtual meetings, practice sessions, with counsel. I reread my 08:04

declaration. I read the declarations from Dr. Bollinger. And then I looked at a few of their other documents that were exhibits.

MR. GROSSMAN: Apologize. I'm just going to remind Dr. Hausinger not to get 08:05 into any specific documents that you reviewed with counsel.

THE WITNESS: Okay.

BY MR. DeROO:

Q. And how long were these virtual 08:05 sessions that you held with counsel?

A. One to one and a half hours.

Q. In reviewing documents in preparation for your deposition today, did you review any documents that were not listed in your table of 08:05 exhibits at Appendix 1 to this declaration?

A. No.

Q. Did you meet with anyone other than Mr. Grossman, Mr. Picozzi, or Ms. Ryen in preparing for your deposition? 08:06

A. No.

Q. Please turn to paragraph 61 in your second declaration here.

A. I'm there.

Q. In the middle of this paragraph you 08:06

1 cite the Valmsen, Ijima, Baerga-Ortiz, and Coffa
2 references, correct?
3 **A. That is correct.**
4 Q. And those are Exhibits 1079 through
5 1082? 08:06
6 **A. Yes.**
7 Q. In the previous paragraph of your
8 declaration at the top of the page you also cite
9 Nakajima 1999, which is Exhibit 1078, correct?
10 **A. Correct.** 08:07
11 Q. Were Exhibits 1078 through 1082
12 provided to you by counsel or did you search for
13 and select them yourself?
14 **A. My recollection is that 1078 was**
15 **provided by counsel. The other four I found** 08:07
16 **myself.**
17 Q. In your box of documents please
18 retrieve Exhibit 1079.
19 **A. Okay. The Valmsen, yes.**
20 Q. Yes. This is the Valmsen publication 08:08
21 you relied on in your declaration concerning COX
22 enzymes, correct?
23 **A. That is correct, yes.**
24 MR. GROSSMAN: Pier, are you
25 providing a copy virtually or -- just so I 08:08

1 know for purposes of --
2 MR. DeROO: If it's in the record, do
3 you have --
4 MR. GROSSMAN: I can. I do have
5 them. I just wanted to make sure that I 08:08
6 had time to pull them up.
7 MR. DeROO: I'm happy to slow down.
8 I think it will be easier if you have
9 electronic copies.
10 MR. GROSSMAN: No. That's fine. I 08:08
11 just needed to make sure that I had them
12 pulled up.
13 MR. DeROO: Fair enough. I won't be
14 offended if you ask me to slow down.
15 MR. GROSSMAN: I've got it. 08:08
16 BY MR. DeROO:
17 Q. Dr. Hausinger, these COX enzymes
18 convert arachidonic acid to either (S)- or
19 (R)-prostaglandins; is that right?
20 **A. Yes.** 08:09
21 Q. If we could turn in the discussion
22 session to Exhibit 1079 to page 3537, please.
23 Just let me know when you're there.
24 **A. I'm there.**
25 Q. In the bottom left paragraph, a few 08:09

1 lines down, it says that the wild-type R- and
2 S-variant COX enzymes formed almost pure 15R-
3 and 15S-PGs.
4 Do you see that?
5 **A. Yes, I do.** 08:09
6 Q. And PGs are prostaglandins?
7 **A. Correct.**
8 Q. The next sentence tells us that the
9 mutant 15R-COX enzyme formed 70 percent
10 (S)-prostaglandins, correct? 08:10
11 **A. That is correct, yes. So a single**
12 **substitution can alter the (audio distortion).**
13 **(Stenographer clarification.)**
14 THE WITNESS: A single substitution
15 can alter the stereospecificity of the 08:10
16 reaction.
17 BY MR. DeROO:
18 Q. And the mutant 15S-COX enzyme formed
19 35 percent (R)-prostaglandins?
20 **A. Correct.** 08:10
21 Q. If we turn to the previous page,
22 3536, are those results shown in Table 2 in the
23 left-hand column?
24 **A. Yes, that's what's shown.**
25 Q. Looking at the bottom two rows of 08:11

1 Valmsen's Table 2, the wild-type R-COX enzyme
2 formed 98 percent (R)-prostaglandins and the
3 mutant formed 30 percent (R)-prostaglandins.
4 Do you see that?
5 **A. Yes.** 08:11
6 Q. Does the wild-type R-COX enzyme have
7 (R)-enantioselectivity?
8 **A. The wild-type enzyme is specific in**
9 **creating the (R) epimer, the (R) product.**
10 Q. Does that mean it's (R) selective? 08:11
11 **A. That would mean that it is specific**
12 **for creating the (R)-enantiomer.**
13 Q. Is it selective for creating the
14 (R)-enantiomer?
15 MR. GROSSMAN: Objection to the form 08:12
16 of the question.
17 THE WITNESS: I'm not sure exactly
18 what you're saying. It's -- it is creating
19 specifically selectively the (R)-enantiomer.
20 BY MR. DeROO: 08:12
21 Q. Is there a difference in your mind
22 between an enantioselectivity and
23 enantiospecificity?
24 **A. So perhaps you're getting at -- well,**
25 **the point of this article is that there are** 08:12

1 **residues that are very specific for the**
2 **chemistry going on related to**
3 **enantiospecificity.**
4 **And so the -- the enzyme is using the**
5 **-- the two enzymes are using the same substrate** 08:12
6 **in creating different products. It's a little**
7 **bit nuanced difference from a -- two enzymes**
8 **using different starting substrates. But it's**
9 **still focused on very subtle changes. Single**
10 **substitutions can make a huge difference in** 08:13
11 **terms of the reactivity of the enzyme.**
12 Q. I appreciate that. But my question
13 is a little bit simpler.
14 When I'm asking if a wild-type R-COX
15 enzyme has (R)-enantioselectivity, you answer in 08:13
16 terms of enantiospecificity.
17 **A. Right.**
18 Q. So is there a difference in your mind
19 between enantioselectivity and
20 enantiospecificity here? 08:13
21 MR. GROSSMAN: Objection to the form
22 of the question.
23 THE WITNESS: So as I thought I was
24 trying to say, the specificity is where you
25 have two enantiomers and so the enzyme 08:13

would be specific for one of the two enantiomers. Here you're creating the two different products, the two enantiomers.

BY MR. DeROO:

Q. Does the mutant R-COX enzyme in Table 2 have S-specificity? 08:14

A. The isoleucine 349 valine variant enzyme -- I prefer not to call it a mutant enzyme because it mutates DNA, not protein -- is able to create both the 15S and the 15R epimers but it favors the 15S epimer. 08:14

Q. Does the variant R-COX enzyme have R-specificity?

A. The variant 15 -- say it again. 15S or 15R? 08:15

Q. 15S -- I'm sorry, the variant FT -- why don't I start again.

A. Okay.

Q. Does the variant R-COX enzyme have R-specificity? 08:15

A. So as I just said, the variant R-COX enzyme creates both the 15S and 15R epimers but it preferentially creates the 15S epimer.

Q. Is that a yes for R-specificity?

Is it a maybe because it creates 08:15

both?

A. Well, it's the --

MR. GROSSMAN: Objection to the form of the question.

THE WITNESS: It's dealing with selectivity. It's dealing with preference for making 15S epimer but it is creating both. But again, a single substitution can alter the reaction dealing with stereochemistry. 08:16

BY MR. DeROO:

Q. Does Valmsen report any variants of S-COX enzymes that produce exclusively (R)-prostaglandins and no (S)-prostaglandins?

A. No, they do not. 08:16

Q. Does Valmsen report any variants of R-COX enzymes that produce only (S)-prostaglandins and no (R)-prostaglandins?

A. No, they do not. But again, I cited this -- I thought this was a pertinent publication because a single substitution can create dramatic changes in the stereochemistry of the reaction. 08:17

Q. So to be clear, Valmsen does not report variants of R-COX enzymes that produce 08:17

exclusively (S)-prostaglandins, correct?
MR. GROSSMAN: Objection to the form of the question.
THE WITNESS: The publication here only focuses on two variants and they do 08:17
not completely swap the reactivity to the other enantiomer. It's somewhat of a mixture.
(Stenographer clarification.)
THE WITNESS: It's somewhat of a 08:17
mixture of products.
BY MR. DeROO:
Q. Thank you, Doctor.
In your box would you please retrieve Exhibit 1078. 08:17
A. Got it. Nakajima 99.
Q. And Dr. Hausinger, the enzymes in Nakajima 1999, Exhibit 1078, are tropinone reductases, correct?
A. That is correct. I will point out 08:18
that reductases by their nature are, in fact, reversible enzymes. And so they do the reduction but then they can also catalyze the reverse reaction, the oxidation reaction.
Q. And the two tropinone reductases 08:18

1 referred to in Nakajima here, they convert the
2 substrate tropinone into alcohol products that
3 have either R- or S-stereospecificity, correct?
4 **A. That is correct. But as I was just**
5 **saying, they do the reverse reaction where they** 08:19
6 **can take the (R)-enantiomer in one case and form**
7 **the keto group or they can take the**
8 **(S)-enantiomer, the alcohol, and form a keto**
9 **group. So it's a little bit closer to the type**
10 **of chemistry seen with RdpA, for example.** 08:19
11 Q. In your box would you please retrieve
12 Exhibit 1080.
13 **A. Okay. That's the Coffa, et al.**
14 Q. Yes. And the enzymes in Coffa are
15 LOX enzymes, correct? 08:20
16 **A. Lipoxygenases, yes.**
17 Q. The substrate these enzymes act on is
18 linoleic acid; is that correct?
19 **A. Yes.**
20 Q. And the LOX enzymes convert linoleic 08:20
21 acid to (S) or (R) hydroperoxide products,
22 correct?
23 **A. Yes.**
24 Q. Would you please retrieve Exhibit
25 1081. 08:20

1 **A. Okay.**
2 Q. This is the Ijima paper you rely on
3 in your declaration?
4 **A. Yes.**
5 Q. The enzymes in Ijima are AMDases, 08:21
6 A-M-D, capitalized?
7 **A. Right. So it's arylmalonate**
8 **decarboxylase.**
9 Q. And looking at the one-sentence
10 abstract, the substrate these enzymes act on is 08:21
11 arylmethylmalonate?
12 **A. That is the substrate that they**
13 **studied.**
14 Q. And the AMDases convert that
15 substrate to produce optically active products, 08:21
16 correct?
17 **A. Yes, that is correct.**
18 Q. And optically active means that those
19 products are enantiomers, (S) or (R), correct?
20 **A. Right. So they probably use circular** 08:22
21 **dichroism, for example, to monitor the optical**
22 **activity.**
23 Q. Would you please retrieve Exhibit 1082
24 from your box.
25 **A. Baerga-Ortiz.** 08:22

Q. Yes. The enzymes in Baerga-Ortiz, Exhibit 1082, were ketoreductase domains; is that correct?

A. That is correct.

Q. These are domains from a multi-enzyme that has multiple domains? 08:23

A. Yes, polyketide synthase.

Q. In a multi-enzyme do the multiple domains catalyze different types of reactions?

A. Typically that would be the case, yes. 08:23

Q. And in Exhibit 1082 here, single ketoreductase domains were isolated and used in this study, correct?

A. Yes. 08:23

Q. If you look to the abstract -- I think I'm going to ask you to pronounce this. But going halfway down, there is a compound beginning (2R, S)-2 methyl.

Do you see that? 08:23

A. Yes.

Q. Is that the substrate used with these KR domains?

And can you read that into the record, please? 08:24

A. So yes, they did use the (2R, S)-2-methyyl-3-oxopentanoic acid and N-acetylcysteamine thioester.

Q. Thank you.

In your box, Dr. Hausinger, would you please retrieve Exhibit 1035. 08:24

A. Okay. That's the Müller, et al., paper from 2006.

Q. Exhibit 1035 names you as an author, correct? 08:24

A. That is correct.

Q. And Tina Müller is also an author?

A. Yes.

Q. Did she work in your lab?

A. Yes, she did. 08:25

Q. How did she come to work in your lab?

A. She came to know about some of our work on TfdA. As a graduate student she had been working on RdpA and SdpA and wanted to get more into the understanding of the biochemistry of those enzymes and so came to my lab as the best place to be able to do that. 08:25

Q. In your experience, is Dr. Müller a good scientist?

A. Oh, she was excellent, yes. 08:25

Q. She was careful and accurate with her work?

A. Yes.

Q. In the abstract of Müller 2006, a little more than halfway down, it states that "Four SdpA variants were (slightly) active with (R)-mecoprop," correct? 08:25

A. That is what it states, yes.

Q. Would you please turn to Table 1 of Müller 2006 on page 1361. 08:26

Just let me know when you're there.

A. I'm there.

Q. In the lower half of Table 1, those four SdpV -- those four SdpA variants mentioned in the abstract are the ones showing a value in the right-hand column for activity on (R)-mecoprop, correct? 08:26

A. That is correct.

Q. For the first of those four SdpA variants, E69A, did it have greater activity on (S)-mecoprop or (R)-mecoprop? 08:26

A. The specific activity was slightly higher on (S)-mecoprop than on the (R) -- I'm sorry. Where am I here? -- than on the racemic mixture of (R)- and (S)-mecoprop. But it was 08:27

1 **within standard error. So it was really**
2 **basically equivalent, which means that all of**
3 **the activity seen was from the (S)-mecoprop.**
4 Q. I see you're comparing the
5 (R)-mecoprop activity in the last column to 08:27
6 racemic mixture of mecoprop and the -- we'll
7 call it the third column of data.
8 **A. Okay. I see what you're --**
9 Q. Does it make more sense to do a
10 comparison of the first column, (S)-mecoprop at 08:28
11 4 millimolar to (R)-mecoprop at 4 millimolar?
12 **A. Yeah. It has been quite a while**
13 **since I looked at this paper.**
14 **So you're correct, those comparisons**
15 **amplify the results that the activity is much** 08:28
16 **greater with the (S)-mecoprop.**
17 Q. Does the first SdpA variant there,
18 E69A, have (R)-enantioselectivity or
19 (S)-enantioselectivity?
20 **A. The E69A has almost essentially** 08:28
21 **(S)-mecoprop specificity and has just a very**
22 **tiny amount of specificity for the (R)-mecoprop.**
23 Q. And is the answer the same for the
24 other three SdpA variants showing some
25 (R)-mecoprop activity? Those are R207A, R207B, 08:29

and G97I/N98G.
MR. GROSSMAN: Objection to the form of the question.
THE WITNESS: The variants you indicate all are active with (S)-mecoprop 08:29
but then also have a small amount of activity with the (R)-mecoprop.
So the point of this is that making very small changes in protein can change it from one that is exclusively 08:30
S-specific to one that relaxes the specificity so that it does act on the other enantiomer. Small changes, big effect.
BY MR. DeROO: 08:30
Q. Table 1 shows the wild-type SdpA as having zero activity on (R)-mecoprop, correct?
A. Yes.
Q. Did any of the variants reported in Müller 2006 completely switch selectivity from 08:30
wild-type SdpA so that there is only activity on (R)-mecoprop and no activity on (S)-mecoprop?
MR. GROSSMAN: Objection to the form of the question.
THE WITNESS: None of the variants we 08:31

1 studied had swapped the activity. We were
2 excited to see the relaxation of
3 specificity. It would have been requiring
4 additional mutagenesis studies to identify
5 something that had swapped that activity. 08:31
6 BY MR. DeROO:
7 Q. Would you please turn to page 1362.
8 **A. I'm there.**
9 Q. The lower right paragraph refers to
10 RdpA variants. 08:32
11 Do you see that?
12 **A. Yes.**
13 Q. And it states that the Q93A variant
14 retains 60 percent of wild-type RdpA activity,
15 but it dropped to 35 percent when the racemate 08:32
16 was provided, suggesting that glutamine 93
17 prevents the incorrect enantiomer from binding
18 to and inhibiting the enzyme.
19 Correct?
20 **A. That is what it states.** 08:32
21 Q. And does that indicate that the
22 glutamine was believed to sterically exclude
23 (S)-mecoprop from binding in RdpA and the
24 mutation and the Q93A variant removed some of
25 that steric hindrance? 08:33

1 MR. GROSSMAN: Objection to the form
2 of the question.
3 THE WITNESS: It means that the
4 glutamine 93 is disallowing the wrong
5 enantiomer from binding. And so when it 08:33
6 was substituted with an alanine, then some
7 of that wrong enantiomer could bind and
8 prevent binding of the proper substrate.
9 BY MR. DeROO:
10 Q. In Table 1, the Q93A, RdpA variant 08:33
11 still retained some ability to degrade
12 (R)-mecoprop, correct?
13 MR. GROSSMAN: Objection to the form
14 of the question.
15 THE WITNESS: The Q93A had reduced 08:33
16 specific activity, whether looking at
17 4 millimolar or 2 millimolar of the
18 substrate. In both cases you see a
19 reduction in specific activity from 7.11
20 down to 4.3 or from 5.6 down to 3.27 units 08:34
21 per milligram.
22 BY MR. DeROO:
23 Q. And so Q93A was still able to degrade
24 (R)-mecoprop at about 60 percent compared to
25 wild-type activity? 08:34

MR. GROSSMAN: Same objection.
THE WITNESS: Q93A has about 60 percent of the wild-type activity with the (R)-mecoprop.
BY MR. DeROO: 08:35
Q. In your box would you please retrieve 1001.
A. Okay. That's the '555 patent.
Q. Would you please turn to Claim 1.
Let me know when you're there. 08:35
A. I'm there.
Q. Let's look at the first part of Claim 1 stating, a transgenic plant cell comprising polynucleotide that encodes an AAD-1 protein that exhibits aryloxyalkanoate dioxygenase 08:35 activity wherein said activity enzymatically degrades a phenoxy auxin herbicide and an (R)-aryloxyphenoxypropionate herbicide.
Did I read that correctly?
A. That's what it states. 08:36
Q. The first type of herbicide referred to in Claim 1 is the phenoxy auxin herbicide, correct?
A. Yes.
Q. Is 2,4-D a phenoxy auxin herbicide? 08:36

1 **A. 2,4-D is a phenoxy auxin herbicide,**
2 **yes.**
3 Q. 2,4-D is a chiral, correct?
4 **A. Yes.**
5 Q. Is (R)-mecoprop a phenoxy auxin 08:36
6 herbicide?
7 **A. Yes.**
8 Q. And it's an (R)-enantiomer as the
9 name says, correct?
10 **A. Correct.** 08:37
11 Q. The AAD-1 protein of Claim 1 can
12 degrade both a chiral and (R)-enantiomers of the
13 phenoxy auxin herbicides, correct?
14 **A. RdpA --**
15 MR. GROSSMAN: Objection to the form 08:37
16 of the question.
17 THE WITNESS: RdpA can degrade to 4-D
18 and (R)-mecoprop and similar (R)-phenoxy
19 auxins.
20 BY MR. DeROO: 08:37
21 Q. The second type of herbicide referred
22 to in Claim 1 is an (R)-aryloxyphenoxypropionate
23 herbicide, correct?
24 **A. Correct.**
25 Q. Can we agree to call this an (R)-FOP, 08:37

(R)- F-O-P?
A. That works for me.
Q. Perfect. (R)-FOPS include (R)-enantiomers like (R)-haloxyfop?
A. It has the same substructure, the same chirality, yes. 08:38
Q. Does Claim 1 require any minimum level of degrading activity on phenoxy auxin or (R)-FOP herbicides?
MR. GROSSMAN: Objection. Objection to the form of the question. 08:38
THE WITNESS: Claim 1 does not specify how much of a compound needs to be degraded. And so -- yeah, it's just not specified. 08:38
BY MR. DeROO:
Q. Is the term (R)-enantioselective stated anywhere in Claim 1?
A. It doesn't have --
MR. GROSSMAN: Objection to the form of the question. 08:38
THE WITNESS: It doesn't have to be because it states that it is able to degrade the (R)-aryloxyphenoxypropionate, which means that it is able to degrade that 08:39

type of compound, that enantiomer.
BY MR. DeROO:
Q. The question was a little bit different.
Do you see the term "(R)-enantioselective" in Claim 1 or is that something you're interpreting? 08:39
MR. GROSSMAN: Objection to the form of the question.
THE WITNESS: That term is not part of Claim 1. 08:39
BY MR. DeROO:
Q. Is the term "(R)-enantiospecific" part of Claim 1?
MR. GROSSMAN: Same objection. 08:39
THE WITNESS: That term "(R)-enantiospecific" is not part of Claim 1. And I think it would be inherent in -- a POSA looking at this would assume that they are seeking specific chemistry here that is for the (R)-enantiomers. And so probably assume that it means it's only acting on (R)-enantiomers. 08:39
BY MR. DeROO:
Q. Will you return to your declaration, 08:40

please.

A. Okay. Where?

Q. At the back of your declaration you have an Appendix 1 that is a table of exhibits, correct? 08:40

A. Yes.

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

A. Yes.

Q. Is it an accurate and complete list of materials that you considered? 08:41

A. Yes.

Q. I understand from your declaration that you reviewed some sequences of RdpA that were published in a Monsanto patent application, Exhibit 1017, and then the Larue 2019 publication, which is Exhibit 1052. 08:41

And my question is actually pretty simple, Dr. Hausinger, which is whether Exhibit 1017 and Exhibit 1052 are both on your list of materials considered? 08:42

A. Yes.

Q. Did Bayer provide you access to any amino acid sequences beyond those reported in Bayer's patent application or the Larue 2019 08:42

publication?

A. Did Bayer provide me with any? So there were some variants that were created by Bayer beyond those shown -- beyond those shown in Larue. 08:43

Q. And that's kind of what I'm getting at, Dr. Hausinger.

Some RdpA variants were published by Bayer either in Larue or in the patent application. 08:43

And my question is whether you were provided access to amino acid sequences of variants beyond what was published, so internal Bayer information.

A. So in my declaration on page 51 you'll see a list of a number of different variants that had been created. And only a subset of these were in Larue. 08:43

Q. Right. So we have variants that were in Larue. We have variants that were published in the patent application. 08:44

Did Bayer provide you with access to any additional RdpA variants?

A. No, I don't believe so.

Q. Would you please retrieve Exhibit 08:44

1027 in your box.

A. Okay. Hogan, et al., 2000.

Q. In the author line you're an author of Exhibit 1027, the Hogan publication?

A. That is correct. 08:45

Q. In the abstract about 13 rows down you stated that variants of TfdA were created starting with H167A.

Do you see that?

A. Yes. 08:45

Q. This states that the H167A, H200A, H213A, H245A, and H262A forms of TfdA formed inclusion bodies when overproduced in E.coli, correct?

A. That is what it states. 08:46

Q. What is an inclusion body?

A. It's where the protein is insoluble and so comes out sort of as a precipitate within E.coli cell.

Q. Your article goes on to state that, these proteins were soluble when fused to the maltose-binding protein (MBP). 08:46

Correct?

A. Yes.

Q. What is maltose-binding protein? 08:46

A. It's a protein that is often used in protein engineering studies because it's highly soluble. And so when you fuse this protein to a desired protein it can retain its solubility of that desired protein. The actual function of a maltose-binding protein is to bind maltose. 08:46

Q. And if you're able to fuse MBP to a desired protein then you could test it in purified form, correct?

A. That is why we used it, to get soluble material. 08:47

Q. Would you turn to page 12402, please.

A. Okay.

Q. Do you see the header Results?

A. Yes. 08:47

Q. In the second sentence of the first paragraph you referred to a standard protocol here that was used and the H8A, H113A, D115A, H216A, and H235A variants existed as soluble proteins. 08:48

Do you see that?

A. Yes.

Q. It says all of the other TfdA variants were present as inclusion bodies even when grown at lower temperatures 08:48

(22 degrees Celsius), in M9 minimal medium, or in LB broth containing 660 millimolar sorbitol and 2.5 millimolar betaine, correct?

A. That's correct. They're a set of standard approaches that people use to try to get soluble protein. 08:49

Q. What effect does lowering temperature have on enzyme expression or solubility?

MR. GROSSMAN: Objection to the form of the question. 08:49

THE WITNESS: When you place the cells at lower temperature, they are metabolizing more slowly. They are producing proteins more slowly. And so there are enzymes within the cells, 08:49 chaperonin proteins, that are present to help fold the proteins properly.

And at lower temperature, if they are formed more slowly, then the chaperonins have a greater ability to do 08:49 their function and fold the proteins properly. Whereas at high temperature if you have very rapid formation of the proteins they overwhelm the chaperonin system. 08:50

BY MR. DeROO:
Q. Can pH also have an effect on enzyme solubility?
MR. GROSSMAN: Objection to the form of the question. 08:50
THE WITNESS: When you're dealing with purified proteins, a lot of times people will look at the pH stability of the proteins. You can unfold the protein and so forth. But at high temperature -- I 08:50 mean high pH or low pH. But in the cell the cytoplasm -- the cells are homeostatic. They maintain pretty much of the same pH within the cell. That's not a trick that's often used for enhancing stability and 08:50 solubility of proteins.
BY MR. DeROO:
Q. And enzymes typically exist in cells in nature, not in a purified form, right?
A. That is -- 08:50
MR. GROSSMAN: Objection.
THE WITNESS: That is correct.
BY MR. DeROO:
Q. And so once an enzyme has been extracted and purified, can it be important to 08:51

maintain it at its natural pH to confer solubility?

MR. GROSSMAN: Objection to the form of the question.

THE WITNESS: When you are dealing with a purified protein, you want to keep that protein at a -- within a pH regime where it's going to stay soluble usually, depending on what your -- your effort is, your experiment. 08:51

BY MR. DeROO:

Q. What is the M9 minimal medium that is referred to under the results section of Hogan here?

A. So it's a medium in which all of the components are well characterized. You put together the phosphate buffer and all -- all of the different components. Unlike the LB where it just contains something like hydrolyzed proteins and you don't know exactly what all is in that milieu. 08:51 08:52

Q. So for the insoluble TfdA variants you tried both the M9 minimal medium and the LB broth.

A. Right. 08:52

Q. Is that right?
A. Yes.
Q. What effect does including sorbitol have on stability?
A. I frankly don't recall why it acts in a positive faction -- fashion in many cases. But I know that that is a standard approach for enhancing solubility of proteins preventing inclusion body formation. I used to know it but I don't remember now. 08:52 08:53
Q. Do you recall what effects betaine can have on solubility?
A. That's the same quandary, that this was 24 years ago and, yeah, I don't recall. It's just one of the tools that we have in our arsenal. 08:53
I would guess that it's referenced in -- yeah, reference 32 would have that information. The Blackwell and Horgan FEBS Letter would probably have it. But... 08:53
Q. Would you please look at the bottom of the right-hand column of page 12402 of Exhibit 1027. I'm looking at the last two sentences here.
It says, MBP-H245A and MBP-H262A 08:54

proteins were soluble; however, gel filtration analysis indicated the presence of only highly aggregated material eluting in the void volume. Because these mutant proteins exhibited aberrations in their folding properties, the 08:54
catalytic role of histidine-245 and histidine-262, if any, could not be assessed.
Do you see that?
A. Yes.
Q. In this project did you conclude that 08:54
these aggregated 245 and 262 TfdA variants had no activity or could they not be tested?
MR. GROSSMAN: Objection to the form of the question.
THE WITNESS: So the highly 08:55
aggregated samples there was clearly something non-natural about how they behaved. I don't recall if we actually tried to test for activity or not. It's just been too long. But in any case, we 08:55
didn't want to try to extract information from these proteins that are clearly not folded properly.
BY MR. DeROO:
Q. Were there additional techniques that 08:55

you could have carried out on them to try to get them in position for accurate testing or did you reach the end of the road?

MR. GROSSMAN: Objection to the form of the question. 08:56

THE WITNESS: One can always devise additional experiments to try to push the limits here and overcome whatever barriers you have, such as with these proteins. But we wanted to get this publication wrapped 08:56 up and chose to stop looking at those variants at that point.

BY MR. DeROO:

Q. Do you still have the '555 patent in front of you here? 08:56

A. Let me --

MR. GROSSMAN: Pier, I was actually going to say, if you're moving on to a new topic, we've been going for about an hour, can we take a short break? 08:56

MR. DeROO: Yeah, that works for me. Dr. Hausinger, five or ten minutes?

Let's go off the record.

THE STENOGRAPHER: We're off the 08:56

record at 8:56 a.m.
(Whereupon, a recess was taken
from 8:56 a.m. to 9:08 a.m.)
THE STENOGRAPHER: We're back on the
record at 9:08. 09:08
BY MR. DeROO:
Q. Welcome back, Dr. Hausinger. I
assume you didn't discuss the substance of your
testimony with counsel during the break, but
would you please confirm? 09:08
A. I confirm.
Q. We were just turning to the '555
patent before the break.
Do you have it in front of you?
A. Yes. 09:08
Q. Could you please turn to column 18.
Let me know when you're there.
A. I'm there.
Q. Towards the top of column 18 do you
see what's referred to as a consensus motif with 09:09
variable spacing for alpha-kg-dependent
dioxygenases, beginning HX(D/E)?
A. Yes.
Q. In that consensus motif the first
spacer must be 1 amino acid, the second spacer 09:09

must be 23 to 26 amino acids, the third spacer must be 114 to 183 amino acids, and the fourth spacer must be 10 to 13 amino acids, correct?

A. I wouldn't phrase it as "must be." Those were the spaces that were identified back around 2004 for the known enzymes. There have been a lot of other enzymes in this family since then. And the spacing could have been expanded, for example. I just don't know about that. But that was the conical motif at the time. 09:09 09:10

Q. And in your declarations, do you provide any expanded consensus motif since 2004 or 2005?

A. No, that wasn't part of what I was asked to look at. 09:10

Q. Okay. Would you please turn to paragraph 26 of your second declaration.

A. Okay.

Q. And towards the bottom of your paragraph 26 you referred to I think eight plant enzymes. 09:11

Do you see that?

A. Yes.

Q. And in this paragraph 26 you're referring to a Hausinger 2004 publication, which 09:11

is Exhibit 1025, correct?
A. Yes.
Q. Would you please retrieve Exhibit 1025 from your box.
A. Okay. 09:11
Q. And would you please turn to Table 1 on page 22 and confirm this is the Table 1 that you cited in your paragraph 26.
A. That is correct.
Q. And about one-third of the way down 09:12 Table 1, do you see the enzyme beginning Petunia hydrida?
A. The flavanone 3 beta-hydroxylase, yes.
Q. So the eight enzymes from plants that 09:12 you identify in your paragraph 26 in Table 1 -- I'm going to go in the order of Table 1 here -- but it is the petunia enzyme, the citrus enzyme, the arabidopsis enzyme, the two gibberellin oxidases from cucurbita, the 09:12 caranthus enzyme, the hyoscyamus niger enzyme, and then we jump all the way to the bottom and it's the tomato oxidase -- ACC oxidase, correct?
A. Yes.
Q. Are those the eight that you referred 09:13

to in your paragraph 26?
A. I believe so, yes.
So the point that I was making was that you can have identical spacing in different representatives of this enzyme family working on very different substrates. 09:13
Q. And for those eight plant enzymes, they all have 53, 54, or 55 amino acids in their third spacer, correct?
A. It looks like it. 09:13
Q. And they all have nine amino acids in their fourth spacer, correct?
A. I believe so, yes.
Q. And these eight plant enzymes do not have between 114 and 183 amino acids in their third spacer; do they? 09:14
A. I think I've answered that, but -- I agreed with the prior statement.
(Stenographer clarification.)
THE WITNESS: I agreed with the prior statement. 09:14
BY MR. DeROO:
Q. You had one other comparison of enzyme spacing in your paragraph 26, which was between TauD and AtsK? 09:14

1 Do you see that?
2 **A. Yes.**
3 Q. You did not identify the overall
4 sequence between TauD and AtsK in your
5 declaration; did you? 09:14
6 **A. No, I did not.**
7 Q. And I think I've seen both TauD and
8 AtsK in a few of your publications, like this
9 one and in Elkins.
10 Are you familiar with TauD and AtsK? 09:15
11 **A. Yes. We had done work on TauD from**
12 **one organism. There are actually multiple TauDs**
13 **known that are not all identical in sequence.**
14 **And I'm familiar with a couple papers that have**
15 **been published on AtsK.** 09:15
16 Q. And do you know roughly what the
17 sequence identity is between TauD and AtsK?
18 **A. I do not recall.**
19 Q. Would it surprise you if the sequence
20 identity between TauD and AtsK is about 09:15
21 33 percent?
22 **A. That does not surprise me. They work**
23 **on quite different substrates. They retain the**
24 **same overall fold. But yeah, they are different**
25 **enzymes within the family.** 09:15

Q. Would it help if I showed you a sequence comparison between these two enzymes?
A. Help in what way?
Q. To confirm the -- the sequence identity between these two. 09:16
A. I have no reason to doubt you. I don't think a sequence alignment is necessary.
Q. In your declaration did you identify the overall sequence identities between any of the eight plant enzymes that you cited in 09:16 paragraph 26?
A. That was not the point of the paragraph. And so, no, I did not include overall sequence identity.
Q. Does any enzyme listed in your 09:16 Table 1 of Exhibit 1025 have the exact same spacings as in the sequence of RdpA?
A. I don't recall but I don't think so. Yeah, I don't think so.
Q. Two rows below AtsK in your Table 1 09:17 is TfdA.
Do you see that?
A. Yes.
Q. And TfdA was at one time mistakenly believed to be a monooxygenase, correct? 09:18

1 **A. Before the biochemistry was**
2 **elucidated it was called a monooxygenase.**
3 Q. And you published an article in 1993
4 reporting that TfdA is actually a dioxygenase,
5 correct? 09:18
6 **A. That is correct. So we showed that**
7 **one atom of oxygen ends up being incorporated**
8 **into this TfdA in the 2,4-D substrate. The**
9 **other atom of oxygen ends up going into the**
10 **alpha-ketoglutarate, the other cosubstrate which** 09:18
11 **was not known to be a cosubstrate at the time.**
12 Q. And is that why TfdA is now known as
13 an alpha-ketoglutarate-dependent dioxygenase?
14 **A. Yes.**
15 Q. RdpA is also an alpha-ketoglutarate- 09:18
16 dependent dioxygenase, correct?
17 MR. GROSSMAN: Objection to the form
18 of the question.
19 THE WITNESS: RdpA is an
20 alpha-ketoglutarate-dependent dioxygenase. 09:18
21 BY MR. DeROO:
22 Q. Since you published your article in
23 1993, would it be scientifically invalid to
24 refer to TfdA as a monooxygenase?
25 **A. It would be incorrect in the same way** 09:19

in some ways that referring to these ADD (verbatim) enzymes as dioxygenases is invalid because the two atoms of oxygen do not end up in the -- that single substrate. But yes, that is correct. 09:19

Q. I'd like to focus on TfdA for now. We'll get to AAD-1.

Since you published your article in 1993, would it be misleading to refer TfdA as a monooxygenase? 09:19

MR. GROSSMAN: Objection to the form of the question.

THE WITNESS: We showed that TfdA is not a monooxygenase even though the activity looks like a monooxygenase in 09:20 terms of only one atom being incorporated into the substrate. It is, in fact, a dioxygenase and the name of the enzyme should include both 2,4-D and alpha-ketoglutarate. 09:20

BY MR. DeROO:

Q. Since you published your article in 1993, have you ever taken the position that TfdA and AAD-1 have monooxygenase activity?

A. So there was a patent issued that I 09:20

was an expert witness in. And I tried to explain that the monooxygenase was a natural understanding, a natural assumption at the time in the original patent. Because the biochemistry had not been carried out, it was not known to be alpha-ketoglutarate-dependent. And I was emphasizing that, again, one atom of oxygen ends up being incorporated into the 2,4-D. So it's like a monooxygenase but it is, in fact, a alpha-ketoglutarate-dependent dioxygenase. 09:20 09:21

Q. In that previous expert witness role, was that a case where you were an expert for Bayer against Dow AgriSciences?

A. Yes. 09:21

Q. And that case involved AAD-1, correct?

MR. GROSSMAN: Objection to the form of the question.

THE WITNESS: That case did -- was -- I don't recall AAD-1 being a focus of that case, no. 09:21

MR. DeROO: Mark, could we please transfer Exhibit 2065 into the publish folder so counsel can retrieve it. 09:22

MR. GROSSMAN: I'm going to object to the introduction of new exhibits at this phase, which patent owner is not permitted to do.

MR. DeROO: Okay. So I think the 09:23
exhibit is in there. If you guys can refresh it, a link, or do we need...

MR. GROSSMAN: I don't see the exhibit in the chat.

MR. DeROO: So it's in the ShareFile 09:24
that was attached to the court reporter email with the Zoom link. Let's see if we can get it in the chat, which might be simpler.

Dov, do you see it in the chat? 09:25

MR. GROSSMAN: I'm still trying to open it.

I'm going to object to this exhibit again on the basis that patent owner is not permitted to introduce new 09:25
exhibits at this phase of the case, number one.

Number two, I'm going to object to this on relevance grounds.

BY MR. DeROO:
Q. Dr. Hausinger, could you please retrieve Exhibit No. 2065 from your box.
MR. GROSSMAN: I'm also going to object to this as incomplete. 09:26
THE WITNESS: I have 2065.
BY MR. DeROO:
Q. Dr. Hausinger, this is your declaration in that previous case between Bayer and Dow AgriSciences, correct? 09:26
A. Yes.
Q. And you signed this declaration on page 20, correct?
A. Yes.
Q. At the top of the page there's a filing date on December 2011. 09:27
Do you see that?
A. Yes.
Q. Your declaration is about 18 years after your 1993 article reporting that TfdA was a dioxygenase, correct? 09:27
MR. GROSSMAN: Objection to form.
THE WITNESS: Right.
BY MR. DeROO:
Q. Would you please turn to paragraph 21 09:27

of your Bayer litigation declaration on page 13, please.

A. Okay.

Q. And the last sentence stated that, the clear and unequivocal association of the name "2,4-D monooxygenase" with TfdA and enzymes like TfdA renders it an unambiguous identifier of the class of biological activities to which the claims of the '401 patent refer. 09:28

Correct? 09:28

A. I see that. That is what it states.

But I'd like to point out that the biochemistry was not known at the time this particular patent was filed. And so --

Q. Would you look at -- 09:28

(Simultaneous speaking.)

BY MR. DeROO:

Q. Sorry.

A. So earlier in that paragraph I talk about how TfdA hydroxylates by monooxygenation but has the separate distinct reaction in which the second oxygen atom is added to alpha-ketoglutarate. 09:29

And so I'm saying that the patent as it was written was the best known at the time 09:29

1 **and it was later corrected to show that it does**
2 **more than add the single atom of oxygen.**
3 Q. Would you please retrieve Exhibit
4 1043 from your box.
5 **A. Okay. The Streber, et al., patent.** 09:29
6 Q. Yes. This is the Streber '401 patent
7 you referred to in your Bayer litigation
8 declaration and also in your declarations in
9 these IPRs?
10 **A. Yes.** 09:30
11 Q. Would you please turn to Claim 1 of
12 the '401 patent.
13 Let me know when you're there,
14 column 32.
15 **A. Okay. Got it.** 09:30
16 Q. Do you see that Claim 1 of the '401
17 patent requires a DNA sequence encoding a
18 polypeptide having the biological activity of
19 2,4-D monooxygenase?
20 Do you see that? 09:31
21 **A. That is what it states.**
22 Q. That's the monooxygenase activity you
23 associated with TfdA in paragraph 21 of your
24 Bayer litigation declaration, correct?
25 **A. So that was the biological activity,** 09:31

which turns out when you get into the enzymology it's actually a 2,4-D alpha-ketoglutarate dioxygenase.

Q. You gave the opinion in the Bayer litigation that AAD-1 infringes this '401 patent claim by having that monooxygenase activity, correct? 09:31

MR. GROSSMAN: Objection to the form of the question.

THE WITNESS: So can you clarify where I state that? 09:31

BY MR. DeROO:

Q. Would you turn to page 14 of your Bayer litigation declaration.

MR. GROSSMAN: I'm going to make a continuing objection to patent owner's attempt to use a document that patent owner is not properly permitted to put into evidence at this stage to try to have testimony about it. 09:32 09:32

BY MR. DeROO:

Q. Are you on page 14 of your declaration?

A. I was on paragraph 14. Sorry.

Q. Oh, I'm sorry. So on page 14 you 09:32

have a section titled Infringement by DAS.
Do you see that?
A. Yes, I see that.
Q. And DAS is Dow AgriSciences?
A. I'm assuming so. It's been a long 09:32
time since I've looked at this. I assume so.
Q. Below the heading Infringement by
DAS, in paragraph 25 you refer specifically to
AAD-1, correct?
A. Yes, I do. 09:33
Q. Would you please turn to paragraph 33
of your Bayer litigation declaration?
A. Okay.
Q. You said here in paragraph 33, I
understand that DAS has asserted as its defense 09:33
to infringement that the accused recombinant AAD
genes, code for dioxygenases, not
monooxygenases; and therefore they are not
encompassed by the '401 patent claims, which all
require recombinant genes that encode 09:33
monooxygenases.
Correct?
MR. GROSSMAN: Objection to the form
of the question.
THE WITNESS: What you said is what 09:34

is stated in the document.
BY MR. DeROO:
Q. In the next sentence you said that DAS's argument that its AAD proteins were dioxygenases rather than monooxygenases was, 09:33
quote/unquote, "simply indefensible."
That was the word you used, correct?
MR. GROSSMAN: Objection to the form of the question.
THE WITNESS: That is the word that I 09:34
incorporated there.
BY MR. DeROO:
Q. Did the Court in this previous Bayer litigation agree with your argument that AAD-1 had the monooxygenase activity required by the 09:34
'401 patent claims?
A. I know that the -- the case was viewed in favor of Dow. I don't know how they weighed all the different components of it.
Q. Dr. Hausinger, do you recall giving 09:35
live testimony before the judge in this previous Bayer litigation?
A. I do recall that, yes.
Q. And that testimony was under oath, correct? 09:35

1 **A. Of course, yes.**
2 MR. DeROO: Mark, would you please
3 drop Exhibit 2062 into the chat, please.
4 And Dr. Hausinger, can you
5 retrieve Exhibit 2062 from your box. 09:36
6 Dov, do you have the exhibit?
7 MR. GROSSMAN: Not yet.
8 THE WITNESS: I have it.
9 MR. DeROO: Let's wait for counsel
10 for a second here. 09:36
11 MR. GROSSMAN: I'm going to -- I have
12 it.
13 I'm going to object to this
14 exhibit, again, on the basis that what
15 patent owner is doing by trying to 09:37
16 introduce new exhibits at this phase of the
17 case is improper and, number two, for
18 relevance reasons.
19 BY MR. DeROO:
20 Q. Dr. Hausinger, this is a transcript 09:37
21 from the Markman hearing in Bayer CropScience AG
22 versus Dow AgriSciences, LLC, Civil Action
23 10-1045 before Judge Bumb, B-u-m-b.
24 And if you turn to page 3, are you
25 the Dr. Hausinger identified there in the table 09:37

of contents for your direct and cross-examinations?

A. Yes.

Q. Let's turn in your direct testimony to page 64 of the transcript, please. 09:37

Starting at line 6 of page 64, you were asked if the TfdA enzyme is a metal-containing enzyme.

Do you see that?

MR. GROSSMAN: Objection to the form of the question. 09:38

I'm making again a continuing objection to patent owner's attempt to try to find a way to get a document into evidence at this stage of the proceeding. 09:38

THE WITNESS: I do see that.

BY MR. DeROO:

Q. And you answered that, yes, TfdA is a metal-containing enzyme.

A. I answered: "Yes. We demonstrated that it requires an iron atom in its ferrous state." 09:38

Q. Then were you asked on line 10: "And do you know whether the AAD enzyme that Dow uses is also a metal-containing enzyme?" 09:39

Do you see that?
A. Yes.
Q. And you answered: "It's the same reaction mechanism, it has the same requirements, yes." 09:39
Correct?
A. That's what I said.
Q. Would you turn to page 69 of the transcript, which is still in your direct examination, please. 09:39
A. Okay.
Q. Starting on line 17 of page 69 it referred to a paper by Tiedje and Alexander.
Is that one of the papers that mistakenly referred to TfdA as a monooxygenase? 09:39
MR. GROSSMAN: Objection to the form of the question.
Again, a continuing objection to patent owner's use of this exhibit in this manner. 09:40
THE WITNESS: That was the original publication where 2,4-D was shown to generate the 4 dichloro- -- 2,4-dichlorophenol and glyoxylate. And based on what was known at the time, the 09:40

1 author suggested that it was a
2 monooxygenase reaction.
3 BY MR. DeROO:
4 Q. Starting on line 22 of page 69, you
5 explained that the author: "...suggested that a 09:40
6 similar action was being carried out in these
7 intact bacteria, but they did not characterize"
8 -- "they did not purify the protein and
9 characterize it."
10 That protein you were referring to is 09:40
11 TfdA?
12 MR. GROSSMAN: Objection to the form
13 of the question.
14 THE WITNESS: The supposed
15 monooxygenase that was characterized in 09:41
16 cells by Tiedje and Alexander is TfdA that
17 we ended up characterizing as a 2,4-D
18 alpha-ketoglutarate dioxygenase.
19 BY MR. DeROO:
20 Q. You explained: "They did not purify 09:41
21 the protein and characterize it. So that's what
22 we wanted to do."
23 Did your lab purify TfdA as part of
24 determining that it was a dioxygenase?
25 **A. Yes, we did.** 09:41

Q. Would you please turn to page 143, which is in your cross-examination.
A. I'm there.
Q. Starting at line 4 of page 143, you were asked a question showing you your deposition testimony in this case. 09:42
Do you see that?
A. Yes.
MR. GROSSMAN: Object to the form of the question. 09:42
I'm also going to object to this exhibit as incomplete.
BY MR. DeROO:
Q. At line 10 of page 143 a piece of your testimony was read back to you: "If one knows that it's a 2,4-D alpha-ketoglutarate dioxygenase, I think it's misleading to call it a 2,4-D monooxygenase." 09:42
And you were asked to confirm that's testimony you gave, line 16. 09:43
Your answer: "That is correct."
Correct?
MR. GROSSMAN: Objection to the form of the question.
THE WITNESS: That is what the 09:43

1 document shows.
2 BY MR. DeROO:
3 Q. And line 13 you were also provided
4 with your previous testimony: "If one calls it
5 a 2,4-D alpha-ketoglutarate dioxygenase, a 09:43
6 2,4-D monooxygenase, that's scientifically
7 invalid."
8 That was also your testimony in this
9 case, correct?
10 MR. GROSSMAN: Same objection. 09:43
11 THE WITNESS: When one knows what the
12 reaction mechanism is, and it is a 2,4-D
13 alpha-ketoglutarate dioxygenase, then that
14 is what it should be called.
15 BY MR. DeROO: 09:44
16 Q. Would you please turn to page 176,
17 please. At the bottom of this page you were
18 asked about some legalese language in your
19 affidavit.
20 On line 22 you were asked: "Do you 09:44
21 ever in your scientific writing say that
22 somebody made an admission?"
23 Do you see that?
24 **A. I see that.**
25 Q. You answered: "This is not 09:44

scientific writing."
Correct?
MR. GROSSMAN: Same objection to the form of the question.
THE WITNESS: That was my answer. 09:45
BY MR. DeROO:
Q. And at the top of the page 177 you attributed legal words like "admission" in your declaration as being provided by the lawyers who helped you write your declaration, correct? 09:45
MR. GROSSMAN: Same objection.
THE WITNESS: That is what it says.
BY MR. DeROO:
Q. This is the transcript of your testimony, correct? 09:45
A. Yes, that is correct.
Q. You can put that aside now.
Could you please turn in your second IPR declaration, to paragraph 27, please.
A. Okay. 09:46
Q. You start paragraph 27 saying, I understand that Corteva has suggested a briefing to the Board that, at my deposition, I somehow acknowledged that Figure 2 of Schleinitz 2004 discloses the AAD-1 motif. 09:46

My question is: Is this information that was provided to you by counsel?

A. Writing a declaration was an iterative process. I contributed some parts and counsel offered some suggestions. I don't remember specifically who provided this sentence or who came up with this sentence. 09:46

Q. Did you review the briefing to the Board or was that information just conveyed to you by counsel? 09:47

A. That was just conveyed to me by counsel.

Q. If you look maybe four or five lines up from the bottom of the paragraph, do you see that you referred to me as "counsel for Corteva"? 09:47

Do you see that?

A. Yes.

Q. Is that what you call people in real life in your scientific writing or was that written by counsel? 09:47

MR. GROSSMAN: Objection to the form of the question.

THE WITNESS: Again, this was a joint effort to create this document. This 09:47

1 particular line could well have been
2 provided by counsel. Maybe I modified it.
3 I don't recall.
4 BY MR. DeROO:
5 Q. In this -- if you go up just a couple 09:48
6 more lines in your paragraph 27, you wrote that
7 during our first deposition together you
8 identified in RdpA where the five amino acid
9 residues of the consensus motif were located, as
10 well as what the spacing was between the 09:48
11 residues. And then in the next sentence you
12 disagreed that those five amino acids at their
13 particular locations in the sequence of RdpA
14 discloses the AAD-1 motif.
15 Do I have the gist of that correct? 09:48
16 MR. GROSSMAN: Objection to the form
17 of the question.
18 THE WITNESS: Schleinitz did not
19 specify anything about an AAD-1 motif.
20 Schleinitz was talking about the sort of 09:49
21 general type of alpha-ketoglutarate-
22 dependent dioxygenase motif.
23 BY MR. DeROO:
24 Q. And RdpA sequence is provided as
25 Seq. ID 9 in the Corteva patents, correct? 09:49

1 **A. Correct.**
2 Q. And '555 patent claims priority back
3 to a PCT application filed in 2005 and a
4 provisional application filed in 2004; is that
5 correct? 09:50
6 **A. Those patent applications never had**
7 **an AAD-1 motif specified.**
8 Q. In your box would you please retrieve
9 Exhibit 1021, please.
10 **A. Okay.** 09:50
11 Q. And Exhibit 1021 is the priority PCT
12 application, Corteva '437, that you've used in
13 your declarations, correct?
14 **A. Yes.**
15 Q. Would you turn at the back to 09:51
16 Seq. ID No. 9, which starts at page 4/22 at the
17 top.
18 **A. Got it.**
19 Q. I'm going to ask you about a few
20 residues at particular positions, if you can 09:51
21 follow along.
22 **A. 422 shows DNA sequence, not protein**
23 **sequence.**
24 Q. At the bottom of 422, do you see
25 there is an amino acid sequence? Just the first 09:51

line appears on page 422 and it's 5 of 22.
Do you see that?
A. Yes.
Q. So Seq. ID No. 9 in Exhibit 1021 has a histidine at position 111, an aspartic acid at 09:52
position 113, a threonine at position 138, a histidine at position 270, an arginine at position 281, and an arginine at position 285.
Did I identify those particular residues correctly? 09:52
MR. GROSSMAN: Object to the form of the question.
THE WITNESS: The sequence does include the residues as you've listed.
BY MR. DeROO: 09:53
Q. In your opinion does the disclosure in Seq. ID 9 of the histidine at position 111, aspartic acid at position 113, threonine at position 138, histidine at position 270, and arginine at position 281 disclose the AAD-1 09:53
motif of the challenged claims?
MR. GROSSMAN: Same objection.
THE WITNESS: One can apply the canonical alpha-ketoglutarate motif, consensus motif, to this sequence and those 09:53

1 residues will be highlighted.
2 I don't view that as indicating
3 an AAD-1 motif.
4 BY MR. DeROO:
5 Q. So the answer is, no, it does not 09:53
6 disclose an AAD-1 motif?
7 **A. Correct.**
8 Q. In your opinion, it is not sufficient
9 for Seq. ID No. 9 to have the required amino
10 acids at those positions; is that correct? 09:54
11 **A. State the question again.**
12 Q. In your opinion, it's not sufficient
13 to disclose the AAD-1 motif by having Seq. ID
14 No. 9 with the required amino acids at those
15 positions that we just went through? 09:54
16 **A. Absolutely. The AAD -- not. The**
17 **AAD-1 motif, if there's such a thing, would**
18 **require something dealing with**
19 **(R)-enantiospecificity. And nothing is**
20 **indicated in the patent about that, what** 09:54
21 **residues are necessary.**
22 Q. So I have the same questions for you
23 regarding Seq. ID No. 10 in Exhibit 1021. So
24 this starts on page 6 of 22.
25 Just let me know when you're there. 09:55

1 **A. I'm there.**
2 Q. Would you confirm for me that
3 Seq. ID No. 10 has a histidine at position 111,
4 aspartic acid at position 113, threonine at
5 position 138, histidine at position 270, 09:55
6 arginine at position 281, and arginine at
7 position 285.
8 Did I identify those positions
9 correctly?
10 **A. The sequence does include those** 09:55
11 **residues as you've stated.**
12 Q. Same questions as before, does the
13 disclosure in Seq. ID No. 10 with the histidine
14 at position 111, aspartic acid at position 113,
15 threonine at position 138, histidine at position 09:56
16 270, arginine at position 281 disclose the AAD-1
17 motif of the challenge claims?
18 **A. And I would say no.**
19 Q. And again in your opinion, it's not
20 sufficient to disclose the AAD-1 motif for 09:56
21 Seq. ID 10 to have the required amino acids at
22 those positions, correct?
23 **A. In my opinion, there is no AAD-1**
24 **motif denoted in this patent. It's really the**
25 **consensus motif just applied to these sequences.** 09:56

MR. DeROO: Why don't we take another short break here.
THE STENOGRAPHER: We're going off the record at 9:56 a.m.
(Whereupon, a recess was taken from 9:56 to 10:07 a.m.) 09:57
THE STENOGRAPHER: Back on the record at 10:07.
BY MR. DeROO:
Q. Dr. Hausinger, would you turn in your Appendix 1 to your list of materials considered, please. 10:07
A. Okay.
Q. And would you confirm that you listed Exhibit 2004, "Protein Sequences"? 10:07
A. Yes.
Q. Would you please retrieve that exhibit from your box, please.
MR. DeROO: And at this point I'll mark the transcript confidential under the protective order. 10:08
THE WITNESS: Okay.
BY MR. DeROO:
Q. And this is the Exhibit 2004 you considered in forming your opinions in your 10:08

second declaration?

A. Correct.

Q. And on this document are [redacted].

Do you see that? 10:09

A. Yes.

Q. [redacted], correct?

A. Correct. [redacted]. 10:09

Q. And [redacted], correct?

A. That's correct. [redacted]. 10:09

Q. The sequences for [redacted]; is that correct?

A. Yes. 10:10

Q. And would you also confirm the [redacted].

A. [redacted]. **Oh, okay.**

Q. And you can see at the top of 10:10

page 6 --

A. Page 6, yes.

Q. -- [redacted]?

A. Yes. 10:10

Q. So there is a standardized way here where I think I can help with counting residues.

Would you mind confirming for me that the full rows here have 50 amino acids.

A. Each row has 50 amino acids. 10:11

Q. At the end of the first row it would be position 50, the end of the second row would be 100, third row would be 150, et cetera, correct?

A. Correct. 10:12

Q. Looking at the native AAD-1 sequence, it has a glycine shown as G at position 59, correct?

A. Yes.

Q. Looking at [redacted], 10:12

[redacted], correct?

A. That is correct.

Q. Would you confirm for me that

[redacted] 10:12

[redacted].

A. That seems to be the case, yes.

Q. Turning back to the native AAD-1 sequence, there is a threonine at position 145, correct? 10:13

A. That's correct.

Q. Can you confirm for me that [redacted].

A. That is correct. 10:14

Q. The native AAD-1 sequence has a lysine at position 213, correct?

A. That is correct.

Q. Would you please confirm for me that [redacted]? 10:14

A. Yes.

Q. In the native AAD-1 sequence there is an alanine at position 231, correct?

A. Correct. 10:15

Q. Would you please confirm for me that [redacted].

A. I can confirm that.

Q. And last one, the native AAD-1 10:16

sequence has a leucine at position 236, correct?

A. Yes.

Q. Would you please confirm for me that

[redacted]. 10:16

A. That's correct.

Q. Would you please retrieve Exhibit 1042 from your box of documents, please.

A. The Schleinitz paper.

Q. And actually we have the blowup again of the sequence alignment as Exhibit 2042 from your last deposition, if that would be easier to look at. 10:17

A. Okay.

Q. For the record, this is a blowup of Schleinitz Figure 2. 10:17

Would you please confirm for me that this is a sequence alignment of RdpA, TauD, TfdA, and SdpA, those four enzymes?

A. I confirm that. 10:17

Q. And would you please using the -- let me start again.

Using the numbering for the RdpA residues, turn to position 59 in the sequence alignment. 10:18

And at position 59 RdpA has a G shaded in gray, correct?

A. Yes, that is correct.

Q. And this glycine at position 59 is conserved in three of the four sequences in the alignment, correct? 10:18

A. Yes.

Q. Would you turn to position 145, please.

RdpA has a T while all three other enzymes have an A shaded in gray, correct? 10:18

A. That is correct.

Q. That alanine is conserved in three of four sequences in this alignment, correct?

A. Yes. 10:19

Q. Would you turn to residue 213, please.

Can you confirm that RdpA has a K shaded in gray.

A. Yes. 10:19

Q. This lycine is conserved in three of the four sequences, correct?

A. Correct. It's a proline in SdpA.

Q. Let's turn to position 231, please.

RdpA has an A shaded in gray, 10:19

correct?
A. Yes.
Q. This alanine is conserved in all four sequences, correct?
A. Yes. 10:20
Q. And let's turn to position 236, please.
RdpA has an L shaded in gray, correct?
A. Yep. 10:20
Q. And this leucine is conserved in three of four sequences, correct?
A. That's correct. It's a phenylalanine in SdpA.
MR. DeROO: Dr. Hausinger, thank you for your time. I don't believe I have more questions for you at this moment. 10:20
I will confirm marking the transcript confidential.
MR. GROSSMAN: Can we confirm here that the portion that you're marking -- just for clarity, the portion that's confidential is the portion that was talking about Exhibit 2004? 10:20
MR. DeROO: I believe that's right. 10:21

1 MR. GROSSMAN: If you want to do 2004
2 through the end of the depo, that's fine.
3 But at least for present purposes until
4 it's filed. But prior to that, it's not
5 confidential. 10:21
6 MR. DeROO: I think that's right,
7 Dov.
8 (Whereupon, a discussion was had
9 off the record at 10:21 a.m.)
10 MR. GROSSMAN: Why don't we take a 10:21
11 break now.
12 THE STENOGRAPHER: Off the record at
13 10:21 a.m.
14 (Whereupon, a recess was taken
15 from 10:21 a.m. to 10:36 a.m.) 10:37
16 THE STENOGRAPHER: The time is 10:36
17 and we're back on the record.
18 EXAMINATION
19 BY MR. GROSSMAN:
20 Q. Good morning, Dr. Hausinger. 10:37
21 **A. Hi, Dov.**
22 Q. Dr. Hausinger, if Claim 1 were
23 understood to allow for degradation of both
24 (R)-FOPS and (R) phenoxy auxins as well as
25 (S)-FOPS and (S) phenoxy auxins so long as it 10:37

still had activity on the (R) enantiomers, would that change your opinions in this case regarding written description?

A. No, it would not.

Q. Why not? 10:37

A. So the -- the claims really focused on (R)-enantiospecificity. But, in fact, they don't have any idea of which residues are responsible for that.

And so all of the concerns that I expressed in my declaration about the AAD-1 motif, including the lack of arginine 285, for example, in Claim 1 and the 85 percent sequence identity, all of those issues are still present. They don't know what is necessary in order to have the (R)-enantiospecificity, which is really what they are aiming for in their engineered constructs. 10:38 10:38

MR. GROSSMAN: Thank you, Dr. Hausinger. I have no further questions. 10:38

MR. DeROO: I have just one.

FURTHER EXAMINATION

BY MR. DeROO:

Q. Dr. Hausinger, did you consult with 10:38

Mr. Grossman and your counsel in the break between my questioning and his?

A. Yes, we did discuss --

MR. GROSSMAN: I'll let the witness answer "yes" or "no." 10:39

THE WITNESS: Okay. Yes.

BY MR. DeROO:

Q. And you did discuss.

And what did Mr. Grossman tell you he was going to ask? 10:39

A. He --

MR. GROSSMAN: I'm going to instruct the witness not to answer. Those conversations are privileged.

MR. DeROO: And my understanding is that if there is consulting in between cross and redirect, that's valid for discovery. 10:39

Do you disagree with that?

MR. GROSSMAN: I do disagree with that. 10:39

But Dr. Hausinger, if you'd like to generally describe if you agree it's not a waiver here.

MR. DeROO: Okay. 10:39

1 THE WITNESS: Okay.
2 MR. GROSSMAN: You may at a high
3 level generally describe what was
4 discussed.
5 THE WITNESS: So counsel asked me if 10:40
6 there were any concerns that I had. And
7 then we focused in on one question where I
8 was perhaps less clear than I should be.
9 And the counsel suggested one line of
10 argument -- or of questioning that he would 10:40
11 proceed on.
12 BY MR. DeROO:
13 Q. Dr. Hausinger, did you help craft the
14 questions that you were asked in redirect by
15 your counsel? 10:40
16 **A. I would not say that, no.**
17 Q. Okay. Did counsel provide any
18 suggestions on what you should include in your
19 answers?
20 **A. Counsel --** 10:40
21 MR. GROSSMAN: I'm going to object.
22 I've given you enough leeway
23 here.
24 MR. DeROO: That's a "yes" or "no."
25 It's a "yes" or "no." 10:40

MR. GROSSMAN: Did you -- fine. You can answer that question "yes" or "no."

THE WITNESS: I would say no.

MR. DeROO: All right. No further questions. 10:41

THE STENOGRAPHER: We're off the record at 10:41 at the conclusion.

(Time concluded: 10:41 a.m.)

CERTIFICATE OF REPORTER

I, Janice M. Kocek, Certified Shorthand Reporter, Certified LiveNote Reporter, and Notary Public in and for the State of Illinois, County of Cook, the officer before whom the proceedings were taken, do hereby certify that the foregoing transcript is a true and correct record of these proceedings; that said proceedings were taken in Stenotype notes by me on the 1st day of August, 2024, via Zoom videoconferencing, commencing at 8:01 a.m. EST and ending at 10:41 a.m. EST.

I further certify that present on behalf of Petitioner Bayer CropScience LP, Monsanto Company, and Inari Agriculture, Inc., were Dov P. Grossman, Ben Picozzi and Jessica Palmer Ryen of Williams & Connolly, and present on behalf of Patent Owner Corteva AgriScience LLC were Pier DeRoo and Mark Lampert 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 4th of August, 2024, at the County of Cook, State of Illinois.

JANICE M. KOCEK
CSR NO. 084-002871

ACKNOWLEDGMENT OF DEPONENT

I, _____, do hereby acknowledge that I have read and examined the foregoing testimony, and the same is a true, correct and complete transcription of the testimony given by me, and any corrections appear on the attached Errata Sheet signed by me.

_____ _____
(DATE) (SIGNATURE)

NOTARIZATION (If Required)
State of _____
County of _____
Subscribed and sworn to (or affirmed) before me on this _____ day of _____, 2024, by _____, proved to me on the basis of satisfactory evidence to be the person who appeared before me.

Signature: _____
(SEAL)

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