IN THE UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF ILLINOIS
EASTERN DIVISION

WENDY B. DOLIN Individually and as Independent Executor of the Estate of STEWART DOLIN, deceased,	No. 12 CV 6403
Plaintiff,	
vs.	Chicago, Illinois
SMITHKLINE BEECHAM CORPORATION D/B/A GLAXOSMITHKLINE, a Pennsylvania Corporation,	March 15, 2017
Defendant.	9:15 o'clock a.m.

VOLUME 2A
TRANSCRIPT OF PROCEEDINGS
BEFORE THE HONORABLE WILLIAM T. HART

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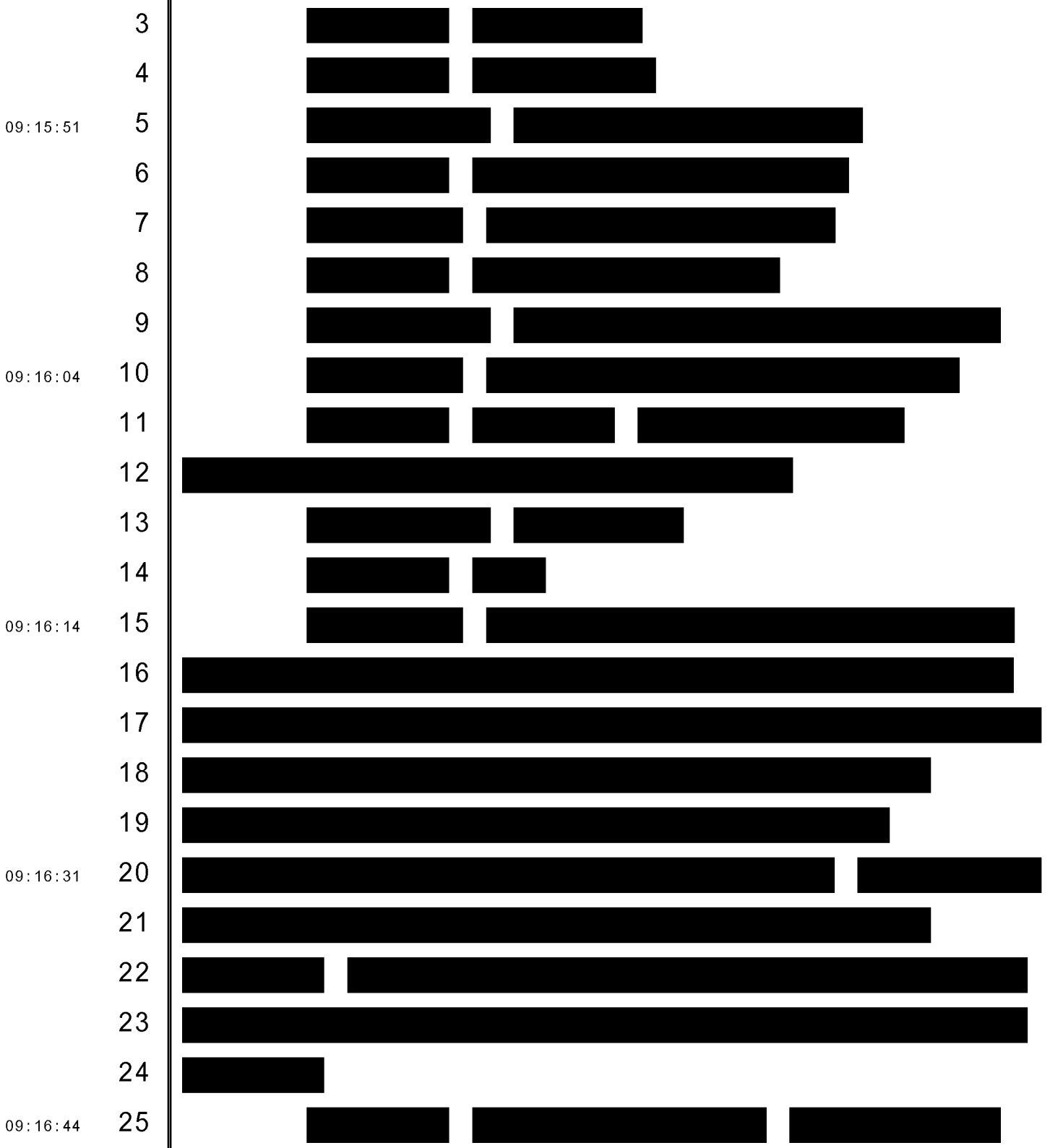
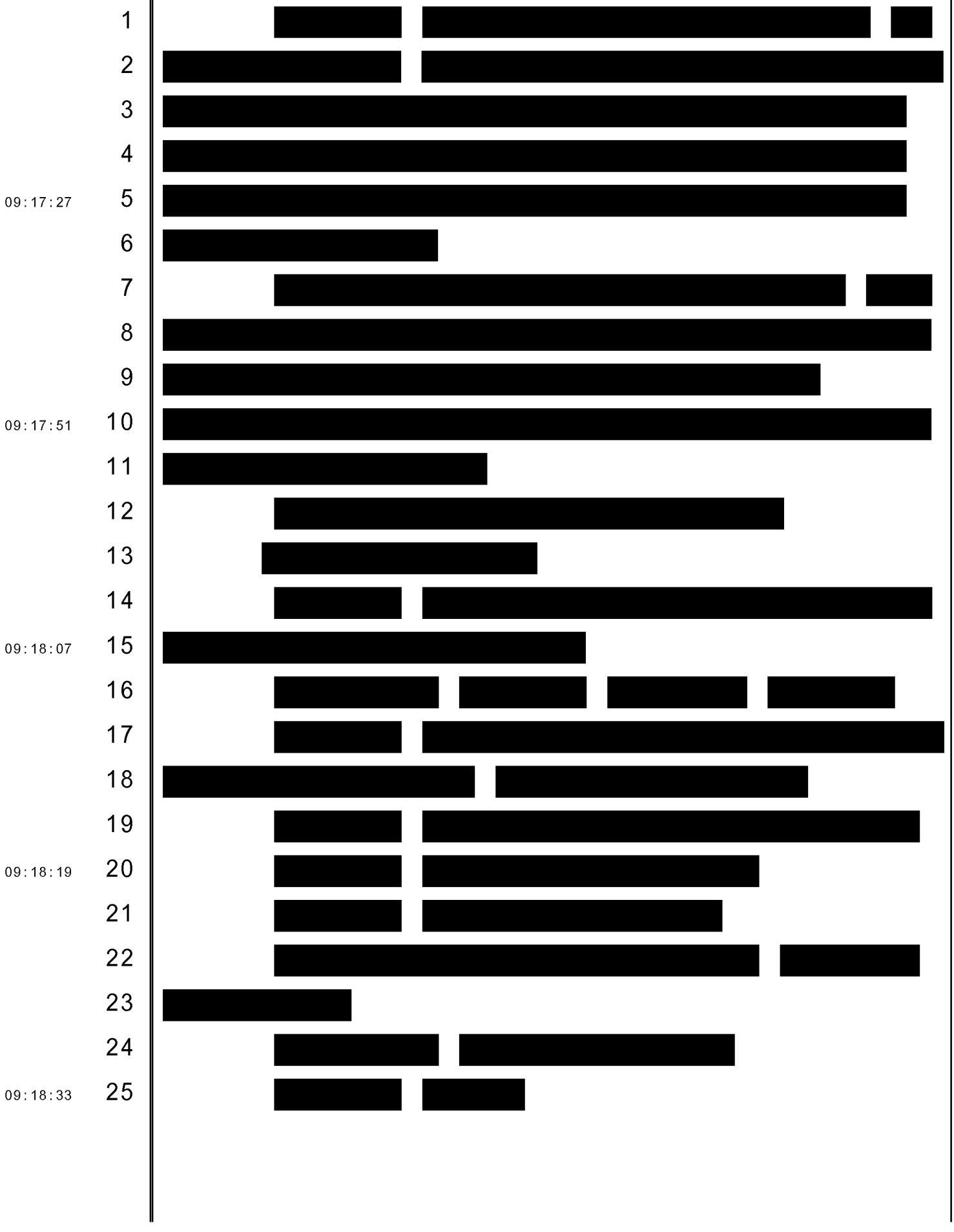
(The following proceedings were had out of the presence of the jury in open court:)

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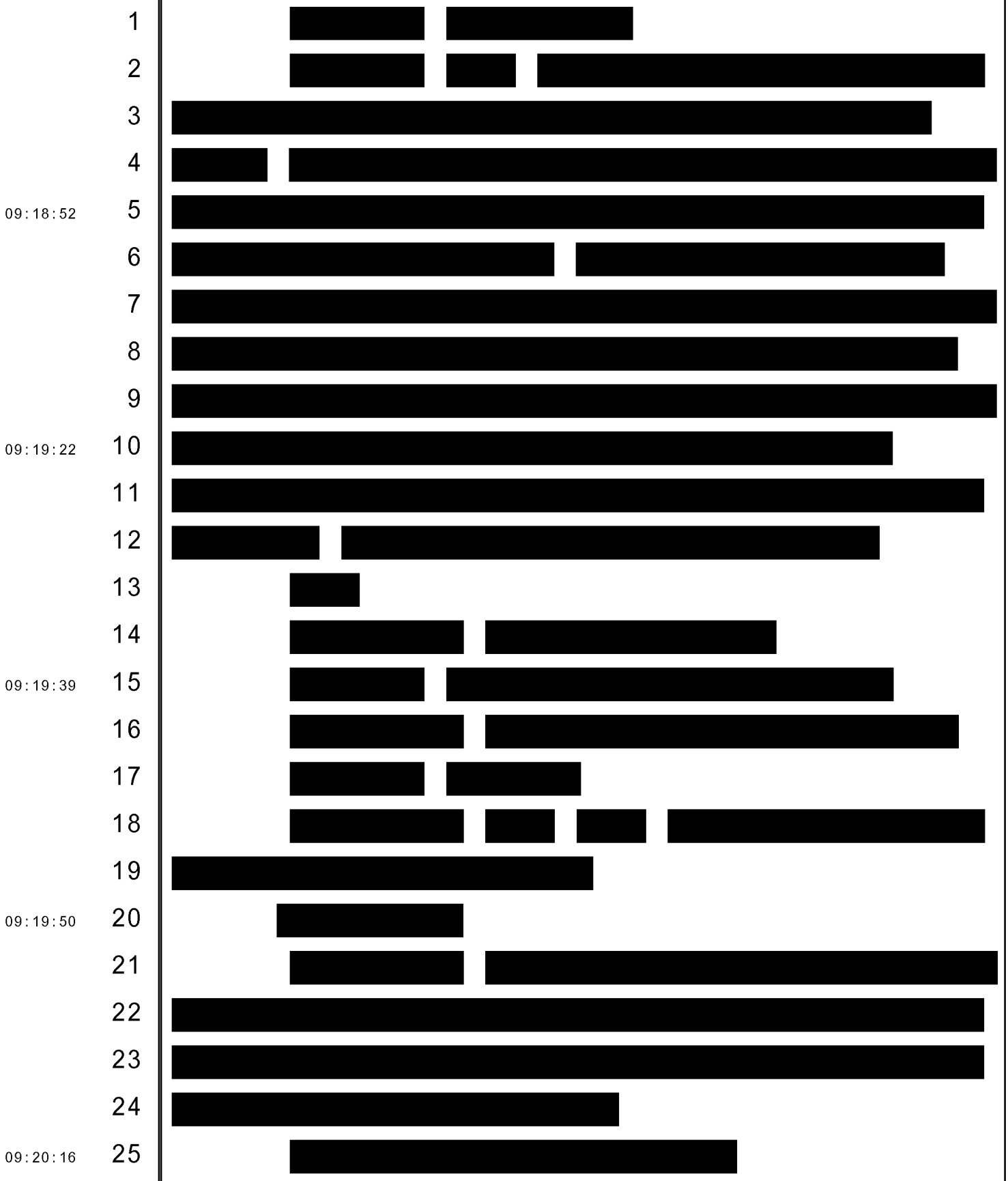
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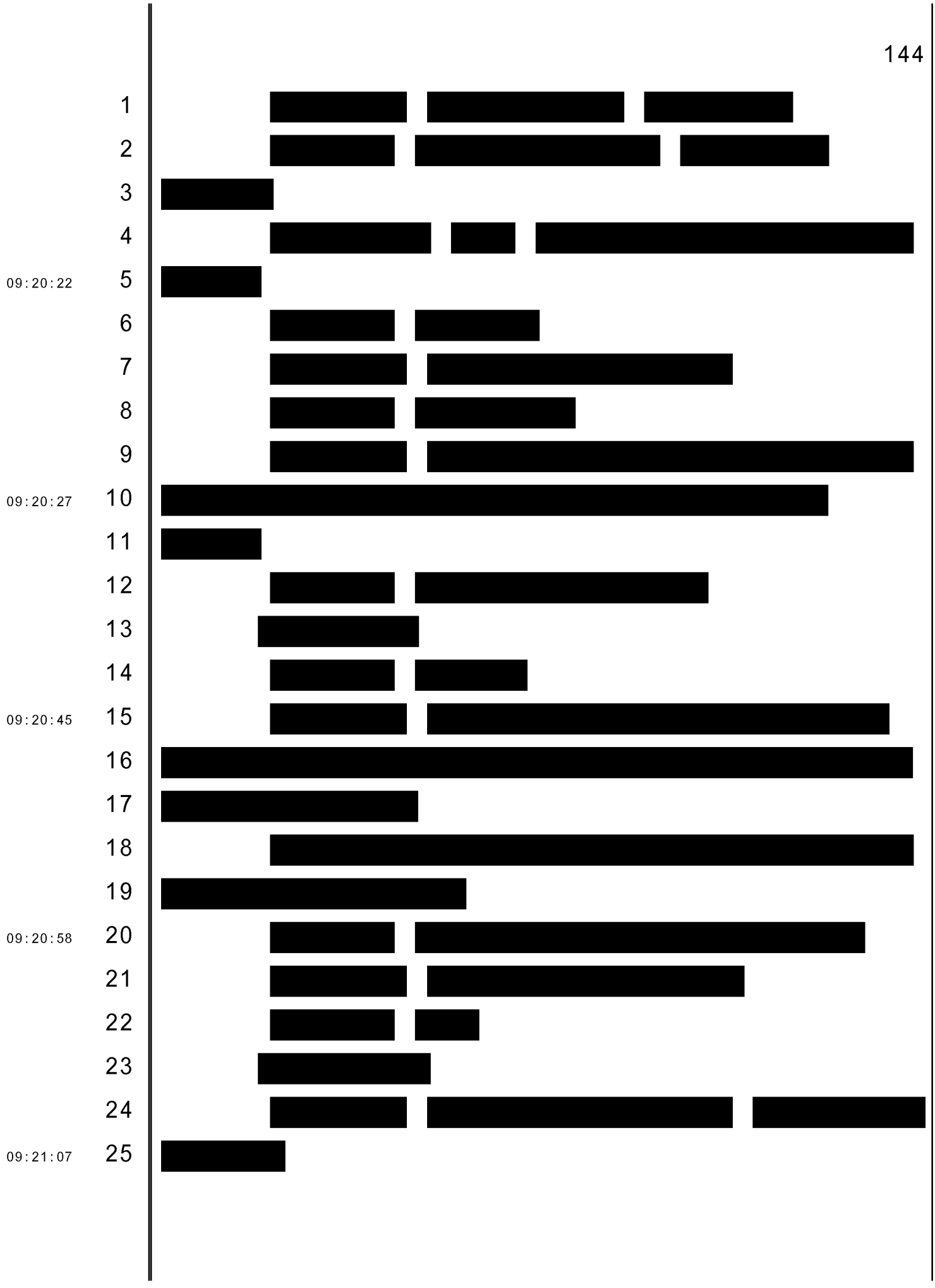
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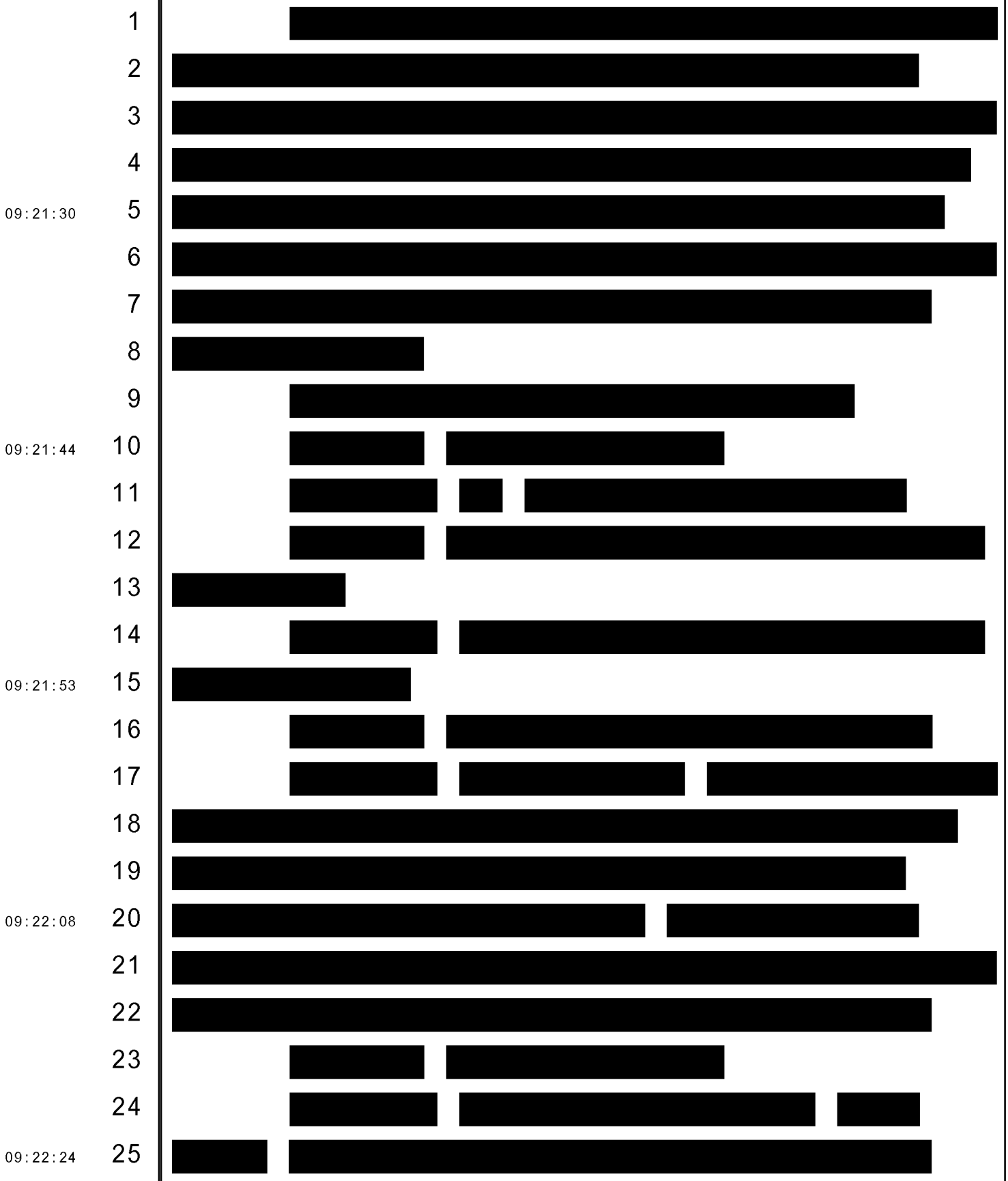
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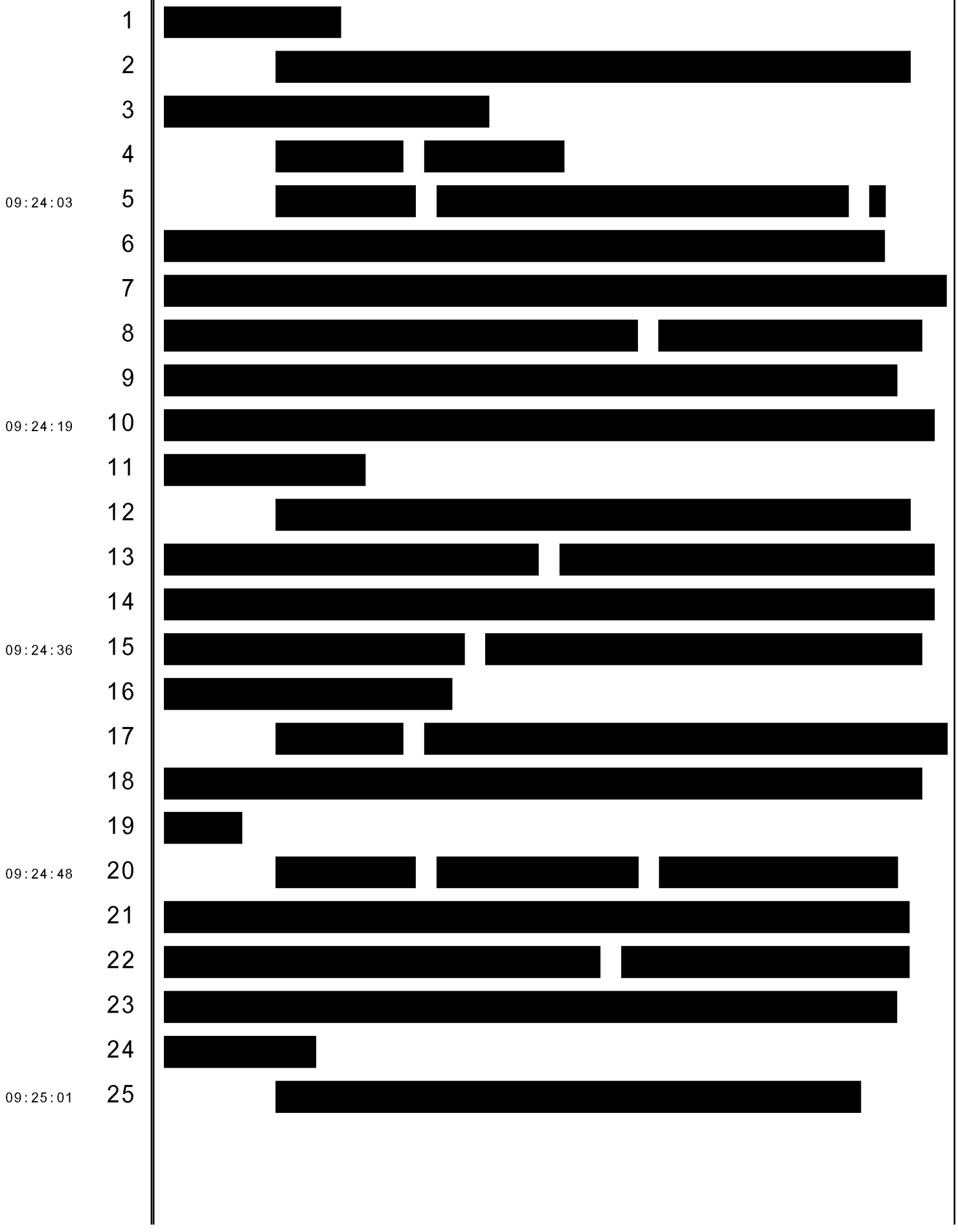
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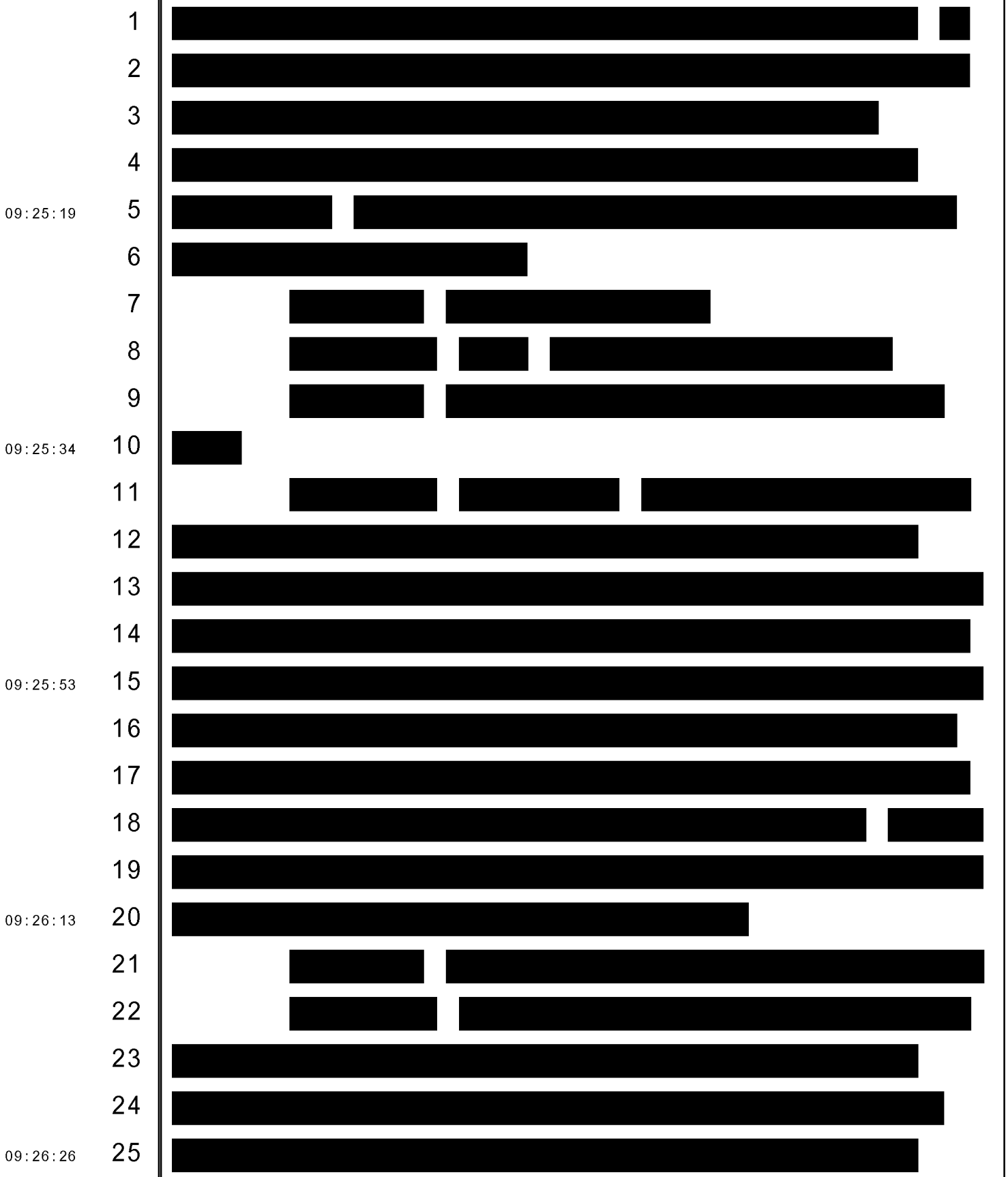
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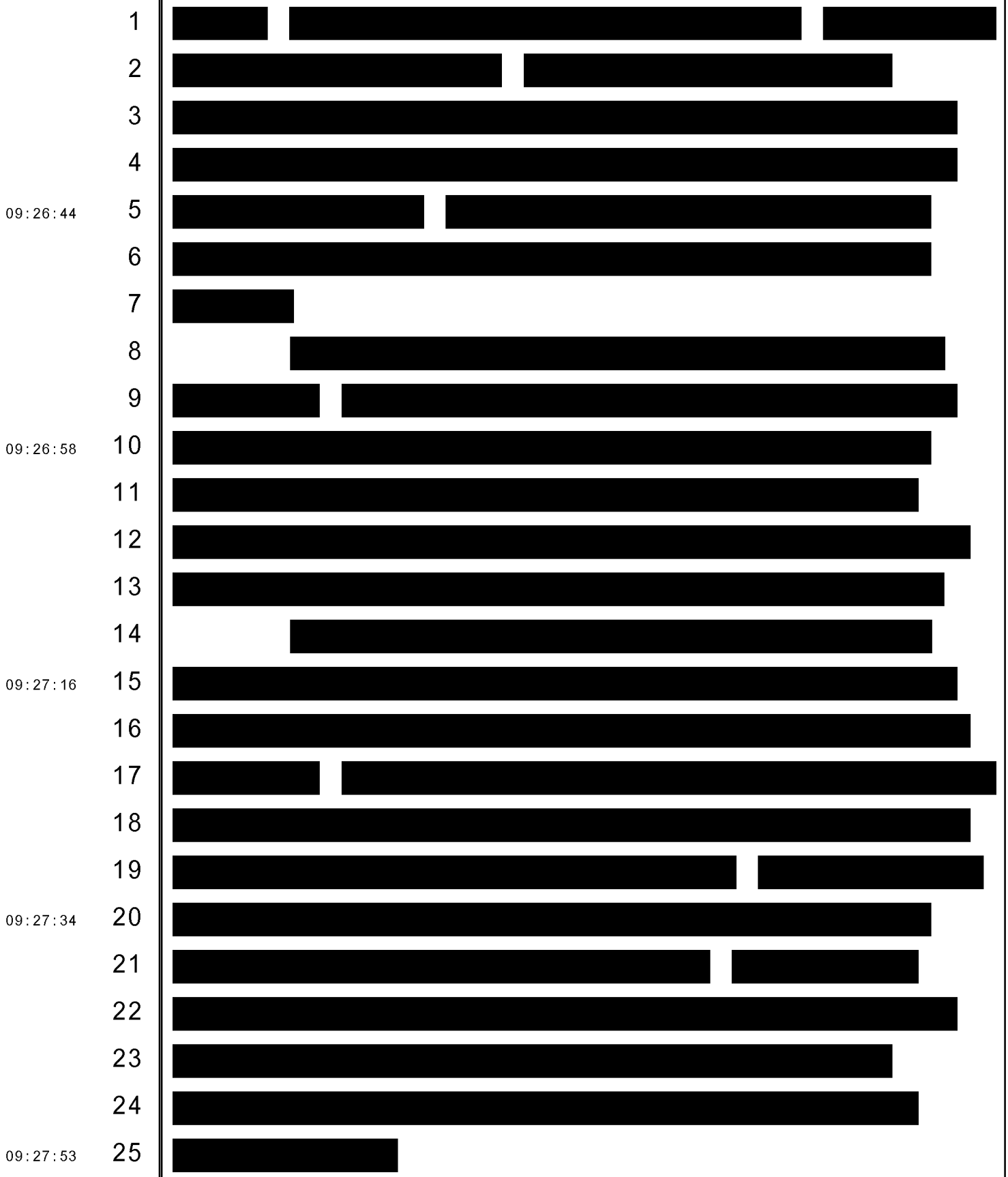

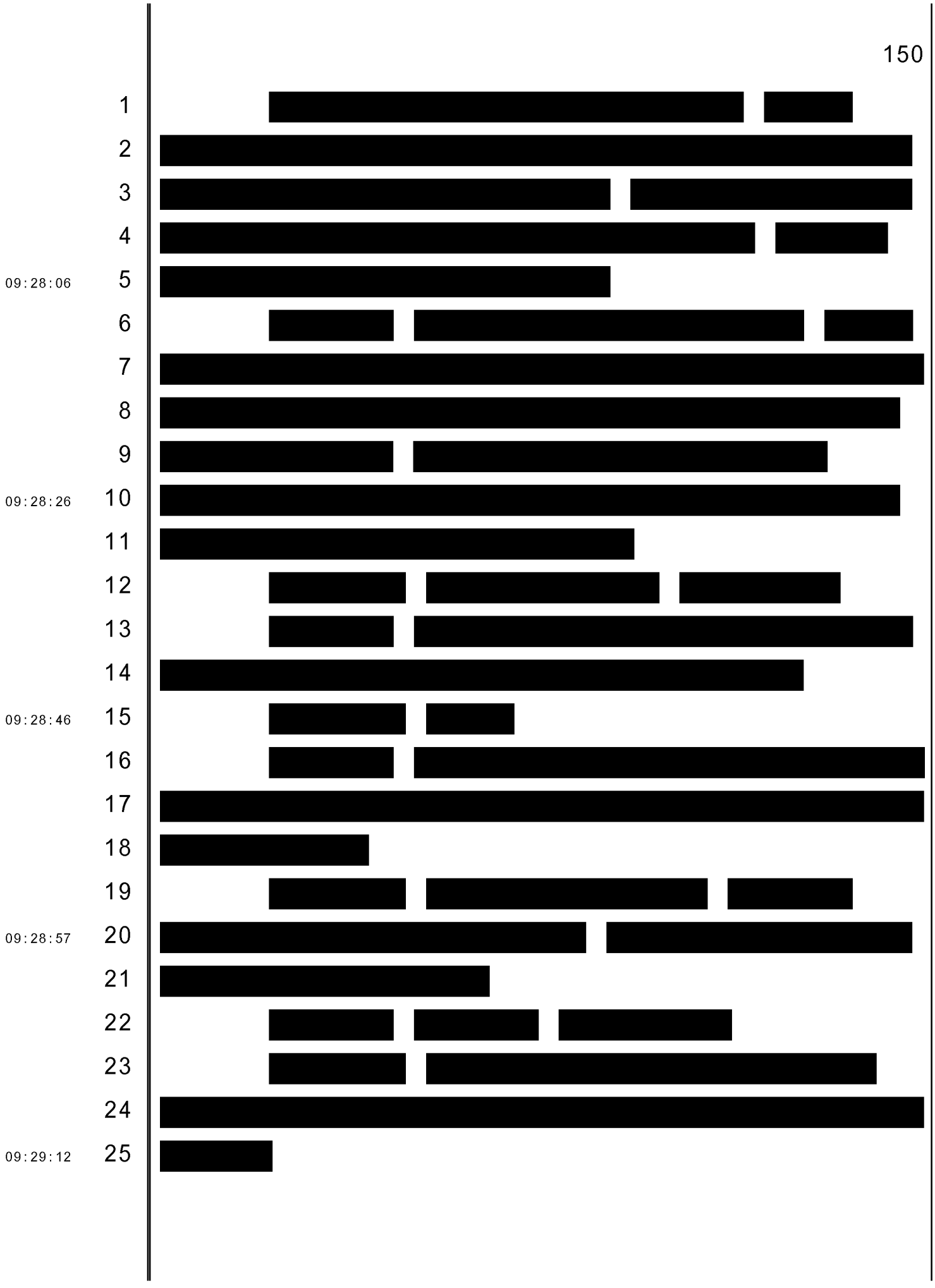
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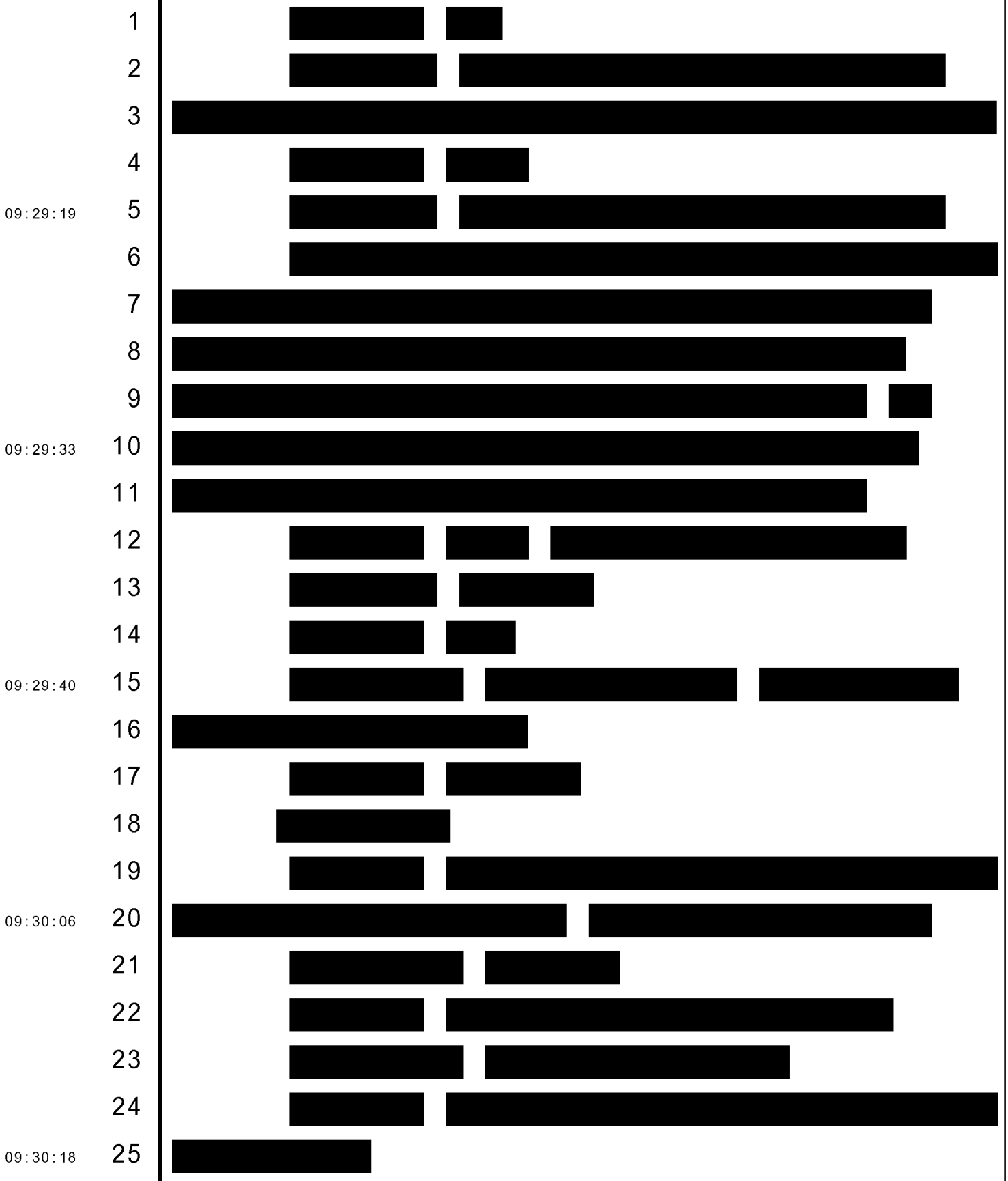
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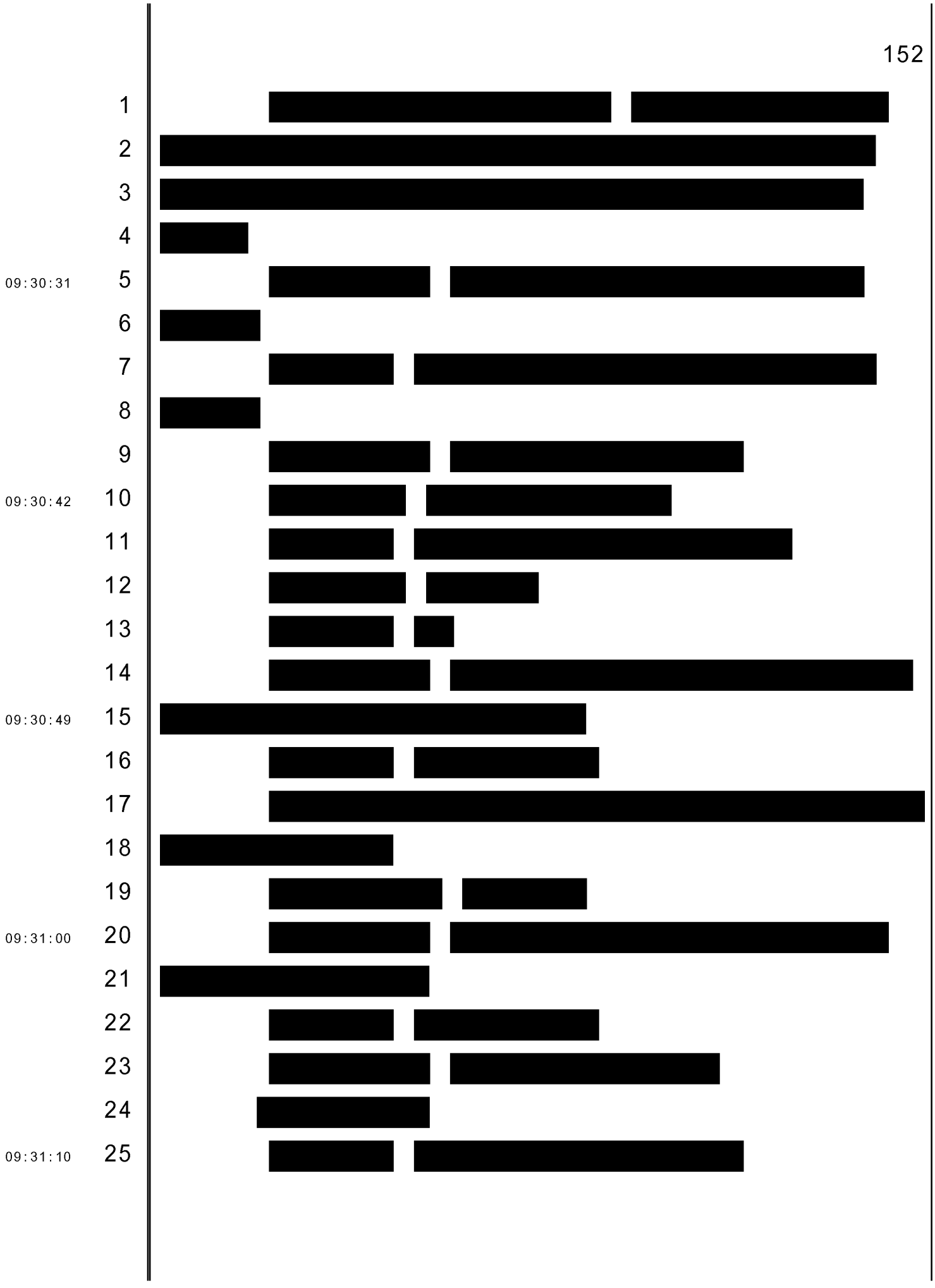
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(The following proceedings were had in the presence of the jury in open court:)

THE COURT: All right. Thank you very much, ladies and gentlemen. Please be seated and we will resume.

(Brief pause).

THE COURT: At this point in time, ladies and gentlemen, we will hear the conclusion of defense opening statement.

Mr. Bayman, you may proceed, sir.

MR. BAYMAN: Thank you, Your Honor.

OPENING STATEMENT ON BEHALF OF DEFENDANT (resumed)

MR. BAYMAN: Good morning, ladies and gentlemen. Just a little bit to cover this morning.

When we left off yesterday, we were talking about the third question, did GSK communicate with the FDA and doctors about the possible risks of Paxil.

And I had told you, when I left off, that in early 2005 GSK had -- the FDA required GSK to revise the Paxil label slightly so that the language more closely resembled language

put in a black box warning for all antidepressants regarding concern of suicidality with patients under age 18.

Regarding adult patients, the FDA approved class labeling language starting in January of 2005. And that language is in front of you. The label stated:

09:35:46

> "... it is also unknown whether the suicidality risk extends to adults. And a causal link between the emergence of such symptoms and either the worsening of depression and/or the emergence of suicidal impulses has not been established."

09:36:01

Starting in January of 2005, GSK changed the Paxil label in another way. It changed the label to add a separate precaution entitled "akathisia." And that precaution said:

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> "... the use of Paroxetine or other SSRIs has been associated with the development of akathisia, which is characterized by an inner sense of restlessness and psychomotor agitation such as an inability to sit or stand still usually associated with subjective distress."

09:36:40

Now, akathisia is a word you probably haven't heard about before in this trial, but what you'll hear during the course of the trial is that it's a medical condition that compels people to be in constant motion. It can't be turned on or off.

09:36:57

This language explaining akathisia that you see on this slide was put in the label over 5 years before Mr. Dolin took his own life in 2010. And this is particularly important because the only plaintiff's expert who will tell you that Paroxetine caused Mr. Dolin to commit suicide is Dr. Joseph Glenmullen, an expert that Mr. Rapaport referred to yesterday.

09:37:13

Dr. Glenmullen has testified that Paroxetine caused akathisia in Mr. Dolin which caused him to commit suicide.

And I was surprised to hear that Mr. Rapaport didn't mention the word akathisia, because plaintiff's complaint in this lawsuit alleges that Paroxetine caused Mr. Dolin to have akathisia which caused him to commit suicide. And Dr. Glenmullen has testified multiple times in his deposition in this lawsuit that this was his claim of how Mr. Dolin's Paroxetine caused akathisia which then led him to commit suicide, but there will be no placebo-controlled trials that show that Paxil or Paroxetine causes akathisia which then causes suicidal thoughts or behavior.

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Now, GSK sent out a dear-healthcare provider letter about this labeling change in February of 2005. And according to that February 2005 letter, the new warning also emphasizes the need for close monitoring of patients especially at the beginning of therapy.

09:38:19

GSK also told doctors about the changes to the precaution section, including the new section titled

09:38:37

"akathisia" and a subsection addressing clinical worsening and suicidal risk and said:

> ".. creating a subsection for revised language dealing with risk of suicide and the need for monitoring patients."

09:38:54

The evidence will show that Dr. Sachman received this letter also.

Now, as I mentioned yesterday, FDA requested all the pharmaceutical companies to submit all their adult clinical trial data related to suicidality in adult patients, the most comprehensive analysis that had ever been done. And the FDA wanted the data from placebo-controlled trials.

09:39:09

GSK submitted its data, but it also decided to do its own analysis of the data. And that's the analysis I told you about yesterday that showed no difference in adult patients taking Paxil and those taking placebo on the main analysis of suicidal thoughts or behavior.

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GSK told the FDA about its analysis in April of 2006 in what was called a briefing document, which you see before you on the screen. And as you can see, the briefing document specifically referenced the 11 patients that I mentioned yesterday and the 6.7 number that Mr. Rapaport kept telling you about.

09:39:48

Well, what else did GSK do with the information about its finding for adult patients with MDD you might ask. GSK

09:40:05

changed the Paxil label per FDA regulations and then submitted that change for approval by the FDA and shared that change with doctors.

Here's the May 2006 label. In addition to submitting this data to the FDA and waiting for FDA to approve the label change, GSK also went ahead and told doctors about this change in another dear-healthcare provider letter in May of 2006. The letter stated:

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> "... GSK would like to advise you of important changes to the clinical worsening and suicide risk subsection of the warning section in the Paxil labeling.

This letter addressed GSK's 2006 analysis that I mentioned a minute ago. And this letter told doctors, importantly, that:

09:41:02

> "... the higher frequency observed in the younger adult population across psychiatric disorders may extend beyond the age of 24."

And, in fact, if we compare this statement against the one sent in the briefing document to the FDA, you can see that GSK included the same figures and the same information. And most importantly, ladies and gentlemen, and the evidence will show that Dr. Sachman also received this letter and knew about the May 2006 label change before he last prescribed Paroxetine to Mr. Dolin.

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Now, I told you yesterday in more detail about the FDA's 2000 analysis of data submitted from all the pharmaceutical companies. So what did the FDA do based on its analysis and the findings from that analysis? FDA made GSK get
09:41:59 rid of the new language that GSK had added in 2006 about its findings of an increased risk in adult with major depressive disorder in favor of using the same warning for all the medications in the same class as it had done previously, the so-called class labeling that I mentioned yesterday.

09:42:18 FDA did this because it had conducted extensive analyses of the adult data, not just for Paxil but for 11 other antidepressants also. And it determined what needed to be said or not said in the labeling, because the FDA controls the label, ladies and gentlemen. The evidence will show that FDA
09:42:37 didn't reach its decision without first analyzing the Paxil studies and the studies on the other medications. So let's look at that labeling.

The labeling language that went into effect in 2007, and remained in effect in 2010 when Mr. Dolin took his own
09:42:56 life, included a black box warning that you see on the screen today, and that labeling remains in effect today.

It noted a concern for pediatric patients and then stated:

> "... regarding adults, short-term studies did
09:43:12 not show an increase in the risk of suicidality

with antidepressants compared to placebo in adults beyond age 24. There was a reduction in risk with antidepressants compared to placebo in adults age 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior."

And the labeling included the precaution that you see here about clinical worsening and suicide risk, which again alerted patients, their families, and their caregivers to be alert to these concerns.

Now, Mr. Rapaport said yesterday that the Paxil label contains no information about a risk for suicide, but he didn't show you this label, the Paxil labeling in 2007 and in 2010 and today continues to address akathisia. The specific side effect the plaintiff claims led Mr. Dolin motion to commit suicide, and it goes it in four different places. In the warning section, under a warning entitled "clinical worsening and suicide risk." In the specific precaution about "akathisia" that I mentioned a few minutes ago. In another precaution section addressing information for patients, "clinical

worsening and suicide risk." And finally, among the post-marketing reports of adverse reactions reported by patients after the medicine first came on the market.

Plaintiff's expert, Dr. Ross, who Mr. Rapaport told you about yesterday, has testified that GSK should have not taken the Paxil-specific language that it added in 2006 out of the label. Ladies and gentlemen, the evidence will show that the FDA told GSK on four separate occasions that they couldn't use the Paxil-specific language and that GSK must use class labeling language, the language which the FDA approved and required for all medicines in the class to have in their labels.

Mr. Rapaport said yesterday that the 2010 label was false and misleading, but the evidence will show that the FDA's approval of the 2010 label means that that label is neither false nor misleading --

MR. RAPOPORT: Your Honor, its argument. He should stick to the facts.

MR. BAYMAN: It's what the evidence will show, Your Honor.

THE COURT: Tell the jury what the evidence will show. Don't argue.

MR. BAYMAN: Mr. Rapaport told you there was nothing in the label that could've warned Dr. Sachman about a possible risk of suicide, but given what we reviewed yesterday with the

labels and given what we reviewed today with the labels and the letters, when we look back at our third question the answer is also yes, GSK communicated with the FDA and doctors about the possible risks.

09:46:29 That bring us to our fourth and final question, was Mr. Dolin's close friend, Dr. Sachman, aware of the possible risks of Paxil or Paroxetine. The evidence will show, ladies and gentlemen, that the answer to that question is also definitely yes.

09:46:46 Mr. Rapaport said yesterday this case is about the fact that doctors need to be informed. Well, the evidence will show that Dr. Sachman was informed.

Ladies and gentlemen, you will recall the very first slide that Mr. Rapaport showed you yesterday that said a 09:47:04 prescription drug company is responsible if they don't warn. And GSK did warn, but that's not the whole story, because what matters is what Dr. Sachman knew, and not just what he knew from the Paxil labeling in 2010.

You're going to hear from Dr. Sachman in this 09:47:24 courtroom. Mr. Rapaport said yesterday, Dr. Sachman had no idea about the risks of Paxil and suicide, but previously Dr. Sachman testified under oath at his deposition, and we will expect that he will testify here, that he received and knew about all the changes in the warnings, including about the 09:47:45 possible risk of suicidal thoughts or behavior.

You heard some commentary yesterday from Mr. Rapaport about pharmaceutical companies manufacturing --

MR. WISNER: Your Honor, I hate to interrupt again, but all of this Mr. Rapaport-comparison is argument and he should talk about facts.

THE COURT: Tell us about the evidence, sir.

MR. BAYMAN: The evidence will show, ladies and gentlemen, that with respect to pharmaceutical companies marketing to general practitioners, Dr. Sachman will testify that the GSK reps that he interacted with were always professional and courteous; that he does not remember any discussions with any GSK sales reps about Paxil; that if there were any differences between what a sales rep told him about medicine and what the label said, he would go with what had been disclosed in the labeling. And the evidence will show that Dr. Sachman has testified, and will testify, that if he didn't understand things in the label, he would do his own research. So that the idea that doctors are somehow held in concrete based on what pharmaceutical companies say is just not how the process works, ladies and gentlemen.

Now, you remember the letters that I showed you yesterday and earlier that GSK sent to doctors across the country in 2004, 2005 and 2006 about Paxil. Dr. Sachman was one of the doctors who got each of these letters. Listen carefully to his testimony. In testimony that he gave, because

in testimony he gave before this trial even started Dr. Sachman said he had a special place on his desk for these very kinds of letters. He understood the warnings and precautions and he discussed them with his patients, specifically the Dolins.

09:49:36 In fact, Dr. Sachman got each of these letters shortly before or during the time he prescribed generic Paroxetine for Mr. Dolin for 13 months, from 2005 to 2006. Dr. Sachman got GSK's February 2005 letter that added the akathisia precaution only a matter of months before he started Mr. Dolin on

09:50:00 Paroxetine in October of 2005.

You will hear how Dr. Sachman knew to be on the lookout for akathisia because it was described as one of the possible side effects of taking Paxil or Paroxetine.

The evidence will also show that he admitted that he

09:50:19 discussed the information in the GSK February of 2005 letter with both Mr. Dolin and Mrs. Dolin.

The evidence will show that Dr. Sachman knew of the Paxil-specific information because GSK sent him a letter about the 2006 label change and Dr. Sachman testified that he

09:50:39 received it and reviewed it.

You will hear testimony from Dr. Sachman that he got the May 2006 dear-healthcare provider letter that had told them what he needed to know about Paxil and the issue of suicidality, and also that the increased risk of thoughts or

09:50:59 behavior may go beyond the age of 24. After receiving this

letter, Dr. Sachman testified that he most likely discussed this information in the letter with Mr. Dolin. Don't forget that this was during the time that Mr. Dolin was still taking generic Paroxetine as prescribed by Dr. Sachman. And when
09:51:19 Dr. Sachman last prescribed Paroxetine to Mr. Dolin in 2010, he went over with him the signs and symptoms disclosed in the Paxil labeling and told him that if he had any problems with the medication, he should call him.

Now, ladies and gentlemen, looking back at the four
09:51:38 questions I've asked you to consider, listen carefully to the answers to those questions as you hear the evidence in this case, because you are the ones to decide. We don't think you'll hear those answers in the plaintiff's case, and we don't believe the plaintiff can meet her burden of proof.

09:51:56 The evidence will show that generic Paroxetine did not cause Mr. Dolin to make the decision to take his own life and that the warnings were appropriate.

The evidence will show that his behavior did not change after he took generic Paroxetine, but rather, his
09:52:11 long-standing fears and work stressors, as far back as 2007, were becoming real in his mind.

I will sit down now, ladies and gentlemen, but my last word is to ask you to keep an open mind and reserve judgment since the plaintiff gets to go first. The plaintiff is going
09:52:28 to start her case with a witness who is not here to provide you

with any information about Mr. Dolin. Some of our evidence will come in during the plaintiff's case and then we will get to put on GSK's case. So please keep an open mind.

These are difficult facts to hear and you're going to hear a lot of information over the next few weeks. A lot of it will be technical and scientific, but a lot of it will simply allow you to use your common sense. In the end, it's up to you to decide why Mr. Dolin took his own life.

09:52:44

Again, on behalf of GSK, I thank you for your willingness to take time away from your families and your jobs and to do the hard work of being jurors.

09:53:00

Thank you very much.

THE COURT: All right. Thank you, Mr. Bayman.

The plaintiff may proceed.

09:53:11

MR. RAPOPORT: Thank you, Your Honor.

As our first witness, we will call Dr. Pierre Garnier, and that's going to be by video.

THE COURT: By video deposition.

(Brief pause)

09:54:47

MR. RAPOPORT: Just will take a moment to get that set up.

(Brief pause).

MR. RAPAPORT: Your Honor, this should be up in a moment. It's all been pretested before the trial. They're just switching wires, to the best of my knowledge.

09:55:01

(Brief pause).

THE COURT: Can you find some 7-year old kid to come and fix this?

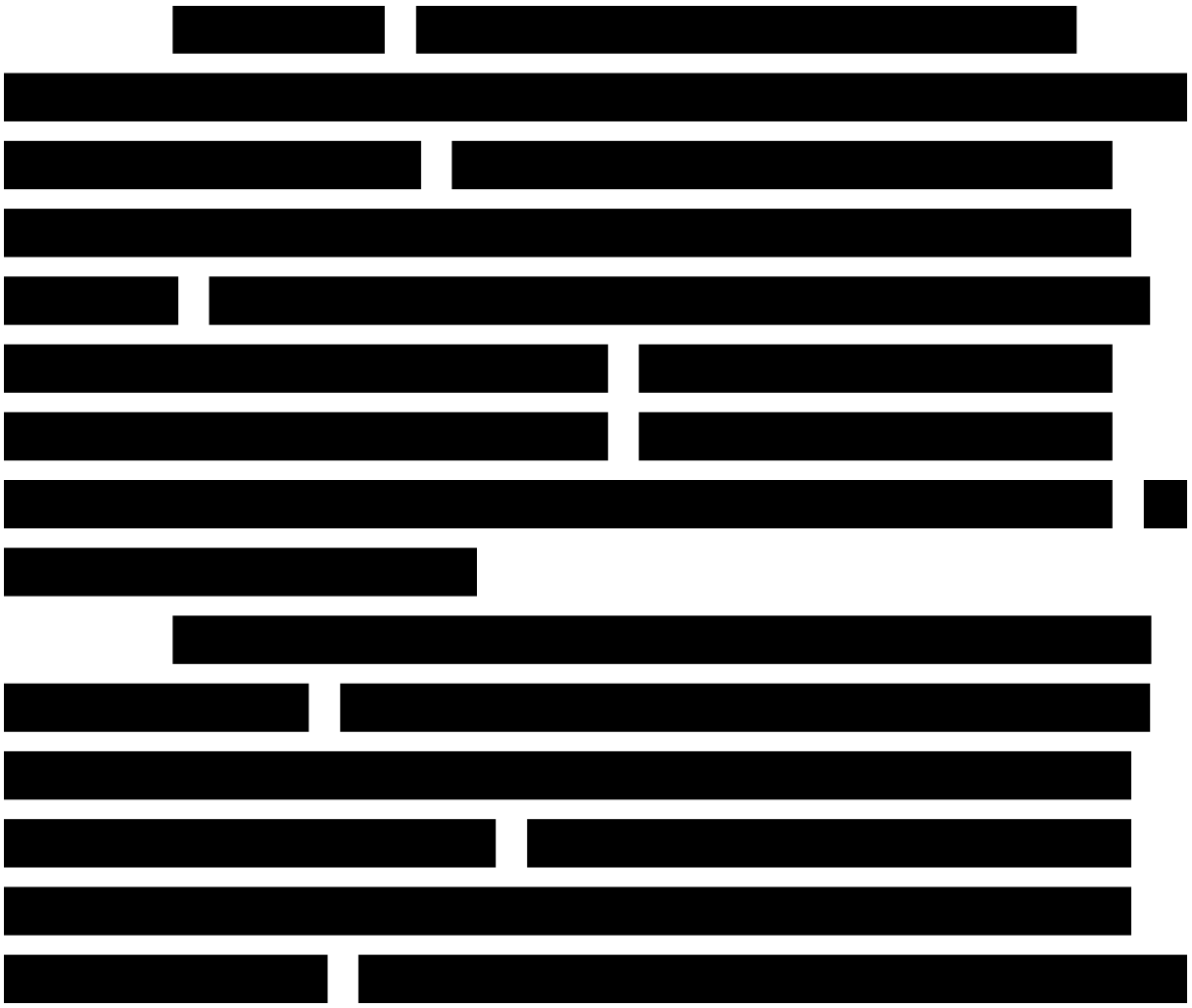
MR. RAPOPORT: Right. I'll call smarter than a fifth grader.

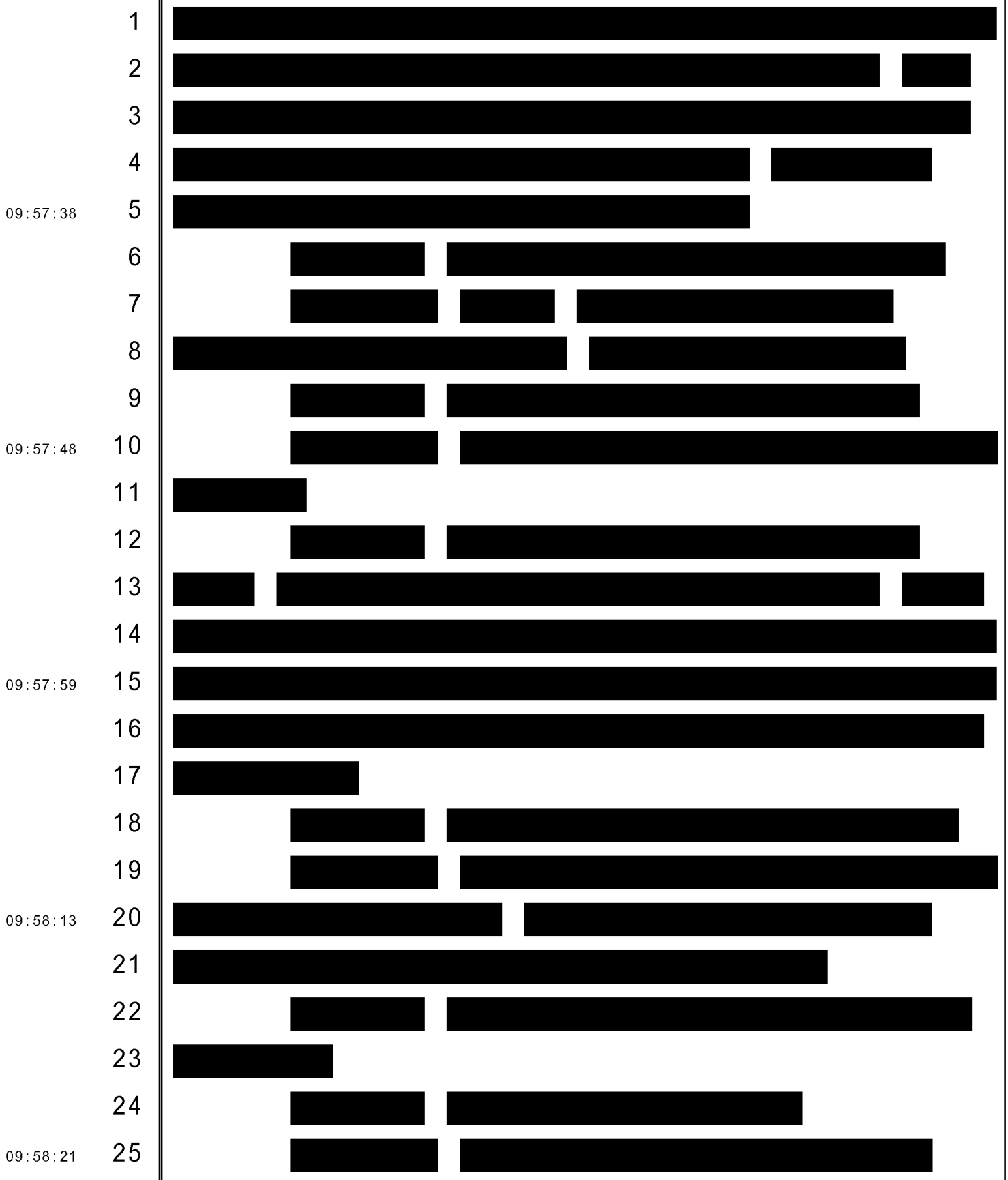
MR. DAVIS: Can we have a sidebar real quick about the video?

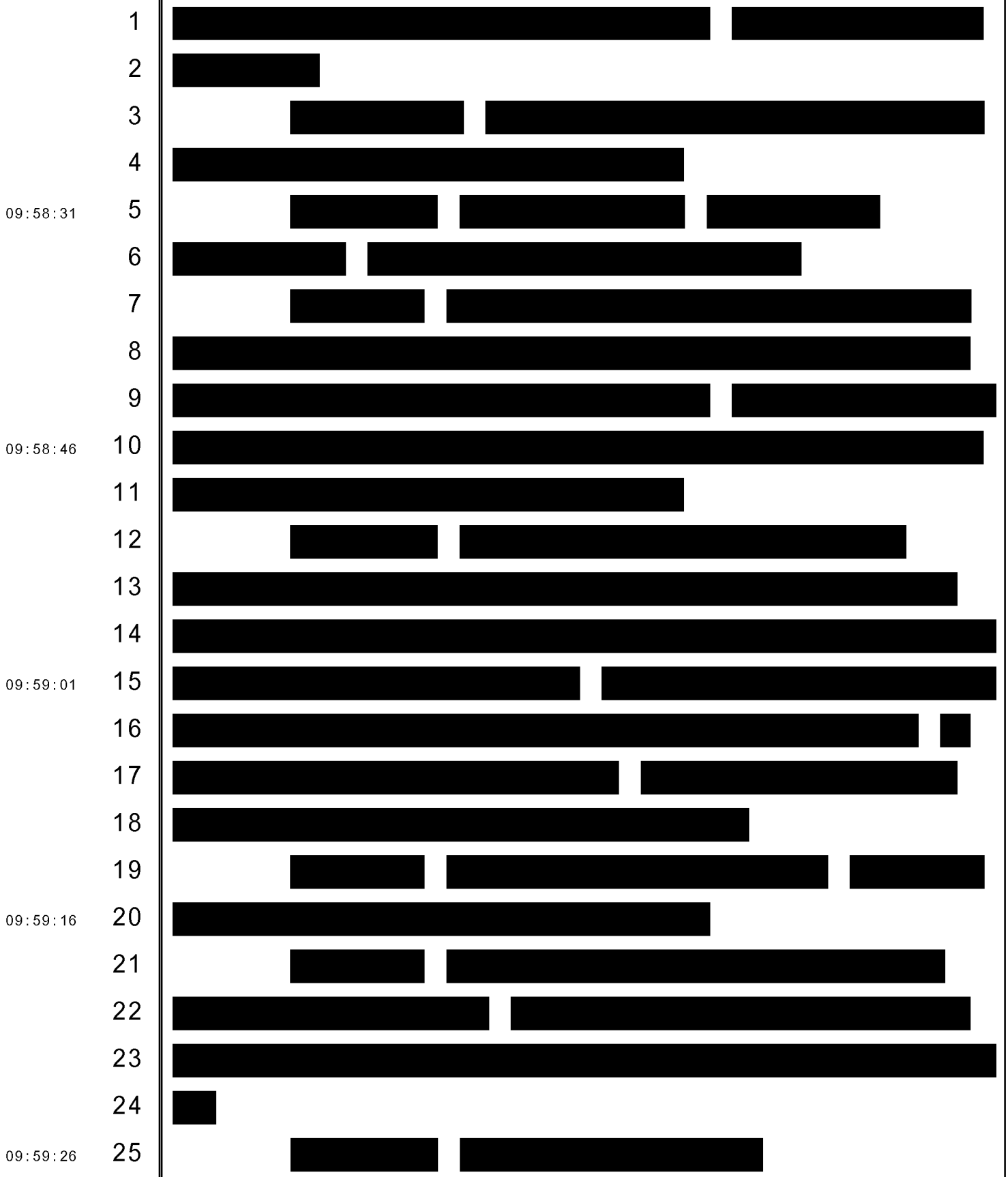
THE COURT: You want a sidebar?

MR. BAYMAN: Yes. A short sidebar.

(Proceedings heard at sidebar on the record.)



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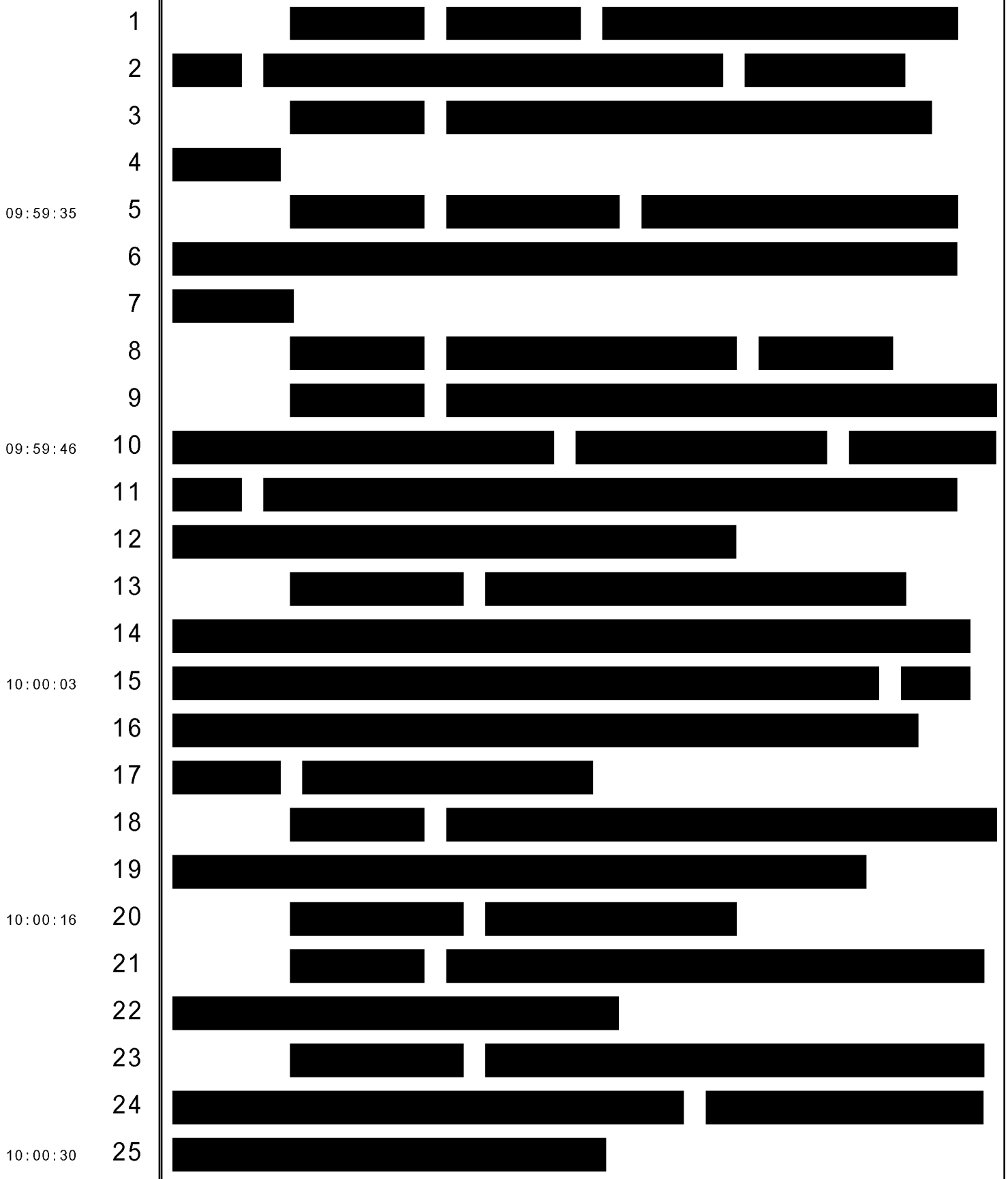
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(Proceedings resumed within the hearing of the jury.)

THE COURT: All right. Proceed.

(Audiotaped deposition of Pierre Garnier played in open court).

THE COURT: That concludes the proceedings.

MR. RAPOPORT: And we can go with another one or break, whatever you say.

THE COURT: All right.

MR. RAPOPORT: Ready for the next one?

THE COURT: Ready.

MR. RAPOPORT: Great, Your Honor. Our next witness is Dr. Davies.

(Audiotaped deposition of John Davies played in open court).

THE COURT: Does that complete the reading?

MR. RAPOPORT: That completes that testimony, yes, Your Honor.

THE COURT: Okay. Call your next.

MR. RAPOPORT: Our next is Geoffrey Dunbar.

I should mention before we begin this, Your Honor, the run time here is 37 minutes just so you know for case

management purposes.

THE COURT: All right.

(Audiotaped deposition of Geoffrey Dunbar played in open court) .

11:06:53 THE COURT: All right. Ladies and gentlemen, we'll take about a ten-minute recess break now.

You may step into the jury room.

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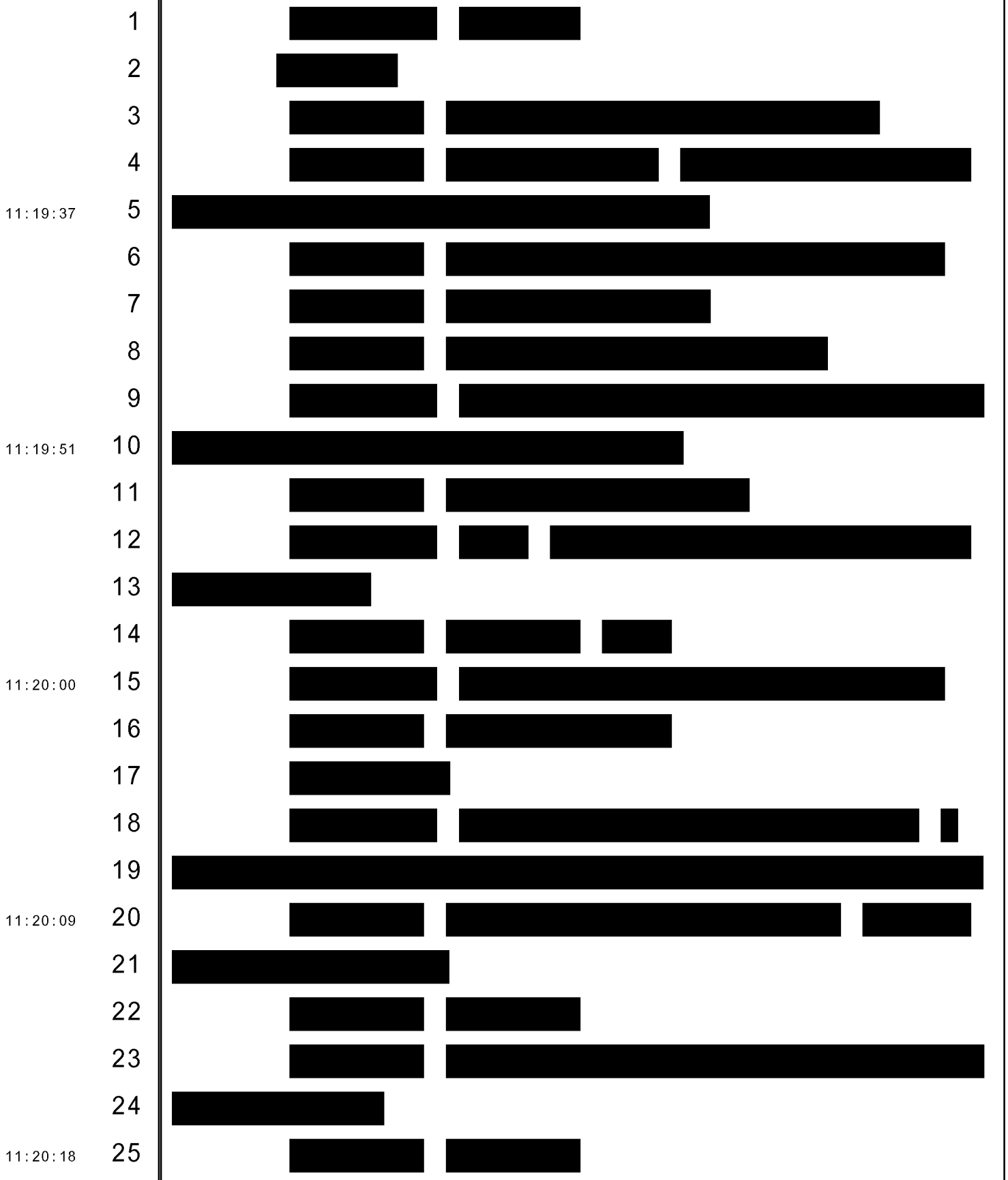

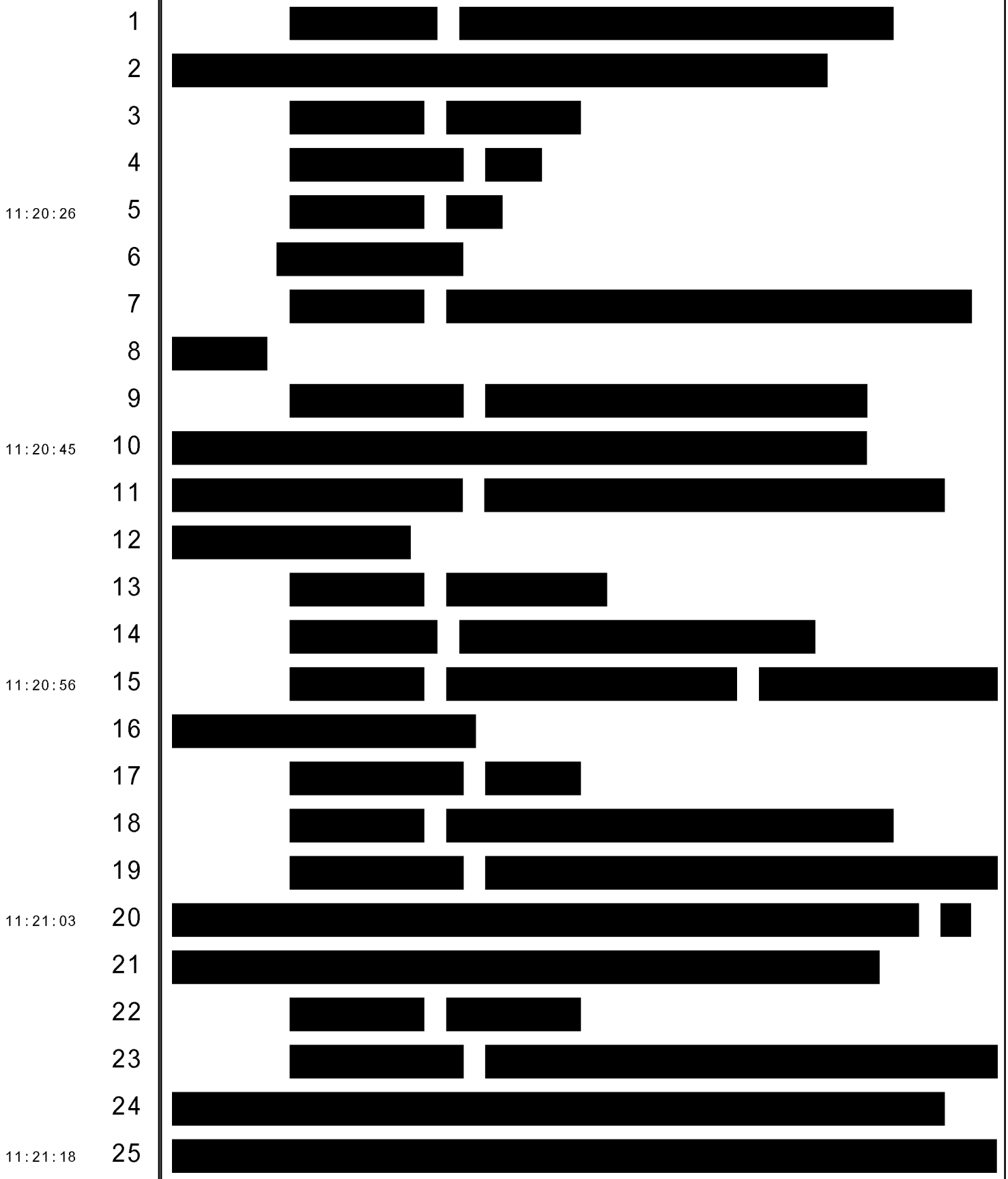
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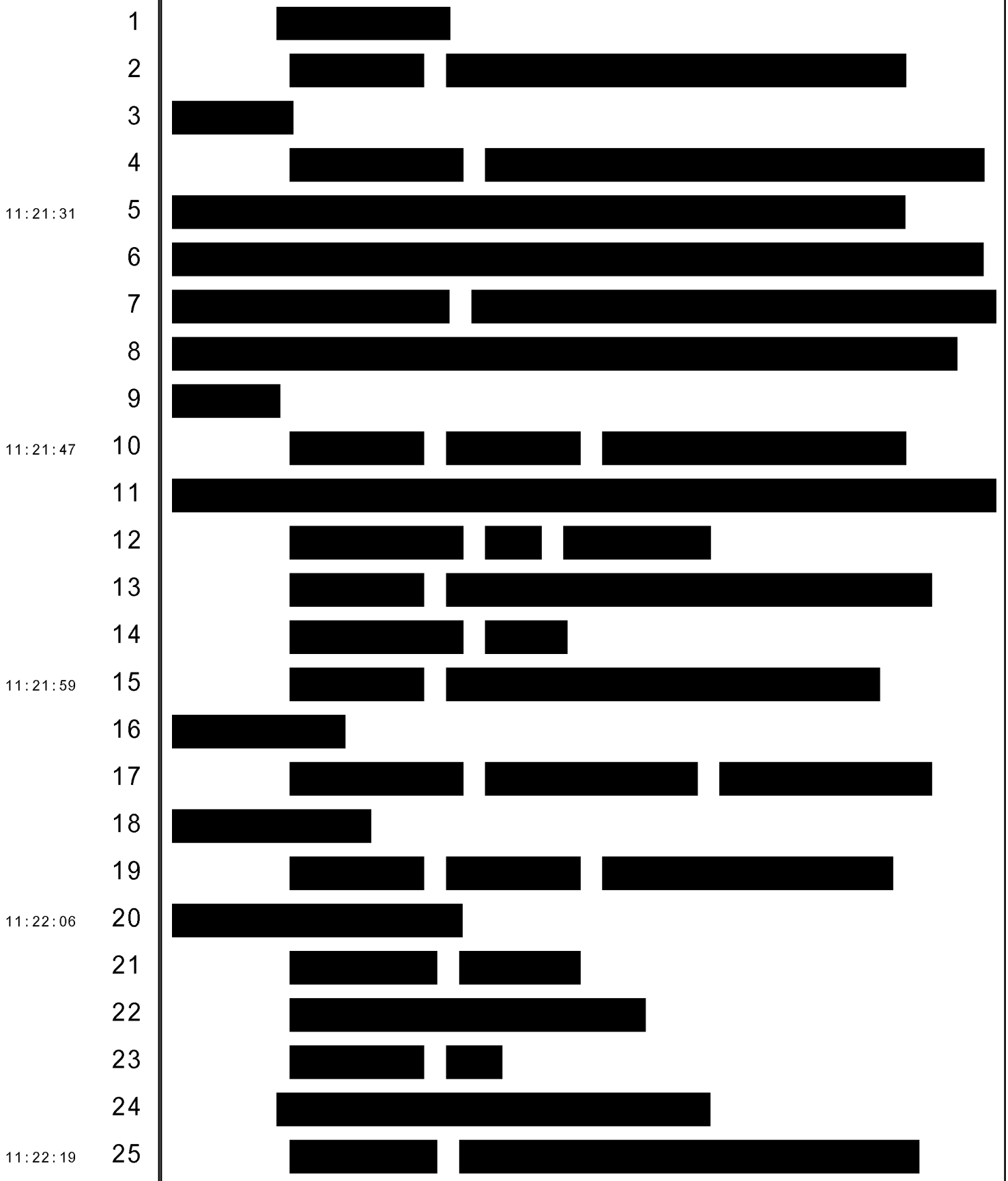
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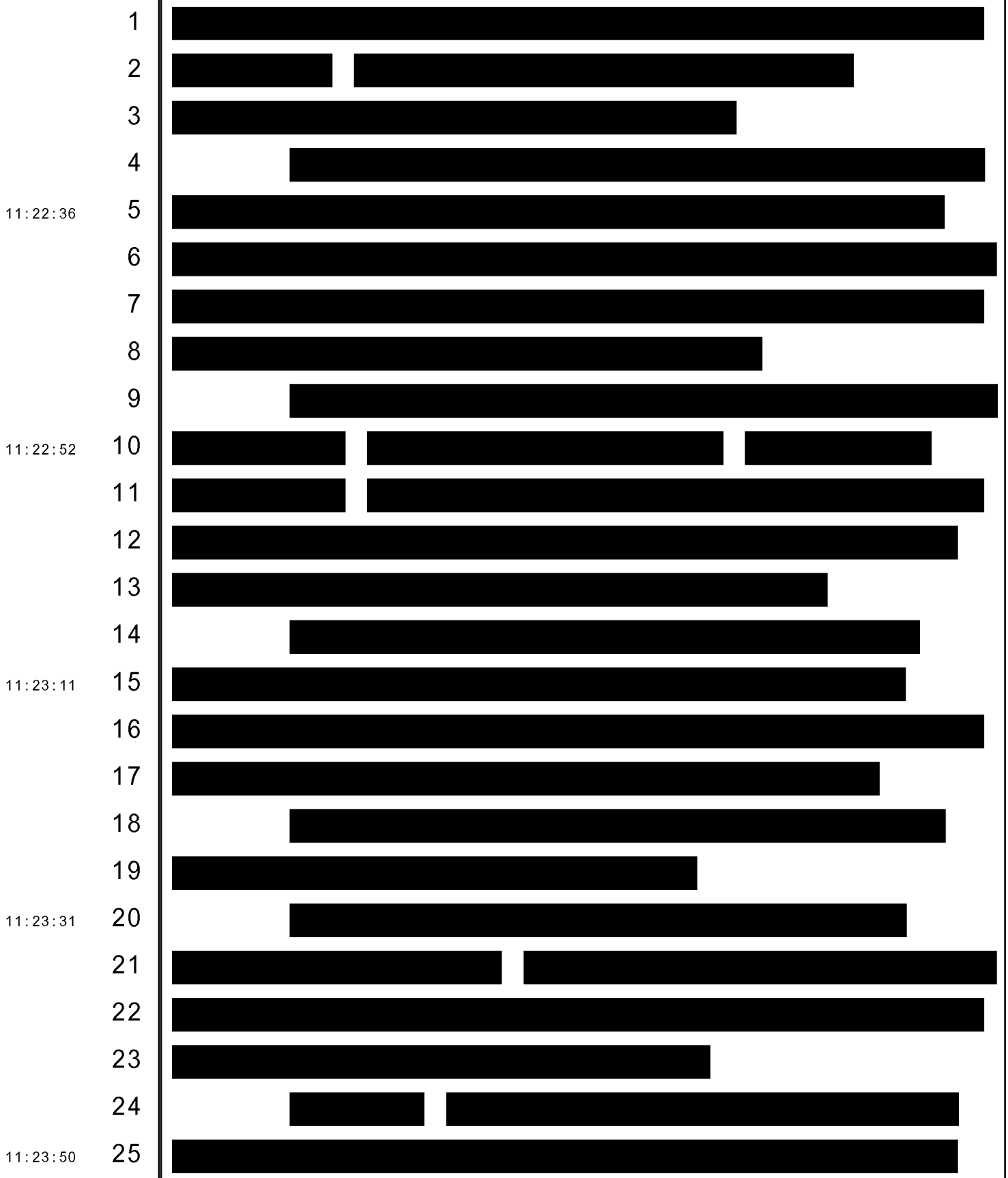
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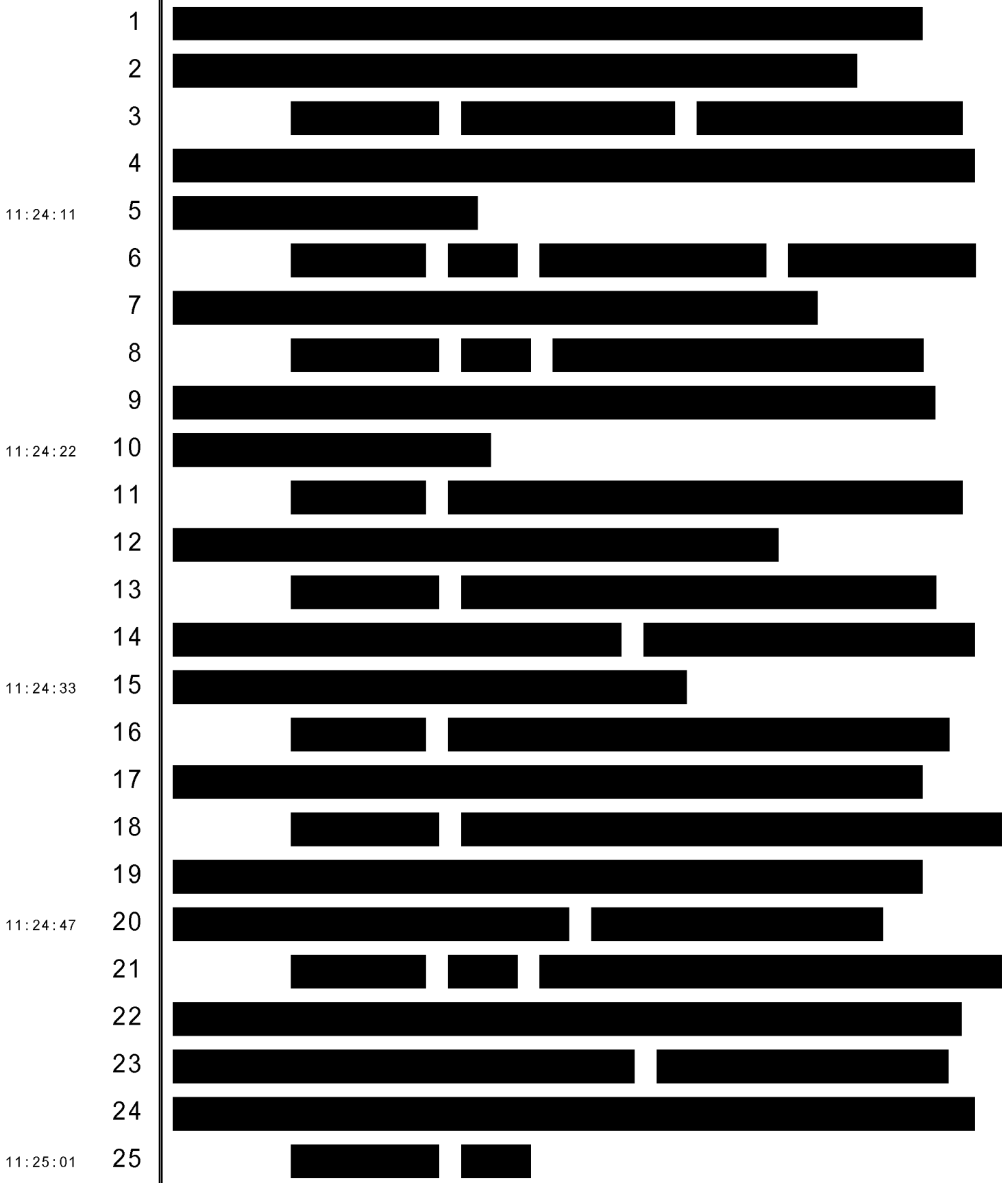

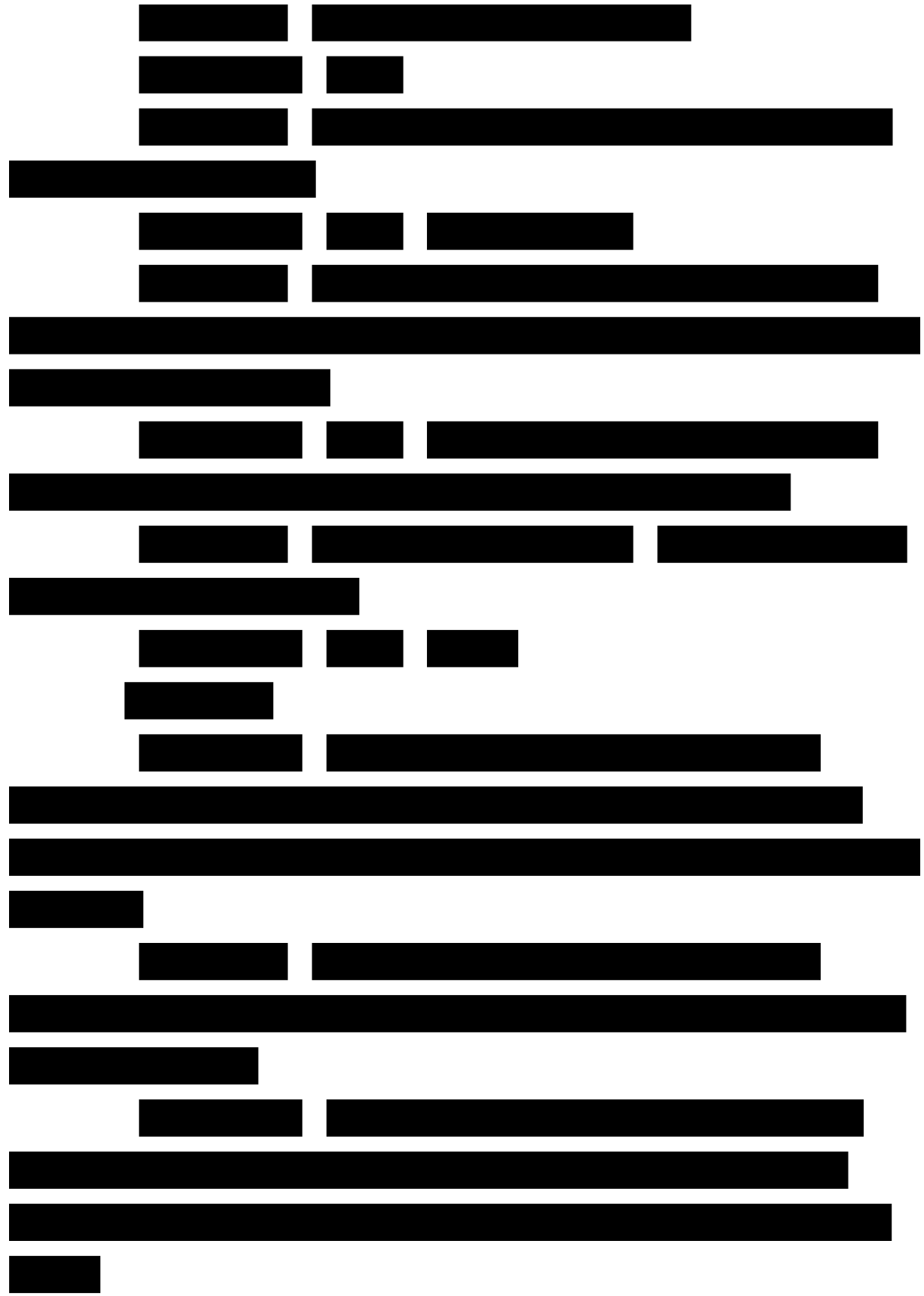
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(The following proceedings were had in the presence of the jury in open court:)

THE COURT: All right. Thank you very much, ladies and gentlemen.

And please be seated. We'll resume.

Call your witness, sir.

MR. WISNER: Yes, Your Honor. The plaintiffs call Dr. Healy to the stand.

THE COURT: All right.

(Brief pause).

THE COURT: All right, doctor, step up here, please. Right around there, if you will (indicating).

(Brief pause).

THE COURT: Please raise your right hand.

(Witness duly sworn.)

THE COURT: You may take the witness stand.

11:28:26 THE WITNESS: Thank you.

THE COURT: You may proceed, sir.

DAVID HEALY, PLAINTIFF'S WITNESS, SWORN

DIRECT EXAMINATION

BY MR. WISNER:

11:28:30 Q. Good morning.

A. Good morning, Mr. Wisner. Excuse me, while I pour some water. Just one minute.

Q. Not a problem.

(Brief pause).

11:28:38 BY THE WITNESS: Okay.

BY MR. WISNER:

Q. Could you please introduce yourself to the jury.

A. Yes. I'm David Healy.

Q. Dr. Healy, are you a medical doctor?

11:28:51 A. I am, yes.

Q. What sort of medical doctor are you?

A. Well, I've trained in general -- in -- hang on. I've trained in general medicine, first of all, but after that I did research and I moved into the mental health area. So I'm

11:29:09 actually a practicing clinical psychiatrist.

Q. Are you familiar with the area of pharmacology?
A. I am, yes, because the research that I did after I did my general training first, and before I went into mental health, was based on pharmacology, because at that point in time, in
11:29:29 the early '80s, the new drugs we had looked like good tools to probe why people behave the way they do.
Q. And can you just briefly explain to the jury what pharmacology is.
A. Yes. I mean, there's a broad range of things that they can
11:29:48 be. You've got a group of people in there who are interested in what we can tell about how the drug works in either the heart, the kidneys, or the brain, or whatever. What does it actually do. How does it latch on to a brain cell, for instance, and tell that brain cell what to do.
11:30:04 And then there's people who work all the way in sort of -- I mean, they don't work in the lab, looking at what actually happens to the drug in the brain, they look at what can we tell about what this drug does when we give it to people. Does it actually work, does it cause problems. And
11:30:23 that involves getting involved in things like clinical trials.
So it goes all the way from the lab to the bedside. At the bedside end of it, the people who are doing it are mostly doctors, but in the lab they're usually Ph.D. scientists.
11:30:37 Q. Doctor, I understand you are a medical doctor, are you

also -- do you also have a Ph.D.?
A. Yes.
Q. And what is your Ph.D. in, specifically?
A. Well, it was looking at what could be said about people who
11:30:50 are depressed. What happens to them. And this is back in the early '80s, you need to remember, before we could look at your genes, before we could do brain scans on you. There's a whole bunch of things we could do now that we couldn't do back then, but one of the things we could do back then was to use the new
11:31:06 antidepressant drugs, and things like that, to check and see what happens to people who were depressed when they began to get well, after they put on the actual treatment, to see does there -- do their hormones change, do their serotonin levels change and things like this.
11:31:24 So that was the kind of work that I was involved in. Looking at is there anything abnormal in people who are depressed to begin with. Could we generate a test which would actually show our people clinically depressed as opposed to just unhappy.
11:31:40 And if we could, then the next issue was what changes when you give a treatment that works or even that fails to work, what's the intact of the treatment and what's the impact of the recovery.
Q. And, Dr. Healy, I'm sure everyone has heard that you have
11:31:55 an accent. Where are you from?

A. I'm Irish.
Q. And where was your medical training done?
A. Well, it was done actually in University College Dublin and the research was then done in a place called University College
11:32:07 in Galway.
Q. And your Ph.D. work, where was that done?
A. Well, that was done in, at the first instance, over in Galway and then later Cambridge, England.
Q. And where did you presently live?
11:32:20 A. I live in the United Kingdom and I live in a part of it called Wales.

MR. WISNER: This time, Your Honor, I'd like to proffer his credentials to the jury.

THE COURT: All right. Proceed.

11:32:43 MR. WISNER: Dr. David Healy is a professor of psychiatry at Bangor University in the United Kingdom and operates a clinical practice treating patients at the Hergest Medical Unit, inpatient unit, in North Wales.

He is both a medical doctor and a
11:32:58 neuropsychopharmacologist. He is -- he has done research specifically in the field of selective serotonin reuptake inhibitors, or SSRIs, of which Paxil is a member.

He achieved his doctorate from his study and thesis specifically on the subject of the serotonin reuptake system,
11:33:18 and the system that Paxil works on.

He has written peer-reviewed medical journal articles concerning SSRIs, including Paxil and about their ability to induce suicidality in some patients.

Dr. Healy has published over 200 peer-reviewed journal articles specifically relating to pharmaceutical medications of which 50 have specifically related to the relationship of psychotropic medications and suicide.

He has presented lectures specifically about the issue of suicidality all around the world, including Harvard Medical School, Columbia, Yale, University of California or UCLA, University of Toronto, as well as various organizations, such as the Royal College of Psychiatrists, the American College of neuropsychopharmacology, or the ACMP, the European College of neuropsychopharmacology, the Irish College of Psychiatrists, et cetera.

He has in addition to his peer-reviewed work in medical journals, published over the 22 books in the field of mental health and psychiatric drugs. A selection of those books are displayed here (indicating). I won't go through all of them. Of note are the psychopharmacologists, which are textbooks specifically relating to the field of psychopharmacology.

In addition in the early years Dr. Healy has been a consultant to most of the SSRI manufacturers at some point in his life, including the manufacturers of Paxil, specifically

GlaxoSmithKline. He's -- years before he was ever asked to be an expert witness for any plaintiff, he was, in fact, asked by Eli Lily, the maker of Prozac, to provide his expert opinions concerning the SSRI induced akathisia and suicidality related to Prozac or fluoxetine.

11:35:32

Dr. Healy has been studying the issue of Paxil-induced suicidality for well over 20 years.

With that, Your Honor, I'd like to proceed.

THE COURT: Proceed.

11:35:45

BY MR. WISNER:

Q. All right, doctor, let's start off with the things that we're going to cover today. I first want to talk to you about antidepressants and how they relate to the treatment of depression and anxiety, then I want to talk to you about

11:36:15

whether or not antidepressants specifically relate to suicidality, and if so, how that happens. Third, I want to talk about Paxil specifically and the data that you have seen, conducted yourself, and you will testify about relating to whether or not Paxil is associated with suicidal behavior. And

11:36:35

then finally, I want to go into your evaluation of the methods by which GSK has conducted its research on suicidality and whether or not those methods were scientifically legitimate or not.

So with that sort of rough outline, let's start at the

11:36:53

beginning. What is an antidepressant, doctor?

A. Well, the group of drugs that we use within -- at the mental health field these days begin in the early 1950's. And the first drug was a drug called Thorazine that's now called an antipsychotic.

11:37:17 And the companies who were in the business of trying to make drugs like these made a whole load of them. And in the midst of all this they found one that seemed -- that looked like Thorazine but actually didn't seem much good for people who had major mental illness. On the other hand, it did seem 11:37:39 to be good for people who had a condition called melancholia.

And this drug that they'd found was a drug called imipramine and it was the first of what are called the tricyclic antidepressants. We now know that it's also a serotonin reuptake inhibitor, but it does a lot more than that. 11:37:56 And it was a very good drug, a very potent drug for treating people with, as I say, this profound what we would call depressive illness now but what was called melancholia back then.

Q. You mentioned a few terms there. Let's clarify them for 11:38:10 the jury.

The first was, you mentioned, serotonin reuptake. What is that and can you explain how that relates to antidepressants, doctor.

A. Okay. One of the things that was closely related to the 11:38:23 discovery of the new drugs was beginning to become aware that

the brain operates using chemical neurotransmitters. And one of the first of these to be discovered was serotonin. And later when drugs like LSD were made, and it was actually found, that that works on the serotonin system, the link between
11:38:48 serotonin and people being severely mentally ill was made for the first time.

But also -- and can I just ask you to quickly repeat the question there?

Q. Sure. I'll ask you another question, doctor.

11:39:04 So you mentioned that there is a serotonin relationship to behavior. How does that work or do we know how that works?

A. Okay. Well, yes. And what we actually know now is, we got over a hundred neurotransmitters, a hundred different ones. We
11:39:21 know that serotonin is one of the most primitive ones. That's way back when were just single celled, and clearly we weren't every single cell creatures, but just when they were single-celled creatures they had serotonin also.

And it's -- it's -- it's -- it's clear that serotonin,
11:39:43 while it's primitive, however, isn't necessarily needed. You can remove, at the serotonin system, from a lot of animals, and after a while, so they don't eat and sleep right for a while, but after that they seem to be able to function not too bad. So that was actually discovered. And there were hints that it
11:40:02 was in the brain as of the early 1950's when drugs like LSD

came along. And when it had impact on it, the link, as I said, was made to mental illness then.

There was a theory based on the fact that a drug called reserpine, which came on stream in the early 1950's also, and it was the one that made the link between serotonin, really, and behavior. And that what we knew was, that it could cause people to become suicidal. And one of the things we did was to deplete serotonin. It lowered it.

In the 1960's the idea came about that, you know, our brain chemicals can be low when we're depressed --

MR. BAYMAN: Your Honor, objection. This is way beyond what's even in his report now. He's giving a speech.

THE COURT: Proceed.

BY MR. WISNER:

Q. Dr. Healy, just answer my question. We'll get to all these things in due time, I promise.

A. Okay. Fine. Okay.

Q. So the other thing that you mentioned earlier was melancholia. What was that in the 1950's and how does that relate to our understanding of antidepressants?

A. Before we had the antidepressants as indicated earlier, the depressive illnesses we had, the main illness was one called melancholia. Most people who had nervous problems weren't thought of as being depressed at all. They were thought of as being anxious.

Melancholia was the kind of condition where you came to a full stop. You often would stop eating and we had to force-feed you in order to maybe save your life. You weren't able to sleep, you got to slow down, you couldn't move physically or mentally.

11:41:41

And we knew that there was a big risk that when you were slipping into this state, that you might try to kill yourself, and as you recovered from this state, you might also try kill to yourself. So people were very concerned about this. And when there was any hint that a person might have melancholia, they were quickly removed to -- to a hospital.

11:41:53

When the first antidepressants came on stream, they seemed to be a good treatment for melancholia --

MR. BAYMAN: Your Honor, that is not even the question.

11:42:07

THE COURT: Overruled. Proceed.

BY THE WITNESS:

A. They seem to be a good treatment for melancholia, and that led to people being aware that actually there's other cases out there that we aren't picking up at all.

11:42:17

And as these cases got picked up, the idea of melancholia began to change into something closer to what we think of as people being depressed now, but there was a big change later on.

Q. Let me ask you another question. How has our understanding

11:42:31

of depression in the mental field change from what was previously melancholia?

A. Yeah. Well, compared with back then, the estimates I have are that there is about 1,000 people being diagnosed for being depressed, as being depressed, when there was only 1 person diagnosed with melancholia back then or even now.

Melancholia still happens, but this profound illness is quite rare compared with the number of people who actually get diagnosed as depressed now.

And part of what's happened is this, you'd expect when a treatment works, that the condition clears up, but, in fact, we seem to have the opposite.

And a little bit of what happened was, as I explained to you, people had nervous problems back during the 1950's, but they weren't called depressed they were called anxious. And we had a good treatment for that, we had the benzodiazepine group of drugs, and you've heard of drugs like Valium and Ativan. These seem to be excellent drugs, but then they ran into problems in the early '80s, people who are concerned that you might get hooked to them.

And that that time, the SSRI group of drugs, that stands for selective serotonin reuptake inhibitors, were coming to the market. And the companies could've put them on the market as anxiolytics or tranquilizers, but --

MR. BAYMAN: Objection, Your Honor. Now what the

companies could've done?

THE COURT: Overruled. It's background.

Go ahead.

BY THE WITNESS:

11:44:02 A. Well, what the companies did was to say, look, from our point of view, let's treat these nervous problems as people being depressed rather than being anxious.

And to a degree, this was probably right. The kind of message for doctors like me was that when you see a patient

11:44:19 who's anxious, there's an underlying depressive illness beneath this. If you treat that, the anxiety will clear up.

But, in fact, what began to happen was, people who had been seeing as cases of Valium or Ativan in the 1980's were actually becoming cases of Prozac and Paxil. People who are

11:44:41 anxious, were becoming depressed. We now have this huge explosion where, as I said, about this seems to be thousand-fold increase in the illness compared with where we were during the 1950's.

Q. Back in the 1950s, you mentioned that there was the

11:44:58 emergence of tricyclics for treatment of depression. Were they effective in treating depression back then and were there alternatives?

A. Yes. And there were two groups. And at almost exactly the same time when the tricyclic group of drugs were actually first

11:45:17 discovered, and that was in Europe, there was a group of drugs

called the MAOI's. Now, that stands for Monoamine oxidase inhibitors and they were discovered over here. And one of the things that was noted early on was when somebody -- I mean, lots of people did awfully well when they got the tricycle
11:45:41 antidepressants, but it was noted that some of them responded poorly, and the people who responded poorly to the tricyclics often responded very well to an MAOI, and people who responded very well to an MAOI often responded poorly to the tricyclics, and one of the reasons for this is that the drugs do completely
11:45:56 different things to the serotonin system.

Q. Were tricyclics and MAOIs a popular form of treatment back in early '60s and '70s?

A. No, they weren't, and for two reasons. The general view, as I've indicated, was this was a rare condition. Nobody
11:46:15 thought much about any of the pharmaceutical companies could make much money out of it, but the other aspect was the MAOI group of drugs, the ones who were invented over here, came with a major problem, which was you couldn't eat cheese with them and you couldn't drink wine with them because there was a real
11:46:34 risk you might actually have a stroke. And that was because of an odd quirk to these drugs, which meant that when you took them, your body can absorb a compound called tyramine, which pushes your blood pressure up. So these were terribly tricky group of drugs used. Very good drugs, but, you know, and
11:46:54 tricky to live with.

Q. Well, that brings us into the '80s, doctor.

What is an SSRI?

A. Right. Well, the tricyclic group of drugs are called that because, when you look at them, they all have three rings. And
11:47:12 to most people looking at them back then, me, you, these all look the same. But a man called Albert Carlson looked at them, said, well, they all look the same, but when I listen to doctors and I listen to patients they tell me that they aren't all the same. Some of them do different things to others. And
11:47:36 does this group over here that people say to me, look, there's some emotional effect of these ones compared to these ones, and I happen to know, looking at the structure of them, that the thing that these drugs are doing which these don't is these act on the serotonin system. So let's try and make a cleaned up
11:47:57 drug that acts more on the serotonin system and less on some of the other things.

And that led to the first of the what's now called SSRI group of drugs, it was a drug called sell met and made by drug called Zelemet (phonetic) and was made by Albert Carlson.

11:48:11 Q. Now, you said it was to be a cleaner drug. How does that supposed to physically work within the body?

A. Well, the talk, the things people talk about is that it's a cleaner drug, but, in fact, it's not.

The big deal with this early group of molecules was
11:48:31 that they all work in a bunch of different things, and the two

key things was they work on norepinephrine and serotonin. And when you hear SSRI and you hear the word "selective" it sounds clean, but what it means really is, it's acting on the serotonin system and not the norepinephrine system. It also
11:48:53 acts on a bunch of other things.

So some of the problems with these drugs come from the action of at the serotonin system and some come from the other things that it acts on. In terms of the serotonin action, what you might guess, given they cleaned it up in a drug that was
11:49:11 going to focus much more on this, is a turbocharged action. So if there's any problem that comes from the serotonin system, these drugs risk causing it.

Q. Now, these are in the context of being treatments for depression. Is a depressed person's serotonin system
11:49:28 deficient?

A. No, it's not. There was an idea during the 1960's that we had the all -- you hear these days about we have a chemical imbalance when we're depressed. These ideas came from the 1960s. The main focus back then was on the norepinephrine
11:49:49 system. People thought that the chemical that's lowered is epinephrine, because that's more a get-up-and-go neurotransmitter.

There were also ideas back in the 1960s that people didn't pay much heed to but that maybe it's serotonin that's
11:50:07 low, but by the end of 1960s most of academic medicine had

thrown these ideas out. They said, look, whatever is wrong and people who have alluded to it, it's nothing to do with a lowering of either of these neurotransmitters.

Q. When you treat a depressed person with an SSRI, do you see a change in their serotonin levels?

A. Well, you certainly do. And this can vary hugely. Again, the word "selective" probably gives you the feeling that we've engineered things and we know what we're doing. In fact, it's a -- if I give an SSRI to anyone here in the court, it's a little bit like dropping a little bit of ink into a glass of water. You can control where it goes and what actually happens. There's much less control -- we know much less about what we're doing than we like to let you know we know, okay.

MR. BAYMAN: Objection, Your Honor. This is outside the scope.

THE COURT: Sir, this is background. It's not damaging to either side. I'm going to let him explain this to the jury. This is the way the jury, I hope, and I will, will understand the case better for your benefit as well as for the plaintiff's benefit.

You may proceed.

BY THE WITNESS:

A. Okay. What -- there was an idea, there was a hope, I guess, that what we find with the serotonin reuptake inhibitors, that there was low serotonin in the brains of

people who were depressed and that with treatment it increases.

The trouble is, there's lots of serotonin on different bits of the brain. And we now know that areas of the brain where it goes up and areas of the brain where it goes down. There's people where, overall, your brain serotonin levels treatment can go up, there's lots of people when they take the treatment the serotonin levels go down.

11:51:50

So, you know, we really don't have any good test based on serotonin to test anyone does anyone here in the court would they be suited to an SSRI or not. The best test we have is to give the pill to you and say, look, let me know how you feel when you get this pill because, you know, that's the single thing that's going to best tell me if this pill suits you or not.

11:52:09

BY MR. WISNER:

11:52:26

Q. You mentioned earlier that LSD was observed to have an effect on the serotonin system. Is there a relationship between impacting the serotonin system and influencing erratic human behavior?

A. Yes. And it's clear on the serotonin system, if you act, all kinds of strange things can happen, including people go -- going quite mad.

11:52:48

While the SSRIs don't work on the bit of the serotonin system that LSD normally works on, they leave a lot of serotonin washing around the place. And some of it can have

11:53:16

effects even like an LSD. You rarely get the full-blown effect, but, you know, things like this can happen for sure.

The other aspect to it is, we don't have any test showing anyone who is depressed has low serotonin levels, but what we can show is that if we take the jury, or the court, or whatever, there's variations among serotonin among all of us, and that colors our personalities. Just like there's variations in dopamine and norepinephrine, the kinds of personalities we are, whether we're outgoing or introverted, do seem to be shaped by these neurotransmitters.

But the point here is that when I give a pill to people, that I should bear in mind that the serotonin system of this person here might be completely different than the serotonin system of that person over there. That doesn't mean that either serotonin systems are abnormal, but it does mean that when I give you a pill, I might get a completely different response here to over there (indicating).

Q. So in the '80s we have the emergence of these selective serotonin reuptake inhibitors. You mentioned the first one, what were the first few SSRIs that entered the medical profession?

A. Okay. Well, in the early '80s, it did look like making serotonin reuptake inhibitors was a rational way forward. It looked like a very good idea. And lots of companies got into the business of trying to make them. And I know of at least 20

different SSRIs that have been made by companies and put into clinical trials.

Now, we don't have 20 SSRIs on the market, we only have about 6 or 7, and that's because a lot of compounds ran into problems even before they came to the market. And then the first few that came into the market, the first was this drug called Zelemet, which you didn't hear about over here. It came in the market in Europe and it caused a serious problem, which is Guillain-Barré Syndrome and was removed from the market after about a year.

The next one came in the market in France, which is called Indelphine (phonetic) and that caused liver problems and that was removed from the market.

The third to arrive was Luvox, which you did get over here much later. We had it in Europe a bit earlier and then it came over here much later, marketed for OCD.

And then the one that really made the market for everyone was Prozac, which was approved here in 1987 and comes into the market in early '88.

Q. With the emergence of Prozac, based on your research, how did that influence or affect the way psychiatric conditions were being treated by doctors, medical doctors?

A. Well, there two things here. One is that, first of all, Prozac isn't the only SSRI that came into the market back then. It was followed quickly by Paxil and Zoloft.

And you had some very big companies get into the business of trying to educate doctors, which is a good thing, and educate the rest of us about the nature of the problems we have. And that tends to -- well, it -- and the influencing can be very effective. And it's not necessarily always the right kind of influence.

11:56:40

But what the companies, what the SSRIs did, and one had undoubted advantage compared to the older tricycle antidepressants, which was they were safe in overdose. So in terms of trying to handle the competition in the marketplace, the idea was the SSRIs was sold as being safe in overdose. That if you were on these pills, you weren't likely to kill yourself, was the messages.

11:57:01

The other bit of competition was to compete with drugs Valium and Ativan which were the big sellers. These were the real competition. And the SSRIs sold themselves as being good for the kind of nervous problems that are out there in office practice rather than in hospitals.

11:57:16

And the good thing about them, it was said back then, was that unlike the benzodiazepines, you couldn't get hooked to them.

11:57:33

One of the other features about all this, though, is, the SSRIs turned out to be ineffective for melancholia. They were relatively weak compared with the older antidepressants. So there was a big premium put on treating primary care

11:57:49

problems rather than hospital problems.
Q. And with that focus on primary care, did we see a shift of the treatment of depression from psychiatrists over to family doctors?
11:58:05 A. We did. And probably a greater shift over here than we saw in Europe. Family meds in our primary care, our general practice as it gets called, was always much stronger in the United Kingdom than it was here. Back then, the antidepressants came on the stream first. They were being
11:58:24 given by a psychiatrist over here and rarely by family doctors. Now that's switched and at least 80 percent of the antidepressants that are given over here are given in primary care family medicine. In the U.K., for a long time, it's been 90 percent of them have been given by family doctors and
11:58:49 they're rarely actually being given by people like me.
Q. Now, doctor, I want to shift to more on what this case is focusing on, and that's the issue of suicide. Before we get to that, though, I want to ask you some basic questions.

In your career, have you investigated specifically
11:59:07 whether or not psychotropic medications can induce suicidal behavior?
A. Yes, I have.
Q. And can you briefly explain to the jury, without getting into any specific cases or anything like that, what that -- how
11:59:25 long you've been researching it and what that research has

encompassed.
A. Yes. Well, from way back in the early 1980's when I was working on the serotonin reuptake system first, that meant -- now, this is even before the first SSRI drug came at the
11:59:42 market, because of the research I was doing, I was the kind of person that companies turned to in order to educate other doctors about what the -- what the serotonin system is and what the antidepressants group of drugs might be doing to it.

So this meant a lot of reading about what's known
12:00:02 about the serotonin system in the brain and also the rest of the body, because most of your serotonin isn't in your brain, it's in the rest of your body, in fact, but what's known about the serotonin system, because this will help shape what kind of problems that people get.

12:00:19 For instance, one of the commonest problems you'll get, if you've taken SSRIs, you'll feel nauseated for the first few days. And that can be explained by the fact that actually the biggest amount of serotonin in you is in your gut, but when the drugs came on stream, most doctors didn't know this. They
12:00:32 had to be told basic things like this.

So, you know, there's a role for people like me in helping to educate people.

And --
Q. I was asking about what your investigation and the
12:00:47 relationship between that.

A. Right. Okay. But the other areas of research, then, involved, as I said, taking people who were depressed and looking at what we could tell about the serotonin system.

We couldn't look in the brains. We couldn't look at what the serotonin levels in the brain were, and we still can't, but what we could do is we could look in the blood where there's a blood cell called the platelet that has lots of serotonin in it and seems to handle serotonin in a very similar way to what nerve cells do.

12:01:02

12:01:18

And the antidepressant group of drugs all act on the platelet and its ability to block serotonin reuptake. So there's a lot of things like this you could do with depressed people.

The other aspect then is, when the drugs began to come on the market and there were controlled trials being done, and again, I would've been one of the people who's involved in helping advise companies on the kind of conditions they might do a control trial in and what kind of rating scales they may want to use, and then looking at the results as they came out.

12:01:33

12:01:53

I did a great deal of consulting with the companies during this period. I was also involved in helping put on symposia, and things like that, to educate people more generally about what the drugs did.

So part of the research also involved simply meeting colleagues who were able to talk about the kinds of things that

12:02:11

they'd seen happen with the drugs that didn't necessarily end up in published articles.

Q. So you mentioned you started looking at this issue in the late '80s. Have you systematically kept abreast of the data and information from that point onward?

12:02:28

A. Absolutely. Yes. This has been the kind of thing that I've got. Well, in the U.K. we have a word that I don't normally hear over here, geek. Do you guys have geeks over here?

12:02:44

(Laughter in the courtroom.)

BY THE WITNESS:

A. Well, I guess you'd call me something like that, a serotonin geek. There you go.

BY MR. WISNER:

12:02:50

Q. All right. And as new data has come and arrived related to the relationship between psychotropic medication and suicide, have you incorporated that new data into your opinions?

A. Yes, I have. And it's been -- well, I have to say here, very early on, because of the research I do and the clinical

12:03:15

practice I do, I had people who I gave SSRIs to who became intensely suicidal. So this was an issue for me from very, very early on. I mean, a personal issue when you see people you are actually trying to treat and trying to help and when you've harmed them.

12:03:37

So that meant that I was interested in the issue, the

whole phenomenon of that, the drugs causing this kind of problem, which involves looking at the evidence that comes in, not just to confirm my view that the drugs can cause a problem, say, but also taking the evidence that points to the fact that
12:03:54 lots of people can do terribly well on these drugs, because I was still giving the same drugs to other people and they were doing well.

So there were issues about trying to work out why some people do well and others do poorly and how big a problem it
12:04:07 is, because that's going to shape, clearly, how sort of the whole -- how these drugs get handled, generally, and the wider debate.

Q. You mentioned that -- do you currently practice and treat patients?

12:04:19 A. I do, yes. About half the week I do research and about half the week I treat people.

Q. And then in your treatment of patients, I mean, do you use SSRIs?

A. Yes, of course I do. I mean, they can be wonderfully
12:04:32 helpful. I mean, the paradox here is, right from the 1950s, when the problem of people becoming suicidal on any antidepressant turned up first, the issue goes back way beyond when I began to see it first to the 1950s. You have people who are very enthusiastic about the early drugs they were giving,
12:04:48 because we didn't have anything else, who were describing some

people as better than well and doing hugely well on these pills, at the same time they were saying, look, we have a few other people who become suicidal. There's a bunch of people who were going on to suicide, but there is a bunch of people who, with these older drugs even, which also, as I said, worked on the serotonin reuptake system, that some people who drugs don't seem to suit and in early phase of treatment they may become suicidal.

12:05:07

THE COURT: Doctor, just don't talk quite so fast. We have a wonderful reporter, but we want to get everything you say. So slow it down a little bit.

12:05:22

THE WITNESS: Okay.

THE COURT: All right.

BY MR. WISNER:

Q. Now, doctor, is it your opinion that all SSRIs should be taken off the market?

12:05:35

A. Absolutely not, no. This is a group of drugs that I use. I mean, most drugs come with problems. The trick is not to necessarily get rid of them, but have an honest acknowledgement of what the problems are in order to be able to ensure that we hang on to the drugs that come with problems for one person over here but may be the perfect treatment for a different person over here.

12:05:56

Q. And based on these decades of research and work that you've done, have you come to an opinion about whether or not SSRIs,

12:06:13

and in particular Paxil, can induce adult suicidal behavior?
A. Absolutely. I'm very sure that it can.
Q. And have you arrived at an opinion with a reasonable degree of scientific certainty?
12:06:26 A. Yes, I have.
Q. Okay. Great. So let's get into the basis of that opinion you have about Paxil and SSRIs, generally.
I'd like to focus our first inquiry, and this is part of the outline we outlined to begin with on how. How do these
12:06:43 drugs, like SSRIs, cause someone who's depressed or had anxiety to be induced into suicidal behavior?
A. Well, there's a little bit of a mix, which is that these drugs take ages to work. They can take 4 to 6 weeks to work. That gives you the impression that nothing is happening before
12:07:05 that. In fact, from within 30 minutes of being on these drugs, many people will feel nauseated and a whole range of other things.
So the drugs are very active on people right from the very start. And right from the very start they can leave some
12:07:21 people -- I mean, the aim of the drug is to emotionally numb you. The reason we have the drugs is because Albert Carlson said, people are saying to me these drugs do something to their emotions, they do have numbing. Now, this can sound like many not a great thing to do, but if he can get just the right
12:07:41 amount of numbing for the circumstances in which you're in, so

that you don't feel the need to maybe dot every i and cross every t, you're not totally anxious about the work you're doing, you're a little bit more relaxed about it, that can be a good thing for a period of time.

12:07:57 Most most of the nervous problems we treat with these drugs actually only last a few weeks, at the most a few months. So if he can tie you over by getting the right amount of the emotional numbing, this can be a good thing.

And all of this happens right at the start, but the 12:08:15 other thing that can happen right at the start at the same time is, you can become agitated. You can become more anxious. So there's a bunch of things happening right at the start that the drugs do all of which can potentially contribute to you becoming suicidal.

12:08:49 Q. Doctor, if you could, in front of you, turn to Plaintiff's Exhibit 41.

A. On the screen or --

Q. In the paper.

A. Okay.

Q. It should be in order.

A. Okay. Let's open this.

(Brief pause).

BY THE WITNESS:

A. Yes.

BY MR. WISNER:

Q. Okay. What is this a document that depicts?
A. This reflects some of the things that these drugs can do almost instantly when you go on them.
Q. Would using this document help explain the mechanism behind drug-induced suicidal behavior?
12:09:05
A. It would help me explain it definitely, yes.
MR. WISNER: Your Honor, permission to publish to the jury?
THE COURT: All right. Proceed.
12:09:14
(Exhibit published to the jury.)
BY MR. WISNER:
Q. Okay. Doctor, what are we looking at here?
A. Right. What you're looking at -- well, what I hope you get from it, and what I get from this is, looking at giving the drug and the reaction of the drug on the brain. And we look and try to tease out how this drug might cause people to harm themselves.
12:09:27
And there's three different mechanisms that I have learned here. There's, in fact, more than three, but these are the three main ones.
12:09:44
Q. All right. Let's start with the one on the top.
A. Yes.
Q. Can you please say what that word is to the jury.
A. Okay. This is one of the most unfortunate words in medicine, I think. It's a word called "akathisia." It's a
12:09:55

Greek word which means restlessness. It was coined by a German. And, unfortunately, the field paid heed to the German that coined it, used it in the context od drugs during the 1950's and didn't pay heed to investigate it here over in the United States. We've seen the same thing as this who were using words like "emotional turmoil" and that would've given you a much better feel for what the phenomenon is.

Do you want me to explain it a bit more?

Q. Yeah. I'll ask you some questions about it.

So what is akathisia as we understand it in the medical profession.

A. Okay. It as actually been described first 100 years before, it was the opposite to Parkinson's disease. With Parkinson's disease you come to a full stop and you can't move. Akathisia was just he opposite. You beat around as restless as you can and can't stop.

It was described first, as I said, by a German doctor, called Dr. Hasse (phonetic) in the mid 1950's linked to a drug called Rezipin and he saw some of the people who became intensely restless on rezipin beating around the place, but American investigators looking at the same thing were more impressed with the fact that people were saying to them, often when they weren't beating around the place, they were saying to them, look, I'm full of violent and unusual impulses and I have never had before, I want to crawl out of my skin. It's an

inner restlessness.

The word akathisia points you a little bit towards the outer restlessness that some people see, but for me and for a lot of other people working, and certainly it's pointing to the
12:11:40 inter restlessness that's often the thing that's a little bit unhelpful, and for me and for a lot of other people it's the inner restlessness that's the really pernicious thing, the thing that can lead people to harm themselves or harm others.

People have described it like a state worse than
12:11:49 death. Death will be a blessed relief. I want to jump out of my skin. A lot of doctors like me have tried these drugs and they've said this condition, if you get it, is one of the worst experiences of your life. And some of these drugs were used in the old Soviet Union to torture people. You'd give them the
12:12:19 drugs, you know how bad they feel, and people were --

MR. BAYMAN: Your Honor, objection. This is now highly prejudicial.

THE COURT: Overruled. Proceed.

BY MR. WISNER:

12:12:30 Q. Doctor, you said, "I took these drugs." Did you mean you used them in patients or did you personally take them?

A. No, as part of research, one of the things that a lot of people do, both the companies do them and people like me have done them is healthy-volunteer studies.

12:12:45 If you're interested to find out about behavior and

things of that, one of things you can do is you can give a drug like an SSRI to healthy volunteers, and you it blind so they don't know what they've got. I mean, you know, you'll have things picked out that they may have got the SSRI or they may
12:13:00 have got a completely different drug. So you're able to look at the impact of behavior on people.

Now, it wouldn't be proper for me to give -- well, to run healthy volunteers on my colleagues -- I wouldn't run healthy volunteer trials on some of my colleagues and friends
12:13:17 if I weren't prepared to take the drugs myself. So I have also volunteered for these trials. And it means that I've had a few of these drugs and know what the feelings are like on the inside.

Q. Now, you said that there's an exterior and interior aspect
12:13:29 to akathisia. Let's focus on first the exterior.

Ballpark percentage, what percentage of akathisia is exhibited physically on the outside?

A. I don't think anyone can answer that for you, Mr. Wisner. And part of the problem here is that akathisia, like
12:13:47 Parkinson's disease, comes with an on/off phenomenon. In Parkinson's disease it's well-known that people can be there unable to move and 5 or 10 minutes later they can be walking down the corridor fine.

Some nursing staff and even in medical staff seen
12:14:07 this, sometimes think the patient is playing games: Look, they

were well able to move, so when they were -- whey they come to a full stop over over here, they were just manipulating us. But, in fact, that's not the case. It just that at times, if you've got Parkinson's disease, you simply can't move and then, all of a sudden, it loosens up and you're able to move again.

It's the same with akathisia. It's got an on/off switch. There are times when you're just incredibly restless and you can't stay still and then there are times that it's gone, you're back.

12:14:37 And I've had colleagues who have, when involved in some of the healthy-volunteer studies, who I interviewed and they seemed happy as a clam to me, just didn't seem to be any problem, and a half hour later, they told me, they were feeling suicidal, they were intensely restless.

12:14:53 Q. So what are the physical manifestations of akathisia that one would see?

A. It can involve pacing. You can literally be unable to stay on the one side -- I mean, it -- it -- it can, if you're caught in the one spot like me here, you won't be able to see it, but

12:15:10 I might be kicking my feet, okay, and unable to stop it (indicating).

If you aren't caught in the one spot, if you're able to move around, well then you move, you move around the whole time. You might ring your hands. You might look agitated. If

12:15:23 you imagine extreme agitation and how it looks. A person who

is really in a woe-is-me state, you know, this is awful, this is terrible, you know, walking up and down, totally oblivious to other people around them often, that's the way it will look.

12:15:40 Q. Now, what about internally -- well, before I get there, you said that it has an on/off switch. If someone is experiencing an akathisia reaction, will you expect them to always be exhibiting these physical systems?

A. No. No. No. They may not exhibit the physical symptoms at

12:16:00 all, they may be just inner, but whether it's inner or outer or both, they can have the on/off switch so there are periods of time when you can meet them and they'll look totally normal to you, and then a short while afterwards they may be anything but normal.

12:16:13 Q. Now, let's go to the inner parts of akathisia.

What does that entail, doctor?

A. Well, the words -- over the years the words that I've come to figure out the best is a state of emotional turmoil. Where you get people who might never have thought about harming

12:16:30 themselves or harming others or doing anything strange or violent are plagued with thoughts they have never had before. This can come as a huge shock to people.

One of the other aspects to the shock is, this can be happening to you and you might come along to a person like me

12:16:46 -- I mean, I've just put you on an antidepressant, you are at

work, you are at home, you're functioning, and things like that, I just put you on an SSRI and you are getting thoughts like this and you come along to me and the paradox here is you don't necessarily tell me it for a few reasons.

12:17:02 One is, you don't want to make me unhappy. And now that you have a big problem, I'm your way out of the problem, so you really don't want to make me unhappy.

But the other aspect to this is just, you know, you figure if I tell Dr. Healy what I'm thinking and what I'm

12:17:16 feeling and what I might do, he'll lock me up.

You don't necessarily make the connection to the pill. You don't necessarily realize, well, actually, if I just hold this pill, everything will be okay.

So for a range of different reasons, you simply don't

12:17:31 let me know what is like on the inside. And I might see you -- you know, maybe I see you during one of these phases where it's off and you're looking reasonably okay and reasonably relaxed and you think it's gone maybe, so I don't need to tell him, you know, he would lock me up if he'd seen me a half an hour ago,

12:17:49 but, hey ....

Q. Now, you're talking about akathisia as though you've seen it or spoken to patients. How do you know about this phenomenon?

A. Well, I've seen colleagues with it. I've had a degree of

12:18:05 it, a very mild degree from one of the pills that I took in a

healthy volunteer trial, but much more to the point, I've seen colleagues with a severe form of it. I've a lot of patients with it. And very early on, before there were the first reports over here on Prozac causing akathisia and causing
12:18:20 people to go on to commit suicide, I've given Prozac in the U.K. to a few patients and seen them become akathisic and suicidal.

Q. When akathisia manifests, when would you expect it to manifest, if at all, in a patient relative to starting a SSRI
12:18:42 therapy?

A. It can be anywhere within the first hour. And it's -- and the -- the antipsychotic group of drugs also cause it, and they typically cause it, if they're going to cause it literally, within the first hour.

12:19:00 The SSRIs seem to -- it's a little slower. It's after the few days often that things begin to build up, and the person more obviously akathisic. But the peak times tends to be around sort of 10 days, within a first week or two, that seems to be the worst time.

12:19:19 And when the SSRIs came out first, pharmaceutical companies reps in the U.K. where I work, and maybe over here as well, often said to family doctors, you know, this kind of thing can happen, it wasn't in the label, but the reps on the ground were saying this can happen, you might want to
12:19:35 co-prescribe a benzodiazepine with a drug in order to get

people through the first week or two because that's -- what -- what they called in the U.K., maybe not over here, serotonin pick-up syndrome.

Q. Doctor, I'm a bit confused. How is it that only a few days of therapy can lead to severe psychological side effects?

12:19:51

A. Well, as I've tried to explain to you, within the first hour the SSRIs will have had a major impact on everyone here in the court. Not everyone will feel nauseated, but about a third of you will feel nauseated, but, you know, those of you who are going to feel nauseated will feel it within the first hour or two of having had this drug.

12:20:15

They cause an emotional numbing that many of you will be able to recognize as being there within the first hour or two of going on the drug. And anyone who's been on the drug and see what they can do -- as, for instance, one of our healthy-volunteer studies we ran in the hospital where I work. And of the people of the volunteers were my nursing and medical colleagues. And some of the patients in the hospital at that time were able to point to one of my medical colleagues and say, what's he on. And this was within a day or two of them having been on the drug. They could see he was on a drug and it was --

12:20:29

12:20:47

MR. BAYMAN: Your Honor -

BY THE WITNESS:

A. -- changing his behavior.

12:20:55

MR. BAYMAN: Your Honor, may we approach sidebar for a minute?

THE COURT: Yes.

Well, this may be a good time to take the break.

12:21:05 We'll break now for lunch and we will resume within an hour, 1:30.

MR. RAPOPORT: Just for clarification, Your Honor, is it 1:30 or 1:20?

THE COURT: 1:30.

12:21:21 MR. RAPAPORT: Yeah, 1:30. Great. Thanks.

THE COURT: I thought I said 1:30.

MR. RAPOPORT: You did. You said in an hour but --

THE COURT: That's a little more than an hour. You're right. You're holding me now.

12:21:30 MR. RAPOPORT: Right. We're happy to have it.

(Brief pause).

(The following proceedings were had out of the presence of the jury in open court:)

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12:21:38 [redacted]

[redacted]

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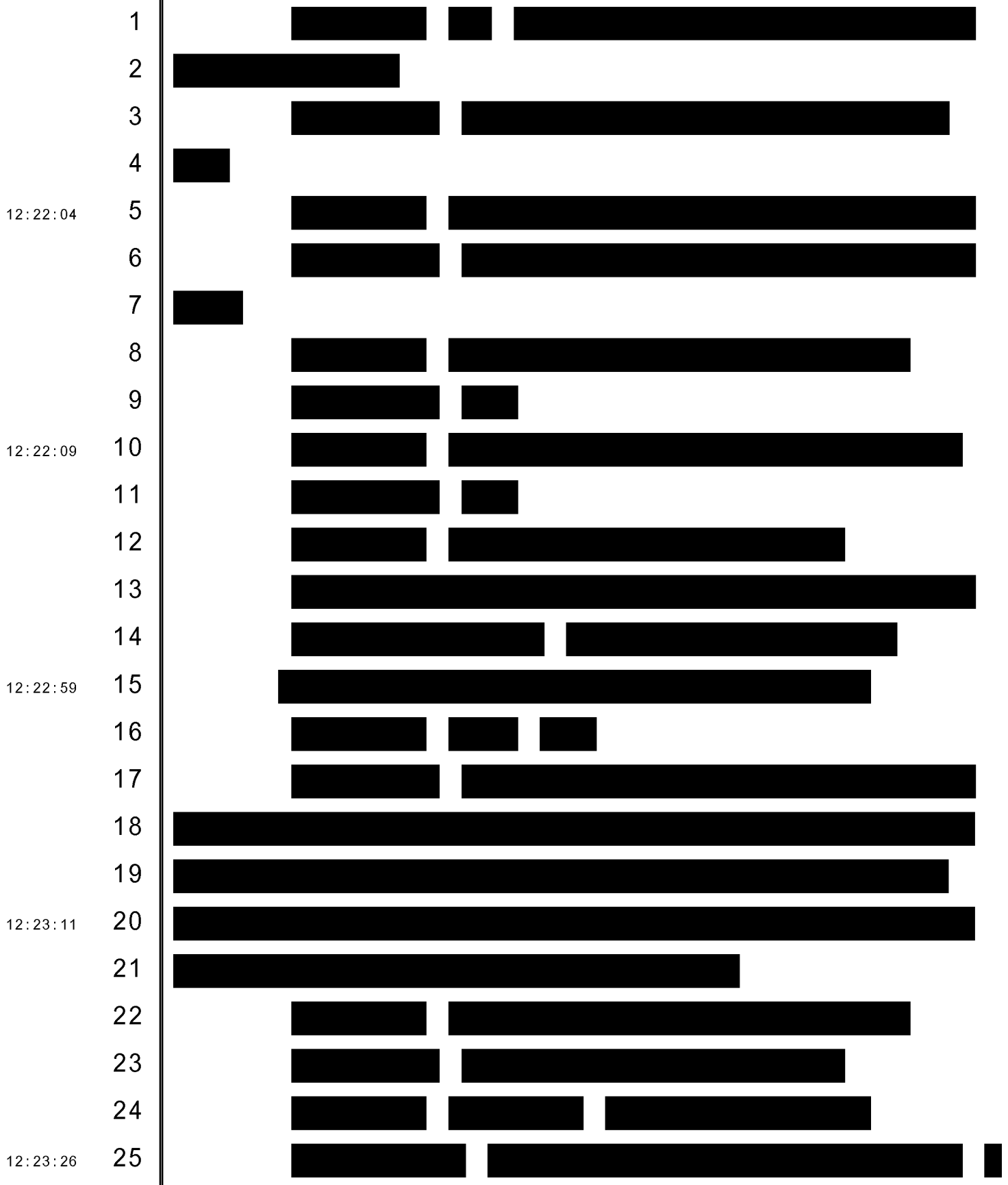
12:21:56 [redacted]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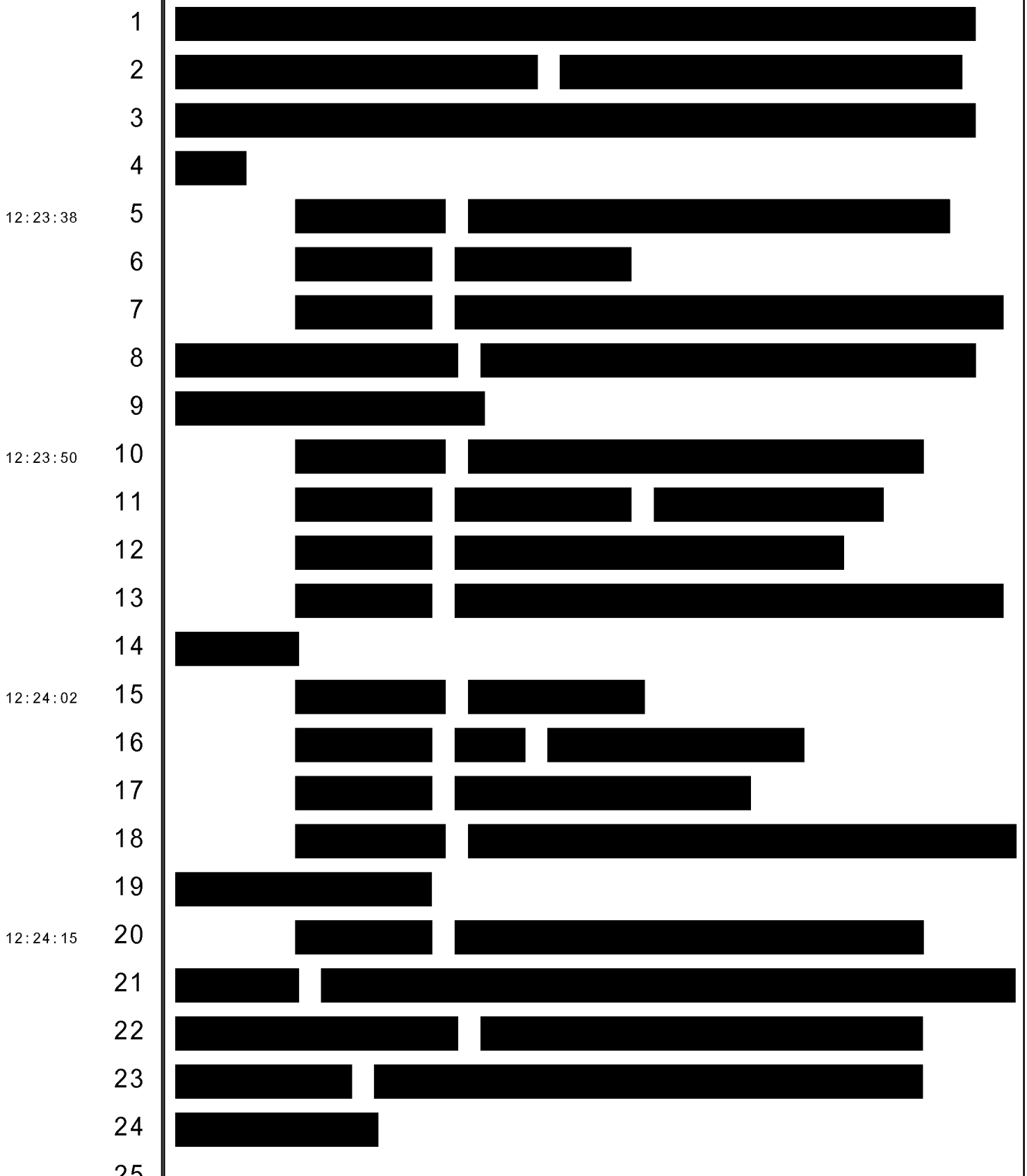
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(Luncheon recess taken from 12:24 o'clock p.m. to 1:30 o'clock p.m.)

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I CERTIFY THAT THE FOREGOING IS A CORRECT TRANSCRIPT FROM THE RECORD OF PROCEEDINGS IN THE ABOVE-ENTITLED MATTER

/s/Blanca I. Lara March 15, 2017