SUPERIOR COURT OF THE STATE OF CALIFORNIA

COUNTY OF SAN FRANCISCO

DEWAYNE JOHNSON,

Plaintiff,

vs. Case No. CGC-16-550128

MONSANTO COMPANY, et al.,

Defendants.

_____/

Proceedings held on Friday, August 3, 2018, Volume 23, Morning Session, before the Honorable Suzanne R. Bolanos, at 9:19 a.m.

REPORTED BY:

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EXHIBITS

(None.)

Friday, August 3, 2018

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Morning Session

San Francisco, California

Department 504

Judge Suzanne Ramos Bolanos

PROCEEDINGS

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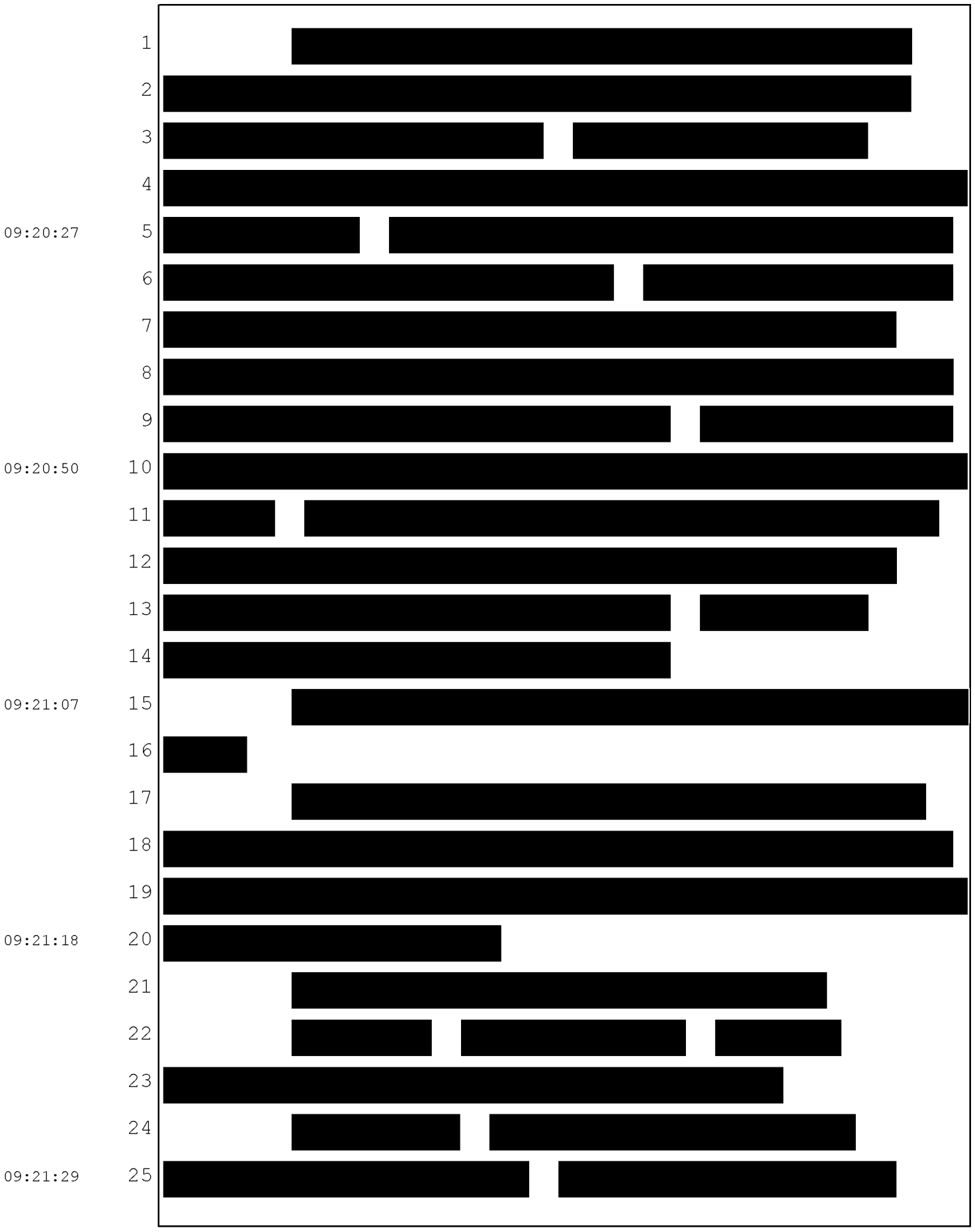
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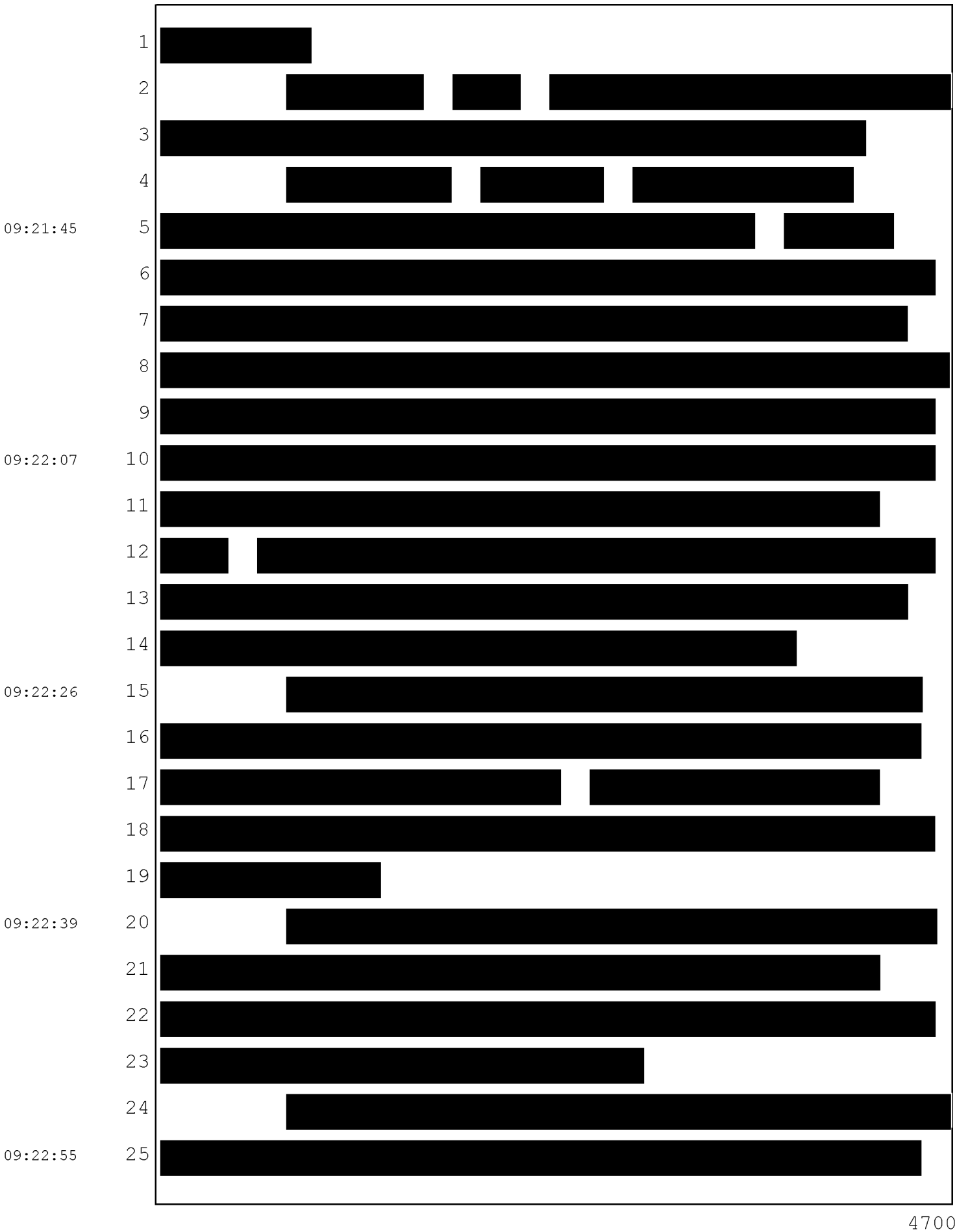
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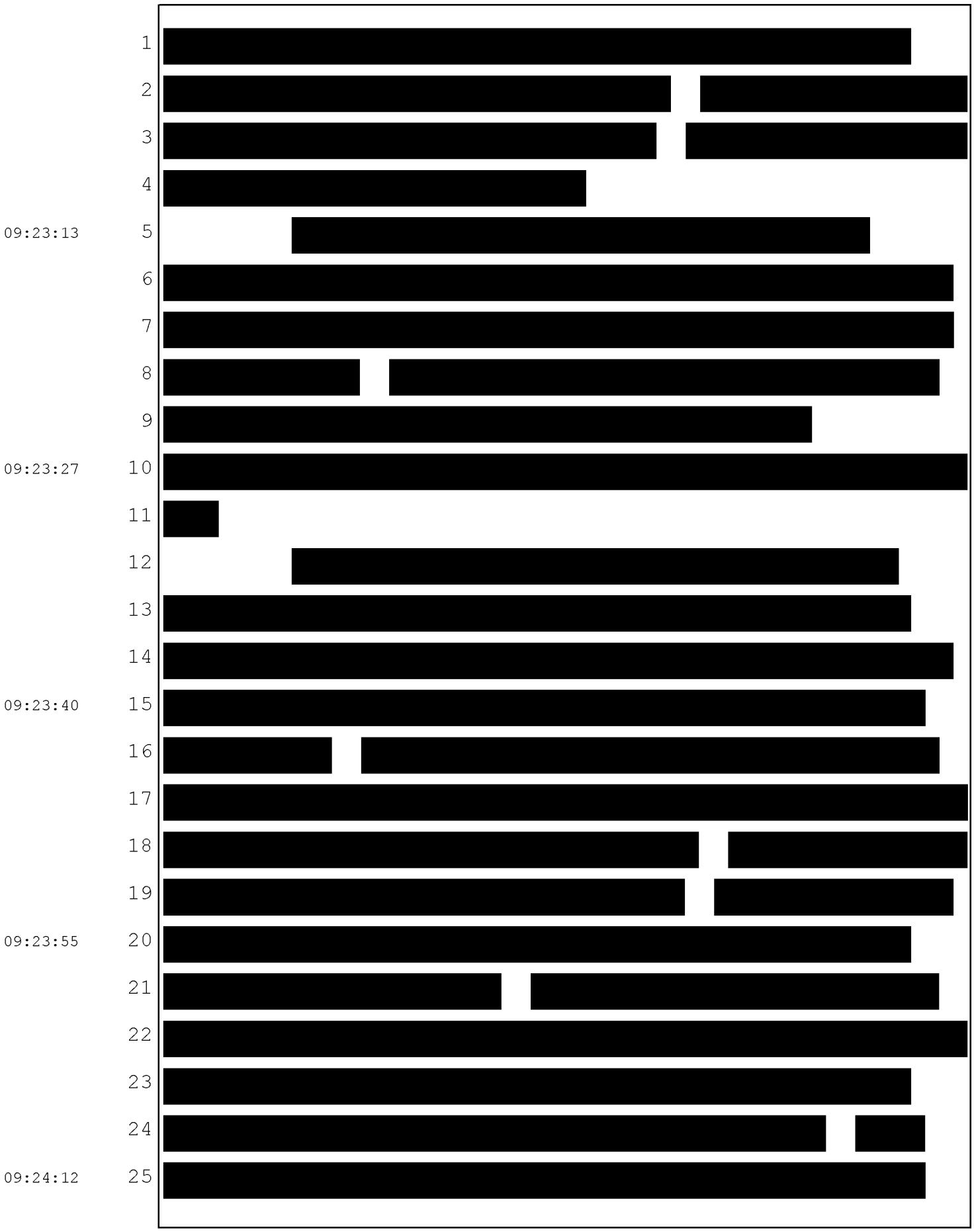
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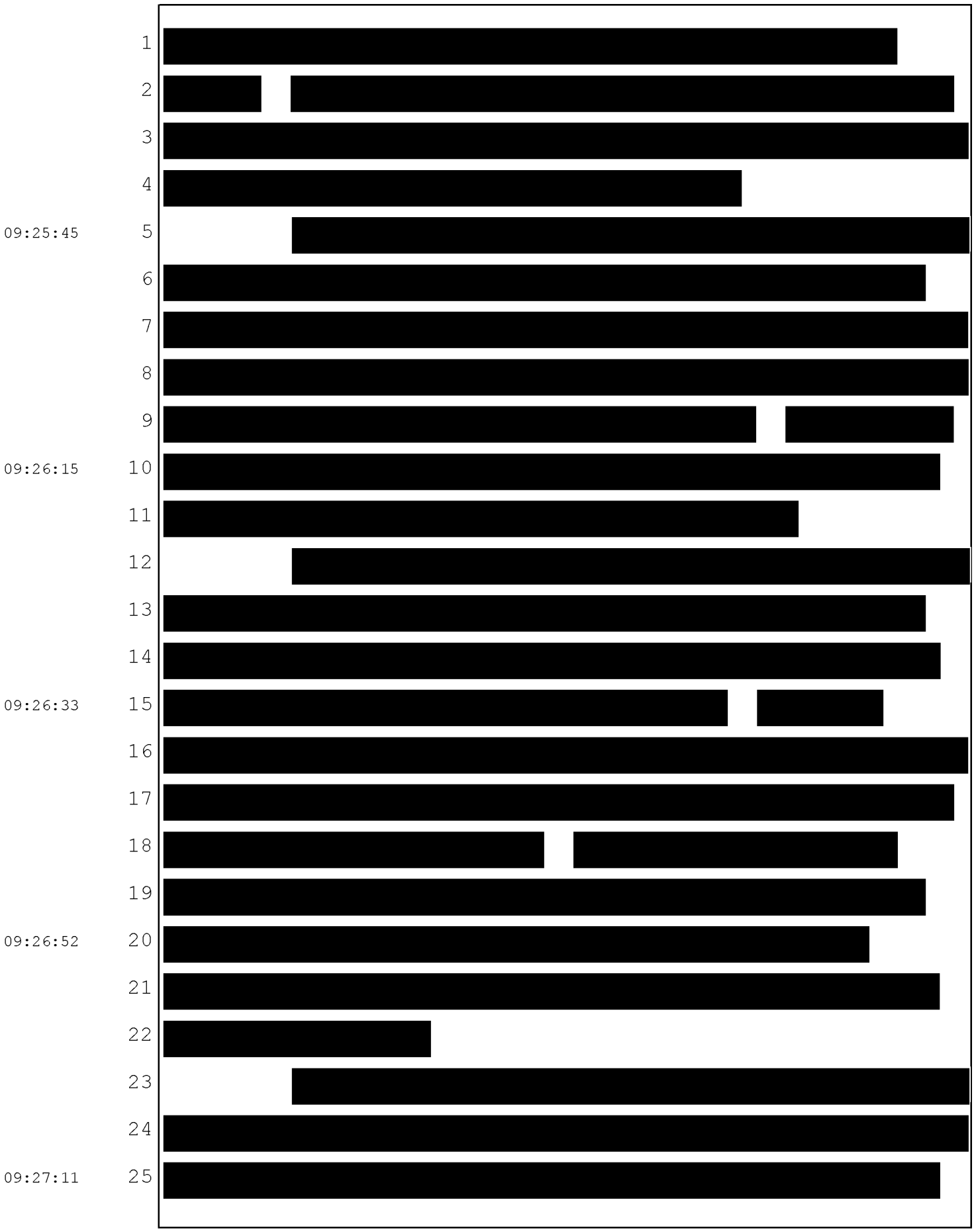
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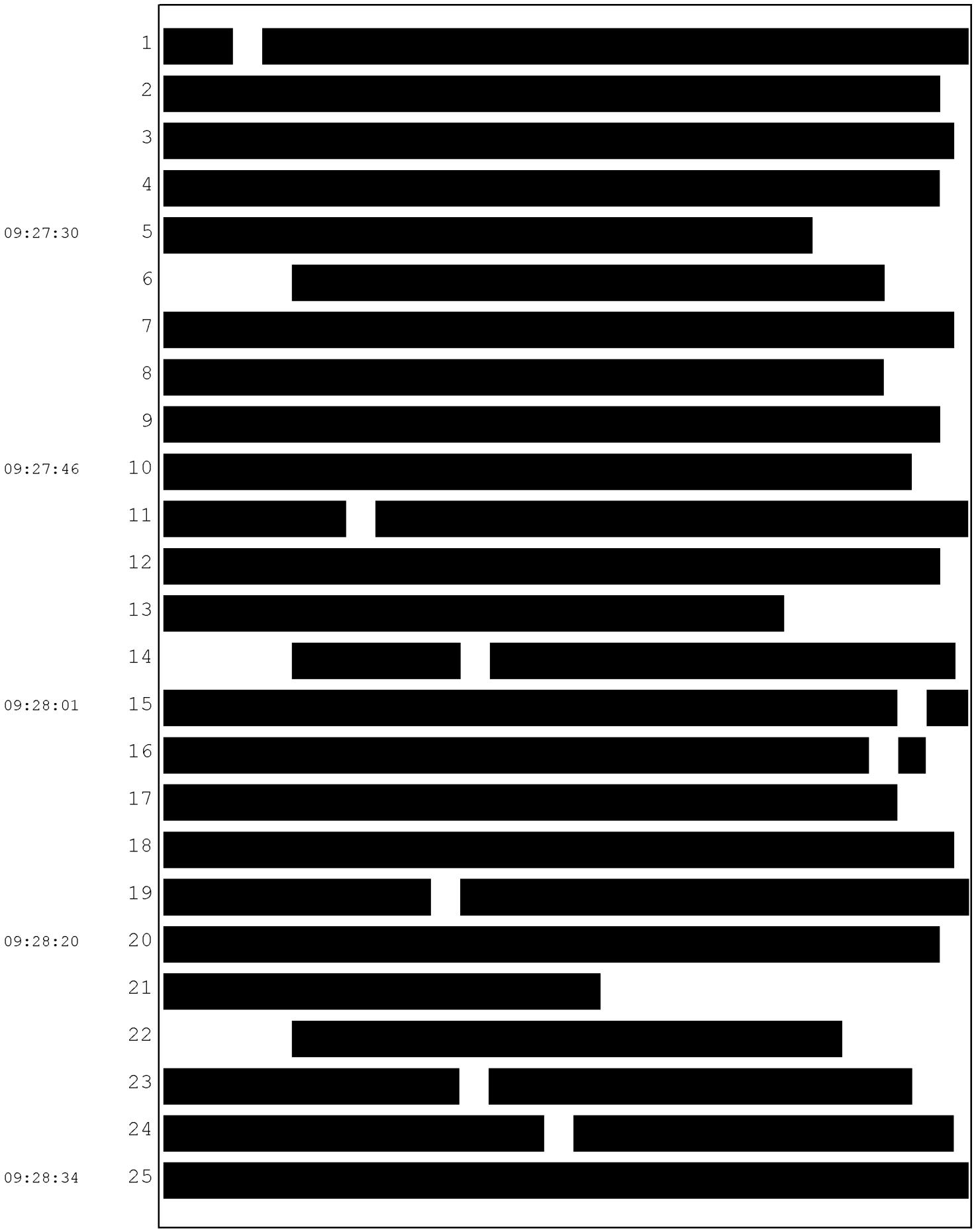
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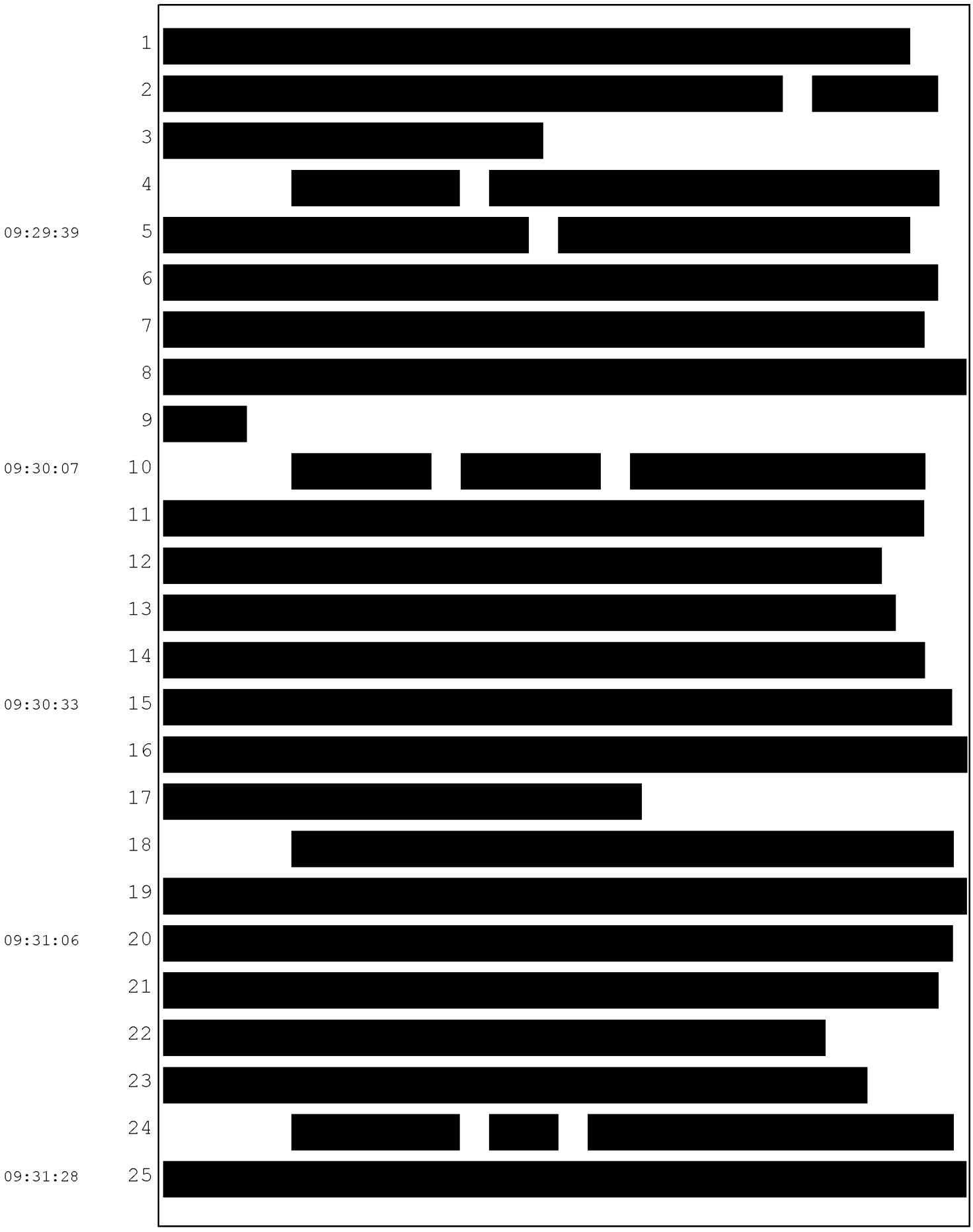
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[redacted]

(Jury enters courtroom.)

09:34:36 THE COURT: Welcome back, Ladies and Gentlemen.

All right. Today, then, we will continue with the defense case. So, Mr. Griffis, you may call your next witness.

MR. GRIFFIS: Monsanto calls Dr. Timothy Kuzel,

09:34:50 your Honor.

THE COURT: Very well.

Good morning, Dr. Kuzel. If you'd please step up here to the witness stand and remain standing while the clerk swears you in.

TIMOTHY M. KUZEL,

having been first duly sworn, was examined and testified as follows:

09:35:36 THE CLERK: Would you please state and spell your name for the record.

THE WITNESS: Timothy M. Kuzel, K-U-Z-E-L.

THE COURT: Thank you.

MR. GRIFFIS: May I approach with a binder for

09:35:48 Dr. Kuzel?

THE COURT: Yes.

MR. GRIFFIS: Thank you.

THE COURT: Thank you.

And, Mr. Griffis, when you're ready, you may proceed.

09:35:59

MR. GRIFFIS: Thank you, your Honor.

DIRECT EXAMINATION

BY MR. GRIFFIS:

09:36:01 Q. Dr. Kuzel, would you please tell the jury your occupation?

A. I'm a physician.

Q. And what kind of physician are you?

A. I'm a hematologist and oncologist.

09:36:09 Q. Where do you practice?

A. I am currently the chief of the division of hematology, oncology and cell therapy at the Medical School in Chicago called Rush University.

Q. And would you please describe your educational 09:36:22 background, sir?

A. Yes. I went to college and medical school at the University of Michigan starting in 1978. Graduated from medical school in 1984. I then moved to Chicago and did my residency and my hematology oncology fellowship at 09:36:41 Northwestern University, and I actually joined the

faculty there in 1990, and I was there until about 2016, when I moved over as the new chief at Rush University in Chicago.

Q. So you were a professor as well as a practicing physician at Northwestern University and then now at Rush University?

09:36:57

A. Right. I obtained the rank of professor of medicine at Northwestern, and I have the same rank at Rush.

Q. And how did your patience treatment duties evolve over that time period, sir?

09:37:06

A. So my research interests during my entire career has really been about novel treatments for cancer, and in particular, the use of immunotherapy to treat a variety of malignancies. We really focused on melanoma, kidney cancer and cutaneous T-cell lymphomas in my career. The lymphoma experience was largely driven by the fact that many of the drugs we use to treat the disease are immunotherapy agents.

09:37:24

Q. So immunotherapy is a common element in the cancers you're interested in?

09:37:46

A. Actually, exceedingly common today. Much less common many years ago, but it's become a real mainstay of the treatment of a variety of cancers today.

Q. And do you currently see patients?

09:38:00

A. I do.

Q. What type of patients do you see?

A. Again, predominantly those that are, sort of, in the area that I focused on in terms of treatment strategies, so melanoma, kidney cancer, prostate cancer and the skin lymphomas are probably the vast majority of my patients.

Q. Now, the jury's heard a lot about non-Hodgkin's lymphoma, and that's a large part of your patient population; is that right?

A. So the cutaneous T-cell lymphomas are, sort of, in the family of non-Hodgkin's lymphomas.

Q. Have you published on cutaneous T-cell lymphomas and mycosis fungoides, which is a --

A. Yes.

Q. -- subcategory of CTCL?

A. Mycosis fungoides and Sézary syndrome are a type of cutaneous T-cell lymphoma, and, yes, I have.

MR. GRIFFIS: Permission to put up Slide Number 1?

THE COURT: Any objection?

MR. DICKENS: No objection.

THE COURT: Very well.

Q. BY MR. GRIFFIS: So this is, sir, some titles from -- we're not going to go through these. It's just

to show some of the sorts of things you've been doing, some of the titles from some of your publications on cutaneous T-cell lymphoma and mycosis fungoides.

Is that what you mainly -- are those diseases mainly what you've published on with regard to non-Hodgkin's lymphoma?

A. Yes, almost exclusively.

Q. And how many publications total do you think that you have in peer-reviewed journals with regard to CTCL and/or mycosis fungoides?

A. Peer-reviewed journals, probably 50 to 75. Additionally, probably another 25 to 50 chapters, reviews, other kinds of publications.

Q. And you've been an investigator for clinical trials, sir?

A. Since I began my career, yeah. That's what you do in academic medicine.

Q. How many clinical trials have you been an investigator on?

A. Probably hundreds.

Q. And have you been a principal investigator for clinical trials?

A. I have.

Q. Would you tell the jury what a clinical trial is in a few sentences and what it means to be a principal

investigator?

A. Sure. So for patients with a variety of cancers, obviously you go see the physician. Many times there's a standard treatment approach that's appropriate
09:40:32 to receive that's been validated, studied and things are easy.

Unfortunately, sometimes there aren't things that have been validated and are straightforward and easy. And in that, sort of, setting we will often
09:40:46 discuss opportunities to participate in what's called a clinical trial.

Those usually involve some sort of either experimental new drug that's been developed for a disease, or it may be a combination of existing drugs,
09:41:02 perhaps, that are being tested for the first time in combination.

So as principal investigator, there's a variety of different, sort of, situations. You may actually write the trial elements yourself. And maybe it's done
09:41:18 at just one place, or it may be through what are, sort of, national -- what are called cooperative research groups. That might be a national trial that's looking to recruit thousands of patients, so you need to have lots of hospitals to participate to get that number of
09:41:36 patients. And some might be being driven by a

pharmaceutical company, because the purpose of the triad was to prove that the drug works and get FDA approval, so the drug would become part of the standard treatment approach.

09:41:51 Q. We've been talking in general terms about clinical trials, and you said you've been involved in quite a few. Have you been involved in clinical trials specifically for mycosis fungoides?

A. Yes.

09:42:00 Q. What kinds of treatments for mycosis fungoides have you participated in exploring through clinical trials?

A. Sort of the full gamut of what's been -- as an oncologist and hematologist, we use today.

09:42:13 So as I said, my interest is immunotherapy. So we've done a number of trials looking at drugs that stimulate the immune system to either treat or slow down mycosis fungoides.

I've done trials with chemotherapy drugs that 09:42:28 are based on, sort of, mechanisms of action that may be relevant to mycosis fungoides.

Less of the targeted agents, unfortunately, are relevant in terms of small or oral pill molecules. But nowadays we even have some targeted agents which attack 09:42:47 specific proteins on the surface of the tumor cells. And

I've done a number of those trials.

Q. Okay. Now, clinical trials are primarily investigating novel treatments and exploratory treatments. Apart from that, have you done research on mycosis fungoides?

09:43:04

A. Yes. Some of our publications -- we have a group at Rush, and we had a group at Northwestern. And some of the work that we did wasn't about developing a new drug or a new treatment. Some of it has been about trying to understand, perhaps, a side effect of treatment or something that we might call a correlative study, where we might not be testing a new treatment, but we might be drawing blood from patients and investigating their tumor cells in some fashion in the laboratory.

09:43:20

09:43:39

Q. Have you done research on the biology and genetics of mycosis fungoides?

A. Yes. But certainly in a more limited fashion than my work with treatment paradigms.

Q. And there's been a lot of work in the area of the genetics of mycosis fungoides with which you're familiar; is that right?

09:43:55

A. Oh, yes.

Q. Generally speaking, what are we talking about when we're talking about investigations of the genetics of mycosis fungoides?

09:44:03

A. Well, it's certainly evolved during my career. When I, sort of, started in this field, we actually didn't know much about the genetics of most cancers. We didn't have the tools to really study them and
09:44:22 investigate them.

Over the years, that's evolved. One of the breakthroughs was initially looking at things that are called karyotyping. And I'm sure every one of you has probably seen the TV commercials for 23andMe, the genetic
09:44:40 testing, where basically they look at your chromosomes.

And in cancer, you can look at the chromosomes the same way. And you are looking for recurring breaks, for example, or pieces of chromosomes that might be missing. So that was probably the first, sort of,
09:45:00 attempts to get into studying the genetics of this disease.

Much more recently, things have become much more sophisticated. And now you can drill down on specific genes, if you want, or you can do what's called whole
09:45:19 genome sequencing, where you literally sequence the entire DNA of a patient's tumor cell.

Q. And I think we've all heard of the human genome project, where they -- a whole human genome was mapped. That's actually, sort of, old news now.
09:45:44 That's the, sort of, technology or better

technology along the same lines but applied to tumor cells to see what the genetics of those look like?

A. Yes. Essentially similar.

Q. Okay. All right. How many new -- new mycosis fungoides patients do you see per year, on average?

09:45:57

A. Currently, I'm not as busy because of my administrative requirements, but I still -- probably still see anywhere from 20 to 30 new mycosis fungoides patients a year.

Q. And at the peak, how many were you seeing a year?

09:46:14

A. When I was busier clinically, I was probably seeing anywhere from 50 to 100 mycosis fungoides patients every year.

Q. Now, Rush is where -- what you would call a tertiary referral hospital; right?

09:46:26

A. It's an academy medical center, medical school with medical students, residents, et cetera.

Q. And tertiary means, kind of, third level, so it's not immediately obvious what that means. What is a tertiary referral center?

09:46:38

A. Yeah. I mean, tertiary sort of implies that it serves as a referral site for patients. Most tertiary hospitals have a primary care area around it, where people in the neighborhood go there for their healthcare.

09:46:56

The difference in a tertiary center is people will come from, you know, multiple counties away or even states away to come see physicians.

Q. So if I understand it correctly, and correct me if I'm wrong, if a patient develops a rare disease requiring some expert attention, like mycosis fungoides, they may first see a primary-level physician, like a family doctor or a general practitioner, who would see that there's a problem and perhaps not quite understand how to do it. They may refer them to someone more specialized. Sort of a secondary referral, like a dermatologist or an oncologist, and they may say, "I'm still not quite sure what's going on with you," and refer you to an academic center, where they specialize in that. And that would be someplace like Rush; correct?

A. Yeah. The patient flow is, sort of, like that. I think nowadays the dermatologists serve as, sort of, the primary stop for most of these patients, because they have a skin rash. And the local dermatologists nowadays are equipped to do skin biopsies and send them out.

So usually they get to the oncologist either in the community setting or in a referral center, because they've already been diagnosed in the community.

Q. Is Stanford also a tertiary referral center?

A. Absolutely.

Q. How would you classify Stanford among the world's research hospitals on the issue of mycosis fungoides?

A. Oh, the team that is at Stanford is known worldwide.

09:48:38

Q. And how about the team at Rush?

A. The team at Rush, probably not as much. The team at Northwestern was similarly known worldwide.

Q. Okay. And do you know Dr. Kim, one of the physicians who treated Mr. Johnson at Stanford?

09:48:53

A. I do.

Q. How well do you know Dr. Kim?

A. Very well. I've probably known her for 15 or 20 years. We've published papers together. I've seen her at numerous meetings and spoken at meetings with her.

09:49:05

Q. And papers you've published are on what subject?

A. Well, Dr. Kim exclusively would be on T-cell lymphomas, mycosis fungoides.

Q. Okay. That's what she does?

A. That's what she does. She's a dermatologist.

Q. And Dr. Richard Hoppe, how well do you know him at Stanford?

A. I don't know him nearly as well as Dr. Kim. I know of him, obviously. He's part of the team there. He's been there a very long time.

09:49:29

Q. What is your understanding of his role at Stanford?

A. He's one of the pioneering radiation oncologists in the field. Many, many, many years ago one of the, sort of, main treatments was a radiation treatment to the entire skin. And, really, Stanford was one of the few centers that, sort of, did it well, developed the treatment approaches that are used.

09:49:43

Q. What is the name of that treatment therapy?

09:50:00

A. Total skin electron beam radiotherapy.

Q. Is that something Mr. Johnson got from Dr. Hoppe?

A. He did.

Q. And is that called the Stanford protocol, the refinements that Dr. Hoppe made to that technique?

09:50:10

A. I mean, I think there's a number of people who do that treatment, and there may be subtle nuances in the way they do it. I don't know that I would call it the Stanford approach, necessarily.

09:50:29

MR. GRIFFIS: Your Honor, at this time I offer Dr. Kuzel as an expert in mycosis fungoides, cutaneous T-cell lymphoma, non-Hodgkin's lymphoma and oncology.

THE COURT: Any *voir dire*?

09:50:42

MR. DICKENS: Just real briefly, your Honor.

VOIR DIRE EXAMINATION

BY MR. DICKENS:

Q. Good morning, Doctor.

09:50:46 A. Hi.

Q. I'm David Dickens. I'm one of the attorneys that represents Lee Johnson in this case.

And just real briefly, you mentioned some of the various cancers that you treat in your current practice.

09:50:58 How big of a percentage is focused on T-cell?

A. Probably 10 percent or less.

Q. So 90 percent is on anything else that doesn't involve non-Hodgkin's lymphoma at all?

A. Yes.

09:51:10 Q. And you don't treat non-Hodgkin's lymphoma patients generally; correct?

A. No. I tightly restrict my patient population.

Q. So the -- you only treat the one subtype of -- or the subtype of T-cell lymphomas?

09:51:26 A. I see some cutaneous T-cell lymphomas that are different from MF and Sézary syndrome, but really restricted to that subject.

Q. Is the majority MF -- that's mycosis fungoides; correct?

09:51:39 A. Yes, MF. Sorry.

Q. And the majority you treat is mycosis fungoides of the T-cell --

A. The majority of the cutaneous T-cell lymphomas are mycosis fungoides.

09:51:49 Q. You mentioned the research you have done on treatment and genetics of T-cell lymphomas. Have you ever published on the causes of T-cell lymphomas?

A. In terms of?

Q. What causes T-cell lymphoma.

09:52:05 A. No.

Q. You have not personally published anything relating to the causes of non-Hodgkin's lymphoma, generally?

A. No.

09:52:11 Q. You haven't published anything on the epidemiological -- or any epidemiological studies on mycosis fungoides?

A. I have not.

Q. You agree you're not an expert in epidemiology

09:52:22 of non-Hodgkin's lymphoma?

A. I agree.

Q. And other than mycosis fungoides specifically, you're not offering an opinion in this case with respect to the causes of non-Hodgkin's lymphoma; correct?

09:52:34 A. Other than the cutaneous T-cell lymphomas, no.

Q. Okay. And you're not offering an opinion here that glyphosate or Roundup is associated with any other subtype, other than mycosis fungoides?

A. I am not.

09:52:48 Q. You mentioned Dr. Kim. Like you, she focuses only on T-cell lymphomas?

A. I think she does some other things, too. I don't want to pigeonhole her quite that much.

Q. Do you know?

09:53:01 A. I don't know.

Q. But is it fair to say the vast majority of her practice is related to mycosis fungoides and T-cell lymphoma?

A. I would say the vast amount of her practice that 09:53:14 I'm aware of is related to those.

MR. DICKENS: Nothing further, your Honor.

We have no objection to qualifying Dr. Kuzel.

THE COURT: All right. Then I'll accept Dr. Kuzel as an expert in mycosis fungoides -- I'm 09:53:24 mispronouncing that, I'm sure -- cutaneous T-cell lymphoma, non-Hodgkin's lymphoma and the other designated areas.

All right. You may proceed, Mr. Griffis.

MR. GRIFFIS: Thank you, your Honor.

DIRECT EXAMINATION (Continued)

BY MR. GRIFFIS:

Q. I'd like to talk about non-Hodgkin's lymphoma and mycosis fungoides in general, before we turn to more specific topics about Mr. Johnson.

09:53:37

MR. GRIFFIS: Could we have Slide 3 please put up?

Q. And, Doctor, would you please talk in real general terms first about what lymphoma is? Not even non-Hodgkin's lymphoma yet. Just lymphoma.

09:54:00

A. So lymphomas are a form of blood cancer. And the malignant -- or the cancer cell is a lymphocyte. So they tend to be in a number of different places. But, sort of, in the way back when, because they were in lymph nodes, they became called lymphomas.

09:54:23

Q. And what is the job or jobs of the lymphocytes?

A. So lymphocytes, they have a variety. They're part of the immune system, so they do, in fact, a lot of different things. There's a lot of different types of lymphocytes. So depending on the type of lymphocyte, they have different roles.

09:54:41

Q. And they circulate through the body?

A. Yes. They circulate in the bloodstream. They start in a variety of places. And some of them circulate always in your blood cells.

09:54:56

Q. And Hodgkin's lymphoma versus non-Hodgkin's lymphoma, what's the basic difference?

A. So -- so one of the earliest differentiators was based on the appearance of cells under a microscope. So
09:55:15 just -- literally just looked at the slides under the microscope. And there was a characteristic cell that was present in what became called Hodgkin's lymphoma.

And if you didn't have that characteristic cell, people tended to be pretty simplistic. They said: Okay,
09:55:31 that cell's not there, so everything else is a non-Hodgkin's lymphoma.

Q. It's a little bit of a historical accident that we have that big division right at the top; is that fair?

A. Yeah. The approaches are different, and the
09:55:43 treatment approaches are different, so it's okay.

Q. Still works?

A. It still works.

Q. Okay. 72,240 new cases in the US per year. That's a non-Hodgkin's lymphoma overall?

09:55:55 A. Yes.

Q. And then mycosis fungoides has a much lower incidence, sir?

A. Yes, much smaller.

Q. So your -- and CTCL, cutaneous T-cell lymphoma,
09:56:09 what percentage of cutaneous T-cell lymphomas are mycosis

fungoides cases?

A. So there are cutaneous lymphomas. And in that category, there are both what we call B-cells and T-cells. Mycosis fungoides is part of the cutaneous T-Cell spectrum. And probably the cutaneous T-cells make up about half of the cutaneous lymphomas. And the MF, Sézary syndrome probably make up two-thirds of the cutaneous T-cell lymphomas.

Q. So your focus on cutaneous T-cell lymphoma is a pretty narrow focus within non-Hodgkin's lymphoma; is that right?

A. It is.

MR. GRIFFIS: Let's have Slide 4 with the subtypes on it.

Q. So this shows -- and we're certainly not going to go through all of these -- a big division in non-Hodgkin's lymphomas between B-cells and T/NK-cells. And without turning this into an oncology lecture, could you just tell us broadly the difference between those two.

A. Well, obviously the biggest is right up at the top. Nowadays -- so if you go back to when I was in medical school, we just looked under the microscope, as I mentioned, at these. And the pathologist's eye was, kind of, what called lymphoma. He had no way or she had no

way of knowing if it was a B cell or a T-Cell.

As science evolved, we developed tools where we can actually now -- on the surface of lymphocytes, we can detect a whole -- a large number of different -- what are
09:57:53 called antigens or proteins that are on the surface of the cells.

So B-cells have a certain characteristic family of these proteins. T-cells have a different characteristic family of the proteins. So that became
09:58:08 another way to, sort of, split the area.

The field keeps changing, because the tools keep getting better. And as we develop new tools, now it's not just looking at the surface, necessarily, of the cells. We actually can look at chromosomes, genes,
09:58:26 fusions of different genes, which aren't supposed to be fused. And that -- actually, lets us drill down on all of these different areas.

Q. Sir, do you know Dr. Chadi Nabhan?

A. I do.

09:58:40 Q. How do you know him?

A. He trained under us at Northwestern.

Q. So were you one of his teachers at Northwestern?

A. I was.

Q. And Dr. Nabhan appeared here and testified. And
09:58:50 one of the things he says was that he specializes in

Hodgkin's lymphoma and non-Hodgkin's lymphoma, all of these together.

And your specialty is -- can we just call it mycosis fungoides, please? Mycosis fungoides, and then the slightly larger family of cutaneous T-cell lymphomas; is that right?

09:59:02

A. Yes.

Q. So how much narrower is your focus within the realm of lymphoma than Dr. Nabhan's, just as a matter of the numbers?

09:59:16

A. Well, I -- I didn't count this up, but it would be a fraction of obviously seeing all of these different kinds.

Q. Okay. Now, you talked about how the antigens and proteins on the surface of the cells can be used to sort it into B-cells and T/NK-cells. Does that sorting just give you the names of these particular subtypes, or are the subtypes different in ways that are important to you as the person who treats them?

09:59:29

09:59:47

A. The reason we do all of this, sort of, academic exercise isn't just because we want to publish papers or we want to try to really finely tune things. The different diagnoses are fundamentally approached in very different ways. They have very different prognoses. The drugs we use to treat them are radically different.

10:00:04

So for some of these, the treatment of choice is observation. For some of these, the treatment of choice is combination chemotherapy and immunotherapy with aggressive upfront treatment.

10:00:21 So the goal of this is to try to avoid over-treating patients that don't need to be treated and under-treating patients who maybe can be cured with aggressive therapy.

Q. Can you give us an example of some of the

10:00:36 subtypes up here having different symptoms than one another?

A. Well, sort of, it's easy on the left side. So the B-cell neoplasms, the vast majority of those present in lymph nodes. So the patient may feel lumps in their

10:00:55 neck or under their underarm or their groin. Occasionally, if the patients have internal lymph node swelling, they may have associated symptoms. Like fevers, night sweats, weight loss, decreased appetite.

The T-cell neoplasms can certainly present

10:01:16 similarly. Obviously the reason they're called cutaneous T-cell lymphoma or B-cell lymphomas is because for that subset they often present in the skin, not in the lymph nodes as, sort of, a first place they present.

Q. We'll get to this a little -- in a little more

10:01:34 detail later, but why do they present in the skin,

cutaneous T-cell lymphomas?

A. We talked a little bit about those, sort of, proteins on the cell surface. It turns out in patients with mycosis fungoides, they actually have some unique proteins on their cell surface that are associated with receptors that are on the blood vessels and in the skin, and they kind of lead to them extruding themselves out of the bloodstream into the skin.

10:01:49

Q. So these cells, the B-cells, the T-cells, the NK-cells, they all have functions within the immune system of the body, which includes finding bad things and seeking them out and killing them; right?

10:02:10

A. Right. So the reason we have these is because they're important to stay healthy. So B-cells are what make antibodies. So when you get a flu shot, what you're doing is you're trying to stimulate B-cells to make antibodies against a specific flu virus.

10:02:23

T-cells are a little different. T-cells are more engaged in, sort of, scavenging the body for other tumors that might be developing or scavenging for, sort of, unique organisms, like tuberculosis or fungal infections. But they both play a role, basically, in the normal human immune system.

10:02:41

Q. And as T-cells circulate in the body -- we'll stick with T-cells, because that's what we care about in

10:02:59

this trial -- how do they tell that they've found one of their targets?

A. There is something on every one of these kinds of lymphocytes that's called a receptor. So there are B-cell receptors and T-cell receptors.

10:03:15

In the normal person, you literally have millions and millions of different possible -- if you, sort of, think of it as a key in the lock, and the receptor is the lock, it's looking for its key.

10:03:32

And those T-cells kind of float around. And if they happen to run into that key, they come together, and it causes all kinds of internal signaling. And those T-cells then proliferate and grow and do their job, which is usually to eliminate the thing that had the key on it.

10:03:52

Q. And does that have something to do with a cell that becomes a mycosis fungoides cell changing its behavior from traveling around the body doing its job to seeking out skin?

A. So the receptors that lead to them being in the skin are different from the T-cell receptor.

10:04:07

Q. Okay.

A. The way the T-cell receptor becomes helpful to us is once that proliferation starts, you can -- actually using sophisticated lab tools, we can actually look for what are called families or clones of cells. And

10:04:24

normally you wouldn't have a clone that would show up.

Once a single cell becomes malignant and begins to proliferate, we can actually see that clone and measure it in the bloodstream or in a skin biopsy.

10:04:41 Q. Do different types of non-Hodgkin's lymphoma look different microscopically?

A. The different types of?

Q. Non-Hodgkin's lymphoma, the cells involved.

A. Right. Yes.

10:04:51 Q. The lymphocytes.

MR. GRIFFIS: Can we have Slide 5, please?

Q. And what does this slide show, sir, this slide of slides?

A. So this is a variety of different types of

10:05:05 lymphomas. Not all T-cell lymphomas. Some of these are B-cells as well. But this is basically what a pathologist would look at, sort of, as this most basic, sort of, first step in diagnosis.

A patient undergoes a biopsy on a piece of

10:05:23 tissue. They put a stain on it, which makes some things turn blue and some things turn red. And their eye is trained to look at these. And they're very good, and they can often look at just this alone, and say, "Oh, I think it's going to be a B-cell lymphoma or T-cell lymphoma."

Nowadays, in general, they would do additional testing to just prove that their eye is right.

Q. We can see that they look -- the various subtypes look different than one another when you look at them microscopically; right?

10:05:56

A. Yes. It general, they slightly have different -- many of these are issue based. The fourth one in the top row from the left is a blood smear. And, you know, some of these are historic names that have little hair-like projections, so it was called hairy cell leukemia. The one in the upper-left corner is mycosis fungoides. That's a skin biopsy. Again, because it's a rash, that's usually where the tissue is from, and the T-cells are distributed in the upper levels of what's called the dermis. And then they creep up into the very superficial layers of the skin. And in this case, they form a small cluster that's actually only seen in mycosis fungoides.

10:06:13

10:06:30

Q. Do the known causes of various types of non-Hodgkin's lymphoma for which there are known causes vary among the subtypes?

10:06:46

A. Yes. As a matter of fact, some of the subtypes are actually subtypes specifically based on some of the cases where we actually do know what's causing the lymphoma.

10:07:04

Q. Okay. Could you give some examples of some of the known causes of some subtypes?

A. Sure. So there is another form of cutaneous T-cell lymphoma that's called HTLV-1 related acute T-cell lymphoma leukemia. The reason it's called that incredibly long name is because HTLV-1 is a retrovirus. And it turns out that there's -- in the northern islands of Japan, the frequency of infection with that retrovirus is exceedingly high. And it turns out that's the place where you see most of those lymphomas and leukemias.

And so the epidemiology is what led to a suggestion that there was something in the neighborhood in the region. And, indeed, there's a retrovirus that causes it. And that retrovirus can be transmitted through the blood. We screen for that in blood donors, nowadays. It can be secreted through mother's milk to infants, and it causes, typically, in -- much later in life, people could get a form of lymphoma leukemia.

There's a form of B-cell lymphoma that presents in the stomach. That's related to the bacteria that causes ulcers. So patients will develop a marginal zone lymphoma in their stomach. We actually treat that now by treating the bacteria with antibiotics, and some patients will go into remission.

So it's those kinds of things where,

unfortunately for the vast majority, we don't have such elegant, sort of, data, and you can't show those same associations.

Q. Are some forms of non-Hodgkin's lymphoma
10:08:45 associated with a specific gene mutation or chromosomal mutation?

A. Yes. So there are some examples where the diagnosis is confirmed specifically because there's a very-well identified genetic chromosomal change, which
10:09:08 leads to a mutation or DNA change.

So a couple good examples, certainly there's a disease called CML, which is a leukemia. It's a blood disorder of leukemic cells, wherever every single patient has a very specific rearrangement in their DNA. So you
10:09:29 make that diagnosis, because you have that rearrangement.

There's a B-cell lymphoma called a follicular B-cell lymphoma, which has always a translocation. Part of chromosome 14 and part of chromosome 18 have broken and inappropriately come together. So when you look at
10:09:50 the chromosomes, you can see that that difference exists. And, again, it's only seen in patients who have that specific subtype of B-cell lymphoma.

Q. Now, we've heard that there is a lot of research with regard to mycosis fungoides on the genetic mutations
10:10:09 that are or are not associated with it. What has that

research found?

A. Well, unfortunately it has not found that single characteristic change in chromosomes or change in genes that everybody who's done that kind of study has been looking for.

10:10:30

So we're all looking for figuring out: Is MF like that follicle center cell in B-cell lymphoma, or is it not like that? And it turns out that any number of investigators have looked at this in different ways. And what we find is that depending on the geographic location and the people doing the study and the types of patients, there's a host of alterations in the tumor cells in patients with mycosis fungoides, but there's never a consistent finding. So that from one patient to the next, it's rare that you would see the same chromosomal or gene mutations or alterations.

10:10:46

10:11:04

Q. So scientists looked really hard but failed to find any particular gene mutation that is consistently associated with mycosis fungoides?

A. Yes.

10:11:21

Q. Now, you said there's a host of different -- when you look at someone with mycosis fungoides, you might find all sorts of individual issues. Why isn't that the answer, that it's all those things that produce the micronuclei?

10:11:33

A. So one of the hallmarks of any cancer is that they're genetically unstable. The cells grow typically at a faster rate than normal cells. And because of that, as they reproduce they tend to make errors in those reproductions.

10:11:54

And, therefore, it's not uncommon in any cancer to see a variety of different genetic mutations, alterations that are present. The tough part for the science is to understand what is just occurring because of these mistakes and which of those might actually be the mutation that actually leads to the cancer that was talking about.

10:12:14

So often these are just what are called passenger mutations. And they're present and there's actually often subclones where the dominant clone is now broken into different family units. It's like children of the original clone. And they've started their own based on a different mutation.

10:12:29

Q. So would it be right to say that when you're doing genetic analysis of cancer cells that have been around for a little while, you would expect to find all sorts of strange DNA and chromosome aberrations just because there's a lot of cell division and a lot of bad cell division going on because they're cancer cells, and what you're looking for is something that they all have

10:12:46

10:13:05

in common? It might be the parent mutation?

A. Correct.

Q. And you haven't found that with mycosis fungoides?

10:13:12 A. We have not.

Q. We've heard at this trial, sir, the hypothesis that genotoxicity -- an action of glyphosate causing DNA damage or oxidative stress, a more general stressing of cells in general -- causes DNA damage leading to

10:13:37 mutations, leading to non-Hodgkin's lymphoma.

Does that -- is that a likely cause of mycosis fungoides, given what you've just told us about the DNA?

MR. WISNER: Objection. Leading, compound.

THE COURT: Overruled. He may answer, if he

10:13:51 understands the question.

THE WITNESS: I think the fact that we don't have any single gene mutation or disturbance suggests that it may be that DNA mutations or alterations may actually not be involved in the process that leads to

10:14:09 mycosis fungoides at all.

Q. BY MR. GRIFFIS: And what's an alternative that's been considered?

A. So we've been talking a lot so far about what's known as genetics. So DNA level. It turns out there's

10:14:24 been, sort of, another field which has emerged over the

last decade or so, which is called epigenetics.

And epigenetics is a field that looks at a variety of cellular mechanisms that don't alter DNA but alter the ability of the cell to turn on the production
10:14:54 of protein, so that rather than being a DNA mutation, it may be an alteration in the ability of the cell to turn on or turn off a gene.

So many of our -- as you grow from a little, tiny embryo to a human being, there are different points
10:15:17 where certain genes are turned on and the protein product from that gene is important for a period of time. Eventually you don't need that anymore, and the cell has ways of turning back off that gene expression.

Epigenetics looks into the possibility that
10:15:36 disregulation of that on/off has occurred allowing cells to proliferate in an uncontrolled fashion.

As a matter of fact, some of our drugs in mycosis fungoides that we use interfere with some of those epigenetic mechanisms as a mechanism of action.

10:15:57 Q. Okay. And at the very highest level, an epigenetic cause would be something that, by definition, isn't a genetic cause. It isn't a DNA change --

A. Correct.

Q. -- or chromosome break change --

10:16:10 A. Correct.

Q. -- like we talked about with the follicular B-cell?

A. Correct.

Q. Is mycosis fungoides a skin cancer?

10:16:21 A. No. It's a blood cancer which shows up typically, in most patients, in the skin.

Q. And what is a skin cancer?

A. A skin cancer would be a cancer that would start in the structures and the cells of the skin. Like

10:16:39 melanocytes in the case of melanoma or the superficial layers of the skin in a squamous cell carcinoma.

Q. So something would go wrong with a cell in your skin, and it would start misbehaving in a way that produced other cells that were also misbehaving, and that

10:16:59 would eventually be a skin cancer; is that right?

A. Yes.

Q. And mycosis fungoides is a blood cancer or a systemic cancer. Would that be fair to say?

A. Yes. It travels through the bloodstream.

10:17:16 Q. And something happens to the cells that make them want to go to the skin in a way that they didn't before; is that right?

A. Yeah. There may be a role for T lymphocytes to circulate to the skin always. But in this disease, the

10:17:31 proteins that need to, sort of, guide you to the skin are

increased.

Q. Where in the body are the T lymphocytes normally?

A. So the place where all T lymphocytes start is there's an organ called the thymus. So when you're a baby, babies have a relatively large thymus. And that's where the T-cells, sort of, grow up and mature.

Over time, as you get older, the thymus shrinks and, kind of, disappears. And those T-cells, sort of, disburse and take up residence in the spleen, the GI tract, the skin, the liver, lymph nodes.

Q. So they're -- they're all over the body?

A. Yes.

Q. And what percentage of them, at any given moment, would be in the skin, if we know?

A. Well, in a normal setting, a tiny fraction of all of your T-cells in your body would be in the skin.

Q. If you had some immunological problem on your skin, they'd send some T-cells to deal with it. But other than that, they wouldn't have a particular reason to be there; is that right?

A. Correct. Correct.

Q. And then something happens to them that we don't understand that makes them want to go to the skin, and they proliferate there, and that's when we start to be

able to detect mycosis fungoides; is that right?

A. Correct.

Q. When was mycosis fungoides first identified in scientific literature?

10:18:56 A. It's largely thought that the first case was a case report in Paris. That was in about 1850.

Q. And, you know, when academics say "the first case," they mean the first one that's reported by them?

A. Exactly.

Q. The first one --

A. The first in the literature was reported in 1850.

Q. When was probably the first mycosis fungoides case in human history?

10:19:18 A. I would hazard to guess that just like many cancers, it's been around for eons.

Q. And, you know, obviously even this first reported case was a long, long time before Roundup or any glyphosate product was available; is that right?

10:19:33 A. Yes. Obviously 1850, the world was a different place.

Q. What causes mycosis fungoides?

A. We don't know.

Q. Are there any known causes of mycosis fungoides?

10:19:46 A. None that I'm aware of.

THE COURT: Doctor, is your microphone on? I want to make sure all the jurors can hear you.

THE WITNESS: Are you okay back there? I'll pull it closer, though.

10:19:59 THE COURT: All right. If any of you are having trouble hearing Dr. Kuzel, please just let me know. Raise your hand.

You may continue, Mr. Griffis.

MR. GRIFFIS: Thank you, your Honor.

10:20:08 Q. We've heard, sir, that mycosis fungoides is more likely to occur in African Americans. Is that a correct statement?

A. Yes.

Q. Okay. And are there any other demographic

10:20:22 statistical features of mycosis fungoides of that sort, like it's more likely in men than women or more likely on the East Coast or the West Coast or whatever?

A. There's a male to female predominance. There's an increased incidence in African Americans compared to

10:20:45 Caucasians compared to Asian people. There are actually certain clusters of what are called HLA types, which, again, relate to your descendants, which are slightly more common in patients than the random population.

Q. And could race be a proxy risk factor rather

10:21:10 than a direct risk factor?

A. Yeah, race usually isn't the cause of any of the cancers that we see. It's usually an association that, kind of, needs investigation to try to understand what -- the underlying reasons why there might be a certain predilection or more common presentation in a given race.

Q. If we look back at the chart, and we don't need to put it up, but --

MR. GRIFFIS: And you can take this slide down, actually.

Q. But if we looked back at that chart and you told us whether it was -- there was an elevated risk for that particular subtype for African Americans, Caucasians, Asians, et cetera, it would be different for each one; is that right?

A. Absolutely.

Q. And for any of them, is it thought to be because of the race or is it because of something that -- some unknown thing that is just a cofactor that race are associated with?

A. The cutaneous T-cell lymphoma in Japan is a great example. It far and away is more common in Asians than typically, of Japanese decent. It's not because they're Japanese. As a matter of fact, there's good examples of Caucasian people, predominantly United States service members, being in -- serving in those Japanese

islands and becoming affected and developing the leukemia lymphoma, so it's not got anything to do with being either Asian or Caucasian. It has to do with having the virus.

10:22:42 Q. And whatever it is here that's causing an increased incidence in African Americans as opposed to Caucasians as a percentage basis for persons of course -- I'm getting all wrapped up in my question.

First of all, let's understand what that means. 10:22:58 It doesn't mean that more African Americans get mycosis fungoides than Caucasians; right?

A. Well, there are more Caucasian cases of mycosis fungoides because there are more Caucasians, but statistically, African Americans have -- the 10:23:13 most frequent as a percentage of the population.

Q. Okay. Do you know of any evidence that being African American somehow interacts with other risk factors to make it more likely somebody is going to develop mycosis fungoides?

10:23:30 A. I am not aware of any work that's been done in that area.

Q. Now, you've treated quite a few mycosis fungoides patients. How many do you think you've treated over the course of your career, sir, new patients?

10:23:47 A. I mean, I've probably managed thousands of

mycosis fungoides patients during my career.

Q. I'd like to talk a little about your experience as a treating doctor with patients coming into your clinical, how they typically present.

10:24:03 In your experience, how do patients typically come to learn that they have mycosis fungoides?

A. So most of the time it's because they have developed a skin rash, which there's a variety of different ways this disease can present, sometimes

10:24:18 relatively mild, and the skin rash is almost irrelevant to the patient, other than perhaps a small area. It might itch a little bit, but it's often present for many years.

Sometimes there's a more generalized

10:24:33 presentation, so as you would imagine, people are concerned about their cosmetics. It causes itching, so they might be concerned about the fact that they're scratching all the time, so they go to a dermatologist.

Q. So they think, "I've got a rash. I wonder

10:24:49 what's causing this rash. Maybe it's the lotion I'm using and I should change to a hypoallergenic lotion"?

A. Right.

Q. And that doesn't work?

A. Right. Do I have ringworm? Do I have something

10:25:04 that's irritating my skin? Detergent? People try some

simple things, and then usually if it's not getting better and they're concerned about it enough, they go see a dermatologist.

Q. What is the rash?

10:25:17 A. Well, the rash can show up in a number of different ways. I mean, it can be something as simple as a small red patch on a patient's skin. It tends to present in what we call the bathing suit distribution, so it tends to, sort of, focused in the groin, buttocks, low

10:25:35 back, lower chest, breast area, which is good. It doesn't typically block the face and arms in many of the cases.

There are some patients who develop not just a red flat patch, but it might be a thicker lesion that we

10:25:51 call a plaque. There are some patients who, then, either will develop later in the disease or sometimes even early on more of -- you know, think of a small golf ball or a marble in the skin, and that would be a tumor stage lesion.

10:26:08 And then the reason there's something called Sézary syndrome is those are patients who uniquely present with total body, usually redness. They tend to have fairly intense itching, dry skin so that literally they'll leave pieces of skin where they've been sitting

10:26:30 from scratching. That group of patients often has blood

cells that we can look at under the microscope and see in the blood cells as well.

Q. Does -- in the early days of mycosis fungoides patients' rash, does it tend to wax and wane?

10:26:48 A. Especially for the patients with the small red patches. Sometimes it can be present for years. Sometimes it does get better with more moisture, moisturizing. Turns out one of the main treatments that we use for early stage mycosis fungoides is exposure to

10:27:08 ultra violet light, so not surprisingly, a lot of patients kind of figure out on their own that, "Gee, I have a mild rash. It itches, but thank goodness summer came," because they go out in the sun and actually sometimes that will make their rash look better, feel

10:27:27 better, so you can understand why patients don't immediately go rushing off to the dermatologist. They often are successfully able to self-medicate even sometimes for a number of years before the diagnosis is made.

10:27:40 Q. And does waxing and waning, kind of, delay diagnosis in some patients?

A. Well, it just results in patients not seeking medical attention right away.

Q. And would you say that mycosis fungoides is

10:27:52 undiagnosable for awhile by pathology?

A. Undiagnosable by pathology?

Q. I'm sorry. By biopsy.

A. By biopsy.

So mycosis fungoides can look like -- especially in the subtle forms, it can look like eczema, psoriasis, ringworm, so there's a lot of things that's -- it's one of the, I think, problems that general practitioners, family doctors have when they see these rashes. Even if you do a biopsy early on with a single small patch, the number of actual cancer cells in that small biopsy is often very small, and unless sophisticated testing is done, it may just come back as a, sort of, vague report that says -- one of my favorites is spongiotic dermatitis, which is a really vague, sort of, term which doesn't help a dermatologist very much on a biopsy.

Q. How many cells do you need to form a patch that you can reliably biopsy and diagnose?

A. Well, again, it depends on the tools that get applied, but in general, when any -- we've, sort of, learned from the solid cancer like lung cancer and breast cancer in the field of literature, that when you develop a tumor lesion that's about a centimeter in size, so a centimeter's about a little less than half an inch, already there's a billion cells in that tumor. So to be visible, you probably have to have a substantial number

of tumor cells interacting with the skin in some way.

Q. Does a patient get a rash as soon as there's one mycosis fungoides cell?

A. No.

10:29:45 Q. And we don't know exactly the number, sir, but how long would it take to go from whatever initially changes a cell into a mycosis fungoides cell to something that's clinically diagnosable?

A. Well, since these cells are also circulating, 10:30:01 you have to have enough of these cells to, sort of, get to even a single spot to have the rash. So it probably takes a long time. Usually years is what it takes for any cancer to develop from the first cell to when it becomes clinically detectable.

10:30:21 Q. Now, the simple big picture that we've heard a couple times during this trial is you start with a cell, it doubles, and now there are two mycosis fungoides cells. They double, and now there are four, et cetera. And I say it's simple because of some things you've told 10:30:40 me about, like, the body's immune regulation, which tends to slow down that process and make it move more slowly, but generally speaking, that's how cancer proliferates, right, by the doubling of the cells?

A. Correct.

10:30:58 Q. And to get to a billion cells, the 1 centimeter

patch in one spot that you told us about, how many doublings would that take?

A. If you do the math, it's about 30 doublings.

MR. GRIFFIS: Can we have Slide 7, please?

10:31:23 Q. So 30 doublings, 2 to the power of 30, is giving us just about a billion. What is the doubling time for non-Hodgkin's lymphoma?

A. So the doubling times of cancers in general have been estimated to be about three months, roughly.

10:31:44 That's, sort of, broadly taking in a variety of different cancer types. Things like -- on the short end of the spectrum are things like acute leukemia, which have probably some of the fastest doubling times we see. Some things very slow growing, prostate cancer for example,

10:32:06 might be six months. The non-Hodgkin's lymphomas, again, depends on the subtype, but certainly it would not be unreasonable to expect it to be in the one, two month range.

Q. One to two months?

10:32:18 A. Yes.

Q. So to get 30 doublings at the bottom end of that range, 1 month, would take 30 months?

A. Yes.

Q. And would -- I mentioned immune regulation.

10:32:32 Would you explain what that is and why that might slow

the process down even more?

A. So it makes this work more difficult because in the laboratory, you can just put one cell into culture, keep feeding it, and you can, sort of, do these kinds of doubling experiments relatively easily. Human beings aren't petri dishes. Human beings have a variety of natural mechanisms for eliminating cancers that form in their body, such as healthy T-cells. So this is not just a, sort of, linear process that you can work out mathematically.

As a matter of fact, in most modeling of human cancers, the, sort of, growth curve looks more like an S on its side, where there's a very long slow period where the cancer cells are adapting to the host. The host is pushing back. Mutations may be occurring within the first tumor cells in subsequent generations that may be enhancing the ability to grow. Ultimately, they really hit their stride, get into the niche that's really right, and they grow much faster for a period of time, and then they actually run into they're own unique issues. They often will out-strip the blood supply, so they can't feed themselves any longer, so that there's some cell death which occurs just because they're growing too fast. So growth tends to slow down again later on.

Q. So there are a number of things that happen in a

human body that don't happen in a petri dish --

A. Sure.

Q. -- that slow down these laboratory rates of doubling?

10:34:18 A. Yes. You can't -- in a petri dish or in a mouse model, you can't recreate the immune system's affect, because you don't have an immune system in a petri dish, and you can't necessarily work out exactly the ability to grow new blood vessels, change the microenvironment

10:34:41 around the tumor cells, because we don't have a microenvironment.

MR. GRIFFIS: You can take that down.

Q. So while we're talking about immune regulations, sir, we had testimony, I think it was about a week ago,

10:34:53 about a substance called Cyclosporin A, and the testimony was that when you give Cyclosporin A to patients, they can very quickly manifest a cancer, like in a few weeks or months. I forget the exact amount of time. Is that an example of a chemical substance causing cancer in

10:35:14 those patients, or is it something else going on?

A. No. Cyclosporin is not causing the cancer. As a matter of fact, in the transplant setting, what causes the lymphoma is typically the Epstein-Barr virus.

Q. So what is Cyclosporin used for?

10:35:31 A. Cyclosporin's a potent immunosuppressant drug.

Q. And it's given to transplant patients why?

A. So whenever you do a kidney transplant or a heart transplant, liver transplant or bone marrow stem cell transplant, the major issue for the patient is
10:35:49 rejecting the new organ, because the body's immune system is designed to identify foreign tissues and reject them.

So to overcome that problem, kidney transplant patients have to take a -- usually several different drugs. Cyclosporin was one of the first immune
10:36:12 suppressant drugs that was designed to keep the T-cells from attacking the new organ.

Q. And when you give Cyclosporin to a patient to suppress their immune system below the point of rejecting a foreign body that you're putting into them, essentially
10:36:32 what happens to make cancer suddenly appear?

A. So there's a fairly well-recognized complication of organ transplant that's called post-transplant lymphoproliferative disorders, and generally, that's because the Cyclosporine and the other drugs, steroids
10:36:52 often that we use, turn off the T-cells. Some patients who -- and we've almost all typically been exposed to a virus called Epstein-Barr virus as children. There are some people who the Epstein-Barr virus has been dormant in their lymphocytes, kind of like the chicken pox virus
10:37:13 can be dormant in their bodies.

When you knock that immune system out to protect the organ transplanted, those lymphocytes are altered by the presence of the Epstein-Barr virus, and they're driven to proliferate, and you end up with a lymphoma often, every one of which has evidence of the Epstein-Barr virus, sort of, sequences in them.

Q. So it's something that never would have happened if you hadn't suppressed the body's immune system?

A. Yeah, we really don't see Epstein-Barr-related lymphomas out of the setting of immune suppression.

Q. Getting back to your experience with patients, Doctor, where we started this, mycosis fungoides patients, do they usually think something in their environment or something that they're doing must have caused this rash they're suddenly having trouble with?

A. I don't think mycosis fungoides patients are any different than any other cancer patient, that they are obviously curious and want to know, "Why did I get this cancer," and they want to know if there's something in their environment that maybe their family also might be affected by.

Q. And what do you tell them when they ask you this question?

A. I tell them that, unfortunately, we don't know why anybody gets mycosis fungoides. There's no

scientific study that has shown a cause for the disease.

Q. Did you read the deposition of Dr. Kim in this case, sir?

A. I did.

10:38:42 Q. And I'd like to read you an answer that she gave at that deposition and tell me if that comports with your experience with your patients.

MR. DICKENS: Objection, your Honor. Hearsay.

THE COURT: Counsel, do you wish to approach?

10:38:57 MR. GRIFFIS: Yes, your Honor.

(Sidebar.)

[redacted]

10:39:16 [redacted]

[redacted]

[redacted]

[redacted]

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10:39:32 [redacted]

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10:39:40 [redacted]

[redacted]

10:40:04 (End sidebar.)

Q. BY MR. GRIFFIS: Have you reviewed the medical records in this case, sir?

A. Yes.

Q. And you reviewed the medical records for what purpose?

10:40:16

A. Just to understand what -- I think what's going on in the patient's, sort of, course of disease, which practitioners he'd seen, what treatment he was receiving.

Q. And you understand, of course, that an allegation in this lawsuit is that glyphosate or glyphosate-based herbicides caused Mr. Johnson's mycosis fungoides; is that right?

10:40:31

A. Yes, that's what I understand.

Q. When you were reviewing the medical records, did you see any of the treating physicians give any sort of opinion that glyphosate or glyphosate-based herbicides were a cause of Mr. Johnson's mycosis fungoides?

10:40:42

A. I did not.

Q. Now, it's been suggested, sir, that if a patient is using any substance that might possibly cause cancer

10:40:59

and they're a patient of yours, you should tell them to stop to be safe, because it's good to avoid things that might cause harm.

A. You mean a known substance?

10:41:16 Q. Well, let's talk about that.

A. Okay.

Q. If -- and no, I don't mean a known substance. I don't mean a smoker with lung cancer asking you if they should stop smoking, but a patient who says, "I'm exposed

10:41:32 to this chemical. I don't know if it might be causing my cancer. Should I stop using it?" What do you tell a patient like that?

MR. DICKENS: Objection. Incomplete hypothetical.

10:41:40 THE COURT: Overruled.

You may answer.

THE WITNESS: I'm sorry?

THE COURT: You may answer.

THE WITNESS: I usually tell them that I -- if

10:41:49 there's no evidence that that chemical has been proven to affect them in some way that would either be adverse for the treatment drugs, perhaps, that I might want to give or proven that it somehow changes their disease, I usually tell them that they should continue to live their

10:42:10 life the way they wish to live their life and need to

live their life.

Q. BY MR. GRIFFIS: And why is it that you don't just tell them, "Don't do this. Don't do this. Don't do this," as a precaution?

10:42:21 A. Because I would never know when to stop saying, "Don't do this." Without some scientific evidence that a particular issue is either affecting the treatment or affecting the disease, where do you stop?

Q. Do you use Roundup yourself, sir?

10:42:38 A. I do.

Q. And what precautions do you take when you use it?

A. None.

Q. How frequently do you use it?

10:42:46 A. I typically use it in the, sort of, spring, summer, when I start getting weeds in my driveway.

Q. It's the commercial hand-spray version?

A. Yes. I use the generic version.

Q. Now, you didn't get to examine Mr. Johnson, but 10:43:03 you reviewed his medical records, as we just discussed. If you had examined him, if he had come to you or you had come to him out here in California and examined him, without running any lab tests, what could you have found out from doing that examination?

10:43:21 MR. DICKENS: Objection. Calls for speculation.

THE COURT: Overruled.

He may answer.

THE WITNESS: I mean, I think the medical records are pretty detailed in terms of what I would have expected to see. I would have expected to see a, sort of, younger, middle-aged gentleman with a fairly diffuse rash, with some evidence of probably at least plaques, maybe even some tumors, depending, I guess, on when I would have examined him and maybe some palpable, touchable swollen lymph nodes.

Q. BY MR. GRIFFIS: For example, could you learn anything about the cause of a mycosis fungoides patient, or Mr. Johnson specifically, their illness by doing an examination?

A. No, not on a routine physical examination, certainly.

Q. Is there a lab test that could tell you the cause of a particular patient's mycosis fungoides?

A. No standard lab test that I'm aware of that even tries to address that question.

Q. We've heard testimony that mycosis fungoides is normally indolent, and is that correct?

A. Again, that's one of the reasons why we do what's called staging. At the time of diagnosis of cancer, we put together a number of features of the

cancer to try to put them into what we call a stage, and prognosis is driven by the stage at diagnosis.

Patients with the early stage of MF actually have a natural life expectancy that's the same as if they were never diagnosed with MF, so I think we could say that's an indolent form of mycosis fungoides. Patients who may present with more extensive disease tend to have some limitation on their life expectancy because of it.

But for an individual patient, you really could never use absolutes. These are just, sort of, population-based estimates. Some patients always do better than you think. Some patients always do worse than you think.

Q. Let's back up a step and talk about the term "indolent." What does that mean?

A. Well, indolent just means that it's relatively slow growing.

Q. Okay. Relatively slow growing.

And overall, is mycosis fungoides generally indolent?

A. Well, the vast majority of patients who are diagnosed with MF are diagnosed with early stage disease, so many people view this as, including grant-fund agencies, as, sort of, an indolent disease process that doesn't need a lot of funding.

Q. So the normal progression, then, is from indolent to less indolent as the disease progresses?

A. No. There's a lot of patients whose it's indolent, indolent and remains indolent, and they die of something else.

10:46:08

Q. It's been suggested, sir, that Mr. Johnson's case of mycosis fungoides is unusual, that mycosis fungoides is supposed to be indolent and stay indolent, but his is super aggressive, moving very fast, and that he's unusual, an outlier in some ways. Is that accurate, in your experience of mycosis fungoides patients?

10:46:22

A. He was diagnosed with a more extensive skin stage of disease. So I wouldn't say that that's really an outlier. I mean, he was actually still -- on the staging system was, kind of, on the lower end of the staging system at presentation.

10:46:39

Q. Is there anything about his case, in your review of all the medical records, that makes him stand out as an unusual mycosis fungoides patient?

A. No, not particularly.

10:46:55

Q. Now, what is the process, the cellular process, by which mycosis fungoides becomes more aggressive? And let's specifically talk about large cell transformation. What is that?

A. So large cell transformation is not, sort of,

10:47:14

why MF becomes more progressive. Large cell transformation is a pathologic term. It just essentially quantifies or counts the percentage of larger malignant cells in a biopsy. If it reaches a certain point, it's
10:47:38 called large cell transformation in that particular lesion.

Now, there's been a variety of studies that have looked at patients' skin biopsies and tried to estimate if you see that, do those patients do worse or do those
10:47:52 patients do better than if you don't see it? And I think there's a mixed bag on that. There are some people who have found that leads to a shortened survival time. There are other investigators who reported the opposite. So I think it's something you think about when you do a
10:48:09 biopsy if you see that.

Q. You're one of the authors of one of the main and most recent papers on life expectancy in association with various indicators like large cell transformation; is that right?

10:48:23 A. Yes.

Q. And it was suggested, sir, that once mycosis fungoides -- this is something that Dr. Nabhan said -- becomes aggressive, it's wrong to say that it was ever indolent. Is that a statement that makes sense to you?

10:48:40 MR. DICKENS: Objection. Misstates testimony.

THE COURT: Overruled.

You may answer.

THE WITNESS: Yeah, I think that it isn't that you were somehow wrong in thinking of it as indolent. As I said, in a lot of the studies that have looked at the genetics of this disease, we find a lot of mutations that pop up this different patients. It may well be that a patient, unfortunately, was unlucky enough to have a mutation develop in a more important or less important signaling protein, and that's why that patient, normally, we might have thought was going to be indolent becomes more aggressive. It may be they don't respond well to treatment as we thought.

MR. GRIFFIS: Would this be a good time to take the morning break, your Honor?

THE COURT: Yes.

Ladies and Gentlemen, let's take the morning recess. We'll be in recess for 15 minutes and resume again at five after 11:00. Thank you.

(Recess.)

THE COURT: Welcome back, Ladies and Gentlemen. Dr. Kuzel remains under oath.

And Mr. Griffis, you may proceed when you're ready.

MR. GRIFFIS: Thank you, your Honor.

Q. Dr. Kuzel, you prepared with us a timeline of some relevant events in Mr. Johnson's medical history?

A. Yes.

MR. GRIFFIS: Can we have Slide 9 on the screen, please.

Q. And we're going to look at some medical records about this, but let's run through what's up here?

Would you lead the jury through this timeline?

A. So as I reviewed the medical records, there were a number of different practitioners who described the first onset of a skin rash on Mr. Johnson in the fall of 2013. He then -- it's described in some of those records as having persistent, sometimes better, sometimes worse of this rash, and then subsequently again he sees a dermatologist in August of 2014 and a biopsy is done and a diagnosis of the T-cell lymphoma is given.

He then is referred to a number of the larger university settings here in San Francisco and ultimately begins what's fairly standard treatment for early stage mycosis fungoides what's called narrow-band UVB. It's a form of ultraviolet light not dissimilar from a tanning bed, but different in terms of the spectrum of the light. He uses that for a period of time. From what I could read, didn't sound like he had a dramatic improvement to the UVB light, has a biopsy of a lesion on a leg which is

a squamous cell carcinoma. I think kind of changes referral centers and is seen at Stanford and Dr. Kim and Dr. Hoppe who agree with these biopsies to reconfirm the diagnosis and recommend starting total skin electron beam
11:09:03 radiotherapy.

Q. One moment, sir. When you say reconfirm the diagnosis, are you talking about the T-cell lymphoma and mycosis fungoides diagnosis?

A. Yes.

11:09:12 Q. Go on.

A. And he starts total skin electron beam, which is sort of a Stanford preferred option and gets a course of that which is usually about 8 to 12 weeks, and then sounds like he gets some benefit but not complete
11:09:35 disappearance. Doesn't get a second course, which it seems Dr. Hoppe wanted to do, and ultimately then starts a relatively new drug which is approved for mycosis fungoides called been Brentuximab. That's an antibody which is linked to a chemotherapy drug, and the antibody
11:09:56 targets a protein on the surface of the cancer cells. And does fairly well with that treatment.

By description, develops chronic side effects from that treatment, so it's discontinued. And then when his disease regrows, recurs, is more symptomatic again.
11:10:19 In the fall of 2017, starts with treatment with a drug

called Pralatrexate, which is a chemotherapy drug. And from what I could see sounds like he has actually a very nice response to a couple of cycles of that therapy and then he stops treatment around early spring of this year.

11:10:38 And that's pretty much most of the records I had.

Q. What is the meaning of complete remission?

A. So as oncologists, we talk about the response to any treatment. There is sort of no response, there's

11:10:54 stable disease. There's what we call a partial remission, which is where patients improve substantially. Usually, it's kind of 50 percent or better. And then there are patients who are fortunate to go into what's called a complete remission, which means you can't

11:11:15 visually or lab testing or CAT scan testing see any evidence of their disease, so that would be called a complete remission.

Q. Okay. The first flag here, the first line -- the first onset of rash being somewhere in the fall of

11:11:34 2013, you said there were multiple providers' records on that point. So let's look at a few of those, sir. In your binder would you turn to defend Exhibit 2297, also tab 2297, and the first page of the records which is page 3 on the Bates stamp?

11:12:02 And would you identify that record, please?

A. Make sure I'm on the right page. Which page?

Q. These have -- the first two sheets of paper are just what was produced to by the people who gather the records, and sometimes it's a lawyer thing. This is the
11:12:18 first page of the actual medical records that I'd like you to look at 2297 and the Bates stamp at the bottom -- the very bottom, the number here is 2297_0003.

A. Okay.

Q. Would you identify that record, please?

11:12:36 A. This looks like it's a note from the University of California San Francisco Medical Center.

Q. Okay. By what doctor?

A. Dr. Ricardo Gonzalez.

Q. Is it on August 26, 2014? It's right next to
11:13:01 his name.

A. Yes.

MR. GRIFFIS: So I move to publish 2297_0003, your Honor.

MR. DICKENS: Objection, your Honor. Hearsay.

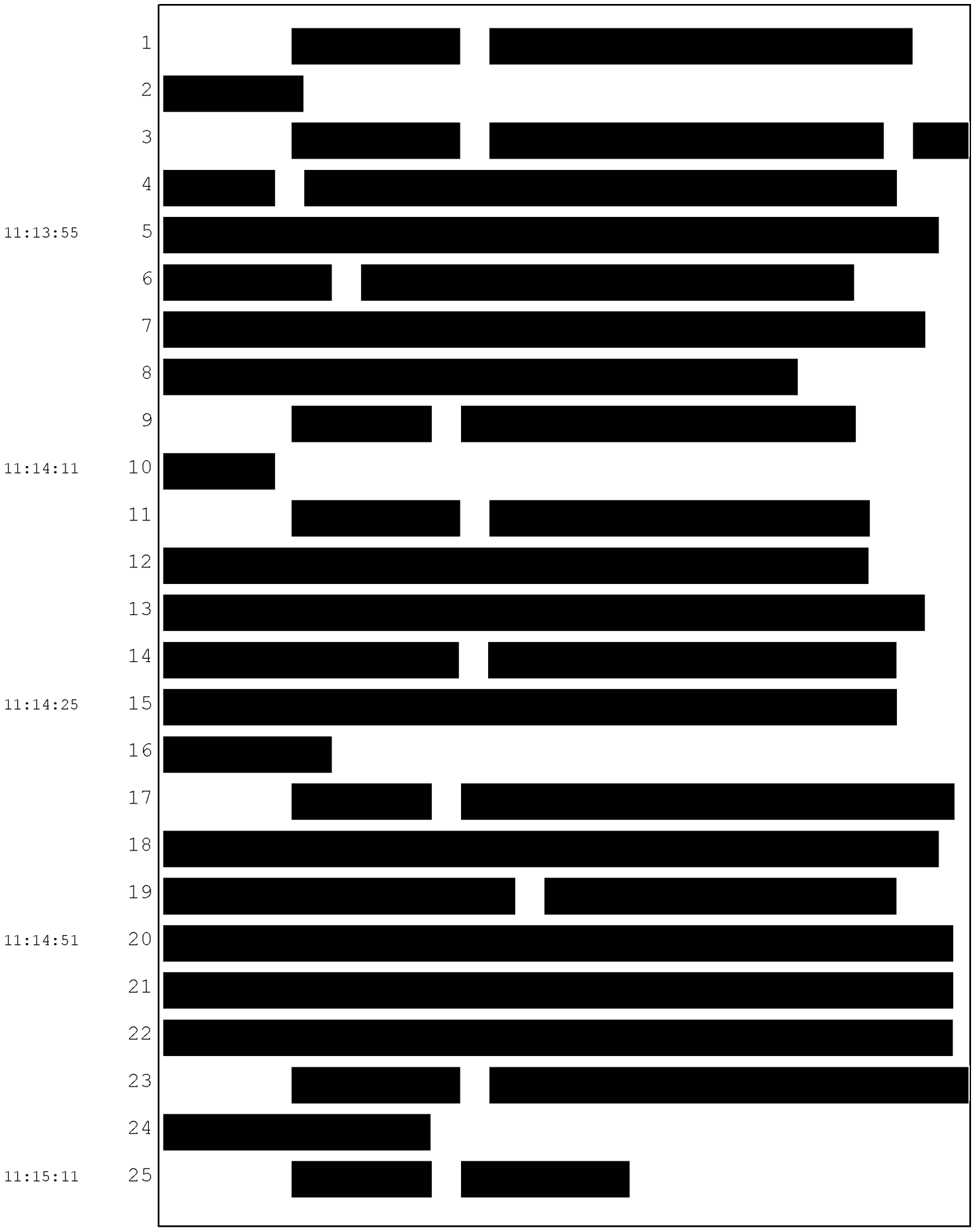
11:13:13 Could we have a sidebar?

THE COURT: Yes.

(Sidebar.)

[redacted]

11:13:45 [redacted]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(End sidebar.)

11:15:45 THE COURT: You may resume, Mr. Griffis.

Q. BY MR. GRIFFIS: We're not going to read to the jury from this record, all right, or show it. We're looking at Dr. Roberto Rafael, Ricardo Gonzalez's August 26, 2014, record, and this is one of the ones you relied 11:16:03 on to conclude that Mr. Johnson's rash dates back to fall of 2013; right?

A. Yes.

Q. Okay. And without reading anything from the record, what is it about this that supports your 11:16:23 conclusion that Mr. Johnson's rash dates back to the fall of 2013?

A. Well, the medical records in multiple places give a history of a rash that started with that time course based on, presumably, discussions with the patient 11:16:43 and describe kind of a gradual course of rash getting a

little better, getting a little worse. A general practitioner tries some interventions and then refers him to a dermatologist.

Q. And when you say gives a history, what is a history to a treating physician?

A. So as part of any doctor's visit, the first thing that usually happens is you sit down with the doctor and tell him why you're there and what has been going on, what the problem is. And usually they'll ask you about, you know, when it started, things that might have happened to you that might relate to that in a fairly standard fashion, and they write it down in the medical records.

Q. And on an issue like how long a patient's had a rash, you're kind of going by what they tell you; right?

A. Yes. I mean, there's nothing else to go by usually.

Q. Did you also rely on this record on the issue of the temporality of the rash, i.e., whether it was there continually or whether it was coming and going during this early time period?

A. Yes, I did.

Q. And which of those did you conclude from what's related in this record?

A. Well, it seems once it started, that it just

gradually was present for most of that year would be the way I would interpreted this.

Q. If you take a look at the start of the next paragraph, sir, does that refresh your recollection about temporality, the start of the second paragraph 2297_0003?

11:18:32

A. I'm sorry, what was the question?

Q. Does that shed any light on what you took from this record on the issue of temporality of the rash, by which I mean not when it started but how it was behaving once it started in terms of being there constantly at the same time intensity or coming and going or something else?

11:19:00

A. Yes. That would have been the kind of thing I would have used.

Q. And which was it? There continually or coming and going or something else?

11:19:13

THE COURT: You can answer.

THE WITNESS: I don't know how I can answer that. Can I cite the medical records or only in general terms?

11:19:30

Q. BY MR. GRIFFIS: You can pick one of the options I just gave you.

THE COURT: Just answer the question. You reviewed the medical records, so you can just answer.

THE WITNESS: I don't want to do anything I'm

11:19:38

not supposed to do here.

THE COURT: That's fine. You can answer based on your understanding.

THE WITNESS: Could I have the question again?

11:19:46 Q. BY MR. GRIFFIS: Yes, sir. I'm trying to ask them carefully. This line that we're looking at starting in the second paragraph -- and you've looked at all the medical records. I'm just pointing you to one here.

But does this refresh your recollection as to

11:20:03 what the medical records report about the behavior of this rash once it started manifesting on the issue of whether it appeared and then was there continually throughout a period of time or whether it was coming and going or whether it was exhibiting some other pattern?

11:20:20 A. My interpretation would be that some aspect of the rash was there throughout the entire continuum.

Q. Okay. Let's turn to 2294 in your binder. Exhibit 2294, and these are Kaiser Permanente records from Dr. Ofodile, and would you find at the very bottom

11:21:01 Bates Number 2294_0123?

A. Yes.

MR. GRIFFIS: I move to publish this record, your Honor.

MR. DICKENS: Objection. Hearsay, your Honor.

11:21:14 THE COURT: Again, he can answer questions based

on his review of the records, what his understanding of the patient's prognosis was.

MR. GRIFFIS: Yes, your Honor.

Q. BY MR. GRIFFIS: So this is from -- the last record we were looking at was from UCSF Medical Center. This is from Kaiser Permanente, a different institution. And the date is what in the upper left-hand corner?

A. I believe it's October 3rd, 2014.

Q. And the provider is Dr. Ofodile?

A. Yes.

Q. And when you look at the history that she took in October of 2014, is that something that you relied on for your conclusion that the start of Mr. Johnson's rash was the fall of 2013?

A. Yes. The history I took from this note was consistent with the previous history.

Q. And sometimes doctors when they're doing -- when they get to the history and physical part, look at a previous note and cut and paste the information from the previous note into this note. Would that apply to either one of these records?

A. Cutting and pasting implies you're sharing the same electronic medical tool that you can actually cut and paste. So I don't know which electronic medical records they used. I don't know that they share the same

tools, so I'm not sure "cutting and pasting" would be the exact term I might use.

Q. Okay. And did these physicians use different language in describing the history of the rash?

11:23:08 A. Yeah. There are some differences in the, sort of, description that's in the two notes.

Q. And did you form a conclusion as to these records, and the other records we'll be looking at, as to whether some of the multiple reports putting the rash

11:23:33 back in the fall of 2013 were cut and pasted from one another.

Did you think they were or not?

A. No. I'm assuming that the practitioner took an independent history and physical and reviewed records on

11:23:50 the outside but generally would confirm things with the patient.

Q. Would you turn to 2285 Stanford records in your binder -- Exhibit 2285 -- and find the Bates number at the very bottom 0007?

11:24:20 A. 007?

Q. 0007, yes.

A. No. Mine goes from 001 to 0064.

THE COURT: Which exhibit number are you in?

MR. DICKENS: 70.

11:24:46 MR. GRIFFIS: 2285. I've also got seven.

Q. The Stanford record with 0007 at the end is a record from Dr. Kim; correct?

A. Yes, this one is.

Q. Okay. And what's the date on it?

11:25:24 A. March 2nd, 2015.

Q. And it's one of the records that you reviewed; correct?

A. Yes.

Q. And based on what Dr. Kim reports in the history

11:25:37 section or what was reported to her, where would Mr. Johnson's rash have begun?

A. Where or when?

Q. When?

A. Again, in the fall of 2013.

11:25:59 Q. And do you have page 89 in that Tab 2285?

A. Which number?

Q. The same one I asked you to open, 2285. Oh, page 89.

A. Thank you.

11:26:14 Q. The very bottom, 0089, the record from Dr. Hoppe.

A. No. Mine ends at 0074 -- sorry, 0076.

Q. The Dr. Hoppe from November of 2015?

A. Yes, it is.

11:26:45 Q. And where does that history place Mr. Johnson's

rash in time, sir?

A. Again, in the fall of 2013.

Q. And, again, was it your conclusion in reviewing these records that these were just people cutting and pasting from one another or people taking independent histories?

11:27:01

A. Well, again, cutting and pasting you can usually identify because the exact same language or phraseology are exactly the same. In every one of these notes, there are differences in the verbiage and the descriptors. So presumably they got that new information or different information from somewhere, and that's usually the patient.

11:27:20

Q. And the normal practice would be to at least confirm information from previous records of the patient?

11:27:34

A. Yes.

Q. So taking all the records together, sir -- and you reviewed all of them in this case -- what was your overall conclusion about the time when Mr. Johnson's rash began?

11:28:00

A. Well, I think -- I think probably the fall of 2013.

Q. I'd like to talk for a moment about the squamous cell carcinoma which was diagnosed in March of 2015 and removed pretty shortly thereafter. I think it was

11:28:18

actually removed the very same month, wasn't it?

A. Yes, and that would be typical.

Q. You want to get those off quickly.

It's been suggested that the squamous cell carcinoma was caused by his treatments with UVB phototherapy. And UVB phototherapy is a possible cause of squamous cell carcinoma; right?

A. Yes.

Q. Do you believe that it's likely that the UVB phototherapy caused this squamous cell diagnosis?

A. I don't.

Q. Why is that?

A. Because generally when you see squamous cell carcinomas as a complication of narrow-band UVB, it's usually in patients that receive narrow-band UVB for many years and it's usually something that manifests 5, 10, 15 years out. It's actually very unusual in an African-American because they have darker, pigmented skin so that it even probably requires more UVB therapy rather than less compared to a very light-skinned Caucasian patient.

Q. So whatever caused this squamous cell carcinoma, nobody thinks it's related to the mycosis fungoides as far as you know; right?

A. As far as I can tell.

Q. One's a skin cancer that's caused mostly by sun

and one is a non-skin cancer, as you explained at some length, for which we don't know the causes; right?

A. Correct.

Q. And whatever caused the squamous cell, it's probably off the chart in this direction in terms of time; is that right?

A. Yes. That would almost take a second detailed history to try to figure that one out.

Q. You didn't focus on that?

A. I didn't nor did any of the practitioners, really.

Q. Okay. And the total skin electron beam therapy, of course, was after the squamous cell was already gone?

A. Right. Squamous cells are also a complication of light after electron beam radiation therapy.

Q. The jury's heard the suggestion, sir, that maybe Mr. Johnson's cancer progressed because he continued spraying Roundup and Ranger Pro. Do you have an opinion as to whether exposure to glyphosate-based herbicides could worsen a case of mycosis fungoides?

A. I've never seen any evidence of that being the case.

Q. And did you see anything in the medical records suggesting that Mr. Johnson's doctors didn't believe that his disease was going to get worse if he continued to

spray?

A. I didn't see anything in the notes that would suggest that the doctors were concerned about that.

Q. Okay. There was a record from Dr. Ofodile, kind of, on the subject; right? She made a recommendation to avoid environmental toxins?

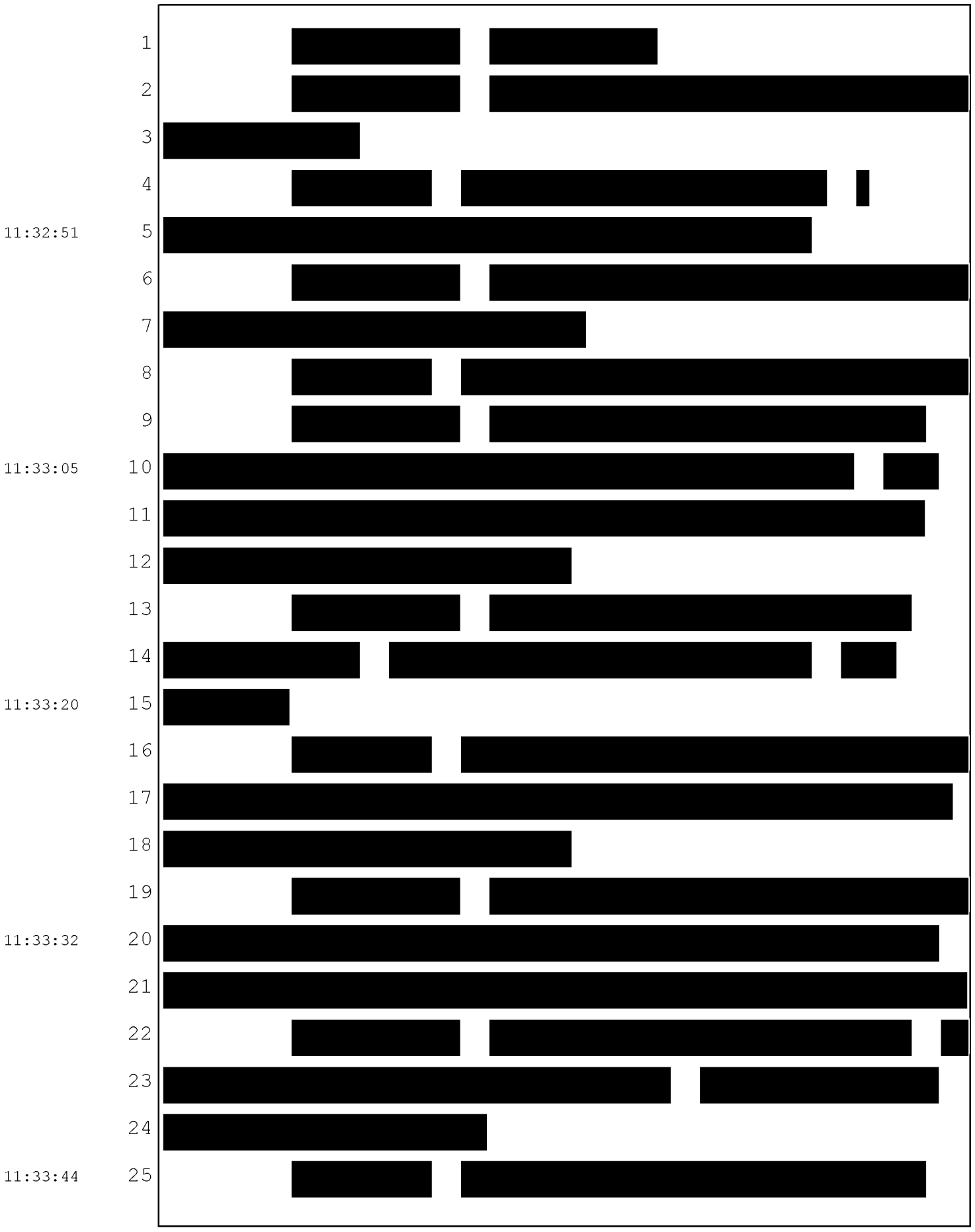
MR. GRIFFIS: Permission to publish 30270123.

MR. DICKENS: Objection, your Honor. Hearsay. Can we have a sidebar on this particular document?

THE COURT: Yes.

(Sidebar.)

[redacted]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(End sidebar.)

THE COURT: All right. You may continue, Mr. Griffis.

Q. BY MR. GRIFFIS: Okay. I would like to turn to this event. November 2015, Dr. Hoppe's letter saying Mr. Johnson can go back to work. This was following -- this was following what? What can he go back to work from?

A. Well, the electron beam radiotherapy is actually a fairly rigorous treatment program. It may require coming in three times a week to Stanford. It's fairly involved in terms of getting prepared and getting the treatment, so it's not the kind of thing that you probably are going to work around. So I assume there was a period of time when he was excused from work.

Q. And these are both right here together, but the electron beam therapy was a little bit before, you come

in multiple times a week for a few weeks, and that's your course of treatment; right?

A. Right.

Q. So the return-to-work letter, would you turn to 22870675?

11:35:20

A. 2287?

Q. 2287, the only thing that's there, really.

A. I've got a whole bunch of stuff on 2287.

Q. I didn't do very good quality control 22870675, the Stanford letter from Dr. Hoppe.

11:35:57

A. I don't think I've got that.

Q. Here you are.

A. Thank you.

Q. So Dr. Hoppe did release Mr. Johnson to return to work. And did you conclude from that, sir, that Dr. Hoppe at Stanford wasn't concerned about Mr. Johnson's continued activities at Benicia including spraying Ranger Pro?

11:36:22

MR. DICKENS: Objection. Calls for speculation.

THE COURT: Overruled.

11:36:42

THE WITNESS: In the letter he basically returns to work with no restrictions, so that would assume that he had no concerns about the type of work.

Q. BY MR. GRIFFIS: Would you turn to Defendant's Exhibit 3155, also Tab 3155? At the bottom 3155_3235.

11:37:04

A. Got that one.

Q. Good. What is this record, sir?

A. This is a report from Kaiser Permanente from, it looks like, March 14, 2018, and this is the report of what's called a PET scan. A PET scan is an imaging technique that's particularly sensitive for lymphomas.

Q. And at the bottom of the page with 3235 on it, there's an impression from the PET scan?

A. There is.

Q. Okay. And what does that -- don't read it to us, but tell us what that shows you as an oncologist, sir.

A. Well, he's had a very nice response to treatment.

Q. And this is part of your conclusion that he's in remission; is that right?

A. Yes.

Q. Now, given his chemotherapy history -- and we haven't had time to go over every chemotherapy treatment that he's had and his course under the treatment -- would you expect similar results if he needs to have another around of chemotherapy?

A. With a different drug? Same drug?

Q. Same drug first.

A. Well, he had a very limited course of treatment

with the Pralatrexate, so I think generally most practitioners who had given something that worked, if the patient begins to show signs of relapse, I think probably most of us would go back and give the same drug again.

11:39:15 Q. Okay. So you'd at least want to see if he would have a similar response the second time around?

A. Yes.

Q. If someone said, sir, that Mr. Johnson, at some point after he was diagnosed with mycosis fungoides, was

11:39:30 not terminal and later at some point in time he became terminal, does that make sense to you as a mycosis fungoides doctor?

A. No. Every patient with the exception, as I said, at the very earliest stages of this disease are

11:39:48 going to have an altered life expectancy and they're likely going to die of their disease unless they're quite old and have other major medical problems.

Q. And the people in the early phase, you're also not going to cure them, but their disease might move so

11:40:06 slowly that they'll eventually die of something else before they die of the mycosis fungoides?

A. Right. So in general, we don't cure anybody with this disease. This is a disease that people live with often for many, many years. Then in some cases for

11:40:21 the earliest stage patients, they live decades and live a

natural life expectancy. But for patients with more advanced presentations, generally their life expectancy is limited. And with the exception of relatively newer more aggressive treatment, in general, I tell patients
11:40:42 that it's incurable.

Q. And what is that relatively new treatment that you just alluded to?

A. It appears with a stem cell transplant, you can actually cure patients with this disease.

11:40:55 Q. How standard a treatment is that for mycosis fungoides -- for a fairly advanced mycosis fungoides these days?

A. So stem cell transplants, just like everything else I've talked about today, have evolved significantly
11:41:07 over the years. When they were first devised, stem cell transplants were something that we did where we took a patient's own blood cells and gave them back to the same patient. So you were basically getting your own cells back. That's called an autologous stem cell transplant.
11:41:26 That was done in a variety of lymphomas: Hodgkin's lymphoma, non-Hodgkin's lymphoma. It showed curative benefits. We tried it in patients with this disease, and it didn't work. So nobody was cured with this disease.

So as the field evolved, the next sort of
11:41:47 development was something called a allogeneic stem cell

transplant. So that's where we actually get donor cells not from the patient themselves, but, rather, from a relative, ideally, a sibling. Sometimes there's no sibling or the siblings aren't healthy enough to give the
11:42:07 cells. In those cases we now have very large international donor databases where people have been generous enough to allow their tissue to be typed, and we now can get cells from unrelated donors who match the cell types pretty closely, and you can do a allogeneic
11:42:31 stem cell transplant.

The difference is you require significant immunosuppression during the period of the transplant. When those were first developed, you had to get high-dose chemotherapy to destroy your own immune system, and then
11:42:45 the donor cells would go in. So there was a period of time when you, sort of, had no defense against infection and the risk of dying of infection and complication was pretty high. In addition, you had to be pretty healthy, so it was often restricted to 40, 45 and younger
11:43:03 patients.

We evolved the field further, because we then understood more recently that it's actually not the chemotherapy that does anything for the patients. It's actually the immune reconstitution with the new immune
11:43:17 system that fights the lymphoma and cures it. So now we

do what's called reduced intensity allogeneic stem cell transplants, and it's much lower doses of chemo.

Now the risk of death isn't from the chemotherapy. The risk of death is from what's called graft-versus-host disease where the donor's immune cells are too vigorous and they attack some of your normal organs like GI tract, the skin, the lungs.

11:43:34

So with that treatment, though, a number of us -- Stanford is a major player in this field -- have developed different regimens, different drugs, different approaches, and it looks like we probably can cure now about 50 percent or so of the patients that we actually do an allogeneic stem cell transplant on.

11:43:53

Q. Do you know if Mr. Johnson could be a candidate for allogeneic stem cell transplant?

11:44:11

A. A candidate for allogeneic stem cell transplant isn't as simple as saying you're 40 or you're 50. It's really more complicated. At Rush, there's an entire team that's involved with these decisions ranging from social workers, psychologists, the medical doctors, and it's focused on is the patient healthy enough, does the patient have the right support system to get through those vulnerable periods. And we try to put everything together.

11:44:35

Sometimes we can't find a donor. Unfortunately,

11:44:52

there are some populations that are under represented in the donor pools. It's easier to find a match for Caucasians, but now we're actually using parents sometimes, so we've pushed it even further away from being fully matched to being partially matched.

11:45:13

Cord transplants, if you've had babies, I'm sure they've approached you about saving the baby's blood cells. We use cord donors sometimes.

Q. So if Mr. Johnson were to be evaluated, it wouldn't be by a single person like you or like Dr. Nabhan or anyone else? It would be a whole team of people?

11:45:29

A. I tend to be pretty peripheral for my stem cell transplant group. They're in my group and if I have a patient I think is appropriate, I refer to them to make the final decisions. I may take care of them later when they finish, sort of, the acute phases. I may manage them again post-transplant, you know, a year out.

11:45:43

Q. Okay. Sir, I want to turn to a somewhat different topic. Dr. Nabhan, when he was here, performed something he called a differential "diagnosis" on the issue of whether Mr. Johnson's mycosis fungoides was caused by glyphosate. I know you don't like that term as applied to figuring that out so let's call it a differential etiology instead of saying differential

11:46:04

11:46:22

diagnosis.

What's wrong with saying "differential diagnosis" there?

A. In my world, a differential diagnosis is not so much what causes it. A differential diagnosis is what it could be, sort of all the different possible diagnoses. Actually in this disease, usually that's what we wrestle with in some of the subtle presentations. Is it eczema? Is it psoriasis? We don't want to tell people they have lymphoma if they really have psoriasis. So that's a differential diagnosis.

Q. So the differential diagnosis for Mr. Johnson is done, and the answer is mycosis fungoides?

A. Correct. I think maybe in August of '14 when he first presented before he had a skin biopsy, there was, again, a differential diagnosis in the head of the dermatologist, but there is no differential at this point.

Q. Let's put that aside and call it a differential etiology, which is acceptable to you.

A. Sure.

Q. Differential etiology.

And he was looking at various factors and wrote on the flip chart, I think, some factors and said that he'd ruled some out and came to the conclusion that

glyphosate was the cause of mycosis fungoides. When you're doing that sort of thing, when you're doing a differential diagnosis, you start out with a list of possibilities like eczema, psoriasis, et cetera; correct?

11:47:49 A. Yes.

Q. And those all have to be things that are actual conditions to be on the list; right?

A. Generally, we hope so, yes.

Q. And they have to reasonably match the patient's

11:48:02 symptoms; correct?

A. Yes.

Q. So when you're doing a differential etiology, does something need to actually be a cause before you put it on the list?

11:48:11 A. I don't usually do this exercise. But yeah, if I was going to put something in front of a patient and suggest that it was a cause, I would expect certainly that there was some basis in fact for why I'm putting that on the list for a patient.

11:48:29 Q. Now, Dr. Nabhan testified, sir, that the majority of non-Hodgkin's lymphoma is idiopathic, meaning of an unknown cause. Do you agree with that?

A. Yeah. I think that's true.

Q. And what about for mycosis fungoides?

11:48:45 A. That's true.

Q. And would you use a stronger word than the "majority" for mycosis fungoides?

A. I would say every case of mycosis fungoides is of unknown etiology.

11:48:57 Q. So if you have something that is majority idiopathic or 100 percent idiopathic, is there any way to rule out idiopathic when you're evaluating cause, in your opinion?

A. You can't rule out idiopathic unless you can, 11:49:14 with absolute certainty, pin things down. I don't tell every lung cancer patient that I encounter, even if they smoked, that cigarette smoking is the cause of their lung cancer, because there are lung cancers which arise in nonsmokers. There's always the possibility that it was 11:49:35 something else. Unless there's a clear, absolute certainty such as the viral etiologies, without scientific facts, there's no way to see what caused any patient's cancer.

Q. Even if you have some other real causes up there 11:49:52 like HTLV, for example, if you have something that's majority idiopathic, how can you pick anything but that as the most likely cause, sir?

A. Well, if a patient has cutaneous T-cell lymphoma and is HTLV-1 positive, have they have HTLV-1 acute 11:50:10 T-cell lymphoma leukemia, I would tell them it's from the

virus.

Q. Because that straight up caused --

A. Straight up. It's the only cause.

Q. The only cause.

11:50:15 A. And I would tell them that.

Q. Did you reach a conclusion about the most likely cause of Mr. Johnson's mycosis fungoides?

A. The same conclusion that I have for every other patient that I see with mycosis fungoides.

11:50:25 Q. What is that?

A. I tell them that we don't know why they got mycosis fungoides. Just like most cancer patients, it may he have just been bad luck in the fact that some of their cells changed.

11:50:38 MR. GRIFFIS: Thank you, sir. I have no further questions.

THE COURT: All right. Thank you.

Mr. Dickens.

11:50:47 CROSS-EXAMINATION

BY MR. DICKENS:

Q. Now, Doctor, you agree mycosis fungoides is non-Hodgkin's lymphoma; we can agree on that?

A. Absolutely.

11:50:59 Q. And once again, your opinion in this case is

specific to the question of whether or not glyphosate can cause mycosis fungoides; correct?

A. Yes.

Q. You didn't look at anything with respect to non-Hodgkin's lymphoma?

A. That's correct.

Q. You didn't look of epidemiology of non-Hodgkin's lymphoma generally?

A. Only in the setting of some of the recent epidemiologic work that I think we brought up earlier in the agricultural worker survey which was more focused on that.

Q. That's the Agricultural Health Study you're referring to; correct?

A. Yes.

Q. And you're aware that that found a quadrupling of the risk of T-cell lymphoma?

A. It didn't.

Q. You say that because it's not statistically significant; is that the reasoning?

A. Yes. There was a wide range of possible impacts on the diagnosis.

Q. So we'll get to that later, but that's the study you reviewed; correct?

A. Yes, regarding more global non-Hodgkin's

lymphoma.

Q. And you didn't do a literature search on your own in this case?

A. No.

11:52:07 Q. The documents, the epidemiology you reviewed came from the attorneys at Monsanto?

A. No. Most of the documents that I reviewed in terms of epidemiology I've written chapters on for many, many years prior to every meeting Monsanto.

11:52:21 Q. That was epidemiology with respect to mycosis fungoides generally?

A. Correct.

Q. But the only epidemiology with respect to glyphosate or Roundup came from the attorneys at

11:52:30 Monsanto?

A. Yes.

Q. You didn't rely on any animal studies in this case?

A. I did not.

11:52:39 Q. You did not rely on any toxicological studies?

A. I did not.

Q. Any genotoxic studies in this case?

A. I did not.

Q. You have no opinion whether Roundup or Ranger

11:52:54 Pro can cause NHL, generally?

A. Generally, no.

Q. Any expert opinion that glyphosate as a human carcinogen would be outside the realm of your experience?

A. Yes.

11:53:12 Q. Now, in your opinion, are there any studies in this case specific to Roundup and Ranger Pro and mycosis fungoides?

A. None that I've ever seen.

Q. Do you agree there are studies with respect to

11:53:25 Roundup, Ranger Pro and T-cell lymphomas?

A. What kind of studies are we talking about?

Q. Epidemiological studies.

A. Yes. There are epidemiologic studies that do include T-cell lymphoma with regard to herbicide use.

11:53:41 Q. With respect to Roundup or glyphosate?

A. I think some have tried to ask the question about glyphosate.

Q. And did you review those?

A. I think it's all in the agricultural health

11:53:57 studies.

Q. So literally the only case that you reviewed with respect to Roundup glyphosate and non-Hodgkin's lymphoma -- the only case you reviewed was the Agricultural Health Study?

11:54:08 A. Yes.

Q. The case that Monsanto claims is the biggest and the best?

A. I think whether who claims is biggest or best, I reviewed the study.

11:54:19 Q. And that was, once again, provided to you by Monsanto?

A. Yes.

Q. Did they provide you any other epidemiological studies on the question of whether or not glyphosate or

11:54:29 Roundup can cause non-Hodgkin's lymphoma?

A. No.

Q. And you didn't go out and do your own literature search to find additional studies, did you?

A. I was not looking for causes of non-Hodgkin's

11:55:10 lymphoma.

Q. Now, this is a slide that you helped prepare; is that right?

A. Yes.

Q. And it says that nearly all NHLs have no cause;

11:55:18 is that right?

A. Correct.

Q. And, once again, you're not an expert in NHLs, generally?

A. Correct.

11:55:23 Q. You're not an expert in the epidemiology of

non-Hodgkin's lymphoma?

A. Correct.

Q. And you have American Cancer Society up there. You're aware that the American Cancer Society lists glyphosate as a known probable carcinogen for non-Hodgkin's lymphoma? Are you aware of that?

11:55:35

A. I am not aware of that.

Q. Are you aware of whether or not the National Cancer Institute, Mayo Clinic or Leukemia and Lymphoma Society mention it?

11:55:51

A. I have not seen them mention it.

Q. Did you look?

A. No.

Q. You are aware of IARC, though, however?

11:55:59

A. Yes.

Q. And you're aware IARC has found Roundup, Ranger Pro, to be a known probable human carcinogen?

A. I don't think that's exactly the way they phrased it.

11:56:09

Q. How about glyphosate? Did they find glyphosate is a known -- or a probable human carcinogen?

A. I think they said there was weak evidence for it to be a carcinogen.

Q. So your review of IARC, you took away that there's weak evidence, not that it's a probable human

11:56:23

carcinogen?

A. I didn't take that away. That was their words, not mine.

Q. And we will turn back to that after lunch.

11:56:41 Now, with respect to thousands of scientific and medical journal articles, what are you referring to there?

A. With regards to?

Q. In your slide.

11:56:51 A. The general practice of malignant hematology and hematology as a Board-certified hematologist.

Q. Are you talking thousands of scientific and medical journal articles saying there is no known cause of NHLs?

11:57:05 A. There have been lots of articles about non-Hodgkin's lymphomas. And thousands of them, probably tens of thousands of them, and -- with those few exceptions that I've, kind of, alluded to, most of them don't show any clear-cut cause for non-Hodgkin's lymphomas.

Q. You understand that there have been other epidemiological studies that have looked at T-cell lymphoma in Roundup, other than AHS; correct?

A. There were earlier versions of the AHS. And I

11:57:41 haven't seen some of the other studies from an

epidemiologic standpoint. The -- probably.

Q. So you're not aware if any other studies have even looked at the question?

A. I wasn't here to talk about non-Hodgkin's lymphoma. Rather, mycosis fungoides.

11:57:55

Q. We've heard a lot about the North American Pooled Project. Did you review that at all?

A. No.

Q. Have you reviewed the Eriksson study?

11:58:07

A. No.

Q. Once again, neither of those were provided to you by Monsanto?

A. My basis for -- sorry. This case is focused on the mycosis fungoides world view, in particular.

11:58:22

Q. Okay. Was there any mycosis fungoides in the Agricultural Health Study?

A. No.

Q. Do you know that?

A. None was broken out.

11:58:30

Q. Okay. So you don't know; right?

A. And it wasn't reported that way, correct.

Q. Okay. Did you ask? Did you ask for any information that Monsanto had as to whether or not there were mycosis fungoides cases in the Agricultural Health

11:58:41

Study?

A. I did not.

Q. Wouldn't that be important to know for you, Doctor?

A. In the setting of the small number of cases of T-cell lymphoma reported, it wouldn't have changed anything.

Q. So your basis that there are no known causes, that's on the basis that there have been no studies that have actually looked for it; correct?

A. No. There have been lots of studies that have looked for causes of mycosis fungoides.

Q. How about for glyphosate and whether or not glyphosate causes mycosis fungoides?

A. There have been large numbers of studies that have looked at various exposures that patients with mycosis fungoides may have had, both casually and occupationally, that have failed to show a convincing link of anything.

Q. But that's not my question. My question is specific to glyphosate. Your opinion that glyphosate cannot cause T-cell lymphomas or mycosis fungoides is on the basis there haven't been sufficient studies to even look at that question?

A. There have been no studies that have shown that any compound has caused mycosis fungoides.

Q. Okay. And mycosis fungoides --

THE COURT: Mr. Dickens, I think this might be a good place to break now for lunch.

MR. DICKENS: That's great. Thank you, your Honor.

11:59:52

THE COURT: All right. Ladies and Gentlemen, we're going to take a lunch recess now. We'll be in recess until 1:30. Please remember: Do not discuss the case. Do not do any research. And we'll resume again at 1:30.

12:00:06

(Time Noted: 12:00 p.m.)

REPORTER'S CERTIFICATE

I certify that the proceedings in the within-titled cause were taken at the time and place herein named; that the proceedings were reported by me, a duly Certified Shorthand Reporter of the State of California authorized to administer oaths and affirmations, and said proceedings were thereafter transcribed into typewriting.

I further certify that I am not of counsel or Attorney for either or any of the parties to said Proceedings, not in any way interested in the outcome of the cause named in said proceedings.

IN WITNESS WHEREOF, I have hereunto set my hand: August 3rd, 2018.

<%signature%>
Leslie Rockwood Rosas
Certified Shorthand Reporter
State of California
Certificate No. 3462