

Thursday, 28th February 2008

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(10.30 am)

MR NASH: My Lord, before we resume with Dr Simmon's cross-examination, a few housekeeping matters.

Discussion re housekeeping

Firstly, we promised you a document setting out our case on data error and data handling error and we've got that.

MR JUSTICE BURTON: That's very helpful.

MR NASH: My learned friends have seen it very, very briefly and I don't expect them to react to it right away. At some stage no doubt they will.

MR JUSTICE BURTON: Thank you.

MR NASH: We have been trying to agree an order.

MR JUSTICE BURTON: Yes, I've seen your recent attempts. Are we any further on than we were then or not?

MR NASH: I don't think beyond the recent attempts.

MR JUSTICE BURTON: At the moment I'm temperamentally in favour of making the order that Mr Bear wants because it avoids the need for any argument until the end of the hearing.

At the end of the trial, it will be known whether the CTSA agreement is at an end or not, and we can then sort out the apparently disputed issue as to who is entitled -- what your entitlements are under the various

1 clauses. But you're not going to want to use any
2 unblinded material during the trial, are you, other than
3 for the purposes of the trial?

4 MR NASH: I think that's right, my Lord.

5 MR JUSTICE BURTON: So as long as we make the order with --
6 you've got liberty to apply under Mr Bear's version,
7 haven't you:

8 "The claimants shall have will have liberty to apply
9 for an order varying or revoking this order" obviously
10 reserved to me. There's no presumption that you've got
11 some burden on you on making that application any more
12 than you would have otherwise. We'll just decide the
13 question as to what use you can make of it in the light
14 of my decision at the end of the hearing. It may be
15 obvious, because, if you fail, the agreement continues
16 in place anyway.

17 MR NASH: Provided it's clear that this order is simply
18 provisional to hold the position until --

19 MR JUSTICE BURTON: No question about it, yes. It's
20 a holding.

21 MR NASH: We know the result, then I think we can proceed on
22 that basis.

23 MR JUSTICE BURTON: Thank you very much. Is that all right,
24 Mr Bear?

25 MR BEAR: Yes.

1 MR JUSTICE BURTON: Clearly this doesn't give any
2 presumption --

3 MR BEAR: No, it's just about time management as much as
4 anything else.

5 MR JUSTICE BURTON: Yes, thank you very much.

6 Now, how are we on agreement about which witnesses
7 are coming when?

8 MR NASH: I don't think it's disagreement about batting
9 order. As far as timing is concerned, I have been more
10 pessimistic than my learned friend, but my learned
11 friend believes that he can finish, I think,
12 Dr Simmon -- perhaps I'll let him tell you what he
13 believes.

14 MR BEAR: My Lord, I'm conscious when I say this that this
15 could be proved wrong within the course of the working
16 day, but at the moment I'm tolerably hopeful that I can
17 finish with Dr Simmon today. It does depend to some
18 extent --

19 MR JUSTICE BURTON: We can sit a little late if it's
20 a question of half an hour.

21 MR BEAR: I don't say this critically of Dr Simmon at all,
22 but as with many witnesses he sometimes wants to add
23 a point, and it may be that if we can all control
24 ourselves and your Lordship may be able to assist in
25 that if you know what I mean --

1 MR JUSTICE BURTON: I'm anxious not to control anything
2 that's relevant, but clearly if he goes -- if either you
3 or he go outside the issues in the case, then we'll --
4 I'll make sure that --

5 MR BEAR: I was thinking more of questions that could be
6 answered quite simply rather than followed by a little
7 speech, but there we are.

8 MR JUSTICE BURTON: A lot of money and principles are at
9 stake for him, and this is his moment to stake a stand.

10 MR BEAR: I know, and I did say I didn't criticise him at
11 all for that, because one often sees it and it's very
12 understandable. But anyway, regardless of that, the --
13 at the moment, I'm hopeful that we can finish Dr Simmon
14 today and I include in that a short period, I hope 15 or
15 20 minutes or so, for Dr Basch from HPM because your
16 Lordship will have seen there's a short witness
17 statement from her.

18 MR JUSTICE BURTON: That closes -- that's the end of his
19 witnesses?

20 MR BEAR: No, because there's then Mr Furcha.

21 MR JUSTICE BURTON: Oh yes, of course.

22 MR BEAR: Who will be I think not that long. His statement
23 is quite carefully --

24 MR JUSTICE BURTON: So what, by lunchtime tomorrow we
25 finish?

1 MR BEAR: Yes, I'm hopeful that it might even be a bit
2 before then.

3 MR JUSTICE BURTON: Let's assume we finish your evidence --
4 Mr Nash's evidence, your cross-examination, by lunchtime
5 Friday --

6 MR BEAR: Yes, could I just say one thing. I'm assuming
7 that there won't be any supplementary questions for
8 either Dr Basch or Mr Furcha, because we had an hour
9 yesterday with Dr Goedkoop in chief.

10 MR JUSTICE BURTON: That was with my encouragement in
11 relation to the tables.

12 MR BEAR: Of course.

13 MR JUSTICE BURTON: But I don't ask for any
14 evidence-in-chief on the other two, except, as I say,
15 just a few minutes to settle people in. I always prefer
16 that.

17 MR BEAR: Yes, if it's confined to, you know, literally five
18 minutes -- with Dr Basch it may not even be necessary,
19 because her statement really is pretty short.

20 MR JUSTICE BURTON: Yes.

21 MR BEAR: But it's a matter for my learned friend.

22 MR JUSTICE BURTON: Subject to that, that's lunchtime
23 Friday.

24 Now, what's the position in relation to your witness
25 who can only come tomorrow?

1 MR BEAR: Well, that's Professor Sandercock. So we'll start
2 with him, which isn't a problem because he's an
3 important witness anyway.

4 MR JUSTICE BURTON: Yes.

5 MR BEAR: And even if cross-examination of the claimant's
6 witnesses goes up to lunchtime tomorrow, I think my
7 learned friend feels that half a day would be sufficient
8 for Professor Sandercock.

9 MR NASH: I think so, my Lord, yes.

10 MR JUSTICE BURTON: So we finish Professor Sandercock by
11 tomorrow. Then we've got Professor Roberts on Monday?

12 MR BEAR: If we slip to that point. If I make better
13 progress than that implies with Dr Simmon today, then
14 obviously we may start Professor Roberts on Friday, but
15 I wouldn't be keen to start him at 3.30 on a Friday.

16 MR JUSTICE BURTON: I'm going to assume pessimism and that
17 we don't start Professor Roberts until Monday.

18 MR BEAR: Yes.

19 MR JUSTICE BURTON: And then what other witnesses have we
20 got after that? He's all day Monday, I'm sure. We've
21 got Mrs Shakur who may be longer, perhaps he won't be
22 all day Monday.

23 MR NASH: I think the balance is slightly the other way.
24 I would think probably a little more than half a day
25 with Professor Roberts and then I think we must budget

1 for a day with Mrs Shakur.

2 MR JUSTICE BURTON: So if we finish about lunchtime on

3 Monday with Professor Roberts, about lunchtime on

4 Tuesday with Mrs Shakur, and then -- that may be even

5 middle afternoon on Tuesday, because Mr Brady will only

6 be short.

7 MR NASH: He will be very short I would think, yes.

8 MR JUSTICE BURTON: So we finish the evidence by Tuesday

9 night, comfortably?

10 MR NASH: The factual evidence, yes.

11 MR JUSTICE BURTON: What's happening on the experts? On the

12 face of it we've got four of them, although Wells and

13 the other witness seemed to have dwindled a little.

14 MR NASH: I think that's right, my Lord. I think the real

15 expert battle is between Charnley Nickols and Gray and

16 that I think is half a day for each of them, yes.

17 MR JUSTICE BURTON: Yes.

18 MR NASH: Half a day for each of them. So it's a full day

19 on that, and then probably less than a full day --

20 a short day -- on Montgomery and Wells. I think we're

21 agreed we take them in that order, so

22 Charnley Nickols --

23 MR JUSTICE BURTON: The other?

24 MR NASH: The database expert, yes.

25 MR JUSTICE BURTON: We say Tuesday, perhaps mid-afternoon,

1 finishing factual evidence, so we could start -- perhaps
2 get rid of the minor expert witnesses Tuesday possibly,
3 and Wednesday all day on the other experts, and then
4 Thursday and Friday for speeches, that's the present
5 hope, is it?

6 MR NASH: Yes.

7 MR JUSTICE BURTON: Right. I'll make the order in
8 accordance with Mr Bear's draft, and that means that the
9 public is now bound, if it wasn't before, not to make
10 any use of the material set out in paragraph 1(a), (b)
11 and (c) and not to disclose the information in 5(a), (b)
12 and (c).

13 MR NASH: I think that's all the housekeeping.

14 MR BEAR: That is all the housekeeping.

15 Before we resume with Dr Simmon, there's a point
16 I need to mention to your Lordship which is to correct
17 something I said on Day 1 in opening.

18 It relates to information that was provided, a line
19 listing that was provided in early November to HPM, and
20 I think what I said to your Lordship was that -- or may
21 have suggested at any rate -- that this was a line
22 listing of the SAEs in the trial database, the 94. That
23 wouldn't be correct. What I am told, in fact, is that
24 it was a line listing which was a line listing of the
25 SAE report forms as they appeared in one module in the

1 trial database.

2 You will recall in Mr Simmon's table there's that
3 middle column headed "TCC", and it's the figure for that
4 total rather than the column on the right which is the
5 94 --

6 MR JUSTICE BURTON: This is on 14th November, is it?

7 MR BEAR: No, this is on 8th November. So it's only that.

8 On 14th November, they got everything, which is the
9 email that went between the solicitors.

10 MR JUSTICE BURTON: I doubt that six days is going to make
11 all the difference, but there it is.

12 MR BEAR: No, I don't think it is, but simply for the
13 record. I wanted to --

14 MR JUSTICE BURTON: You wanted to correct it, thank you.

15 I've initialled this order. I hope I've initialled the
16 right one, yes, it is, because it's the one with
17 "liberty to apply" in both paragraphs 1 and 2.

18 MR BEAR: Yes.

19 MR JUSTICE BURTON: That needs -- I don't know -- there's
20 no-one here from the Commercial Court. That's going to
21 need to be drawn out, if you can make sure someone gets
22 it in the Commercial Court.

23 Thank you very much.

24 DR VINCE SIMMON (continued)

25 Cross-examination by MR BEAR (continued)

1 MR BEAR: Dr Simmon mentioned before you came in that he
2 would appreciate a break every hour or so, and what
3 I have suggested subject to your Lordship is if he could
4 just signal that to you and you will decide --

5 MR JUSTICE BURTON: If you say every hour or so, Mr Simmon,
6 unless you literally mean every hour, we've got between
7 now and lunchtime two and a half hours, if we could just
8 have one break which would coincide with the shorthand
9 writers' break. So the plan would be to break at about
10 11.55, if that's all right?

11 A. That's fine, thank you very much.

12 MR JUSTICE BURTON: Then we'll agree -- everybody will
13 agree, we'll break from everyone's point of view, unless
14 it's a bad time, at 11.55 and start again at 12.00.
15 Thank you.

16 MR BEAR: Thank you. Dr Simmon, just to close off
17 yesterday, I was asking you about the rate of
18 recruitment and can I make it plain to you and to his
19 Lordship, I'm not asking about this simply because it
20 may go to your credit, if you understand that term --
21 the general fairness as it were with which you approach
22 matters -- I'm asking it because I say there's a further
23 relevance to the case.

24 Now, what I'd like to do is put some propositions to
25 you and see if you can either agree with them or

1 disagree, and if you disagree tell me where. Okay?

2 A. Yes, sir.

3 Q. First proposition: you had a business expectation that
4 Xytis would finish recruiting patients by February 2008.

5 A. At a point in time, that is correct, but as you and
6 I discussed yesterday, that point changed several times.

7 Q. During the spring and summer of 2007, that was your
8 business expectation?

9 A. I believe you're correct.

10 Q. LSHTM would have had an understanding from the protocol
11 that they could recruit up to August/September 2008?

12 A. I believe that is correct.

13 Q. And that understanding would have been part of the
14 agreed basis on which the contract was entered into?

15 A. I wasn't there when the contract was entered into.
16 I wasn't -- I don't recall the status of the protocol,
17 which version, et cetera, so I'll take your word for it.

18 Q. Well, let's go very quickly to protocol bundle 1,
19 please. This is a bundle we haven't looked at. It's
20 one of the thematic bundles which have been prepared by
21 the claimant.

22 Could we go to protocol bundle 1, page 254? This is
23 a version of the protocol which is from 17th August
24 2006.

25 A. Which would have, by a few -- by a week or so postdated

1 the CTSA, if I remember correctly.

2 Q. No, you're incorrect in that.

3 A. Okay.

4 Q. The CTSA was signed by my clients on 18th August, wasn't
5 it?

6 A. 18th. So this predates the agreement?

7 Q. Yes, it predates it by one day. Yes?

8 A. I don't have the other document in front of me, I accept
9 your word.

10 Q. I think we can do it by what I'm telling you. Do you
11 agree that page 254 shows the same rate of recruitment
12 as we get in the final version of the protocol?

13 A. Is this the final version? You're asking me a question
14 about --

15 Q. No, this is a draft version.

16 MR JUSTICE BURTON: We looked at the final version
17 yesterday. If you want to refresh your memory, but --

18 A. I think that page and this page are the same. I do not
19 think it changed in terms of the recruitment plan, if my
20 memory serves me.

21 MR BEAR: This is dated 17th August, isn't it?

22 A. The one I'm looking at is, yes, sir.

23 Q. This shows recruitment ending, in fact slightly
24 later, September/October, rather than August/September,
25 but roughly the same. It's the final version?

1 A. You're saying it's roughly the same, and I don't have it
2 in front of me --

3 Q. Dr Simmon we can spend a long time on this. You can
4 pick up every point or you can accept what I say.

5 A. I said I would take your word for it before.

6 Q. Okay let me put this to you again. Having seen it do
7 you now accept that the agreed basis on which my clients
8 went into the CTSA was that they would have recruitment
9 ending in the autumn of 2008?

10 A. In the autumn more or less as you said, yes, sir.

11 Q. Thank you very much. Now, can I put a number of points
12 to you again and tell me if you disagree or if you
13 agree.

14 First of all, in June 2007, you were critical of
15 LSHTM both to them and to the board in relation to
16 recruitment rates?

17 A. I disagree.

18 Q. Do you think you weren't critical of LSHTM?

19 A. I had a discussion with LSHTM at a meeting in their
20 facility, which is minuted, about recruitment. We
21 discussed it as any pair of partners in our proposition
22 would discuss it and we wished that recruitment could be
23 accelerated. We expressed that.

24 Q. When you wrote to them on 12th June saying that the
25 board was understandably concerned about recruitment

1 rates, do you not accept that that is some form of
2 criticism of them?

3 A. If the board was concerned because of the fact, as
4 I explained yesterday, of when the contract we had to
5 license Anatibant might expire, the fact that they are
6 concerned does not mean per se criticism, and I don't
7 accept that.

8 Q. All right. Whether you call it criticism or not, do you
9 accept that you put forward a desire that LSHTM should
10 recruit patients more quickly?

11 A. We discussed that, and we put forward that desire, yes,
12 sir.

13 Q. Do you accept that, therefore, that was something you
14 wanted from LSHTM which was more than the contract
15 required them to provide?

16 A. No, it was the same number of people. When you say
17 "more" --

18 Q. More quickly.

19 A. More quickly?

20 Q. Yes.

21 A. Yes, I agree.

22 Q. Do you also accept that you were prepared to use any
23 necessary means including coercion to get your way?

24 A. No, sir, I deny that, and there's no evidence to that.

25 Q. Let's look, then, at page 1691 in bundle 6,

1 chronological bundle 6/1691.

2 Do you remember this email?

3 A. I'm rereading it, but I vaguely remember it, yes, sir.

4 (Pause).

5 Q. Then can we also look, while we're on it, before I ask

6 you a few questions, at the following page. This is

7 Mr Furcha's reply. We can see your email at the bottom,

8 his reply at the top.

9 A. Okay. Yes, sir.

10 Q. Now, you recorded an urgent need to boost recruitment in

11 your email, didn't you?

12 A. Yes, sir.

13 Q. And you used LSHTM to do that, correct?

14 A. Not entirely. We were also involved in adding sites

15 which was permitted under the contract in, I believe

16 Estonia, at that time.

17 Q. In part you used LSHTM didn't you to boost recruitment?

18 A. Yes, sir.

19 Q. If we go back, just for the moment -- keep a finger in

20 1691 if you could -- to page 1678. This is the notes of

21 the meeting you had with LSHTM on 18th June.

22 A. Yes, sir.

23 Q. And if we look at 1679, please, Dr Simmon, the first

24 subheading "recruitment":

25 "VS expressed anxieties that recruitment is very

1 slow. The venture capitalists funding the trial have
2 expectation of finishing recruitment in April 2008. The
3 recruitment plan is feasible with the original sites
4 recruited by TCC, 17 sites. End date is predicted to
5 be June 2008. This is ahead of the original plan taking
6 into account the three-month delay in finalising the
7 contract with Xytis. VS stressed that a July end date
8 is too late and needs to be brought forward
9 to April/May 2008."

10 LSHTM were a little reluctant at that meeting,
11 weren't they, to speed up recruitment, would that be
12 fair?

13 A. I don't see that anywhere in here.

14 Q. I'm asking you whether it is a fair --

15 A. It's not.

16 Q. No? That they were happy to fall in with your plans,
17 were they?

18 A. We talked about it, and we -- I recall at that meeting
19 that I discussed with Ms Shakur what her recommendation
20 would be for logistics and she did these minutes, so
21 I think if she was upset about that, she would have
22 expressed that in these minutes.

23 Q. The fact is that very swift results followed, didn't
24 they: recruitment ramped up quickly thereafter?

25 A. July was much better, and August was a high point.

1 Q. And by 21st August, 121 patients had been recruited as
2 opposed to 40 by mid-June, that's correct, isn't it?

3 A. I believe those numbers are correct, yes, sir.

4 Q. So you got the immediate boost that you needed in terms
5 of recruitment, correct?

6 A. Yes, sir.

7 Q. Going back now to page 1691, your email to Mr Furcha of
8 20th June, you said in the middle:

9 "Let's end up suggesting things to them."
10 Before that you said:
11 "We need them to do what we want without telling
12 them to do it."
13 Then dropping down a couple of lines:
14 "It is not really the normal approach for a sponsor
15 but I am hopeful it will work. At the end, we may have
16 to result to [and I suggest that means resort to] brute
17 force."
18 What does "brute force" mean?

19 A. We didn't have to resort to it, so I was speculating, we
20 might have to do -- take other measures.

21 Q. You don't need to speculate about the meaning of what
22 you wrote, do you, Dr Simmon?

23 A. Excuse me?

24 Q. You don't need to speculate about the meaning of
25 language that you used. What did it mean when you used

1 it?

2 A. That we would have to potentially add additional sites
3 which we began doing from the end of the contract in
4 other places including Latvia, and that I authorised us,
5 the company, to do that.

6 Q. You're saying that "brute force" means adding additional
7 sites, is that your evidence?

8 A. Yes, sir.

9 Q. I suggest "brute force" means something else. I suggest
10 it means that if LSHTM didn't comply with what you
11 wanted you would have them threatened legally and, if
12 necessary, removed from the trial. That's right, isn't
13 it?

14 A. I disagree. That's not my intent.

15 MR JUSTICE BURTON: On any basis, brute force means
16 coercion, doesn't it, Dr Simmon?

17 A. No, not necessarily, sir.

18 MR JUSTICE BURTON: I don't understand the difference.
19 What's the difference between brute force and coercion?

20 A. First of all this, does not say brute force with or on
21 or to LSHTM.

22 MR JUSTICE BURTON: Who is it brute force towards?

23 A. I've already indicated that what I was doing, it was
24 instructing Mr Furcha to pursue additional sites, and we
25 did that in that timeframe, we began --

1 MR JUSTICE BURTON: Isn't the normal approach for a sponsor:
2 but I hope it will work. At the end we may have to
3 result with brute force, but let's start with sugar and
4 see how far we get. If we disagree with what they are
5 doing, suggest alternatives. Are you not saying that
6 this means brute force on LSHTM -- various forms of
7 brute force are being suggested, but I don't need to
8 worry about that. But brute force of some kind,
9 coercion of some kind to LSHTM?

10 A. Well, again, it does not say use brute force to LSHTM,
11 sir.

12 MR JUSTICE BURTON: You stand by, do you -- I'm looking back
13 at the reply that you gave. You were prepared to use
14 any necessary means including coercion to get your way:

15 "No, sir, I deny that and there's no evidence to
16 that."

17 Do you want to reconsider that answer? That's an
18 answer you gave at page 156 the transcript.

19 A. I'm sorry, would you, my Lord, read that again, please?

20 MR JUSTICE BURTON: Yes:

21 "Do you accept [said Mr Bear] that you were prepared
22 to use any necessary means including coercion to get
23 your way?"

24 And you said:

25 "No, sir, I deny that, and there's no evidence to

1 that."

2 A. I'm comfortable with that statement, my Lord.

3 MR BEAR: Did you read Mr Furcha's response on page 1692 as

4 endorsing a strategy of coercion directed against LSHTM

5 if the strategy of persuasion did not work?

6 A. Well, he uses a term in here, the soft psychology before

7 the baseball bat.

8 Q. You're smiling. Do you think that was amusing?

9 A. I -- in retrospect, I think he didn't choose very good

10 language here, sir.

11 Q. Why do you think that in retrospect?

12 A. Excuse me?

13 Q. Why do you now think that?

14 A. For the reasons we've just discussed. It certainly

15 implies here that he was inferring, in this case, to the

16 London School, yes. Because the soft psychology was an

17 attempt to work closely with them, there was a lot of

18 friction between the groups which is evidenced in lots

19 of discussions we've had --

20 MR JUSTICE BURTON: Being critical of Dr Furcha, is it

21 really any different to your words:

22 "If we disagree with what they are doing suggest

23 alternatives as opposed to being confrontational."

24 Are you are you really saying that in your words

25 "brute force" and "confrontation" were not supposed to

1 be addressed to the school, and that it's all
2 Dr Furcha's fault in his reply?

3 A. No, it's not all Mr Furcha's fault, sir, my Lord.
4 I think he was trying to carry out what he felt were my
5 instructions.

6 MR JUSTICE BURTON: Yes. What were those instructions?

7 A. My instructions were to work with LSHTM, try to get them
8 to understand our need, used, as I said, sugar as -- try
9 to work better with them to get enrolment out. That was
10 my request. That was my specific request.

11 MR BEAR: That was the first half of it, wasn't it? Then
12 the second half was, if that didn't work you'd have to
13 use brute force. That was the second half of your
14 instructions, wasn't it?

15 A. That's the second half, yes, sir.

16 Q. Thank you. Now, standing back from the particular issue
17 of recruitment and recruitment rates, the things that
18 Xytis might want from the collaboration with LSHTM were
19 the things which would suit your business objectives.
20 Do you agree with that?

21 A. Would you repeat it? I believe the answer is "yes".

22 Q. Standing back from the particular issue of recruitment
23 and recruitment rates, the things that Xytis might want
24 from the collaboration with LSHTM were the things which
25 would suit your business objectives.

1 A. Business and ethical objectives, yes.

2 Q. What do you mean by "ethical objectives"?

3 A. What I mean by ethical objectives, sir, is that if this
4 trial was not completed in a time leeway and Xytis was
5 unable to obtain a relationship with a large
6 pharmaceutical partner, it was my belief there would be
7 no phase 3 trial.

8 Q. So this is getting to the next phase in time before your
9 licence runs out?

10 A. That is correct, and thus we would be treating patients
11 with no hope of a future trial, which is unethical, if
12 the drug had proved to be safe and effective.

13 Q. Someone else could take the benefit of your trial then,
14 couldn't they?

15 A. Possibly.

16 Q. Yes, so there would be nothing unethical there, just,
17 you wouldn't be making the business objective, the
18 lawful one, of a profit?

19 A. I'll accept your statement.

20 Q. Now, as you've agreed, the things that you might want
21 from the collaboration were those things which would
22 suit your business objectives, and I suggest that was so
23 whether or not those things were consistent with what
24 had been agreed in advance with LSHTM. Is that fair?

25 A. Yes, the agreement preceded me, and I was discussing

1 changes to that agreement, yes, sir.

2 Q. You could see that LSHTM were somewhat independent
3 minded, could not you?

4 A. Very much so.

5 Q. And, for example, it might be difficult in terms of
6 finishing off the data analysis and doing the academic
7 work on the study at the end, within the timeframe that
8 you and your investors were hoping to achieve, you could
9 see a potential problem there, I imagine?

10 A. Yes, sir.

11 Q. Did you start, then, to look for ways to force LSHTM
12 out?

13 A. No, sir.

14 Q. Well, I'd like to challenge that. Let's go to page 1853
15 in bundle C7. So bundle C7/1853. At the bottom of the
16 page, please, an email from you which is dated in the
17 American fashion, so 11th July:

18 "Dear Ian, thank you for the phone call. I think we
19 sorted through some of the issues."

20 Then you say:

21 "I can't say often enough we believe Haleema is
22 working very, very hard ... I just wish she was able to
23 delegate more. Our goal is to help, not hinder.
24 I would appreciate a copy of your enrolment plan. Have
25 a good trip to Colombia. I would be interested in

1 hearing your impressions. Kind regards ..."

2 So those were warm words from you, weren't they?

3 A. Yes, sir.

4 Q. And that's an example of the sugar?

5 A. I think that we had conversations among us at a times

6 that were more difficult and some that were less

7 difficult. This was a time --

8 Q. This email was an example --

9 A. Less difficult.

10 Q. -- of sugar?

11 A. Sugar, yes, I would accept that.

12 Q. Professor Roberts replies above, perhaps rather in

13 accordance with your plan:

14 "Dear Vince, thank you very much for being so

15 positive. Have a great trial that is making excellent

16 progress..."

17 And he sends you a letter with some other specific

18 suggestions for continuing to --

19 A. I think these -- that email preceded mine, if I read

20 these correctly, because I refer to his trip in

21 Colombia, but I might be wrong.

22 Q. No, I don't think that can be right. Your email is at

23 the bottom. Can you see those little chevrons that come

24 before "Vincent Simmon"?

25 MR JUSTICE BURTON: 10.48 am, do you see, and then the reply

1 is 19.09 pm. I think, even allowing for time
2 difference, it looks as though the one above as is
3 normal on these emails, predates the one below.

4 A. Perhaps I've made an error in that. I just thought
5 since I referred to his trip to Colombia, I wasn't aware
6 that I knew it ahead of time. I might have from our
7 conversations.

8 MR BEAR: I'm assuming you discussed it in a call.

9 A. Maybe that's where I got it from, thank you.

10 Q. Then you see that's why he says:
11 "Thank you very much for being so positive."

12 A. Got it.

13 Q. Thank you. So Professor Roberts then attached the
14 letter at 1854, did he not?

15 A. 1854?

16 Q. If you could cast your eye over that quickly, Dr Simmon.
17 (Pause).

18 A. Okay.

19 Q. Do you agree that he is seeking to respond
20 constructively and positively to the dialogue as it
21 stood?

22 A. Yes, sir.

23 Q. Now can we go forward to page 2014? It's still in the
24 same bundle.

25 Is this your reply to his letter that we've just

1 been looking at?

2 A. I believe that is correct.

3 Q. Could you again just cast your eye over it to remind
4 yourself of its terms? (Pause).

5 A. Yes, sir, I'm ready.

6 Q. Thank you very much. Is it fair to say that your letter
7 of 18th August contains a series of demands?

8 A. It has a series of suggestions of what we would like to
9 see, and if you were to demand, I would have said "you
10 must do this or else", and there is no "or else" in
11 here, it's a request. It's a listing of things that my
12 regulatory and medical people suggested to me that would
13 be required to conduct the trial under GCP, and
14 I formally wrote the letter, that is, I am the person
15 who signed it, but this was prepared by my regulatory
16 and clinical people.

17 Q. Whether demands or suggestions, do you agree they were
18 for work to be done by LSHTM on short timescales?

19 A. When you're running a clinical trial, sir, you have to
20 be in compliance with GCP. My people --

21 Q. No, I didn't ask you to go into any justification.

22 A. And therefore --

23 Q. I'm sorry, Dr Simmon, I simply asked you to say whether
24 or not there was a series of suggestions for LSHTM to do
25 work within short timescales. Can you agree or

1 disagree?

2 A. I agree when it was required for GCP.

3 Q. Well, look at 2015.

4 "All requests for information on trial progress will

5 be centralised through the project director or

6 designee."

7 That's on your side, isn't it? I'm looking at the

8 first bullet point under "general communication"?

9 A. Yes, I'm reading that.

10 Q. "TCC will respond within one week."

11 That's a short timescale, isn't it?

12 A. I do not believe that is correct. If one looks at the

13 correspondence between the groups, there was frequently

14 correspondence with requests that were turned around

15 within 24 hours.

16 Q. Does GCP contain a requirement for a CRO to respond to

17 any request that the sponsor makes for information on

18 trial progress, is that a requirement of GCP?

19 A. There are some instances where, as we've discussed in

20 SAEs, that there is information that needs to be

21 transferred in a specific time. But in general to your

22 answer, there's certainly nothing in the guidelines that

23 requires this. This is a request.

24 Q. So GCP is a red herring, isn't it? This is just about

25 you trying to put pressure on LSHTM, isn't it?

1 A. No, sir, as I said, this letter was prepared by my
2 regulatory and clinical people who were concerned about
3 issues and asked me to express these to
4 Professor Roberts in response to his letter, and I did
5 so.

6 MR JUSTICE BURTON: Did you ask the regulatory people to
7 draft this letter for you to send?

8 A. Yes.

9 MR JUSTICE BURTON: It wasn't their initiative?

10 A. No, it was not their initiative. I had a letter from
11 Professor Roberts.

12 MR JUSTICE BURTON: Yes.

13 A. To which I needed to respond, and I asked for assistance
14 from my clinical and regulatory people in preparing the
15 response. So they did it at my request.

16 MR JUSTICE BURTON: Yes.

17 MR BEAR: Would you agree it was an unusual level of
18 reporting that you were asking them to provide?

19 A. No, I would not. I've worked with CROs in the past,
20 extensively, as I indicated, and such a request would
21 not be seen as out of the ordinary.

22 Q. Could you look at 2016, please, the first line:
23 "Frequency of reporting might appear high."
24 Doesn't that suggest it's an unusual level of
25 reporting, even by your own standards?

1 A. It gives an explanation of that in the next couple of
2 sentences, which you've omitted.

3 Q. Yes, but it suggests it's unusual, doesn't it, whether
4 or not there's an explanation --

5 A. It says it may "appear high", but it explains why the
6 request is being made in the subsequent sentence.

7 Q. Let's go forward again. We have to look at the next
8 bundle for the moment, please, chronological bundle 8.

9 MR JUSTICE BURTON: Page?

10 MR BEAR: 2046. Sorry, I may have given you an incorrect
11 reference for which I apologise. Forgive me, my fault.
12 Can we go back to C7? I had some questions which
13 I should have put to you on the document we were on,
14 I apologise.

15 What I want to do is to pick up what happens to the
16 document. We need to go forward. It's in bundle 7, but
17 it is 2046.

18 A. Yes, sir.

19 Q. What we've got here -- correct me if I'm wrong -- is an
20 electronic version of your letter into which
21 Professor Roberts has put comments.

22 A. That is correct.

23 Q. Although it ends up looking rather different, but it is
24 your text, plus his in response?

25 A. That's correct, and in the original I believe they were

1 in different colours to make it even easier to
2 distinguish.

3 Q. I'm sorry we haven't been able to carry that through
4 into our trial bundles.

5 Now, could we pick up what is said, please?

6 If we look in the fourth bullet point on page 2046,
7 you had raised this point. It is under the overall
8 heading of "Communication plan and trial progress
9 report", isn't it?

10 A. Yes, sir.

11 Q. SAEs/deaths at the bottom of the page:

12 "It seems that there are some discrepancies [you
13 would say] between HPM and TCC databases. This needs to
14 be rectified."

15 Just pausing there, that was presented by you as a
16 communication issue, correct?

17 A. Yes, sir, it was -- and in the context of progress
18 reports, et cetera, that's an event -- that
19 reconciliation, we felt, was a necessary event, and we
20 were not in the loop on it, so to speak, because LSHTM
21 and HPM were communicating between each other. We only
22 saw it when it came out the other end.

23 Q. Professor Roberts' response is in the bold type in this
24 version, isn't it?

25 A. Yes, it is.

1 Q. So he tells you that your team has to understand that
2 there will be, always, some discrepancy between the two
3 databases, and then on the third line of the next page:

4 "Resolutions of these discrepancies are constantly
5 ongoing and will only be finally resolved at the end of
6 the trial."

7 Do you see that?

8 A. Yes, sir, I'm just rereading this, please. (Pause).

9 I'm somehow not seeing the end of the trial. I know
10 that's a fact that that's what the plan was, but I just
11 can't see it in writing here.

12 Q. Can you see it now? It's on the fourth line of
13 page 2047?

14 A. "... resolved at the end of the trial."

15 There it is.

16 Q. Yes. Then let's look at your response. We have to go
17 forward in the bundle now to a letter which starts at
18 2080.

19 A. Correct.

20 Q. So you continued the mode of interspersing comments.

21 A. Yes.

22 Q. Then 2081 we can see, about halfway down the page, the
23 bullet point:

24 "SAEs/deaths."

25 Have you got that?

1 A. Yes.

2 Q. So your original in light type and then in bold type
3 Professor Roberts' comments with the sentence I drew
4 your attention to, containing "at the end of the trial"
5 and then beginning "yes" underneath, is that your reply?

6 A. Yes, it is.

7 Q. "Yes, we agree and understand that at any moment in time
8 discrepancies can exist between the TCC database and the
9 HPM databases. However, we would like to know that such
10 discrepancies are being resolved in current time. We do
11 not want the discrepancies to accumulate until the end
12 of the study, at which time resolving them could add
13 months to the conclusion of the study. Therefore, the
14 status of the discrepancies should be reported monthly
15 so that we can ensure that SAE discrepancies are being
16 dealt with in a timely manner."

17 So your point in response can be summarised in this
18 way, I suggest: you don't want a delay at the end of the
19 trial on account of this reconciliation?

20 A. That would be a fair summary.

21 Q. And you're not worried, therefore, about the earlier use
22 of the HPM database, are you?

23 A. I'm not worried about the?

24 Q. Use beforehand in the trial of the HPM database. Your
25 concern here is just to make sure that the

1 reconciliation doesn't hold up things at the end?

2 A. That's what it says, yes, sir.

3 Q. Yes. And you don't say, do you, that Professor Roberts,
4 how can DSMB consider safety during the course of the
5 trial if it does not have the reconciled HPM database?

6 A. What is reflected here is what I knew at the time, sir,
7 and as events unfolded, our concerns came to life in the
8 form of an SAE database that had twice as many SAEs
9 as -- approximately twice as many SAEs as the HPM
10 database.

11 That creates a lot of issues, including, if they
12 believe they had true SAEs, why weren't they reported,
13 which is a regulatory requirement, to the authorities.
14 We didn't have that information; they did. So it's --
15 my concerns and those of my people came to life
16 in October 19th when it was discovered by them that
17 there was a huge difference between their database after
18 they prepared it --

19 MR JUSTICE BURTON: But what you knew there was that they
20 were not going to reconcile the two databases before the
21 end of the trial?

22 A. My Lord, that is precisely what the language states. In
23 good clinical practice, there is an ongoing process. If
24 you waited until the end for everyone, you might --
25 doctors forget, they leave the hospitals and go other

1 places, the CRFs are old, cold and stale and nobody
2 remembers. It's a process that should be ongoing to
3 keep it current as best you can. It's always realised
4 it will be a step or two behind, but not months and
5 months behind, as we found. And the final
6 reconciliation at the end of the trial goes through
7 a process of cleaning that data probably -- for SAEs or
8 efficacy measurements, four or five times in a real
9 trial. You don't wait for everything to pile up at the
10 end, but that final thing, before you submit -- you say
11 "done", would be at the end of the trial obviously.

12 MR BEAR: I thought your case was that as a point of
13 principle, a DSMB should be presented with evidence
14 which is based on a database that has been reconciled to
15 the pharmacovigilance database, isn't that your case?

16 A. No, it's not, although if we look back in time, I can
17 understand why you say that, because Xytis at the time
18 of November 1 had only the SAEs listed from HPM. We
19 subsequently got additional information, some of it
20 difficult to interpret from the data dump.

21 We learned from Rene the number 94, but we did not
22 know how far out of sync these things were at the time
23 when I wrote this. We had some evidence that they were
24 becoming further and further out of sync --

25 Q. Sorry, I don't want to interrupt --

1 A. Our case, initially, was based on information we had at
2 the time that the cases were filed, and that involved
3 only what we knew, a number 94 and the HPM database.
4 That is not the case, as I understand it from my
5 lawyers, that was ultimately filed as such.

6 Q. I just want to know what your case is now, because if
7 you're not saying this, it's important. Are you not,
8 therefore, saying that as a point of principle a DSMB
9 should be presented with information which is based on
10 and reconciled with the pharmacovigilance database?

11 A. I think that would have been a good practice. If they
12 chose not to do it, which they apparently did, that's
13 their decision, ultimately.

14 Q. I see. You agree with me, don't you, that looking at
15 2081, the only concern that you express there was one to
16 keep the work ticking over so that there wasn't undue
17 delay at the end of the trial?

18 A. I wanted things -- if you go through this, it's done in
19 current time, is what it refers to, so that you don't
20 have this pile-up at the end, that is correct.

21 Q. So that there wasn't a pile-up at the end, that was your
22 objective?

23 A. It was my objective, for several reasons I have
24 disclosed to you.

25 Q. Yes, you have, that's quite correct. Now, can we go

1 forward to 2086? This is Professor Roberts' response,
2 and at this point, he departs from the system of
3 interspersing, doesn't he?
4 A. Yes, he does.
5 Q. Perhaps the colours had run out. At any rate, it is his
6 response, do we agree on that?
7 A. I agree.
8 Q. Can you just cast your eye over it to remind yourself of
9 it, unless you're already familiar with it.
10 A. Did you want me to focus on that SAE reporting or the
11 whole thing?
12 Q. Yes, please. Just look over the whole thing briefly,
13 but --
14 A. Okay. (Pause).
15 Q. Okay?
16 A. Yes, sir.
17 Q. It's fair to say that he gives you no specific
18 commitment at all, does he, on this issue of timing of
19 reconciliation?
20 A. That's fair to say:
21 "Resolving these discrepancies requires the input of
22 HPM and we cannot commit to a schedule of doing this."
23 That's what you are referring to, sir?
24 Q. Yes, I am. So he's refusing to commit to a schedule
25 isn't he?

1 A. He also says:

2 "We can reassure you that we can and do make every

3 effort to resolve these in a timely manner."

4 Q. Yes, but that's a phrase which could mean anything,

5 couldn't it? He's refusing to commit to any schedule.

6 A. He is refusing to commit to a schedule other than being

7 timely.

8 Q. Right. Now can we go forward to bundle C9, please?

9 MR JUSTICE BURTON: Page?

10 MR BEAR: 2651. This is a document which we may not have

11 looked at before. It's a little way ahead.

12 A. Way up to October, yes.

13 Q. 29th October. This is you to the other members of the

14 board, isn't it?

15 A. This is a letter to the board of directors of --

16 Q. It's an email to the board of directors, isn't it?

17 A. Well, it's an email, I'm sorry.

18 Q. Let's just read it out:

19 "Subject: GCP.

20 "Attachments: Response to Ian 8/24 letter.pdf.

21 "The enclosed communication document describes

22 a number of GCP issues we have previously brought to the

23 attention of LSHTM. Black was our original comments,

24 blue their response and orange our response to their

25 response. Nothing has been improved or changed as

1 a result of this series of communications which had
2 significant input from Joann, Rene, Rowland and
3 Desiree."

4 Those are your various regulatory and medical
5 advisers, aren't they?

6 A. Yes, they are.

7 Q. Yes.

8 A. Medical and regulatory.

9 Q. Then you attach to the 30th August letter, don't you?

10 A. That is correct.

11 Q. Did you tell the board about Professor Roberts' letter
12 of 3rd September?

13 A. No, I did not.

14 Q. If we can just go forward in bundle 9 towards the end of
15 the bundle to look at an email from Mr Guerin of the
16 board, it's 2702. This is part of a chain which we may
17 come back to later. We have to turn it round, I'm
18 afraid, it's the only place it appears. I want to look
19 at the last email on 2702 which is from Monsieur Guerin,
20 sent on 28th October 2007. Do you have that?

21 A. I do.

22 Q. 14.25, subject: LSHTM.

23 He says:

24 "LSHTM better have [and this is to you] the complete
25 list of the alleged violations with medical

1 explanations, why those violations are important for the
2 safety of the patients. I disagree with your statements
3 about having warned the board of specific items
4 requiring urgent corrections. You mentioned many times
5 your dissatisfaction about the LSHTM performance but we
6 never got any specific details."

7 Just pausing there. On 28th October, Mr Guerin
8 complained about a lack of specificity in your
9 dissatisfaction, didn't he?

10 A. Yes, he did.

11 Q. And your email at 2651 of 29th October was in response
12 to that complaint, wasn't it?

13 A. The previous one, I'm sorry?

14 Q. Yes, the previous one in the bundle, I'm suggesting it
15 was sent in response to Monsieur Guerin's complaint.

16 A. I'm just wondering why this follows instead of leads,
17 but --

18 Q. It's the way your solicitors have put the bundle
19 together, so let's not worry about that.

20 A. If the dates indicate you're correct, I accept your
21 statement.

22 Q. Thank you. Now, by showing the board the letter of
23 30th August, which contained, at the end of it, your
24 comments in response to Professor Roberts, but by not
25 showing them his comments in response in the letter of

1 3rd September, the board were being given an incomplete
2 impression, weren't they?

3 A. They were given my impression of concerns which is what
4 they asked for, not Professor Roberts' response to my
5 concerns, which happened to be in the first letter, but
6 they didn't ask: what is he doing about it, please tell
7 us. And, no, I did not include the letter.

8 Q. Do you agree that they were being given an incomplete
9 impression?

10 A. What they asked for was the particulars of my concerns.
11 I gave them that.

12 Q. So when you said at page 2651, having referred to the
13 enclosed communication document:

14 "Nothing has been improved or changed as a result of
15 this series of communications", do you not think it was
16 unfair to omit Professor Roberts' response of
17 3rd September in which he refused to commit to any
18 particular schedule before coming back to you?

19 A. Well if he refused to commit to a schedule, that would
20 be part of a "nothing has changed", wouldn't it, so --

21 Q. Do you or do you not think it was unfair to omit his
22 letter?

23 A. No, I don't.

24 Q. No?

25 A. No, I don't.

1 Q. His letter of 3rd September was quite acceptable to you,
2 wasn't it?

3 A. His letter of 3rd September at the time was quite
4 encouraging to me. Events, as they unfolded
5 subsequently, indicated to me that nothing had changed.

6 Q. I'm putting his -- putting this to you: what he said in
7 his letter of 3rd September was quite acceptable to you,
8 wasn't it?

9 A. It was encouraging to me, yes.

10 Q. Do you disagree that it was quite acceptable to you, his
11 refusal to commit to a schedule?

12 A. I would have preferred to have a schedule. He said: we
13 will try to do it timely. I accepted it.

14 MR JUSTICE BURTON: Can I ask you what this is a reference
15 to by Monsieur Guerin, when he says:
16 "LSHTM better have the complete list of the alleged
17 violations with medical explanations why those
18 violations are important for the safety of the
19 patients."
20 What's that a reference to? What violations?

21 A. Monsieur Guerin is French writing in English and I --
22 I didn't always understand what he was asking me for.
23 I gave him what I thought he was asking for, my Lord.

24 MR JUSTICE BURTON: He appears to have thought that it was
25 being suggested that the defendant was acting in

1 violation, in breach, of some kind of obligation which
2 could have an effect on the safety of the patients.

3 A. Which goes to the issue if, if you are not in compliance
4 with GCP, by definition, the patient safety is at risk.
5 It doesn't mean you'll hurt a patient --

6 MR JUSTICE BURTON: I haven't seen any suggestion anywhere
7 that was being passed on by you to the defendant that
8 they were in violation of GCP. I've seen a number of
9 requests and such like.

10 A. I believe the correspondence, if we go through it, back
11 as early as June, I mentioned concerns about GCP
12 compliance in communications with Dr Roberts. So this
13 is not -- and I discussed with the board my concerns
14 about it.

15 MR JUSTICE BURTON: But you didn't -- you were asked, or it
16 was thought that you were going to, by your board
17 members, that you were going to send a complete list of
18 alleged violations, which suggests to me that you had
19 told your board members that there had been
20 a substantial number of violations and that there was
21 a capability of compiling a list of them.

22 A. I'm at a loss here, my Lord. Monsieur Guerin asked me
23 for some information. I believe I complied with it
24 because he didn't say otherwise. I did -- provided him
25 with what I had at that time. I also instructed my

1 chief medical officer, Dr Joann Data to prepare
2 a document where she expressed those concerns. So it
3 wasn't just this back and forth between Dr Roberts and
4 I. There was a longer letter prepared by Dr Joann Data.
5 MR JUSTICE BURTON: That's the one we've been looking at,
6 18th August.
7 MR BEAR: No, this is later on that Dr Simmon is referring
8 to.
9 MR JUSTICE BURTON: At the moment, I want to know about
10 29th October.
11 MR BEAR: Sorry, yes, I meant later on than the one that
12 Dr Simmon just referred to.
13 MR JUSTICE BURTON: I follow. I won't interrupt, thank you.
14 MR BEAR: Let's just deal with this compendiously, because
15 I will come back to it, but in short you alleged to the
16 board during October that LSHTM was failing to comply
17 with GCP, didn't you?
18 A. I expressed my concerns that the board -- prior, even,
19 to that date, that LSHTM was not in compliance with GCP.
20 I expressed those to Professor Roberts --
21 Q. So you alleged non compliance with GCP to the board?
22 A. And to Professor Roberts.
23 Q. I'm just talking about the board for the moment.
24 A. I did, yes, sir.
25 Q. And Monsieur Guerin was saying: where are the details,

1 wasn't he?

2 A. Yes, sir.

3 Q. And the letter of 30th August was sent by you, on 2651,
4 in response to that, wasn't it?

5 A. Yes, sir.

6 Q. But in fact we've agreed a few minutes ago that the only
7 concern you expressed in the 30th August letter was
8 a concern to have the trial run on time so there wasn't
9 a pile-up at the end, correct?

10 A. Wrong.

11 Q. We didn't agree that?

12 A. We agreed that that's one, but that's not the only issue
13 in that letter that has to do with GCP. That's what
14 you're trying to limit it to.

15 Q. I'm sorry, Dr Simmon --

16 A. If I didn't understand your question, would you please
17 repeat it?

18 Q. I think you understood my question perfectly well. The
19 letter of 30th August only expressed a concern about
20 managing matters in a timely way so that there wouldn't
21 be a pile-up at the end of the study, and that was
22 a business concern to do with getting your product into
23 phase 3 in time.

24 MR JUSTICE BURTON: Do you want to look at that letter,
25 Dr Simmon, and identify --

1 A. I'm familiar with the letter and what I'm saying --

2 MR JUSTICE BURTON: Just a second. Do you want to identify,

3 in that letter of 30th August, where you are alleging

4 violations of GCP?

5 A. One of them -- would you direct me, sir, to the correct

6 page?

7 MR JUSTICE BURTON: It's 2080, is that right, in

8 chronological bundle 7?

9 MR BEAR: Yes or we can look at the copy behind 2651.

10 MR JUSTICE BURTON: Where you are now, behind 2651.

11 MR BEAR: Page 2653 is the relevant page.

12 A. Thank you. One of the ones that we expressed had

13 previously, for example, expressed concerns about was

14 record logs of patients that were screened.

15 When you're running a clinical trial, it's important

16 that the regulators know at the end that you have not

17 what we call cherrypicked patients. That is the -- not

18 you, the hospital, when they decide who meets criteria,

19 hasn't excluded people for some reason, who actually

20 meet criteria, but for some reason the doctor decides

21 they don't get into the trial. So there's -- what we

22 were requesting was clarity on an issue about which

23 there had been a substantive back and forth between

24 Mr Furcha and Ms Shakur which still left us uneasy that

25 that requirement, that GCP requirement, was being met.

1 That is another example.

2 Q. That's on a different point, isn't it? That's
3 screening.

4 A. That's my point.

5 Q. I think his Lordship was asking you whether or not there
6 was any GCP concern expressed in relation to the SAE
7 databases.

8 MR JUSTICE BURTON: No, I'm happy to understand what the
9 long list of -- of a complete list of violations of the
10 GCP were, and, in this letter or otherwise, and one of
11 them, you say, related to a possible concern -- it
12 doesn't seem to me to be a list of violations --
13 a possible concern in relation to screening patients.
14 But is there anywhere in this letter of 30th August in
15 relation to any matter, not limited to screening of
16 patients, not limited to the database, is there a list
17 of violations of -- a complete list or an incomplete
18 list of violations of GCP with which you were taking the
19 defendant to task?

20 A. I believe, if I'm correct, my Lord, that the word
21 "violation" is used by Monsieur Guerin, not by me.
22 I said we had concerns about compliance with GCP. Now,
23 he translated that in Anglo-French, or whatever, into
24 "violations".

25 The only way you could prove violations of GCP is

1 through audits, et cetera. We had concerns that we
2 expressed about --

3 MR JUSTICE BURTON: Of course he says "alleged violations",
4 I understand that. Whether you call them "alleged
5 violations" or whether you call them "concerns as to
6 breach of GCP", just tell me how many there were in this
7 letter of 30th August where you were alleging,
8 suggesting, proposing breach or risk of breach of the
9 GCP.

10 A. My Lord, I did two things in response to
11 Monsieur Guerin's letter. I immediately provided
12 something I had in hand, but then I asked my chief
13 medical officer to please prepare a response to that
14 letter, which took several days, I believe she was
15 travelling at the time, and that's where Dr Joann Data
16 then responds more fully to that requirement, that
17 request of Monsieur Guerin.

18 MR BEAR: Let's go to page 2703, please, at the back of
19 bundle 9.

20 MR JUSTICE BURTON: That's the same page as the other --

21 A. My Lord, may I say one other thing?

22 MR JUSTICE BURTON: Yes.

23 A. If you read the ICH-GCP guidelines, the sponsor may
24 delegate activity to the CRO, but the sponsor retains
25 responsibility for anything that happens in the clinical

1 trial. It retains all that responsibility. If the CRO
2 is making mistakes, it's my job, our job, the sponsor's
3 job, to inform them of their concerns and ask that they
4 be corrected. This is a responsibility of any sponsor,
5 and we were acting in that fashion. We did not have
6 proof of violations, certainly. We had concerns that we
7 expressed to the LSHTM in the hopes that they would be
8 corrected.

9 MR BEAR: You didn't have proof of violations, is that what
10 you just said?

11 A. I don't believe at this time in August 30th we had
12 "proof of violations". We had concerns.

13 MR BEAR: No, we're talking about late October now.

14 A. I don't -- I have to read through Dr Data's letter to
15 answer that more fully.

16 Q. Did you or did you not have proof in late October?

17 A. I don't remember, sir.

18 Q. Let's go to 2703. Let's look at the bottom email --
19 let's start on 2704 because it will be easier. There's
20 an email from Monsieur Guerin sent on
21 Saturday 27th October, and he says to you:

22 "I still do not understand the patient safety issues
23 which have been alleged. I am waiting to see in writing
24 from Vince what we are really talking about."

25 Then he goes on to make some other points.

1 Now let's look at your reply, we can see that
2 starting at the bottom of the next page, please. So
3 right at the bottom of 2703. Can you see:

4 "Original message from Vincent Simmon to
5 Herve Guerin and others, sent on Sunday, October 28th at
6 1.17 am."

7 Right at the bottom --

8 A. I turned to the wrong page, I'm sorry.

9 Q. Going back to 2703, it's all in reverse order,
10 Mr Simmon. Count up six or seven lines from the bottom
11 of the page:

12 "Original message from Vincent Simmon to Herve
13 Guerin, sent on Sunday, October 28th at 1.17 am."

14 Are you with me, right at the bottom of the page?

15 A. I'm on 2703. Am I on the right page?

16 MR JUSTICE BURTON: Take it slowly. 2704, Mr Guerin says:

17 "I do not understand the patient safety issues which
18 have been alleged."

19 Then we are on to 2703, in which he says:

20 "What are the evidences that the trial is not being
21 run under GCP? Please list them."

22 MR BEAR: Yes, I was coming to that, after showing Mr Simmon
23 his intermediate reply. So first of all Mr Guerin says:

24 "I do not understand the patient safety issues ..."

25 Then you come back, on the last three lines of this

1 page:

2 "Dear Herve, the simple answer to your question is
3 that if the trial is not being run in compliance with
4 GCP, it is, by regulation, a safety problem for the
5 patients and for Xytis."

6 A. That is correct.

7 Q. And then he says, and it's squashed up just above your
8 message:

9 "What are the evidences that the trial is not being
10 run under GCP? Please list them, HG."

11 Do you see that?

12 A. Yes, I do.

13 Q. So he's asking you for the evidences, as he calls it.
14 Then let's look at your reply above that, diligently
15 working into the morning, 3.40 am:

16 "Dear Herve, of course we will give you a list.
17 However, we have already pointed out during the phone
18 call today that the refusal of LSHTM to enforce
19 screening data collection is but one example of
20 a violation of GCP."

21 Do you see that?

22 A. Yes.

23 Q. You used the phrase -- you seem to have introduced the
24 phrase "violation of GCP"?

25 A. I didn't introduce it. Excuse me for interrupting you.

1 Q. You did use it, didn't you?

2 A. I did use it, but I didn't introduce it.

3 Q. But you wouldn't use a phrase if you didn't know what it
4 meant, would you?

5 A. No.

6 Q. To your fellow directors? No, of course not?

7 MR JUSTICE BURTON: It's the first time it's been used in
8 this exchange of correspondence, isn't it? It's not
9 Mr Guerin's Anglo-French which used it, as far as I can
10 see. He's talking about not being run under the GCP,
11 and you say:

12 "This is but one example of a violation of GCP."

13 A. And I accepted that, okay?

14 MR JUSTICE BURTON: You said you didn't introduce the
15 word --

16 A. I didn't believe I did.

17 MR JUSTICE BURTON: -- and at the moment I can't see who
18 did, if it wasn't you.

19 A. Excuse me?

20 MR JUSTICE BURTON: At the moment, I can't see who did
21 introduce the word "violation" if it wasn't you.

22 A. I thought we had read that before. If I'm mistaken,
23 I sit corrected.

24 MR BEAR: Okay so, then if we go back to 2651, even though
25 we must bear in mind that because of the way the bundle

1 has been put together, this is after in time,
2 29th October, so the next day you told --
3 Monsieur Guerin says:
4 "What are the evidences that the trial is not being
5 run under GCP? Please list them."
6 You wrote back and said:
7 "The screening log is but one example of violation
8 of GCP."
9 Then 2651, you send the enclosed communication
10 document --
11 A. Correct.
12 Q. -- describing a number of GCP issues, correct?
13 A. Correct.
14 Q. Can you tell us by reference to the communication
15 document what were the GCP issues that you had -- and
16 I'm reading from your covering email -- previously
17 brought to the attention of LSHTM?
18 A. We've discussed two of them, the screening issue and the
19 SAE issue.
20 Q. You haven't told us so far that the SAE database issue
21 had been brought to LSHTM's attention as a GCP issue.
22 Is that now your evidence or not?
23 A. Yes, it is my evidence now. I was --
24 Q. Where did you bring it to their attention as a GCP
25 issue?

1 A. I didn't -- at the time I didn't realise the
2 implications which Mr Furcha has subsequently pointed
3 out to me, which is if they believed there were 45 more
4 serious adverse events than was in the pharmacovigilance
5 database, which was reporting to the authorities, that
6 in essence that meant that they were sitting on adverse
7 events they believed existed, but hadn't reported, and
8 that's a GCP issue.

9 Q. I'm so sorry, but we are talking here about what you
10 said on 29th October and I'm asking you to identify
11 where you had previously brought issues to LSHTM's
12 attention as GCP issues. Now, so far you've told us
13 about the screening log issue --

14 A. Yes.

15 Q. -- which is mentioned at 2653. Are there any others,
16 please?

17 A. I would still say that the SAE one, in my mind, was
18 a potential violation of GCP, because there is an
19 expectation in GCP that there's a timely reconciliation
20 of issues, which wasn't occurring, and --

21 Q. But I'm asking about what you brought to LSHTM's
22 attention as a GCP issue. Did you bring it to their
23 attention as a GCP issue?

24 A. I did make an assumption that they were familiar with
25 the requirements of GCP, that is true.

1 Q. Did you bring it to their attention as a GCP issue?

2 A. I believe I did in this letter, yes, there are a number
3 of them.

4 Q. Can you point to the words that you used?

5 A. I pointed out in the screening one it's a GCP issue, and
6 I don't other places.

7 Q. That suggests that the GCP issue is the one you flag up
8 as a GCP issue and that the others are business issues,
9 doesn't it, Mr Simmon?

10 A. Well, I would point out, sir, for example, we're talking
11 about site audits, and the concern for that is, while
12 it's not flagged as a GCP issue, is a GCP issue.

13 Q. I think I've taken that as far as I can take it with
14 you.

15 On the screening log, that's not raised in this
16 action, is it, as a problem? That's not one of the many
17 things that you have sought at any stage ever to
18 complain about, agreed?

19 A. I believe that's correct.

20 Q. But you were telling the board, by sending them this
21 letter of 30th August, that that was a GCP issue.
22 Agreed?

23 A. Yes, sir.

24 Q. Professor Roberts on 3rd September had responded to you
25 in relation to the screening log as well, hadn't he? Do

1 you want to check?

2 A. Yes, please.

3 Q. It's in bundle 7 at 2086. We should probably keep open
4 your letter of 30th August. We were looking at the copy
5 of 2653 in bundle 9. Let's pick it up from 2653, shall
6 we, Mr Simmon, so that you can follow how it went?

7 A. Sure.

8 Q. Your original statement:

9 "... screened patients considered for the trial but
10 not randomised. This serves as a diagnostic tool if
11 there are large numbers of patients being considered and
12 few being enrolled as well as being a GCP requirement."

13 The response from Professor Roberts -- are you on
14 it?

15 A. The screened patients?

16 Q. Yes. He says:

17 "This will be reported as per the trial procedures,
18 will be based on monitoring reports received by the TCC
19 and accordingly will be behind recruitment status."

20 Do you see his response there?

21 A. I was looking down at the -- where it says "screened
22 patients" and I may have --

23 Q. Yes, I'm reading from what he says under "screened
24 patients"?

25 A. He says:

1 "We are happy to update you ..."

2 Am I on the wrong page?

3 Q. Are you on 2653?

4 A. No, I was on 2086.

5 Q. It's the same document, I think. It's the first bullet

6 point on the page, which starts off:

7 "Screened patients."

8 MR JUSTICE BURTON: 30th August letter, yes?

9 A. Yes, sir, I'm there.

10 MR JUSTICE BURTON: Second page, is that right?

11 A. And I respond to him the response to -- again: "The

12 response is not clear." Again, I don't handle these

13 screening issues myself. That's the responsibility of

14 the people who work for me.

15 MR BEAR: No, I understand, so he had replied and you said:

16 "The response is not clear."

17 And you mentioned GCP. No dispute about that. Now

18 let's look at what he said in the 3rd September

19 correspondence which is out of the electronic loop,

20 okay? So 2086:

21 "Screened patients. We are happy to update you on

22 the number of patients who meet the inclusion criteria

23 but who are not enrolled."

24 A. That's what he says, yes, sir.

25 Q. And that was quite acceptable to you, wasn't it?

1 A. If it was done, yes, sir.

2 Q. So why didn't you tell the board that he had responded
3 to you in a way that was quite acceptable?

4 A. I don't recall, sir.

5 Q. You were giving them a misleading impression, weren't
6 you?

7 A. It was my impression that from the email correspondence
8 that it wasn't being done.

9 Q. That's not an allegation --

10 A. Despite his answer.

11 Q. That's not an allegation that you are making in this
12 action, is it, Dr Simmon?

13 A. I said it was my impression, sir.

14 Q. It's not an allegation that you are making in this
15 action, is it, Dr Simmon?

16 A. Not to my knowledge.

17 Q. No. And do you have any evidence at all that it wasn't
18 being done? Can you give us a single piece of evidence
19 now?

20 A. No, sir.

21 Q. So in that case, it was, I suggest, misleading of you
22 not to put forward to the court what Professor Roberts
23 said on this issue in his letter of 3rd September, which
24 was quite acceptable to you?

25 A. If it had been -- if it was followed through, it would

1 have been acceptable to me, yes.

2 Q. You had no reason to assume it wasn't being followed,
3 did you?

4 A. As I said in October, nothing is changed. So it doesn't
5 seem like it was followed through, and belief later is
6 that it was not followed through on.

7 Q. You've just told us you don't have any evidence to
8 support that. Can you not agree, Mr Simmon -- I'm going
9 to give you one final chance, just reflect a little,
10 okay, before this answer, because his Lordship has to
11 assess your evidence overall -- can you not agree as you
12 sit here now, a little back from the hurly burly of
13 day-to-day events, that it was misleading of you not to
14 send Professor Roberts' letter of 3rd September to the
15 board?

16 A. Upon your suggestion and reflection, it would have been
17 better if I had done so, yes, sir. But I did not do
18 that.

19 Q. Can you explain why you didn't?

20 A. I do not remember.

21 MR JUSTICE BURTON: You told me that in relation to that
22 letter -- 3rd September -- in relation to the two
23 matters where you say that there were, in your mind,
24 possibly GCP concerns, his response to the screened
25 patients was acceptable and his response to the SAE

1 reporting and discrepancies between databases was
2 acceptable?

3 A. Yes.

4 MR BEAR: My Lord, would that be a convenient moment?

5 A. What I'm saying is -- excuse me for interrupting.

6 MR JUSTICE BURTON: Give your answer. It was only suggested
7 that there be a break.

8 A. So, if we look now, in October, when I'm responding to
9 Monsieur Guerin's concerns, I'm saying my concerns here,
10 despite the effect of this letter, I'm still getting
11 input from over a two month period, roughly --

12 MR JUSTICE BURTON: Well, we'll have to see whether that is
13 so, but at the moment the answer I thought you had given
14 in relation to the screened patients was that you had no
15 information that there was any failure by
16 Professor Roberts to comply with his assurance in
17 relation to screened patients on 3rd September.

18 A. I was informed by the people who worked for me that we
19 still had this as an issue in late October, and it
20 hadn't gone away, and I said, in my response, these
21 issues that we raised, including the reconciliation,
22 et cetera, were not getting fixed.

23 So I -- that's what I responded. It's two months
24 later, have things been fixed? To the best of my
25 knowledge, sir, they had not been.

1 MR JUSTICE BURTON: We're going to look between September
2 and October to see if there was anything else on
3 discrepancies, but I thought you said that you still
4 don't know now anything to differ from the suggestion
5 that the response on screened patients was acceptable.
6 A. You asked me if I had evidence, sir.
7 MR JUSTICE BURTON: Yes.
8 A. If I understood the correction.
9 MR JUSTICE BURTON: Well Mr Bear did.
10 A. One of you did, if I had evidence. I don't have here,
11 sitting with me, evidence per se that I could point to,
12 but my best recollection, to respond to the question, is
13 that when I -- and prior to sending my response, I had
14 enquired if we still had concerns about this, because,
15 again, I'm not handling all these day-to-day issues, and
16 I was informed that we did.
17 MR BEAR: Did you tell Professor Roberts that his response
18 of 3rd September was quite acceptable?
19 A. I don't recall.
20 MR BEAR: My Lord, shall we have a break?
21 MR JUSTICE BURTON: If you'd like to follow this up and
22 finish this topic?
23 MR BEAR: I thought that's why I would depart from my
24 intention. Can I ask you to look at a document which as
25 far as I know is only in witness statement bundle 4?

1 Could you go to tab 31? This is a bundle of exhibits to
2 interlocutory statements. You'll see from the front
3 page that tab 31 is the exhibit to Professor Roberts'
4 statement that he made on 11th December. Do you have
5 that?

6 A. Yes.

7 Q. Then could you turn most of the way through to page 193?
8 At the bottom half of the page, Ian Roberts to you
9 on September 3rd:

10 "Dear Vince, please find attached two letters in
11 response to your recent correspondence on (a) extending
12 the period of observation [that's the protocol amendment
13 issue which we'll come to after the break] and (b)
14 communication. Look forward to talking to you on
15 Wednesday."

16 Your response:

17 "Dear Ian, thanks for your letters. I am not
18 corresponding to you on the correspondence letter
19 because, as you have suggested, we have sufficiently
20 corresponded and your correspondence was quite
21 acceptable."

22 Yes?

23 A. Yes, sir.

24 Q. As it happens, Dr Simmon -- you'll have to take this
25 from me and I'll be corrected by your legal

1 representatives if I'm wrong -- this email has not been
2 disclosed by Xytis in this action. Were you aware of
3 that?

4 A. No, I'm not.

5 Q. Did you conduct a search of your emails before you gave
6 documents to your solicitors for disclosure in this
7 action?

8 A. I certainly did, and I --

9 Q. Can you explain why this exchange between you and
10 Professor Roberts does not appear in your disclosure
11 list, discovery as you call it in America, in this
12 action?

13 A. No, I thought the process I used to respond to this
14 discovery was one of looking for -- doing a search for
15 any email to Professor Roberts on my laptop, which is
16 my -- essentially has my correspondence on it, either on
17 the hard disk or accessible through the email files, and
18 copied those and forwarded them to the -- to Dechert,
19 and if I didn't get this one there was no -- I don't
20 know why I wouldn't have. I don't know how it happens.

21 Q. Do you think that you selected it as one you wouldn't
22 disclose?

23 A. No, I can assure you, sir, did I not select,
24 selectively --

25 Q. Might you have deleted the email? How would it not come

1 up on your search?

2 A. I don't have an answer to your question, sir, but I'm
3 under oath, and I assure you that I did not selectively
4 delete any information that was due to --

5 Q. Are you in the habit of deleting emails in your normal
6 working life as you go through, to clean up the inbox?

7 A. I occasionally go through, and I was looking for some
8 documents, and I -- things that are fairly old,
9 I wouldn't classify this in that group, it's September.
10 I don't think I would have deleted it.

11 Q. Have you made any checks in relation to deleted emails
12 on the servers?

13 A. I have not made any such checks, no.

14 Q. You haven't. So we don't know if your disclosure
15 includes any emails that might have been deleted? Do
16 you know if your disclosure includes --

17 A. No, I didn't do such a search and the server actually
18 exists in Nyon or Geneva.

19 Q. One of the things we've noticed in the bundle is that
20 there are no internal emails from you, and again I'll be
21 corrected if I'm wrong, internal emails within Xytis
22 relating to the BRAIN Trial or LSHTM, until 20th June,
23 the "brute force" email. Is that in accordance with
24 your recollection of what's been disclosed? Am I fair
25 in that?

1 A. I vaguely recall that, yes.

2 Q. Can you explain why that is?

3 A. No, I don't believe there was a selective deletion.

4 I don't --

5 Q. There must have been some emails from you between you

6 and Mr Furcha, for example, relating to this trial

7 before 20th June.

8 A. If there were, Mr Furcha would also have a copy of

9 those, and I presume in one of the bundles they would

10 have come up.

11 Q. Do you think it's likely that there were emails between

12 you and Mr Furcha relating to this trial and LSHTM before

13 20th June?

14 A. Don't know. I don't know, honestly I do not know.

15 MR BEAR: Would that be a convenient --

16 MR JUSTICE BURTON: Just one final question just to wrap up

17 this topic.

18 A. Yes.

19 MR JUSTICE BURTON: Looking back upon your answer in

20 relation to 3rd September, when Mr Bear suggested that

21 it was misleading of you not to send to the board

22 Professor Roberts' letter of 3rd September, and you

23 said:

24 "Upon your suggestion and reflection it would have

25 been better if I had done so, but I didn't.

1 "Question: Can you explain why you didn't?

2 "Answer: I don't remember."

3 Now that you know that you actually sent an email to
4 Professor Roberts saying 3rd September, and indeed the
5 entire correspondence "was quite acceptable", do you
6 want to reconsider your answer as to why you didn't send
7 Professor Roberts' letter of 3rd September to the board
8 and left them with the impression that things were not
9 acceptable to you?

10 A. Again, my response would be now, as I've kind of --
11 ordering these things chronologically, sir, is that my
12 statement at the time in late October to Monsieur Guerin
13 and the other board members, was that things had not
14 changed. So given that on October 29, which was the
15 impression I had from the people who worked for me, that
16 the situation was basically unchanged, with our
17 concerns --

18 MR JUSTICE BURTON: Neither unchanged for the better nor
19 unchanged for the worse, is that it?

20 A. Unchanged according to our requests and discussions from
21 the August 30th letter, that these were our concerns.

22 MR JUSTICE BURTON: Shall we break there for now? Five
23 minutes.

24 (12.02 pm)

25 (A short break)

1 (12.07 pm)

2 MR BEAR: Let's move on to a different topic, bundle C7,
3 page 2011, chronological bundle 7/2011.

4 This is a letter in which you sent to
5 Professor Roberts --

6 A. I'm sorry? Volume 7?

7 Q. Yes, volume 7, page 2011. This is the covering email by
8 which you sent Professor Roberts some comments on the
9 Hireos scale.

10 A. Yes.

11 Q. Which you said were very, very troubling to you.

12 A. Yes.

13 Q. "Therefore it may be necessary to modify the trial
14 design ... Based on discussions with several experts,
15 I believe that the reliability of measuring a positive
16 effect on Anatibant can best be achieved by extending
17 the observation period to a last assessment of 80 to 100
18 days post-trauma. Obviously this will have no impact on
19 the amount required of work at the clinic. The time of
20 trauma will require some outreach to find and bring
21 patients back in. Obviously the sooner this change is
22 implemented, the more patients' data can be captured.
23 I have asked Rowland to make implementation of such
24 a change a priority."

25 Then you go on to congratulate LSHTM on the

1 outstanding work. And you say this:

2 "... enrolment continues to accelerate and now my

3 investors feel much more comfortable."

4 So that statement was correct, wasn't it? Your

5 investors felt much more comfortable?

6 A. Correct.

7 Q. So I suggest the pressure on you to have a trial in

8 progress which was meeting expectations on the timeframe

9 was off by then, that things were on course for an early

10 finish?

11 A. Yes, sir, they seemed to be.

12 Q. Now, what you sent included comments from a Dr Bermak,

13 didn't they?

14 A. Yes, sir.

15 Q. Who's an American medical man?

16 A. American MD, UC, San Francisco.

17 Q. He had already discussed the Anatibant trial at an early

18 stage with Dr Tschollar, didn't he? Did you catch the

19 question?

20 A. Yes, with Dr Tschollar?

21 Q. Yes.

22 A. He was involved early prior to me coming to the company,

23 yes, sir.

24 Q. Yes. And not all of Dr Bermak's ideas had been accepted

25 by Dr Tschollar, had they?

1 A. No.

2 Q. So I suggest Dr Bermak, if asked about the Hireos scale,
3 was always likely to offer a negative view, wasn't he?

4 A. I had no way of knowing that.

5 Q. It would be a fair guess, wouldn't it, that someone who
6 was consulted about the trial initially and whose
7 recommendations weren't accepted would be likely to
8 offer a negative opinion if asked about its design later
9 on. As a man of the world, could you see that?

10 A. That wasn't my concept. I sent it to someone who
11 I thought could look at the trial and I knew he was
12 familiar with it from early on. I wasn't aware of how
13 deeply he was or wasn't involved in the trial design.
14 He could have been in favour of the trial as it was
15 designed for all I knew. I just didn't know.

16 Q. You were hoping to get favourable comments, were you, on
17 the trial design?

18 A. I was -- by this time, I had focused a bit more,
19 pressure was off, as you kindly pointed out for the --
20 for enrolment, and I began to look at the trial design
21 and wonder in my mind if this was the best trial design,
22 a trial that would meet with the original objective back
23 in December 2005, which was to show benefit in a patient
24 population, show efficacy, was in that original
25 document, was a first objective, December --

1 Q. That wasn't the objective of the phase 2 trial, was it?

2 A. It was part of that, in my belief, yes, because we had
3 safety as the primary end point, but showing a dose that
4 could be effective in a patient population -- now, let
5 me distinguish here slightly. Efficacy, as it's used in
6 regulatory work, generally means at a statistically
7 significant efficacy, and that will be a phase 3 trial.

8 In a small trial like this, there was no expectation
9 of seeing statistically significant efficacy. What we
10 were hoping for -- and I said many times in discussions
11 with -- both in emails and personal discussions with
12 Dr Roberts -- is a signal, something that showed
13 a trend, so that we could then get a sponsor for
14 a larger phase 3 trial.

15 My concern became that the -- what I believed to be
16 the primary efficacy end point, the Hireos scale --
17 because it's the only outcome scale in there -- was
18 perhaps not as good as I had thought it might be
19 originally.

20 So I chose to ask someone, who might know more about
21 it, who was involved in the trial before I came, that
22 was Dr Bermak, I had consulted with him on other things,
23 and he gave me back, in reasonably short time,
24 a response. But I did not send it to him, because he
25 was critical of the trial. I did not know his standing

1 with respect to the trial.

2 MR JUSTICE BURTON: You didn't know he'd had any previous
3 involvement?

4 A. No, I didn't say that. I said I didn't know what he
5 thought about the trial design prior to this letter. He
6 explained that he would have done it differently.

7 MR JUSTICE BURTON: But he must presumably have explained at
8 that stage that he had been asked about it originally
9 and had expressed the same views originally.

10 A. I did not know that, sir.

11 MR JUSTICE BURTON: But didn't he say that: oh, well, it's
12 interesting you should ask me, because I advised your
13 predecessor about it?

14 A. In the response letter, he says that -- which is the
15 only communication I had -- I sent it by email, I got an
16 answer back by email from him.

17 MR JUSTICE BURTON: You're looking to see whether there is
18 such communication in the bundle, are you? Have we got
19 it?

20 MR BEAR: Prior communication between Dr Bermak and
21 Dr Simmon, do you mean?

22 MR JUSTICE BURTON: Yes.

23 MR BEAR: Yes, there is some --

24 MR JUSTICE BURTON: And he is one of the several
25 individuals, is he?

1 A. There was also a Dr Donald Berry, a statistician,
2 I believe at Dallas at the University of Texas who is
3 a world renowned statistician.

4 MR JUSTICE BURTON: But the primary person you consulted was
5 Dr Bermak?

6 A. I sent both Dr Berry and Jason Bermak the Hireos scale
7 and the -- under confidentiality, as well as the
8 protocol and asked them about it.

9 MR JUSTICE BURTON: It's in the bundle, is it, Mr Bear, the
10 communication with Mr Bermak?

11 MR BEAR: I'm just trying to find it.

12 MR NASH: Page 1951, I believe.

13 MR JUSTICE BURTON: Thank you very much.

14 MR BEAR: It starts at 1954 -- 1953 rather, sorry. So this
15 is the usual reverse order email string, okay? So this
16 is the first one:

17 "Jason [on Monday, July 23rd] I cannot find my
18 electronic version of this. Could you send me a copy,
19 please."

20 You had obviously had some form of communication
21 with Dr Bermak prior to this email, hadn't you?

22 A. Excuse me --

23 MR JUSTICE BURTON: 1953.

24 A. Okay, 1954?

25 MR BEAR: No, 1953. 1954 is a spreadsheet.

1 At some point in the future, someone will invent
2 a machine that reorders emails in an easier way to read,
3 but --

4 A. I couldn't agree with you more.

5 Q. So 1953, and my point is --

6 A. Yes, you're reading correctly, on July 23rd, I sent to
7 Jason Bermak this -- when I was reviewing this
8 information previously, I thought that request --

9 Q. No, you didn't send him anything, you asked him for
10 something. My point is there must have been some prior
11 communication, whether written or verbal, between the
12 two of you.

13 A. Yes, sir.

14 Q. Can you tell us what that was?

15 A. No, I can't. I thought -- as I was about to say when
16 I read through this bundle -- that I sent this to
17 Mr Furcha, which would have made sense. Why I asked
18 Dr Bermak for a copy of it I don't know.

19 Q. You told his Lordship a moment ago, if I understood you
20 correctly, that the communications were only by email,
21 between you and Dr Bermak.

22 A. No, I said we had telephone conversations.

23 Q. You had telephone conversations, did you?

24 A. Yes, sir. I have his cell phone number and he has mine.

25 Q. Sure, and you're writing to him in fairly familiar terms

1 in this email, aren't you?

2 A. Yes, as I said, we had consulted on a number of
3 different matters.

4 Q. Oh, I see, so you knew him from previous projects?

5 A. Involving Xytis, yes.

6 Q. Involving Xytis, okay. So I suggest you must have got
7 the impression before you started to ask Dr Bermak to
8 look into the Hireos scale, that he didn't think very
9 much of Dr Tschollar and didn't think very much of the
10 way the BRAIN Trial was designed. That would be fair,
11 wouldn't it?

12 A. No, it wouldn't.

13 Q. No?

14 A. I do not have that impression.

15 Q. So when he wrote to you at 1952, saying under the first
16 heading, in which he congratulates you on recruitment:
17 "In terms of Hireos, indulge me for a moment and
18 just try to guess the answers to the following and then
19 I will show you the data so you can have a sense of the
20 usefulness of Hireos versus 'Vince's guesswork'. Be as
21 realistic as you can."

22 That seems to be suggesting that he doesn't think
23 very much of Hireos, doesn't it? Do you agree with me?

24 A. I didn't know -- first of all, I was very busy when
25 I did this test, and I didn't know where he was going,

1 I just tried to answer his question. Quite frankly, it
2 was -- I had no idea what the outcome would be.

3 Q. I see, so when you got the outcome at 1951, which is the
4 extract that you later sent to various people, to LSHTM
5 and the board --

6 A. Yes.

7 Q. -- that was a complete surprise to you, was it?

8 A. I was badly disappointed in what Dr Bermak alleged was
9 a scale that might not be useful to the company. I was
10 shocked.

11 Q. When Dr Bermak said, at the end of his first paragraph:

12 "I would have run a smaller trial with more
13 information gathered on each patient at two weeks but
14 alas."

15 And then when he said at the start of the third
16 paragraph:

17 "Other conclusions I have made from Hireos is that
18 such and such [second sentence] from day number one
19 I lobbied to Werner to have GCP 328 [that's Glasgow Coma
20 Scale] as the inclusion. He said 5 to 13 which is
21 a terrible idea. In my opinion, I told him this
22 over-and over again, finally convinced him to include
23 patients at 3 to 5, but he never dropped the high end
24 down. So a lot of patients are being enrolled with
25 minor symptoms. Mark my words you will find that

1 patients with initial GCS 9-13 will screw up the drug
2 effect."

3 Didn't you get the impression from that that
4 Dr Bermak was someone who felt a little aggrieved that
5 his suggestions hadn't previously been accepted by
6 Dr Tschollar?

7 A. I -- when I read this, I assumed these things were in
8 his current mind of concerns, that he didn't like the
9 way the trial design had ended up, and I certainly had
10 that impression, sir, at this time.

11 Q. My question was: didn't you get the impression that he
12 was aggrieved that his advice hadn't been accepted?

13 A. He was suggesting what he thought would be a better
14 trial design, and I don't --

15 MR JUSTICE BURTON: If you look at the last sentence of the
16 first paragraph, he says:

17 "I would have run a smaller trial but alas."

18 Doesn't "alas" mean: nobody took any notice of me?
19 Isn't that what it means?

20 A. I accept that, yes, sir.

21 MR BEAR: And you would have appreciated that at the time,
22 wouldn't you? The whole tenor of this is someone who's
23 saying: I told you before and no-one would listen and
24 now look it's all coming wrong rather as I predicted.
25 That's the whole tone of this email, isn't it? Correct?

1 A. The suggestions that he had made -- the tone of this
2 email is that suggestions he had made prior to me coming
3 to the company were not followed, yes, sir.

4 Q. It's not written in a particularly objective, scientific
5 way, is it? Do you agree with that?

6 A. It's an email, it's not a formal report, and I did copy
7 Dr Roberts on it and asked him for his comments.
8 I didn't just take this at face value. I also sent it
9 on to Dr Berry and asked his comments.

10 Q. I'm just asking to you agree with me, if you can, that
11 this is a pretty unscientifically worded email, "screw
12 up", "abysmal", "terrible", that sort of language, it's
13 all rather emotive, isn't it?

14 A. Yes, sir.

15 Q. So I suggest that you appreciated from the start that
16 Dr Bermak was going to give you a negative view. Can
17 you now agree with that?

18 A. I will never agree with that.

19 Q. Then you sent it on, didn't you, to --

20 A. My hope would have been, sir, if I may interrupt you,
21 a trial that would give a successful outcome, for me to
22 want this trial, to allege that I wanted this trial to
23 fail and therefore I sought somebody to tell me it was
24 going to fail, is --

25 Q. I'm not suggesting that at all. I'm suggesting this --

1 A. So I would have wanted this scale to be good, in his
2 opinion, not bad.

3 Q. Let me put the point to you. What you wanted was
4 a pretext to have an assessment at three months because
5 an assessment at three months, you thought, would be
6 more acceptable to investors or funders for phase 3.

7 A. It would have been -- it was my concern, and it's
8 expressed in many places -- that a trial which did not
9 have an outcome that would result in a pharmaceutical
10 company seeing some sign of efficacy, as I've used that
11 term where it's not statistically significant, if it
12 didn't have that, a phase 3 trial would never be
13 undertaken, and I wanted, as a result of that, to have
14 the trial design changed to increase the probability of
15 such a signal.

16 Q. I'm suggesting specifically that what you wanted is
17 a three-month assessment because that would be something
18 which, in your business view, would be more familiar to
19 big pharmaceutical companies or investors and would look
20 more like the primary end point for a phase 3 trial
21 which would be a six month assessment. Is that fair?

22 A. I would say to -- with the limitation not to investors,
23 more to pharmaceutical companies.

24 Q. Apart from that qualification, is what I've said fair?

25 A. Yes, yes, sir.

1 Q. My point to you is: you wanted to find a pretext for
2 a three-month assessment. Is that fair?

3 A. No.

4 Q. No? Well, let's take a look. The first thing that you
5 did was to send the comments of Dr Bermak on to
6 Professor Roberts, correct?

7 A. To? I sent the comments of Jason Bermak to Dr Roberts?
8 I certainly did that.

9 Q. Let's look at page 2011?

10 A. I certainly did that. I'm not disagreeing that I did
11 that.

12 MR JUSTICE BURTON: 2011, is it still is in the same bundle?

13 MR BEAR: Still in C7.

14 A. And I said it was troubling to me. His comments were
15 troubling to me.

16 Q. Well, let's look at it. Look at the end of the first
17 overall paragraph.

18 A. Yes.

19 Q. The line beginning:
20 "Evaluation ..." and you say:
21 "Obviously the sooner this change is implemented the
22 more patients' data can be captured. I have asked
23 Rowland to make implementation of such a change
24 a priority."
25 A. Correct.

1 Q. You're referring to it as a fact, aren't you? You're
2 referring to it as something that's going to happen.

3 A. It was my belief it needed to happen, yes, sir, and
4 I would -- excuse me for interrupting.

5 Q. Not at all, no. Go on.

6 A. In the information we have here Professor Roberts
7 communicated with MHRA about what a sponsor could or
8 couldn't do in a clinical trial, and that evidence shows
9 that the MHRA sponsor says that it's the perfect right
10 of a sponsor to change the design of a clinical trial.

11 Q. I'm not talking about that at all for the moment. I'm
12 suggesting that you had already instructed Mr Furcha to
13 implement a change to include three months' assessment,
14 correct?

15 A. You're -- the answer is "yes".

16 Q. Right. Now let's look at what you sent to the board in
17 bundle C7, page 2026. I'm afraid this is yet another
18 string of emails: 2026 and we're starting at the bottom
19 of the page.

20 A. Yes.

21 Q. What I want you to find is your original message sent to
22 Monsieur Guerin and the other board members on
23 Tuesday, August 21st, okay?

24 A. Yes, sir.

25 Q. So you'd sent your communication -- you'd sent

1 Dr Bermak's comments on to Professor Roberts on the
2 17th, which was a Friday, we can see, because this is
3 a Tuesday.

4 A. Okay.

5 Q. Okay? So a working day elapses and then you write to
6 the board saying:
7 "Issue with the Anatibant trial."
8 Let's just cast our eye over this, okay?

9 MR JUSTICE BURTON: Sorry, whereabouts are we on?

10 MR BEAR: Bottom of 2026 in C7, which is the first email in
11 the string:
12 "I have made the assumption that the efficacy scale
13 being used in the Anatibant trial been fully vetted."
14 Then you refer to Bermak and various other matters.
15 And then you cite Dr Bermak's comments and then you cite
16 some comments from someone called Don Berry, and then
17 two-thirds of the way down the page, you say:
18 "That is the bad news."
19 Then the good news, first of all you refer to the
20 contract and to what you were expecting to hear from
21 LSHTM and then:
22 "Second, enrolment continues to ramp up. 35 to 40
23 patients this month", et cetera.

24 A. Yes.

25 Q. Then you refer to additional centres and you say at the

1 bottom of the page:

2 "As a result we should be able to complete enrolment
3 late in the first quarter of 2008."

4 Then you refer to another disability scale which
5 again you say is only after two weeks:

6 "Therefore, I think we must do the following:

7 " extend the final visit and patient evaluation to
8 three months."

9 You go on to say that you won't be able to do this
10 initially for every patient because a small number have
11 already passed the three-month timeframe:

12 "However, as we painfully recall, enrolment was
13 very, very slow initially so we won't lose that many
14 patients by the time the protocol amendment is improved
15 and implemented."

16 Then the next paragraph:

17 "As part of the protocol amendment we should request
18 permission to increase the patient number to up to 500
19 patients."

20 You go on to discuss potential regulatory issues:

21 "Since we have not had any safety issues to date it
22 may be improved. Hopefully we will be able to have at
23 least 400 patients with three-month data."

24 You refer to the fact that the trial was originally
25 designed for 500, cut back to 400 for budgetary

1 purposes. Then you say the reduced trial cost to LSHTM
2 should permit both changes, control timing and cost, and
3 then this:

4 "The net result of the above would be to greatly
5 enhance the quality (and possibly the quantity) of the
6 data coming out of the trial, while not increasing
7 costs. We do add three months to the end of the trial,
8 but if we continue on the upward trend in enrolment, we
9 still have all of the data by mid 2008.

10 "We have given LSHTM a heads-up on our thoughts but
11 have not heard back from them yet."

12 Then you say you:

13 "... will have more specifics by the time of the BOD
14 meeting [the board meeting] on September 4th."

15 Okay, you recall that email?

16 A. I do.

17 Q. The position on the 21st was that LSHTM had had
18 Dr Bermak's comments, and indeed your suggestion made to
19 them for the first time about an amendment, since
20 Friday. You sent this email on the Friday and they had
21 had it since the Friday?

22 A. Right.

23 Q. Professor Roberts is obviously a well-known clinical
24 trialist, correct?

25 A. In -- he is very well known in traumatic brain injury

1 and for quite a number of other things he's done.

2 Q. And this is a traumatic brain injury trial, isn't it?

3 A. It is, but it's a registration trial, which is totally

4 different from an epidemiological study.

5 Q. So you say. Now --

6 A. So the experts say.

7 Q. He's also the designer of the trial, correct?

8 A. Excuse me?

9 Q. He designed the trial, basically his design, with

10 Dr Tschollar?

11 A. In some consultation with Dr Tschollar, yes.

12 Q. Yes, and obviously he's very familiar with Hireos,

13 because that's a scale developed by LSHTM in a previous

14 trial of theirs?

15 A. Yes.

16 Q. Yes. Dr Bermak's comments, however emotively worded,

17 would you agree, were on a scientific topic, because

18 they concerned the predictive power of the Hireos scale?

19 A. Yes.

20 Q. So why not get Professor Roberts' comments before you

21 raised with the board the desirability of making

22 a change which, in your email to the board, was

23 predicated on inadequate predictive power of the Hireos

24 scale?

25 A. This is a -- you're sort of looking in the middle of the

1 sausage factory, so to speak. I don't just bring to the
2 board final conclusions. I communicate with the board
3 about my thinking at the time and why I'm thinking
4 certain things, and give them the information, I think,
5 that helps them understand why I'm thinking these
6 things.

7 Q. You communicated a view which was a firm one, did you
8 not?

9 A. A view. I told them: this is my belief, yes, I did.

10 Q. I'm asking you why, before you sent your belief and the
11 reasons for it and Dr Bermak's comments, before you sent
12 all of that over to the board, why you didn't first get
13 Professor Roberts' comments on it.

14 A. We had a board meeting, as I recall, from your reading
15 of this, coming up, I wanted to give them a heads-up to
16 one of the topics of discussion, give them some
17 information about it, and what my thinking was.

18 Q. One answer, which is not the one you've just given, but
19 I'd like you to consider, is that you didn't in fact
20 care about what any scientific answer might be to the
21 concerns that you had raised; you took a business view
22 that three months' assessment would help find funding
23 for phase 3.

24 A. If you mean by funding the partnership with the
25 pharmaceutical company, that's -- that is correct.

1 I felt this would be necessary to have some signal that
2 the drug was potentially effective in order for the
3 development of the drug to continue into a phase 3
4 study, and it was my belief that a longer three-month as
5 opposed to two-week examination period, and additional
6 patients -- which had been factored into the trial
7 originally, but then removed -- would be more likely, be
8 more likely, to achieve that goal, yes, the goal being
9 a business goal.

10 Q. We're not quite on the same point.

11 A. Okay.

12 Q. What I'm suggesting is -- let me approach it like this:
13 Professor Roberts, as we know from the initial
14 correspondence explained to you his view that the Hireos
15 scale did have predictive power, correct?

16 A. He did.

17 Q. Yes. So, if your concern was simply "do we have
18 something which will give us predictive power", my
19 suggestion is that you would have waited to see what
20 Professor Roberts -- the expert -- told you, and I'm
21 suggesting that your real concern was just to find some
22 way of getting a three-month assessment, because that
23 would attract the pharmaceutical companies.

24 Now, that's fair, isn't it?

25 A. I think that's fair.

1 Q. Yes. So all this business about Hireos not being
2 predictive is just a vehicle for trying to get
3 a three-month assessment, correct?

4 A. No, and let me explain my answer. If Dr Bermak had come
5 back to me and said, "This is the best thing since
6 sliced bread", I would have been relieved and happy for
7 all kinds of reasons that I'm sure you can imagine,
8 because we had -- it was going to take time to implement
9 any kind of a change, there were logistical and
10 financial issues involved, and I would have preferred
11 a different answer from him, but having that answer in
12 hand I felt, in the best interests of Xytis, and
13 I understood from all the regulations it was Xytis's
14 capability as a sponsor to change the clinical trial
15 design.

16 Q. You see, what that doesn't explain, with respect,
17 Dr Simmon, is why -- okay, you've got Dr Bermak's view,
18 expressed in the way it is, from the source that it is.

19 A. Yes.

20 Q. But what you haven't explained is why you didn't put
21 first to Professor Roberts those concerns and wait to
22 see what his response is and then weigh that up and
23 present the two together to the board before you
24 launched off, and I'm suggesting that the reason why you
25 didn't follow that obvious procedure was because you

1 weren't interested in the scientific potency of Hireos
2 as a tool. What you wanted was a reason to get an
3 assessment done at three months, because that would, in
4 your view, look right for a pharmaceutical company, just
5 the fact of an assessment at three months. Have I got
6 it right?

7 A. I believe that it -- a Glasgow outcome scale measurement
8 at three months would be a good -- a better than the
9 Hireos scale at two weeks, indicator of potential
10 efficacy, yes, I believe that, and that was what I put
11 forward.

12 Q. But the trouble is that 400 patients is not going to be
13 enough, is it, to deliver a significant signal?

14 A. It won't deliver significance, but if this trial at 400
15 patients had no signal, it should never have been
16 conducted, because you're not going to get a big
17 pharmaceutical company, which is seeing so many failures
18 as Dr Roberts is pointing out, in this indication -- if
19 you don't have any signal you're not going to get
20 anybody to do the next trial. It's -- A follows B and
21 there's certainly no assurance -- and then I'll let you
22 get in your words -- there's no assurance that you're
23 going to see such a signal with 400 or 500 patients.

24 Q. I understand that's your business point of view. It's
25 fair to say that that is a criticism of the design of

1 the trial, isn't it?

2 A. Yes.

3 Q. And it's a criticism of the way the contract has been
4 set up?

5 A. It is a criticism that after I consulted with several
6 experts in statistics and one who had an analysis -- had
7 been involved in a trial design, came up and I felt it
8 was my responsibility to inform the board of it and take
9 action.

10 Q. I'm not challenging that at all.

11 A. Okay.

12 Q. What I'm talking about is the means by which you pursued
13 it, because what I suggest is you've identified what, in
14 your business judgment, was a basic flaw with the trial
15 as a business proposition, correct?

16 A. Correct.

17 Q. But what that meant was that you wanted to change the
18 terms on which the arrangements had been set up with
19 LSHTM, correct?

20 A. Yes, it would have meant changes in the protocol and
21 potentially changes in the contract as well, yes.

22 Q. Yes, and what you have done, since then, ever since
23 then, is you've been looking for ways to try and get
24 LSHTM to agree to go along with a different bargain and,
25 if they wouldn't agree, to evict them from the trial.

1 That's correct, isn't it? Get them off and get someone
2 else in who will agree to a different trial.

3 A. I have to say that -- I think this correspondence
4 reflects this -- I was surprised -- and perhaps that was
5 naively so -- that Dr Roberts wouldn't be interested in
6 a trial that collected more data -- including safety
7 data -- at three months and had more patients in it than
8 the original trial.

9 I was surprised at that response.

10 Q. But I'm asking about your motivation, not about what you
11 think about him?

12 A. Okay, my motivation came through scanning through the
13 literature and looking at trials that had been run in
14 stroke and traumatic brain injury and looking at how
15 many of them had a two week end point, and basically,
16 there weren't any.

17 This scale, the Hireos scale, was developed as
18 a part of a trial that actually, I believe, had a six
19 month Glasgow outcome scale outcome, and it was my
20 business belief, reading the science -- which guided
21 me -- to say: nobody is doing this, so here is a little
22 company, Xytis, that is going to suddenly create a new
23 scale and have somebody invest, as you say, in a phase 3
24 trial, which was our goal from day one.

25 Q. I'm just asking you to agree -- again to stand back from

1 the day-to-day events and see if you can either agree or
2 not with this proposition, that what you've been doing
3 is trying either to get LSHTM to go along with
4 a different trial from the one they signed up to or get
5 them off the trial and get someone else in. Is that
6 a fair overall summary of your approach?

7 A. My original goal -- and I've looked through all the
8 correspondence up through, you know, middle
9 of October -- my original goal was, yes, get LSHTM, not
10 to get them out of it, but to get them to change the
11 trial design. That was my goal. I thought they would.
12 They resisted.

13 MR JUSTICE BURTON: But once they wouldn't?

14 A. Once they wouldn't, because I felt that this was -- that
15 this trial was then being run for science, which --
16 ICH-GCP guidelines say: you can't just run a trial just
17 for running a trial, you have to have an expectation
18 that patients in this trial and future patients may
19 benefit. I lost that expectation based on the comments
20 of Dr Bermak, and reinforced by Dr Berry.

21 MR JUSTICE BURTON: So?

22 A. And, therefore, I believed it was necessary to change
23 the trial design or it would be unethical to continue.

24 MR BEAR: Did you ever tell the board that it would be
25 unethical to continue with this trial as it currently

1 stood? Because I haven't seen that.

2 A. I don't know, I don't remember.

3 Q. Let's look in bundle C7, please -- I'm afraid we're
4 going to have to go through this in the light of your
5 answers -- let's look first of all at 2103.

6 This is Professor Roberts' letter of 30th August
7 now.

8 "Thank you for your email message of 17th August
9 about extending the observation period in the
10 BRAIN Trial."

11 MR JUSTICE BURTON: I'm sorry, page?

12 MR BEAR: 2103, my Lord. I'm afraid it is a detailed
13 letter, but because of the witness's answers we need to
14 go through it.

15 He starts off with the scientific issues, yes, which
16 he says are the most important, and the heading is:

17 "Low statistical power for efficacy end points."

18 Do you see that heading under the 1?

19 A. Yes.

20 Q. He goes on to explain:

21 "The primary objective of the trial is to evaluate
22 safety. Assessing the effect on mortality and morbidity
23 is a secondary objective and for good scientific reasons
24 the BRAIN Trial with only 400 randomised patients has
25 very little statistical power to detect a plausible

1 treatment effect."

2 He cites a section of the protocol which says the
3 same thing.

4 So the protocol itself -- let's just look at it,
5 because I think it bears on the answer you gave:

6 "Absence of any well-established surrogate measure
7 for patient outcome after acute TBI is an important
8 methodological consideration in the context of clinical
9 trials in this patient population. The second important
10 consideration is that realistic treatment effects in
11 this context are likely to be modest. Indeed, there is
12 now widespread recognition that large absolute
13 reductions in death or disability cannot realistically
14 be expected in the treatment of acute traumatic brain
15 injury."

16 Let me move on:

17 "Nevertheless, even modest improvements in patient
18 outcome, absolute risk reductions of the order of
19 3-5 per cent, would be clinically important if this
20 could be achieved by a treatment as widely practicable
21 as XY2405. Taken together, these methodological
22 considerations suggest that it would be unrealistic to
23 expect unambiguously clear signals of treatment efficacy
24 to emerge from a phase 2 trial, first because there is
25 no established surrogate measure, second because the

1 modest improvements in patient outcome that might
2 reasonably be expected from XY2405 might be obscured by
3 the play of chance in a phase 2 trial. The primary aim
4 of this phase 2 trial is, therefore, to provide data
5 that will allow an assessment of the effect of treatment
6 on patient safety that will inform the judgment as to
7 whether it is appropriate to proceed to the phase 3
8 trial."

9 My point to you is this, Dr Simmon: this is the
10 document which is actually been approved by the
11 regulators, and it says in terms: we are not expecting
12 to get any evidence of efficacy. We just want to find
13 out if it's safe to run this trial on several thousand
14 people. Do you agree with that?

15 A. No.

16 Q. Tell me why you disagree?

17 A. Because there are efficacy end points. If we -- to say
18 that you are going to do those measurements and say we
19 don't expect statistical significance -- and I disagree,
20 although Professor Roberts has run one very large trial
21 and I believe he is involved in another trial in
22 traumatic brain injury, let me tell you what the basis
23 of this original starting point. It was a trial known
24 as Bradycor. In that trial, which enrolled ultimately
25 139 patients -- I think they had about 133 evaluable --

1 there was a reduction in mortality at six months from
2 28 per cent to 20 per cent.

3 In that trial -- and I believe it's one of the
4 literature -- it should be one of the literature
5 citations in the investigator's brochure, maybe it's in
6 the protocol -- there was an improvement of not
7 statistically significant, anything I'm telling you
8 right now is not statistically significant. There was
9 an improvement of 10 per cent -- 10.3 per cent at three
10 months and 12 per cent or 12.5 per cent at six months in
11 the Glasgow outcome scale, that's the Bradycor study
12 published in 1999 by Marmarou et al.

13 Dr Roberts asserts that the results in this trial
14 will only be 3 or 4 per cent. Anatibant -- the only
15 test of Anatibant -- excuse me, of this mechanism of
16 action that Anatibant has, which is interfering with
17 a specific receptor, the only test ever run suggested
18 the effect could be larger than 3 or 4 per cent. It
19 didn't prove it; it just suggested that that was
20 possible at three months and at six months in terms of
21 Glasgow outcome scale and one can see how, at three
22 months, there's a 27 per cent reduction in mortality,
23 and at six months it was a 28 per cent reduction in
24 mortality. That's a scientific published study, it's
25 not the speculation of one man. It's a scientifically

1 published study. Our drug works by the same mechanism.

2 I hope that the effect is larger than 3 or
3 4 per cent, but I don't know, I don't know if it will
4 have any effect whatsoever, but I think that the chance
5 of detecting an effect, not statistically significantly,
6 but enough so that someone, hopefully Xytis and its
7 partner, but possibly not, would conduct a phase 3
8 clinical trial.

9 Q. I understand all that.

10 A. My --

11 Q. Sorry, but the point I was on was your assertion that
12 you thought it would be unethical, you said it wasn't
13 really a matter of business convenience, but you thought
14 it would be unethical to run the phase 2 trial without
15 going for some further evidence of efficacy.

16 The point I was making to you was that the protocol
17 itself, the approved document, accepted and acknowledged
18 that there was unlikely to be any significant evidence
19 of efficacy.

20 So from that it surely follows that there is no
21 ethical problem, because the regulators have approved
22 a trial in which there is no expectation of achieving
23 any data that will tell you anything about efficacy.

24 A. Then why are the (inaudible) measurements in there?

25 Q. They are in there because they might as well be

1 collected.

2 MR JUSTICE BURTON: I was looking in the protocol to find
3 where it is. What paragraph number in the protocol is
4 this?

5 MR BEAR: I'd need to check.

6 MR JUSTICE BURTON: We've got the protocol in the core
7 bundle at tab 3, no doubt someone can find it.

8 MR BEAR: I think it's probably in section 9.

9 MR JUSTICE BURTON: At any rate, Dr Simmon, the point that's
10 being made to you is --

11 A. It refers to a modest effect. That's what the
12 protocol --

13 MR JUSTICE BURTON: The protocol says it would be
14 unrealistic to expect unambiguously clear signals of
15 treatment efficacy?

16 A. That to me means statistically significant. When it's
17 unambiguous it is statistically significant. That's
18 unambiguous and that's all I'm asking. I'm not
19 expecting a statistically significant unambiguous
20 answer.

21 MR JUSTICE BURTON: I think Mr Bear accepts that you wanted
22 commercially -- and you've accepted that -- a change in
23 the protocol and a change in the contract at this stage
24 once you realised, fully at any rate, with the benefit
25 of Mr Bermak's advice, that you weren't going to get,

1 really, any particular indications of efficacy on the
2 basis of the trial as then constituted. You've accepted
3 that that was going to mean changing the contract and
4 changing the protocol. But you've then gone further in
5 saying that it would be unethical to continue with the
6 trial -- or in your view it was unethical to continue
7 the trial -- if you didn't get some indication of
8 efficacy.

9 Mr Bear then asked you: did you ever tell your board
10 members that? And you couldn't remember whether you
11 had. He was then further asking whether you could
12 really say that it was unethical given that the protocol
13 itself authorised -- and that was approved by the
14 regulators -- the trial knowing that it was not likely
15 to come out with any signs of efficacy.

16 Of course, there would be some indications of
17 efficacy. You wanted more indications of efficacy.
18 Understood all that. But it's this question that you've
19 raised of "unethical" that he's asking you about. Are
20 you really saying, in the light of that protocol, that
21 the trial was unethical if it wasn't going to come out
22 with some indications of efficacy?

23 A. No, I mean -- excuse me, my Lord, when do you a clinical
24 trial, it's an experiment. You don't know what the
25 outcome is going to be.

1 MR JUSTICE BURTON: No.

2 A. And I didn't say: if we do 400 at two weeks, we won't
3 get anything. What I suggested was, if we do
4 a three-month at 500, we would improve the chances of
5 seeing if anything was there, improve the chances.

6 MR JUSTICE BURTON: Yes, no doubt about it.

7 A. I don't know if the drug is safe or efficacious, and
8 I won't know really the answer to that if this trial had
9 gone to 400 patients, because --

10 MR JUSTICE BURTON: I understand all that. That's why you
11 had commercial reasons for wanting to change it.

12 A. Okay.

13 MR JUSTICE BURTON: But if it was your point that to carry
14 on with the trial in the light of what Mr Bermak had
15 said, to carry on the trial in its present form would be
16 unethical, that's what you're being probed about.

17 A. Okay.

18 MR JUSTICE BURTON: Do you really say that, given the
19 approved protocol in this form?

20 A. If, in my belief, if, in my belief, I am in charge of
21 a trial, and it has no chance of going to a phase 3 --
22 and I continue treating patients -- it's my belief
23 I would be acting unethically according to the ICH-GCP
24 guidelines, where I am putting patients at risk, but
25 I have no belief -- because I don't think the pile is

1 big enough and whatever -- that there is going to be
2 a signal which will result in a phase 3 trial. Signal,
3 not a proof.

4 MR JUSTICE BURTON: Did you put it to Professor Roberts that
5 it would be unethical to continue in those
6 circumstances?

7 A. No, I don't think I did.

8 MR BEAR: We can see that from the last page in the bundle,
9 2107, your letter of 3rd September:

10 "Dear Ian, I am in only partial agreement with the
11 recommendations and comments from Dr Bermak ...
12 A shorter, more complicated trial is not what Xytis is
13 recommending. We believe that more patients ... not
14 fewer, are desired and that a three-month observation
15 would increase the possibility of detecting a positive
16 signal, not statistically significant in all likelihood
17 in this trial.

18 "I of course understand that safety is the primary
19 end point. It is equally important to understand that
20 if the results show Anatibant is safe, there is no
21 evidence of efficacy, there will be no phase 3 trial."

22 You go on to say: no-one will ever put money into
23 it, whether it's a pharmaceutical company, investor or a
24 government.

25 So I understand that's your business position.

1 A. Yes, that is my business --

2 Q. But surely, if you had an ethical concern, you would
3 have mentioned it in this letter, do you not think?

4 A. At this time?

5 Q. Yes, at that time.

6 A. Yes, sir, I agree with you.

7 Q. And the reason you didn't is because, putting it
8 bluntly, this is an argument that's occurred to you now,
9 and you think you might as well put it into the mix.

10 A. That I might as well, I'm sorry?

11 Q. You might as well advance it in court. It's
12 something -- a point that's occurred to you now.

13 A. It didn't occur to me now, I'm not sure -- I couldn't
14 put a date on it, but I was concerned about running
15 a clinical trial in two ways.

16 Q. When do you think it occurred to you?

17 A. I expressed in a board meeting -- I realise the board
18 meeting minutes are quite vague -- my concerns of the
19 CEO running a trial in which I had concerns about GCP
20 compliance, couldn't be sure we were in compliance, and
21 that in a trial where there was no expectation for
22 either business reasons or ethical reasons that an
23 outcome would lead us forward.

24 However, having said that -- if I may finish --

25 Q. Go on.

1 A. -- I will say to you that as CEO of the company it was
2 my responsibility to utilise the investments we had made
3 the best way I thought fit for the company, and that
4 included running the phase 2 trial that had the highest
5 probability of success, success being defined as just
6 some signal, and that would have been my primary concern
7 at that time.

8 MR JUSTICE BURTON: You'd lost confidence in there being any
9 point in the phase 2 trial at this stage, is that right?

10 A. Yes, sir, that's correct.

11 MR JUSTICE BURTON: As constituted?

12 A. As constituted, yes, sir.

13 MR JUSTICE BURTON: I thought that was it.

14 MR BEAR: You referred to the board minutes. Let's look at
15 2098. These are the minutes of a regular meeting of the
16 board of directors of Xytis held at Irvine, California,
17 on September 4th, 2007, and they are redacted, but we're
18 given to understand that we've got everything that
19 relates to the trial we're concerned with.

20 A. Yes.

21 Q. So we can see who's present, the directors, and also
22 someone called Curtis Mo, the company's outside counsel,
23 do you see that at 2098?

24 A. Yes, sir.

25 Q. He's from a law firm, isn't he?

1 A. He's from a law firm, yes.

2 Q. And then you chaired the meeting, and Mr Mo kept the
3 minutes thereof?

4 A. Yes.

5 Q. Is that correct?

6 A. Yes.

7 Q. And then operations update, next Mr Simmon and then
8 I think Kelvin Gee must be concerned with your other
9 product, so we can ignore him?

10 A. Yes.

11 Q. "... updated the board on the status of the company's
12 clinical trials, product development projects and
13 regulatory strategy for [the other one] and Anatibant as
14 well as the status of research and development in
15 pre-clinical trial efforts of the company for other
16 compounds. Questions were asked by the board and
17 answered and discussion ensued."

18 And that's it, isn't it, that's the whole of the
19 minute?

20 A. That's the unredacted, I think -- that's the redacted
21 version.

22 Q. This is the redacted.

23 A. The redacted version, sorry.

24 Q. Is that really all you keep as a company in terms of
25 board minutes?

1 A. Yes, sir.

2 Q. So Mr Mo from his law firm, is this the full extent of
3 his minute?

4 MR JUSTICE BURTON: Well, it's redacted in order to remove
5 any reference to anything which has got nothing to do
6 with this case.

7 A. That's correct.

8 MR JUSTICE BURTON: But is there anything else relating to
9 this case which was said, or is that all there was?

10 A. That's all that's in the minutes that's related to this
11 case. I asked Mr Mo to provide the minutes to Dechert.

12 MR JUSTICE BURTON: So after that it deals with other
13 things, but in relation to this trial that's all there
14 was in the minutes?

15 A. Yes, sir, that is correct.

16 MR BEAR: Because all your minutes are in this very vague
17 and formulaic form, and it occurred to me -- it may be
18 I'm wrong -- that perhaps there's some other note that's
19 kept somewhere or some other record so that the
20 directors can see what was actually said and what was
21 actually decided, which we don't get from here. Is
22 there some other note that's kept somewhere if it's not
23 called a minute?

24 A. Not to my knowledge.

25 Q. No?

1 A. And I don't do that.

2 Q. Did you notice Mr Mo writing anything down during the
3 meeting?

4 A. I --

5 Q. You always have an outside lawyer present.

6 A. Yes, either on the phone or in person, yes.

7 Q. When they're in person, do you notice them keeping --
8 keep notes?

9 A. Yes, they keep notes.

10 Q. Notes of the discussion?

11 A. Yes, sir.

12 Q. We haven't seen those, Dr Simmon.

13 A. I don't have those notes. I sent a request specifically
14 to Mr Mo to provide to Dechert the minutes of the
15 meeting.

16 Q. But there are some other notes --

17 A. I don't know that he still has -- I cannot tell you
18 about his notes.

19 Q. What would happen if somebody said: hang on a second, at
20 board meeting six months ago I think I said this, and
21 there was such and such a discussion, and there's some
22 sort of need to find out what happened, perhaps because
23 a director has changed. How would you go about
24 exploring that?

25 A. You would have to rely on the memory of the board, and

1 the reason I say that is that the minutes are kept, and
2 then whatever Mr Mo then puts into a minuted form is
3 circulated to the board members for their approval, and
4 then that's usually discussed at the next board meeting
5 for any changes, comments or whatever. If they want
6 something put in, they can request it. That's the
7 process.

8 I've seen this on the boards of several companies.
9 This is typical in the United States, where we're even
10 more litigious.

11 Q. You said you don't know if Mr Mo still had the notes
12 that he took during the meeting?

13 A. I have no idea.

14 Q. Can you tell us whether you put Professor Roberts'
15 letter of 3rd -- of 30th August which set out his
16 rationale for disagreeing with the amendment, to the
17 board on 4th September?

18 A. I don't think I did, no.

19 Q. You didn't?

20 A. No, I gave them a subsequent one or two letters from
21 Dr Roberts. I don't think I said --

22 Q. So on 21st August, as we saw, you'd sent the board
23 Dr Bermak's comments incorporated in your email at
24 page 2027, and you'd sent them a detailed view of your
25 dissatisfaction with the trial and the predictive power

1 of Hireos, but you didn't then send the board the
2 detailed response from Professor Roberts, correct?

3 A. I don't recall that I did.

4 Q. No, and if you didn't -- and there is no evidence in
5 writing that you did -- again, that would be giving the
6 board a one-sided and selective impression, wouldn't it?

7 A. I gave them what I thought was -- should be done, that's
8 correct.

9 Q. Do you now think on reflection it was giving them
10 a one-sided and selective impression?

11 A. No, I still hold to the view that the trial should be
12 changed.

13 MR JUSTICE BURTON: Yes, but this letter from
14 Professor Roberts ended:

15 "I think the proposed change is unwise."

16 A. Yes.

17 MR JUSTICE BURTON: "If Xytis is intent that such a proposal
18 should be put before the trial steering committee
19 I think a much more carefully reasoned expert opinion is
20 needed."

21 It's the last paragraph, do you see, on page 2015?
22 It's the end of that. Sorry, 2105, my fault, the last
23 paragraph.

24 So you didn't put this letter before the board, and
25 you didn't get a more carefully reasoned expert opinion?

1 A. Ultimately, I did, but, we're sort of looking at the
2 sausage in the middle of the factory at this point.
3 When I --

4 MR JUSTICE BURTON: Just so we know, when was the
5 "ultimately" that you received this more carefully
6 reasoned expert opinion, when was that?

7 A. That would have been from Yossi Tal, a statistician at
8 Technostat with whom the company had a working
9 relationship, and I'm not sure, but I did in fact
10 provide information to and set up a telecommunication
11 between Yossi Tal and Dr Roberts to discuss this issue.

12 MR JUSTICE BURTON: And when was that?

13 A. It's in a document. Sir, it was
14 late September/early October, I'm not sure when.

15 MR BEAR: Just before we leave this letter, if you go back
16 to 2104, After making the point by reference to the
17 protocol, can you see the next subheading:
18 "A simple ordinal ratings scale can provide useful
19 information."
20 And then --

21 MR JUSTICE BURTON: You're on the wrong page. 2104.

22 A. I'm on 2104.

23 MR JUSTICE BURTON: It's the headline, just -- that's it.

24 A. Thank you.

25 MR BEAR: So:

1 "A simple ordinal rating scale [which is a reference
2 to Hireos, it's a five point scale] can provide useful
3 information."

4 Then he goes on to refer to the genesis of Hireos
5 and he concludes over the page at the end of the
6 paragraph after giving some percentages about its
7 sensitivity and specificity, he says:

8 "We know that the Hireos scale is not perfect.
9 However, it was included at almost no extra cost and we
10 do have data to show that it predicts outcome at six
11 months with a high degree of specificity."

12 So he's actually saying that this scale can provide
13 information that relates to the primary end point, isn't
14 he?

15 A. Yes, he is.

16 Q. And I suggest, by not putting this before the board you
17 were being selective. On reflection, can you not agree
18 with that?

19 A. No, the board was aware of the Hireos scale long before
20 I came on the scene. We had copies of it that were
21 given to board members to the best of my knowledge. It
22 was talked about extensively. There were concerns
23 within the board which you can see in some of Roger
24 Flugel's emails to me, that there had been concern in
25 the past, but Werner pushed through this agreement

1 despite their concerns, and so I -- these numbers
2 appear, I'm assuming Dr Roberts in that publication by
3 one of his masters degree students had these numbers in
4 it and that's where he's getting it from.

5 That Bermak letter considers that and says, well, it
6 has those characteristics if you leave the dead people
7 in. Those people who died in two weeks, sir, are
8 invariably dead at six months, but if you take that
9 population out and look at what happens, the status of
10 people at two weeks, and see how that compares with six
11 months, you get a different answer.

12 So that was the concern that I had. It was
13 confirmed by a statistician, Dr Donald Berry, and so
14 I had a concern.

15 We knew about -- we knew about what Dr Roberts
16 thought.

17 Q. The board hadn't seen his response to Dr Bermak's
18 criticisms, had it?

19 A. When did I -- can you tell me quickly when I got that
20 response?

21 Q. 30th August.

22 A. No, I don't believe it had.

23 MR JUSTICE BURTON: Is that a convenient moment?

24 MR BEAR: Yes, it is, thank you, my Lord.

25 MR JUSTICE BURTON: Thank you. Mr Nash, I've seen this and

1 it's very helpful, but I just want to be absolutely
2 clear what it is -- I know Mr Bear hasn't yet seen it --
3 this is a very clear basis of your case on what I call
4 the primary case, that is, all revolving round different
5 ways of alleging that there was a failure with regard to
6 reconciliation, sufficiently taking into account,
7 cleaning, et cetera, et cetera, et cetera, with regard
8 to SAEs or AEs.

9 What I really want to know is is this now your sole
10 case, put in a number of different ways, because what
11 I said to you was I had a complete lack of
12 understanding, and Mr Bear said he did as well, about
13 any allegations about data collection or management
14 otherwise than as it refers to SAEs, and how and if you
15 were relying on the first audit report, or the second
16 audit report, or any other errors, et cetera et cetera.

17 Now, if this is now your case it's clear and
18 I understand it, but are you intending, by this, to not
19 proceed with all the other subsidiary allegations,
20 because that's the way I understand it from your
21 producing this document.

22 MR NASH: We're proceeding and maintaining a case on the
23 defects in the database, which is the subject of the
24 Wells and Montgomery reports.

25 MR JUSTICE BURTON: That's what I wanted -- you see --

1 MR BEAR: I'm not sure that it is.

2 MR JUSTICE BURTON: -- set out. This is all, as
3 I understood, your main case. What I didn't
4 understand -- though it's very helpful to have it in one
5 and a half pages -- was the fall-back ballpark
6 allegations about data control and data management and
7 errors in audit reports, which I did want set out if it
8 was going to be pursued.

9 MR NASH: My Lord, I think we're talking about perhaps two
10 different things. There's the question of whether or
11 not the database was compliant with GCP and whether it
12 functioned properly, that's all the subject matter of
13 the Wells and Montgomery expert reports.

14 MR JUSTICE BURTON: Yes.

15 MR NASH: That remains live. There is the --

16 MR JUSTICE BURTON: I'd like you to put on a piece of paper
17 the respects in which you are pursuing a case that
18 database management was inadequate. All this is -- as
19 I say, it's very helpful, but I'd largely understood
20 this, this all relates to the adverse events.

21 If you remember Mr Bear's tendentious skeleton in
22 which he said -- and his answer to your issues: I'm not
23 even going to respond to this because I don't know what
24 it is, et cetera. It was that area where I thought we'd
25 all be helped by clarification.

1 MR NASH: Perhaps you misunderstood, my Lord, we
2 certainly -- well, in any event --

3 MR JUSTICE BURTON: There's plenty of time.

4 MR NASH: -- I think we are agreed that is a helpful
5 document.

6 MR JUSTICE BURTON: This is certainly a helpful document,
7 but none of it comes new to me.

8 MR BEAR: I'm not sure at all, actually. With great
9 respect, just looking at this literally now, some of it
10 does look a bit surprising, and --

11 MR JUSTICE BURTON: If it's a surprise, then so be it, but
12 I've gone through and highlighted some of it. I haven't
13 highlighted all of it, about discrepancies, timely
14 reconciliation, et cetera, non-fatal events, deaths.

15 If it goes further than the pleaded case, I'm not
16 shutting you out in any way from having time to consider
17 it, but at least it's, in general, SAEs as a headline.

18 MR BEAR: It is in general. What I'm going to suggest from
19 this -- I see from the bottom it looks like a Dechert
20 document -- perhaps it's not too difficult for someone
21 just to cross-refer this to the expert report.

22 MR JUSTICE BURTON: I'm sure that's capable of being done.
23 At any rate, it's all helpful, this, and if it
24 identifies that you are making a case which goes beyond
25 the pleadings, that's a separate issue, but what I'm

1 more concerned about is knowing what your case is on
2 what I've called the subsidiary case, if there is one.
3 At the moment I'm not impressed by it in the sense that
4 it hasn't got through to me as to whether it has any
5 strength. If there is some strength, fine. If you
6 aren't pursuing it, well then let's know as soon as
7 possible or at any rate what parts of it you're not
8 pursuing.

9 MR NASH: My Lord, there is just one timing issue. Dr Basch
10 needs to be dealt with completely today. It may be
11 necessary to interpose.

12 MR JUSTICE BURTON: We'll interpose Dr Basch.

13 MR BEAR: Shall we take her after the short adjournment?

14 MR JUSTICE BURTON: Yes, shall we do that? We'll take her
15 at 2.05.

16 (1.10 pm)

17 (The short adjournment)

18 (2.05 pm)

19 MR NASH: My Lord, we call Dr Veronique Basch.

20 MR JUSTICE BURTON: Thank you. I should mention I've got
21 a judgment from last week to hand down on Friday at
22 2.00. At the moment, there is some argument about
23 interest in costs, but it may well slim down. It's
24 certainly going to be 15 minutes. Thank you.

25

1 DR VERONIQUE BASCH (affirmed)

2 Examination-in-chief by MR NASH

3 MR NASH: Dr Basch, will you give your full name to the
4 court, please?

5 A. Veronique Basch.

6 Q. And your address, please?

7 A. I live in France, in Collonges-Sous-Saleve.

8 Q. Perhaps your professional address would be easier.

9 A. Sorry, HPM Geneva in Geneva, Petit-Lancy.

10 Q. Thank you. I think you'll have in front of you a bundle
11 of witness statements. If you go to tab 3 within that,
12 can you please confirm, first of all, that that is your
13 statement for the purposes of these proceedings?

14 A. I confirm that this is my statement.

15 Q. And I think there is one thing you want to make
16 a comment on within this statement, if you go to
17 paragraph 18, please, within that statement --

18 A. That is correct. In point 18, I specify that the CIOMS
19 forms were more complete because we asked questions
20 about things which were not covered in the CRF or on the
21 TCC database and we analysed this data.

22 I would like to correct that, as I did not have
23 access to this TCC database. That was actually an
24 assumption, but I cannot really confirm that.

25 Q. So if we delete from that sentence the words "or on the

1 TCC database", the remainder of that sentence is your
2 evidence, is that right?

3 A. Correct, that's correct.

4 MR NASH: Thank you. Would you wait there, please,
5 Dr Basch?

6 Cross-examination by MR BEAR

7 MR BEAR: If you could try to keep your voice up as much as
8 possible, Dr Basch.

9 A. I will try to.

10 MR JUSTICE BURTON: Can I just ask about the C-I-O-M-S
11 forms. They were the ones in which the longer -- the
12 really worrying events were recorded, is that right,
13 what was it called, the --

14 MR BEAR: SUSARS.

15 MR JUSTICE BURTON: The SUSARS, is that right?

16 A. Well, actually the CIOMS form is a format where you
17 would put the data -- it's just a form to put the data
18 in, which is recognised as a standard for reporting
19 adverse events, serious adverse events to the health
20 authorities.

21 In clinical trials, most of the health authorities
22 want to see SUSARS only, although in some European
23 countries, they want to see SARs as well.

24 So it is used for reporting to health authority.
25 However, it can also be used for communicating on the

1 case data to anyone who wants to see this, or may see
2 this data, because it's a very practical pragmatic
3 point.

4 MR JUSTICE BURTON: I am a little unclear. I thought there
5 were the CRF forms, which the CRAs filled out with all
6 the basic information in the format we've seen. Then
7 there was the SAE forms which were sent for
8 pharmacovigilance purposes?

9 A. Correct.

10 MR JUSTICE BURTON: And that CIOMS forms were only filled
11 out if there was a SUSAR. Otherwise it would seem to be
12 completely duplicative of the SAE forms, if you had to
13 do a CIOMS form as well.

14 A. That is something I would like to clarify, is that the
15 CIOMS form, we call it CIOMS forms, they contain not
16 only information which is on the SAE form. They can
17 contain other information which was received after
18 follow-up requests to get queries that could contain
19 information which could be in an autopsy report which
20 was separately received. So it's like -- all the
21 information we receive we actually put it in a database,
22 which contains much more information than the CIOMS
23 form, much more fields, and the CIOMS form is an output
24 of certain data items which are -- which is in our
25 database. But it's not per se just a duplicate of the

1 SAE form, otherwise --

2 MR JUSTICE BURTON: In this trial, where I've heard a lot

3 about CRF forms and the SAE forms, were there any CIOMS

4 forms?

5 A. Yes, we actually internally -- if we want to -- we can

6 print out a CIOMS form from any case which is in the

7 database at any time.

8 MR JUSTICE BURTON: But were any CIOMS forms sent into you

9 by the CRAs on this trial?

10 A. No, CIOMS forms is a form which we, at the

11 pharmacovigilance department, would -- our database

12 can --

13 MR JUSTICE BURTON: So you just compile it from information

14 which you have been sent in?

15 A. Yes, yes, but the --

16 MR JUSTICE BURTON: Sent on the SAE forms?

17 A. On the SAE form and other information we may have

18 received from other pages of the CRF, for example, or

19 from additional questions or MDs have asked --

20 MR JUSTICE BURTON: I'll leave it to you to explore, but, as

21 I understand it so far, the CIOMS forms are not

22 originating forms, they don't come in from down below

23 like the CRF forms and the SAE forms, but are compiled

24 from information which is obtained on one or other of

25 the two primary forms.

1 MR BEAR: Or from further information that HPM request, they
2 effectively dig around, and what you do is you conduct
3 a medical analysis, don't you?
4 A. That's correct.
5 Q. Then you put that medical analysis into the CIOMS form?
6 A. We put it in our database.
7 Q. Okay and then out of the database you can print a CIOMS
8 form?
9 A. From the database, we can print a CIOMS form, and that
10 could be included in there, yes.
11 Q. Yes, so it's your work product as a company?
12 A. Yes, it's basically the raw data plus the added value of
13 our work.
14 Q. Yes, and the added value of your work isn't part of the
15 trial study, as such; it's the safety reporting that
16 needs to go on in conjunction with the trial study?
17 A. I'm not sure how you formulate the beginning of the
18 question. It's part of the trial, because of course
19 it's mandatory by regulatory requirements --
20 Q. It's not part of the work of study in the trial; it's
21 a separate requirement for there to be safety reporting.
22 A. Work of the study? I'm not sure --
23 Q. You don't understand the word "study", do you?
24 Les etudes.
25 A. You mean the clinical trial?

1 Q. The clinical trial is a study, isn't it? This CIOMS
2 form isn't part of the study that is the clinical trial,
3 is it?

4 A. It's an output of the safety data which comes from this
5 trial.

6 Q. It's a separate piece of work that has to go on --

7 A. It's separate --

8 Q. Please let me finish, because I don't want to have to
9 keep you longer than I have to, so don't interrupt and
10 you will be out more quickly.

11 A. I apologise.

12 Q. Now, there's a separate piece of work that has to go on
13 with every clinical trial, which is safety reporting.

14 A. That's correct.

15 Q. And that is not part of the study of the drug; it is
16 a separate flow of work?

17 A. You can put it this way, yes.

18 Q. Thank you. Now, were HPM aware, in general terms, of
19 the rate of recruitment into the trial?

20 A. No, we were not really aware.

21 Q. Not aware? Have no idea how many patients were coming
22 into the trial?

23 A. I think that from time to time we would receive a report
24 on how many patients or informal information, yes.

25 Q. We've seen various print-outs which are said to be from

1 your database and they record SAEs on patients. Are you
2 saying that you had no idea what proportion those SAEs
3 and those patients bore to the total number of patients
4 in the trial?

5 A. I actually, myself, had no access to this information --
6 I didn't receive an email about this.

7 Q. So there's no formal reporting process whereby you are
8 kept up to date with the number of enrolled patients, is
9 that correct?

10 A. Not to my knowledge.

11 Q. And you are a responsible company, I take it?

12 A. Absolutely.

13 Q. If you thought that procedures were defective in any
14 way, you would say so at once and very clearly, wouldn't
15 you?

16 A. Yes.

17 Q. You haven't in fact said that any of the procedures in
18 this trial are defective, have you?

19 A. We have raised a certain number of points whenever we
20 had doubts, we have requested procedures at some points,
21 we have provided our procedures.

22 Q. Can you answer my question? Have you said that any of
23 the procedures in this trial are defective?

24 MR NASH: I think, my Lord, Mr Bear must bear in mind that
25 this isn't this witness's first language, and I think

1 she's struggling a little bit.

2 MR BEAR: Do you understand the word "defective"?

3 A. Yes, I'm trying to remember if we did that.

4 Q. That's fine, you take your time remembering, because

5 it's an important point. (Pause)

6 A. I don't think we have raised that point according --

7 I mean, in relationship to a certain procedure.

8 Q. In relationship to any procedures, Dr Basch, have you

9 said that they are defective?

10 A. No, I don't think we have. But this is not our role.

11 Q. I'm so sorry?

12 A. This is not our role.

13 Q. I think you agreed with me that you are a responsible

14 company?

15 A. Absolutely.

16 Q. And that if procedures were defective you would say so

17 at once and very clearly?

18 A. Yes, if they were deck if I have it in terms -- I mean,

19 we have our own procedures for what we are doing and we

20 are responsible as you pointed out very clearly at the

21 beginning for a part of the work which is a bit aside.

22 Q. Did you know that there were, by the end of August,

23 a large number of patients who had been recruited?

24 Would you have been aware of that in general terms?

25 A. I was not aware of the planned recruiting rate, so --

1 Q. No, I'm talking about the actual number.

2 A. Personally, I was not.

3 Q. You personally didn't have much to do with the trial,
4 did you?

5 A. I was -- actually, I'm leading the team, and my
6 colleague, Mrs Aubes is project manager for this study.
7 She would come to me every time she would have
8 a question, a specific question or an issue, and I was
9 copied on most of the emails.

10 Q. Did you personally have much to do with the trial?

11 A. At the beginning of the study, I was actually --
12 Mrs Aubes was not there, and I was actually --
13 I attended some of the meetings, and, yes, I was
14 involved at the beginning.

15 Q. When did the beginning come to an end, as it were?

16 A. I was very involved at the setting up and Miss Aubes was
17 more involved on the case processing, like day-to-day
18 case processing.

19 Q. All right.

20 If recruitment in a trial is going on fast and let
21 us say 100 or more patients have been recruited, your
22 company would expect a DSMB, if there was one on the
23 trial, to have started meeting and considering patient
24 data, wouldn't it?

25 A. We are not involved in what the DSMB should do or not.

1 I mean, this is a different aspect.

2 Q. I know that English isn't your first language so I'll
3 put the question again and listen carefully.

4 If recruitment in a trial is going on fast and 100
5 or more patients have been recruited, your company would
6 expect a DSMB to have started meeting and considering
7 patient data?

8 A. Our company was not involved in expecting or deciding or
9 even taking -- giving her -- its opinion on what the
10 DSMB should do, because the DSMB is setting its own
11 roles, and we were here to collect the data, analyse it,
12 and provide it to the health authorities, if needed, be
13 in compliance with the regulatory requirements, but not
14 involved at all in the level of recruitment, because we
15 collect all SAEs. Whatever the level of recruitment is,
16 that's what we have to do. We have no opinion to give
17 on --

18 Q. I see, so you're just like a robot, you just follow the
19 tasks you're given to do, and you do them to the best of
20 your abilities and you make your medical analysis and
21 that's it, correct?

22 A. I don't think we were like robots, because we analyse
23 the data on a patient-by-patient basis and it's much
24 more personalised, a personalised approach.

25 Q. But you don't do anything outside your remitted task,

1 you have no expectations outside that task, you don't
2 offer any opinions, correct?

3 A. If we are asked to. We are service provider, and we
4 provide services and advice on what we're asked to, yes.

5 Q. What advice were you asked to provide in this case, in
6 this trial?

7 A. In general?

8 Q. Well, at all.

9 A. We were asked to discuss the definition of the adverse
10 event. We were asked to review the safety path of the
11 protocol, and we were asked to provide feedback on
12 the -- you actually provide the SAE form, the guidelines
13 for completing the SAE forms. Our responsibilities
14 included the collection of the data, putting it in
15 a validated database in order to comply with all
16 regulatory requirements, and report any appropriate SAE
17 to the health authorities, and to the ethics committees.

18 Q. Okay.

19 Now, the database that you provide, have you given
20 print-outs from that to Xytis or to Xytis's lawyers for
21 the purpose of these proceedings?

22 A. We have been requested to give an access to the database
23 recently.

24 Q. We have various print-outs in these bundles. Let me
25 show them --

1 A. Line listings, you mean?

2 Q. Let's look at bundle number 10, please. Could you go to
3 page 2808? There's a document here that runs through to
4 page 2815, if you could just glance through it,
5 Dr Basch?

6 A. Yes.

7 Q. Now, this comes in the bundle -- just keep your finger
8 in the database. If you go back to page 2806, so two
9 pages before where we started, there's a copy of an
10 email which in fact I see you were copied in on?

11 A. Correct.

12 Q. So it's from your colleague, Dr Aubes or Mrs Aubes?

13 A. Yes.

14 Q. "Please find attached the SAE line listing."
15 Do you think that what we have at 2808 is the line
16 listing that was attached to this email?

17 A. Looks like it.

18 Q. It looks like it. Does your database have a date on it
19 that says what date the data is presented at?

20 A. You mean the date the line listing was issued?

21 Q. Well, on the document beginning at 2808 -- and there are
22 obviously lots of dates associated with individual
23 patients and information, but there's no date for the
24 document. It doesn't say: this is the database as at
25 such a date. Do you see what I mean?

1 A. Yes, I see what you mean.

2 Q. Now, is that always the way that your database comes
3 out, one doesn't have a date for when the document is
4 compiled?

5 A. I would think that -- let me check. (Pause). I think
6 this is a standard line listing.

7 Q. How are we to know -- how is the reader to know at what
8 date this database is being presented? You see, it
9 purports to show the SAEs but up to what final date?

10 A. My colleague actually ran a line listing which I believe
11 is according to the request which was made, all SAEs
12 reported to date. Of note, this line listing was
13 prepared in less than an hour, so it was an urgent
14 request which was dealt with very urgently, and it's not
15 like -- if we would prepare line listings for official
16 documents, of course there would be titles which would
17 define this very quickly -- very, very accurately, and
18 this was done very quickly because it was an urgent
19 request.

20 Q. I understand.

21 A. And it was run and there were no reasons why -- it was
22 not stated in the request why this line listing was
23 needed, and it was (inaudible).

24 Q. Can you tell us up to what date this database is
25 accurate?

1 A. Up to what date it is accurate?

2 Q. Yes, look, what your database shows is a -- it's

3 a compilation of the SAEs, isn't it?

4 A. Yes.

5 Q. And that must mean up to a certain terminal date,

6 a final date?

7 A. Yes, I believe that this is the exact -- what was

8 provided that day was all the SAEs which were in our

9 database for this trial.

10 Q. As at when, though? On that day, do you mean?

11 A. On that date.

12 Q. We have no way of knowing that from the document, do we?

13 A. From the line listing, no.

14 Q. No. How many -- do you know how many SAEs there are in

15 this document?

16 A. Well, I would have to count them. You mean SAEs or

17 cases?

18 Q. Well, let's just take it by stages. If we just look at

19 the first page, 2808, if we look at the penultimate

20 column, please, it's got the heading which says: "Main

21 event", "verbatim" and "other symptoms."

22 A. Yes.

23 Q. As I interpret that -- but you must tell me if I'm wrong

24 because it's your company's document -- the first entry

25 in each row under this column gives what your company

1 considers is the main SAE, is that correct?

2 A. We have, a requirement is by A to B, which, I mean, is
3 a guideline which defines how the -- the safety
4 databases are formatted and how the data should be
5 presented, that one event should be always chosen as the
6 main event. This is because in some instances, we would
7 have to provide line listings for periodic reports where
8 we have to classify them by system (inaudible).

9 Q. I didn't ask you to justify it. I simply wanted you to
10 agree or disagree. Does the first entry in each row for
11 this column show what your company considers is the main
12 event, yes or no?

13 A. Yes.

14 Q. Yes?

15 A. Yes.

16 Q. And then does the second entry -- in italic text --
17 record the original doctor's description, the verbatim
18 entry?

19 A. That's correct.

20 Q. And then sometimes -- but not in every case -- there
21 will be a description of other symptoms, correct?

22 A. That's correct. It's other events.

23 Q. Yes, I was going to say symptoms of what?

24 A. It's events.

25 Q. So is the word "symptoms" wrong?

1 A. The word "symptoms", yes, is --

2 Q. Why have you put it in your database, then, if it's

3 a validated, audited database, why is the terminology

4 wrong?

5 A. It's the terminology which is used in this line listing,

6 it's a standard --

7 Q. Has an auditor said to you: this is wrong?

8 A. No.

9 Q. When was your database audited, on what date?

10 A. I don't have the precise date in mind, but it was

11 audited -- I think it was a year ago.

12 Q. Was it still being developed?

13 A. Well, we have -- this database has not been developed by

14 us. It's a product which has been developed by a third

15 party company which was audited, and because the

16 regulations change very regularly, the products can be

17 updated, yes.

18 However, every time there is an update, we run

19 scripts and validation tests.

20 Q. When was it validated, your database?

21 A. When?

22 Q. Yes.

23 A. Well, actually, the product is validated at the vendors,

24 and we validate the changes and we validate the fact

25 that the changes occur as they should at our end,

1 because it's a web based product.

2 Q. If we look at this document at 2808, will you take it
3 from me, because I've tried to count it, that there are
4 50 cases, 50 patients, and we can go through it if you
5 want, or I can ask you to -- after you've finished your
6 evidence.

7 A. I can take your word.

8 Q. Okay, if I'm wrong, someone will tell us afterwards,
9 because it's visible on the face of the document. What
10 I've counted, Dr Basch, is: 50 cases plus or including
11 six cases where there is what is referred to as "other
12 symptoms", okay?

13 So, for example, we can find another symptom at the
14 top of page 2809.

15 A. You mean an additional event in a case?

16 Q. I'm just using the terminology of your line listing.

17 A. Yes, yes.

18 Q. "Other symptoms". Okay, is there an example of that in
19 the entry which actually crosses over the page:

20 "Xytis 00006."

21 The main event is cardiac arrest, the verbatim
22 description is cardiac arrest on mechanical ventilation,
23 then there's what you call another symptom or another
24 event, haemodynamic instability. Have I interpreted
25 that correctly?

1 A. I think this is correct.

2 Q. So there are six of those. So that gives us a total of
3 56 SAEs, doesn't it, in this line listing?

4 A. I will have to count because I am just wondering if
5 there are not more.

6 MR JUSTICE BURTON: Take it for the moment that that's
7 right, 56.

8 MR BEAR: I'm quite happy to be corrected, because
9 barristers are notoriously very bad at maths.

10 MR JUSTICE BURTON: There are 50 entries, six of which are
11 double entries, in the sense of having two SAEs within
12 the same column, so that makes 56, right. So take that
13 as a given for the moment.

14 A. 56 events and 50 cases, that's what you say.

15 MR BEAR: Can you go forward in the bundle to 2820,
16 Dr Basch?

17 A. Right.

18 Q. Here we've got another print-out from your database, is
19 that correct?

20 A. Yes, it looks so.

21 Q. I want to you look through it. Go to the last page
22 which is 2827. Yes?

23 A. Yes.

24 Q. Can you see the last patient is number 68 in the first
25 column?

1 A. Yes.

2 Q. And if you go back to the previous listing that we were
3 looking at -- keep your finger in this document, but go
4 back to page 2815, please?

5 A. Yes.

6 Q. That ends with the same last patient, doesn't it?

7 A. 68, yes.

8 Q. 68, okay. Now, go to page 2820. Can you see the
9 heading that's been put on there:
10 "48 SAEs, seven non-fatal."

11 A. Yes.

12 Q. As you read that -- I appreciate you may not have
13 prepared this document -- did you prepare it?

14 A. No.

15 Q. But as you read it, does that mean there are 48 serious
16 adverse events? Is that what it appears to mean?

17 A. Yes, yes, that's what I --

18 Q. You see, because again -- and I may have to be
19 corrected -- I have counted 48 cases with then a further
20 four additional events.

21 A. Right.

22 Q. Okay?

23 A. But I don't know what is this -- when this was provided
24 and for which --

25 Q. You don't know what?

1 A. When this line listing was provided --

2 Q. I don't know, it's come from Xytis's solicitors. So we

3 just have it in the bundle. It's been put forward as

4 your company's document, and I think you think it is.

5 A. It is.

6 Q. What about the heading? Who put 48 SAEs on it?

7 A. I'll have to count them. (Pause).

8 MR JUSTICE BURTON: You're being asked about heading. Take

9 it from us for the moment that there are 48 entries,

10 four of which have double entries --

11 A. Right.

12 MR JUSTICE BURTON: -- of SAEs, and all you're being asked

13 about is who put the heading on.

14 A. I believe it is my colleague, Ms Aubes.

15 MR JUSTICE BURTON: And that would be accurate insofar as it

16 refers to 48 numbers of patients, but it would be wrong,

17 wouldn't it, if what you're being told is right, to say

18 48 SAEs. It's 48 patients, but it's 52 SAEs, isn't that

19 right?

20 A. It would be 48 case -- yes, SAE cases, obviously from

21 what --

22 MR JUSTICE BURTON: Yes, on the assumption it's 48 entries,

23 four of which are double entries, it should have been

24 described as 52 SAEs?

25 A. Yes.

1 MR JUSTICE BURTON: 48 patients, yes?

2 A. I believe so.

3 MR BEAR: Yes, but the point that I'm trying to put to you
4 is that, if my maths is right, my arithmetic, then the
5 heading is wrong because it refers to SAEs.

6 MR JUSTICE BURTON: She's accepted that.

7 MR BEAR: You have accepted that?

8 A. I said yes.

9 MR JUSTICE BURTON: Yes.

10 A. If your maths is right, I agree.

11 MR BEAR: Entirely on that assumption, and I stand to be
12 corrected. Do you know what date this document refers
13 to, what is the point in time up to which this document
14 applies?

15 A. No, this document is just presented to me like this.
16 I don't know.

17 Q. Unless we have some external evidence such as a letter
18 to which a database is attached, or somebody's knowledge
19 that it was prepared on a certain date, we can't tell
20 from the document which date it applies to, can we?

21 A. From this document, we cannot. What I can just add as
22 a comment is that we -- the only situation where we had
23 to provide official line listings from our database, for
24 regulatory reasons, was when we prepared the annual
25 safety reports and whenever we do these line listings,

1 they have all the dates and the titles and everything.
2 We have been requested several times for informal line
3 listings which look like these ones.

4 Q. Can you tell us what the number of SAEs -- not patients,
5 but SAEs -- was in your company's database as at
6 19th October 2007?

7 A. By heart, I can't remember. I think it's somewhere in
8 my witness statement.

9 Q. Is it in your statement?

10 A. I think it's somewhere:

11 "On 19th October, the HPM database showed 43 safety
12 cases and 49 SAEs."

13 Q. Where are you reading from?

14 A. This is point 21 from my witness statement.

15 Q. And how did you satisfy yourself when you made your
16 statement? What evidence did you have that this
17 sentence was correct?

18 A. Well, we looked -- we looked at our database and counted
19 the cases.

20 MR JUSTICE BURTON: As I understand it, this document comes
21 in the bundle after 1st November, so someone has guessed
22 that this date is 1st November, and if that's right,
23 it's 52 SAEs on 1st November.

24 A. But here we're talking about the 19th October.

25 MR JUSTICE BURTON: Of course, but -- yes, indeed, but

1 1st November was of course the date of the meeting of
2 the DSMB. The DSMB based itself, as I understand it, on
3 statistics as of 19th October.

4 So it may be the suggestion is, of whoever put this
5 in the bundle, that this is the 19th October document,
6 but I don't know.

7 MR BEAR: It's not a suggestion we can make, because this is
8 evidence coming --

9 MR JUSTICE BURTON: Whoever put the bundles together has
10 assumed, I think, this is the 19th October document.

11 MR BEAR: I don't know whether they --

12 MR JUSTICE BURTON: But on any basis that's 52 and not 49.

13 MR BEAR: I just want to ask Dr Basch a little more, if I
14 may, my Lord, about --

15 MR JUSTICE BURTON: Of course. Counsel's question is, just
16 so that he goes on: where did you get your statement at
17 the end of paragraph 21, which is not backed up by any
18 documentation, that on 19th October the HPM database
19 showed 49 SAEs, because at the moment I for one am
20 unhappy that that is necessarily accurate given that we
21 have got a document saying 48 SAEs which you have
22 accepted is inaccurate. That's the problem I have. So
23 what did you look at when you said 49 SAEs, and is it
24 possible that you were looking at a document which was
25 just as inaccurate as this one?

1 A. I believe that the only thing which was inaccurate in
2 this document is writing SAEs instead of SAE case
3 reports.

4 MR JUSTICE BURTON: Yes.

5 A. This was done manually, and we redid the counting after
6 running a line listing on 19th October -- from the
7 19th October data log point, and came out with the
8 numbers which are in my witness statement.

9 MR JUSTICE BURTON: I see that. You're not able help us at
10 the moment what the document is that you looked at when
11 you gave that evidence in paragraph 21?

12 A. I looked at the database and --

13 MR BEAR: What, on the screen or on paper?

14 A. Whenever you run a line listing, it appears in a pdf so
15 you can look at it.

16 MR JUSTICE BURTON: This statement was given on
17 12th February 2008.

18 A. Correct.

19 MR JUSTICE BURTON: So what counsel is asking is whether you
20 looked at a screen, which presumably would have been as
21 of February 2008, or whether you were looking at
22 a database -- a print-out which at least purported to be
23 as of 19th October?

24 A. I remember -- I think we took a line listing which had
25 been prepared around these dates and eliminated the

1 cases which had been received after the data log of
2 19th October.

3 MR BEAR: So you actually did some work, did you, to work
4 back to what you thought would be the position as at
5 19th October?

6 A. Because we were asked for this date, to provide data on
7 that date, what was the case on that date.

8 MR JUSTICE BURTON: Well what does it show now? We're not
9 very long after 12th February, we're 26th or
10 27th February now. Without doing any work on it, what
11 does your screen say today was the number of SAEs? Are
12 you able to tell us? Obviously not at this minute.

13 A. So how many SAEs are in our database today?

14 MR JUSTICE BURTON: Yes.

15 A. I think it's about 76 or something. But I'm -- around,
16 around 76.

17 MR JUSTICE BURTON: SAEs or patients?

18 A. SAEs.

19 MR JUSTICE BURTON: So that would be how many patients?

20 A. I don't know precisely. This is a living -- really
21 a living document, and we receive data daily.

22 MR JUSTICE BURTON: Yes.

23 A. To add on SAEs.

24 MR JUSTICE BURTON: Presumably it didn't very many less than
25 76 two weeks ago when you did this statement. So

1 whatever it said then -- say it said 70 -- you worked
2 back to 49. How am I to have confidence that that's an
3 accurate statement?

4 A. Actually, the safety databases are set up in a way that
5 you can really extract data which starts from one date
6 to another date, which we call data lock point, and so
7 you can really ask the database to provide you with that
8 line listing which covers a certain period of time, and
9 that's what we can use.

10 MR BEAR: If we can look at the document that we were
11 looking at, 2820, take a look at the last entry again on
12 page 2827, Dr Basch:

13 "Xytis 000068."

14 A. 2827?

15 Q. Page 2827, in the final entry, please.

16 A. Yes.

17 Q. You see, if we look at the pre-penultimate column, there
18 are three dates in it, aren't there: 19th October,
19 23rd October, 29th October.

20 A. Right.

21 Q. How can you tell now what this database would have said
22 if one had looked at it on 19th October? How can you
23 tell?

24 A. Well, we know when we receive the data this is entered
25 in a database, also from follow-up information, this is

1 all in the database.

2 Q. You can estimate when it might have been filled in, but
3 can you actually tell what the database would have
4 looked like on 19th October? Can you tell us, can you
5 assure us of that or not?

6 A. I can assure you of which cases had been received on
7 19th October.

8 Q. No, I'm asking about the database, not about the receipt
9 of cases. Can you tell us what the database looked like
10 on 19th October or not?

11 A. Say the database is a living document. Whenever we
12 change something in a case, let's say a case was
13 received on 18th October, it is in the database, and it
14 would appear in the line listing.

15 Say we receive a follow-up after that date,
16 in January, for example, which says: okay, we know now
17 that the patient -- that the patient took this or that,
18 other drugs, this is added up to the case.

19 There is an audit trail which allows us to exactly
20 know which data was entered on which date by who, and
21 this is -- because it's a validated database.

22 However --

23 Q. Have you gone through that exercise?

24 A. No.

25 Q. You personally? No.

1 A. For that line listing, you mean?

2 Q. I'm sorry?

3 A. For that line listing or in general to look at some
4 cases?

5 Q. For the purposes of this statement, Dr Basch?

6 A. No.

7 Q. Your answer is no, I think?

8 A. No.

9 MR BEAR: Thank you, I don't have any --

10 MR JUSTICE BURTON: So it's possible that paragraph 21 of
11 your statement should read 52 SAEs rather than 49? This
12 document does look as though it's pretty close to the
13 time of 1st November, because it's got these October
14 entries, and if that SAE in relation to the last patient
15 was recorded on 19th October -- it's one of the dates --
16 and if the penultimate one was reported on
17 18th October -- which is two of the three dates that
18 antedate 19th October -- then you could say that all
19 these SAEs were in place on 19th October, and that means
20 that it would be 52, not 49?

21 A. Our database comes from the date the SAE is received by
22 anyone in the sponsor or representing the sponsor.

23 MR JUSTICE BURTON: Yes.

24 A. The date which counts here is the first receipts date,
25 that's the fourth column.

1 MR JUSTICE BURTON: In that case, why is this not the answer
2 that, as of 19th October, according to this document,
3 there were 52 SAEs and not 49? Because all the dates
4 here show the first received date, a date prior to
5 19th October.

6 A. Well, here it says 30th October. If I take page 2827,
7 last case, for example, the fourth column which
8 represents the first received date --

9 MR JUSTICE BURTON: Which page is that on?

10 A. 2827.

11 MR JUSTICE BURTON: Yes, which page is that? I'm so sorry,
12 2827, yes.

13 A. If you look at the last case and you look at the fourth
14 column, it says 30th October. That's the date which
15 counts.

16 MR JUSTICE BURTON: I see. I was looking at the last
17 column.

18 A. That's the therapy start.

19 MR JUSTICE BURTON: I see, thank you very much. So that may
20 be the answer, that you did use this document in
21 arriving at your 49. You took this document, which
22 is -- you ignored the heading, and you got it correct at
23 52, and then you took off those last three entries, is
24 that right?

25 A. Yes, we counted --

1 MR JUSTICE BURTON: Those last --

2 A. We took off the ones which were received after that

3 date, after the 19th.

4 MR JUSTICE BURTON: You should have taken four of them off,

5 looking at the last page.

6 A. I'm confused about which one you're looking at.

7 MR JUSTICE BURTON: The page you're referring me to, 2827.

8 A. Yes, you should take off --

9 MR JUSTICE BURTON: All four of those came in after

10 19th October, so in fact --

11 A. 68, 67, 66, 65.

12 MR JUSTICE BURTON: Yes, so there are four of them?

13 A. Yes, it is four.

14 MR JUSTICE BURTON: So in fact on this -- if this is the

15 right document, it's 48 SAEs, not 49?

16 A. If this was -- I believe my -- actually my countings are

17 correct, so I would have to recount everything to agree

18 with you, but --

19 MR JUSTICE BURTON: Yes.

20 MR BEAR: In this document starting at 2820, Dr Basch, how

21 many additional events which is headed "other symptoms",

22 can you see? Can you tell us now, while you're on the

23 document. So start at 2820. Just take us through it,

24 each case where there's an additional symptom,

25 additional event?

1 A. So the first would be 006 on page 2821.

2 Q. Yes. Go on.

3 A. Then there would be 31.

4 Q. Yes.

5 A. Then there would be --

6 MR JUSTICE BURTON: Just stopping on each one, in relation

7 to the ones where there were these extra events, you

8 don't have a date for when that extra event was first

9 reported, do you?

10 A. Not in this line listing, no. We have it in our

11 database. We receive a set of information, and every

12 time we receive a set of information counts for what we

13 call day zero is when the regulatory clock starts.

14 That's what counts for us. Whether we receive one or

15 two or seven events, it doesn't make a difference.

16 MR BEAR: All right, so we had identified patient 006 and

17 patient 31.

18 MR JUSTICE BURTON: You've counted four, Mr Bear, and the

19 witness hasn't disagreed with you about it.

20 MR BEAR: No, I suggest 34 is another one, correct?

21 A. 34, yes.

22 MR JUSTICE BURTON: Do we need to look at them?

23 MR BEAR: It's simply the total. Then I've got one more on

24 the next page, which is 42?

25 A. Yes.

1 Q. I can't see any more.

2 MR JUSTICE BURTON: No, well, there it is.

3 A. 64.

4 MR BEAR: Yes, you're quite right.

5 MR JUSTICE BURTON: If I have understood the case

6 accurately, Mr Bear -- I'll be corrected no doubt if

7 I've misunderstood by either party -- the CRF forms

8 would come in earlier than the SAE forms. One could

9 have a situation in which the CRF forms show 92 SAEs but

10 the SAE forms are lagging behind.

11 MR BEAR: The evidence is that sometimes that might happen

12 or sometimes the doctor might not complete an SAE form.

13 MR JUSTICE BURTON: If he doesn't complete it at all that's

14 understood.

15 MR BEAR: In theory the SAE form is supposed to be done very

16 quickly, so in theory -- and I think Dr Basch may be

17 able to confirm this -- the SAE form is supposed to be

18 filled in straightaway, faxed to LSHTM, who then fax it

19 on to you, correct?

20 A. That's correct, per protocol the investigator has

21 24 hours to declare any serious adverse events to the

22 TCC.

23 Q. All of that assumes that you're getting one SAE report

24 form per adverse event that is coded as serious.

25 MR JUSTICE BURTON: Yes.

1 MR BEAR: That is the assumption.

2 I don't have any further questions, my Lord.

3 MR JUSTICE BURTON: Thank you very much.

4 Re-examination by MR NASH

5 MR NASH: Just before you go, Dr Basch, one or two further
6 questions.

7 You were asked whether you had raised any queries or
8 suggested to the school that any of the procedures were
9 defective, do you remember that question being raised?

10 A. Yes.

11 Q. Can I show you just one or two documents? Will you take
12 up, please, volume 5 in the chronological bundle? You
13 may need some help with the bundles.

14 Within that bundle, please, look at page 1381. This
15 is an email from you to "brain brain" whom we know is
16 the school, Eva Cachin, who's one of the CRAs, that's
17 right, isn't it, and to Mr Furcha of Xytis. It's an
18 early email, 23rd March 2007, so just about when the
19 trial begins, that's right, isn't it?

20 A. That's correct.

21 Q. And after the first part of the email, you're clearly,
22 from the first part of it, discussing a particular case
23 that has arisen, that's right, isn't it?

24 A. It's the first case which we had received.

25 Q. The first case. And having made some comments about

1 that, you give a series of requests and record some
2 replies to those requests. That's right, isn't it?

3 A. Sorry, I didn't -- couldn't hear very well.

4 Q. Sorry. You make a series of requests in this email at
5 the bottom, about information, do you see that?

6 A. Yes, I'm asking for additional information on this case.

7 Q. If you read this correctly:

8 "Request 1: please provide autopsy report as soon as
9 possible and hospital/surgery report if available."

10 Then the next line is:

11 "Please note that we are collecting death
12 information in the CRF."

13 Where does that comment come from?

14 A. I believe this was an exchange of emails, and I believe
15 that Ms Shakur and myself were actually answering under
16 the paragraph directly, and it doesn't look very obvious
17 here, but I believe that this is -- this is a first
18 answer to the question of -- I had raised. So she said
19 that, because they were collecting death information in
20 the CRF, that's her answer to my request, and then after
21 you can see my further comment on this issue.

22 Q. So she -- you originally request:

23 "Please provide autopsy report as soon as possible
24 and hospital/surgery report if available."

25 She replies:

1 "Please note we are collecting death information in
2 the CRF."

3 Then you respond:

4 "The autopsy report is definitely important for the
5 safety analysis of the cases. The case by itself, it
6 would complete the story and for the analysis of similar
7 reports in the future potential trend, it would
8 definitely be important to have all information there."

9 Similarly, you query or you ask for information
10 about the circumstances and the time of injury. She
11 says:

12 "This is collected in the CRF and would be baseline
13 information. This is a nice to have information."

14 Can I take you through to the end of this series of
15 requests now, please --

16 MR JUSTICE BURTON: Whose statement is that:

17 "This is a nice to have information."

18 Is that you or is that Ms Shakur?

19 A. I believe it was Ms Shakur.

20 MR JUSTICE BURTON: Sorry?

21 A. I believe it was Ms Shakur.

22 MR JUSTICE BURTON: This is collected in the CRF in the
23 baseline information, that's Mrs Shakur, isn't it?

24 A. As well.

25 MR JUSTICE BURTON: They both are Mrs Shakur? Unlike the

1 first one, which Mr Nash suggested to you was -- the
2 first sentence was her and the second was you, this one,
3 unusually, these are both her, is that it, and you don't
4 make any reply at all? I don't know.

5 MR NASH: It may help if you go over to 1382 and see
6 a similar exchange in request 3, again:

7 "This is a nice to have."

8 And request 5 the same sort of thing. Does that jog
9 your memory?

10 MR JUSTICE BURTON: Again it looks like, under request 3:

11 "Time of admission to hospital is not required."

12 That looks like Shakur.

13 "Time of randomisation are collected."

14 That again looks like Shakur. Who says:

15 "This is a nice to have information?"

16 There's a similar one under 5. Then number 6:

17 "Thank you for the answer."

18 That's you certainly.

19 MR NASH: If you look at request 4, please, Dr Basch, you'll
20 see there:

21 "Time study of drug administration, investigator
22 reported the condition was pre-existing, see his email."

23 Then:

24 "Thank you for the answer. This information is of
25 high importance."

1 That I think must -- is that you?

2 A. Yes.

3 MR JUSTICE BURTON: It does look like, "This is a nice to
4 have information", is your response.

5 A. It looks like it. It's difficult to recall, because
6 it's a long time ago, and this email is confusing.

7 MR JUSTICE BURTON: I don't know, but the significance of it
8 may be that I think "This is a nice to have information"
9 refers back to original words used by Mrs Shakur,
10 I don't know. It seems to be her wording in a later
11 email at 1399 where she says:

12 "Anything not asked as part of the SAE report should
13 only be nice to have."

14 It may be a form of expression you were using
15 between the two of you from time to time. It may not
16 matter.

17 MR NASH: Bottom of page 1382, please, Dr Basch.

18 A. Yes.

19 Q. Having given your -- having had your exchanges, there is
20 then a text which I have assumed is you, but correct me
21 if I'm wrong:

22 "Regarding the provision of a line listing every two
23 months, this delay is definitely not satisfactory to us
24 to allow timely analysis and update of the case, except
25 for the "nice to have information". I am not sure how

1 time-consuming for you it is to get a hold of this
2 information, but would it be an option to give us access
3 to the clinical database? Is this even possible?"

4 Then:

5 "I think that it is now up to Xytis to decide on the
6 level of detailed data collection they would like to
7 have in the safety database."

8 The safety database, pausing there, is you, is that
9 right?

10 A. Yes.

11 Q. "For unrelated cases, we could limit our queries to all
12 the questions above except the "nice to have" ones. In
13 addition, we would appreciate if you could send us the
14 SOP of the DSMB. Their opinion would certainly help in
15 raising the line for all of us. Looking forward to your
16 feedback", et cetera.

17 So this appears to be you corresponding with the
18 school --

19 A. Yes.

20 Q. -- about certain procedures and communications?

21 A. Yes, it was about the first case in which -- discussing
22 the level of detail.

23 Q. If we can follow this through by going to page 1404,
24 please, the email which begins halfway down 1404 is from
25 Haleema Shakur, we can see that if we go over the page

1 to 1405. This is her response to your longer email
2 which we've just looked at, you can see that, can't you?
3 A. Yes, it was even before my --
4 Q. I don't think that's right. Your email which begins at
5 the top of 1405 is timed at 1818 on 23rd March. And
6 then on 24th March, page 1404, she replies to that.
7 A. Okay.
8 Q. Do you see that?
9 A. Mm-hmm.
10 Q. "Dear Veronique, thank you very much for your reply.
11 Procedures I find are only truly tested once patients
12 are in the trial."
13 Then:
14 "Regarding the need for autopsy report we have two
15 issues to address."
16 Perhaps, Dr Basch, if you read that through to
17 yourself first just to remind yourself.
18 A. Okay.
19 Q. Then you take this question to Dr Furcha at Xytis, which
20 is the email at the top of the page:
21 "Dear Rowland, I think we should discuss the issue
22 below. All SAEs are different and we cannot think the
23 same as for clinical trial data management. The SAE
24 form is a starting point for data collection and
25 I understand that we have to be pragmatic for most

1 cases, but we will get in trouble if we do not
2 investigate further, at least for a cluster of cases.
3 What is your opinion there?"

4 Summarising what is said here first of all, it
5 appears that Mrs Shakur is saying to you that the
6 information you have on the SAE will be supplied as
7 absolutely required information. That's right, isn't
8 it?

9 A. Yes.

10 Q. And then there's further information which you wish to
11 have which she regards can be supplied by way of a line
12 listing every two months?

13 A. Yes, she was referring to the information which is
14 presented somewhere else in the CRF.

15 Q. What was the outcome of that debate? What was agreed
16 finally on these procedures?

17 A. Well, finally, my colleague, Mrs Aubes, was given access
18 to the database, the clinical database, to look by
19 herself at some of these details which was already
20 somewhere in the CRF, so that it would reduce some
21 exchange and then she could get the information directly
22 from the database -- would reduce queries.

23 Q. So she had a direct access, unrestricted access, to the
24 database?

25 A. Yes, yes, and that covered any queries we may have for

1 information which was present somewhere else in the CRF,
2 but that's just the other ones.

3 MR NASH: Thank you. I have no further questions, Dr Basch.

4 MR JUSTICE BURTON: Does this mean that you were suggesting
5 that their procedures were defective? I can't see any
6 such suggestion here. Were you doing that?

7 A. No. To say, actually, this was the first case we
8 received, so at that time it's always -- there is always
9 like a little -- little adjustments to be done on how
10 we're going to work together and how it would be all
11 set.

12 The only thing -- the only little difference in
13 approach we had is that we thought that for the benefit
14 of the completeness of the data we would really want to
15 get as much information as possible in order -- further
16 along the line -- for Xytis to have a full data set, to
17 be able also to be proactive to detect any trends of
18 safety issues which may arise, and also to be able to
19 rule out potentially safety issues because you have
20 other information which may explain the occurrence of
21 a serious adverse event in a patient.

22 I think -- I believe that maybe Haleema Shakur was
23 of the opinion that we should restrict maybe the
24 requests to the minimum which was useful, which was
25 required maybe, to avoid unnecessary queries to the

1 MR BEAR: Dr Simmon, when you seek an amendment to
2 a clinical trial that's already started, you have to
3 justify with a rationale for that amendment to
4 regulators, don't you?

5 A. Yes, sir.

6 Q. In the case of the amendment that you were proposing
7 in September of last year, you got a company called
8 Technostat to draft the amendment for you, didn't you?

9 A. The statistical part of it in response to what
10 I perceived as the new design, yes, sir.

11 Q. And the individual concern was a Dr Tal, wasn't it,
12 T-A-L?

13 A. That is correct.

14 Q. If you could be given bundle C8, please? Go to
15 page 2121.

16 You can see the covering email on the previous page
17 from Dr Tal, whose first name is Yossi, and then over
18 the page:

19 "Protocol amendment number 3."

20 Now, this first part of it is dealing with the
21 increase in sample size, correct, so this is the --

22 A. The first part of it? Yes, that's the header, that's
23 correct.

24 Q. The sample size was proposing to up from 400 to 500?

25 A. That is correct.

1 Q. And that was, wasn't it, a function of the wish to have
2 a three-month end point. The increase was to allow
3 a suitably large group to participate in the three
4 months?

5 A. A larger than 400 group to participate, yes, sir.

6 Q. Yes. Now let's look at the rationale for the amendment
7 that is put forward here.

8 "The sample size in this trial was specified to
9 provide at least 90 per cent of power to detect
10 a difference of 20 per cent in SAE rate in favour of
11 placebo when compared with combined treatment arms."

12 Then some further technicality in the end of the
13 sentence.

14 Just pausing there, what that's saying is, isn't it,
15 that the size of 400, mathematically, would provide
16 90 per cent power to detect the difference of
17 20 per cent when you looked at all the treatment
18 groups -- all the Anatibant treatment groups -- compared
19 with the placebo group, correct?

20 A. Yes.

21 Q. Then go on:

22 "The power to detect this magnitude of difference
23 between arm pairs, however, is well below 90 per cent."

24 Just pausing there, arm pairs would mean any of the
25 dose groups versus the placebo, correct? I'm just

1 asking you what the words "arm pairs" means.

2 A. I think you're right.

3 Q. It seems to mean something less than the combined
4 treatment group, doesn't it?

5 A. Yes.

6 Q. Go on, look at the last sentence now -- this is the one
7 I want you to focus on:
8 "We wish to increase sample size to provide power of
9 at least 90 per cent to detect search differences
10 between arm pairs."
11 Okay?

12 A. Yes, sir.

13 Q. Now, this is saying that the reason that Xytis would
14 want to increase the sample size is to provide suitable
15 statistical power to detect differences between arm
16 pairs, it is saying: that's your reason for wanting the
17 increase in sample size, is that correct?

18 A. Between arm pairs for SAEs, yes, sir.

19 Q. The fact is, that wasn't your company's reason at all
20 for wanting the increase in sample size, was it?

21 A. The -- we wanted to increase the sample size to detect
22 if there was a signal. However, when you do this --

23 Q. A signal of what?

24 A. I'm sorry, a signal of efficacy.

25 Q. Yes, nothing to do with safety, was it, Dr Simmon?

1 A. Nothing to do with safety, although you get an
2 improvement -- as he points out -- in your safety
3 analysis. So Dr Tal's task here is to explain to
4 regulators what the impact of this is.

5 Q. It's a bit more, isn't it, because when we say
6 rationale, we're talking about the purpose, do you see
7 what I mean, not just what the effect would be, but
8 about the purpose. Is that a fair comment?

9 A. It is a fair comment.

10 Q. Now, what I'm suggesting here is that your company was
11 willing to use a scientific pretext for a business
12 decision. On reflection, is that a fair comment?

13 A. No.

14 Q. No?

15 A. No.

16 Q. Well, tell me why that isn't an accurate description --

17 A. No, sir, I had --

18 Q. Sorry, let me finish the question. Tell me why that
19 isn't an accurate description of what you're doing here.

20 A. To say "that is correct" would pre-assume that I knew
21 what the statistical impact of the size increase would
22 be, which I didn't. I had -- on the --

23 MR JUSTICE BURTON: No, it has nothing to do with
24 statistical impact. What you're being asked about is
25 the purpose. You've accepted that your purpose was to

1 introduce some element of efficacy.

2 A. Right.

3 MR JUSTICE BURTON: The purpose here, on the face of it, is
4 to increase safety and it's being suggested to you that
5 you were -- you may have thought that the purpose of
6 efficacy might include some side effect of improving
7 safety, but your purpose was efficacy and not safety
8 improvement. It's being suggested here that it was
9 being said to have the purpose of safety improvement
10 when in fact your purpose was something different.

11 A. I am -- I understand, my Lord, your argument. I had no
12 idea what the impact on statistical significance in the
13 safety end point would be at the time of the request.
14 Dr Tal is asked in that to come up with the effects of
15 these and explain it if there is any value at all, which
16 there might not have been, in terms of safety, or if
17 there is something that changes in terms of safety, what
18 that is, and this is what he sent me.

19 MR BEAR: I'm asking you to stand back a little and look at
20 the way you operate. It may be it's become second
21 nature to you.

22 Can't you see that what's going on here is you are
23 making a business decision, you're finding an expert,
24 and you're getting him to clothe the business decision
25 in some technical concept? Just think about that.

1 A. I don't have to think about it very long, because that
2 is not the case, sir, because I had -- as I said, the
3 increase of 25 patients per arm might have had no
4 effect, might have had no effect.

5 If you were to challenge me and say: did you know in
6 advance this was going to be it, and then you asked him
7 to arrange it this way? I would say, no, I didn't, and
8 I neither knew it in advance nor asked him to arrange it
9 in that way. I asked for the protocol amendment. This
10 is a format that is used and required for regulators --

11 Q. Just one final question then we'll move on. Did you
12 care whether there was any extra statistical power for
13 detecting safety as between arm pairs? Did you care at
14 all?

15 A. I was pleased that it did, but it was -- as you have
16 stated and I have agreed, my purpose in asking for the
17 number to go up was based on my concern that there would
18 not be any signal of efficacy.

19 MR JUSTICE BURTON: Your rationale?

20 A. My rationale, yes, my rationale.

21 MR BEAR: Yes.

22 Now, you said before lunch that Dr Tal gave
23 statistical input to the board. Did I hear that
24 correctly?

25 A. I don't recall him giving statistical input to the

1 board.

2 Q. His Lordship asked you if there was expert statistical
3 advice provided to the board. I don't want to suggest
4 anything that's wrong, but my recollection -- I'm afraid
5 I haven't found it on the computer, as I haven't tried
6 to scroll back -- is there was a discussion as to
7 whether or not you had given expert statistical advice
8 to the board -- not yourself but through an expert --
9 because you are saying: well, I didn't provide
10 Professor Roberts' letter of 3rd September to the board,
11 I got other people to give an opinion, and in that
12 context I think you mentioned Dr Tal, didn't you?

13 A. No, I mentioned Don Berry from the University of Texas.

14 Q. But Don Berry gave his opinion before --

15 A. He's a statistician.

16 Q. Yes, but he gave his view, his two line view, before
17 Professor Roberts had responded to you, didn't he?

18 A. That's correct. That's the statistician I was referring
19 to.

20 Q. I see. So was there any occasion afterwards, after
21 Professor Roberts' letter of 30th August, in which he
22 disagreed with the statistical basis for seeking the
23 three months' assessment, was there any way in which you
24 either put forward Professor Roberts' views to the board
25 or put forward an expert opinion on those views to the

1 board?

2 A. I did two things subsequently. I copied a full letter
3 of Dr Roberts and his arguments on the issues to the
4 board.

5 Q. What, the 30th August letter on the --

6 A. No, not 30th August, I said subsequently, and I don't
7 remember the date, I would have to look.

8 Q. I'm thinking specifically about the argument that had
9 arisen on the statistical issues, and on 30th August
10 Professor Roberts sent through his letter which
11 contained -- we looked at it before lunch, didn't we --

12 A. Yes, sir.

13 Q. -- a detailed scientific exposition of his reasons for
14 disagreeing with the amendment?

15 A. Yes.

16 Q. Did you put that letter before the board, yes/no?

17 A. Not that letter. Another letter.

18 Q. Did you put any outside statistician's advice relating
19 to the content of Professor Roberts' letter before the
20 board?

21 A. No, sir, I did not.

22 Q. In fact, Dr Tal of Technostat and Professor Roberts
23 spoke in September, didn't they, about the amendment?

24 A. I arranged that meeting. They did speak by telephone.

25 Q. If we look in bundle C8, please, at page 21 -- sorry,

1 it's 2164. It's an email that actually begins at the
2 very bottom of the previous page.

3 MR JUSTICE BURTON: I'm sorry to interrupt, I have found the
4 reference to Dr Tal. It was page 106, and it was --
5 you're right -- in the context of my asking the witness
6 about whether he got any more carefully reasoned expert
7 opinion. That was in response to the last paragraph, if
8 you remember, of Professor Roberts' letter when he said:
9 "If you were going to think of getting an amendment,
10 you ought to get more carefully reasoned expert
11 opinion."

12 I then said:

13 "So you didn't put this letter before the board and
14 you didn't get a more carefully reasoned expert
15 opinion?"

16 Then I said:

17 "When was the 'ultimately' that you received this
18 more carefully reasoned expert opinion?"

19 And you said:

20 "That would have been from Mr Yossi Tal, a
21 statistician at Technostat with whom the company had
22 a working relationship, and that was
23 late September/early October."

24 I don't know whether that was what you had in mind.

25 MR BEAR: It was, so what Dr Simmon was saying there was not

1 that he provided Dr Tal's view to the board, but that he
2 obtained it as an expert opinion himself. That's how
3 I read it.

4 MR JUSTICE BURTON: Is that right?

5 A. That's correct, sir.

6 MR BEAR: That's very helpful, thank you. If you look at
7 the very bottom of page 2163, yet another of these email
8 strings, so you can see the last line, from Yossi, okay,
9 right at the foot of the page?

10 A. Yes, sir.

11 Q. Okay, then we go over. On 11th September at 9.26 to
12 yourself and others, subject:

13 "Amendment discussion with Ian."

14 And after an apology in the first paragraph, he says
15 this:

16 "I had a rather long and I feel productive
17 discussion with Ian. He presented his case for not
18 measuring three-month outcome and, truth be told, he all
19 but convinced me. There are of course arguments for and
20 against, some of which have been mentioned, and some new
21 ones, but for me the bottom line is what will provide us
22 with the greatest likelihood of showing some promising
23 trend towards efficacy. He claims ..."

24 Then he goes on to summarise what he sees
25 Professor Roberts as having argued. Then in the last

1 full paragraph:

2 "The issues seem to me complex, aren't they always,
3 and require additional discussion. What I suggested to
4 Ian is that I write a document summarising our
5 discussion, send it along to him to ascertain that what
6 I heard was actually said, and then send the final
7 version to Xytis. Is this acceptable..."

8 Okay?

9 A. Yes, sir.

10 Q. So Professor Roberts has all but convinced Dr Tal not to
11 amend, hasn't he?

12 A. He has all but convinced Dr Tal -- and he didn't;
13 convince him, that's what it says, "all but" -- and this
14 is on the efficacy end point, the three-month efficacy,
15 not the 500, I believe, but I wasn't part of that
16 conversation, but I -- if my recollection serves me,
17 Dr Roberts wasn't really against 500. The concern that
18 Dr Roberts had in his arguments to me, in writing and to
19 the ones I presented to the board, were against the
20 three-month end point.

21 Q. Didn't you read this as saying, Dr Tal saying to you:
22 look, Professor Roberts has more or less convinced me?

23 A. No, I read it for -- as the words are written. He is
24 "all but".

25 Q. So your evidence is this, that you read this as Dr Tal

1 saying: I'm not really convinced at all by
2 Professor Roberts?

3 A. No, that's not what I said.

4 Q. What do you understand by the words "all but"?

5 A. I said "all but", he didn't quite get there, that's my
6 understanding.

7 Q. He's come very close, hasn't he?

8 A. That's what I -- I would agree with that.

9 Q. Dr Tal doesn't say anywhere here: I actually disagree
10 with Professor Roberts, does he?

11 A. Yes, he said there are pros and cons, and in that
12 I believe he's saying that he agrees with some things
13 and some things he doesn't agree with.

14 Q. He hasn't said I disagree with Professor Roberts'
15 conclusion, has he?

16 A. I interpreted the pros and cons to mean that.

17 Q. You weren't interested in the pros and cons in the
18 slightest, were you, Dr Simmon?

19 A. (Pause). If Dr Tal had come back with a very negative
20 analysis of this I think I would not have proceeded on
21 that basis. The fact that he said there's pros and
22 cons, which Dr Roberts said there are many pros --
23 I don't think he enunciated any cons -- this is another
24 expert doing a statistical analysis, not a biologist,
25 and he says there are pros and cons.

1 MR JUSTICE BURTON: Well, he says:

2 "The issues seem to me complex and to require some
3 additional discussion."

4 A. Which I believe, my Lord, he refers to between himself
5 and Ian, if I understood the rest of that.

6 MR BEAR: What I want to suggest, Dr Simmon, is that you
7 weren't interested in any additional discussion. Can
8 you answer yes or no to that, please?

9 A. I don't believe that's correct.

10 Q. Let's look at your email at the top of 2163, please. So
11 this is -- not your email -- forgive me -- Dr Tal's
12 email but referring to you. So he emails Mr Furcha on
13 12th September the following day:

14 "Subject: Amendment discussion with Ian. It is no
15 problem. I have spoken to Vince in the meanwhile and it
16 would seem that the three-month follow-up is a final
17 decision so that he wants the matter referred to the
18 steering committee ASAP. I will call Ian today and do
19 my best to convince him that despite his opinion, and to
20 some degree mine, the follow-up should be done."

21 You had told Dr Tal, hadn't you, that you weren't
22 interested in the pros and cons, it was a business
23 decision, and it was final. Do you agree?

24 A. I believe the follow-up would be the three-month study,
25 that I believed -- and we've only looked at the SAE part

1 of this and not the efficacy part, which is part of that
2 three-month follow-up, because it was a different
3 measurement scale, and I felt, as I have expressed
4 previously, that this drug, if it showed no efficacy in
5 its phase 2 trial for 400 people would effectively be
6 dead, and if it did have benefit to society, that would
7 be a tragic loss, and that I felt that our company
8 should do the utmost to determine if there was a signal
9 of efficacy.

10 Q. Had you told Dr Tal that you weren't interested in the
11 pros and cons, it was a business decision and it was
12 final? I suggest you had, and I suggest that's what
13 this email records. Can you agree with that
14 proposition?

15 A. I will agree with that proposition.

16 Q. Thank you. Now, can we move forward to 2190.

17 Can you look at the bottom half of the page as there
18 are two emails that are on this page?

19 A. Yes.

20 Q. Can you see those little arrows? There's an email that
21 you sent on 19th September, isn't there, at 12.37 am,
22 beginning:

23 "Gentlemen, thanks for hanging in there."

24 A. Yes, sir.

25 Q. And you sent that to -- we can't see who, but presumably

1 to people including Professor Roberts?

2 A. Yes, sir. I mean, may I comment?

3 Q. Well, just look at the second paragraph beginning:

4 "Ian ..."

5 Can you see that?

6 A. Yes, sir.

7 Q. "Werner made some significant errors while at Xytis.

8 I include among them not having Xytis recognised as the

9 sponsor of the trial and having no voting members on the

10 TSC."

11 Just pausing there, what was the error in not having

12 Xytis recognised as the sponsor of the trial and what

13 was the error in having no voting members?

14 A. I was referring specifically, as sponsor of the trial,

15 to something that we discussed -- although I don't think

16 it's minuted -- at the meeting with Joann Data and

17 Rene Goedkoop, at a meeting at the London School, and we

18 talked about the fact that on the "brain brain" site, or

19 the BRAIN Trial site, Xytis was essentially invisible.

20 So that's the reference to the sponsor part.

21 Q. What about no voting members on the TSC?

22 A. The TSC is strictly Dr Roberts, Haleema Shakur, Mr Frost

23 and two other outside members. We had no voting

24 membership in it. It's really the London School telling

25 the London School how to run the trial.

1 Q. Do you agree that that was built into the contract, the
2 situation you've just described?

3 A. It was -- yes, and I said that was a mistake.

4 Q. And recognition of the -- well, let's focus on this
5 voting members. So you were saying that the contract
6 was a mistake?

7 A. That element, that element, correct.

8 Q. So you thought it was a bad bargain that Dr Tschollar
9 had struck for Xytis?

10 A. Bad, incorrect, I'll accept bad.

11 Q. Okay, sub-optimal?

12 A. Thank you. I accept.

13 Q. Thank you.

14 You wanted to change the terms of the bargain,
15 didn't you, in what you saw as Xytis's interests?

16 A. I did not propose that we change the structure of the
17 trial steering committee. If, to be done all over
18 again, I would have, perhaps, but that's speculation at
19 this point. I only say that -- you know, it seems to me
20 that was a bad idea.

21 Q. The trial steering committee had jurisdiction under the
22 contract to decide whether to change the protocol for
23 any reason, didn't it?

24 A. Yes.

25 Q. And you wanted to change the protocol, but you couldn't

1 do it because of the trial steering committee which
2 Professor Roberts chaired, correct?

3 A. Correct.

4 Q. And you wanted to end that situation one way or another
5 either by getting LSHTM to relinquish the scientific
6 controls built into the contract, or by getting them out
7 of the trial?

8 A. I think if we follow this through you will see there
9 were a lot of attempts to get the trial changed, none of
10 which were successful.

11 Q. I am trying to put a slightly more general proposition.
12 Do you agree with my general proposition.

13 A. Would you repeat it, please, sir?

14 Q. Yes. You wanted to change the situation with the trial
15 steering committee, with Professor Roberts chairing it,
16 stopping the amendment. You wanted to get LSHTM to
17 relinquish that scientific control, or else get out of
18 the trial.

19 A. If I may restate what you've said to more expressly be
20 clear about what my intent was, I never proposed
21 a change to the trial steering committee. It is my
22 understanding -- and it's been confirmed by emails from
23 MHRA -- that the sponsor ultimately has the authority
24 over the protocol, ultimately is responsible for the
25 trial, and that the structure, as it stood, did not give

1 the sponsor what it has a responsibility for, yes.

2 So, to your question, I have restated, yes, I wanted
3 the protocol changed and I did perceive, I think
4 incorrectly at first because there were these series of
5 documents, I referred to the PC and I think Dr Roberts
6 subsequently corrected me, to look at different
7 documents which gave that authority to the TSC.

8 Q. On this issue of the amendment, you thought it was very
9 important, didn't you?

10 A. Yes, sir.

11 Q. And I suggest you wanted to get the amendment either by
12 getting LSHTM to agree or, if they would not agree, by
13 getting them out of the trial. That's correct, isn't
14 it?

15 A. Not at this time. I felt we could get the amendment
16 achieved. It wasn't until --

17 Q. At what time, then?

18 A. In reviewing this information, I think that it was some
19 time after the meeting that was held in London where
20 I thought -- and Mr Furcha thought when we left -- that
21 we basically said, you know, to use my Lord's words,
22 we've got a bad marriage here, we want to get divorced
23 and how do we do it. I thought that was -- and both of
24 us communicated that to --

25 Q. That was the meeting of 26th September, was it?

1 A. I believe that's the correct date, yes, sir.

2 Q. Yes.

3 A. So there were some subsequent things and numerous
4 attempts to try to find a way not to get the London
5 School out, but to keep it in.

6 Q. I suggest that what you did, Mr Simmon -- Dr Simmon
7 forgive me -- was this: that you started on a campaign
8 of legal threats against LSHTM in an attempt to force
9 them either to back down or else to provide a pretext
10 for getting them out of the contract. Do you agree with
11 me?

12 A. I don't remember when the first what we'll call "legal
13 letter" was, I don't recall.

14 Q. Forgetting the timing, do you agree that's an adequate
15 description of the overall campaign?

16 A. The goal, being advised by attorneys Dechert, was to
17 have the London School change the protocol and stay
18 a part of the trial, and there were discussions between
19 me and lawyers at Dechert about -- under English law --
20 how that might best be done.

21 Q. What if they wouldn't go along with that, then what was
22 the goal?

23 A. We were quite surprised that they wouldn't go along, so
24 there was sort of an escalating series of letters which
25 ultimately Dr Roberts said to me on -- after -- at first

1 agreeing on 29th October to submit this to the TSC and
2 two days later he wrote: basically I'm not doing it,
3 period.

4 MR JUSTICE BURTON: Can I go back to a question you were
5 asked a little bit ago, page 173?

6 Mr Bear said to you:

7 "I suggest you wanted to get the amendment either by
8 getting LSHTM to agree or, if they would not agree, by
9 getting them out of the trial. That's correct, isn't
10 it?"

11 And you said:

12 "Not at this time. I felt we could get the
13 amendment achieved. It wasn't until ..."

14 Then you were interrupted before you completed that
15 sentence. Can you help me what you were going to say?

16 A. It wasn't until Dr Roberts, some time late in October --
17 and I believe it was on the 31st when it was sort of
18 like, no way will I do this, up until then there had
19 been some back and forth -- I had sent things where
20 I felt that he had been willing to consider it under
21 certain circumstances. I looked at ways to try to
22 achieve that. We even discussed going up to 600,
23 because he felt that would be even better than 500. So
24 it's looking at ways to accommodate and find a way that
25 the London School would be willing to change the

1 protocol and would stay on as the CRO.

2 And ultimately, when I got this letter on the 31st,
3 it was pretty clear nothing -- there wasn't any way.

4 There was no way.

5 MR JUSTICE BURTON: So then you did form the view that was
6 put to you by Mr Bear, you wanted to get the amendment
7 either by getting LSHTM to agree or, if they wouldn't
8 agree, by getting them out of the trial.

9 By 31st October, that was your aim?

10 A. The 31st October, receiving that letter, it was clear to
11 me that he was not going to change his mind, and the
12 next day was the DSMB meeting, and he didn't have to
13 change his mind.

14 MR JUSTICE BURTON: Yes, I follow.

15 MR BEAR: Go to 2207, please. This is your email to
16 Professor Roberts of 20th September.

17 A. Yes.

18 Q. You refer to the trial in general terms, three-fourths
19 of the way down the page:

20 "One of the problems we have had is that the rules
21 of the game contract between us has been interpreted
22 differently by each side. As a result, we sometimes see
23 the other party as not playing by the rules. This was
24 certainly true in the case of the reimbursement versus
25 fixed price contract. We face that issue again over the

1 issue of the amendment of the clinical trial. Nowhere
2 in the contract is the TSC given control over the design
3 of and amendments to the clinical trial. According to
4 the contract, GCP, EMEA and FDA guidelines, that remains
5 the responsibility of the sponsor.

6 "I have carefully listened to your arguments for not
7 doing a three-month or greater end point, but my
8 business decision is to attempt to obtain as much data
9 as possible on this trial. If you are [then that should
10 be "unwilling"] to accept my decision, then we will need
11 to make an orderly transition for LSHTM to turn over the
12 trial to another ..."

13 MR JUSTICE BURTON: I think we're both having difficulty
14 following you. You said 2287?

15 A. I heard 07, but I lost where you were too.

16 MR JUSTICE BURTON: The transcript says 2287 (transcript
17 amended). There we are.

18 MR BEAR: That's my voice.

19 MR JUSTICE BURTON: And I was on 2287: you were on the right
20 page, I'm so sorry. 2207, thank you.

21 MR BEAR: My Lord, I picked it up at the penultimate break
22 on the page:

23 "One of the problems ..."

24 MR JUSTICE BURTON: Thank you.

25 MR BEAR: I've read that paragraph, and then the next

1 paragraph over to the end.

2 MR JUSTICE BURTON: Yes.

3 MR BEAR: "My business decision is to attempt to obtain as
4 much data as possible from this trial. If you are [and
5 that should be "unwilling"] to accept my decision then
6 we will need to make an orderly decision for LSHTM to
7 turn over the trial to another entity."

8 I suggest, Dr Simmon, by this stage you were
9 entirely clear that if LSHTM wouldn't agree, they had to
10 go.

11 A. I was suggest that as a possibility, yes, sir.

12 Q. You weren't suggesting it as a possibility because you
13 used the words "will need". You were suggesting it as
14 an inevitability, weren't you?

15 MR JUSTICE BURTON: And then the next sentence.

16 A. "If you are unwilling". Yes, sir.

17 MR BEAR: So it was either: agree to something which is not
18 in the contract, or else get out. That is a fair
19 summary of your position.

20 A. Through an orderly transition, yes, sir.

21 Q. The reality is that you told them it was in the
22 contract, but it wasn't, was it? They didn't have to
23 agree to an amendment under the contract, did they?

24 A. I think I referred to the fact that the sponsor,
25 according to the regulation under which we were

1 functioning, gave that authority to the.

2 Q. The protocol is the governing instrument of any clinical
3 trial, isn't it?

4 A. It is until modified.

5 Q. Until modified?

6 A. Yes.

7 Q. And LSHTM were not obliged to agree to try and modify
8 the protocol, were they?

9 A. They were not obliged to try to mod -- I think what
10 you're saying is to modify the protocol per my request.

11 Q. Yes, they weren't obliged to do it at your request, were
12 they?

13 A. I believe that's correct.

14 Q. So why did you threaten them with an allegation of
15 breach of contract in this document:

16 "We see the other party as not playing by the rules.
17 We face that issue again over the amendment of the
18 clinical trial."

19 Why did you threaten them with that, Dr Simmon?

20 A. I'm looking for the word "breach the contract". Am I --
21 or is that an inference?

22 Q. I didn't use the words "breach of contract". What you
23 said is:

24 "... the rules of the game contract between us has
25 been interpreted differently by each side. As a result,

1 we sometimes see the other party as not playing by the
2 rules. This was certainly true in the case of [the
3 costs issue]. We face that issue again over the issue
4 of the amendment to the clinical trial."

5 That is -- whether you use the word "breach" or
6 not -- a suggestion that they are not abiding by the
7 contract, and I'm asking you to explain to his Lordship
8 why you chose to make that suggestion to my clients.

9 A. I explain this. I say "according to the contract", and
10 that, I would have to say -- I probably wrote this
11 poorly.

12 "According to the contract and GCP" would be:

13 "According to the contract we must follow GCP, and
14 GCP, ICH, EMEA and FDA guidelines give authority to the
15 sponsor for the design of the trial."

16 Ultimately. Ultimately the sponsor is responsible
17 for that in the guidelines. If I were to re-write that,
18 I would probably try to do that correctly. It's clearly
19 not in my best recollection in the agreement, the CTSA.

20 Q. I'm just going to ask you one more time: can you explain
21 why you threatened my clients with a suggestion that
22 they were breaching the contract? If you can't explain
23 it, say so and we'll move on. If you have an
24 explanation, give it to us?

25 A. I've given my response to the best of my ability.

1 Q. Now let's look forward to 2228, please. This is
2 a redacted email. We don't know the reason for the
3 redaction. It's dated 26th September, from yourself to
4 the members of the board:
5 "Subject: LSHTM."
6 Then the bit we can see starts:
7 "Rowland and Ian met last week to discuss these and
8 other problems ..."
9 We have no idea of knowing what that refers to.
10 "... to hopefully find a way to resolve them.
11 I joined them for two hours, about, by teleconference.
12 We seemed to be making some progress, although Ian was
13 refusing to accept that we had the right to modify the
14 trial design."
15 MR JUSTICE BURTON: Mr Nash, have you looked at the original
16 of this email?
17 MR NASH: I haven't personally, my Lord.
18 MR JUSTICE BURTON: Would you kindly do so overnight?
19 MR NASH: I will.
20 MR JUSTICE BURTON: It does look as though there ought to be
21 some part of the earlier part of the text which would
22 seem to be material, because "these and other problems"
23 suggests that although there may be other immaterial
24 matters, "these problems" must be referred to.
25 MR NASH: I'm being told something from behind, my Lord.

1 I'm told it's been redacted on privilege grounds.
2 David Schulman is a lawyer at Dechert, but I will make
3 some further enquiries about that.

4 MR BEAR: My friend will bear in mind that just by copying
5 a lawyer in on a document it doesn't become privileged,
6 whatever may be the position taken in some American
7 jurisdictions.

8 MR JUSTICE BURTON: Yes, it's widely distributed. Mr Mo is
9 a lawyer as well.

10 MR BEAR: Yes, Mr Mo is a lawyer.

11 MR JUSTICE BURTON: Mr Furcha is not.

12 MR BEAR: I think Emmanuelle Trombe may also be a lawyer.
13 But Mr Furcha is not. If you choose to copy a lawyer
14 in, that doesn't alter the status of the document.

15 MR JUSTICE BURTON: Mr Nash knows the position full well and
16 I'm sure we can rely on him.

17 MR BEAR: Of course we can, we have to.

18 MR JUSTICE BURTON: Thank you very much.

19 MR BEAR: So you refer to a meeting then in the previous
20 week, so that would be the week containing the
21 19th September, and then:
22 "Yesterday afternoon, Rowland and I flew to London
23 to meet with Ian and Haleema to hopefully find the way
24 forward. When the meeting started, Ian launched into
25 a tirade about the failure of Xytis to make payments and

1 several other topics. He refused to yield on the
2 three-month time point amendment issue. What had been
3 planned as a meeting to find some reconciliation turned
4 into a dust-up that lasted just over an hour. The only
5 agreement reached was that we would part ways in an
6 orderly fashion."

7 Then you go on to say:

8 "We are just beginning the process of determining
9 how best to go about an orderly transfer to a new CRO.
10 In the meantime, we had enrolled 178 patients as of
11 24th September."

12 Just pausing there, was it correct that an agreement
13 was reached to part ways in an orderly fashion?

14 A. I listened to everything you said then, and you asked me
15 to focus on one thing and I'm --

16 Q. Was it correct that there was an agreement reached
17 between you and LSHTM the day before this email to part
18 ways in an orderly fashion, which is what you were
19 telling your board directors?

20 A. That is my belief.

21 Q. You see, I suggest that was untrue. Can you go forward
22 to 2235 --

23 MR JUSTICE BURTON: Can I just interrupt a moment to see
24 what would be convenient for you? This case that I have
25 fixed at 2.00 for tomorrow for the convenience of one of

1 the parties, because he was in the Court of Appeal, it's
2 now occurred that the Court of Appeal have shifted their
3 case to 2.00. So I'm now going to put them in in the
4 morning.

5 What would be more convenient for you? To start
6 a little late and then we will sit until 5.00 to make up
7 time, rather than to break off in the middle? I would
8 have thought that's the more sensible course, isn't it?

9 MR BEAR: Yes.

10 MR JUSTICE BURTON: If I say not before 11.00 -- well, not
11 before 11.00 for the start tomorrow, and we'll sit until
12 5.00, is that all right?

13 MR BEAR: Yes. Thank you very much.

14 We don't need to look at the detail of this letter,
15 Dr Simmon. It's dated 26th September.
16 Professor Roberts refers in detail again to the
17 discussion on the proposed amendment, gives more
18 reasons, and then at the end, on the next page, the last
19 sentence:

20 "We do accept, however, that more power to assess
21 safety could be an advantage and so, as we have
22 indicated, we would be willing to discuss this issue
23 further."

24 Do you see that?

25 A. Yes.

1 Q. No-one would write that if they had agreed to part ways,
2 would they?

3 A. I took this as a -- Ian sort of coming back to the table
4 and saying: look, maybe there is something we can do.

5 Q. No, my point is that no-one would write this if they had
6 previously agreed to part ways.

7 A. I've responded to the best of my ability, sir,
8 I believed that this letter was Dr Roberts coming back
9 to me and saying: you know, maybe there is something we
10 can do.

11 Q. Look at 2238, please.

12 A. Sure.

13 Q. This is your letter of 27th September.

14 A. Yes.

15 Q. Lengthy reference to the clinical trial services
16 agreement at the top:

17 "Dear Ian, let me first thank both you and Haleema
18 for meeting with Rowland and me in London this past
19 Tuesday and the frank nature of our discussions."

20 Go forward please to the next page and to the
21 subheading halfway down:

22 "Ongoing LSHTM to enrol."

23 Do you see that?

24 "Lastly, at the conclusion of our meeting I was left
25 with the impression that you may still have an open mind

1 as to whether LSHTM would continue to carry out its
2 responsibilities under the services agreement."

3 Do you agree with me that, if you had an open mind
4 about whether LSHTM would continue, that's inconsistent
5 with a belief that there had been an agreement to part
6 ways?

7 A. I would agree with your assessment, sir.

8 Q. Yes. So the evidence that you gave just now must be
9 wrong, mustn't it, because it contradicts your own
10 letter?

11 A. Contemporaneously with my email, there's one from
12 Mr Furcha that also reached the same conclusion. As we
13 left that meeting, we both had that conclusion. I had
14 assistance of counsel in this letter who recommended we
15 try to keep this open and not get to an impasse, and
16 there was something that Dr Roberts had said toward the
17 end -- and I can't put my finger on it, in my memory.

18 MR JUSTICE BURTON: What are you referring to with this
19 contemporaneous email from Mr Furcha? I'm not familiar
20 with that. Do we have this in the bundle?

21 A. I believe sent to Yossi Tal.

22 MR BEAR: Have you seen it in the bundle?

23 A. I have, but I couldn't tell you where it is.

24 MR JUSTICE BURTON: You say it's contemporaneous. Your
25 email, the one that's been redacted, is the

1 26th September. Are you saying it was round about the
2 same time?

3 A. I thought it was the next day, to tell you the truth.

4 MR JUSTICE BURTON: 29th September at 2241?

5 MR BEAR: Shall we start at 2229?

6 MR JUSTICE BURTON: Yes.

7 MR BEAR: There's an email that you weren't involved in from
8 Mr Furcha to Dr Goedkoop:

9 "Subject: London School is falling down, falling
10 down. Rene had meeting with TSC yesterday. The only
11 option was to mutually separate."

12 A. That's not --

13 Q. That doesn't suggest --

14 A. That --

15 Q. Sorry, just pausing there, that doesn't suggest an
16 agreement to part ways, does it? It's just someone
17 saying: this is the only option. Do you agree with me?

18 A. I would agree with you.

19 Q. Yes. Can I make a suggestion, Dr Simmon, and tell me if
20 you agree with this -- again trying to stand back as
21 best you can from the heat of battle, but not agreeing
22 if you don't agree -- what you want to suggest is that
23 you decided, because they wouldn't agree to the
24 amendment, that they had to go, correct so far?

25 A. I had not made that decision at this point.

1 Q. All right. So we disagree about that. And that you
2 were looking for a way to manoeuvre them out. Fair?

3 A. No, I disagree with that as well. There were no -- in
4 fact, my letter which we've gone back and forth on --

5 MR JUSTICE BURTON: Can we look at the next page, possibly,
6 please?

7 A. Sure.

8 MR JUSTICE BURTON: I'll leave this to you, Mr Bear, if
9 you'd prefer, but --

10 MR BEAR: My Lord, maybe it's more helpful for your Lordship
11 to do it?

12 MR JUSTICE BURTON: The exchange of emails at page 2240
13 seems even more relevant, the email from Mr Furcha to
14 Mr Tal at the bottom of the page.

15 Would you like to read that? It refers to your
16 rupturing the contract with LSHTM and then response from
17 Mr Tal is:

18 "I am sorry to hear things did not go well. Might
19 there still be a possibility for Xytis presenting the
20 case and convincing them? Technostat would be more than
21 willing to take things over and we obviously need to
22 talk about it."

23 Does this assist at all?

24 A. My Lord, this is the email I was referring to. If you
25 look at the middle of Mr Furcha's email to Yossi,

1 there's a single line:

2 "The long and short is that we mutually decided that
3 we could not move forward as partners any longer."

4 "mutually decided". That's was Mr Furcha's word,
5 contemporaneous with my email of the 26th.

6 MR JUSTICE BURTON: What was the "rupturing the contract"?

7 Obviously, we may have to ask Mr Furcha about this,
8 "rupturing the contract"?

9 A. Well, we had to -- it's his words and I would prefer
10 that -- my Lord, that you --

11 MR JUSTICE BURTON: Technostat were all lined up to take
12 over, it seems?

13 A. No, they were not at that time lined up to take over.
14 We had been talking with them for some time about doing
15 a statistical analysis plan for us, for a variety of
16 reasons that I'm not going to go into, but a part of
17 which started with the fact that when we wanted to have
18 a meeting with the FDA, it's my understanding that the
19 statistician at the London School, Chris Frost, was not
20 interested -- I don't know if it's unwilling or not
21 interested in doing such a meeting.

22 We had an open IND at the FDA that had been done at
23 the time of the phase 1 study by Fournier, I believe.

24 So we planned to give them a progress report, talk
25 about the study and make sure that we had all of the,

1 particularly animal toxicology in place, there were some
2 issues about dosing levels in animals. So we needed
3 a statistician there, Chris Frost at the London School
4 indicated to Mr Furcha and others, I believe, that he
5 wasn't going to participate in that, and so we began our
6 discussion with Technostat, and all -- for the simple
7 reason of getting an FDA compliant statistical plan,
8 I think there was an email in here which says that the
9 analysis by Yossi Tal was that it was a great academic
10 plan, but it did not meet FDA requirements.

11 That was the reason we had Technostat in place, or
12 were beginning to work with them, and they did some
13 consulting, as previous discussion about the protocol
14 amendment indicated, but we did not have them in place
15 to take over the trial, that is to say to -- we had not
16 requested them to prepare a proposal until later for
17 a database.

18 MR JUSTICE BURTON: What's the explanation for the next
19 page, 2232, at the top of the page, 26th September, your
20 email generally distributed as before, but in particular
21 addressed to one of your investors, as I understand it,
22 Mr Flugel:

23 "Our strategy at the moment is to inform LSHTM we
24 intend to implement the amendment which we have a right
25 to do under the contract. If they refuse, they would be

1 in breach. If it turns out we would have no further
2 financial obligation to them, maybe they will come to
3 their senses."

4 This is on 26th September, which is the week after
5 the alleged meeting when you say it was all agreed
6 voluntarily.

7 MR BEAR: It's two days after.

8 A. Two days.

9 MR JUSTICE BURTON: Two days after. Is that -- can you
10 explain that?

11 A. The -- with respect to, in this context, I was being
12 advised extensively by --

13 MR JUSTICE BURTON: Leave aside whether the advice was right
14 or not about whose obligation it was under the contract.
15 I was asking you about your stated intention. You
16 thought you had right on your side, let's leave that
17 aside for the moment. But that was your stated
18 intention on the face of that email.

19 A. Yes, sir.

20 MR JUSTICE BURTON: And its inconsistent, isn't it, with
21 saying that it had all been agreed voluntarily that you
22 would part.

23 A. It is inconsistent. I still would have -- my best
24 recollection is that we, Rowland and I, after the
25 meeting, felt that we had -- "reached agreement" might

1 be too strong a word, but we had certainly discussed
2 with Dr Roberts and Miss Shakur, going apart and, if we
3 did do that, what it would involve.

4 MR JUSTICE BURTON: What would it involve?

5 A. It would have involved Xytis retaining someone else to
6 manage the database, for example, which would have been
7 Technostat. It would involve other -- many other
8 elements which are in here which we'll probably see
9 later on about a plan that we -- the board wanted to
10 know: okay, if that happens, how are you going to -- how
11 would you implement this, and --

12 MR BEAR: Just look at 2232, Dr Flugel's -- I think you told
13 us he was Dr Flugel yesterday -- email to you at 1733:

14 "Vince, this sounds like a mess."

15 He goes on to say that it's a significant problem
16 because he said:

17 "A situation with a non-CRO such as LSHTM is
18 something we were concerned about."

19 Then he goes on to say:

20 "Would it make sense to have a meeting with you and
21 the lawyers on both sides?"

22 Then in response to that -- just pausing there, what
23 he's telling you is, he -- this particular director --
24 does not want to see matters come to an end, correct?

25 A. What he said was --

1 Q. No, just answer yes or no, if you can. He's telling you
2 he doesn't want to see matters come to an end with
3 LSHTM.

4 A. Correct.

5 Q. Now, in response you, I suggest, then change tack and
6 say: all right, we're going to threaten them with breach
7 of contract and perhaps they'll come to their senses.
8 Is that a fair summary?

9 A. Upon advice of counsel, that was the strategy I had
10 adopted, yes, sir.

11 Q. Then go forward to 2301. This is two emails again on
12 the page, so the bottom half the page is your email of,
13 again 5th October, 3.45 pm:

14 "Dear Ian, as indicated to you in my letter [then
15 you cite your letter] Xytis intends to modify the
16 protocol. I offered LSHTM the opportunity to reverse
17 its position that it would not participate in the
18 clinical trial if amended, other than to provide an
19 orderly transition. Since I have yet to hear back from
20 you, despite my request for your response, I must assume
21 you have not changed your mind and do not intend to file
22 the amendment or continue longer term as a participant
23 in the trial. Therefore, Xytis will begin the
24 transition next week by independently filing the
25 amendment."

1 So he was saying: I'm going to go ahead with the
2 amendment and the inevitable consequence is that LSHTM
3 will leave the trial. That's the gist of what you're
4 saying, isn't it?
5 A. That is correct.
6 Q. You are actually doing that without the support of your
7 board, weren't you, Dr Simmon? Again, just try to
8 answer yes or no.
9 A. Without Roger Flugel's --
10 Q. Was Mr Guerin on your side?
11 A. No, I don't suppose so, but I hadn't heard from him at
12 this point.
13 Q. Did any member of the board give you his support prior
14 to this email?
15 A. No.
16 Q. So you did it without the support of the board?
17 A. I will accept your statement.
18 Q. Now let's move forward can we go, please, to 2306,
19 Professor Roberts then did send the response that we
20 could see on the page we were just on, he had promised
21 you he was going to send.
22 A. Correct.
23 Q. And there are scientific arguments that he puts in some
24 detail against the changes, aren't there?
25 A. Yes, sir.

1 Q. And also arguments of law about what the contractual
2 position is, correct, at 2308 to 2309?

3 A. Yes, he expresses --

4 Q. Then under the LSHTM's position, he says, do you see
5 this in the middle of 2309:

6 "We wish to continue with the current trial in its
7 current format. We also consider that we are legally
8 entitled to continue in that role" and so on?

9 A. Yes.

10 Q. And he concludes by saying at the end of the letter on
11 2310:

12 "LSHTM remains committed to the trial and to
13 performing its obligations under the CTSA. I believe
14 this provides clear confirmation as requested in your
15 letter."

16 Yes?

17 A. That's what it says, yes, sir.

18 Q. You didn't have any difficulty understanding any of
19 that, did you?

20 A. No, sir.

21 Q. Now, if we could go forward -- I'm afraid we have to
22 pick up a bundle because it's not in this one, unless
23 I'm wrong -- can we go forward to, keeping this open --

24 A. I would note that Dr Roberts does threaten legal action
25 against Xytis as well.

1 Q. Yes, because you were threatening to try and amend the
2 protocol on your own without going through the trial
3 steering committee, that was what his threat related to,
4 wasn't it?

5 A. It says:

6 "We must formally reserve our right to take legal
7 action to preserve our position under and in connection
8 with the TSC ..."

9 Q. Dr Simmon, you said in your email of 5th October that:
10 "Next week [and the 5th was a Friday] we will begin
11 the transition by independently filing the amendment."
12 Do you remember saying that in your email?

13 A. Yes, sir. As a practical matter --

14 Q. That would have been contrary to the protocol on the
15 CTSA which gives the trial steering committee the power
16 to decide whether to change the protocol for any reason,
17 correct?

18 A. Correct.

19 Q. Now, can we then go forward, please, in the bundle, to
20 look at -- sorry, not in the bundle, in witness
21 statement bundle 4, because I'm afraid there's another
22 document that isn't in the chronological bundle, unless
23 I'm mistaken. Page 71, please, my Lord, of bundle 4.
24 Witness statement bundle 4.

25 A. Is there a tab? Am I looking at the right --

1 Q. Tab 31, I'm so sorry, page 71.

2 A. Yes.

3 Q. Professor Roberts sends his letter to you on 8th October
4 and then now we see a letter from Dechert, your
5 company's attorneys -- in fact this is from Dechert in
6 the US, page 71?

7 A. No, I apparently have the wrong -- tab 31?

8 Q. Witness statement bundle 4.

9 MR JUSTICE BURTON: If you can just find it for him because
10 it's right in the middle of the largest -- it's there,
11 page 71. It's in the great chunk. Thank you.

12 A. Thank you.

13 MR BEAR: So he is writing to the lawyers for LSHTM
14 on October 11th and then looking at point 1 first of
15 all:

16 "Incomplete invoices lacking. Required detailed
17 supporting documentation."

18 Then without going through the detail, what happens
19 here is a very large number of questions are posed by
20 your lawyer on the invoices, correct? It's the tenth
21 line or so -- let me take you to it. Can you see the
22 line beginning "supporting data" ten lines down in
23 section 1?

24 A. I don't believe that's the subject of this hearing.

25 Q. Can you just look at the line beginning "supporting

1 data"? I'm not going to ask you about the contractual
2 arrangements as such. But:
3 "In addition, we have a number of questions we have
4 been asked to pass along."
5 Do you see that? Do you see that sentence?
6 A. No, I'm not there yet.
7 Q. Okay, supporting data is a line beginning about ten
8 lines down in section 1.
9 A. Yes, I have that.
10 Q. Okay:
11 "In addition, we have a number of questions we have
12 been asked to pass along ..."
13 That obviously means asked by their clients, you.
14 "... including ..."
15 And then a whole list of questions followed. Just
16 cast your eye over them?
17 A. Yes, sir.
18 Q. Agreed those are some onerous questions, whether or not
19 they are justified, are they onerous questions?
20 A. I do not believe they are. I think these are, as you
21 said, justified by the contract.
22 Q. I said: whether or not justified, do you agree that they
23 are heavy questions to answer?
24 A. No.
25 Q. Okay. Let's look at number 2:

1 "Protocol amendment."

2 Reference to the issue of the protocol. I'm not
3 asking you any questions about it, but just note that
4 it's there. He is saying: no, we have the final say.
5 Then 3, escrow offer:

6 "As a means to resolve matters, Xytis has asked me
7 to propose the following:

8 "Although Xytis is not as you recognise in any way
9 obligated under the agreement to do so, Xytis is
10 nevertheless prepared to place a mutually agreed amount
11 into escrow as a good faith measure, if LSHTM
12 immediately agrees to the proposed protocol amendment.
13 All fees to be borne by LSHTM. As an alternative to
14 escrow, if LSHTM immediately accepts the amendments to
15 the protocol, Xytis is prepared to convert the contract
16 into a fixed price arrangement, which would avoid the
17 need for the required invoice documentation to be
18 reviewed and resume payments."

19 So you were offering to trade LSHTM's objections for
20 a more beneficial arrangement as to payment than the
21 arrangement that you were asserting, which was
22 reimbursement?

23 A. That is correct.

24 Q. Do you think it was appropriate to offer to trade
25 scientific objections for money?

1 A. Scientific?

2 Q. Objections of LSHTM for money?

3 A. Again, I would refer back to the ICH-GCP guidelines
4 which suggest that trials aren't done just for science;
5 they're done for society. If you can't show benefit of
6 a drug, you shouldn't be testing it.

7 MR JUSTICE BURTON: That's not the question you're being
8 asked, Dr Simmon. The point is, on the face of it,
9 unless you're suggesting some bad faith,
10 Professor Roberts' objections to the amendment were set
11 out on scientific and technical and professional
12 grounds, in some long letters.

13 A. Correct.

14 MR JUSTICE BURTON: What you're being asked is whether you
15 think it was appropriate to trade a financial dispute,
16 an offer from your point of view of more money, in
17 return for him giving way on the amendments to the
18 protocol?

19 A. I think it was appropriate as a way to seek a solution
20 to the problem, yes, sir.

21 MR BEAR: Do you think that LSHTM were raising objections in
22 bad faith, not genuine scientific objections?

23 A. No, but I had --

24 Q. Sorry, did you answer "no"? I didn't hear your answer.

25 A. I said no, but ...

1 Q. Hold on to the but. Go to your witness statement,
2 please, can you be given your witness statement in
3 bundle 1. Page 9, paragraph 41. Because I have read
4 this in a different way from your last answer. Page 9
5 of the witness statement, paragraph 41.

6 The heading on the page is:

7 "Proposed changes to the protocol."

8 You refer to the amendment issue in paragraph 40,
9 and then you say:

10 "I began to raise this with Ian Roberts who was
11 resistant, although I believe that his scientific
12 rationale was more from a point of view of convenience
13 than genuine science."

14 Do you withdraw that allegation now, Dr Simmon?

15 A. I would prefer to amend it as opposed to completely
16 withdrawing it. In my discussions with Dr Roberts, at
17 times what I found is that his responses to my requests
18 changed, it seemed to be a moving target. That part of
19 it, I thought, was the convenience. I do believe, and
20 would -- that Dr Roberts, if this implies otherwise,
21 was -- I would withdraw it, if it implies otherwise. If
22 it does. And I do believe that Dr Roberts, in good
23 faith, believed his scientific opinion was more
24 important than any other ones that I had received.

25 Q. If that's your belief, why did you say what you said in

1 41, look at the words carefully, beginning at the end of
2 the first line:

3 "I believe that his scientific rationale was more
4 from a point of view of convenience than genuine
5 science"?

6 A. And I believe I responded to your prior question of
7 would I amend or withdraw it -- excuse me, withdraw it,
8 and I have responded to your question, I think.

9 Q. I'm asking why you said what you said in your witness
10 statement?

11 A. And I am saying, sir, I would amend it, and I would
12 further state that I believe that Dr Roberts believed in
13 his mind that he had a sound scientific rationale.

14 Q. So, then, that's not a point of convenience, is it, a
15 point of view of convenience?

16 A. That is correct.

17 Q. So why did you say what you said in the second line of
18 paragraph 41? It's a serious allegation to make against
19 a distinguished professional scientist, and I want an
20 explanation, please --

21 A. I refer to --

22 Q. I want an explanation why you said it.

23 A. I was specifically referring here to discussions that
24 I had had with Dr Roberts, telephonically, and found
25 that when I had those discussions at times I felt we

1 would get some place and then it suddenly would turn
2 around and I thought he did those as a matter of
3 scientific convenience, or convenience for his argument.

4 MR JUSTICE BURTON: You, just a little ago -- referring back
5 to page 200, Mr Bear said:

6 "Do you think that LSHTM were raising objections in
7 bad faith, not genuine scientific objections?"

8 And you said:

9 "No, but I had ..."

10 And Mr Bear said:

11 "Hold the 'but' ..."

12 Can we come back to the "but"? Do you want to
13 finish that sentence now?

14 "Do you think that LSHTM were raising objections in
15 bad faith, not genuine scientific objections?"

16 "Answer: No, but ..."

17 What's the "but"?

18 A. I believe I was referring to, my Lord, or thinking at
19 that point, was that Dr Roberts' opinion was his
20 opinion, and that I had sought and obtained some other
21 opinions as well. That's the "but" part.

22 So while he thinks that this is the absolute best,
23 that wasn't the uniformly or universally held opinion.

24 Q. That doesn't go to his good faith, does it, the fact
25 that there are other people who take a different view?

1 Do you understand that general proposition?

2 A. I'm sorry, but I've lost exactly where we are in the
3 thread.

4 Q. It's my fault because my voice is going a little. The
5 fact that, for example, I might disagree with Mr Nash
6 doesn't mean that either of us are conducting ourselves
7 in bad faith.

8 A. Correct.

9 Q. Good faith is about believing what you say, and what
10 you've just said to his Lordship is that there were
11 other people who had a different view from
12 Professor Roberts?

13 A. Correct.

14 Q. I understand the words that you have used, but that
15 doesn't provide any basis, does it, for challenging
16 Professor Roberts' good faith?

17 A. And if you're referring then back to 41 as --

18 MR JUSTICE BURTON: I'm referring you to your answer.

19 A. Okay.

20 MR JUSTICE BURTON: "Do you think that LSHTM were raising
21 objections in bad faith ..."

22 A. And I said no.

23 MR JUSTICE BURTON: "... not genuine scientific objections?
24 "Answer: No, but ..."
25 What do you want to do with the "but"?

1 A. What I want to do with the "but" is, sir, my Lord, is to
2 further explain that I don't think they had the sole and
3 only opinion on this --

4 MR JUSTICE BURTON: Shall we just get rid of the "but", yes?
5 Delete the "but". It can stand as "no", can it?

6 A. Yes, sir.

7 MR BEAR: My Lord, I wonder if that would be convenient?

8 MR JUSTICE BURTON: Yes.

9 I just want to clarify one position very clearly for
10 the purpose of these proceedings. The defendant's case
11 is, I take it -- and that's their presented case -- and
12 their real position, bad faith, good faith or otherwise,
13 is that they want to carry on with this trial, is that
14 right?

15 MR BEAR: Yes, they do.

16 MR JUSTICE BURTON: And indeed they're going to ask me for
17 orders to ensure that they do?

18 MR BEAR: Correct. That is absolutely correct. They
19 appreciate, of course, that there can be difficulties if
20 you are in what Dr Simmon called "a bad marriage", but
21 they consider that this isn't a contract such as
22 personal services contracts.

23 MR JUSTICE BURTON: Subject to the points that are being
24 made, there's no attack on your good faith, and there's
25 only the matters we've heard mentioned which are attacks

1 on the way in which you carried out the trial.

2 MR BEAR: Yes. Professor Roberts does explain towards the
3 beginning of his statement some of the reasons, the
4 institutional and scientific reasons why the school
5 wants to carry on.

6 MR JUSTICE BURTON: Given the fact that it is quite clear
7 that there is no challenge to the defendant's bad faith
8 and that it's now well known what the criticisms, if
9 any, of the defendants are, I don't know whether there's
10 any point overnight in the claimants considering whether
11 or not they want to see if they can derupture the
12 relationship, but there it is. I mention that. If, for
13 that purpose, you need to talk to Dr Simmon, you have my
14 permission to do so.

15 MR NASH: Thank you, my Lord.

16 (4.25 pm)

17 (The court adjourned until 11.00 am the following day)

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