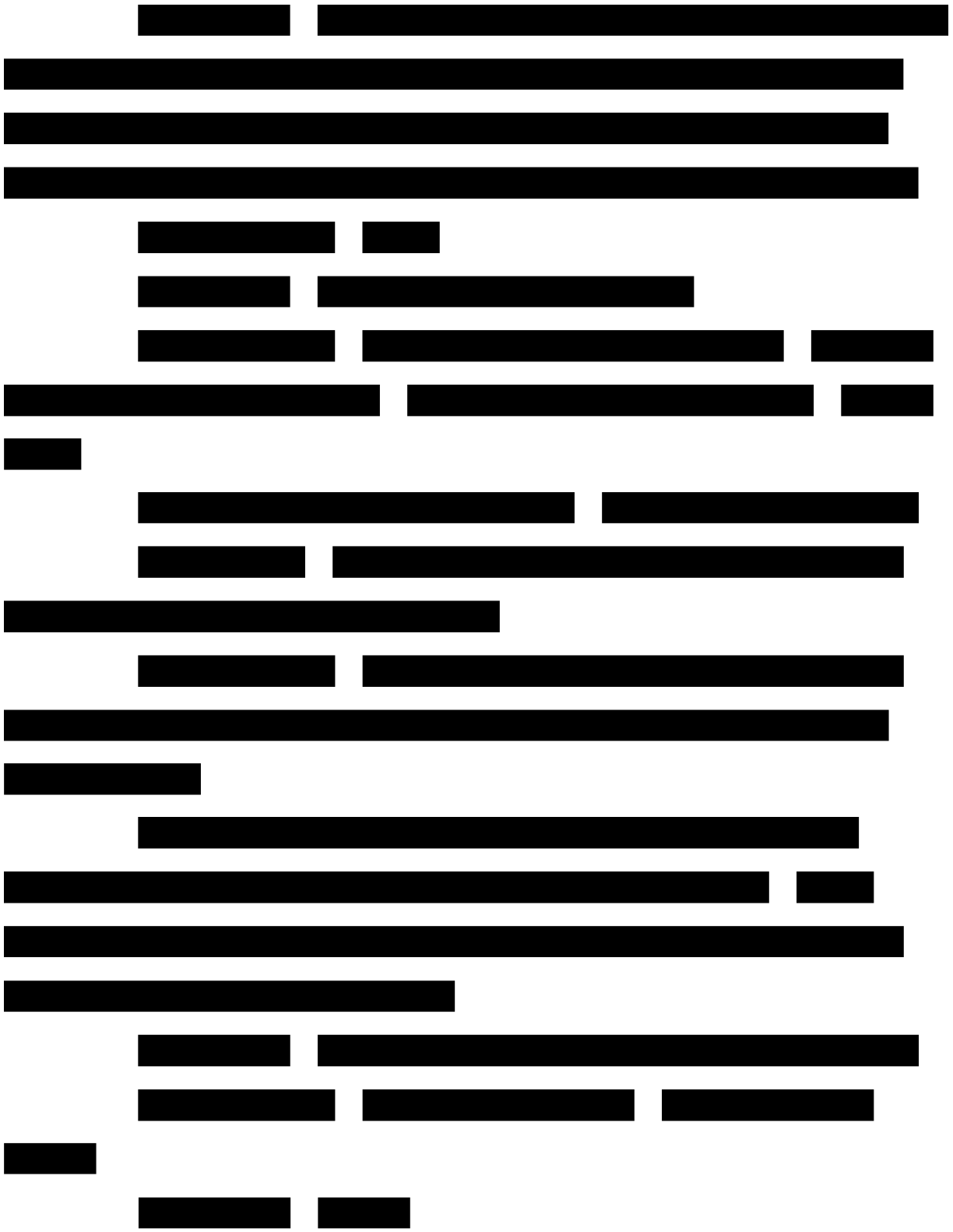
(Change of reporters - Volume 1-C)

(In open court outside the presence of the jury:)



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(Jury in at 3:22 p.m.)

THE COURT: All right. Thank you very much, Ladies and Gentlemen. Please be seated. We will resume.

(Witness enters courtroom and resumes the stand.)

MR. WISNER: May I inquire, your Honor?

THE COURT: You may.

DIRECT EXAMINATION (Resumed)

BY MR. WISNER:

Q Dr. Healy, we were talking about coding maneuvers before the break.

Do you believe it is appropriate to code suicidal events as emotional lability?

A No, I don't.

MR. BAYMAN: Objection. He's not a regulatory witness.

THE COURT: Overruled.

BY THE WITNESS:

A No, I don't believe it to be appropriate and I think it's misleading, unless, when the wider public like me and the jury, say, are told, look, you know, this is what's happening.

Q How did you learn about this emotional lability issue?

A Well, I became aware of it from a few sources: One is from colleagues who had noticed the problem in the adult data; and then from a media program in the U.K., which were --

MR. BAYMAN: Objection. Hearsay, your Honor. Media --

BY THE WITNESS:

A No, I was a participant in the program --

THE COURT: All right, then he may answer --

BY THE WITNESS:

A -- and advisor to the program. And the journalist who had read the article -- as I said, lay people were quicker to spot

this -- the journalist who read the article said what does this mean --

MR. BAYMAN: Objection. Hearsay, your Honor. He's now talking about what a journalist did.

MR. WISNER: Your Honor --

THE COURT: It is hearsay, but he's an expert, and he may rely on what he's heard.

BY THE WITNESS:

A As part of her research trying to understand what was happening, she consulted me. And, you know, I tried to offer a view and said this is what I would usually think it meant. But it became clear through her research and closer reading of the materials she had unearthed that that's not what it meant. It didn't mean what people would usually think.

BY MR. WISNER:

Q Do you know, based on the documents and information that you've reviewed, whether or not people within the FDA were concerned about coding suicide events as emotional lability?

MR. BAYMAN: Objection, your Honor.

THE COURT: Sustained.

BY MR. WISNER:

Q All right, Doctor. What happens practically with the suicide signal when you start talking about emotional lability and coding maneuvers?

A Well, there's a few different things that can happen with

emotional lability, which includes things other than suicidal events. So, again, the picture gets clouded.

It's a bit like akathisia. If you include other things in to -- well, it's in a sense almost the opposite. It's drowning out the signal by including other things in.

There are other ways to code things as well. I mean, when you've got emotional lability then, this is a behavioral change. And you can do things like include in the behavioral changes which are linked to the brain, for instance, you can talk about central nervous system effects. And if you do that, as opposed to teasing these out as mental health effects of a drug, you can put them under central nervous system effects. And if you do that, you can include in headaches, of which there are an awful lot of headaches in clinical trials, both on placebo and on active treatment. And this is rather like what we saw with Study 057 and 106. You drown out the signal, because all of a sudden there might be 6 or 8 or 10 emotional lability events, but if you add in 30 headache events to active treatment and placebo, both having a lot, then you drown out the signal.

Q All right, Doctor. That was Number 5 in our list of 13.

What's Number 6?

A We're going to --

Q Exhibit 36.

A -- 36.

Not reporting events.

Q What do you mean by that, Doctor?

A Well, there's a few ways that events may not be reported.

First of all, when anyone -- this can happen in any trial, it may not be a company trial, it can happen in any trial -- where events may happen, such as the person goes on to a suicidal act, and I've got a whole stack of reports from a bunch of patients, and there's suicidal acts here, there, and everywhere, and I'm transcribing them over to a spreadsheet, and somehow some may just not migrate over. There may be some dropped out. This, you know -- it's the kind of thing you can see happen. It does happen in company trials. It has happened in Paxil trials. And it has happened to suicide events in Paxil trials.

Q So when you say it happened in a Paxil trial, I don't want to get into the specifics of the trial, Doctor, but how did you go about figuring out that events just weren't reported?

A Well, again, I mean, people don't want to take out of this weren't report -- they don't want to read weren't -- or deliberately weren't reported. My take on this is if we're going to get --

MR. BAYMAN: Objection, your Honor. This is outside the scope of his report and now it's his take on this. He's talking about intent and motive.

BY THE WITNESS:

A No, I'm saying the opposite. I'm saying you don't want to infer intention.

BY MR. WISNER:

Q Dr. Healy --

THE COURT: You've got a lawyer here. Let him do the arguing.

I think we're getting kind of far afield here with this -- it's not specific. It's too general.

Sustain the objection.

Move on to something else.

MR. WISNER: Yes, your Honor. Let me -- let me -- let me focus in so it's very specific.

If your Honor doesn't like this question, let me know and I'll just let it --

MR. RAPOPORT: Just ask the question.

MR. WISNER: Okay.

BY MR. WISNER:

Q In Paxil trials that you reviewed, have you looked at the raw data?

A Yes.

Q And in looking at the raw data, have you compared whether or not what's reported in the raw data was reflected in the report?

A Yes.

Q And what have you seen on that issue specifically as it

relates to suicide?

MR. BAYMAN: Objection. This is outside the scope of his report, your Honor. It's nowhere in there.

MR. WISNER: Actually it is, your Honor. I can show you if you would like.

THE COURT: Overruled.

BY THE WITNESS:

A Not all the events that happen in the trial end up in the documents. So the documents we have seen earlier, I don't have confidence that the 42 events versus 6, even if the -- it ought to be 42 and 1, I don't have confidence that they're necessarily the correct figures. It could be higher.

BY MR. WISNER:

Q And when you went and looked at the raw data for that one Paxil trial that you're referring to, did the incidents of --

MR. BAYMAN: Your Honor --

BY MR. WISNER:

Q -- suicide increase or decrease?

MR. BAYMAN: -- may we have a sidebar on this?

THE COURT: Okay.

(At sidebar outside the hearing of the jury:)

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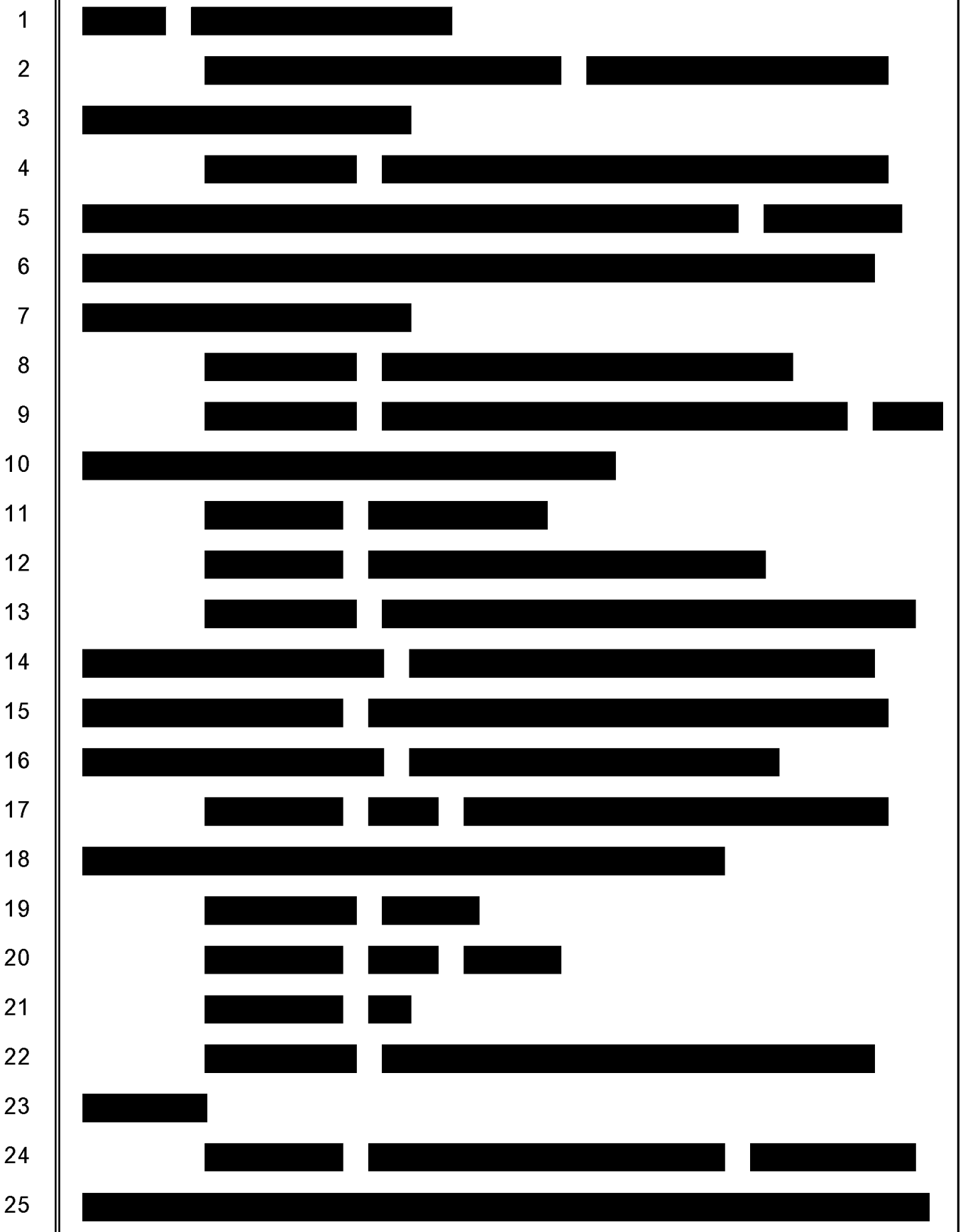

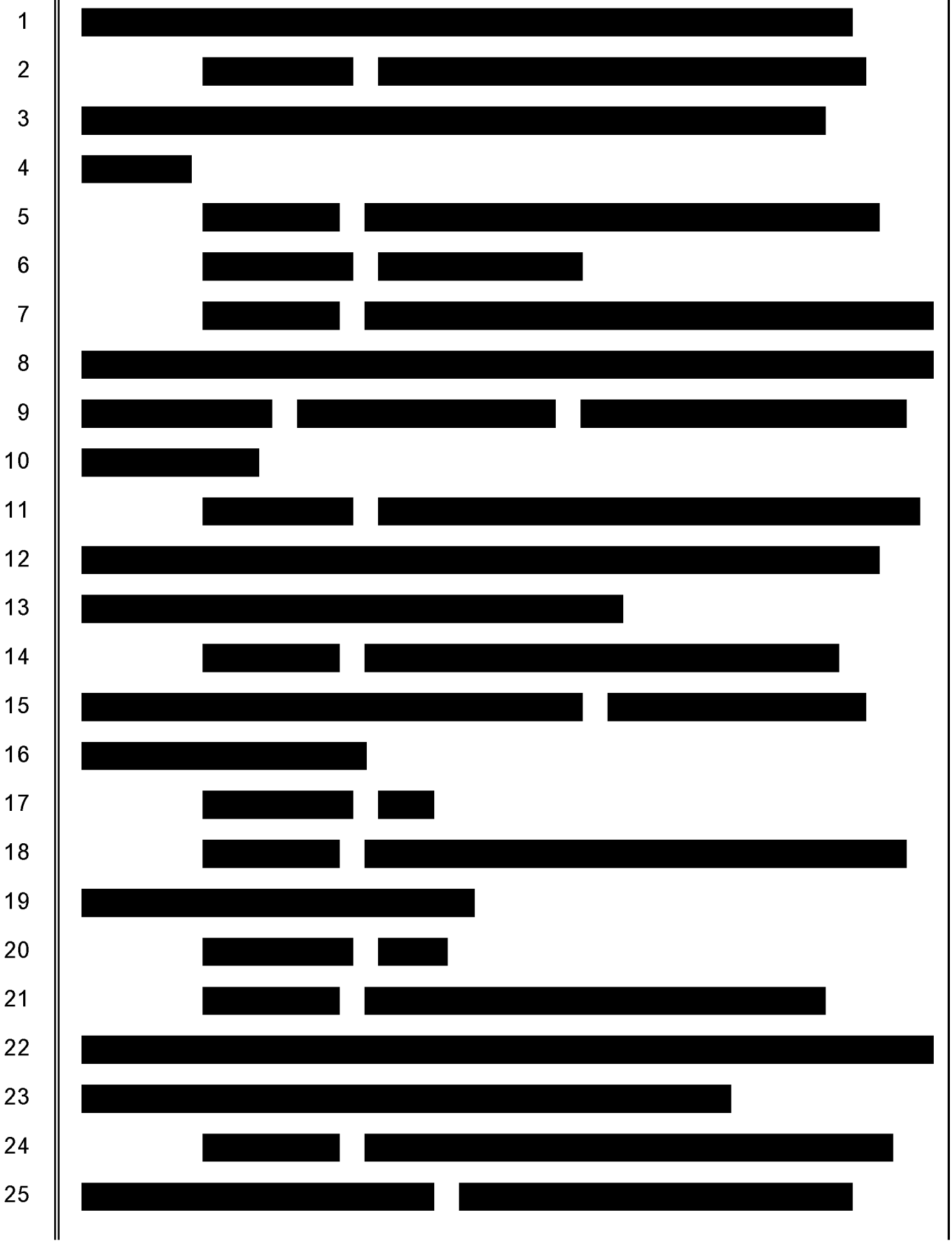

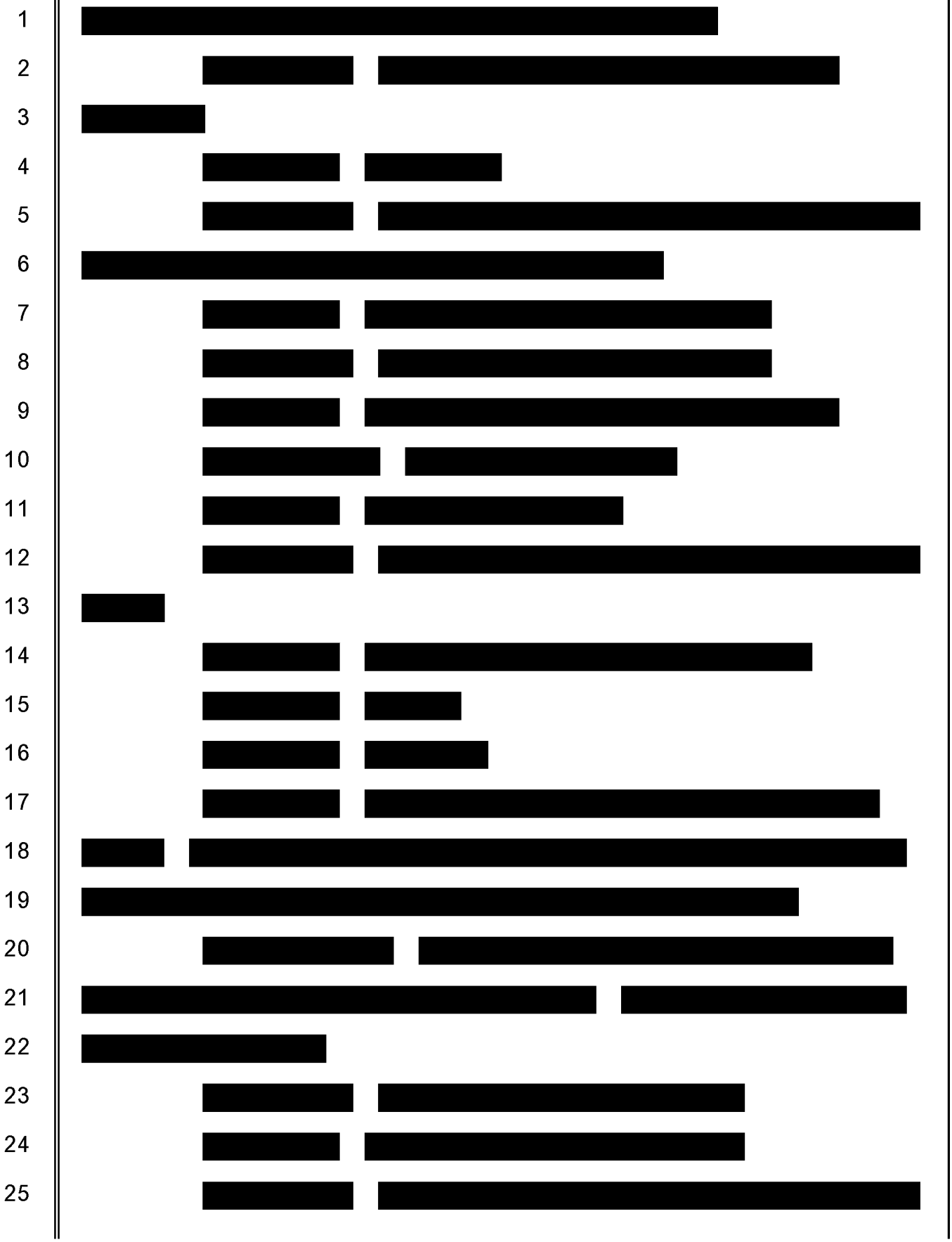

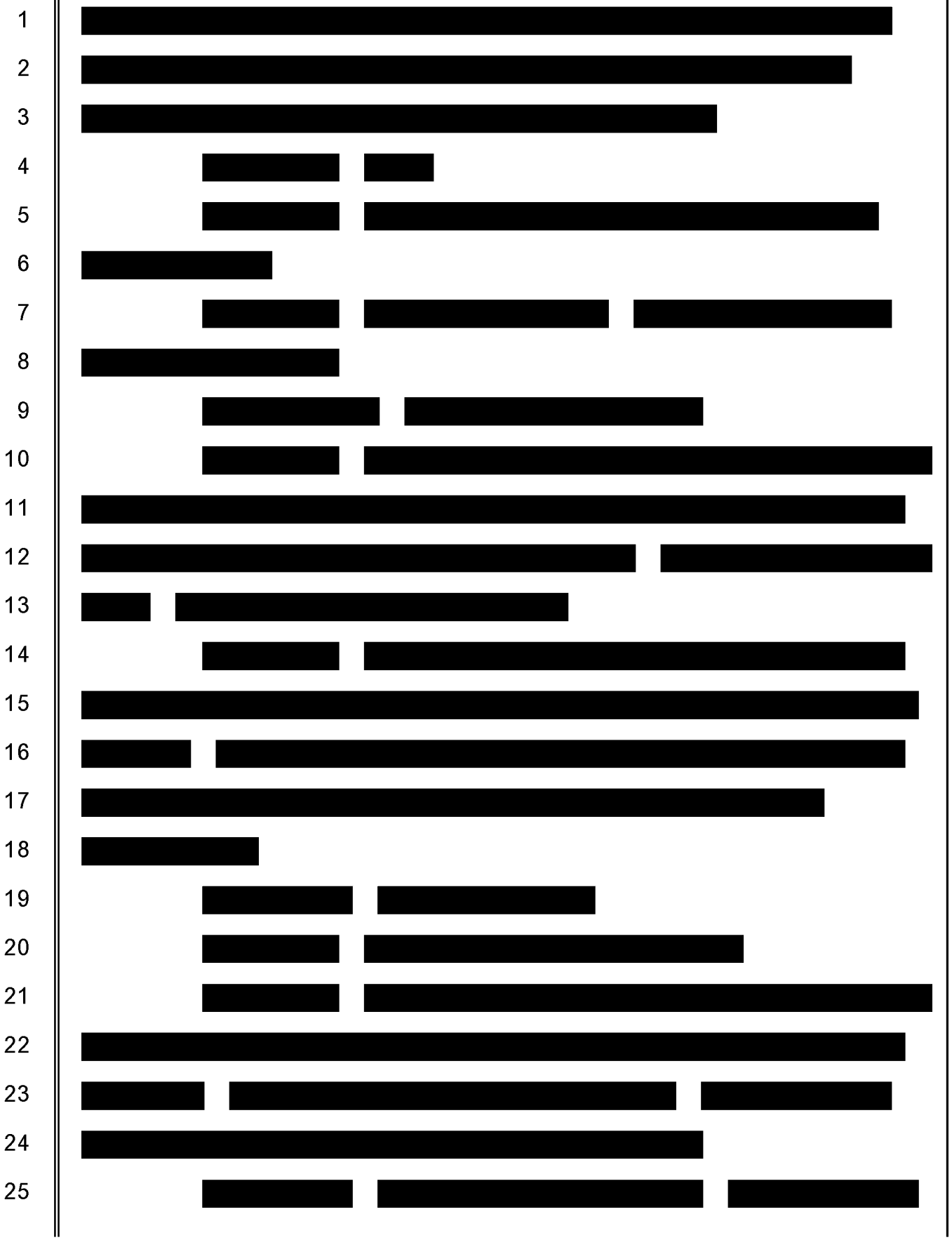

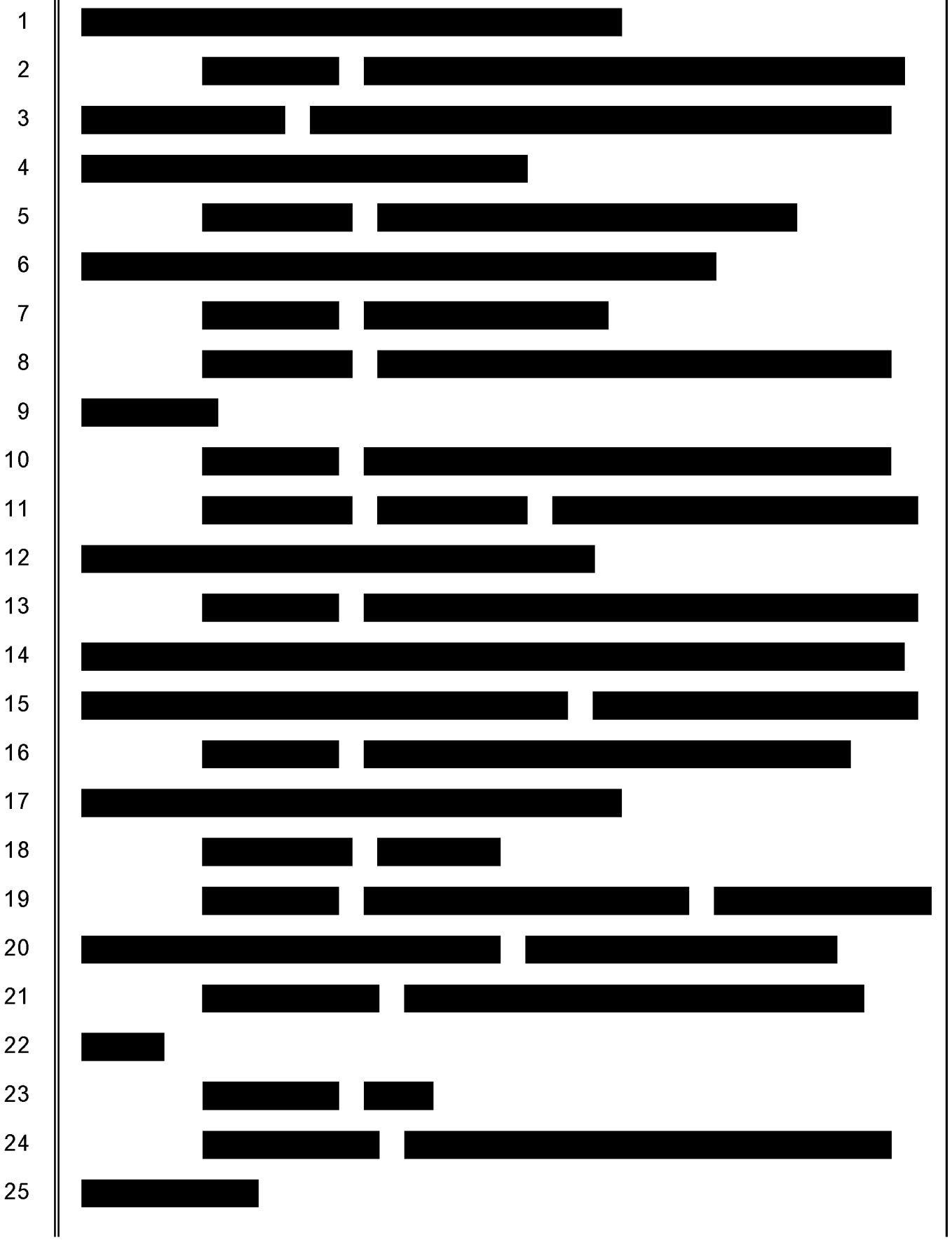

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MR. WISNER: May I proceed, your Honor?

THE COURT: Yes.

BY MR. WISNER:

Q All right, Doctor. Let's step away from the non-reporting specific thing we're talking about here and just talk generally about -- let's move on to the next item.

After not reporting events, what do you have, Doctor?

A You've got focusing on suicidal ideation.

Q And what does that mean?

A Well, that's specific in this case to this event, and it's -- in the course of going on to commit suicide, people usually start thinking about it and then planning it, and this is what we mean by suicidal ideation. There may be fleeting thoughts or it may be plans.

Suicidal ideation is very, very common.

Suicidal behavior -- actually doing something, cutting your wrists, taking an overdose, jumping off a building -- that's much less common.

Completed suicides is less common again.

There's typically ten suicidal behavior events for every one completed suicide.

There may be hundreds of suicidal ideation events for

every one suicidal behavior -- behavior.

Q So why does looking at ideation, why does that obscure the suicide signal?

A Well, it drowns it out. It's very like, again, as I said, including headaches in with other central nervous effects, which may be quite different to headaches, but if we end up just reporting the central nervous effects of our drugs, and if the headache signal in there is awfully big, it can make everything look equal between active treatment and placebo.

It's a little bit the same here.

If in the suicide box we include ideation, it can equal things out, and it can do more than that, because we do expect in the course of the trial that Paxil, for instance, is going to be effective and it will lower Hamilton Rating Scale scores; but as I've indicated to you earlier, it's not the case that I've necessarily asked you every single question on that scale. I may have got the general impression you're improved, and I may be rushed, and I might just fill in a score afterwards consistent with your overall improvement, as I might do on libido issues. The drug might have wiped out your sexual functioning, but overall I probably haven't asked the question, and I've rated you as being a little bit improved overall. We know that the Hamilton Rating Scale score for libido improves in the course of treatment with Paxil. We also know that 100 percent of people who take Paxil have some sexual

dysfunction linked to the drug.

Q Now, Doctor, are you saying that we should not look at suicidal ideation?

A No. It's important. And this can help us if it's done well. If we put a suicidal ideation scale in there, I expect a lot of people to improve. They may have been suicidal to begin with. Paxil may have been a good treatment for them. But if in the midst of things we've got some people who are improving, but some people who are getting worse, then it can all get mixed up.

It's a bit like what we reported as regards sleep. You may have some people who aren't able to sleep on the drug, some people sleeping too much. If we average it out, we may overall say, well, Paxil improves sleep a bit, when there's a bunch of patients in there who are having a tremendous problem.

It's the same with eating. Some people lose weight, some people gain weight. If you look at the average effect, you may conclude that Paxil has no effect on weight when, in fact, it's having a big effect but in opposite directions on a large number of people.

Q Now, Doctor, could a drug conceivably, like Paxil, induce suicidal behavior but not ideation?

A It -- well, this is awfully tricky and, you know, there are people who commit suicide without having prolonged and protracted ideation.

It does seem that people in the midst of an akathisic episode, where they haven't been thinking about the issue much beforehand, go on quite quickly to kill themselves, but I think it would be rather unusual to have a person actually try to harm themselves or kill themselves without having a degree of ideation. It's built in to the akathisia. It's built in to the emotional blunting to some extent in that that has an effect on the ideas you might be having from your illness. It means you're numb to the thoughts the illness may actually suggest. But on top of this, you've got a bunch more ideas coming from akathisia, for instance, or possibly from psychotic features that have been triggered by the drug.

Q Now, we've seen it broken down: Suicidal ideation, suicide attempts, and completed suicides.

Would it be fair to group completed suicides into a suicide attempt category?

A I believe that's fair. I mean, you should tease the two apart and report both, but I think suicidal behavior is distinct from ideation.

Once you throw ideation in, because of the way we collect it -- you know, we're not as rigorous in trying to collect it -- then you can cloud the signal.

But the other thing that comes up in terms of the suicide ideation debate is just people saying, well, the score on the Hamilton Rating Scale, the suicidal ideation score

improves, and that gives the impression that if it's improving overall in the group as a whole, and even more than on placebo, that there's no problem here, when this isn't the case.

Q Doctor, I want to focus for just a quick second, not on ideation, but simply on suicide attempts and suicides, completed suicides.

Can someone complete a suicide without also making an attempt?

A Well, clearly, no -- well, first of all, there's a debate over whether it should be called suicide at all. Do they intend. But, I mean, it's a lethal attempt. Some of the attempts may be events that people survive by accident. They've -- you know, they -- they were trying hard to kill themselves and don't end up dead.

Q You actually brought this up yesterday, and I kind of wanted to follow up with you on this.

If you say "suicide" is not the right term, do you got a better one?

A Well, it's awfully tricky to know -- and, again, the jury may be able to kind of suggest views, too -- it's -- it's -- this is -- this is a treatment-induced problem. And a lot of people I know when their partners or their children or their parents kill themselves having been put on a drug are very keen that suicide is not the right term. I don't know that anyone has come up with a different term. But a lot of people feel

awfully strongly, this was completely out of character, to say that this person whom I knew well would have killed themselves is just wrong.

Q Would a drug-induced reaction be an appropriate way to phrase it?

A Except that includes every other reaction, so -- it's a treatment-induced death.

Q Okay. All right. So we -- we were just talking about what happens when you add ideation in and how you believe it should be examined.

A Unfortunately I think, yeah, if you hear the word "ideation," you have to be suspicious.

Q Okay. What do you mean you have to be suspicious? What do you mean by that, Doctor?

A Well, in the context of the debate, the way it has played out, ideation has been used to I think conceal the signal, so you have to be -- well, it's not inappropriate to look at it; but to emphasize that this is the only thing that counts is a way to hide the problem.

Q Now, if someone were to say there's no statistically significant risk of increased suicidality, what does that mean?

A Well, that will often include ideation. It won't be looking at just events. It will be including ideation. And as I said, this is a new term, "suicidality." It appears in the documents we've seen here for almost the first time. If people

look back through the documents, they'll be able to see some of the first mentions of this term ever, and it includes ideation and attempts and completed suicides.

Q Now, earlier when we were looking at that GSK study, just the placebo-controlled trial data, and it showed a risk ratio of 6.7 -- do you remember that?

A Yes.

Q What was that? Was that -- was that ideation? What was that?

A No, that's events. That's behavioral events. That's attempts or acts. And the one -- the 6.7 one doesn't include a completed suicide, but it's suicidal acts.

Q So to be clear, that study showed that there was a 6.7 times increased risk that a person not necessarily would be thinking about it but would actually do something about suicide.

A Yes.

Q Okay. All right. Let's go on back to your 13 list here. We just focused on ideation and what that has.

The next one you have here is what, Doctor?

A This is using significance testing.

Q What is significance testing?

A Well, it can be totally appropriate to use statistical significance. And the creator of the whole idea used it in the context of people knowing what they were doing. And when you

had a statistically significant result, it meant to most people that you knew what you were doing.

You only ran a trial that would give you statistical significance for plaster casts if you are pretty sure, for instance, that the plaster cast was going to be helpful for a broken bone. And you were prepared to accept that 1 in 20 people the bone mightn't heal even though you put the plaster cast on. But it was a demonstration that you knew what you were doing. It confirmed people understood what they were doing.

Q So do you think it's appropriate to use statistical significance in prospectively designed studies?

A Yes. But it's appropriate for the -- what's called the primary outcome. You've heard that before.

In our randomized controlled trial, this is used properly. And it means the focus -- all the rating scales, all of the things we're looking at -- are designed to look at does this drug work. And in that context, it can be appropriate to use it.

While you're focused in this way, you might miss completely that the person is not able to function sexually, so the result wouldn't be statistically significant, but, in fact, 100 percent of the people going through the trial may not be able to function.

I mean, you may get a more -- you might have, in fact,

had a more reliable result with the sexual functioning than you had with the mood change.

Q Well, Doctor, if -- you know, these clinical trials are not prospect -- are these clinical trials prospectively designed to study suicidality?

A No. There haven't been any.

Q So then would it be appropriate to apply statistical significance to whether or not they show suicidality?

A It wouldn't because you're not focused on that issue and you're not collecting all the events as thoroughly as you would want to.

Now, the key point about this is, though, as a result we might have a few people going through the trial who are deemed as having sexual dysfunction or becoming suicidal; but because you haven't designed the trial to look at this, the results may end up not being statistically significant. And when you apply that to does the drug work, if the finding is not statistically significant, that usually means that -- people infer this means that the treatment doesn't work.

If you apply it to an adverse event, and the suicidal events are not statistically significant, people -- some people infer -- not all, most people don't, some do -- that this means people didn't become suicidal at all. You know, that -- not only was there not an increase in risk, but actually it's just not there, the drug is protective potentially or sexual

dysfunctioning. As I say, you can look at the data and it's not statistically significant, and you can figure this drug has no effects on sexual functioning, when 100 percent of the people who get the drug have an issue.

Q So if you think that statistical significance testing isn't valid --

A I didn't say it's not valid.

Q Strike that.

A Yeah.

Q Let me ask you a better question.

Considering your views on statistical significance, what does it tell you when a study does have statistical significance?

A Well, let me be clear. When you said "your views," I want to emphasize these are the standard views in the field. They're just not idiosyncratic to me.

MR. BAYMAN: Objection, your Honor. He's talking about now other people's views here.

THE COURT: Overruled.

Proceed.

BY THE WITNESS:

A And -- well, it should be just, as I said, from my point of view, it should just be applied to the efficacy measures. And there are trials when -- where Paxil shows a statistically significant effect in terms of the benefit. And I'm not

arguing with that. Okay?

But when it's applied to adverse events, I don't think it should be applied how I see it being applied, unless I see it being applied to adverse events, and people conclude when you've got 42 events versus 1 or 2 or 3, that because they're not statistically significant, 42 equals 1 or 2 or 3, which is not the case. In the normal universe, you know, the universe that juries and the rest of us operate in, 5 is greater than 1 or 5 is greater than 0 or 42 is greater than 1.

BY MR. WISNER:

Q That said, Doctor, let's say we went down the rabbit hole and we focused on statistical significance. What does it tell you when even there you have a risk for Paxil -- let me strike that.

The GSK study, the 6.7, was that statistically significant?

A Well, it was reported as being so, yes. And the issue I guess is a lot of people who do believe in that kind of thing would say that if the trial was designed to pick this up, we'd have a terribly strong signal, given that we've such a strong signal from a trial that's not designed to pick it up.

Q Thank you, Doctor.

And the FDA study with Paxil, the FDA study for SSRIs that had the data for Paxil, was that result, that 2.7 result, was that statistically significant?

A It was. But, again, I'm -- you know I talked about Catholics and Protestants. Well, I'm on the confidence interval side.

Q I understand. I just wanted to know if it was statistically significant, Doctor.

Okay. Let's move on to the next one.

What's your next -- next list of the 13 to hide the signal?

A Excluding withdrawal.

Q Okay. And I don't want to get into withdrawal, Doctor, but please explain to me how excluding withdrawal can obscure a suicide signal?

A Well, the warning on the antidepressants at this date says that the problems are linked to going on the drug and when the dose gets changed and when the dose gets reduced are halted. So that's a tricky period. It's a bit like, you know, the space shuttle going out into orbit and coming back in. They're the risky periods. And they can be the risky periods for a lot of drugs with a lot of problems. They're not the risky period for all drugs and all problems, but they can be the risky period for a lot of drugs and a lot of problems, and they're the risky period for this group of drugs.

The FDA data that you've seen only has the going into orbit data. It doesn't have the coming back to earth data in it.

Q And excluding the re-entry data, what happens to the data?
A Well, the data excludes a number of problems linked to re-entry, and there are a significant number of problems linked to re-entry.
Q And by excluding the re-entry, is that -- are those problems linked to the drug itself?
A The signal from the drug will be reduced.
Q All right. Let's move on to the next one, Number 10.

Using -- what do you have there, Doctor?

A I've got using age stratification.
Q What does stratification mean?
A Well, where you stratify the results by age. And, strictly speaking, if you've got a randomized controlled trial, that that should take care of age issues completely. And the outcome that you get from it should be one that applies to everyone.

If you then start stratifying by age and pick up an effect that's different by age, you potentially are in the ballpark of saying something has gone badly wrong with these trials.

For instance, in some trials in this area, the problems have appeared in the United States -- well, actually appeared in venues outside the United States and not in the United States. And that suggests something funny has happened in the trials. Randomization is supposed to take care of this.

Everybody should be equal, regardless of age and sex.

Q If you focus in on just the very narrow age bracket, what can happen to the data?

A Well, if you focus in on a very narrow issue -- I mean, ultimately this can be -- can be reduced to a certain absurdity.

If we had a bunch of suicides happen in 52-year-olds, suicidal acts in 52-year-olds, and none in 53-year-olds, you could end up arguing this is only a problem in 52-year-olds and not in 53-year-olds.

So when -- you know, this is -- this is -- just when you look at the data, you've got to assume that the signal that you get out of the trial applies across age groups.

Q All right. Let's move on to the next one. Number 11.

Relying on relatedness assessments.

Do you see that, Doctor?

A Yes, I do.

Q What is that about?

A Well, this is one of those areas where, looking at the adverse effect that has happened, as we've explained, companies as well as everyone else tries to work out in this case was our drug linked to the problem? And they, using the criteria we all use, some doctors can come to the conclusion, yes, it was, and some company personnel can come to the conclusion, yes, it was, but they can also come to the conclusion, no, it wasn't,

when retrospectively we figure out lots of other people, you know, the jury, for instance, might look at it and say, well, we think there's a good case for saying it is related.

When it comes to handling the data overall, companies generally tend to emphasize when the investigator thinks a person has got better and that this is related to the drug, they'll emphasize that. They won't say this is an anecdote. They won't say you should only depend on what the RCTs show. But when it comes to an adverse event, they'll often not go by what the RCT shows, the signal that comes out of the controlled trial. They'll say, well, the investigators didn't think this was related. So they treat the good events in a different way to the adverse events.

Q And how does that -- how does it hide the signal, Doctor?

A Well, if -- you know, we're not looking at a huge number of adverse events here, so if the investigators figure some of them are not linked to treatment, this can compromise the signal completely.

Q And have you seen that happen in Paxil trials?

A I have.

Q Okay. And actually for all of these, Doctor, have you seen all of this happen in Paxil trials?

A I have.

Q Okay. So Number 12. Let's move on to the next one.

A Ignoring concomitant drugs. And this is --

Q For those of us who are not doctors, what does "concomitant" mean?
A It means other drugs the person may be on.
Q Okay.
A Okay? And when the trial starts, we've taken care to remove people who are on other antidepressants so this doesn't cloud the picture. We haven't necessarily removed antihistamines, say, and lots of people are regularly on antihistamines. And the placebo patients will be on antihistamines as well as the Paxil patients. And why this is significant is a number of the antihistamines they may be on are serotonin reuptake inhibitors. Paxil is an antihistamine as well as being a serotonin reuptake inhibitor. All of the SSRIs were antihistamines to begin with. So if you've got a bunch of patients on placebo who are also on an antihistamine, well, some of the SSRI adverse events are going to leak in there, and that's going to cloud the signal coming from --

MR. BAYMAN: Your Honor, objection. This is now outside the scope of his report again.

MR. WISNER: Actually I believe this was brought up in deposition as well. This is a clear part of his opinions and it's been expressed in numerous reports, your Honor. I don't think this is anything new to the defendants.

MR. BAYMAN: It's not in his report, your Honor.

THE COURT: Is it --

MR. WISNER: Sorry, I didn't hear, your Honor.

THE COURT: Are there instances that you can point to?

MR. WISNER: About concomitant drugs? Yeah, absolutely. He's discussing them.

BY THE WITNESS:

A I have an article on this, your Honor, which shows this and is referred to in the report and certainly I handed to GSK in that deposition.

THE COURT: All right.

BY MR. WISNER:

Q So, Dr. Healy, about this concomitant issue, I'm sorry, have you seen this occur that patients in Paxil trials, for example, in the placebo arm were taking drugs that had a serotonin effect?

A Yes. We've looked at this and shown that this happens. It's an effect that happens. It's just one of the things that's going to cloud the picture.

Q Well, how does that -- how does that affect the suicide signal?

A Well, it's not clear. I have -- I mean, to be able to answer that for you, I'd have to have the raw data from all of the clinical trials here.

What we've seen is a few different ways in which the signal has been handled, and I guess this makes GSK feel a little nervous, maybe. But the problem really is without

access to the data --

MR. BAYMAN: Your Honor, "makes us feel nervous," we've produced --

THE COURT: That may go out.

Proceed.

BY THE WITNESS:

A Okay. Without access to the data, it's all of us that should be feeling nervous. It's a bit like going --

MR. BAYMAN: I'm going to move to strike that comment, your Honor.

MR. WISNER: I don't know how many people are objecting over there, your Honor, but we'll strike it, no problem.

THE COURT: That will go out.

BY MR. WISNER:

Q Doctor, you keep mentioning raw data. What does that actually mean?

A It's the patient record. In the trial -- there's two things. First of all, there's the actual medical notes. And, strictly speaking, that's the raw data. When any of the juries, say, got involved in a trial, I've got a big folder of rating scales and things of that for an antidepressant trial, and I fill up the scores and the rating scales, the answers to each of the questions that I ask, and I fill up the reports where an adverse event, and this is -- this is -- this is,

well, what's called the clinical record. And it's not the actual medical record, but that's essentially the raw data, the closest we're likely to get to it.

What happens after that is the figures and all the different things that have happened in the trial get moved over into a data sheet, because you have to do that in order to start computing things and trying to work out what's happening more commonly in the drug or less commonly or what the different things are, adding things up.

And that's essentially what gets handed over to FDA. FDA can have access to the clinical records, but it's the company working from the data sheets prepares a report about what they think this shows. And it's the report they have, along with the tables, that FDA work from.

They may audit to make sure that the patients actually all existed, but they don't -- beyond that, they actually don't look at the raw data.

And the problem for all of us is while there's some access, there's increasing access -- and GSK have played a part in helping increase access to the data from trials -- but it's been the spreadsheets. It's not the actual record.

And when you get the record, it becomes clear that actually, you know, for us --

MR. BAYMAN: Objection, your Honor. He said a few minutes ago he could not give an opinion without access to the

raw data. Now he's saying if you had the raw data, here's what it shows. There's no way he can say what the raw data shows.

MR. WISNER: I'm not sure we know what he's going to say, your Honor, but --

THE COURT: Let's proceed. Go ahead.

BY THE WITNESS:

A Yeah, in my experience -- and I'm one of the few people in this universe who have had access to the raw data -- then it becomes clear that you can tell a lot more about the things that are happening on the drug with access to the raw data. It doesn't require specialist expertise. I think the jury could do a great job on what the effects of Paxil are if they had access to the raw data, for instance. But without access -- and the experts in the field, anyone else who turns up here, who gets called by either side, won't have had access to the raw data. And the data arguably is ours. It's not clear that it's not ours. But without access to that, you can't be fully sure. We have to work from what we get instead. And my experience is that the raw data shows there are more issues, more things to be collected. It's richer than the data sheet.

MR. BAYMAN: Same objection, your Honor. Move to strike.

THE COURT: Overruled.

BY MR. WISNER:

Q You said the data is not ours. Who are you referring to

there, Doctor?
A Well, I'm saying the data, strictly speaking, probably is ours --
MR. BAYMAN: Your Honor, it's not in his expert --
BY MR. WISNER:
Q Who --
MR. BAYMAN: -- report. This is really far afield now.
MR. WISNER: I'm trying to have him clarify what he said, your Honor.
BY MR. WISNER:
Q What are you -- who are you referring to when you say the data is actually ours? Who is "ours"?
A It's not clear to me that the data belongs to a company in the case of a clinical trial, for instance.
Q Got you.
A They hold on to it, but it's not clear that they own it.
(Counsel conferring.)
BY MR. WISNER:
Q How do you -- you said you have looked at some raw data; is that right?
A Yes.
Q What raw data have you looked at, specifically as it relates to Paxil and from the defendant GSK?
MR. BAYMAN: Objection, your Honor. This is what we

took up at sidebar, the raw data that he reviewed.

THE COURT: Overruled.

BY THE WITNESS:

A I've had the opportunity to look at the raw data from a GSK Paxil trial.

BY MR. WISNER:

Q What did you do specifically with the raw data? What did you do?

A Well, a team of us spent the better part of a year looking at the raw data, trying to work out what this clinical trial of Paxil showed, both in terms of the benefits and in terms of the adverse profile of the drug.

And the publication that came out of it --

MR. BAYMAN: Objection, your Honor. We're now going into what your Honor overruled earlier at sidebar, the publication --

MR. WISNER: Actually your Honor did not rule --

MR. BAYMAN: What you -- what you sustained --

THE COURT: Overruled, sir.

Please proceed.

BY MR. WISNER:

Q Sorry, you were saying about the publication.

A The publication that came out of it gave a different profile. And this is, as far as I understand it, the only trial in the field where you've got two articles in two

journals -- our article was in the *British Medical Journal*. You have two articles in two journals saying totally opposite things about the drug -- I mean two articles about the same trial --

Q How big was the trial, Doctor?

A Sorry?

Q The trial that you looked at the raw data for, how big was it --

MR. BAYMAN: Same objection, your Honor, as to the trial. This was the objection you sustained at sidebar.

THE COURT: Overruled.

BY THE WITNESS:

A It was a fairly substantial trial. It was one of the bigger trials GSK have done of Paxil.

BY MR. WISNER:

Q And in that trial that you looked --

MR. BAYMAN: Your Honor, may I have a continuing objection to this line?

THE COURT: Yes, you may.

MR. BAYMAN: Thank you.

BY MR. WISNER:

Q And in that trial that you looked at the raw data for, did you look at the issue of suicide?

A Yes.

Q And did you compare the raw data from what was reported in

the tables?
A Yes.
Q Specifically about suicide?
A Specific -- well, about all of the adverse events.
Q Sure.
A But, yes, the suicide issue came up. And it became clear that in our publication there was a different profile compared with the publication that had been out there prior to ours.
Q And when you say a different position, are you referring to you found a signal and GSK didn't?
A There was a three-fold higher rate of suicidal events compared with the previous publication.
Q Do you know that publication, the previous one, do you know if it was ever retracted?
A No, it hasn't ever been retracted.
Q And when did you publish the re-analysis?
A Approximately two years ago. A little less than two years ago now.
Q All right. Okay. So sorry I went down that area of raw data.

Let's go back to your list here.

We finished ignoring the other drugs.

What about Number 13, Doctor?

A Well, we've -- we've -- we've in essence covered this, which is that you can drown out the signal from emotional

lability, for instance, if you include it in a group where headaches are also included. So that's -- I mean, it's -- the reverse happens with akathisia where it gets split up and put into a few different groups.

So generally the coding issue is a very sensitive issue, and the grouping issue is very -- these are acts of authorship.

When we think about authorship, you usually think about the person that writes the words; but actually authorship starts happening from the time the first table is made and from the time the coding is done. These are acts of authorship. And then as you group the data together, it will make it look one way or the other.

Now, to get authorship that we're all comfortable with, a lot of different people should get access to it. Like the jury, for instance, they might decide to group it in a different way, and we might all see different things from the data, depending on how different people group it.

There's a lot of bias that comes into play, like I might have a bias or other people might have a bias.

At the end of the day when everybody can see the data, others can see which is the best grouping proposed.

And, for instance, when we grouped the data from the GSK trial, I made it clear to everyone -- it's written in the paper -- that GSK themselves might not agree with everything

we've done, but the properly scientific approach is for us to put our best guess up there, and if GSK make a case that certain events should have been coded in a different way, we would be open to changing those in order to fit in if they can put forward a reasonable argument.

Q Now, you mentioned how akathisia can get put into different categories.

Has GSK ever gone back through all the data and specifically looked at the issue of akathisia?

A I don't believe they have.

Q Do you know if GSK has ever gone back to the raw data and said, okay, this agitation or this restlessness, this really was akathisia, and done a retrospective analysis of the data?

A These things may have been done in-house. They haven't been published that I'm aware of, and I haven't seen anything.

Q Do you think something like that would be helpful?

A It would.

Q Now, we talked about akathisia yesterday quite a bit. And we discussed the Juurlink article. Do you remember that?

A We did.

Q And we also talked a bit about how the Juurlink article was talking about elderly patients. Do you remember?

A Yes.

Q Now, that article started from 60 years on up, right?

A Sorry?

Q That dealt with 60-year-olds and up?
A 65 or so. I don't quite meet the criteria.
Q Now --
(Laughter.)
BY MR. WISNER:
Q Now, Doctor, you mentioned that akathisia was pretty bad in the elderly. How is it in 57-year-olds?
A Well, my clinical experience, what hit me when I reported first on this, the first person that I saw become intensely akathisic on a drug like Prozac was in his mid-60s, and the next person was in his early 50s. So when I saw the problem first, it was in people in this age bracket. And all of my clinical experience since has told me that people in their 80s can have a severe akathisic reaction. Some of the most violent suicides that I've been made aware of have occurred in an older age group.
Q Now, have you taken it upon yourself -- strike that.
Have you reviewed all of Stewart Dolin's medical records and things of that sort?
MR. BAYMAN: Objection, your Honor. He's here for general causation.
MR. WISNER: I think he can answer the question then.
THE COURT: He can answer that question.
MR. BAYMAN: Okay.
BY THE WITNESS:

A I've reviewed a substantial amount. I haven't gone into the depositions because I'm not providing a specific causation view, but I wouldn't be here offering you the views I'm offering on what --

MR. BAYMAN: Your Honor --

THE COURT: Don't interrupt until he answers.

MR. BAYMAN: Well, I'm afraid he's going to --

THE COURT: I know you are.

MR. BAYMAN: -- put something out --

THE COURT: Well, we'll handle it, but let him answer.

BY THE WITNESS:

A Okay. I've been approached before to offer views that an SSRI, Paxil or other SSRIs, can cause a problem; but if I have reason to believe, looking at the specific causation, the clinical record for the person, that the drug didn't in this case --

MR. BAYMAN: Objection, your Honor.

BY THE WITNESS:

A -- I don't offer the view.

BY MR. WISNER:

Q You have not offered a view -- an in-depth view to a reasonable degree of scientific certainty for Stewart Dolin, have you?

A I haven't been asked to. But I have reviewed the material to the point where, as I say, I'm comfortable there's a prima

facie case, but others --

MR. BAYMAN: Objection --

BY THE WITNESS:

A -- will be arguing this.

MR. WISNER: No, he's not, your Honor.

COURT REPORTER: I'm sorry, I didn't hear your objection.

MR. BAYMAN: Objection. He's getting ready to offer an opinion. He said I'm now -- I have a *prima facie* view. And I want -- I'm objecting before he blurts something out. He does not have a specific causation opinion in this case.

THE COURT: He hasn't -- he hasn't formed an opinion, so why don't we just drop it.

BY MR. WISNER:

Q Precisely. I was -- I don't want your opinion, Doctor.

A Sure.

Q Okay. My point is you haven't -- you haven't rendered a scientifically rigorous opinion in this case, correct?

A I have offered lots of views on people that I have been approached by where there's been issues of homicide or people going on to commit suicide, and if -- if -- if I haven't thought the drug has played a part, I haven't engaged in the case.

Q Got you.

So here have you -- are you familiar with

Dr. Glenmullen?
A I am. Yes.
Q Have you reviewed his report?
A I have.
Q Okay. I'm not asking for any opinions about whether or not it's accurate or not; but having reviewed it, do you have any concerns?
A Concerns about his report?
Q That's right.
A No, I don't.
MR. BAYMAN: Your Honor, now he's asking to vouch for another expert.
THE COURT: Yes, that's true.
MR. WISNER: Well --
THE COURT: He can't vouch for him, sir.
MR. WISNER: Fair enough.
MR. BAYMAN: Move to strike.
MR. WISNER: Fair enough.
THE COURT: Yeah, that may go out.
MR. BAYMAN: Ask the jury to --
THE COURT: Disregard his testimony.
BY MR. WISNER:
Q You also mentioned yesterday -- I'm just going to clean up some stuff before we finish off your testimony today -- you mentioned yesterday that there are alternatives to patients

besides SSRIs.

A Yes.

Q What are some of those alternatives? Medical alternatives.

A Well, one of the useful ones, if the person isn't terribly severely ill, simply supporting the person. You know, if they come along to me, I'll outline the nature of the fact that the conditions often are ones that clear up of their own accord. And if they clear up of their own accord, people are often more resilient afterwards if they feel, you know, they didn't need the pill or they didn't need talking therapy.

One of the things that support -- I mean, support includes things like being available on the end of the phone if there's an issue; it may include weekly visits; it may include things like problem-solving. If there's issues at work, we might talk through them. If there's issues at home, we might talk through those. If there's issues with the children, we might talk through those. But it's not necessarily, you know, that I'm an expert on all these things. It's just another human being who has seen a lot of difficulties patients go through so I can offer a little context and things like that. But, you know, it's so this person feels supported and that they'll know that I'm a person who will use drugs to help treat them, so if things don't clear up, that we always can turn to a drug.

Q Is there -- is there another --

A Now, it may be the case -- there's a bunch of patients as well for whom what are called -- in the U.K., at least, and maybe the same here -- talking therapies. There's a -- a lot of people have a prejudice that talking therapies are better than drug therapies. They like the idea. It sounds better. I don't have that prejudice. I don't think talking therapies are better than drug therapies. Actually, I think the best thing is if you don't get involved in the health system, if I just support you so you don't get either.

But if it looks like you're the kind of person who has got the kind of condition that talking therapy will help, or we can refer you to a person who will do specialized talking therapy, as opposed to the general support that I may be offering. If it looks like a drug may be helpful, then I'm the kind of person who will be specialized in this area. And -- does that help? Does that answer?

Q Absolutely.

My other question, though, is there other drugs that you can give besides SSRIs?

A Oh, of course there are. The ones we've referred to earlier, there's the tricyclic antidepressants, which generally speaking are regarded as more potent, more effective if you're severely depressed, and they tend to have a gentler action on the serotonin system. They're not designed to produce a mega horsepower effect on the serotonin system.

There are other drugs then that have an opposite effect on the serotonin system that we've known for 50-odd years that people who respond poorly to an SSRI might respond well to an MAOI.

And the Teicher report we referred to earlier said that, look, some of these people who became intensely suicidal on Prozac did well when switched over to an MAOI.

And often we know that these things run in families.

So, again, before I put you on a drug, I might be checking things like that out. Does anyone you know related to you, have they had a poor response to an SSRI. That might slow me down. Equally the other way around. If someone closely related to you has a good response, that might lean me towards using an SSRI.

THE COURT: Not so fast.

BY MR. WISNER:

Q Slow down, sir.

A Aside -- aside from all that, there's a bunch of other drugs that get referred to as "other," because they don't fall into one clean group. "Other" isn't a group. I mean, there's the SNRIs, but "other" isn't a clean group. It's a bunch of drugs that have unusual actions. They don't fit in to one or other of the counts.

Q If you're treating a patient and they had a history of being okay on an SSRI, but then they suddenly start having

problems with them, would you consider an alternative to an SSRI?

A Yeah, well, there can be a big difficulty here in that some people can be treated very successfully with an SSRI or other drugs, but more obviously with an SSRI, and seem to be doing fine for a long time, and then something happens that the drug isn't working as well as before, things get unstable. It can be very tricky trying to get the person off the SSRI. You know, it's not necessarily clear that this is a person who is going to respond well to other drugs. It can become -- this is one of the most complex clinical problems people can have.

Q Now, we also talked about how akathisia, emotional blunting, and decompensation can have an effect on human -- human behavior.

I want to be clear. Do you need to have all three of those before someone will engage in a suicidal act?

A No. You may have none of them. There's another -- I mean, there's a few other ways we haven't gone into in which SSRIs can trigger people to become suicidal.

They're one of the commonest drugs, Paxil --

MR. BAYMAN: Your Honor, this is not in his expert report, and this is far afield of this case.

MR. WISNER: Yeah --

THE COURT: I think this is interesting, but not on point.

BY MR. WISNER:
Q Yeah, let's go back to my question, Doctor.
My question is do you need to have all three to become suicidal?
A No, you don't. I've picked out the three commonest forms here, but there are -- I mean, you don't have to have all three together --
MR. BAYMAN: I think he's answered, and now he's going on.
BY THE WITNESS:
A You don't have to have --
THE COURT: Okay. Doctor, you've answered it.
BY THE WITNESS:
A -- two of them together. You can have just one.
BY MR. WISNER:
Q That was my next question.
Could you just have one of those and that itself induce a suicidal state?
A You could.
Q Could you have two of them and that induces a suicidal state?
A Yes.
Q And you can have three of them that induces --
A Yes.
Q Okay. All right. I also want to clear up, I -- we got

into a conversation yesterday about Juurlink. Do you remember that?

A I do.

Q And I asked you some really confusing questions about whether or not the cohort in one group was the same as the cohort in the other.

Here's my question:

Are the people that were studied in the Juurlink article that showed that five times increase, were they both equally depressed?

A Yes. What you've got is two groups of people who are on antidepressants: There's the SSRI antidepressant group and the non-SSRI antidepressant group. These were controlled so that both groups were the same. There was the same severity of the illness in both groups. The same male/female ratios. And that's important because completed suicides is more linked to men. There's -- there were the same ages, broadly speaking. And there were the same issues about the same rates of alcoholism in both, for instance. So the groups are as closely matched as Dr. Juurlink and his colleagues could make them.

And given these closely matched groups, they then find the ones given the SSRI during the first month of treatment were the ones who seemed to have a much higher likelihood of going on to actually kill themselves.

Q And that involved 1.2 million patients and over 1,000

suicides. Is that right?
A That's correct.
MR. BAYMAN: Your Honor, we went all over this yesterday. We're going back --
MR. WISNER: I was just cleaning up some stuff, your Honor. I'm coming to the end of my -- on my direct.
BY MR. WISNER:
Q Now, Doctor, we spent the last two days going over a lot of stuff, a lot of data, a lot of articles.
Do you, as a psychiatrist and psychopharmacologist, have any doubt that Paxil can induce suicidal behavior in adults?
A No.
Q In your research, do you believe GSK has told that fact to doctors?
A No.
Q Have you ever seen an article published by GSK to doctors stating that fact?
A No.
Q Sitting here today, having investigated this for over 20 years, do you know how many people have committed suicide because of that failure?
MR. BAYMAN: Your Honor, objection. This is subject to the motion *in limine*. And it's not in his report either.
MR. WISNER: I'm asking if he knows.

MR. BAYMAN: It's speculative.

MR. WISNER: I think his answer will clear up the objection, your Honor.

THE COURT: All right. You may answer.

BY THE WITNESS:

A I don't know specifically to Paxil. With colleagues, we've looked at the issue for all SSRIs --

MR. BAYMAN: Your Honor, he said he didn't know specifically with Paxil, and that's what we're about in this case.

BY THE WITNESS:

A Yes, that's true.

MR. WISNER: So let's -- let me just wrap it up, I think, your Honor.

BY MR. WISNER:

Q So to be clear, Doctor, you do not know to this day, after 25 years of GSK not telling doctors about this risk, how many people have died because of it, right?

MR. BAYMAN: Objection. Leading and argument --

THE COURT: That's argument, yeah. Sustained.

MR. WISNER: All right. We pass the witness, your Honor.

THE COURT: All right.

MR. BAYMAN: Thank you.

THE COURT: Do you want to start? You have about five

minutes -- I think we better wait --

MR. BAYMAN: I'll wait, sure.

THE COURT: All right. Ladies and Gentlemen, before you leave, I want to remind you again that it's very important that you not conduct any private research on this case while you're out of the courthouse and also that you not discuss it with anyone.

Remember, in fairness to yourselves and in fairness to the parties, I ask you to follow these rules, and I assure you it will be much easier to deliberate when that day comes.

So thank you very much for your attention. Don't forget us now. We are looking forward to seeing you again on Monday.

Thank you.

MR. RAPOPORT: Have a nice weekend, folks.

(Jury out at 4:20 p.m.)

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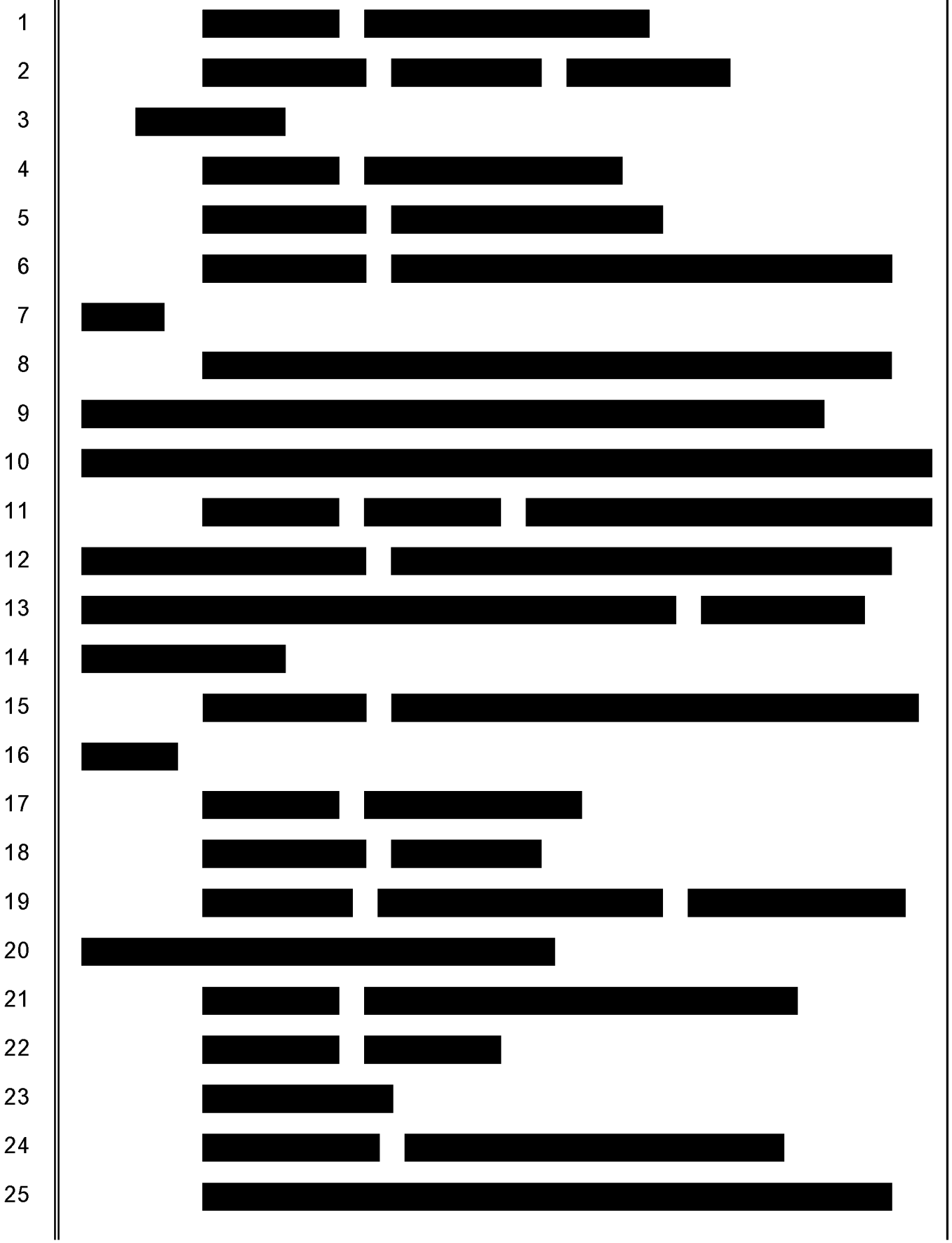

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(Proceedings adjourned at 4:23 p.m., to resume on 3/20/17 at 9:30 a.m.)

C E R T I F I C A T E

We, JUDITH A. WALSH and GAYLE A. McGUIGAN, certify that the foregoing is a correct transcript of the record of proceedings in the above-entitled matter.

/s/ JUDITH A. WALSH March 16, 2017
JUDITH A.WALSH, CSR, RDR, F/CRR
Official Court Reporter

/s/ GAYLE A. McGUIGAN March 16, 2017
GAYLE A. MCGUIGAN, CSR, RMR, CRR
Official Court Reporter