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 Thursday, July 12, 2018, Volume 8, Afternoon Session, before the Honorable Suzanne R. Bolanos, at 1:20 p.m.

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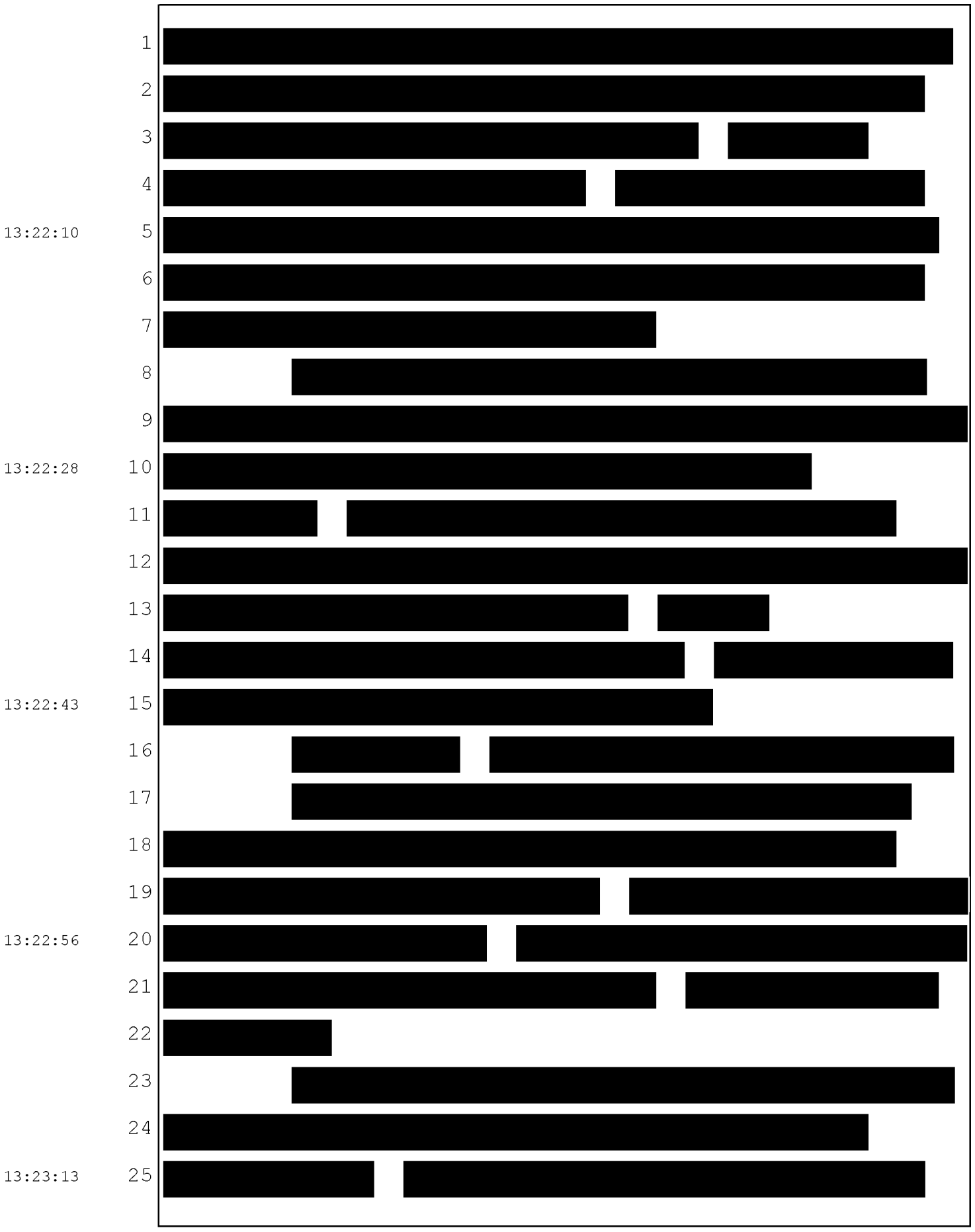
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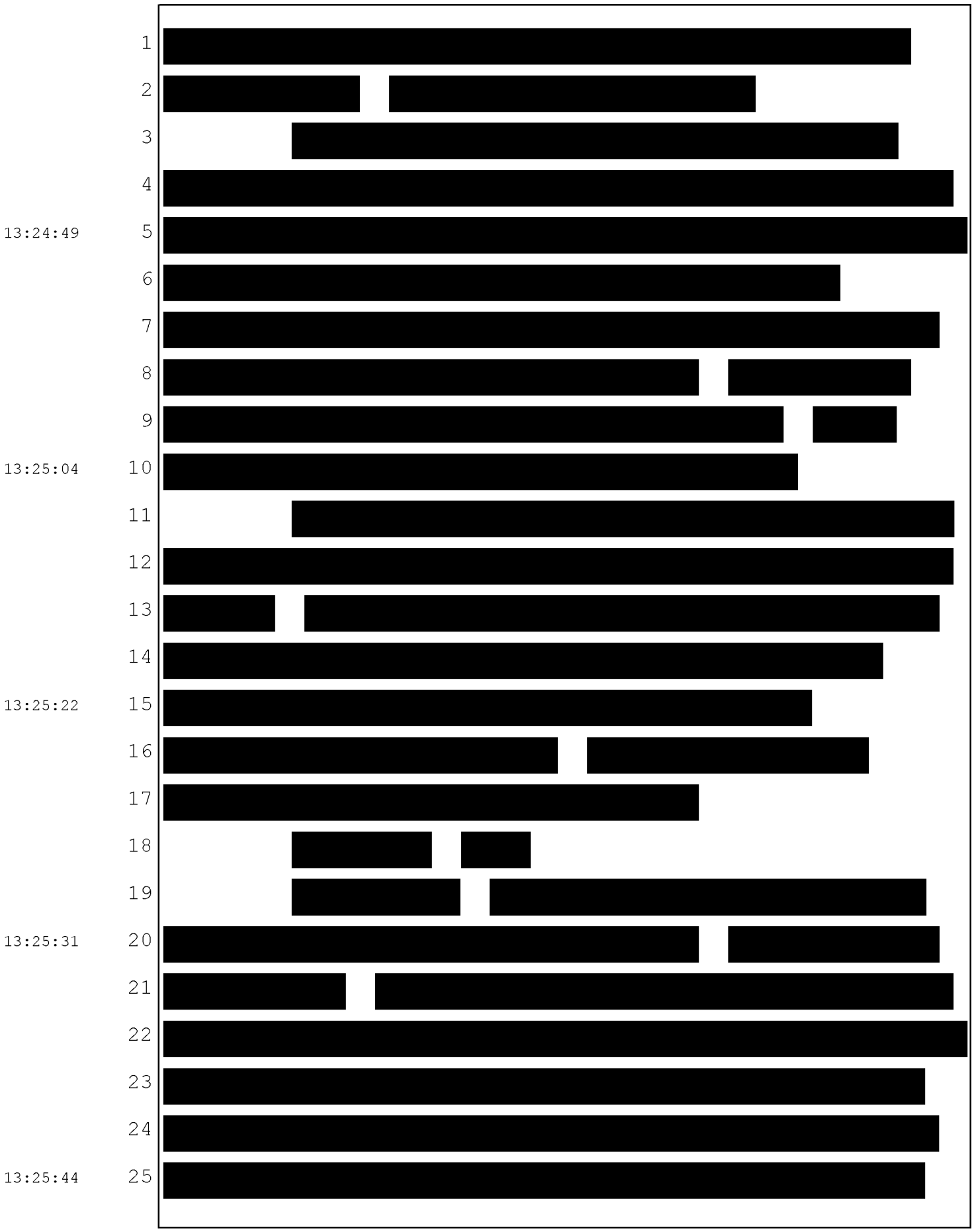
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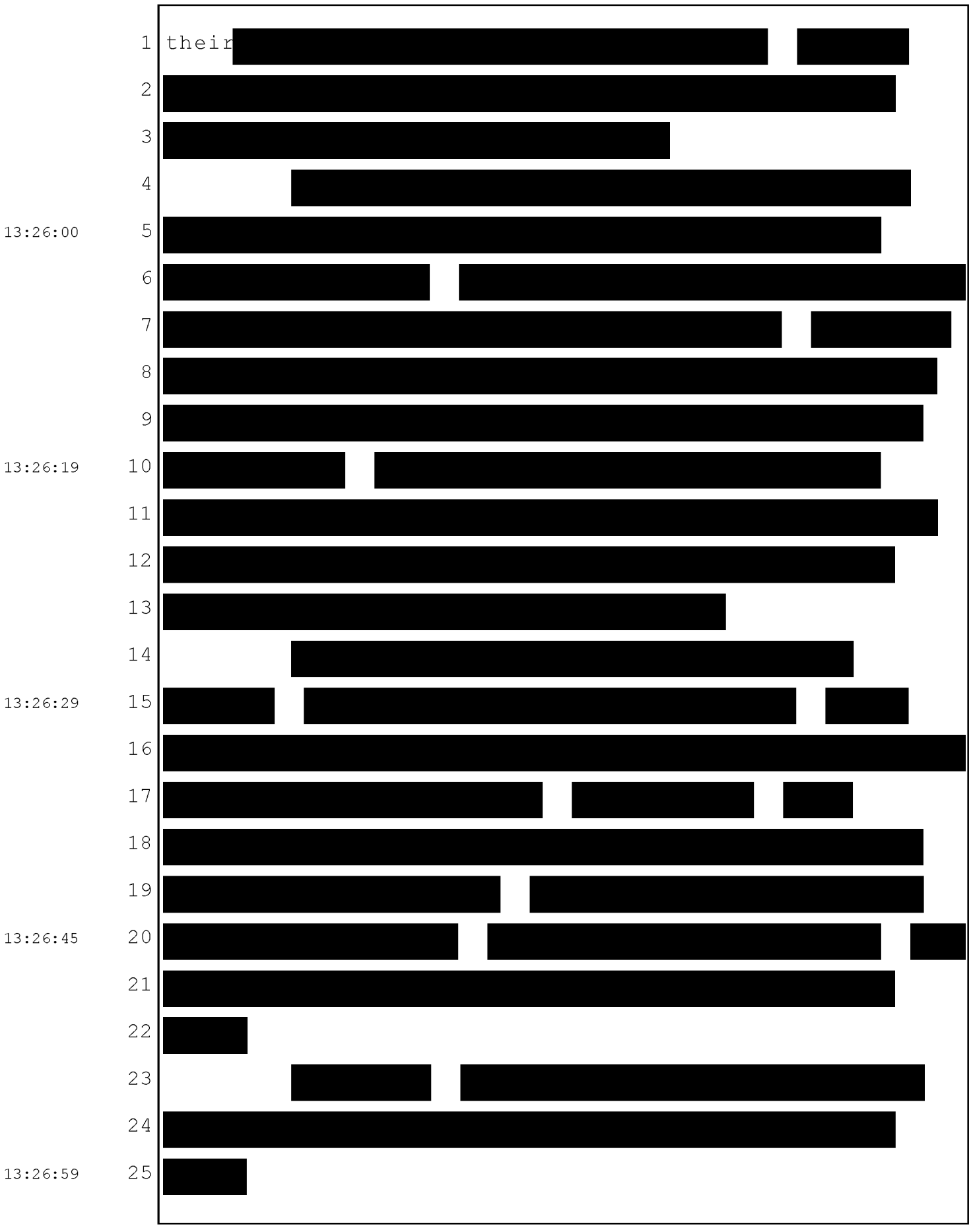
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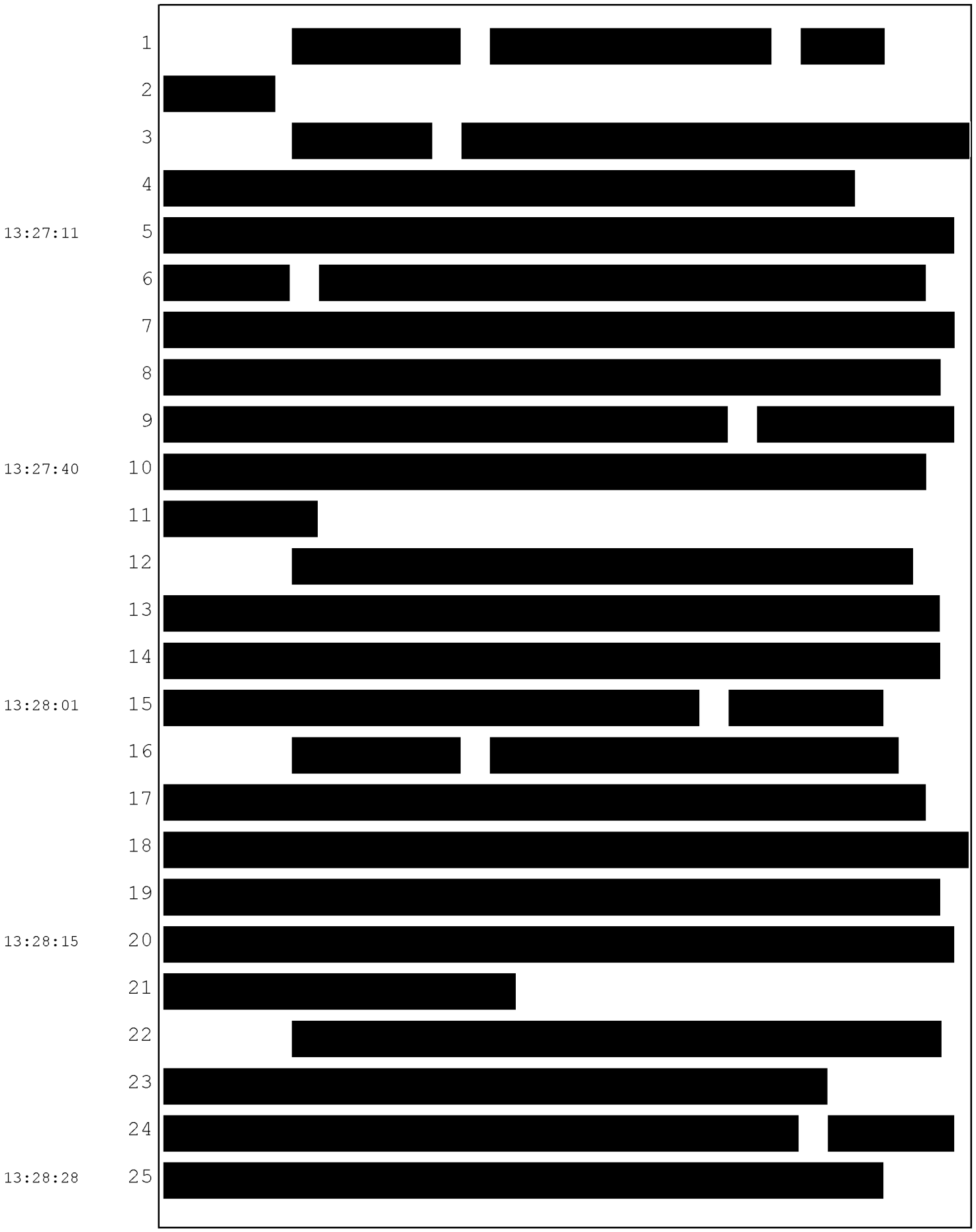
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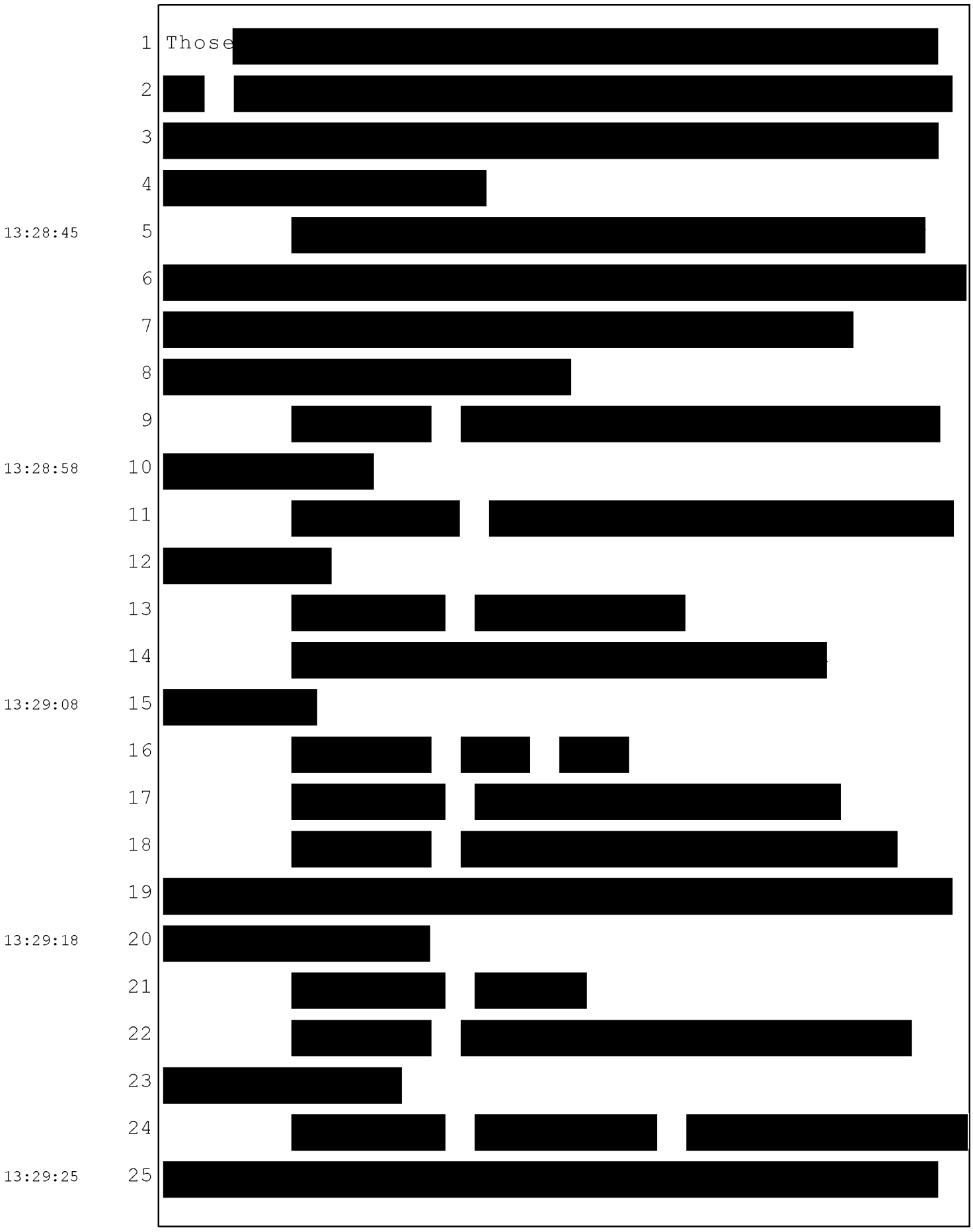
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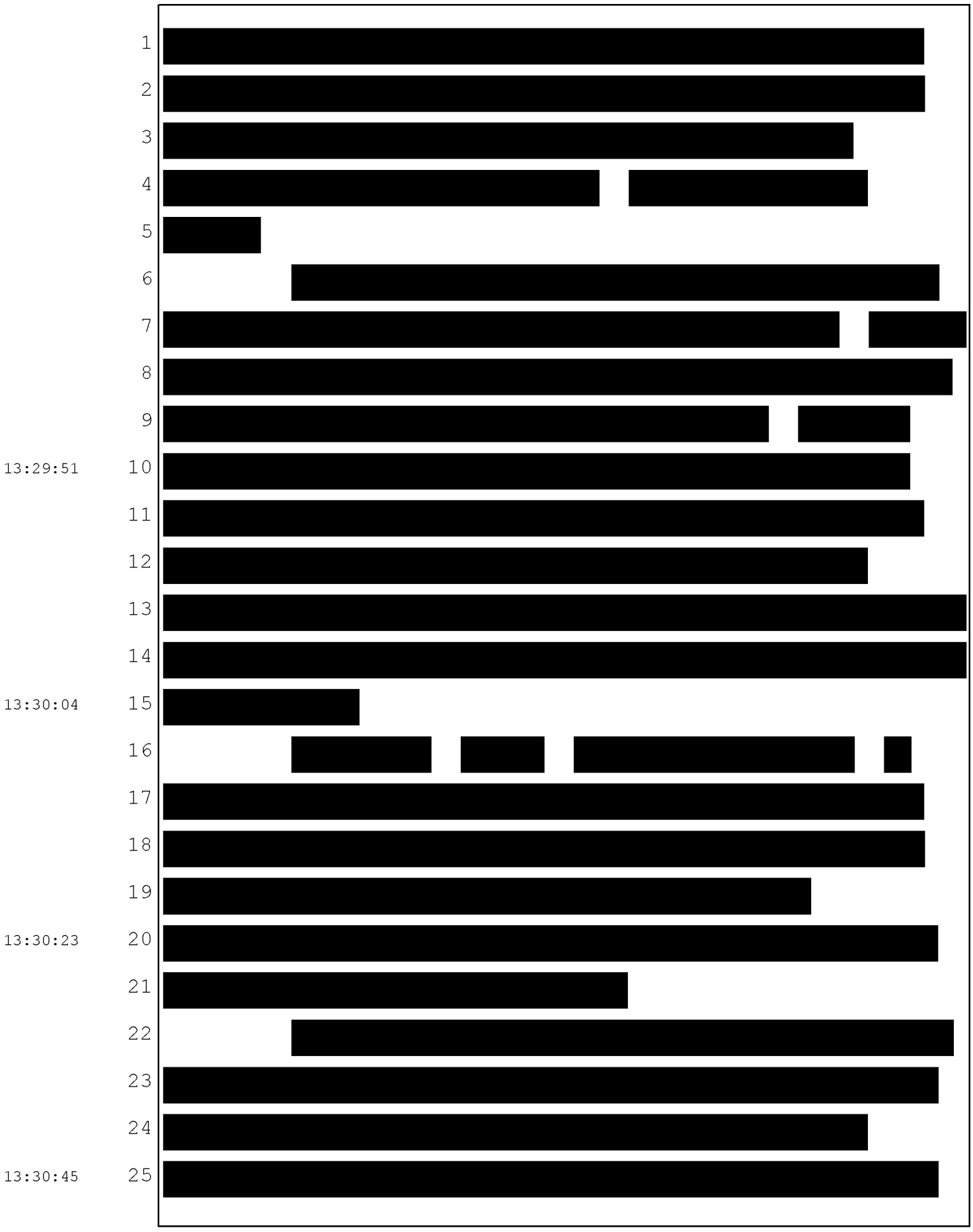
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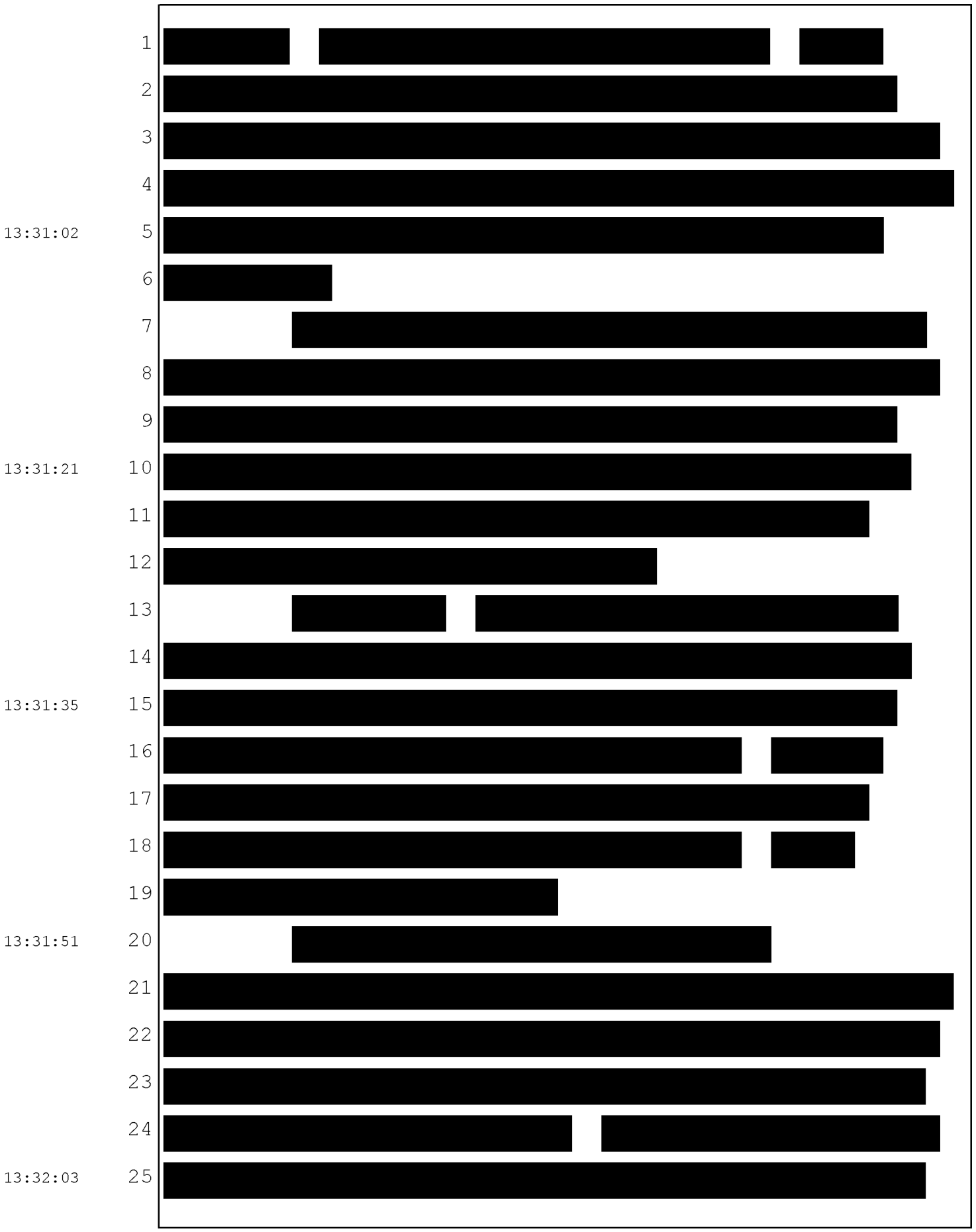
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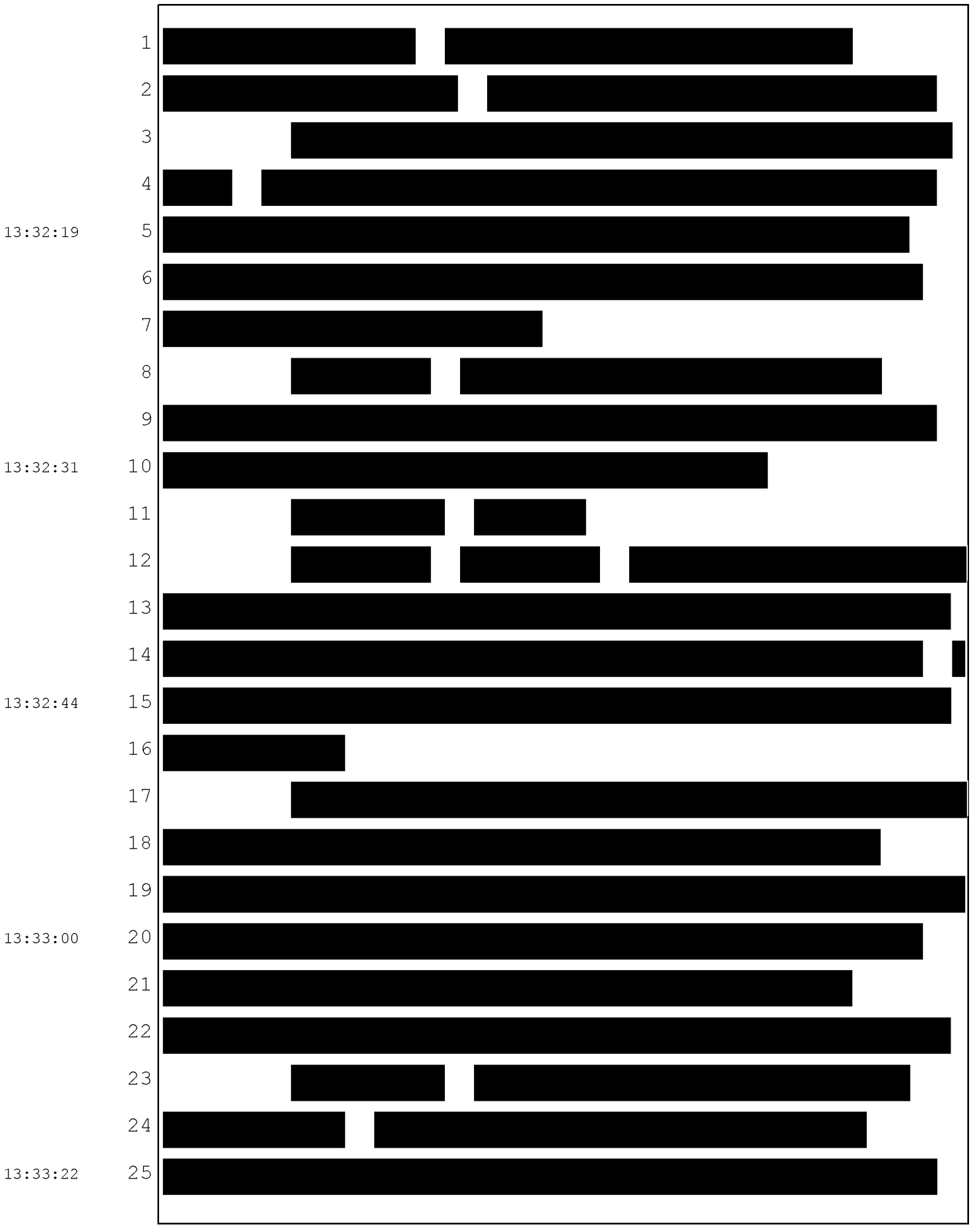
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13:35:24 (Jury enters courtroom.)

THE COURT: Welcome back, Ladies and Gentlemen.

Mr. Wisner, do you wish to recall Dr. Portier?

MR. WISNER: Yes, your Honor. At this time, I recall Dr. Portier to the stand.

13:37:02 (Christopher Portier takes stand.)

THE COURT: Good afternoon, Dr. Portier. If you'd please return to the witness stand.

And, Ladies and Gentlemen, Dr. Portier remains under oath.

13:37:21 MR. WISNER: Thank you, your Honor.

THE COURT: All right. Mr. Wisner, you may proceed.

DIRECT EXAMINATION (Continued)

BY MR. WISNER:

Q. Did you have a good lunch, Doctor?

A. Sorry?

Q. Did you have a good lunch?

A. Yes. Thank you.

13:37:32 Q. All right. Good.

All right. Just before we ended off, we were talking specifically about the reactions that you experienced after the IARC Monograph was issued.

Do you recall that, Doctor?

13:37:48 A. Yes.

Q. And we discussed that there had been, sort of, an outcry that emerged following the classifications?

A. Yes.

Q. And I think you testified you weren't sure where

13:37:58 that came from; right?

A. Correct.

Q. Okay. I'm going to show you a document that's in evidence. Exhibit 292.

A. Okay.

13:38:08 Q. This is a document that came in earlier in the trial, Doctor. And as you can see, the first page is dated February 23rd, 2015, and it says, "Glyphosate and IARC."

Do you see that?

13:38:20 A. Yes.

Q. All right. Now, if we go down this document, I just want to show you -- now, Attachment A to this document says, "Preparedness and engagement plan for IRAC carcinogen rating of glyphosate."

13:38:42 Do you see that?

A. Yes.

Q. And (inaudible) February 17th, 2015?

A. February.

Q. It's back far enough; right? Right here

13:38:49 (indicating).

A. Yeah, I see it. It's one at the top, too, February 23rd.

Q. Yeah. And this is before the IARC actual classification; correct?

13:38:57 A. Correct.

Q. Okay. And then down here it says, "Inform, inoculate, engage in industry partners."

Do you see that?

A. Yes.

13:39:04 Q. All right. This is the part that I wanted to show you. Sorry. It's at the bottom of this page. Post-IARC.

Do you see this section, Doctor?

A. Yes.

13:39:14 Q. And it states: "Orchestrate outcry with IARC decision, approximately March 10th of 2015."

A. Uh-huh, yes.

Q. As part of your work on the IARC panel, did you keep in touch with some of the Working Group members

13:39:31 after the classification?

A. Yes.

Q. And do you understand whether or not they were sent letters or intimidated in any way by Monsanto or other organizations?

13:39:43 MR. GRIFFIS: Calls for hearsay, your Honor.

THE COURT: Sustained.

Q. BY MR. WISNER: As part of your work, have you had to consult with anyone from the IARC program to respond to subpoenas or requests for information?

13:40:12 A. I have talked with IARC on those issues.

Q. You personally have?

A. Yes.

MR. GRIFFIS: I apologize. This is the subject of a motion *in limine*.

13:40:25 THE COURT: Mr. Wisner, do you wish to move on?

MR. WISNER: Was the motion granted?

MR. GRIFFIS: Yes.

THE COURT: Counsel, do you wish to approach?

MR. WISNER: Sure.

13:40:42 (Sidebar discussion.)

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

Q. BY MR. WISNER: Following this outcry, Doctor, do you know if the IARC director issued a letter

13:41:10 responding to these criticisms?

A. Yes, he did.

Q. And have you read that letter?

A. Yes, I have.

Q. And have you considered it?

13:41:16 A. In what I've done here?

Q. Yeah.

A. Partially, but not totally.

Q. But there's portions of it you did read and consider?

13:41:25 A. Yes.

Q. I'd like you to turn to Exhibit 793. It's in your second binder, Volume 2.

Are you there, Doctor?

A. Yes, I am.

13:41:57 Q. Is this a fair and accurate copy of that letter?

A. Yes. This is the -- the letter the directors sent to the governing council and made public. Made widely public.

Q. And it was published online and available for

13:42:11 anyone to see?

A. Correct.

Q. And this is the one that you reviewed, sir?

A. Yes.

Q. And, obviously, minus these redactions at the

13:42:18 front, does this appear to be a fair an accurate copy of that later letter?

A. It appears to be, yes.

Q. And to be clear, it was written by the director of IARC. Who is that?

13:42:28 A. Chris -- Chris Wild.

Q. And Chris Wild wrote this letter in his official capacity as the IRAC director; is that correct?

A. That's correct.

Q. And this was made in the regular course of his

13:42:37 working at IARC; correct?

A. Correct.

MR. WISNER: Your Honor, at this time I move 793 into evidence.

THE COURT: Any objection?

13:42:45 MR. GRIFFIS: Objection of hearsay, your Honor.

THE COURT: All right. Then why don't we take this up at a later time.

MR. WISNER: So don't discuss the document, your Honor? I want to make sure I understand what the ruling

13:43:02 is.

THE COURT: Yes. Not at this time. It's not in evidence.

Q. BY MR. WISNER: All right. Let's get off of IARC, Doctor. Let's take about the science. What --

13:43:16 what were you asked to do in this case?

A. Originally I was asked to provide expert scientific opinion to the law firm that I contracted with about the science related to glyphosate.

Q. And were you asked to determine whether or not

13:43:37 glyphosate or Roundup can cause non-Hodgkin's lymphoma?

A. Not originally.

Q. Okay. But at some point were you asked to do that?

A. Yes, I was.

13:43:46 Q. And did you go about trying to answer that

question?

A. Yes, I did.

Q. What did you do to examine or come to an opinion about that question?

13:43:53 A. Say that again.

Q. What did you do to arrive at or come to a conclusion -- an opinion about that question?

A. I did a systematic review, study of the literature. I looked for all possible publications, both

13:44:07 in the peer-reviewed literature and anything else that was available through regulatory sources, et cetera.

I read all of that material that I found relevant and then used what's called the Bradford Hill criteria to walk through all of that science and come to

13:44:24 a conclusion about the causality.

Q. And when you looked at all this different science and studies, did you look at things that IARC did not look at?

A. Yes.

13:44:35 Q. What did -- what else did you look at that IARC did not look at?

A. Well, there were -- at the time of the IARC Monograph meeting, there were studies that were unavailable to them in enough detail for them to review

13:44:50 and act on it.

In my review, having combined information from multiple sources, as well as those studies that IARC decided not to do, and not being required to have it in the public domain in my review, I reviewed those studies as well.

13:45:09

These are cancer studies in animals that are proprietary to the industry. And genotoxicity studies, again, proprietary to the industry. And then any new studies that came out since the IARC review.

13:45:24 Q. So let's break that down just quickly.

So IARC, you said, only looks at stuff that's publicly available; is that right?

A. That is correct.

Q. Why is that?

13:45:34 A. Because they have a very strong belief in transparency. They are a public agency. They feel that their scientific reputation is -- it's important to their scientific reputation to be transparent in everything they do.

13:45:49 Q. And you weren't bound by that requirement in your assessment; is that right?

A. That is correct.

Q. And so you got the chance to look at, you said, proprietary studies; correct?

13:45:59 A. Correct.

Q. To be clear, we're talking about studies that were done by industry that just weren't publicly available?

A. Well, parts of them were publicly available but not in a form with enough detail for IARC to feel like they could review them.

13:46:09

Q. And since you are obviously a part of legislation here, you had a chance to, sort of, look at stuff that IARC didn't have a chance to look at; is that fair?

13:46:22

A. Partially fair. I mean, many of the documents -- IARC does not generally reference articles where someone else has reviewed the literature and come to a conclusion. The whole purpose of the IARC Working Group is for them to come to a conclusion.

13:46:39

But some of those reviews contained appendices that had raw data that, given time, the IARC Working Group could have potentially used. Again, doing everything I did. So it was there. They looked at the review articles but not at the appendices.

13:46:56

Q. So to come to your opinion in this case, you went and looked at studies that IARC did not look at; is that fair?

A. That is correct.

13:47:07

Q. And what percentage? What are we talking about

here in volume?

A. In terms of the full -- full -- oh, 5 percent?

Q. Five percent of --

A. The whole set of science.

13:47:24 Q. What did you look at?

A. That IARC did not look at?

Q. Oh, okay.

A. No. The part that I looked at that IARC didn't look at was probably 5 percent of everything I looked at.

13:47:37 Q. Okay. So about 95 percent of the same, but you looked at about an additional 5 percent; is that correct?

A. Correct.

Q. All right. So I understand IARC has these different categories of information. You know, animal, 13:47:52 toxicology, epidemiology, mechanistic studies. Did you take a similar approach in your evaluation?

A. Yes, I did. All -- all reviewers generally take that approach.

Q. Okay. And why is that, Doctor?

13:48:03 A. Because they're separate science. They -- they really complement each other, but you have to have, sort of, a different kind of scientific framework to look at each of those three sections.

Q. So let's talk about the three sections. Start 13:48:20 off with toxicology. Please explain to the jury what an

animal study is and how it's performed.

A. So, generally, to assess the chronic effect of chemicals in humans, we use what's called an animal carcinogenicity study. These studies are typically done in rats and mice. They're typically done for approximately two years. Some of the ones we're looking at are 18 months.

13:48:43

The rats and mice will generally live about 30 months if they're left to go to the end of their life span.

13:49:00

Let me take this out. Sorry. My -- I have a bit of a cold.

Let see. So length of time. The animals are from one colony. So basically you have these companies that grow these animals for this type of laboratory work. And when the study gets ready to be started, they want to choose animals that were all born at approximately the same time, in the same facility, under the same conditions, so that there's no problem with "I got animals from here and here, and they gave me different answers."

13:49:17

13:49:36

So basically everything is controlled. The animals go on study when they're about six weeks of age. That's because that's when rats and mice reach puberty. That's sort of the end of puberty time for them. They're

13:49:52

beginning to become adults. So it's intended to be like the adult lifespan of the animal.

They start exposing them at that point. In all of the studies we have here, they mixed the chemical in food, and the animals eat it every day for their entire two years or 18 months.

13:50:10

Again, during that time, everything is controlled in these laboratories. The amount of time they see light, the amount of time they see dark, the water they drink. Everything they can possibly control, they control in these studies.

13:50:27

At the end of this time, they kill any animals that remain alive. Many animals die during the course of the study just from natural problems in the animals. Every animal that dies -- in most study, not all of the studies we're looking at -- they go in and pathologists review all the tissues in the animal and look for cancer. Both for large tumors that they can see, as well as they slice the tissues and look in the microscope to see if they can see smaller tumors in these tissues.

13:50:43

13:51:06

That -- so the first phase takes about two years. That phase takes about half a year to a year, depending on how big the study is. It takes a lot of time to read all these slides.

After that, it goes to the, sort of, statistical

13:51:21

toxicological group who then analyze it, interpret it, write the report. Then that's the end of it.

That's a typical animal cancer study.

Q. In that study, there's a control group; is that right?

13:51:35

A. Oh, right. I'm sorry. I didn't cover that.

A typical study -- in fact, virtually all the studies we'll look at here -- had three groups of animals that were exposed to glyphosate and one group of animals that were not exposed to glyphosate.

13:51:47

These amounts lived under the same conditions. They just didn't get the glyphosate. Ate the same thing, except no glyphosate in the food. The doses given to the other animals went from a low dose to a high does. So you could look at: Does the risk of cancer increase as you increase exposure?

13:52:05

And most of the studies have between 50 and 75 animals in each of these exposure groups. Most studies use males and females. And if you're looking at glyphosate as an agency or something like that, you usually do rats and mice, males and females.

13:52:24

Q. And, Doctor, earlier today you testified that cancer's pretty rare. How can you find out there's cancer in mice but just looking at 50? How does that work?

13:52:41

A. So these studies are intended to -- for two purposes. One is: Can it happen? Can you see this in these animal populations after they're exposed?

And the second purpose is to estimate risk in 13:52:58 human populations if there's no good epidemiology to do that from. So there are two purposes.

For the first purpose, if you believe that the risk of cancer increases with the risk of exposure, then to make the best possible study, you want the highest 13:53:14 exposure that the animal can take without it causing other problems to the animal.

And so what you do, typically, is you do a three-month study instead of a year study. And you take a bunch of doses and feed them to some animals for three 13:53:34 months. And then you look to see how the animals handle the food. Did they lose weight? Did they get sick? Were there toxicological changes of concern? And you find an exposure where none of that happens.

And then you take that exposure as your maximum 13:53:50 exposure, and you run it for two years in the animals and then lower doses.

The reason you do that is because -- what you're interested in, of course, in human populations is much lower exposures. But you're also interested in human 13:54:06 risk in the range of 1 in a million to 1 in 100,000 to 1

in 10,000. And we can't use that many animals to get at that type of risk.

And so you don't do studies at human exposure levels. You extrapolate them. You take what you see in high doses, and you draw a line or some other technique to get you into the low region. That's how you estimate human risk.

Q. And that maximum dose that, I guess, the mouse or rodent can take before, essentially, dying, what's that called?

A. It's called the maximum tolerated dose. And there are guidelines that all the agencies follow that describe how to find that maximum tolerated dose and how to evaluate it to make sure you didn't go too high in the animals.

Q. Doctor, if the study doesn't reach the maximum tolerated dose, or the MTD, how can you learn anything from that study?

A. Well, it depends. If the study actually shows a cancer risk, then, of course, you're going to learn something from that study, because it's positive. Even though it wasn't the highest dose the annual could tolerate, you're seeing cancer at these lower doses. That's good enough.

On the other hand, if you use too low of a dose

and you see nothing, that could mean that you were in a probability arrange that you just wouldn't see. You'd be unlikely to see an extra animal with a tumor. Because the risk to the animal -- let's not worry about humans
13:55:44 yet -- might be 1 in 1,000 or 1 in 100. If it's that small of a risk with only 50 animals, I won't see it. It's unlikely I will see it.

Q. So the rule, then, is: Even if you haven't reached the MTD, if you see a risk, that's a problem. If
13:56:01 you don't see a risk, you're not safe yet.

A. Correct. Well, I wouldn't say not safe.

Q. Fair enough.

A. The purpose of these studies in a regulatory context, like it is here with pesticides, is they --
13:56:13 they -- there's a debate. The debate goes on in the scientific literature. And that's what set up these guidelines. And basically the guidelines are there to say this is the minimum amount of information a regulatory authority needs to make a determination of the
13:56:29 safety. Now, if it's entirely negative, the agency will, of course, determine it's safe and let it on the market. But they come back and look at it again and again and again.

But it's the minimum amount of evidence. So
13:56:43 that's why these cancer studies. They're part of that

minimum amount of evidence.

Q. What is a historical control?

A. Okay. So when you -- when you do these animal cancer studies, every once in a while you see a tumor you've never seen before in your entire life in that animal.

So, for example, NTP, where I worked, we saw osteosarcomas in the leg of a -- in the muscle of a leg of a mouse exposed to fluoride.

13:57:18 MR. GRIFFIS: Doctor?

THE WITNESS: Too much?

MR. GRIFFIS: What is that?

THE WITNESS: Fluoride?

MR. GRIFFIS: No.

13:57:25 THE WITNESS: Osteosarcoma. So it's a bone tumor.

MR. GRIFFIS: Okay.

THE WITNESS: But it appeared in the muscle tissue, which made it extraordinarily unusual. So we 13:57:32 went and said, okay, we've done a bunch of these studies in this animal. For the last five years, we might have done 40 studies. And each one of those studies has a control group. And each control group was treated exactly the same as the one we're doing now.

13:57:47 So we go group them together and say, how rare

is this tumor? And in this case, having never seen it, it's extremely rare. So then the causation argument: Did this chemical cause this tumor? It's very high. Because you've never seen it, it has to have been due to
13:58:06 the chemical.

So in most studies -- in most interpretations of cancer studies, if you have a tumor that occurs less than 1 percent in the animals, it's considered a rare tumor. And when you see those tumors, you go back to control
13:58:22 data sets that were treated the same way, over a period of time not too far away from what you're looking at now, and you look to see how often that tumor has occurred, and then you compare that information to what you see in your current study.

13:58:35 Q. BY MR. WISNER: But from looking at controlled, what's better: The concurrent control in the study or the historical controls?

A. In every guideline that's out there that I've read, the concurrent control is always the best. The
13:58:50 reason for that is because at this time, during this period, they were exposed to exactly the same thing as the treated animals. So they're always the better control.

But if you see these rare tumors, then you
13:59:03 really have to have something else to make a decision.

Because statistically, you'll never see them.

If I see 2 out of 50 versus 0 out of 50 in the controls, that's not statistically significant. It never will be. But it could be biologically significant if it's never been seen before.

13:59:21

Q. So, for example, in that case, you found two in a high dose, zero in the concurrent control. That, itself, is not statistically significant?

A. Not at all.

13:59:30

Q. But if the historical control tells you that the incidence of that tumor is 1 out of a million, right, the fact that you saw 2 out of 50, what does that tell you?

A. That the probability of seeing that is virtually 0.

13:59:44

Q. Okay. All right. So how many rodent studies did you consider for this case?

A. I think -- it's hard to say without looking at my document. I think it was 21 or 22 studies.

Q. And, I'm sorry, when I say "rodent studies," that's probably too general. I mean long, chronic carcinogenicity studies in mice or rats.

14:00:05

A. Correct. And that's 21 or 22 of them. I'd have to look back.

Q. But of those, how many were of sufficient quality to actually be examined by yourself?

14:00:19

A. So, yeah. There were several studies that I discarded as not being of sufficient quality.

I ended up with 13 studies that I felt were sufficient quality: Seven in rats, five in mice. And then one study that's known as an initiation promotion study. A different type of study.

14:00:35

Q. Okay. So let's start off with the mice.

I understand we prepared a demonstrative here to help us get through this relatively complicated topic.

14:00:51

Please turn to exhibit --

MR. WISNER: Well, your Honor, actually, permission to set up the demonstrative?

THE COURT: Any objection?

MR. GRIFFIS: No, your Honor.

14:01:03

THE COURT: All right. Very well. Is it marked as an exhibit?

MR. WISNER: Yes, it is. I have to look at it. It's Exhibit 1020.

Q. All right, Doctor. I'd like you to come off the

14:01:32

stand and use these markers to help us walk through this chart. Okay?

A. I'll need my notes.

Q. Sure. You should probably use black, so you can see much more --

14:01:52

All right, Doctor. So what are we looking at

here? What is this a chart of?

A. So these are the five different mouse studies that I looked at. Each one was done in a different laboratory. Each one was done in different years. These
14:02:11 first four were done in exactly the same strain of mouse. So mice --

Q. Sorry, Doctor. Stop. I don't think some of the jurors can see. I'm going to bring this up much closer.

All right. Continue.

14:02:31 A. So mice are like cats. You know, cats come in different types of cats. You have your tiger-looking cat, your black cat. There are different strains. It's the same with mice.

But in laboratory studies, they're very, very
14:02:47 carefully breeded and controlled as to which mice you look at. So that one laboratory using this mice, this laboratory using it, they should get the same basic results. So you try to keep them clear.

These are all CD-1 mice. But CD-1 mice also
14:03:06 have substrains. So it's not just one type of CD-1 mice. So these -- some of these have different substrains. But the idea is they're approximately the same animal.

This study went for two years, these two studies (indicating). These two studies went for 18 months
14:03:22 (indicating). So we have to look at them differently,

because an 18-month old CD-1 mouse is more in the range of a 50-year old, person. Whereas a 24-month-old mouse is more like a 60-year-old or a 65-year-old human. So we're going to consider them separately.

14:03:43 This is a different mouse. This is a Swiss Webster -- new mouse. Well, Swiss Webster mouse. And so they did a different study.

Q. All right. So these different columns represent different studies; is that right?

14:03:54 A. Correct.

Q. And they have dates underneath them. The earliest one on here is what date? I can't see.

A. 1983.

Q. Okay. And then the last one is 2000 --

14:04:05 A. 2009. They're not in chronological order. They're in biological order.

Q. Okay. And which ones of these were actually conducted by Monsanto?

A. Sometimes I don't know these things. I think 14:04:17 the Knezevich & Hogan.

Q. Okay. We'll deal with that later. All right. Fair enough.

So these different boxes underneath here reflect what?

14:04:28 A. So each box is a different tumor where some sort

of statistically significant finding exists that says there's an association between glyphosate and this tumor and this study and these animals.

There are two ways in which we do that. One is trend test. And what a trend test -- remember, I said they do multiple doses, starting at the lowest dose going to higher dose.

So what a trend test does, it says: Okay, I've got these data points. Let's put a line through the data points -- am I doing -- let's do it this way. It's easier.

You fit a line through a data point, and the line has a slope. You know, this has a slope of 0 (indicating). It's flat. And you can measure by drawing that line the size of that slope.

And what the statistical test does is tells you if that slope is bigger than 0. It gives you a probability that that is bigger than 0. Roughly.

A dose test is where you take each dose group and compare it to the control separately. So you looked to see if the lowest dose is -- response is bigger than control, the next dose is bigger than control, et cetera.

And so you have, in this case, three tests for dose and one test for trend in each sex species group for each tumor.

Q. Doctor, quick question: What is the vehicle for exposure for these animals?

A. Food.

Q. Okay.

14:06:08 A. Meats in their food.

Q. Okay. And does that mean you're only looking at it from a dietary perspective, or are there other types of exposure as well?

A. Well, when an animal eats, rats and mice, they 14:06:22 groom themselves as well. So they don't just get internal exposure in the stomach. They will get exposure on their skin. Less, but, nonetheless, it's there. And, also, the feed itself, sometimes when they eat they inhale the dry food. So they might get some of it in 14:06:41 their lungs as well.

Q. All right. So let's go through some of these studies. Let's start with the first one in 1983, Knezevich & Hogan.

A. Okay.

Q. This is one of the original registration studies for glyphosate; is that correct?

A. That is correct.

Q. And, also, another important thing. Do any of these involve Roundup?

14:06:56 A. No. These are all pure glyphosate.

Q. All right. So what did we find in the Knezevich & Hogan study?

A. Well, the original evaluation of the data -- it's a complicated story, the Knezevich & Hogan. The original data came in. See here, I have kidney carcinomas and -- or adenomas. A kidney adenoma is a precursor to kidney carcinoma. And so it's like you're getting a lesser tumor, and then you get the really bad tumor. Okay?

14:07:13

And so when you look at the animals, you try to decide whether this bump or tumor that I'm seeing is an adenoma or a carcinoma, so you can look at the progression.

14:07:32

So the original Knezevich & Hogan data was adenomas found in the kidneys of the animals. If I remember correctly, there were 50 or 51 animals per group. It was males only they saw this in. And what they saw was none in control, none in the low dose, one in the middle dose and three in the high dose. All kidney adenomas.

14:07:45

14:08:04

Q. When that data first came in, what was the EPA's assessment of it?

A. The EPA's assessment of that data was that it showed a positive association -- causal association between glyphosate and kidney adenomas in this mouse.

14:08:17

Q. Are you familiar with the term "oncogenic"?

A. Yes.

Q. What does that mean?

A. Causes cancer.

14:08:28 Q. And what did the EPA conclude with regards to this study as it relates to the kidney carcinomas or adenomas?

A. In terms of oncogenicity, a, sort of, general cancer question. Their original draft conclusion was 14:08:38 that this would fall into their Category C, which I believe is possible carcinogen or something in that category.

Q. Okay. Then what happened after that was the initial assessment of those tumors?

14:08:51 A. Well, through some discussion and debate that I read in the documents here and documents that EPA has put out, they allowed Monsanto to re-evaluate these kidneys.

Monsanto got a pathologist. They went back, and they -- usually when you do a kidney, you take three 14:09:15 slices through the kidney, and you look at the three slices, and then microscope to see if you see tumors. Kidneys are -- they're not big on a rat, but in me they're pretty big. But, you know, you take very thin slices in three areas, and you look at them separately.

14:09:32 What they did here, and going back, is they took

ten so that you get a much more detailed picture in each of the animals.

And when they did that and re-evaluated, they brought in some additional pathologists to look at the
14:09:45 data as well. And then when they re-evaluated it, two of the adenomas in the high exposure group became carcinogens. The one in the abnormality in the second group stayed an adenoma. But they found an extra adenoma in the control group -- in one of the animals in the
14:10:03 control group.

Q. And because of that addition of this adenoma that no one had seen before in the control group, what happened?

A. There was a lot of scientific debate within the
14:10:17 EPA about that particular issue, because they couldn't agree amongst themselves exactly. There was a faction that said, "Historical controls tell us this is a very rare tumor. We're seeing three. That's enough. It should be statistically significant and biologically
14:10:34 significant."

There was another group that said, "No. Statistical significance goes away. We're not worried."

So it went to the EPA science advisory board, science advisory panel. And they reviewed it and gave a
14:10:46 recommendation.

Q. What was the recommendation?

A. They recommended that -- I believe they recommended a new study with some modifications to how to do it. And they recommended that until then, EPA put it in this inadequate category. I think that's the category they said.

Q. The category just below C?

A. A different category.

Q. That category D, just below C?

A. Category D.

Q. Okay. Now, this A, B, C categorization, it doesn't exist anymore today; right?

A. They have words that talk about it, but they don't have A, B, C anymore, yes, correct.

Q. I mean, I guess, did Monsanto ever do that study?

A. Not that I'm aware of.

Q. Okay. All right. You've reviewed the data from the study. What did you conclude?

A. So I concluded -- so I'm going to base my claims -- as I think through this, I don't use these dose tests at all in my thinking. I'm strictly looking at trends. Because, to me, that's the more important test. It's -- statistically, it's a better test. It uses all the data at once, rather than one dose at a group. So

I'm going to use trend.

But here's what we saw when I looked at it. There are no individual dose group effects that are statistically significant. The trend, when you look at it, has a P value.

So do we need to talk about P values?

Q. You probably do. What's a P value?

A. Okay. This is where it gets really somewhat complicated and backwards, if you're not a statistician.

Okay. When you do these studies, you have a hypothesis in mind. And the hypothesis is -- you start with the hypothesis: Glyphosate does not cause cancer. And you run the study. And what you're trying to do is decide if the results I got are so strange that I can no longer stick with that hypothesis that it does not cause cancer, and I have to go to the hypothesis that it does cause cancer.

So that's the thinking as you look into this. So what statisticians do is they build these tests where you look at -- in the case of a trend test, you're looking at how steep that trend is, and you're asking yourself: If truly there was no dose response here, what is the probability I would see that trend that I'm seeing? Okay.

So if that probability is very small, then you

reject the hypothesis that it's flat, and you take the hypothesis that it is increasing with dose. That's how you do it.

Now, typically in science, we look for probabilities -- these are called P values -- that are less than .05 or less than .01. This is a tradition. That's all it is. One in 20 or 1 in 100. It's -- or 1 in 10 -- .05 -- 1 in 10 -- 1 in 20, 1 in 100. Because that seems rare. And that's what statisticians and scientists usually use.

So that's what we look at here. So when I talk about the trend being statistically significant, I mean the P value was less than .05.

If I talk about it being highly statistically significant, then I'm going to mean the P value was less than .01.

If I talk about it being marginally significant, then I'm talking about a P value between .05 and .01. It's bothersome, it's showing a direction, but it hasn't reached that critical 05 value. But I don't want to forgot that when I look at all this data, that this one sort of said something. Because if I see it in another study, I want to know it was kind of leading in that direction with this study. Okay?

So, here, what you saw were no pairwise

comparisons were significant.

Q. Okay. You can't say words like that and not define them. Pairwise comparison.

A. The dose to control comparisons. None of those were significant.

14:15:00

Q. Okay.

A. So low dose was not significantly different. Middle dose was not, high dose was not. The trend test was marginal. Once you put that extra one animal in there, I believe the trend was -- oh, I didn't write it down. I have to check my report. But it was not .05.

14:15:12

Q. But it was above -- between .05 and .1; is that fair?

A. I think so. I have to check my notes to make sure, because I didn't write it there.

14:15:30

Q. Okay. Why don't you put a star next to "trend." We'll use the star as a marginal.

A. Okay. (Witness complies.) But I also did the trend test. I did a calculation with where I looked at historically what happened with this tumor, and I used that historical rate in a calculation to get at the probability that: If that historical background rate is the true rate, what is the probability I would have seen this response?

14:15:48

And so I did that calculation as well for slope.

14:16:08

And that one is statistically significant. I don't remember where it was. Just above .01.

Q. Okay. Great. So let's circle that.

MR. GRIFFIS: Your Honor, may I approach?

14:16:24 THE COURT: Yes.

(Sidebar discussion.)

THE COURT: All right. You may continue.

Q. BY MR. WISNER: All right, Doctor. Let's continue.

14:21:16 Quickly -- let me ask more questions.

A. Okay.

Q. All right. Let's go through this. All right. So you said there was a historical significantly -- result for the kidney carcinomas and adenomas; is that

14:21:32 right?

A. Correct.

Q. All right. Why don't we circle the trend indicating that.

A. (Witness complies.)

14:21:36 Q. And what species was that -- gender?

A. Males.

Q. Okay. Great.

What else did you find in the study?

A. Well, at a later point, a re-analysis of the

14:21:48 study of multiple tumor sites found what's called a

spleen composite lymphosarcoma. And so a trend in that tumor in these animals.

Q. So why don't we circle "trend." And why don't you tell the jury what that tumor means, if you know?

14:22:08 A. (Witness complies.) The P value here was .015. I wrote that down. And this was in males.

Spleen composite lymphosarcoma, as I understand it -- I am not a pathologist. You should ask a pathologist. But as I understand it, back at the time

14:22:48 that Knezevich & Hogan were doing their studies, this is a type of lymphoma. It's a sub-classification of a certain type of lymphoma that occurs in mice. And here it's only occurring in the spleen.

Now, from the data, it occurred in a lot of

14:22:52 different places. And this was the only one that saw significant trend that I saw.

But it -- nobody looked at all of them, which is the typical way we do it now.

Q. All right. Let's move on to the next study, the

14:23:09 Atkinson study from 1993. It says, "Limited." Why is that?

A. Well, this is -- remember I said for animal cancer studies they look at every tissue and every organ microscopically and look for tumors.

14:23:23 In the Atkinson study, they did not do that. In

the Atkinson study, there was a proposed new approach, which was later dropped by everybody. But at this time, it was supposed to be a reasonable approach.

What you do is look at controls and the high dose, and you look to see if you see any significant changes. And then you look at tumors in the animals below, in the other dose groups. It saves you time, saves you money.

14:23:38

But here they did it slightly differently. They only looked at animals that died during the course of the study and the pathology on those animals, looking at slides. And the ones that died in the end, they did not do that on the middle groups.

14:23:56

So you didn't get to see what was in every animal for every reported --

14:24:13

Q. Notwithstanding those limitations, what did the results show?

A. For malignant lymphoma, they saw a marginal trend. There were no individual doses that were highly significant. And this was only in males.

14:24:26

Q. All right. So why don't we put a star, since that's our current approach, and a circle at the end.

A. (Witness complies.)

Q. All right. What else did they see?

A. They saw an increase in hemangiosarcoma. It's a

14:24:41

trend, that increase, and it's in males. There were no individual significant findings that I found.

Q. Okay. Great. Let's circle it up.

A. (Witness complies.)

14:25:05 Q. Quick question, Doctor: The CD-1 mice, are they more prone to cancer than other strains of mice?

A. No. Not -- not -- strains of mice differ in which tissues get cancers. So you can either look at overall -- but when I think about these things or when

14:25:26 most scientists and toxicologists look at these things, you look at, for example, Sprague-Dawley rats have high mammary tumor rates, but they have mediocre liver tumor rates. Fischer rats have high liver tumor rates, but they almost never get mammary tumors spontaneously. So

14:25:46 it's hard to say more or less. Generally, it's a good testing model.

Q. And when these animals were given the food and the glyphosate in it, how was it dissolved in it? Do you know?

14:25:58 A. I'd have to go back. Generally, there's probably something that's dissolved, but I haven't written it down or paid attention.

Q. And is there any difference between the food given to the control animals and the -- the dosing

14:26:11 amounts that's beyond the glyphosate? Is there any other

difference?

A. No, none at all. But in this study (indicating), the food given to the animals is different than in this study (indicating).

Q. Fair enough.

A. Most of them use diets that are blended for their laboratory.

Q. But for an individual study, the food that's given to the control animals is identical to the food

14:26:33 given to the dose animals, except that the food given to the dose animals has glyphosate in it?

A. That's correct.

Q. Okay. And, also, for all of the mice studies, do you know if any of them actually reached the MTD?

14:26:50 A. No. None of these, in my opinion, exceeded the maximum tolerated dose. All of them, in my opinion, had a high enough dose to be valid studies.

Q. Okay. All right. And -- great.

So why don't we create a little key for this.

14:27:07 Why don't we put a star here that says, "Marginal." You can write bigger, too. Circle, that means significant. I think that's good for now.

A. (Witness complies.) I'd like to put at least one more thing on it.

14:27:32 Q. Sure. Go for it.

A. Because this significant one for here was through historical controls. So I want to put an "HC" next to it, so we remember that. This was the trend with not the historical controls. And that was the trend with
14:27:48 historical controls.

Q. Perfect. Put that in.

A. I can't write on this very well.

Q. Great. Let's move through these studies.

We move on to the Sugimoto study from 1997.

14:28:08 A. I'm just going to put one more thing on here.

Q. All right.

MR. WISNER: For the record, he wrote --

THE WITNESS: We already said that.

Q. BY MR. WISNER: Yeah, I know. I'm just going to
14:28:28 make the record.

MR. WISNER: For the first two columns, he's written, "24 weeks."

THE WITNESS: Months.

MR. WISNER: "Months." Sorry. And then for the
14:28:35 last three, he's written, "18 months."

THE WITNESS: The last two.

MR. WISNER: Last two.

THE WITNESS: Because they're CD-1 mice. The last study is a different mouse, and I don't care.

14:28:44 Q. BY MR. WISNER: Okay. All right. Because you

don't have more than one in that?

A. Correct.

Q. Great. All right. So let's move on to the Sugimoto study. We're still in the CD-1 mice.

14:28:53 A. Correct.

Q. And what -- what did you observe here? It seems like you saw quite a few tumors.

A. Yeah. There were five significant findings in this particular study. Kidney carcinomas or adenomas,

14:29:06 malignant lymphomas, hemangiosarcoma, hemangioma, which is a completely different tumor, multiple malignant tumors or neoplasms. I'll explain that, if you'd like. And harderian gland adenomas.

Q. All right. Why don't you just fill in the

14:29:23 information as you know it, and then we'll just summarize it when you're done.

A. Okay. I doubt if you can see that that's a star.

Q. Okay. Great.

14:30:25 So for kidney carcinomas, you have historically significant, marginally and trend. Also -- why don't you just tell me what it is.

A. Here, without looking at historical controls, you saw a marginally significant finding --

Q. Okay.

A. -- with historical controls. You see a significant finding. This is in males.

Q. Great.

Malignant lymphoma?

14:30:48 A. A significant trend in males.

Q. Great.

Hemangiosarcoma?

A. Marginal trend in males.

Q. Great.

14:30:58 A. Hemangioma.

Q. I can't read it. Hemangioma.

A. Significant trend in females. The high dose group was significantly different from controls. And this is actually highly significant.

14:31:13 Q. And that was in females?

A. Females.

Q. Okay. And just to be clear, are any of these rare tumors?

A. The hemangiosarcomas in males are very rare

14:31:29 tumors.

Q. And the kidney tumors as well?

A. And the kidney tumors.

Q. Okay. And then you had multiple malignant tumors and neoplasms?

14:31:37 A. Yeah. That's an incorrect title. What this is

is looking at the animals, did an animal have at least one malignant tumor, meaning a carcinoma, not an adenoma. A malignant tumor.

So you look to see how many animals, as a
14:31:54 function of exposure, had malathion tumors. Not any one tumor, but just as a group.

So that's what this is looking at. So I'm going to call it malignant tumors or neoplasms. And that had a significant trend. The -- I believe it's high dose. The
14:32:11 high dose was significantly different than controls. And this is in males.

Q. Okay. And then the bottom one is -- I can't read it, sir.

A. Harderian gland adenoma.

Q. Okay.

A. Humans do not have harderian glands. But these mice do.

Here we saw significant trends in the mouse. And it's in females.

14:32:34 Q. Great. Let's go on to the Wood study. Why don't you fill in the Wood study, and then tell us what it says.

All right. What does that show?

A. The first tumor was malignant lymphomas. There
14:33:01 was a high significant trend for malignant lymphomas.

The high dose group was significantly different than controls. And this was in males.

Q. Great. And for multiple malignant tumors, is this a little different than the other one?

14:33:16 A. Yes. This one, they looked at something different. They looked at more than one malignant tumor in each animal. So you have to have two or more for it to be counted here. That's an unusual thing to do in a study. But that's what they did, so I'll report it.

14:33:34 There they saw a significant trend, and it was in males.

Q. And then the last one?

A. Lung adenocarcinoma. That's a lung tumor. This trend was significant. And that was also in male mice.

14:33:48 Q. Great. Let's look at the last one. Now, this was not in CD-1 mice. This was in the Swiss albino mice; right?

A. Yes.

Q. And what -- what did that show?

14:33:57 A. And I believe it was 18 months, but I'd have to check.

Q. Okay.

A. But what this showed is the kidney carcinomas or adenomas. They saw a marginal trend, whatever. And it

14:34:13 was in males. And malignant lymphomas, a marginal trend,

and it's in males.

Q. All right. The last one was what?

A. Hemangioma. It had a highly significant trend, and it's in females.

14:34:35 Q. All right, Doctor. So looking at all of these different tumors and all of these different mice studies, I see a couple of things. I want to know what the significance of that is.

In every tumor done after the Monsanto ones, all 14:34:48 the non-Monsanto studies, it appears that in every one of those there is either a significant or marginally significant observation of mall lymphoma; is that right?

MR. GRIFFIS: Objection. Leading, your Honor.

THE COURT: Sustained.

14:35:05 Please rephrase.

Q. BY MR. WISNER: Is there malignant lymphoma in every single study not conducted by Monsanto?

A. If -- if you want to consider the spleen composite lymphosarcoma as the same. And I'm not 14:35:20 certain. They're certainly a subset of each other in some way, shape or form. Yes, there's at least some indication of malignant lymphoma in all of these studies.

Q. And does that have any significance with the fact that we're talking here today about non-Hodgkin's 14:35:37 lymphoma?

A. Well, there are two important findings there. One is when you look at the animal studies, you look for consistency across the studies to see if they were all giving you the same result. And if they are, then that
14:35:52 strengthens the findings that it causes that tumor in the mice.

And so we have fairly solid strength here that this malignant lymphoma is being caused in these mice by glyphosate.

14:36:05 The second thing is that it's a little different. And it's, again, a little outside my area of expertise, but I've read and looked at it, and they're in my expert reports that have been available. It seems that if you are developing a drug and you want a drug for
14:36:26 some type of lymphoma, B-cell, T-cell lymphomas, which NHLs are, then the best model for doing that is a mouse model. So that says that this tumor in the mouse is closely related somewhat to humans' NHL.

Now, I want to make that this really clear.
14:36:49 Here we're using animals to see if we can cause the tumor. In this case, we're using animals that actually have a fairly low chance of seeing malignant lymphomas.

If I want to do an evaluation of the safety of a drug -- or the efficacy, I want to see if I can stop the
14:37:09 living lymphomas, then I need a mouse strain that gets a

lot of malignant lymphomas, so I can show it goes away.

This is not this strain. So these are the equivalent strains of mice. I just got the observation that the tumors appear to be somewhat similar.

14:37:25 Q. And what is the significance, if any, the fact that we see repeated tumors popping up in different studies in different species?

MR. GRIFFIS: Your Honor, I would need to (inaudible) a sidebar, as to the courtroom rules.

14:37:41 THE COURT: All right. So just be mindful about what we discussed, Mr. Wisner.

MR. WISNER: One more question, and we're going to another chart, so --

THE WITNESS: I'm sorry, what was the question

14:37:50 again?

Q. BY MR. WISNER: Sure. I'll just repeat it. What, if any, significance is there to the fact that there are multiple tumors that are appearing in multiple different studies over the course of 20 years? What does

14:38:01 that tell you?

A. So when you -- the guidelines exist for evaluating this type of evidence. Give you some guidance on what to think about these things. Generally, in the form of: If you see this, your finding is strengthened.

14:38:19 Not -- it generally doesn't say: If you don't see this,

your finding is weakened. It's generally if you see, it's strengthened.

So the things that strengthen your finding is if you have multiple tumors of the same type in multiple studies of the same species -- so here we've got these (indicating), et cetera, you can look at them in here.

14:38:36

The other thing that adds to the strength of causality in the animals is if you see multiple findings in the same study of cancer. That means -- because when you're looking to humans, you're not necessarily going to get the same animal in the rodent that you're going to get in the human. But by seeing lots of different tumor types hit in the animal, it's more important to the human causal. So you use that information as well.

14:38:54

Q. Thank you, Doctor. Let's talk about the rat studies. I understand we have a cart for that as well.

14:39:12

MR. WISNER: Permission to publish, your Honor.

THE COURT: Any objection?

MR. GRIFFIS: No objection.

THE COURT: And this has been marked as number?

14:39:26

MR. WISNER: I'm just going to get the number. It is Exhibit 1021.

Q. BY MR. WISNER: All right. Doctor, what are we looking at here?

A. It's basically the same thing. These are the

14:39:51

different studies in rats done over the years. These are the tumors that were found in those studies, and these are Wistar rats. And these are Sprague-Dawley rats. So they're different strains of rats. And you can see the
14:40:15 difference here with the color at the top, the slight brown -- gray in there versus this.

Q. Now, the same question with the mice studies, with these rat studies: Are these types of rats any more predisposed to cancers than other rats?

14:40:30 A. No. These are common species -- common strains that are used for this type of testing exercise.

Q. And, again, same question for the rat studies: In any of these studies, did the maximum tolerated dose, was it reached?

14:40:44 A. No. One of the studies showed a slight indication that there might have been some problems with the high dose, but it was so small that I wouldn't call it exceeding the MTD. This study did not reach the MTD.

Q. Which one is the one that -- slight change?

14:41:05 A. I'd have to look at my notes, I'm sorry. I can't recall.

Q. It's okay. All right. Let's go through these studies quickly.

A. Okay.

14:41:12 Q. Let's start off with the Lankas study from 1981.

This is a Monsanto study; is that correct?

A. I think so.

Q. Okay.

A. Yes, I think it is.

14:41:24 Q. It's fine.

A. I really didn't pay attention to who did the study. I just looked at the science and the study.

Q. Fair enough.

So what did you find for these tumors?

14:41:34 A. So this was 26 months.

Q. Okay.

A. All the rest are 24. So there's a slight difference there. The highest dose here is substantially smaller than here. That's important to note.

14:41:48 We found testicular interstitial cell tumors. They have a highly significant trend. There was a significant effect at, I believe, the highest dose and in males.

We found thyroid C-cell carcinomas or adenomas.

14:42:05 There was a significant trend. I don't know what I wrote there, but it was in females.

And then there was pancreatic islet cell tumors. There was no significant trend in the data. You saw at the low dose a significant difference with -- from

14:42:26 controls. And this was in males.

Q. Great.

What do we have in the Stout & Ruecker study?

A. This study we found, again, thyroid C-cell adenomas and carcinomas. It was a marginal trend. There were no individual dose effects. And this was seen in both males and females.

14:42:49

Q. Okay. Great.

A. Pancreatic islet cell tumors. That's the pancreas is, sort of, an endochrome -- hormone-controlling organ. There was no trend. There were -- two of the dose groups saw significant difference from controls. And this was seen in the males.

14:43:07

Q. Why don't you put a "2" next to that, so it's distinguishable.

A. (Witness complies.)

14:43:24

Q. Great.

A. Hepatocellular carcinomas or adenomas. That's liver tumors. They are -- there was a significant trend in adenomas and a significant trend in adenomas and carcinomas combined. So there are two findings here. And it's in both carcinomas with adenomas or adenomas alone. There were no individual dose effects. And this was in males.

14:43:36

Q. Okay.

A. Continue?

14:43:53

Q. Yes. Go. Let's do them.

A. Adrenal cortical carcinomas, there was a trend that was significant seen in females.

And for skin keratoacanthoma, which is a skin
14:44:10 tumor, there was a marginal increase in the trend. And that was seen in males. And those single doses were significant.

Q. Okay. Great. So between the Lankas study and the Stout & Ruecker study, we see a repeat of two
14:44:25 different tumor sets; is that right?

A. That's correct. You see a trend in females in thyroid C-cell carcinomas or adenomas in both studies. And in the Stout & Ruecker, you also see that in males. And you see pancreatic islet cell tumors, but these are
14:44:46 at individual exposure groups.

Q. All right. Now we're talking about the Atkinson study. It says, "Limited," here. Is it limited for the same reason the -- study was?

A. Right. It's the same laboratory that did both
14:45:00 studies, rats and mice. And they used the same approach. So that same issue of not looking at every tissue microscopically is in this study.

Q. What did you find in that study, notwithstanding that limitation?

14:45:12 A. A margin trend in thyroid follicular cell,

carcinomas or adenomas. So thyroids have follicles. These are little -- little tubules in the thyroid that release hormones, and they got cancer in those little tubules. And that occurred in the males.

14:45:36 Now, in this study, thyroid follicular cell tumors, as I understand the pathology, but I'm not a pathologist, are generally -- can generally be observed grossly. Meaning you can actually see it or feel it in the tissue when they look at it.

14:45:56 So here, even though they didn't look at the middle dose groups, I did an analysis that included the middle dose groups with all the animals, treating those that they hadn't looked at on the microscope as still having -- not having the tumor. Not at all having the

14:46:15 tumor. And there, I did see a significant trend. That was just for my understanding of how strong this finding was.

Then you see the skin keratoacanthoma again. This was a significant trend, and it was seen in males.

14:46:32 Q. Now, Doctor, you keep mentioning you're not a pathologist. You didn't actually look at the individual slides for these; is that --

A. No, of course not.

Q. So you're relying on the pathology reports from

14:46:42 the studies themselves?

A. Part of a pathology report. I don't actually have the pathologists' written notes, which you typically you would see. All I have is their final tables.

Q. Okay. So someone else had determined these tumors, but they're not -- not necessarily you?

A. Yes, yes. Definitely. Correct.

Q. Okay. Great. I just wanted to make sure that was clear.

Let's talk about Enemoto.

A. Back to kidney tumors again. This showed a significant trend. But it was only in adenomas, not in carcinomas. And it was in males. And this was a highly significant trend.

Q. Now, is there any significance to the fact that we see kidney carcinomas or adenomas, which we discussed were rare, in different species altogether, across rats and mice?

A. Well, to be clear, they're not rare here. It's only rare in the CD-1 mouse. And the Sprague-Dawley rats, they're not as rare. So I wouldn't call this one a rare tumor.

Q. Okay.

A. But, again, in looking at all of the evidence and trying to reach a decision about casualty in the rats -- in the rats and mice, one of the criteria that

helps you with that is if you see the tumor in multiple species.

Q. Okay. All right. Sorry. I didn't mean to cut you off. What else did you see?

14:48:06 A. Again, we saw skin keratoacanthomas. But this was a marginal effect. There were no individual doses that were significant, and it was males again.

And, finally, basal cell tumors, which I'm not going to try to explain to you what basal cells are.

14:48:27 Here we saw a significant trend. And this was also in males.

Q. Okay. Great.

So now we get to the Suresh study. And my question to you is: Was there something about the Suresh

14:48:40 study that's different than the other studies insofar as how it was done?

A. So Suresh also did that pathology where they only did high and low, and then some of the middle dose groups. So that was a limitation.

14:48:58 As you can see, there were no significant findings in the Suresh study at all. This is a Wistar rat. And so I can go look at other historical Wistar rats, the controls, and see what the rates look like. And this study tends to have very unusual rate -- rate of

14:49:21 tumors in the control animals.

For example, they saw -- I think it's a 45 percent -- I'd have to look at it -- 45 percent liver tumor control response.

These two other studies, which are also the same rat, saw much smaller, 3 to 5 percent, control response. So that gives you some indication that it's -- it's somewhat different from these two. But it's only an indication. It is still a Wistar rat.

14:49:42

Q. What happens when you have so much cancer in the control animal? How does that affect the findings, results?

14:49:59

A. Well, for the liver cancers, it would make it very difficult to see an effect. Because, remember, you're trying to see it climb above the controls. And so if the control's low, you've got between 0 and 1 for it to climb, 100 percent response to 0 response.

14:50:18

But if you're already at 50 percent, you've got a lot less room. And so when you fit that slope, it's harder to see that increase.

Q. Okay. All right.

14:50:32

And then we have the Brammer study from 2001. It looks like there was only one tumor finding.

A. That's correct. They saw a statistically significant increase in hepatocellular adenomas, not carcinomas. And that was in males.

14:50:49

Q. And then, finally, the Woodward study. Is that also the same laboratory that did the Woodward study in mice?

A. Yes, it is.

14:51:04 Q. Okay. And what did that study show?

A. Significant trend in skin keratoacanthomas. Again, in male rats. An increase in mammary gland carcinomas or adenomas. There was a significant trend in the combined -- so I have to break these down for you.

14:51:25 There was a significant trend in carcinomas. I'll circle that. A marginal trend in adenomas. I'll put a little star near that. And a significant trend in both of them combined. And I'll circle "trend" for that. And that significant trend was highly statistically

14:51:48 significant. And that was in females.

Finally, pituitary adenomas were significant in both males and females. And both trends were statistically significant.

MR. WISNER: Thank you, Doctor. You can take a

14:52:06 seat.

THE WITNESS: Thank you.

Q. BY MR. WISNER: Can you see the boards, Doctor?

A. Yes.

Q. Well, Doctor, taking a step back and looking at

14:52:39 all of these different mice and the rat studies, and

specifically, I'd like to note the volume of tumors in all of the studies. What, if any, relevance is there to the fact that none of these reached the maximum tolerated dose?

14:52:57 MR. GRIFFIS: Objection to leading.

THE COURT: Overruled.

You may answer this question.

THE WITNESS: It means they're all balanced studies. That is why I've included them in my

14:53:07 evaluation. There's a lot of things you'd look at to determine if it's valid or not. And reaching the MTD is -- or exceeding the MTD is one thing that would make a study probably pushed off to the side. Or at least that dose group pushed out of the evaluation. None of these

14:53:25 have that problem.

Q. BY MR. WISNER: Is that one of the reasons why we don't have every one of these studies that you looked at up on the board?

A. That's one of the reasons. There were a couple

14:53:35 of studies with very low/high doses that saw nothing. But that's expected. There were other reasons.

Q. And then the lack of MTD, that includes the Suresh study; is that right?

A. The Suresh study did fine in terms of maximum

14:53:51 tolerated dose.

Q. It didn't reach it, though?

A. It did reach it.

Q. Oh, it did? Okay.

A. Oh, yes.

14:53:55 Q. All right. I want to talk briefly with these up here, because I want to talk about the standard by which you review this.

Let's take a look at -- in your binder, Doctor, Exhibit 640. It should be in the first binder.

14:54:29 Did you find it?

A. Yes, I did.

Q. Okay. What is this document, sir?

A. This is EPA's guidelines for carcinogenic risk assessment. This is what EPA uses as their guidance for

14:54:40 evaluating animal studies, human studies, mechanistic studies.

Q. Did you have a role in any way of helping to create these guidelines?

A. As I mentioned earlier, many of the scientist in

14:54:54 the federal government who do this type of work were asked to provide comments early on in the process.

Q. And did you provide comments on this, Doctor?

A. Yes.

Q. And, specifically, did you provide comments as

14:55:06 related to the assessment of carcinogenicity from

long-term animal studies?

A. Yes.

Q. Did you rely upon this at all in understanding and informing your approach to looking at animal cancer data?

14:55:21

A. Yes.

Q. And we're discussing some of the issues raised in these guidelines to help you and help the jury understand your testimony today?

14:55:30

A. Yes.

MR. WISNER: At this time, your Honor, I would move Exhibit 640 into evidence.

MR. GRIFFIS: No objection.

THE COURT: All right. 640 may be admitted.

(Exhibit 640 admitted into evidence.)

THE COURT: And, Mr. Wisner, I would like to take the afternoon recess at 3:00. So just keep that in mind.

MR. WISNER: Perfect. We'll be done with

14:55:47

this -- just when we're done with this will be right around 3:00, so --

THE COURT: Okay. Good.

Q. BY MR. WISNER: All right. Doctor, let's take a look at this. This is a digital copy.

14:55:54

MR. WISNER: I hope all of you can see it.

Q. We have the front page here. It says, "Guidelines For Carcinogen Risk Assessment."

Do you see it?

A. Yes, I see it.

14:56:03 Q. All right. So let's turn to page 21 -- or 221. 221.

Are you there?

All right. Do you see it on the screen?

A. Yes.

14:56:24 Q. All right. So at the bottom here, we have "Assessment of evidence of carcinogenicity from long-term animal studies."

Do you see that?

A. Yes, I do.

14:56:31 Q. All right. And it says, "In general, observation of tumors under different circumstances lends support to the significance of the findings for animal carcinogenicity. Significance is generally increased by the observation of more of the factors listed below. For

14:56:47 a factor such as malignancy, the severity of the observed pathology can also affect the significance. The following observations adds significance to the tumor findings."

And then I want to go to those factors. And

14:57:00 that's listed right here.

Do you see that, Doctor?

A. Yes, I do.

Q. All right. Great.

So we can just do a "yes" or "no" here, unless you think it needs more explanation.

14:57:08

The first one, "Uncommon tumor types." Do we see that in the mice and rat studies?

A. "We have two uncommon tumor types," yes. Kidney tumors in mice and hemangiosarcomas in mice at 18 months.

14:57:22

Q. "Tumors at multiple sites." Did you see that?

A. Yes.

Q. And that's demonstrated by all of these different tumors we have on this board?

A. Correct.

14:57:31

Q. "Tumors by more than one route of administration." We'll put a flag on that and come to that later. Okay?

A. We don't have it in this particular set.

Q. Yeah.

14:57:41

"Tumors in multiple species, strains or both sexes."

Do we have that here?

A. Yes.

Q. "Progression of legions from preneoplastic to benign to malignant."

14:57:50

First of all, what does that mean, and do we have it?

A. So when tumors are formed in most tissues, they start off as an irritation. That's soon followed by a little nodule that's considered benign and doesn't, sort of, migrate around. And after a while, that becomes a carcinoma. And a malignant tumor can then metastasize and kill you. Mostly that's the case.

So that progression, you can see that in the pathology if you look carefully. And, yes, we do have that here.

Q. Thank you.

"Reduced latency of neoplastic lesions."

Do we have that?

A. Only if you consider looking at the 18-month studies compared to the 24-month studies. Then you can see some things in the 18-month studies more clearly than you see in the 24-month studies. Because it came earlier, and there's a lower control.

Q. Okay. "Metastasis"?

A. That's not in these tables. But, yes, there were metastasis. That's where the tumor migrates from its primary site. So you still have a tumor there, but cells break off, they go elsewhere and cause a tumor to occur somewhere else. The pathologist can actually

identify that.

Q. Okay. And do we have an unusual magnitude of tumor response in these students?

A. No. That, we do not.

14:59:10 Q. Okay. The proportion of malignant tumors, is that here?

A. I haven't looked at it or thought about it, so I don't have an answer for it.

Q. Okay. And do we have dose-related increases?

14:59:21 A. Yes. Absolutely.

Q. And that's illustrated by all the circled "trends" on the board?

A. Correct.

MR. WISNER: Okay. Great. That means it would

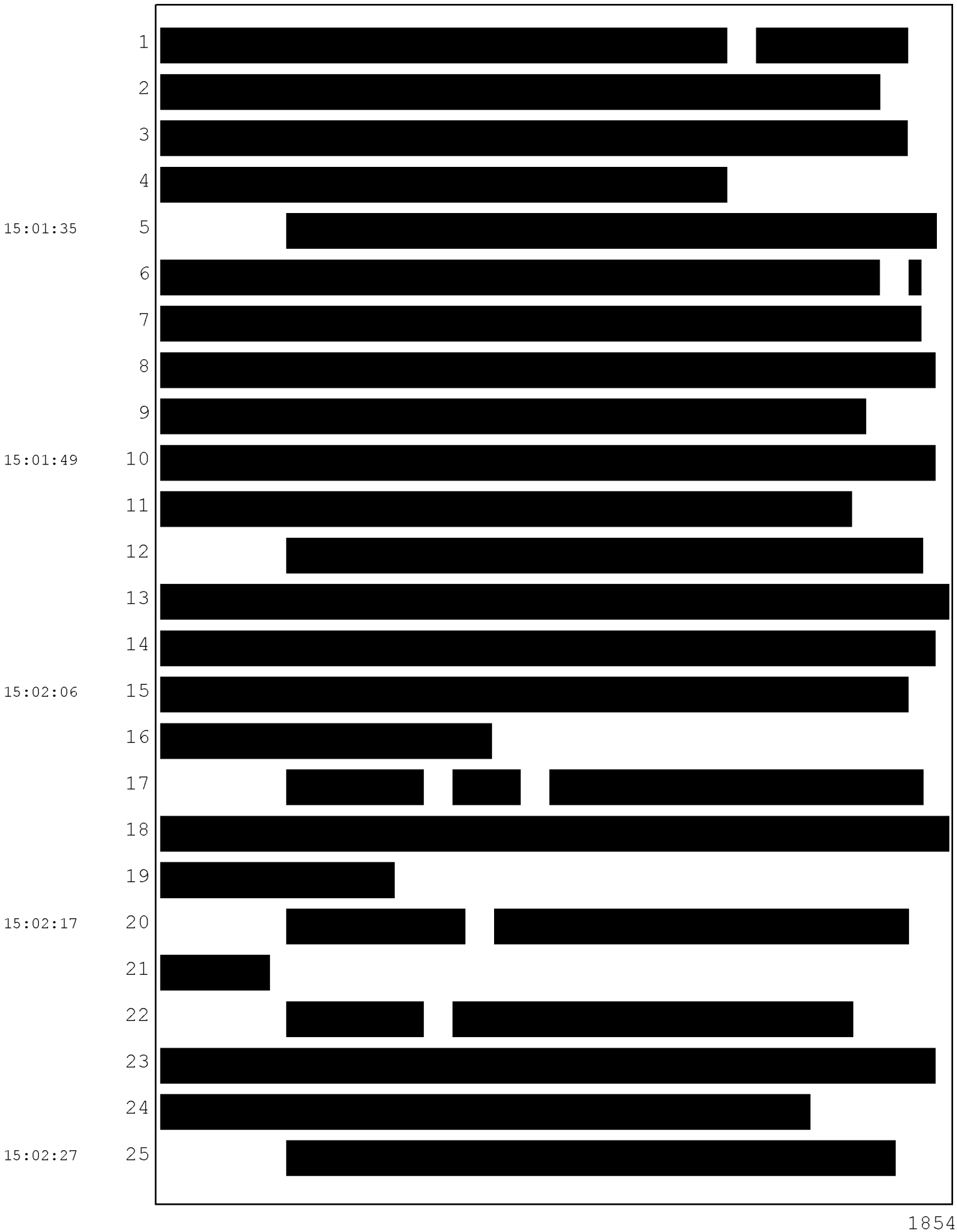
14:59:32 be a good time to take a break, your Honor.

THE COURT: All right, Ladies and Gentlemen. Then we'll take the afternoon recess right now. We'll be in recess for 15 minutes. Please do not discuss the case. Thank you.

15:01:12 (Jury leaves courtroom.)

[redacted]

15:01:20 [redacted]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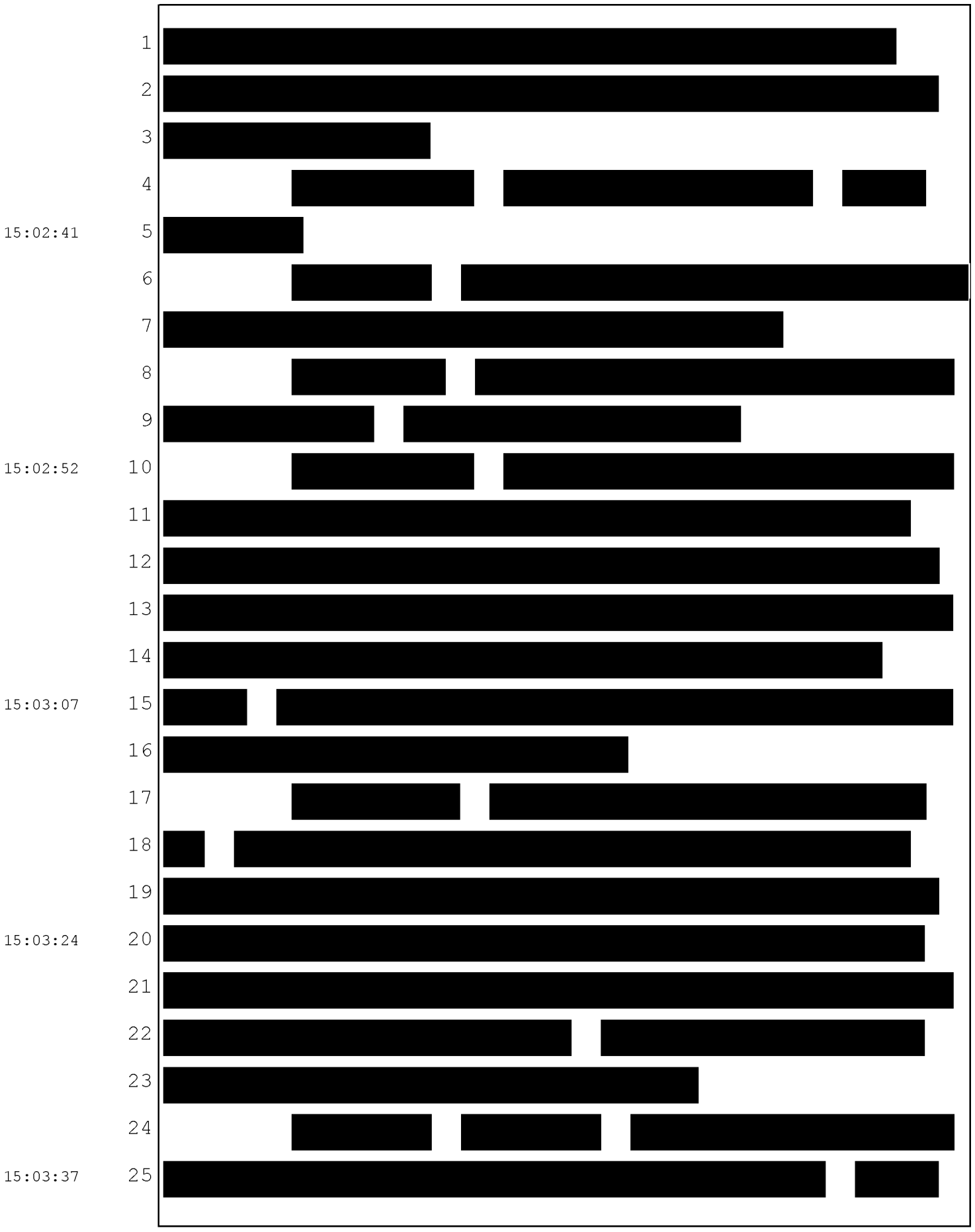
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[redacted]

THE COURT: Welcome back, Ladies and Gentlemen. Dr. Portier remains under oath, and Mr. Wisner, you may continue.

MR. WISNER: Thank you, your Honor.

15:17:42 Q. Doctor, I just want to fill in, make sure we complete this chart. The Lankas study was 26 months; is that right?

A. Correct.

Q. And the remaining studies were how long?

15:17:52 A. 24 months.

Q. So that one was a little bit longer than the other ones?

A. Correct.

Q. So I'm going to do 24 to reflect that.

A. Okay.

Q. I also noticed in the rat studies there is this pink box that appears quite a few times. It says skin keratoacanthoma. What is that?

A. Skin keratoacanthoma. Again, I'm not a pathologist, but my understanding of the tumor is that it's predominantly a benign skin tumor. It can become malignant and in some strains, it's more dangerous than in others, but it's basically a skin tumor.

Q. So it's a tumor in the skin?

A. In the skin.

Q. Okay, great. Now I noticed we talked about five mouse studies and seven rat studies, but you mentioned that there was 13 studies that you thought were of interest; is that right?

A. That's correct.

Q. What is the last study that we're missing?

A. It's what's called an initiation promotion study in Swiss albino mice.

Q. And when was that -- what's that study called and when it was conducted?

A. It was conducted in -- well, it was published this 2010. The lead author was George.

Q. All right. I want to get into what a promotion study is, but before I do that I think it would be helpful to sort of talk about the mechanisms of cancer; is that okay, Doctor?

15:19:29

A. Certainly.

Q. I understand you prepared a demonstrative to help explain this phenomenon; is that right?

15:19:41

A. That's correct.

MR. WISNER: Permission to publish the demonstrative, your Honor.

THE COURT: What is the exhibit number?

MR. WISNER: It is Exhibit 1024.

15:19:55

THE COURT: Any objection?

MR. GRIFFIS: No, your Honor.

THE COURT: All right. Very well. You may proceed, Mr. Wisner.

MR. WISNER: All right. We're going to do this digitally.

15:20:02

Q. What are we looking at here, Doctor?

A. You're missing a line. But what you're looking at here is a theoretical picture of how skin -- how cells go from being normal to being cancer cells.

15:20:22

And then you have some information -- oh, we

don't have other information.

Q. It's on the next slide. We'll get there in a second.

A. Okay, good. Basically you start with normal
15:20:34 cells in the body, and in some way, shape or form the DNA in the cell gets damaged. So you end up with at least one cell in that collection of cells that has genetic damage on it.

Now, the cellular machinery can repair damage.
15:20:50 It has great capacity for protecting us from these types of things. And that can occur in one of two ways. Sometimes the cell spontaneously repairs it when it occurs, but most of the repair occurs when the cell divides to make new cells and they break into two cells
15:21:10 from one cell. During that process, there's quite a bit of repair machinery that comes in.

So if that DNA damage is repaired, you end up with normal cells again. So that's what that bottom arrow is for. DNA repair takes you back.

15:21:26 If that damaged cell is not repaired and the cell undergoes replication, then it duplicates DNA to make the new cell, and when it does that, that damage is fixed in the cell. So from that point onward, it's no longer repairable. It's now called a mutation.

15:21:50 Now, there are lots of mutated cells in our

body, but certain specific mutated cells don't have growth control. They start losing the control of keeping the tissue down in size and they replicate too often.

And as they replicate, you can get more mutations and more mutations, and so you go from an early group of cells that are mutated to a benign tumor to a precursor tumor, benign tumor, and finally to a malignant tumor, and that's additional stages in this process. You can get additional mutations that lead you on to cancer.

15:22:10

15:22:28

Q. So if a chemical compound affects any one of these boxes in these stages, can that help promote or reduce cancer?

A. Yes.

Q. So let's look at the next chart, which is I think what you're trying to show us. Show us what this demonstrative -- explain to us what this demonstrative tells us.

15:22:42

A. Well, this is the same picture, a progression, but what I've now done is put some of the mechanisms of course in the genesis, some of the ways in which chemicals can alter this normal process that increases the chance of getting cancers.

15:22:54

Q. And what is the difference -- using this diagram, what is the difference between an initiator and a promoter of a cancer?

15:23:10

A. So a chemical that goes in and directly damages DNA, or even indirectly damages DNA, would be an initiator. It would be the thing that starts the process from normal cells. All the cells are normal, and it goes and it causes that initial damage.

15:23:30

Q. And then a promoter, what would that be?

A. Pretty much everything else. The tumor comes in, the early progression of the tumor begins, and this chemical comes in and says we're going to take these cells and give them an advantage to grow and provide a variety of different mechanisms. And so you get the tumor faster. That is promotion. It's promoting a cancer that is already started on its way.

15:23:48

Q. Now, Doctor, have you ever -- has there been any -- a carcinogenicity study designed specifically to look at whether or not glyphosate is an initiator or a promoter?

15:24:05

A. Yes, there's a classic protocol used for that.

Q. And what does that protocol usually entail?

A. I'll just talk about this one. It's general like any other. You take instead of 50 animals per group, you choose 20 animals per group. And usually these are hairless animals or you shave the hair off the animal because you're going to paint the glyphosate on the skin. So it's a skin painting study. You're trying

15:24:19

15:24:39

to induce skin tumors in these animals.

An initiation promotion protocol, you take a known chemical that's an initiator. In this case, they're using -- what is the initiator? I think it's DNBA.

Q. Do you have the exhibit in front of you?

A. Yes. No, I have my notes.

Anyway, they take a chemical that's known to attack that first said cell to cause that DNA damage, and they put that on the skin of the animal in one shot usually. And then for the following weeks, they put glyphosate on at a -- at a particular rate, and that tells you if glyphosate is promoting the cancer effect.

Then what they do also in the same type of study is they'll put glyphosate on first, and then they'll take a chemical that's known to promote cancer from previous studies, and they'll put that on top and see if you get more cancers from that. That test where the glyphosate is an initiator.

And then you have appropriate controls which have just DNBA or just TPA or et cetera.

Q. And those different chemicals, those are referring to things that are known promoters or known initiators?

A. Correct. The classic design of this is with

TPA, which is a chemical, and DNBA, which is another chemical, and then the one you wish to study.

Q. And the study that looked at this from glyphosate, is that the George study from 2010?

15:26:11 A. It is, yes.

Q. And what did that study show?

A. If you put glyphosate on first and follow by a promoter, there's no change. If you put glyphosate on by itself, there's no change. If you put the initiator down

15:26:24 and then follow up with glyphosate, there was a significant increase in the number of skin papillomas on these animals. A skin papilloma is a benign tumor.

And there was an increase in the -- both the number of animals -- number of tumors per animal and the

15:26:45 number of animals with papillomas. So both of those were increased.

Q. What does that, the results of that study, indicate to you?

A. That -- that glyphosate has the potential to be

15:26:57 a promoter of carcinogenesis.

Q. Now, Doctor, isn't it true that IARC in its analysis didn't use that study to evaluate the carcinogenicity of glyphosate?

A. They -- they reviewed it. I don't believe they

15:27:16 used it.

Q. And why is that?

A. One, they typically don't use initiation promotion studies, especially if they have good two-year cancer studies because a two-year cancer study is more definitive. You've -- you've not got anything else in there, and sometimes initiation promotion studies don't exactly tell you what will happen in chronic exposure to just the chemical.

But also they had concerns with the study.

Q. What were those concerns?

A. First, they felt that they didn't use an adequate untreated control. I disagree with that. I think their controls were adequate in the study.

The other thing they argued was that the -- they didn't do pathology on the papillomas that appeared on the backs of the animals. You could have either these papillomas or it could be a carcinoma, which would be a more important finding.

I disagree with them there. The classic skin painting studies, not all of them do pathology. Because if you see a bump, it had to have started as a papilloma, not as a carcinoma.

So if they're interpreting the study as only papillomas, then they're perfectly correct. If they want to interpret the study as papillomas and carcinomas, then

they needed to do the histopathology to get a pathologist involved.

Q. Now, were there any papillomas in the control group?

15:28:49 A. None. None at all.

Q. How many of the animals in the glyphosate exposed groups has papillomas?

A. About 40 percent. So with 20 animals, that would -- and in the high dose group. With 20 -- I think

15:28:57 that's the only dose group. Let me be correct. They didn't do multiple dose groups. They did one. With 20 animals, that's, what, 8 of the 20.

Q. And that -- although IARC didn't consider it as part of its carcinogenicity weighting, did they conclude

15:29:19 that it was a study showing a promotional factor?

A. Oh, yes, they did.

Q. Why is it okay for you to consider it even though IARC didn't?

A. I'm interpreting it, I think appropriately. I'm

15:29:35 not interpreting it as a carcinogenic finding; I'm interpreting it as a papilloma finding, which is a benign region, not really a carcinoma. And all I'm using it for is to give me an indication of some of the mechanistic underpinnings of this particular chemical.

15:29:58 Q. All right, Doctor. I'd like to move off of --

we're going to come back to the mechanism issues in a minute, but let's move on to the second sort of broad area of science that's looked at by IARC and yourself. Let's look at epidemiology, okay, Doctor?

15:30:14 A. Okay.

Q. All right. I understand you have prepared a plot summary of the epidemiological studies that form the sort of core of your analysis; is that right?

A. Correct.

15:30:25 MR. WISNER: Permission to publish this, your Honor. It's a demonstrative. It is 1022.

THE COURT: Any objection?

MR. GRIFFIS: No objection, your Honor.

THE COURT: Very well. You may proceed.

15:30:57 Q. BY MR. WISNER: All right, Doctor. We're looking here at Plaintiff's Exhibit 1022. What is it?

A. Okay. This is -- this deals with the epidemiology studies. This is what's known as a forest plot. So in a forest plot you're plotting the findings

15:31:15 from the epidemiology studies on a common scale next to each other so you can compare them.

Epidemiology studies, in their analysis, what they look for is this thing called risk ratio. There's lots of different names for it, but the general concept

15:31:35 is you're looking at the ratio of the tumor appearing in

the exposed people over -- relative to the tumors appearing in the unexposed people.

What does that mean? That means if that ratio is bigger than one, that means the exposed people had more tumors or more exposure than the unexposed people or the control population. If it's below one, it means that they actually had less.

So when you look at these pictures, they -- I believe it's the green line where just above the "T" in not provided. Is that a green line?

Q. Right here. This is a blue line.

A. Blue line. That blue line is one. So in the forest plot, if that -- see, I guess I have to define what the things are in the forest plot.

Q. Let's take it one at a time.

A. Okay.

Q. So let's talk about the concept you just expressed. So let's say we have -- so in epidemiology, we're comparing exposed people and potentially unexposed people; is that correct?

A. Well, it depends on the study. Let's be clear.

Q. Fair enough. Let's make it simple. For here we're talking about never ever; right?

A. Correct.

Q. So this is referring to people who were exposed

to Roundup and people who were not exposed to Roundup; is that right?

A. Correct. Correct.

Q. And here we're talking about the formulated product. We're not just talking about glyphosate; right?

15:33:04

A. Correct.

Q. Okay. And so when we look at the number of people in these two different groups, we count up how many of them have non-Hodgkin's lymphoma; is that right?

15:33:15

A. Not really.

Q. Okay.

A. Depends on the epidemiology study.

Q. Fair enough. But let's keep it at a high level for now. We can get specific with each study. But generally, you look at how many people got non-Hodgkin's lymphoma in the exposed group and how many people got non-Hodgkin's lymphoma in the unexposed group.

15:33:27

A. No.

Q. Okay.

A. It's really -- it sounds technical, but it's really not that.

15:33:40

Q. What is it?

A. Well, it depends on the study.

Q. Okay.

A. In a cohort study, what you've said is exactly

15:33:46

correct. But in a case control study, you're looking to see if the known cases have more exposure than the known controls, the controls being those people who do not have non-Hodgkin's lymphoma and the cases being those who do have non-Hodgkin's lymphoma.

15:34:03

Q. Okay. Fair enough.

So even in the case control studies, right, we pull up cases of exposed people, cases of unexposed people, and then we still compare the number of the cases in each group.

15:34:16

Is that fair?

A. No, we're comparing the number of -- the exposed versus unexposed cases to exposed versus unexposed controls.

Q. Okay, great. I think that, yeah, I got it. All right.

15:34:26

In any event, if we do simple math, for example, let's say we have two groups of a hundred. This is very simple because I want to make sure we understand this. And there is five NHL in the unexposed group, and there's five in the -- ten in the exposed group; right? You'd have twice as many NHL in the exposed than in the unexposed; right?

15:34:40

A. Correct.

Q. And so that would lead to a risk ratio, is what

15:34:57

you were referring to, of 2.0?

A. No.

Q. Okay. I'm trying to be a statistician.

A. Because you're looking at two ratios when you look at case control studies.

Q. Sure.

A. And in the cases you're looking at the ratios of exposed to unexposed, and you're dividing that from the controls, the ratio of exposed to unexposed effectively.

Q. Okay.

A. And so you have to bring the controls in there.

Q. Okay.

A. So it's a little more complicated.

Q. Sure. Fair enough. And maybe that's an easier way of saying it. When you have a risk ratio of 2.0, that means there's twice as much in the exposed?

A. Correct.

Q. Okay. All right. When we say the risk ratio is 2.0, that's the points that are on this chart; is that right?

A. The little black squares, yes.

Q. Okay, great. So, for example, for this one, we have a point -- if you go down about three.

Do you see that?

A. Yes.

Q. And then over here, it's closer to the blue line, it's like 1.3 or 1.2. Actually, we know what it is. It's 1.2.

A. It's written there on the chart, yes.

15:36:08 Q. Okay, great. Okay, good. So now we know what those points are. Now let's talk about the bars that are going through the points. What is that?

A. That is the 95 percent confidence interval around that point.

15:36:21 Q. Okay. We have a demonstrative to talk about confidence intervals. So let's pull that up.

MR. WISNER: Your Honor, permission to publish Plaintiff's Exhibit 1023.

MR. GRIFFIS: No objection.

15:36:47 THE COURT: No objection?

MR. GRIFFIS: No objection.

THE COURT: All right. 1023.

You may proceed.

Q. BY MR. WISNER: All right. So what we have here 15:36:53 on the screen is a fake confidence interval; is that correct?

A. Correct.

Q. And we have a point, just like we do over there, and that's right there; is that correct?

15:37:04 A. That's correct.

Q. And that's supposed to reflect 1.5?

A. Correct.

Q. All right. And then we have a confidence bound stretching between a little bit before one up until another number, and we actually have the rate up here, it's .9 through 5.

Do you see that?

15:37:13

A. Correct.

Q. All right. So what does this tell us, in the simplest terms as you possibly can explain. And the next slide shows the bell curve if you want to let me know when you need it.

15:37:20

A. Okay. So remember when I was talking about in the animal studies you had a null hypothesis or a hypothesis you worked on that said there was no effect and then you had to worry about the alternative.

15:37:34

So what you're doing here is you calculate this risk ratio, this odds ratio, whatever. They use different names for different types of studies. You calculate that ratio, and then you say suppose truth was there was no effect. So you're back to that hypothesis of nothing's there.

15:37:48

Then I want to know, given these data, what's the 95 percent range. So when I look at that, what's the areas where two -- only two and a half percent chance

15:38:12

that it's bigger than this number and there's only two and a half chance that it's less than this number.

So you're looking at -- remember that 5-percent rule we used in the animal studies? You're doing the same thing here, but it's on both ends. Below one or above one, you're looking at that 5 percent.

Q. All right. So let's look at the next part of this diagram. And can you explain to the jury how this bell curve sort of fits into this confidence interval?

A. Okay. So the bell curve is what's called a probability distribution. You might think of it more like a frequency thing. So if -- if I roll a dice, it can have values one to six, and I could roll it lots and lots and lots of times. And if it's a good dice, I roll it a hundred times, I'm like -- well, let's make it 120. It's easy. I'm likely to see 21s, 22s, 23s, 24s, 25s, 26s. And so that distribution looks like from one to six flat across the top.

Here, because we're looking at something that has a lot more values than one through six, then it's more of a curve. And so the middle of that curve, where you see that big peak, that is where the highest chance of getting the -- of the number that we think applies to this data set. And as you go along the edges, you have less and less chance that that number applies.

So when you get down to the bottom of the 95th percentile, which is this .9 at the bottom half, what it's saying is that if you add up all the probability that's in this curve that is less than .9, it's 2.5 percent.

15:40:06

So you only have a 2.5 percent chance that this risk ratio is less than nine -- .9.

Q. Doctor, let me stop you. I think you might actually have misspoke.

15:40:22

A. Okay.

Q. I'm using my statistics degree. That 2.5 percent is the actual end of the confidence interval?

A. Correct.

Q. So what we're talking about below .9 is actually not the red part, but the little part between the red and the one?

15:40:32

A. Say that again.

Q. So when we talk about the confidence interval, the 95-percent probability of the actual true risk is somewhere under this curve; right?

15:40:46

A. You're absolutely right.

Q. So the probability within a 95-percent confidence interval that it's below one here is actually the red is already off. So that's beyond 95 percent. It's just this little area between the red and the one,

15:40:59

the probability?

A. No. No.

Q. Okay.

A. Again, under the consumption that the true risk ratio is one, what is the value that from this data set, from this data set, what is the value that is smaller than -- what data point has a probability of 2.5 percent or less from this data of being that value.

Q. Okay. So when you have a confidence interval like this and you have this distribution, and the vast majority of the distribution is to the right of one, what does that tell you as a statistician?

A. Well, you could actually calculate it, but what it tells me is that the area below one is probably three and a half percent in this example, not two and a half percent. So that tells me I'm not really that far from having that whole line above one.

If that -- if that bottom part of that line is above one, in epidemiology that's usually what they call statistically significant finding. So that's what you want to see here, but this tells me I'm almost there, but I'm not quite.

Q. Okay. Is it also fair for me to say based on this distribution that the likelihood that the actual estimate is going to be above one is I guess over

95 percent?

A. Yeah, it's over 95 percent in this case. It's probably 96 and a half, give or take.

Q. Now that would change, obviously, if this confidence interval would move closer to one.

A. Correct.

Q. And so more of this curve would then get -- be passing the one line and be more and more probability that it's below one or one?

A. Correct.

Q. Okay. All right. So turning to our plot summary -- I'm just going to leave that up on the screen now in case people need to think about it some more. Turning to our plot summary now. These lines are the confidence intervals for these various point estimates; is that right?

A. Correct.

Q. And the wider a confidence interval, that's a reflection generally of the -- what does that reflect?

A. In the case of the case control studies, that reflects more than anything probably the number of exposed cases to the number of exposed controls, basically.

If it's a very few number of exposed people, then you end up with these huge confidence bounds. If

it's a lot of exposed people, you end up with a smaller confidence bound.

In the case of a cohort study, it's a little more complicated, but it's similar.

15:43:57 Q. And would it be fair to say, then, that when you have a larger number, it helps reduce the size of the confidence interval?

A. Correct.

Q. Would it also be fair to say that -- okay, 15:44:10 great. Let's kind of go through some of these studies here that are on this chart.

A. Okay.

Q. So the first one we have here is McDuffie 2001. Do you see that?

15:44:18 A. Correct, yes.

Q. And it says no pesticide adjustment. Do you happen to see that?

A. Yes.

Q. Now, again, this is a never-ever analysis; is 15:44:27 that right?

A. That's correct.

Q. What does that tell us? Just reading the McDuffie numbers, tell us how to read this chart.

A. Remember we talked about confounders early and 15:44:38 what constituted a confounder. Well, some pesticides

beyond glyphosate have been associated with NHL. So that makes those pesticides a potential confounder.

And so I looked at these studies and asked myself which ones adjusted for pesticides, so took into account the potential that there's these confounders, and which ones did not. So I put more weight on things that did adjust for pesticides than those that didn't, but I still used all the information.

15:44:58

In this case, looking at the little bar, what you see is a slight increase above one with a confidence bound that really has grabbed quite a bit of one.

15:45:14

Q. So this is not a statistically significant result?

A. It's clearly not a statistically significant result.

15:45:29

Q. But you would say this is elevated but not statistically significant; correct?

A. That is correct.

Q. And it's only slightly elevated because it's only 1.2?

15:45:38

A. And it has large confidence bounds relative to 1.2.

Q. Okay, great. Now in the McDuffie study, do you recall what that study was about?

15:45:47

A. A case control study in Canada looking at cases

versus controls, cases or people with NHL, controls of people without NHL, and looking into their exposure. I'd have to go back and look and see more detail on this study if you really want more detail.

15:46:07 Q. That's good enough. This is a case control study. Is it -- what kind of size of a population is it pulling from?

A. It depends on the study. I mean, it depends on where they work. I didn't do the calculations except for 15:46:20 one of the studies, I did a calculation. But you can actually do that.

They define when they write the paper how they got their cases and controls, and based on that definition -- for example, if I say all of my cases are 15:46:38 men aged 18 to 55 in the state of North Carolina who have NHL occurring between this year and that year. Okay? If that's my definition, then I can go in North Carolina and look and see how many men in that category existed between those two years, and that's the size of the 15:46:59 population this study is drawing from.

But -- so that's where you've got your support. But that doesn't enter into the evaluations. That just gives you some idea of the magnitude of the support.

Q. Now when we talked about a never-ever analysis, 15:47:15 is there any particular problems that you can run into

with such an analysis?

A. Oh, there are plenty. First of all, if -- if -- exposure matters. If the bigger exposure gives you higher risk, then if you could break it down into those
15:47:32 different exposure groups, you might be able to see that.

So that's -- that's an advantage of the other measures. The disadvantage of the other measures, which becomes an advantage of the ever-never, is people usually get it ever never. They -- people do remember whether
15:47:53 they were exposed to this or not exposed to this. But sometimes getting a quantitative measure for that is a little more difficult, and that can be a problem in some of the studies.

What else do you want to know about it?

15:48:06 Q. No, that's exactly what I wanted to get at.

Now, did Dr. McDuffie in 2001 do a sort of an intensity or duration analysis?

A. I have to look at my notes for a second. Yes, he did.

15:48:20 Q. Okay. If you turn to Exhibit 818. It's in the second binder. Is that a fair and accurate copy of the study?

A. Yeah, that is the McDuffie study.

MR. WISNER: Permission to publish, your Honor.
15:48:47 I believe we've agreed we've published these literature

but not enter them into evidence.

THE COURT: Any objection?

MR. GRIFFIS: No, we haven't.

THE COURT: All right. So you may publish Plaintiff's 818.

Q. BY MR. WISNER: All right. So this is the McDuffie paper, and we can see up here in the title non-Hodgkin's lymphoma and specific pesticide exposure in men across Canada, study of pesticides and health.

Do you see that?

A. Yes.

Q. And we have here it's done by Dr. Helen McDuffie. Do you see that?

A. Correct.

Q. Now, in the table, this is where you got -- oh, sorry.

If we look at table 2, this is where you have the 1.2 number; is that right?

A. I'm looking for it. Give me a minute. Yes, I see it.

Q. Do you see Roundup, glyphosate, and then you have this 1.26 and this 1.2. Do you see that?

A. Yes, I see it.

Q. And you used the most adjusted one which got you that number on the chart, which is 1.2; right?

A. That is correct.

Q. So if you also look at the next table, and this is table 3, and it talks about -- oh, this is insecticides. Let's go to pesticides.

15:50:21 A. Table 4.

Q. Table 4. Oh, thank you. All right, table 4 is fungicides, frequency of exposure to fungicides classified in the major chemical classes as individual compounds.

15:50:33 Oh, wait, Doctor, this is fungicides.

A. Yeah, but they did a separate analysis with glyphosate is a different table, I think.

Q. Yeah, let's find the table. Here we go. Herbicides. All right. Table 8.

15:50:50 Frequency of exposure to selected herbicides. Do you see that, Doctor?

A. Yes.

Q. Okay, great. And if we look in here, do you see this reference to glyphosate?

15:50:56 A. Yes, I do.

Q. Okay, great. All right. So walk us through what these different numbers reflect.

A. So the first is the group of unexposed people. I can't see the top of the table.

Q. Sorry.

A. That's okay. You can keep it there. I'll go look at...

Q. You can see it now.

A. The N is the number of cases that were unexposed. The second line, the next point is percentage of -- total percentage of cases that were exposed -- unexposed. Next line is the controls, the number of exposed, the percentage. And then the final line is the ratio we were talking about. Here it's one because it's comparing itself to itself. It's classically always listed as one.

The next line is compared against that unexposed line, and these are for people who typically use glyphosate more than zero times a year but less than or equal to two times per year. So one or two times a year they will use glyphosate. That's the answer to the survey question with those groups.

And you can see the numbers, 28, 5.4 percent, 97, 6.4 percent. The ratio there is about one. There's just no change based upon that exposure pattern.

The next group is greater than twice per year, and when that's compared to the unexposed, you get a ratio of 2.12 with a confidence bound from 1.2 to 3.73.

Q. So what we have here, then, is a more than doubling of the risk for people who have been exposed for

more than two days a year, and that result is statistically significant?

A. Correct.

MR. GRIFFIS: Objection. Leading.

15:52:43 THE COURT: Sustained.

MR. WISNER: Your Honor, this is an expert.

THE COURT: I sustained the objection. You may rephrase.

Q. BY MR. WISNER: Okay. What do we see here, Doctor?

A. You see that after -- or people who have non-Hodgkin's lymphoma and are exposed for more than two days per year, they are two -- more than two times as likely as the unexposed -- as the controls to be exposed

15:53:11 to glyphosate.

Q. Now you've heard of something called a dose response relationship. Have you heard that before?

A. Correct.

Q. And in the epidemiological context, the fact

15:53:24 that the more that people are being dosed here to glyphosate, is this similar to a sort of dose response?

A. Yes. In epidemiology, they call it exposure response.

Q. And although the never-ever results don't show a

15:53:39 statistically significant risk, the more than two days a

year does?

A. Correct.

Q. Okay. Let's move on to the next study, the Hardell study from 2002. What do the results here show?

15:53:54 A. I want to look at that. I'm not sure if that was the one that was NHL or a subset of NHL. I don't know if that's important to you, but I can look at it if you'd like. Or to combine. That's Hardell and Eriksson?

Q. This is Hardell 2002. So this is not the

15:54:14 Hardell from 1999.

A. Okay. So this is Hardell and Eriksson. This is a combination of two studies. It's what's called a pooled experiment. Hardell was in both of them so he had access to data from both of them. So he took them and

15:54:32 combined them and did an analysis with the combined data. This is Sweden. It's a study in Sweden.

The first line is with no pesticide adjustments. You can see it's a significant increase in the risk.

The second is adjusted for pesticides, other

15:54:54 pesticide use. I could be more specific if you want me to look at that. And there you see it's clearly not statistically significant but elevated.

Q. And when you look at these two confidence intervals together, what, if anything, does that suggest

15:55:13 to you?

A. So my interpretation of these types of numbers is that you're looking at the confounding for pesticides to ask the question how much of the effect that I see, without worrying about the other pesticides, remains after I do the confounding.

15:55:33

And here what you see is that there's still a fairly strong signal; it's just not statistically significant.

Q. Okay. Let's move on to the next study. De Roos 2003. Tell the jury about that study to the best of your memory.

15:55:52

A. So this was a study that was done in the United States. It's again a pooled analysis from three separate studies done in three different states in the United States, or maybe even four. I'd have to look. Anyway, it's a collection from different states.

15:56:03

When they did their analyses, they always presented analyses with adjusting for pesticides. They never showed an analysis without an adjustment for pesticides. Whereas Hardell and others adjusted for only a few pesticides, in this study I think they adjusted for almost 60 other pesticides. So it's a massive adjustment.

15:56:21

And here you see that the first method of analysis, which is called logistic regression, which is

15:56:38

what everybody else used effectively, is statistically significant. It's an elevated risk.

The second method of analysis of the same data but a different method of analysis, using what's called Bayesian statistics, shows a positive finding but not statistically significant.

Q. Doctor, please turn to Exhibit 710. Is that a copy of De Roos 2003 article?

A. Yes, it is.

MR. WISNER: Your Honor, permission to publish.

THE COURT: Any objection?

MR. GRIFFIS: No objection.

THE COURT: 710 may be published.

Q. BY MR. WISNER: All right. Doctor, turning to page 7 of 9, and this is the -- I'm pointing to the paragraph here discussing glyphosate.

Do you see it's on the right column. Do you see that, Doctor?

A. Yes.

Q. It says: "Glyphosate, commercially sold as Roundup, is a commonly used herbicide in the United States both on crops and on non-crop land areas. An association of glyphosate with NHL was observed in another case control study, but the estimate was based on only four exposed cases. A recent study across a large

region of Canada found an increased risk of NHL associated with glyphosate use that increased by the number of days used per year."

That's what we were just talking about with the McDuffie study; correct?

15:58:18

A. That is correct. Referenced the McDuffie study.

Q. "These few subjective findings provide some impetus for further investigation into the potential health effects of glyphosate even though one review concluded that the active ingredient is non-carcinogenic and non-genotoxic."

15:58:35

Do you see that, Doctor?

A. I see that's what it says, yes.

Q. All right. So in this point in the science, we have a couple of positive and suggestive findings linking NHL to glyphosate or Roundup exposure.

15:58:47

Is that fair?

A. Yes, that's fair.

Q. And Dr. De Roos is saying these provide further impetus for investigation even though one review concluded it was non-carcinogenic and non-genotoxic.

15:58:59

Do you see that?

A. Correct, yes.

Q. And that's -- what's the citation? Is that citation 50?

15:59:16

A. Correct.

Q. All right. I'll pop it up on the screen.

If we look here, the citation for number 50 is a study called Williams Kroes Munro.

15:59:28 Do you see that?

A. Yes, I do.

Q. Published 2000. Is this a study that you reviewed?

A. I've read the study. I've reviewed it, yes.

15:59:38 Q. And would you recognize a copy of it if you saw it today?

A. Yes, I would.

Q. Permission to publish -- please turn to Exhibit 884 and let me know if that's a fair and accurate

15:59:51 copy of that exhibit of that study.

A. Yes, it is.

MR. WISNER: Okay. Permission to publish, your Honor.

THE COURT: Any objection?

16:00:05 MR. GRIFFIS: No objection to the Williams review article.

THE COURT: All right. Very well. You may proceed.

Q. BY MR. WISNER: We're looking at the Williams

16:00:13 review article. You see up here the title "Safety

Evaluation and Risk Assessment of the Herbicide Roundup and Its Active Ingredient, Glyphosate, For Humans."

Do you see that, Doctor?

A. Yes, I do.

16:00:23 Q. And you see it has three authors: Gary Williams, Robert Kroes, and Ian Munro?

A. Yes.

Q. All right. Now if we look at the end of this document, there's actually an acknowledgement section.

16:00:37 Do you see it on the last page right here?

A. Yes, I see it.

Q. All right. It says: "The authors acknowledge the assistance of individuals who participated in the preparation of this document. First, we are grateful to

16:00:47 those who gathered and made available the large amount of information used to write the manuscript for this document."

"Second, we thank toxicologists and other scientists at Monsanto who made significant contributions

16:01:00 to the development of exposure assessments and through many other discussions. The authors were given complete access to toxicological information contained in the great number of laboratory studies and archival material at Monsanto in St. Louis, Missouri, and elsewhere. Key

16:01:17 personnel at Monsanto who performed scientific support

were William Heydens, Dr. Farmer, Marian Bleeke, Stephan Bratton, and Katherine Carr.

Do you see that?

A. Yes, I do.

16:01:33 Q. Now, I assume you read this acknowledgement when of course you reviewed this study.

Is that fair?

A. I can't be certain. I don't always read the acknowledgement.

16:01:41 Q. If -- does anywhere in this document it suggest or indicate that a Monsanto employee actually wrote the article?

A. No.

Q. Are you familiar with something called

16:01:57 ghostwriting?

A. I've heard the term.

Q. What is your understanding of it?

A. Somebody writes the article and somebody else puts their name on it.

16:02:05 Q. If in fact this article had been ghostwritten, does this acknowledgement tell you that?

A. No.

Q. All right. Let's move on to the next study.

Well, I want to stop for a second.

16:02:17 You mentioned that De Roos adjusted for, what,

69 pesticides; is that right?

A. Something in that range.

Q. Is that a common thing to do in an epidemiological analysis?

16:02:31 A. That's a bit extreme.

Q. And notwithstanding that fact, the results showed the logistical regression -- a doubling of the risk; is that right?

A. That's correct.

16:02:41 Q. And that risk, notwithstanding adjustment for 69 pesticides, was significantly significant; is that right?

A. That's correct.

Q. Does this study tell you anything about the risk of confounding in these studies?

16:02:55 A. It tells me a little bit. Confounding from pesticides, I assume, is what you're asking, because there's other potential confounders they looked at in here.

It would be better if I saw the unadjusted 16:03:08 analysis, because then I can make the comparison. But here, since they've adjusted by almost 70 pesticides, I'd say that there's probably not a big effect of the pesticides on confounding in this particular study, but I've have to see an unadjusted evaluation first.

16:03:29 Q. And, in fact, in the De Roos article, they did

not see any significant confounding by other pesticides, did they?

A. They didn't discuss it.

Q. Okay. It says here the Bayesian modeling.

16:03:41 Do you see that?

A. Correct.

Q. And Bayesian statistics, it's a type of statistics that makes assumptions a priori before you conduct the experiment; is that right?

16:03:53 A. Correct.

Q. And based on those assumptions, it influences how you assess data that you see?

A. To some degree, yes.

Q. And in this study, they made an assumption about

16:04:05 the carcinogenic potential of glyphosate before conducting this Bayesian model; is that right?

A. That is correct.

Q. And they made an assumption about the likelihood of carcinogenicity based in part upon whether or not

16:04:16 there was an IARC finding; correct?

A. That is correct.

Q. And at this point in 2003, IARC had not, in fact, made an assessment of glyphosate, had it?

A. That is correct.

16:04:27 Q. And because of that, it resulted in a Bayesian

assumption of, like, 30 percent probability of carcinogenicity; is that right?

A. They did that for all pesticides without an IARC review unless they had other reasons to put it lower or higher, but yes.

16:04:43

Q. Okay. So if we were to redo the Bayesian approach today, that starting number would be significantly higher than .3?

A. It would be .6 by their rules.

16:04:54

Q. And if you increase the starting assumption, that would ultimately increase the ultimate risk?

A. It's likely, but it's not guaranteed.

Q. Okay. Less turn to Eriksson study 2008. Are you familiar with this study, sir?

16:05:07

A. Yes, I am.

Q. All right. And what is this study -- where was this study conducted?

A. I think it's in Scandinavia somewhere, but I have to look. I don't know which tab it is, but -- I

16:05:28

can't tell you without looking at the actual document.

Q. Okay. Would you like to look, sir?

A. Yes, please.

Q. All right. It should be Exhibit 758.

Did I skip one? I did. Okay. We'll come back

16:05:49

to that.

A. Again, it's Sweden. It's a case-controlled study in Sweden of -- in this case, they're still looking at "yes" or "no" exposure to glyphosate.

Q. And when they looked at glyphosate and didn't do any adjustments but just looked at the raw impact on the data, what did it show?

16:06:02

A. Significant increase in the relative risk ratio of 2.02 with the confidence bound that did not include 1, so it's significant.

Q. And then they conducted something called a multi-varied analysis; is that right?

16:06:18

A. Correct.

Q. And that took into account other pesticides?

A. If I remember correctly, I think they did two different types of analyses, but, yes, they adjusted for other pesticides.

16:06:30

Q. And what happens to the risk ratio when they did that?

A. It dropped. It drops to 1.5, and it's no longer statistically significant. Although again, it still shows an increase above 1.

16:06:43

Q. I'm going to read a statement to you. I want you to tell me if this is true. "And when Eriksson did that adjustment, do you know what the result was? No effect. No effect of glyphosate." Is that a true

16:06:57

statement?

A. No, of course not. It's a nonstatistically significant positive increase.

Q. And when you read these two numbers together, does it show you or indicate anything to you?

16:07:12

A. It, again, indicates that other pesticides were somehow confounded with the glyphosate result, and it shows it -- they take away some of the significance of that glyphosate finding.

Q. And, Doctor, did Eriksson in this study try to do something different than a never/ever analysis, try to do a, sort of, exposure analysis?

16:07:32

A. Again, I'm going to look at my notes here, but I think yes.

Yes, he did.

16:07:50

Q. And when they did a never, how did they break it down? I know that McDuffie was greater than two days a year. What did they do in Eriksson?

A. They tried two different breakdowns. One was less than ten days' exposure, I believe, per year, and the other one was greater than or equal to ten days of exposure per year.

16:08:03

Q. Great. We'll talk about that one. I don't really care about the other one.

A. Okay.

Q. Let's talk about the greater than ten days of exposure per year. When they looked at people who had more than ten days of exposure to Roundup per year, what did the data show?

16:08:26 A. It was a significant increase. The -- the risk ratio -- the relative number is 2.36, and it's statistically significant in terms of having its confidence bounds above 1.

Q. And the lower one, the less than ten days a

16:08:44 year, what was the results for that?

A. 1.69 risk ratio, and it -- the confidence bound did go below 1, but it is still increased, just nonstatistically significant.

Q. So when we, kind of, compile the two exposure

16:09:01 assessments, we have McDuffie, when they adjusted for greater than two days per year, it's statistically significant, doubling of the risk; is that right?

A. Correct.

Q. And for Eriksson, the other one that did

16:09:13 exposure analysis, greater than ten days per year, again it's statistically significant?

A. Correct.

Q. Is that something you -- from a scientific perspective, is that something you want to see in the

16:09:24 data to help you understand causality?

A. Again, yes. When you look at Bradford Hill, which we'll do later, that's one of the criteria you want to look for.

Q. All right. We skipped over one here, De Roos 2005.

16:09:42

Do you see that, sir?

A. Yes, I do.

Q. We also have Andreotti down here, 2018?

A. Correct. We have Orsi as well.

16:09:49

Q. Sure. Why don't we just talk about Orsi, and then we can talk about those two, because those two are related.

In Orsi, this one, of all of these, is clearly 1.

16:09:57

Do you see that?

A. Correct.

Q. It's exactly -- exact ratio of 1; right?

A. Correct.

Q. And it has a ratio of .5 and 2.2, so it's not

16:10:09

statistically significant?

A. Correct.

Q. What about -- what is worthy or interesting about this stuff?

A. It's a case-controlled study. It was done in

16:10:15

France. It wasn't the smallest study. They were

different than all the other studies, if I recall correctly, because they used hospital-based controls rather than population-based controls. You can do it both ways, although hospital-based controls can sometimes give you problems.

16:10:37

What does that mean? So for the other studies, you found people with non-Hodgkin's lymphomas and then you went to the general population and found people who, sort of, looked like the ones you have that had the non-Hodgkin's lymphoma.

16:10:51

When you use hospital-based controls, you go find patients in the hospital, and in this case, patients with no cancers, patients with no history of immune disease, and I think there were some other criteria, but then they choose those patients as their controls. It makes it easier, because you can go talk to the patient right away, rather than trying to schedule something with someone in the general population.

16:11:05

Q. All right. And this is a study that you reviewed and considered as part of your analysis?

16:11:18

A. Yes.

Q. All right. And then we have this De Roos 2005.

Do you see that, sir?

A. Correct.

Q. And then we have this Andreotti 2018?

16:11:26

A. Correct.

Q. Those are studies that occurred where, sir?

A. Those are studies in the United States. They're based on people in North Carolina and Iowa. They are what are called -- it's the same study. They're the same study -- cohort study. That cohort study is called the Agricultural Health Study in the United States. It was started sometime earlier than that. I don't remember the exact year when they started the study.

16:11:41

16:12:00

But, basically, what they did was recruit farmers and people who have to apply for licenses to spray pesticides and asked them to join this cohort study, and if they agreed, then what they would do would be interview the people right at the beginning and find out all kinds of things about them, and then ask them about their exposure to 60, give or take, pesticides and write that information down. And then they'd wait five years, some period of time. They go back, and they interview these people again, and at the same time or at a different time, they looked to see if any of these people have gotten a disease.

16:12:20

16:12:41

Here they're looking at more than non-Hodgkin's lymphoma. They're looking at any -- at a large variety of diseases. That's why it's the Agricultural Health Study. It's all kinds of things related to working in

16:12:55

agriculture and all kinds of diseases. And then they assess whether you've gotten the disease, and then they do an analysis is -- the people who have never been exposed to this, do they have higher risk of getting the
16:13:17 disease than -- or lower risk of getting the disease than people who haven't been exposed to it.

Q. And the Agricultural Health Study, when was it started?

A. I'd have to look. I forgot.

16:13:30 Q. Okay. Do you want to look at the study, or what would you like to look at?

A. The study would be fine.

Q. Okay. Which one do you want, the Andreotti or De Roos?

16:13:38 A. De Roos is fine. She does a better job of describing it.

Q. Okay. Let's go to -- that would be Exhibit 709.

A. Okay.

Q. So when did this study start, based on your
16:14:00 understanding of this study?

A. Between 1993 and 1997.

Q. And to be clear, we're talking about people who are professional and licensed pesticide applicators; is that right?

16:14:10 A. Yes. There are slight differences between North

Carolina and Iowa as to how they did that, but that's a good description.

Q. And these individuals, they don't just spray glyphosate?

16:14:25 A. That's correct.

Q. But many of them do; is that correct?

A. Yeah, a large faction of them in 2005, when this De Roos study was done, I think it was 76 percent, give or take, spreading glyphosate.

16:14:40 Q. So these people who are getting enrolled in this study in 1993, they take this exam, and then they're asked to fill out a questionnaire; is that right?

A. That is correct.

MR. GRIFFIS: Objection. Leading.

16:14:51 THE COURT: Sustained.

Q. BY MR. WISNER: What happens after they take the examine?

A. They identify people who say they'll do it. They give them a questionnaire right then and there, 16:15:02 because they're -- the way they recruited people is they stood around a state agency where you had to register, and they'd grab you and say, "Do you have time to join the cohort study," and, effectively, that's how they did it.

16:15:15 And so they'd give them a questionnaire, and

then they followed up with a much more detailed questionnaire than they had to do in the paper, and you'd get answers to these all sort of questions, including exposures and things like that.

16:15:28 Q. And the exposure questions, did they relate to all the potential pesticides that they could be using?

A. Yes and no. There were all kinds of different things about it that one has to look at. "Yes" or "no" for the pesticide, that pertained to whether they'd been

16:15:43 exposed to the pesticide or not. They asked a question about how often you're exposed to the pesticide and when was the first time. That's pesticide dependent, but then they calculated these other intensity scores, and that's not really pesticide -- that's not specific for a given

16:16:01 pesticide, because it uses some general rules as well.

Q. Was there a question specifically about protective gear?

A. Yes, there was, but, again, it didn't pertain to glyphosate alone. It pertained to all the pesticides,

16:16:13 and, actually, at that time, they probably weren't -- well, that's speculation. I'll avoid speculation.

Q. Okay. But it'd be fair to say, then, that if somebody was spraying a very toxic pesticide and they used protective gear for that, but they applied

16:16:31 glyphosate or Roundup differently, that couldn't be shown

in the questionnaire?

A. That is correct.

Q. And when they were asked to recall their use of glyphosate -- or sorry -- Roundup in the past, how far did they ask for to go back?

16:16:43

A. In your entire history up to that point.

Q. So right then after taking an exam, they have to remember their amount of use for -- since, I guess, the '70s when Roundup hit the market?

16:16:59

MR. GRIFFIS: Objection. Counsel's testifying, leading.

THE COURT: Please rephrase, Mr. Wisner.

Q. BY MR. WISNER: So right after the exam, they have to remember their entire pesticide use for all the pesticides being studied?

16:17:16

A. Certain aspect of the pesticide use, when was the first time they used it, how often do they use it, I think it's on a yearly basis. Those -- I think those are the two questions.

Q. And that memory of their previous pesticide use and their answer about protective gear, was that used to estimate their exposure moving forward?

16:17:30

A. It was used to estimate certain aspects of their exposure. If they didn't use -- so when they looked at all the chemicals, if they didn't use protective gear,

16:17:49

they got a higher factor in this calculation of intensity than if they did use it, but again, it doesn't pertain to the particular chemical, so it may or may not have made sense for certain chemicals.

16:18:08 Q. Would it be fair or accurate to say that the AHS was a Roundup specific study?

A. Not at all.

Q. Would it be fair to say that the AHS was a non-Hodgkin's lymphoma specific study?

16:18:20 A. Not at all.

Q. In fact, have there been more studies published from the AHS beyond glyphosate?

A. Oh, easily more than a hundred.

Q. When they started the AHS, was there a

16:18:35 hypothesis generated to study glyphosate and NHL?

A. No. But they probably had it in -- well, no. They probably didn't even have it in mind, because there probably wasn't a lot of literature on that at that point when they started the study, so they might have had an

16:18:56 inkling from one or two epi studies that were out there, but in general, they brought NHL in because it was known to be related to a number of pesticides at that point.

Q. Now, Doctor, I understand De Roos published the results as it related to glyphosate in 2005; is that right?

A. That is correct.

Q. Okay. What happened in 2018?

A. It's a later time. They've had another interview or questionnaire sent to the people about their exposure, and they've gone to death registries and cancer registries to figure out who's still around and which ones got cancer and which ones didn't.

Q. And in 2018, did -- well, strike that.

I understand you said it started enrolling in 1993; is that right?

A. Correct.

Q. And then completed in 1997?

A. That is correct.

Q. Now, specifically with regards to Roundup, did Roundup use change during that exact period of time?

A. Yes. Roundup usage has been increasing for the last 10, 15 years.

Q. Well, back in 1993, 1997, did it specifically increase during that period?

A. Yes, it did.

Q. And when we talk about significantly, how much are we talking about here?

A. I don't remember looking at the 1993 to 1997, but in the period of the Andreotti study, the later period, 2000 to 2007, or something in that range, it more

than doubled.

Q. And --

A. Probably since '93 to 2007, it's probably fourfold increase.

16:20:36 Q. Now, previously you were talking about cohort studies. You said they followed them every year to see what their exposure was. Do you recall saying that?

A. It's not every year, but fixed periods they asked about the exposure.

16:20:46 Q. How many times have they followed up in the AHS?

A. They have the original questionnaire, they have the questionnaire for the De Roos paper, and then they have the questionnaire for the Andreotti paper, so they followed up twice.

16:21:02 Q. And that's spanning how long of a period of time?

A. Well, it depends on which study. De Roos' study they -- they stopped asking questions. I'd have to look it up again in terms of the materials and methods.

16:21:23 December 2001 is when they looked at incident cancers or not, so that --

Q. I'm sorry, Doctor. I'm not being clear. How many times did they follow up about exposure?

A. As far as I know, the only follow up on exposure

16:21:43 is Andreotti.

Q. Okay. So for De Roos, all the exposure being used to estimate the exposed group is based upon their answers from either -- between 1993 and 1997?

A. That's my understanding, yes.

16:21:58 Q. Now, you said in Andreotti there was a followup; is that right?

A. That's correct.

Q. And so they called back all those people and tried to get some more exposure information; correct?

16:22:08 A. That's correct.

MR. GRIFFIS: Objection. Leading.

MR. WISNER: I'm trying to get through this before 4:30. I apologize if I lead a little bit, your Honor. He is an expert.

16:22:17 THE COURT: All right. Well, just be careful with the leading.

MR. WISNER: Yes, your Honor.

Q. So, Doctor, when they did the followup on Andreotti, what percentage of people actually responded?

16:22:29 A. Roughly 60 percent.

Q. What effect, if any, does losing 40 percent of your exposure analysis have on your study?

A. Well, it's going to reduce the ability of your study to identify a positive effect. That's quite clear, 16:22:45 but it could also bias your study, and depending on how

you deal with the other 40 percent, it could have a major impact on your findings.

Q. Did Andreotti, did they try to -- how'd they try to deal with that 40 percent?

16:23:02 A. They did what's called an imputation. They -- they took what they knew about people's first exposures and their second exposures, they took some information about their economics and race and, et cetera, and exposure to other pesticides, and they calculated a

16:23:22 formula from that about what they knew and the people they followed up, and then they used that to predict what might have happened in the rest of the people.

Q. And you're a biostatistician. Have you actually looked at how accurate that imputation process was?

16:23:42 A. Yes, I have.

Q. Best case scenario, how off is it?

A. Best case scenario, my guess is that the -- for the estimation of exposure in the 40 percent who didn't respond, they probably put about 14 percent of those who

16:24:06 were really exposed into the control group. At least 14 percent.

Q. And to be clear, Doctor, when you take people who --

A. Or 7 percent. Sorry. 7 percent.

16:24:19 Q. Okay. 7 percent. Okay.

When you take people who are actually exposed and start treating them as though they're unexposed, what happens to your study?

A. Well, that's called exposure bias, and what you probably will see if you do that is a reduction in the risk ratio, because you've taken people who potentially have the disease and are exposed and put them into a group that has the disease but aren't exposed, and so you've moved a group of people from an important category into the unexposed category. It's likely to reduce the risk.

Q. And when you do that, can that make a result -- what happens to a risk ratio?

A. It certainly will likely be reduced. It could go below 1, even though in truth it might be above 1. It can have all kind of effects like that.

Q. Now, that was the best case scenario. What's the worst case scenario of the imputation?

A. Well, they didn't give me enough detail in the paper for me to be exact as to what they did, so I looked and did a best case/worst case scenario. The worst case scenario is, based on what they presented in the paper, they got pretty much everything wrong. Given the numbers that they presented, they could have conceivably missed -- put all the exposed in this predictive group

into unexposed and all the unexposed into the exposed.

Q. Now, let's be fair. Do you think it was the best or the worst case scenario?

A. I don't think it was either. I think it's somewhere in between. It's probably from -- historically, what these types of imputation things do, we're probably looking at 20-percent error, somewhere in there.

Q. Now, if the risk -- let's go back to De Roos here. You see De Roos back in 2005, this is without the imputation problem, when there's no adjustment, you have a risk ratio of 1.2.

Do you see that?

A. Correct.

Q. And then with adjustment, it's 1.1.

Do you see that?

A. Correct.

Q. And neither of these are statistically significant?

A. Correct.

Q. When you -- if you have a modest or low effect like this and you introduce 20-percent misclassification of exposure, what happens to your -- your result?

A. As a general rule, depending on how that misclassification occurs, if it's biased

misclassification, like I just described, it's going to definitely pull that risk ratio down closer to 1, even below 1.

If it's random, so sometimes I make a mistake and put it as a control, and sometimes I make a mistake and put a control as an exposed, and it's really just a flip of a coin, then that's undifferentiated, nondifferential exposure misclassification, and that tends to just bring you down to 1, but it's not likely to bias you below 1 if truth is above 1.

Q. And when you say it brings you closer to 1, what's a -- sort of, a layman's way of describing that?

A. It -- it hides the true effect, so if the true effect would be 1.5 and you had a lot of -- well, there's a paper on that, several papers. In the Agriculture Health Study, one of the papers showed that if the true relative risk was roughly 1.5, then the degree of -- of nondifferential exposure and misclassification can bring that down to 1.01, 1.05, depending on some factors.

Q. So with that kind of misclassification problem, you could have a legitimate risk that just -- you can't see in the data?

A. That is correct.

Q. Now, I understand -- stepping aside from Andreotti for a minute, and we're going to have an

epidemiologist come and testify to talk much more about epidemiology, so --

A. Good.

Q. -- but there was a metaanalysis done.

16:28:28 Do you see that?

A. Yes.

Q. What is a metaanalysis, very quickly?

A. You take -- it's not a pooled analysis, because you don't have access to all the data. When you have all

16:28:37 the data, you pool it. Here they have access to the papers. There's a statistical way where you can take the information from all the papers, combine them and come up with a weighted estimate of what the risks should look like over all of these studies based upon the observed

16:28:53 statistics, observed data.

Q. And are metaanalysis better that individual studies?

A. No, they're not. But they -- they tell you something the individual studies don't tell you. They

16:29:05 tell you about the general trend across all of these individual studies.

Q. And this metaanalysis on your board here, who paid for it?

A. Well, it -- the one I've listed there as Model 1

16:29:18 was done by a group of scientists who, if I read the

acknowledgements correctly, were paid by Monsanto or some -- I think.

Q. And that was in 2016.

A. That is correct, after the IARC Monograph.

16:29:31 Q. And what did that metaanalysis show?

A. When it combined all of these studies for the most adjusted finding, it -- it showed a risk ratio of about 1.3 that was statistically significant.

Q. Now, Doctor, taking a step back and looking at 16:29:51 all of this epidemiology, if, in fact, the risk was 1, so there's no risk in the real world, what would you expect to see by random chance or variation of these point estimates?

A. Well, when you put it that way, it's like 16:30:09 flipping a coin. If above 1 is heads and below 1 is tails, then because truth is 1, then sometimes you're going to be above, and sometimes you're going to be below, and it should be about 50/50. So you'd see about half of these with a risk ratio of below 1 and about half 16:30:27 with a risk ratio above 1.

Q. Is that what we see here?

A. No. What we see here is of the six studies before Andreotti, all of them are equal to 1 or above 1.

16:30:37 Q. And what does that tell you, both as a

statistician and someone who's looking at cancer risk in humans?

A. Well, an epidemiologist looking at this is going to say, "Well, that's an interesting somewhat consistent bit of information." As a statistician, I would look at this and apply what is probably the oldest statistical test ever done. It's called the sign test. And here you can actually calculate a probability of seeing all six studies equal to or above 1, and that's one-half to the sixth power and whatever that number is. I think .03, give or take.

If you want to do greater than 1, and so you keep the RC study off to the side, it's still a fairly small probability, so more complicated.

Q. So would it be fair to say that based on this data, if the true risk was just 1, the probability of seeing so many results to the right of 1 is almost 0?

A. No. Not almost 0, but it's small.

Q. Okay. 1 in 10,000?

A. No, no. It's less than -- it's bigger than that. It's one-half to the sixth power, which is 64 -- it's 1-64th, 1 out of 64.

MR. WISNER: Okay. Thank you. I think this is a good time to end for the day, your Honor.

THE COURT: All right, Ladies and Gentlemen. We

are going to adjourn for today. Please remember do not do any research. Please do not discuss this case with anyone.

Also, we have been receiving a lot of questions. Thank you for paying attention and submitting your questions. I just want to remind you the lawyers are not permitted to answers the questions directly, because anything the lawyers say is not evidence. The questions, if they're relevant and if they're permissible, will be answered by the witnesses.

So at the conclusion of each witness' testimony, I will give you an opportunity to submit questions that you wish to ask the witness or that you wish to have answered by the witness. I'll discuss those questions with the lawyer, and we'll see if they can be answered.

Okay. Thank you very much, and we'll see you tomorrow.

And, Counsel, can you please remain?

(Jury leaves courtroom.)

[redacted]


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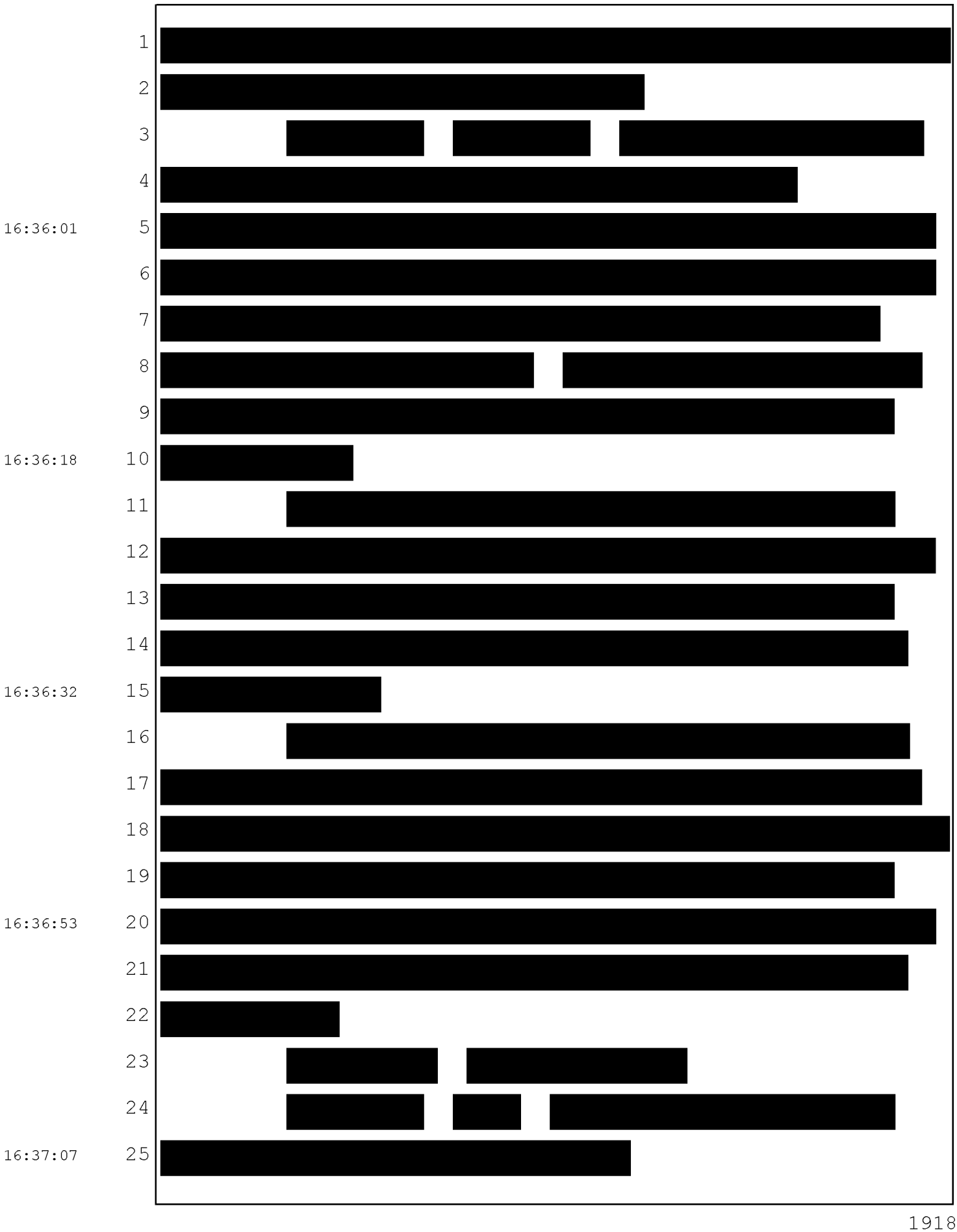
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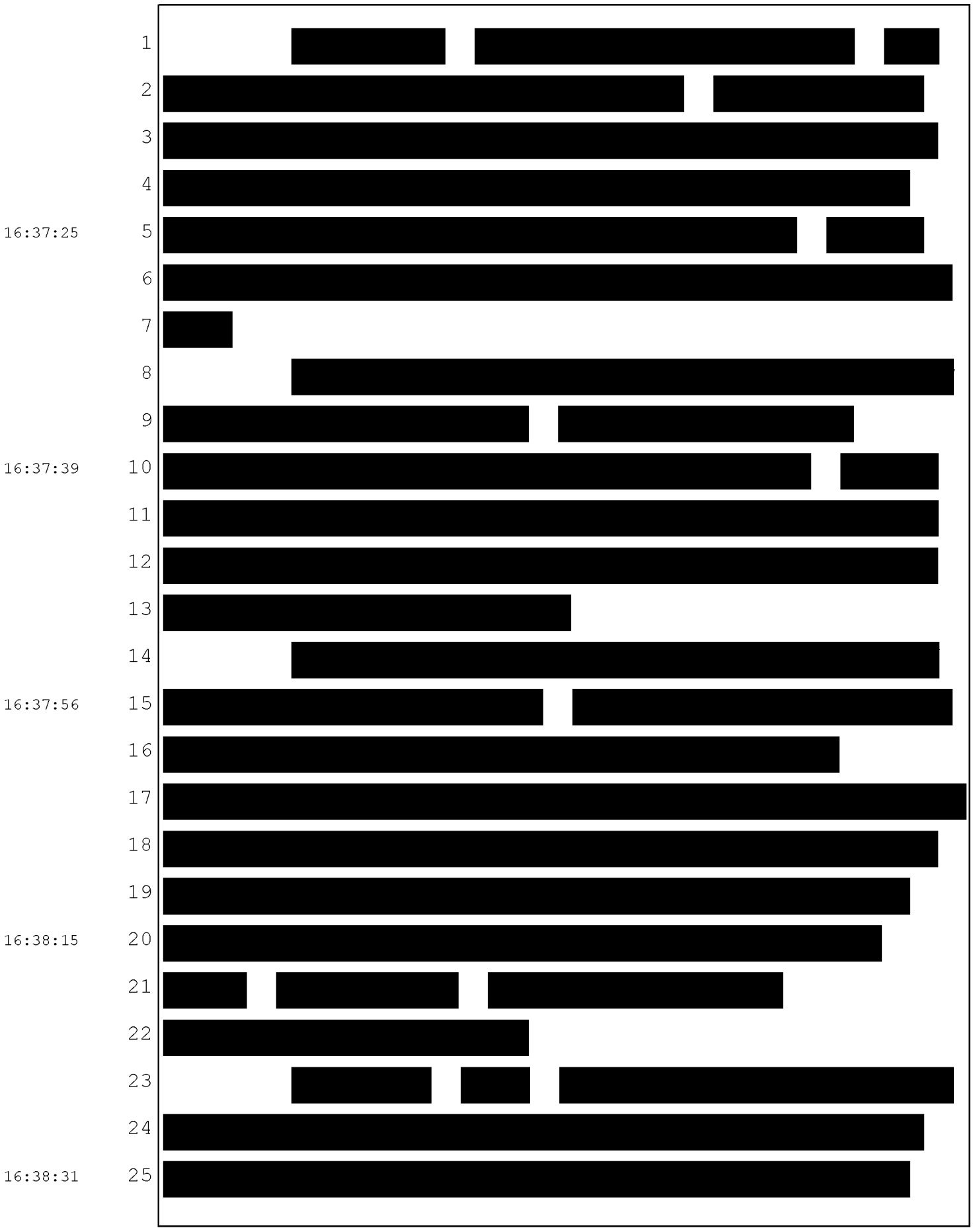
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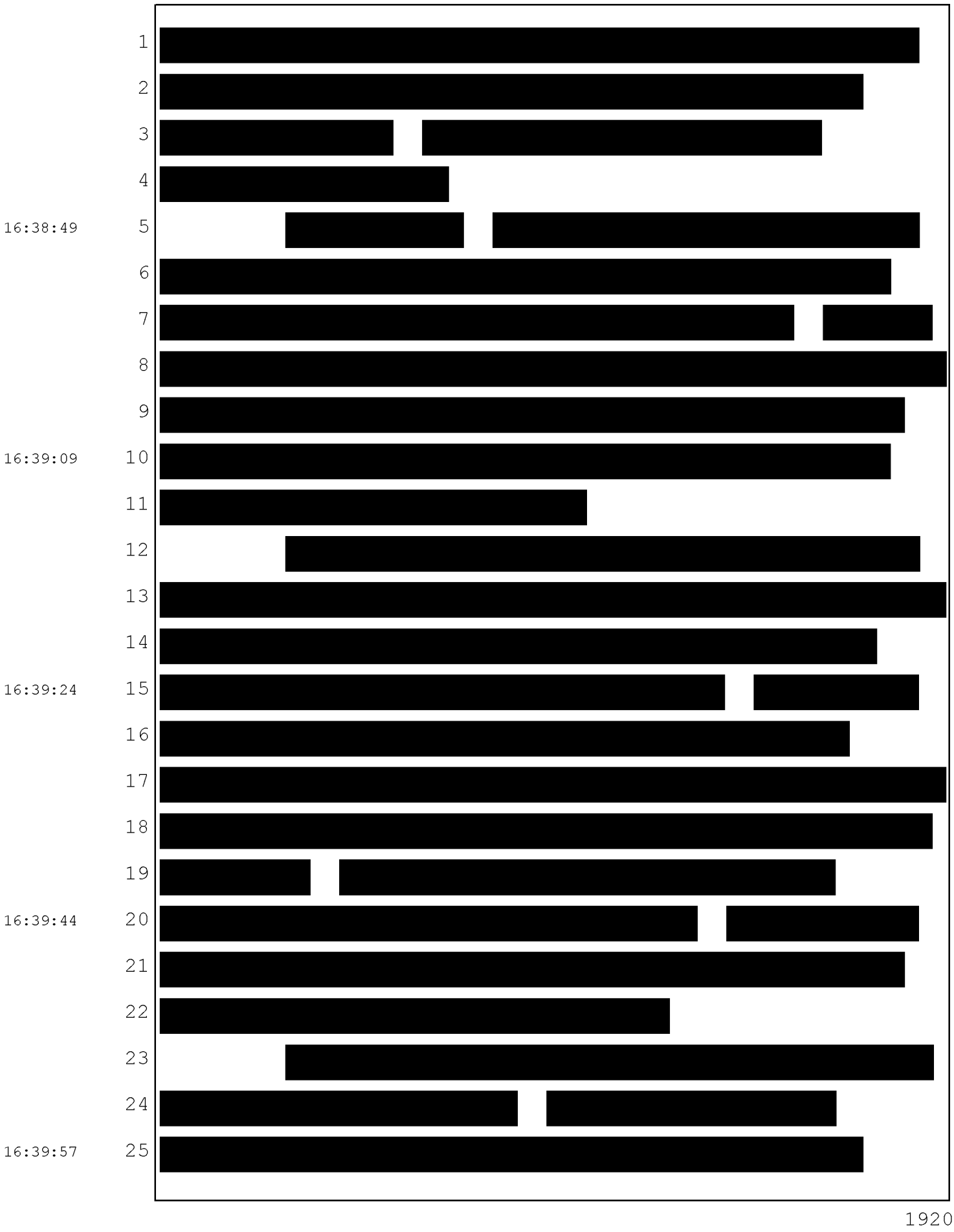
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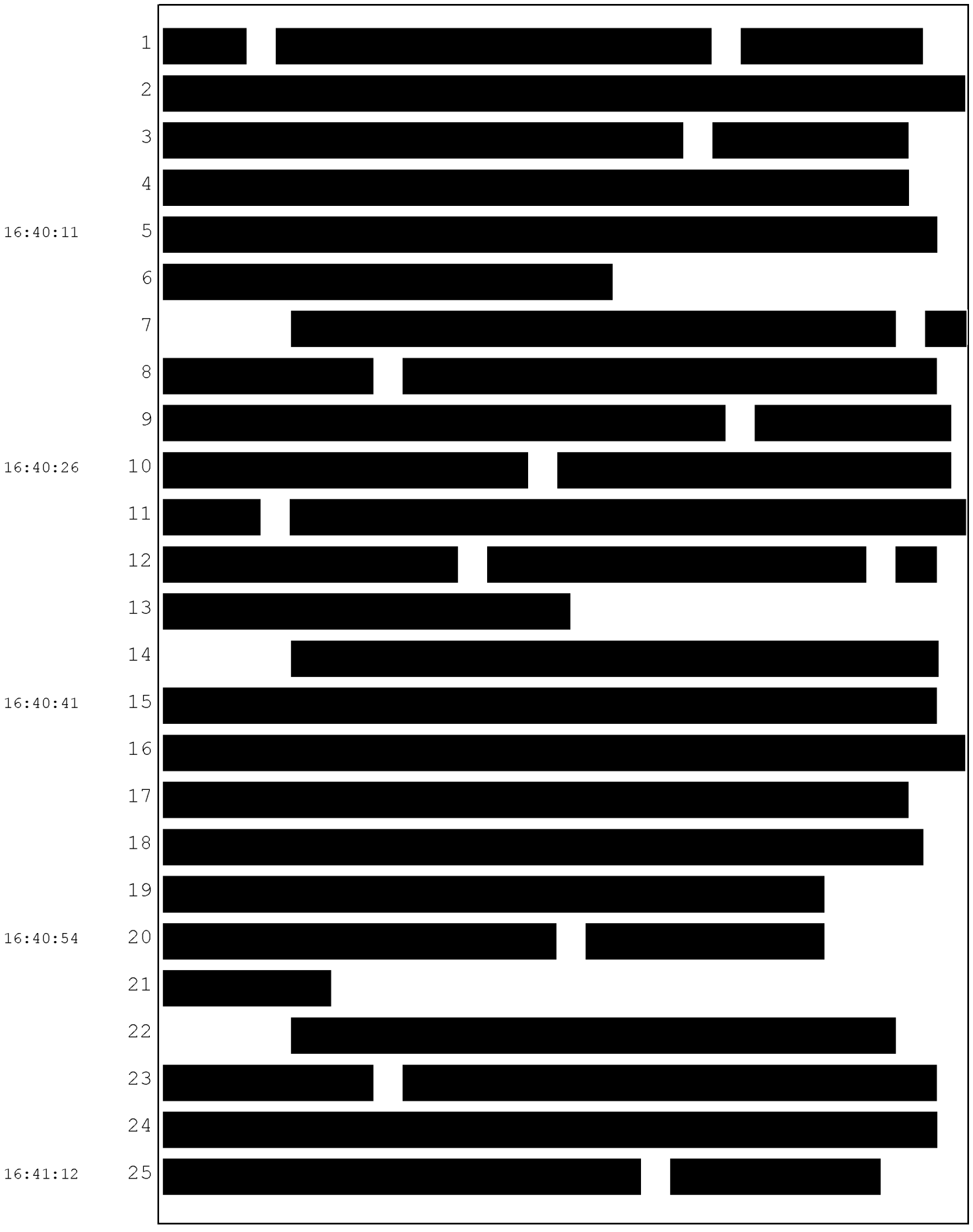
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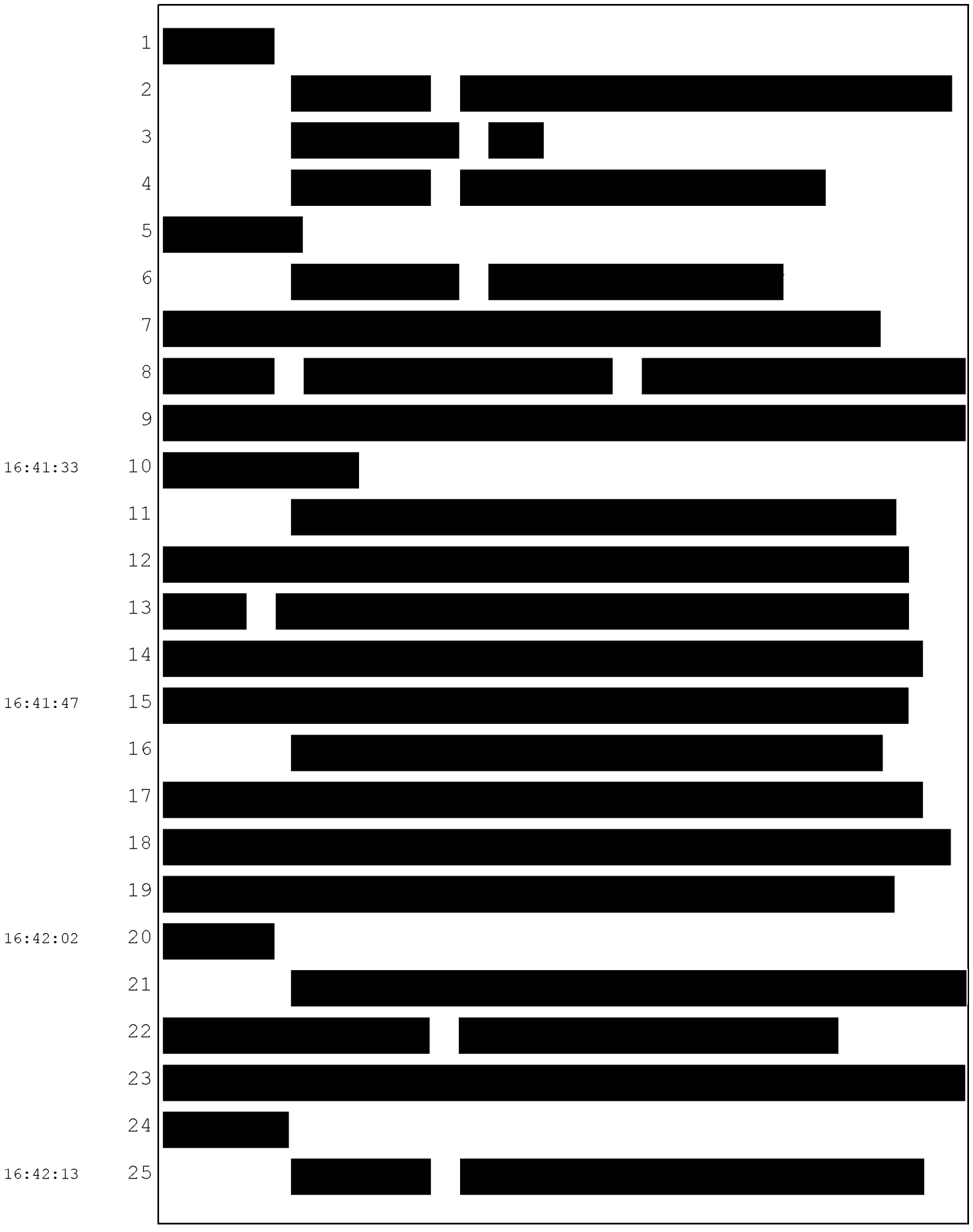
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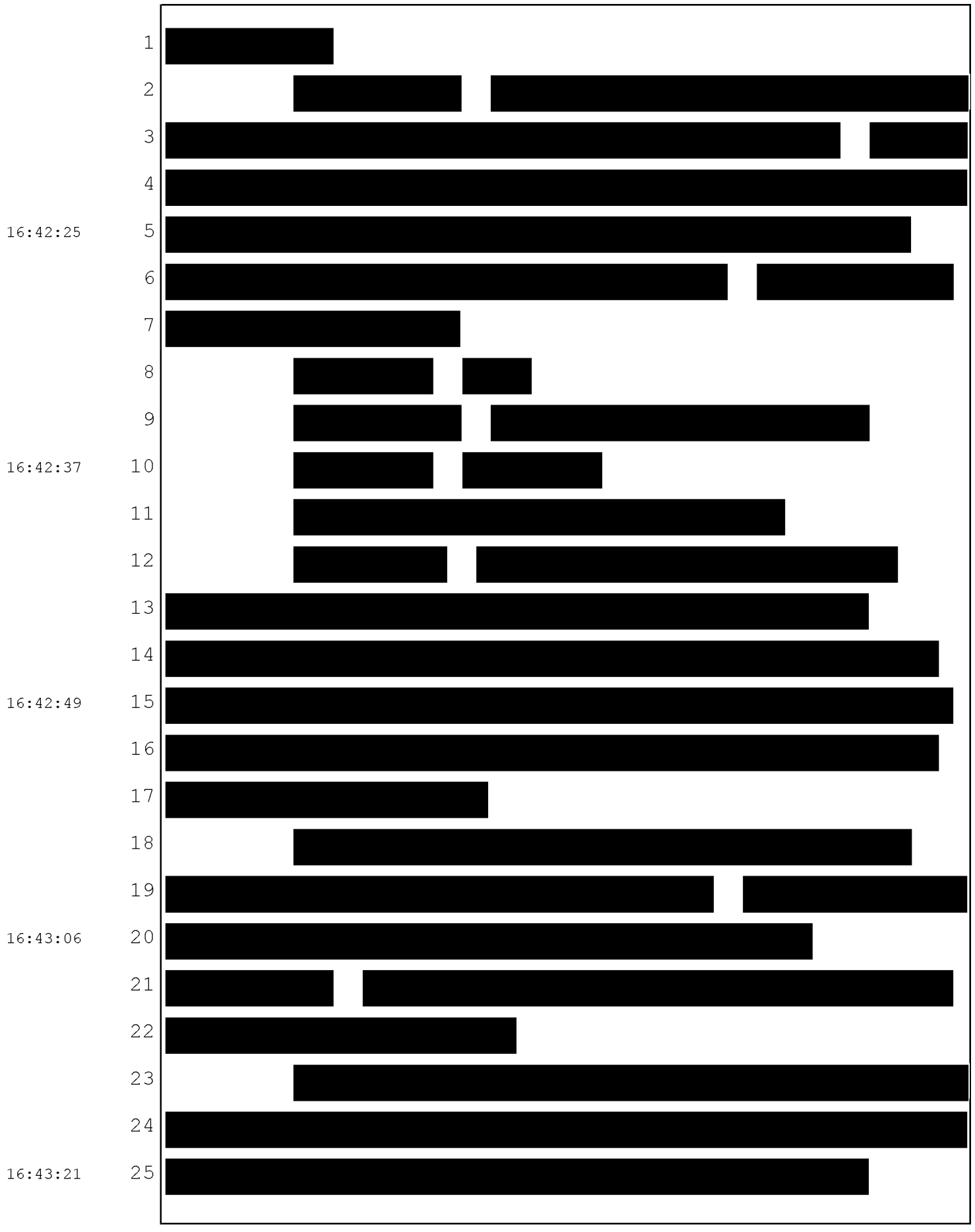
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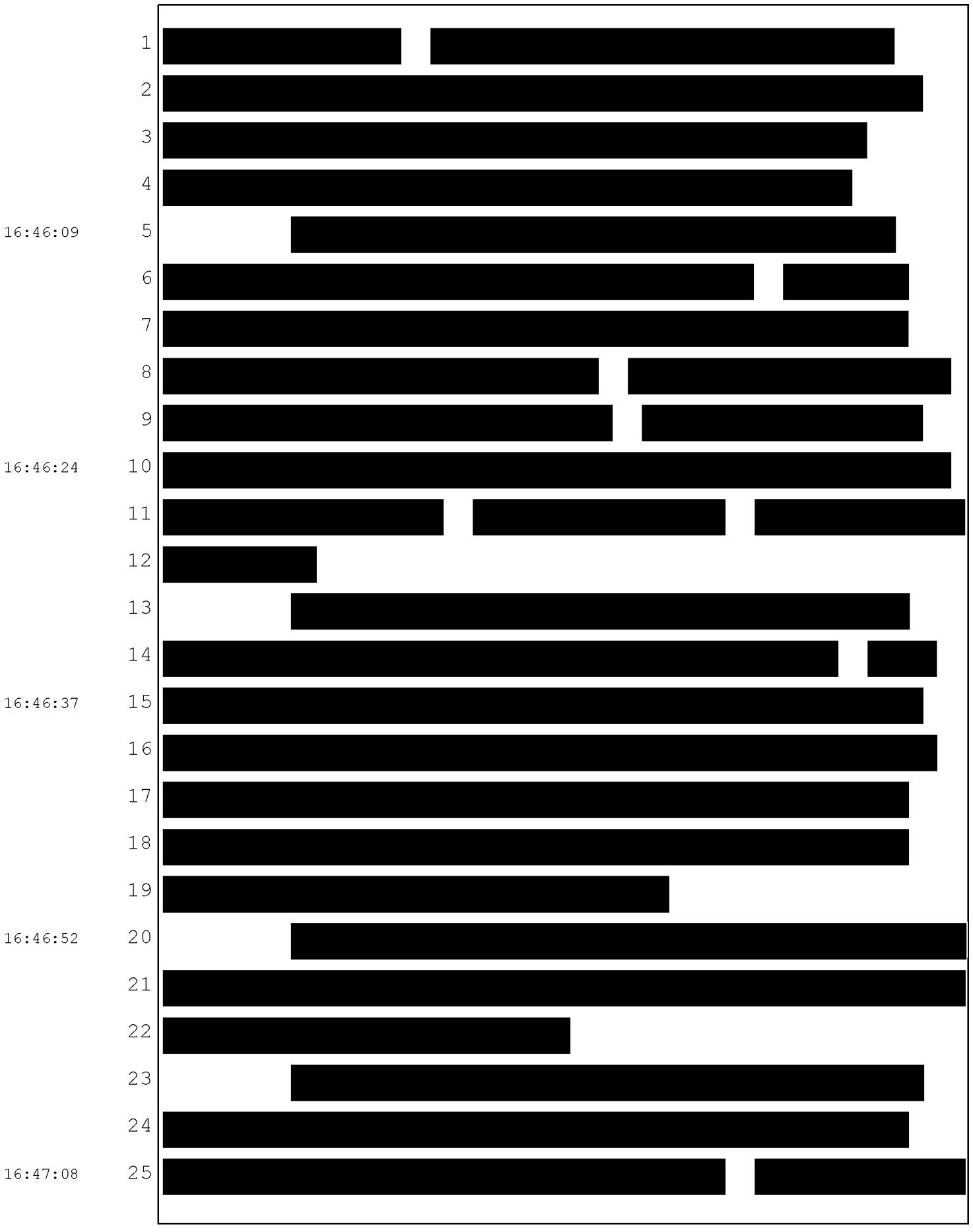
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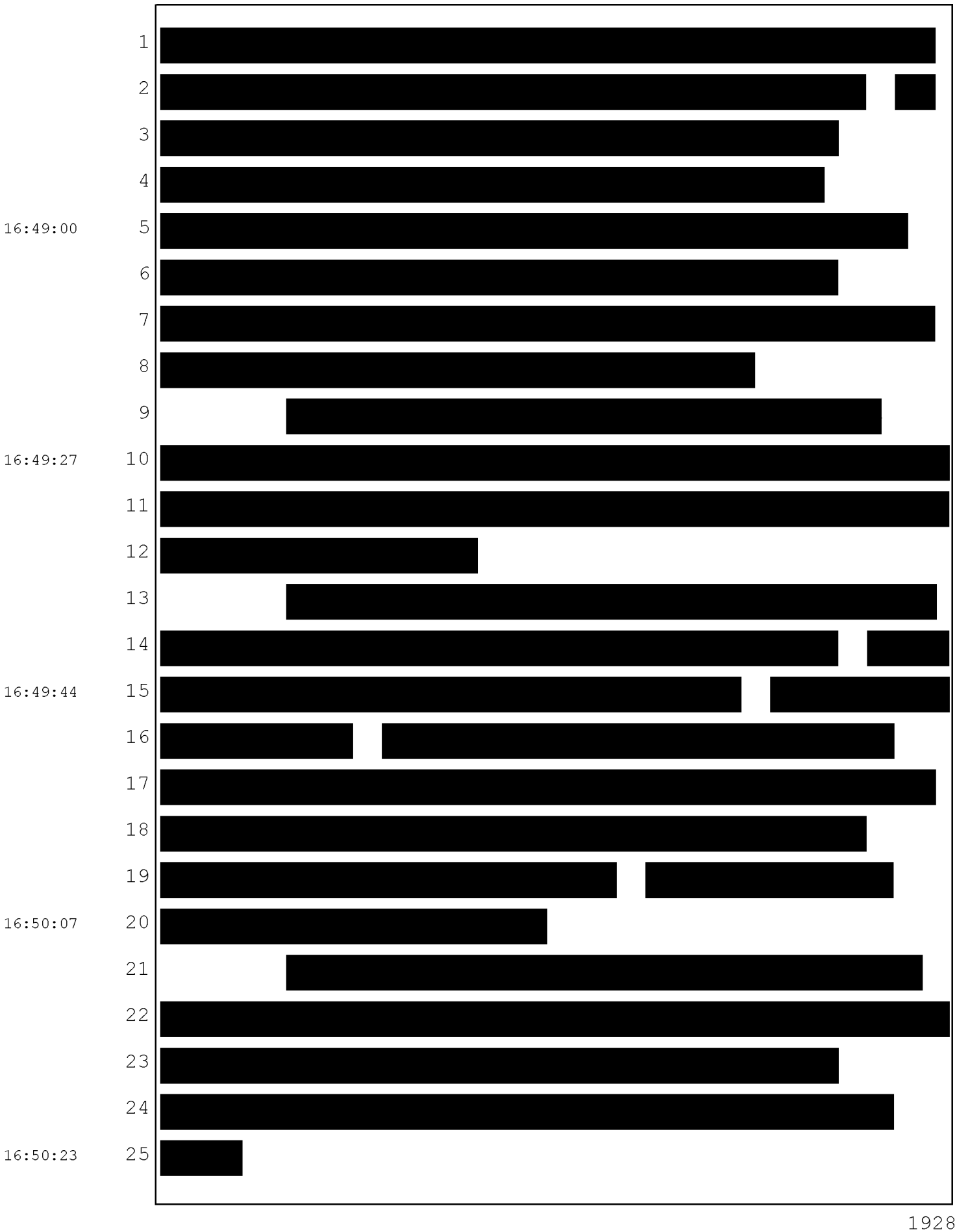
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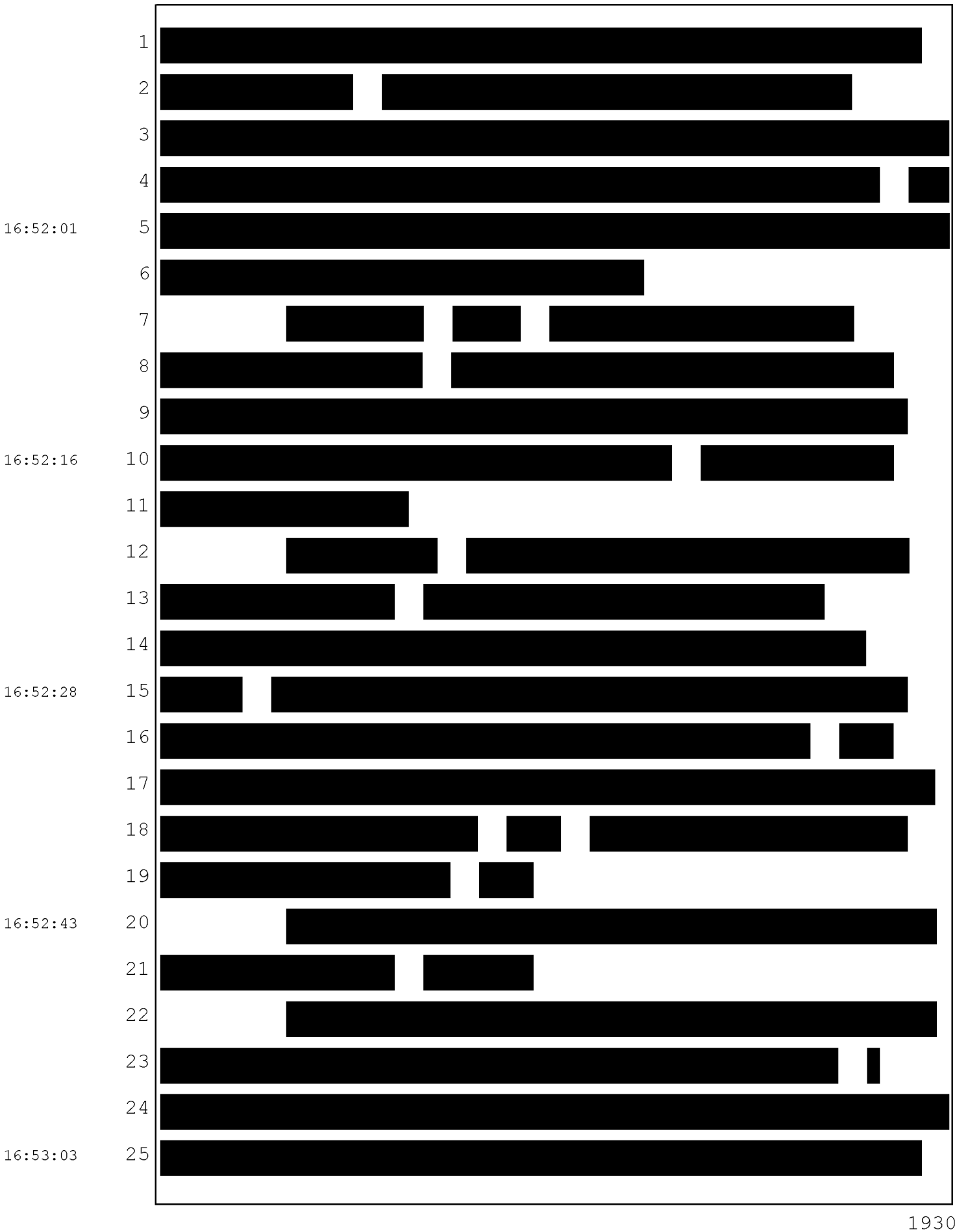
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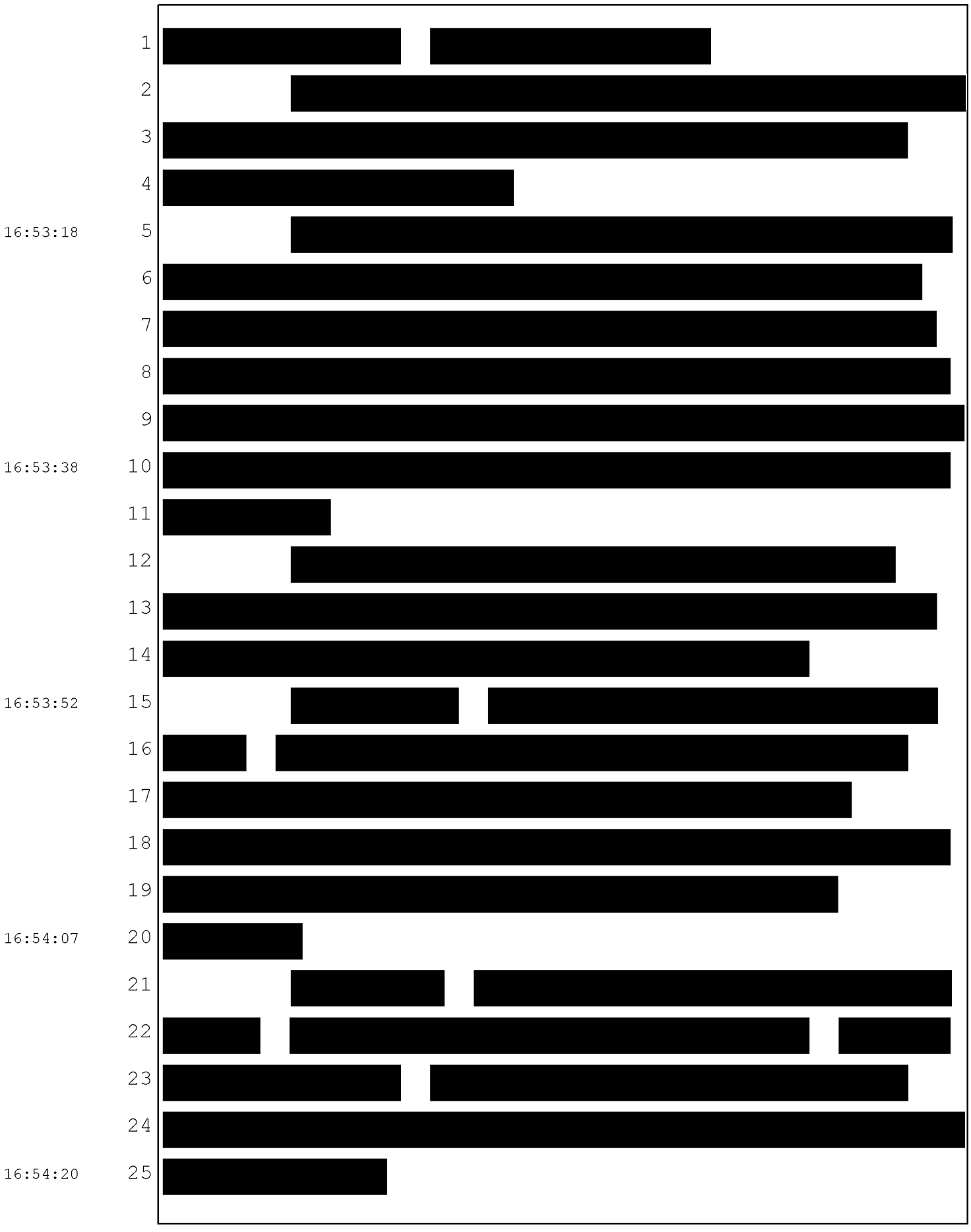
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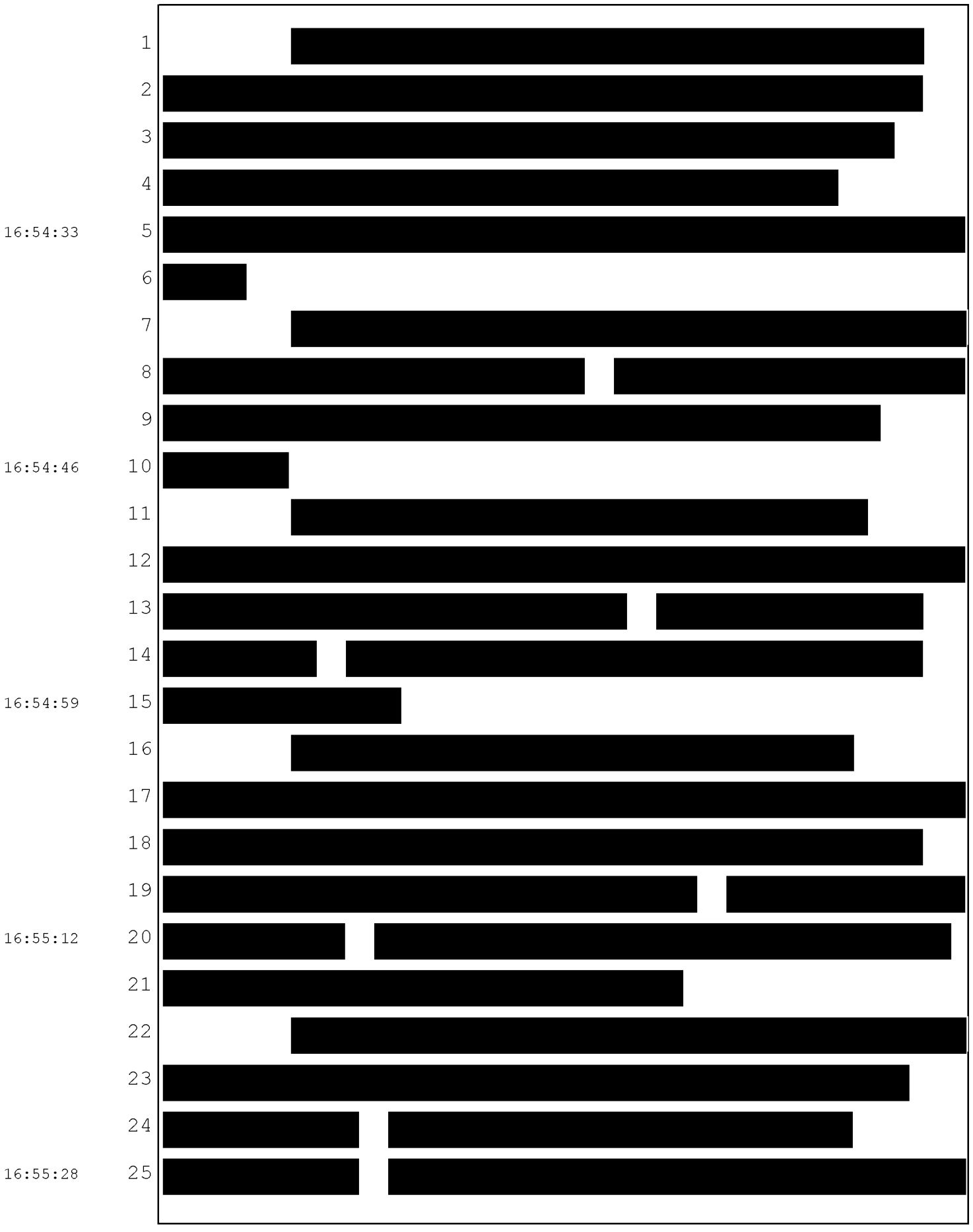
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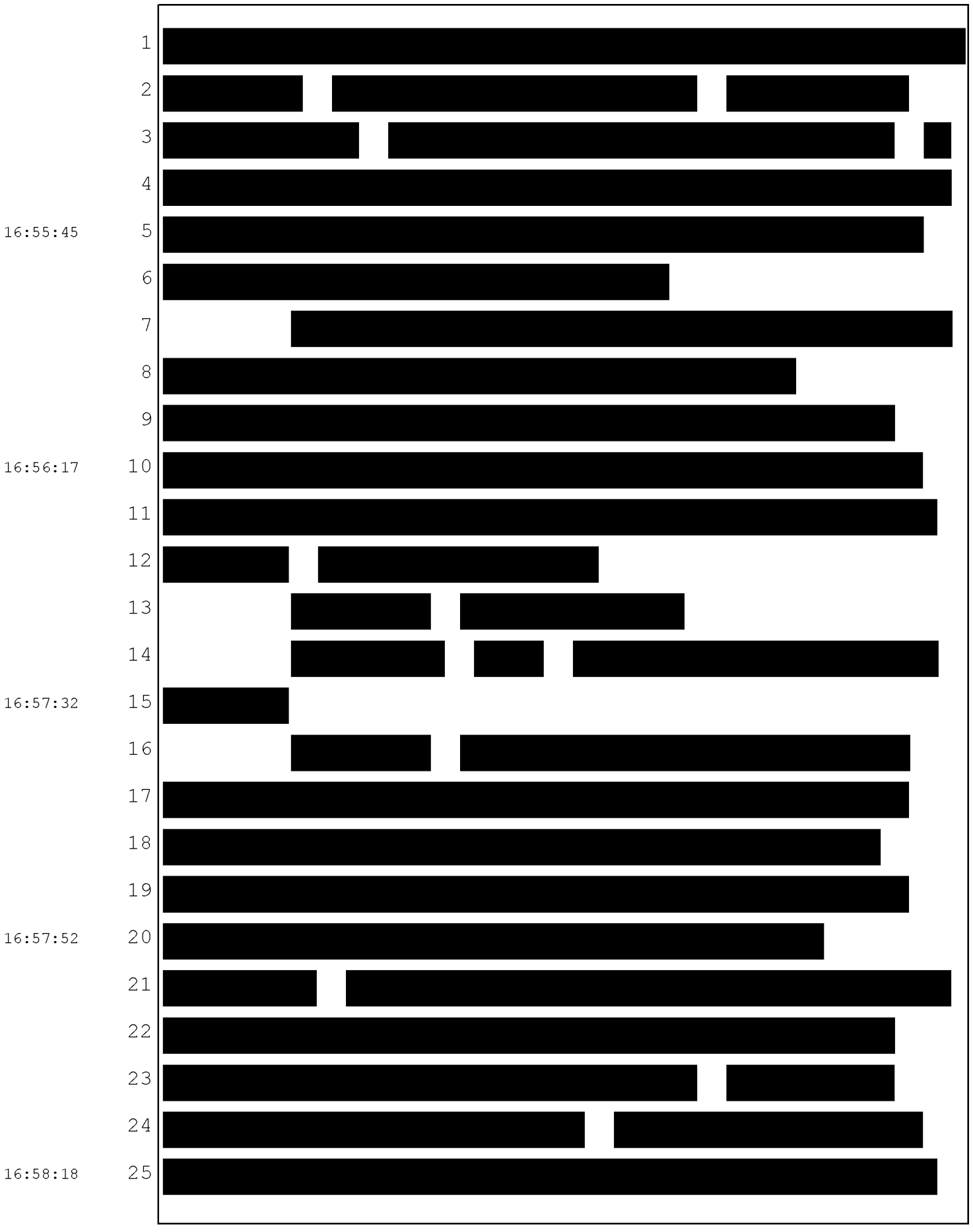
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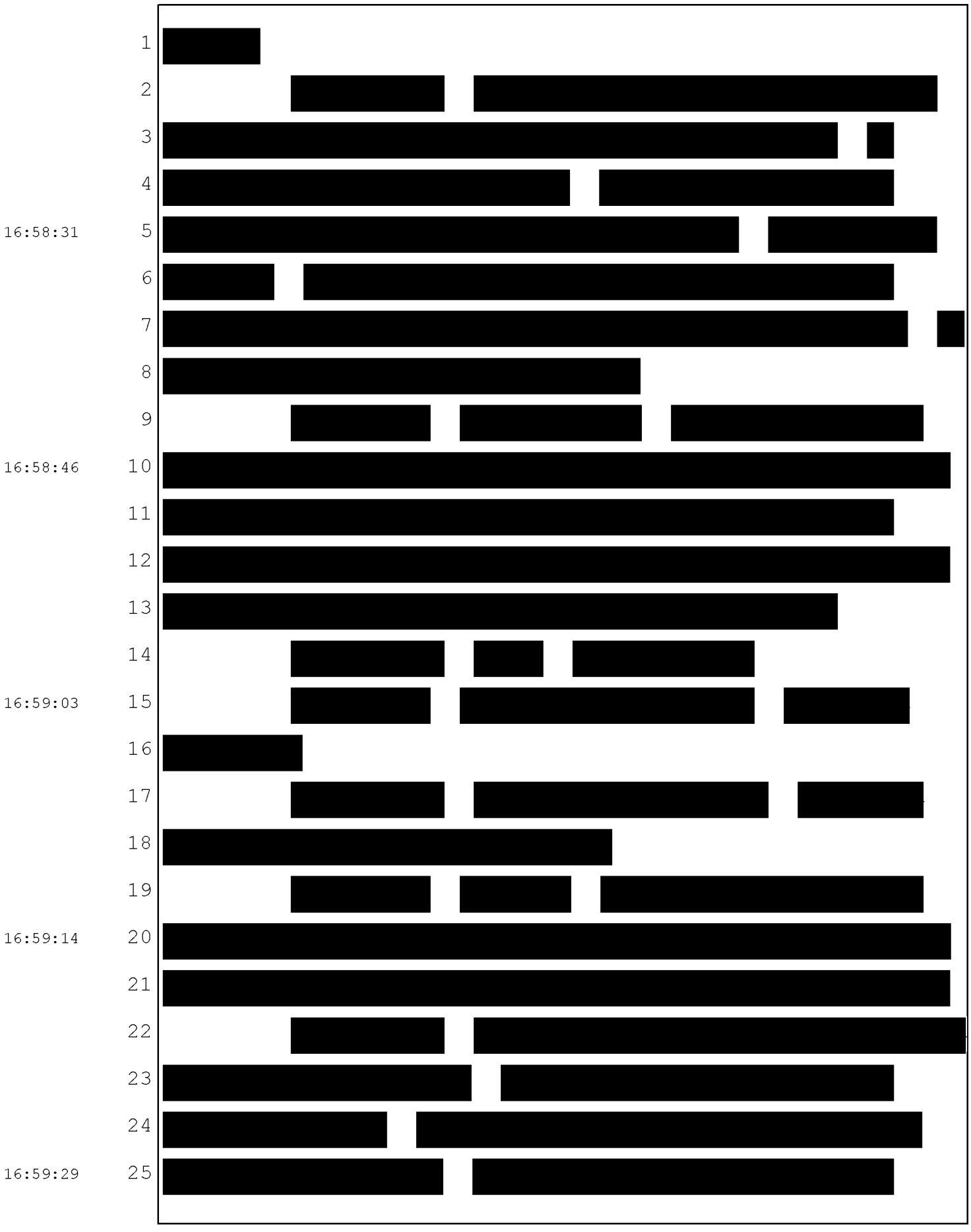
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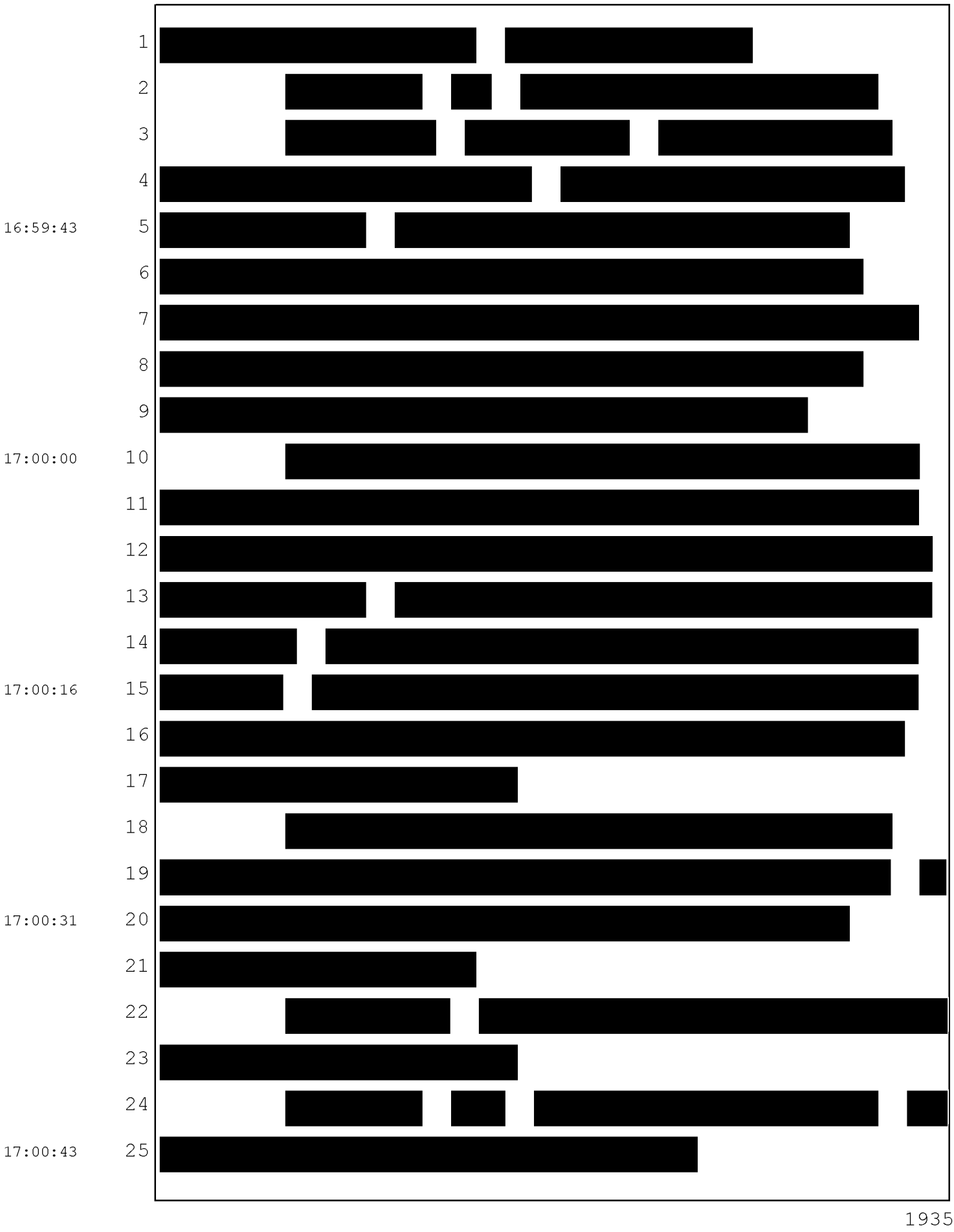
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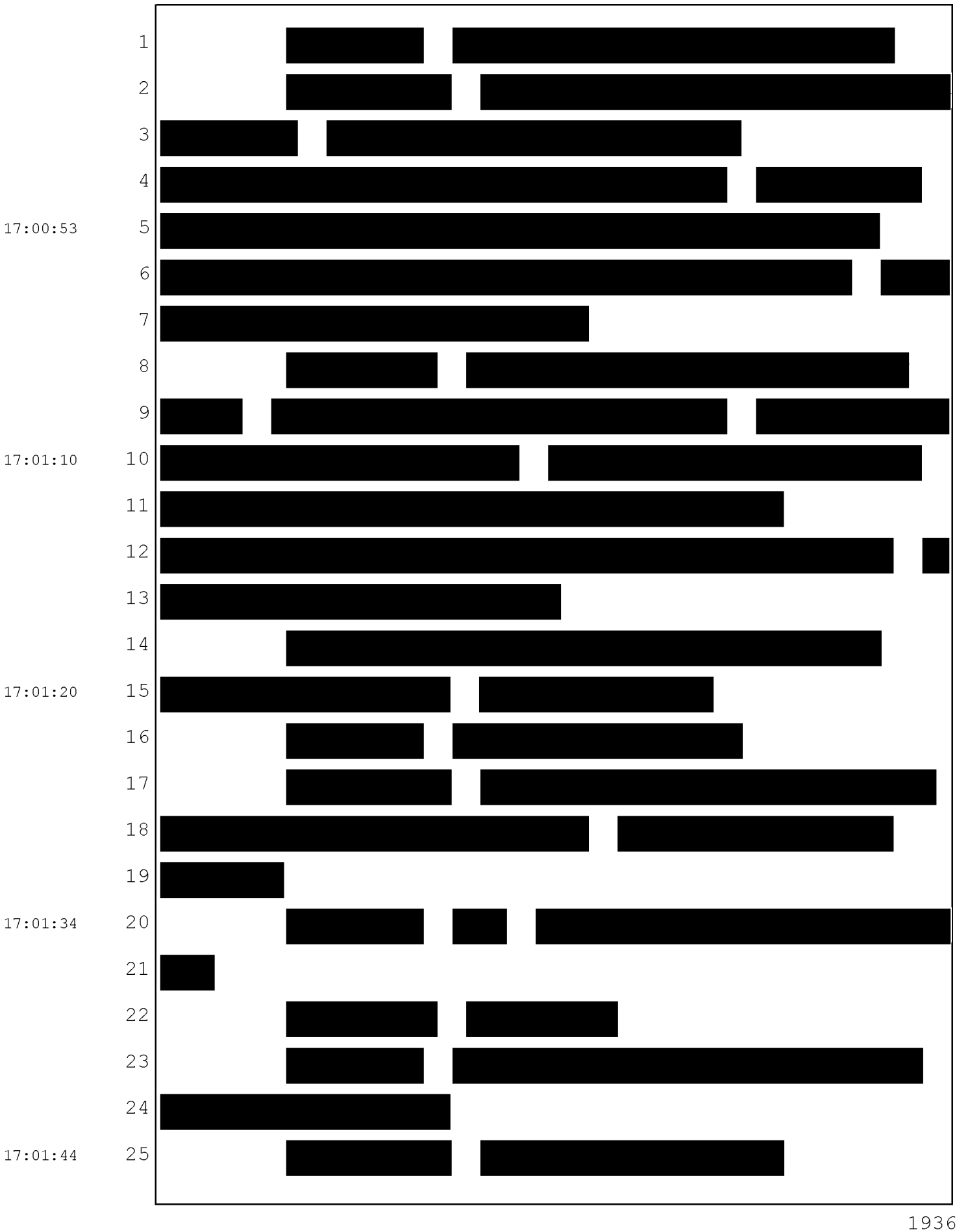
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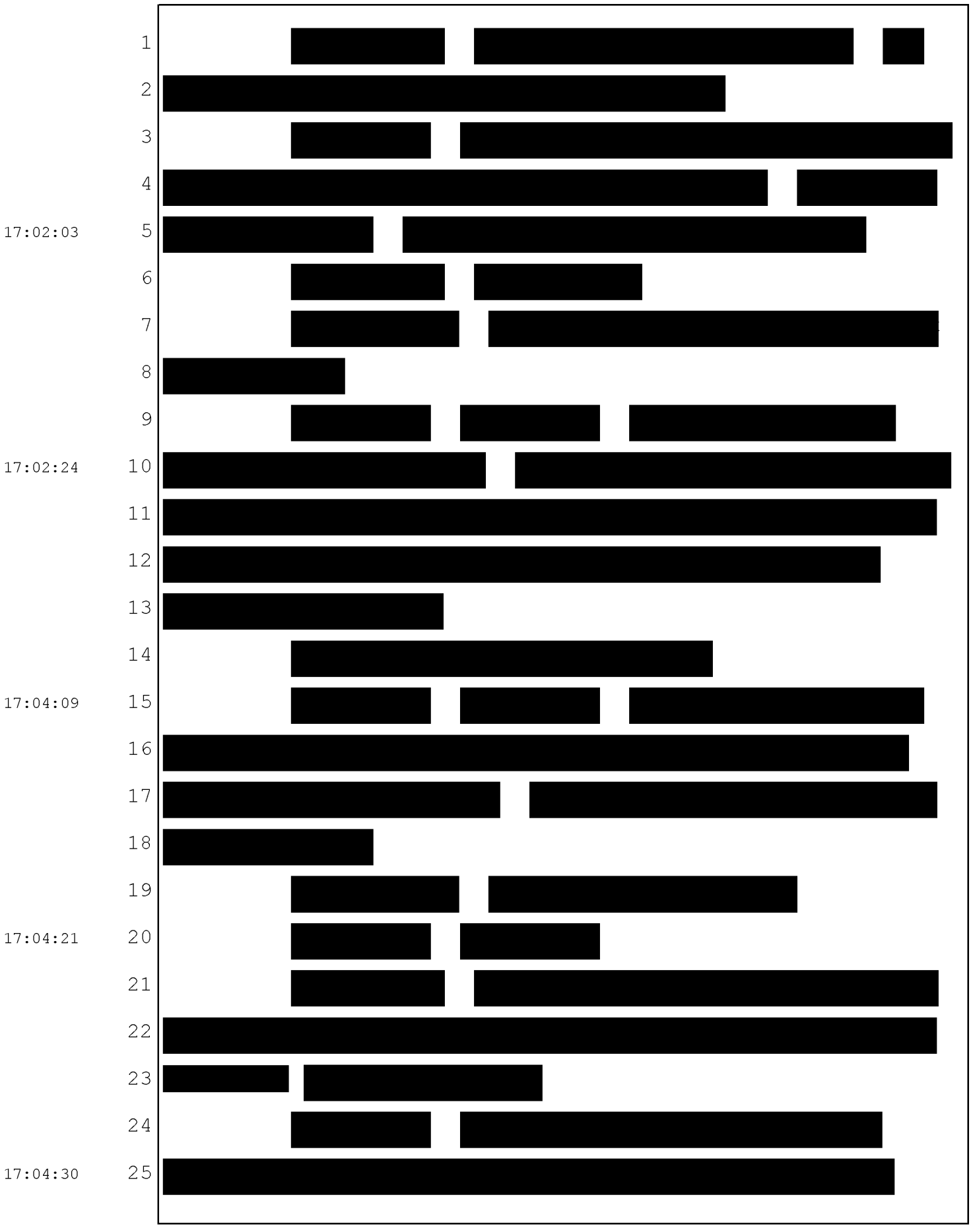
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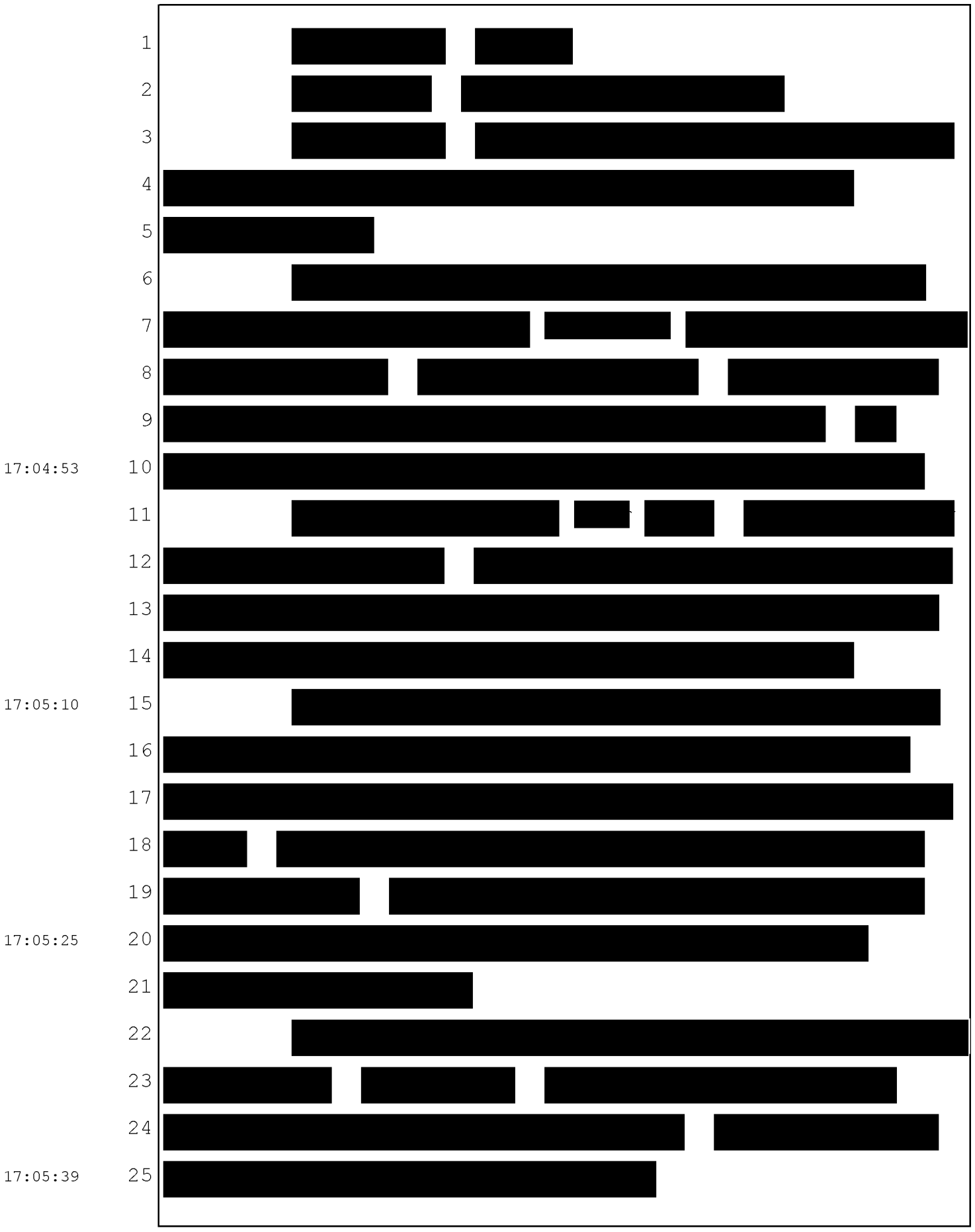
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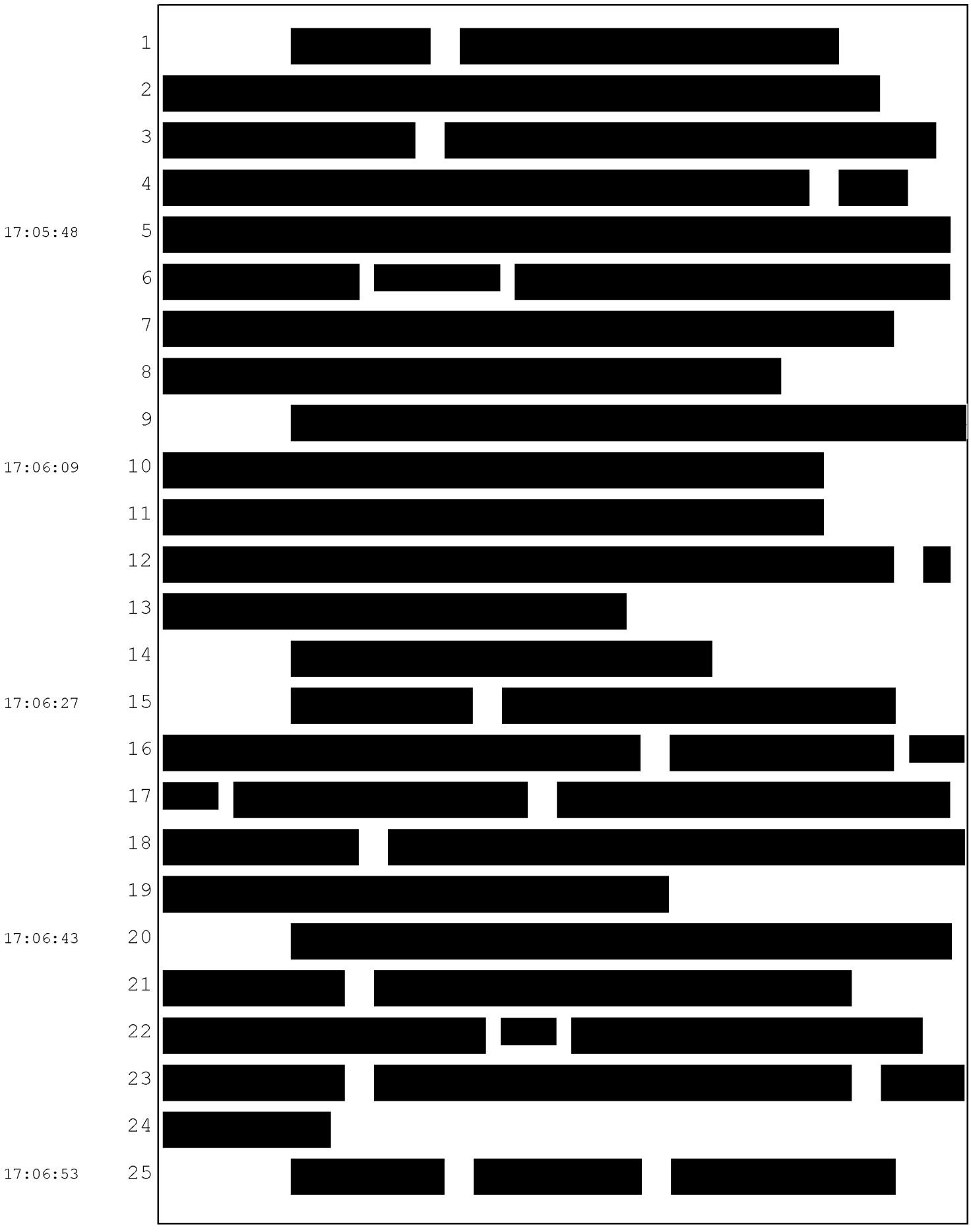
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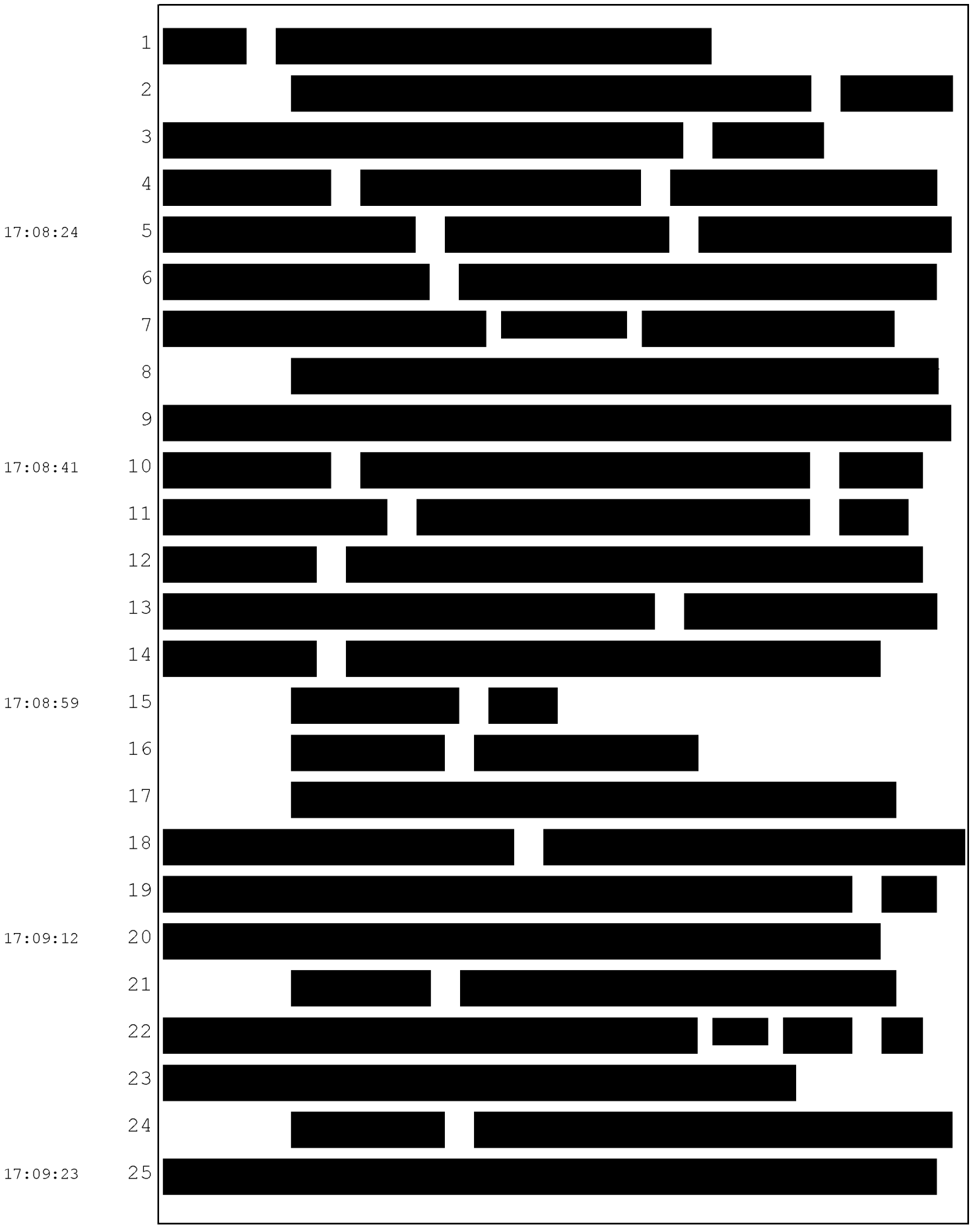
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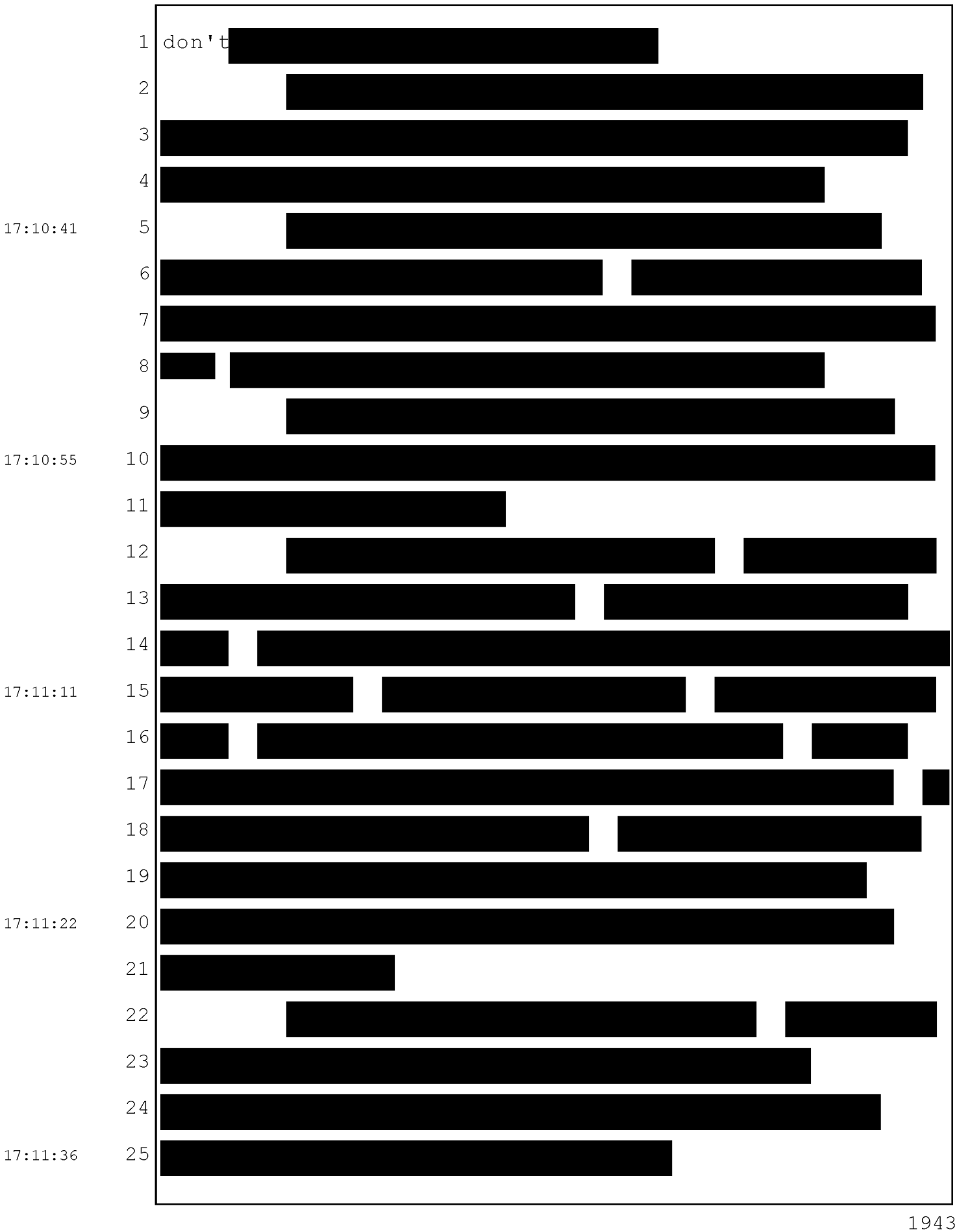
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(Time noted: 5:12 p.m.)

--oOo--

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: July 12th, 2018.

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