

Tuesday 26th February 2008

1

2 (10.30 am)

3 MR NASH: May it please your Lordship.

4 MR JUSTICE BURTON: Yes, Mr Nash?

5 MR NASH: I appear on behalf of the claimant, with my

6 learned friend Mr Dougherty and my learned friends

7 Mr Bear and Mr Casey appear on behalf of the defendant.

8 As your Lordship is aware this is an expedited trial

9 of this matter.

10 MR JUSTICE BURTON: Just hold on one second, if you would

11 before my clerk disappears. I had some notes in front

12 of a bundle, and I wonder what she's done with it.

13 Sorry, yes, Mr Nash? Expedited trial.

14 MR NASH: Expedited trial, my Lord, and your Lordship will

15 have, I think, at least an overview of the issues, the

16 interlocutory hearings we have dealt with. I know your

17 Lordship has had some opportunity for reading. It would

18 be helpful to me at least to have some idea of how

19 much --

20 MR JUSTICE BURTON: Yes, I've had a very full opportunity,

21 thank you very much indeed. What I have done is, apart

22 from preparing a list of questions I want to ask you

23 both this morning, which I'd like to do before you open,

24 just so that you know what I've done, I have built up

25 the two core bundles that you gave me by adding in to

1 the detriment of the chronological bundle -- sorry about
2 my voice, it's better than it was last week, but it's
3 still a bit irritating to everybody -- I've built up
4 a core bundle by taking documents out of the
5 chronological bundle and putting them in here, and
6 I think that means that every document that's been
7 referred to in the two skeletons or in the witness
8 statements, if they have seemed important I have now got
9 in my core bundle. I may prefer to do it in that way.

10 So, yes, I have therefore read and assimilated all
11 the documents in the original core bundles, witness
12 statements volume 1, I've had a brief look at one of the
13 earlier witness statements, I was a little thrown by
14 noting that the witness statements said that they were
15 not repeating everything in the earlier statements, but
16 none of you invited me to read the earlier statements,
17 so all I've actually done is taken out Mr Simmon's table
18 from his earlier statement, but otherwise I've not read
19 the earlier statements. I've read the experts' reports,
20 sufficient of the authorities, and your skeletons.

21 Obviously I've had extra time by virtue of yesterday.

22 MR NASH: Yes.

23 MR JUSTICE BURTON: So I think you can assume that I'm
24 au fait and, as I say, if I can ask a few questions
25 first, then it will be apparent to you where I'm not

1 au fait and where I need to be brought up to date.

2 MR NASH: Yes. Perhaps now is a good time for the
3 questions.

4 Questions from the Bench

5 MR JUSTICE BURTON: Shall I fire away? Yes, that's fine.

6 One or two questions, then I just thought I'd let
7 you know where I'd got to on my understanding of the
8 issues.

9 First question is this: in relation -- they are at
10 no in any particular order of logic -- in relation to
11 your case that they have failed to deliver documents
12 requested, paragraph 109 of Mr Roberts' statement and
13 elsewhere refers to a delivery of the data dump on
14 14th November 2007, but there doesn't appear to be
15 a document evidencing, by way of a cover note or
16 whatever it was, that delivery anywhere in the bundles.

17 If there is such a document, I'd like to put it in
18 my core bundle.

19 MR BEAR: Yes, there is one. It's in a set of bundles which
20 you, I'm quite sure, have not looked at.

21 MR JUSTICE BURTON: That's called supplementary disclosure,
22 is it?

23 MR BEAR: Party and party correspondence. It's an email
24 from Eversheds to Dechert.

25 MR JUSTICE BURTON: I haven't got it. So can I take it out

1 and put it in party and party correspondence bundle 3,
2 I take it.

3 MR BEAR: Yes.

4 MR JUSTICE BURTON: No.

5 MR BEAR: I don't know which bundle it is, I'm sorry, I'm
6 looking to see whether the reference is -- it is,
7 I believe, in the skeleton argument, our skeleton, at
8 page 15, footnote 15 to paragraph 43.

9 MR JUSTICE BURTON: I had missed that, thank you. Anyway,
10 I have now opened 14th November and --

11 MR BEAR: According to our note, it's correspondence
12 bundle 1, pages 18 to 19.

13 MR JUSTICE BURTON: Thank you very much. I had missed that.

14 "Please can you resend your email with the raw
15 data."

16 That's the 14th November. There must have been an
17 earlier email which he was requesting should be resent.
18 Page 19.

19 MR BEAR: Yes.

20 MR JUSTICE BURTON: Good, thank you very much. I shall take
21 that out and put it in.

22 Next question: there is a reference in the experts'
23 reports volume 2, page 22 of 45 of Mrs Chancily Nickols'
24 expert's report, to correspondence between Mr Brady and
25 Ms Shakur dated 19th October referring to a reported AEs

1 that were not real AEs, spreadsheet.

2 Now, I can't find that email of 19th October, or the

3 spreadsheet referred to.

4 MR NASH: I think, my Lord, that's in core bundle 9,

5 page 2 --

6 MR JUSTICE BURTON: Correspondence bundle?

7 MR NASH: Sorry, chronological bundle.

8 MR JUSTICE BURTON: Let's not call it a core, because it's

9 far from core.

10 MR NASH: A recipe for confusion.

11 MR JUSTICE BURTON: Chronological bundle 9, thank you.

12 MR NASH: And I believe it's at 2436.

13 MR JUSTICE BURTON: Well, if it is, I've already taken it

14 out and put it in the core bundle. I'll just find it.

15 I have already taken it out, yes.

16 Now, also for the DSMB:

17 "Do you want to send me an update of your reported

18 AEs that were not real AEs spreadsheet?"

19 Yes, I had pulled one out and put it in here, but

20 what about the spreadsheet, where's that?

21 MR NASH: I don't think we've seen the spreadsheet.

22 MR JUSTICE BURTON: That ought to be produced.

23 MR NASH: I'm told we have seen it, my Lord. Perhaps I can

24 get someone to track that down.

25 MR JUSTICE BURTON: Can you? If it's going to form a part

1 of your case that even by 19th October the defendants
2 appreciated that there were some AEs reported that were
3 not real AEs and failed to pass that information on to
4 DSMB, it may be of some substance.

5 MR NASH: Yes.

6 MR JUSTICE BURTON: Right, thank you. Let me make a note of
7 that.

8 2436, you said, didn't you?

9 MR NASH: Yes.

10 MR JUSTICE BURTON: My next question is for you Mr Bear, by
11 reference to the pleadings people, the defence,
12 paragraph 9.2(c)(ii) and 12.1(b) and 12.3.

13 Now, the same question relating to all of them, it's
14 a similar point: 9.2(c)(ii), last sentence:

15 "The DSMB chose to consider the former set of data
16 [that is the CRFs] as part of a much broader
17 examination", et cetera, et cetera, "and not the latter
18 set [which are the SAE forms], chose to consider CRFs
19 and not SAEs."

20 12.3:

21 "If there was a breach relating to the DSMB's chosen
22 source of data, such breach was rectified."

23 And then 12.1(b) I've passed over, a similar point:

24 "In any event the DSMB made a reasonable scientific
25 judgment in considering data from the CRFs and not

1 considering data ..."

2 Now, that makes it look as though, as far as your
3 clients were concerned, they were positively told not to
4 supply CRFs because of a positive decision to that
5 effect by the DSMB who chose, having been given the
6 option, either by you or of their own motion, to see the
7 one and not the other.

8 If that's a case which you're making -- you seem to
9 make it there -- I don't know when that choice occurred,
10 who made the choice, and whether it was anything to do
11 with you at all.

12 If, however, it's something different -- ie you made
13 the decision to send CRFs, not SAEs -- well, that's part
14 of your expert's case, that's fair enough, and that's
15 a different argument, but it's a different case from
16 saying: we were only too pleased to send the DSMB
17 whatever they want, but they told us "don't bother".

18 MR BEAR: Yes.

19 MR JUSTICE BURTON: Now, which is the case, and if it's the
20 "don't bother" point, what's your case on it, because
21 I can't find it anywhere in the witness statements,
22 either the doctor himself, I can't remember his name,
23 who has given evidence from the DSMB, or Dr Roberts.

24 There's some evidence about "we not it's not clean"
25 which I'll come to in a moment. But this point, a

1 positive choice to have CSFs and not bother with SAEs on
2 the part of the DSMB, if that's part of your case
3 I ought to know about it.

4 MR BEAR: There's a witness statement from someone called
5 Professor Sandercock. He is the DSMB Chair.

6 MR JUSTICE BURTON: Yes, I couldn't remember his name.

7 MR BEAR: He is the DSMB Chair.

8 MR JUSTICE BURTON: I can't find it in there. Sandercock,
9 that's how you pronounce it?

10 MR BEAR: Yes.

11 MR JUSTICE BURTON: It's a good thing to know.

12 I'm very conscious of his evidence, and at
13 paragraph 37 he says he:
14 "... disagrees entirely with the starting point of
15 premises which is that the HPM's database [which is how
16 he describes the SAEs] was in some respect inherently
17 preferable to the defendants."

18 Indeed, he is rather of the opposite view. But does
19 he anywhere say -- and he says it wouldn't have assisted
20 the DSMB to look at the SAE form. But does he anywhere
21 say: we chose not to look?

22 MR BEAR: What he says at paragraph 29 is perhaps putting it
23 in a slightly different way.

24 MR JUSTICE BURTON: "It simply didn't occur to us to
25 request ..."

1 MR BEAR: Yes. So the DSMB does not see case report forms,
2 CRFs. What it sees is tables divided up, and you've
3 probably seen them in the bundle --

4 MR JUSTICE BURTON: Yes, one of my questions was going to be
5 to ask someone at some stage either in opening or
6 through a witness in chief, to explain the shell tables
7 to me. You're going to say the format of the shell
8 tables was decided by the DSMB and that makes it clear
9 it's got to be the CRFs, is that it?

10 MR BEAR: It's got to be information derived from the CRFs,
11 yes.

12 MR JUSTICE BURTON: Information derived from the CRFs.

13 MR BEAR: That's right.

14 MR JUSTICE BURTON: So your case on -- if you would be asked
15 for further information on the word "chose", your case
16 would be: they chose by the format of the shell tables?

17 MR BEAR: That's right, by the prescriptive categories laid
18 down in the shell tables.

19 MR JUSTICE BURTON: That I'll look at. Obviously the
20 earlier I look at it the better. But that's your
21 answer: there wasn't any express instruction otherwise
22 than through their provision, and sanction, of the form
23 of the shell table, is that it?

24 MR BEAR: That's correct.

25 MR JUSTICE BURTON: So all three of your pleading paragraphs

1 that I've referred you to -- "there chosen", "they
2 chose" -- is based on that?

3 MR BEAR: Yes, there was no statement in evidence anywhere
4 with the DSMB saying: we do not want to look at the data
5 derived from these SAE report forms.

6 MR JUSTICE BURTON: Is Dr Sandercock's evidence that he knew
7 at the time of the existence of what he calls the HPM
8 database, ie that he knew that there was one derivation
9 of AEs which include SAEs which was dealt with in the
10 SAE forms which he was delighted to get analysed in the
11 shell forms, but that there was also the HPM database
12 derived solely from SAE forms which he was perfectly
13 happy not to have?

14 MR BEAR: It's a matter of interpretation of his evidence,
15 but perhaps I shouldn't start commenting on it too much,
16 but we would certainly say his statement makes it clear
17 that the DSMB recognised perfectly well, and indeed it's
18 standard practice that there would be a separate body of
19 SAE report forms, that that would be a sort of off-spin
20 of the regular reporting --

21 MR JUSTICE BURTON: A regulatory requirement?

22 MR BEAR: Yes, which ultimately would feed into regulatory
23 requirements and so on, and that he and his colleagues
24 were well aware of that, but what they wanted was to
25 focus on the data held in the trial database.

1 MR JUSTICE BURTON: That's your case, anyway, that's what
2 I'm to look out for, I'm very grateful, thank you.

3 MR BEAR: I should say just by way of a small gloss on what
4 the DSMB did and didn't want to look at, there is
5 evidence that the DSMB was asked whether it wanted to
6 consider data from an HPM form which is called CIOMS,
7 C-I-O-M-S, which I think may relate to what are called,
8 and forgive the yet further acronyms, SUSARS. Now,
9 SUSARS are --

10 MR JUSTICE BURTON: The very, very, very worrying things,
11 which there never were any of, as I understand.

12 MR BEAR: There don't seem to be any in this case. That's
13 if you get an actual reaction, an allergic reaction
14 which appeared to be linked to the drug.

15 MR JUSTICE BURTON: They would want to be told about those,
16 would they?

17 MR BEAR: They would know about those anyway. But I'm
18 simply making a point: there is evidence that the DSMB
19 were to be asked about whether they wanted to look at
20 the form which HPM was producing for SUSARS.

21 MR JUSTICE BURTON: I see, so they did approve that form,
22 did they?

23 MR BEAR: No, they didn't approve that form.

24 MR JUSTICE BURTON: But they were told about it.

25 MR BEAR: There's evidence suggesting that they were told

1 about that, yes. It's a gloss, because I don't think
2 it's actually relevant.

3 MR JUSTICE BURTON: No, I can see that, but if they knew
4 about the existence of that form and didn't ask even for
5 that form, although I suppose they would have assumed
6 they would have been supplied it, then that would be
7 part of your case?

8 MR BEAR: If there were SUSARS, they would have shown up in
9 other ways in the trial.

10 MR JUSTICE BURTON: How would they have shown up?

11 MR BEAR: That I will need to find the detail for, but there
12 are mechanisms for that we will draw to your attention.

13 MR JUSTICE BURTON: Thank you very much. I've got one last
14 rather minor question. Can I just mention that either
15 in opening or in a witness in chief, I want to have
16 explained to me the shell tables and I want to have both
17 Mr Simmon explain what survives of his table in his
18 statement, and Mr Roberts to make his comments on that,
19 in chief, really, so I understand it, and Dr Sandercock
20 also, in the sense that this is all very helpful and
21 I notice I'm given a corrective of it, but it will be
22 much more helpful for me to have the men themselves
23 explaining them, or you, I don't mind.

24 MR BEAR: Well, it's a task one might well choose to leave
25 to Professor Roberts.

1 Could I just say on titles, I don't know if
2 Mr Simmon prefers to be addressed as Doctor. He does
3 have a PhD. It's Professor Sandercock and
4 Professor Roberts.

5 MR JUSTICE BURTON: Thank you very much.

6 MR BEAR: I should mention one small point on the shell
7 tables. If we're looking purely at the shell, there's
8 no difficulty about the information. If we're looking
9 at the populated tables, I just need to mention one
10 point --

11 MR JUSTICE BURTON: Which is confidentiality?

12 MR BEAR: -- which is confidentiality. There's a rule,
13 I think from memory it's CPR 31.22, which says that
14 normally when a document is read or referred to in open
15 court it can be put into the public domain. Obviously,
16 we don't want that, and the court has power to make an
17 order restricting that, and I don't know if that's
18 something that could be common ground, but I certainly
19 wouldn't want our references to it to then make it
20 unconfidential.

21 MR JUSTICE BURTON: I'm sure it would be common ground,
22 wouldn't it, that I can make that order and perhaps you
23 can agree a form of order which I can make at lunchtime.

24 MR NASH: Yes, there is a question about blinding and access
25 to information, which we'll have to debate in a moment.

1 I think this is a more general point about whether this
2 material goes into the public domain merely by reference
3 in court, and I'm sure we can do something about that.

4 MR JUSTICE BURTON: Thank you very much. Two very quick
5 last minor questions.

6 I can understand the word "blind", that's not
7 a problem, information is blinded. And in the case
8 where it's blinded, as here, the only people who had
9 access to it were, as I understand it, Sealed Envelope
10 and the DSMB except for the limited information that was
11 supplied by the DSMB to the TSB for the purpose of their
12 decision making.

13 What I don't understand is the word "double blind".
14 It seems this was multiple blinded. Who was being
15 referred to when you're talking about double blind? The
16 patient doesn't know?

17 MR NASH: I think double blind means that the patient
18 doesn't know and the investigators don't know.

19 MR JUSTICE BURTON: But nobody knows.

20 MR NASH: Well, until the end of the trial, of course.

21 MR JUSTICE BURTON: Yes, of course.

22 MR NASH: So the investigators, both at the site and at the
23 TSC --

24 MR JUSTICE BURTON: The patient is not told the information?

25 MR NASH: Doesn't know whether he's receiving placebo or

1 treatment.

2 MR JUSTICE BURTON: I see, but he will know, will he, or
3 not, how he's getting on?

4 MR NASH: I mean, he of course receives medical attention
5 throughout the trial, but I don't believe he's ever told
6 that:
7 "You have been receiving placebo or treatment."

8 MR JUSTICE BURTON: No, that I understand. Whether it's
9 a placebo or whether it isn't, if he then has some
10 adverse reaction, he will be told about it, won't he:
11 you have just had a stroke, or whatever. He might have
12 had a stroke anyway.

13 MR NASH: If your Lordship is asking whether, if he has
14 a stroke, someone then goes to him and says: oh, by the
15 way, you were receiving the drug --

16 MR JUSTICE BURTON: No, that's not what I had in mind. Once
17 he's on the trial, the only thing that the patient is
18 blinded from is whether it was a placebo or whether it
19 was the drug.

20 MR NASH: Yes.

21 MR JUSTICE BURTON: He won't be blinded from the fact as to
22 what has happened to him.

23 MR NASH: Certainly not, no, he's treated in the normal way.

24 MR JUSTICE BURTON: When we're talking about "blinding",
25 from his point of view, the aspect is what he was

1 having. From the investigator's point of view, of
2 course it's both the fact, as to whether he's having
3 a placebo or having a drug, and the identity of the
4 patient, is that right? Or will the investigator -- the
5 investigator will know the identity of the patient?
6 MR NASH: No, the investigator, even if there is an adverse
7 event, the investigator will not know at that stage
8 whether or not the patient is receiving placebo or
9 treatment.
10 MR JUSTICE BURTON: I understand entirely, but he will know
11 the patient?
12 MR NASH: He will have a randomised number.
13 MR JUSTICE BURTON: A number, but not a name.
14 MR NASH: Well, I'm not sure whether he has the name, but he
15 certainly has randomised numbers for each patient.
16 MR JUSTICE BURTON: Yes, so the investigator will not know
17 (a) whether it was a placebo or whether it was the drug;
18 (b) the identity of the patient. He will only know the
19 number, is that right?
20 MR BEAR: No, as I understand it, the investigator in the
21 local hospital, say in Colombia, is going to be the
22 doctor in charge of the patient. That's got to be the
23 case.
24 MR JUSTICE BURTON: He is the CRA?
25 MR BEAR: No, not the CRA, the CRA is a sort of medical

1 bureaucratic assistant, I don't mean to downgrade their
2 work.

3 MR JUSTICE BURTON: He is local?

4 MR BEAR: The CRA is local, he is a sort of subcontractor
5 engaged to help ensure that the forms are properly
6 filled in.

7 MR JUSTICE BURTON: Will he know the identity of the patient
8 other than by randomised number?

9 MR BEAR: I assume not.

10 MR JUSTICE BURTON: No, that's what I had thought.

11 MR BEAR: The doctor -- ie the investigator at each site --
12 will know, I'm sure, the name of the patient --

13 MR JUSTICE BURTON: Of course.

14 MR BEAR: -- and exactly what's happening to him, because he
15 or she is the one reporting on his condition throughout
16 the trial.

17 MR JUSTICE BURTON: And he, the doctor, will know whether
18 it's a placebo or a drug?

19 MR BEAR: No.

20 MR JUSTICE BURTON: He won't either?

21 MR BEAR: Nobody knows anything about the relationship
22 between, on the one hand, the patient in the trial, and
23 on the other hand what they've received, whether it's
24 placebo or study drug.

25 MR JUSTICE BURTON: So the patient knows he's taking a drug,

1 knows what's happening to him, doesn't --

2 MR BEAR: If he's conscious --

3 MR JUSTICE BURTON: Sorry, a pill, doesn't know whether it's

4 a placebo or a drug?

5 MR BEAR: Yes.

6 MR JUSTICE BURTON: The doctor, ditto.

7 MR BEAR: The doctor is in the same position.

8 MR JUSTICE BURTON: The CRA?

9 MR BEAR: The CRA won't be present in the hospital. He or

10 she will come along afterwards.

11 MR JUSTICE BURTON: Right, he or she will not know whether

12 it's a drug or placebo?

13 MR BEAR: No.

14 MR JUSTICE BURTON: And will not know the name of the

15 patient --

16 MR BEAR: Probably will know, because they have to have

17 access to the medical records. So the doctors, assuming

18 they follow the usual Anglo Saxon system, will have

19 their hospital case notes, and that will be the

20 underlying source --

21 MR JUSTICE BURTON: The investigator will know the name of

22 the patient?

23 MR BEAR: Well, the investigator is the doctor. The CRA who

24 is the bureaucratic assistant --

25 MR JUSTICE BURTON: Will know the name of the patient?

1 MR BEAR: Yes, will be entitled to see who the patient is
2 and check the hospital's notes against the CRF.

3 MR JUSTICE BURTON: Then, one stage up, you will not know
4 whether it's a placebo or a drug, and will know the
5 patient only by randomised number, is that right?

6 MR BEAR: There's also initials and no doubt, if it were
7 necessary for the chief investigator to become aware of
8 the name in order to pursue some enquiry in great
9 detail, LSHTM or Professor Roberts.

10 MR JUSTICE BURTON: Ie is it really an SAE?

11 MR BEAR: If you were checking it out at that level, but in
12 the normal course, the impression I would say the
13 documents create is that, no, the trial centre doesn't
14 need to know that sort of detail. What it looks at is
15 the case report forms.

16 MR JUSTICE BURTON: And the sponsor is one step further
17 removed, will only know randomised number and that's
18 all?

19 MR BEAR: Yes, the sponsor will just get results in terms of
20 what the total figures are.

21 MR JUSTICE BURTON: Thank you very much.

22 Now one other question -- this is really for you,
23 Mr Nash: there is some criticism in your expert's
24 report, at least in theory, of Mr Brady, lack of
25 training, et cetera, et cetera.

1 If that were so, why is that something that's the
2 responsibility of the defendant? I thought Sealed
3 Envelope was a separate contractor, if anything,
4 answerable only to the DSMB.

5 MR NASH: In relation to that, it was contracted -- Sealed
6 Envelope was in a contractual relationship with the
7 school and was there selected database developer, and
8 within the CTSA, the services agreement, one of the
9 services which the school contractually bound itself to
10 supply to us is the production of the database.

11 So we say that, if the database has failings, and if
12 those failings arose because the man who designed it was
13 not sufficiently trained, that, as a matter of contract,
14 lies at the school's door.

15 MR JUSTICE BURTON: I mean, I can see entirely, if what he
16 supplies to the DSMB is wrong, well, not least because
17 it would be capable of them to give him different
18 instructions, I can see that they carry some
19 responsibility, but if Brady is -- I don't get my mind
20 around it, but there's some suggestion that Brady is
21 insufficiently trained. If he's insufficiently trained,
22 is that their responsibility? Surely their job would be
23 to select an apparently competent independent
24 contractor, wouldn't it?

25 MR NASH: Well, I see your Lordship's point on that, but the

1 training point is not simply the state of Mr Brady, if I
2 can put it that way, when it all began, but the state of
3 Mr Brady as he developed the database and what training
4 he should have been seeking for himself --

5 MR JUSTICE BURTON: At that stage?

6 MR NASH: -- as he was developing the database, what
7 training he should be seeking for himself in order to
8 produce the correct product at the end, and we say that
9 if he was failing to obtain the appropriate training for
10 himself as he went through the development of the
11 product --

12 MR JUSTICE BURTON: After the start of the contract he has
13 to get more training?

14 MR NASH: While he is developing the database, my Lord, yes.

15 MR JUSTICE BURTON: There it is. At any rate, that's your
16 case.

17 Now, let me, if I may, then, run through where I've
18 got to, because it may -- either you can put me right or
19 put me on the right road in the course of your
20 respective openings, or possibly it may lead to some
21 shortening of the case.

22 MR NASH: My Lord, before your Lordship does that, can I
23 just pick up on a couple of points arising out of those
24 questions?

25 MR JUSTICE BURTON: Yes.

1 MR NASH: Firstly, we do have a copy of the adverse events
2 which are not adverse events spreadsheets.

3 MR JUSTICE BURTON: Good, thank you.

4 MR NASH: That's in chronological bundle 14 at page 4135.

5 MR JUSTICE BURTON: Right, well I shall take it out.

6 MR NASH: It's at page 4135.

7 MR JUSTICE BURTON: I've seen this somewhere before, but it
8 may be not in this precise form. There it is, yes.

9 MR NASH: That's the spreadsheet.

10 MR JUSTICE BURTON: And where does it say -- it doesn't say
11 "adverse events that aren't in there", but that's simply
12 the comment in the email. Can I call this up? This is
13 all I want, is it, page 4135?

14 MR NASH: Yes, it's a single page.

15 MR JUSTICE BURTON: Yes. And just let me then marry it in
16 to the core bundle, page 2436.

17 "Do you want to send me an update of your reported
18 AEs that were not real AEs spreadsheet?"

19 That's how Mr Brady refers to this document.

20 MR NASH: Yes.

21 MR JUSTICE BURTON: This document, however, is simply
22 adverse event.

23 MR NASH: Yes.

24 MR JUSTICE BURTON: And it says what the problems are. It
25 doesn't purport to be spreadsheets capable of having

1 that description. So there's obviously some subjective
2 judgmental element in what Mr Brady says about it.

3 MR NASH: Well, I believe it's been produced to us as the
4 spreadsheet which has been referred to in that email,
5 that's certainly how it's described in the index to this
6 bundle. So I don't think there's any doubt that that is
7 the relevant document.

8 MR JUSTICE BURTON: Why is it so far divorced from the email
9 in the chronological bundle in terms of time? This is
10 the one that was -- I just wonder why it was put in in
11 the 4000s which suggests that it was somewhere
12 in December.

13 MR NASH: It wasn't an attachment to the email.

14 MR JUSTICE BURTON: No, no, but its date -- you're assuming
15 that having been so told this is the document being
16 referred to on 19th October.

17 MR NASH: Yes.

18 MR JUSTICE BURTON: So shall I put it in my core bundle as
19 2436A?

20 MR NASH: Certainly, my Lord, yes. The reason it's in
21 number 14, I think, is simply because it's undated. You
22 will see that 14 and 15 contain a whole series of
23 undated documents.

24 MR JUSTICE BURTON: Unless I'm told otherwise by Mr Bear,
25 I'm going to assume that this is 2436A.

1 MR NASH: The second point arising out of those exchanges,
2 my Lord, the point about the DSMB being asked whether
3 they wished to see the CIOMS form, which is one of the
4 HPM forms, the position on that is that they replied
5 saying they'd like to have a look at the form at the
6 next meeting to see whether it's a form they wish to
7 see, and that exchange you'll find in chronological
8 bundle 5, right at the back, pages 1505 and 1506.

9 MR JUSTICE BURTON: Again, I think I ought to pull that out.
10 Page?

11 MR NASH: The last two documents in the bundle.

12 MR JUSTICE BURTON: 1505?

13 MR NASH: And 1506. Start at the bottom of 1505.

14 MR JUSTICE BURTON: This would have been a blank form at
15 this stage, obviously.

16 MR NASH: Yes.

17 MR JUSTICE BURTON: "It would be a good idea to see these
18 forms. We can then decide if we want to continue to see
19 them or just a summary of data extracted from them."

20 In fact fortunately there never were any forms
21 filled so there was never any data to be extracted from
22 them.

23 MR NASH: Yes.

24 MR JUSTICE BURTON: But do we know whether they did see the
25 forms at the next meeting? Is there any reference in

1 the minutes?

2 MR NASH: I don't recall that there is a reference, I'll be
3 corrected if I'm wrong, but I don't think there is
4 a reference in any of the documents that suggests they
5 were actually shown the CIOMS forms.

6 MR JUSTICE BURTON: Right, thank you very much.

7 MR NASH: My Lord, those were the points arising.

8 MR JUSTICE BURTON: Now, let me run through where I've got
9 to on the issues.

10 First of all, 9.2, you rely on suspension. Where
11 I am at the moment, having read the two skeletons and
12 the documents, is that I remain to be persuaded that
13 this was a suspension as opposed to a temporary halt.
14 That's before we get on to the question as to whether
15 the -- if it was a suspension, it was an
16 administrative/ministerial decision.

17 So I mean, I'm influenced by regulation 31 and by
18 the way in which it was dealt with at the time in the
19 documents that are in core bundle tabs 23, 46 and 47.

20 But, at the moment, I need some persuasion that this
21 was a suspension of the trial as opposed to the trial
22 continuing but a suspension of any further recruitment.

23 Secondly, your next run, so to speak, is
24 unreasonable refusal -- I'm sorry, your second one is
25 that the trial was capable of being stopped under 9.2

1 because of -- I'm so sorry, 9.3(v) -- because of lack
2 of -- a risk of lack of trial patient protection and
3 safety considerations.

4 At the moment, I am wholly unpersuaded about that.
5 You will have a long way to go to persuade me, only from
6 what I've read. The point is made that, if you have
7 been in any concern about trial patient protection, you
8 would have given notice under 29(a) that your own very
9 understandable reaction when the refusal -- when the
10 suspension, if it was a suspension, takes place is not
11 worry but delay, if anything. Do we really have to
12 report it, et cetera, et cetera, in the correspondence
13 that I've seen.

14 It just doesn't read to me like -- even taking into
15 account your earlier concerns -- like patient protection
16 at all, but in any event, I at the moment conclude that
17 I've got to be satisfied that it was, at the time,
18 a decision based on a fear of patient protection and I
19 don't see it. I'm influenced by the other motives which
20 you plainly had and continue to have for unloading the
21 defendant, commercial and otherwise.

22 At the moment I'm persuaded that, in your sole
23 discretion, or whatever the words are, require that you
24 be not capricious and that you're going to have
25 difficulty.

1 Then there's the waiver issue. It isn't of course
2 waiver, because it wasn't breaches, but it's a question
3 of electing against terminating under 9.2 by keeping the
4 contract going, and I shall have to hear you on that as
5 well.

6 But so far your case to me is a very difficult one.

7 Then moving on to number 4, which is your assertion
8 that there was no compliance with your request for
9 information, there too I'm at the moment wholly
10 unpersuaded, either that you made a reasonable request
11 or that it wasn't complied with within a reasonable
12 time, or, notwithstanding what you say about only
13 wanting the blinded information -- subject to,
14 obviously, what you were supplied on 14th November -- it
15 looks to me as though you can't show that you were
16 taking sufficient care to bear in mind the unblinded
17 status of the information you were seeking.

18 So there too I think you're facing considerable
19 difficulties.

20 We then move on to what I see as the nub of the
21 case, and the one on which I can see the force of your
22 case, and for my part where I would like to see most of
23 the effort devoted, and that is your case that there was
24 an obligation on the defendant to reconcile the
25 information from The SAEs and the CRFs so far as they

1 could, before it was supplied to the DSMB on two bases:
2 one, an obligation to clean the information so far as
3 you could or they could, and secondly, if you are right
4 that the result of the protocol requirement, 8.1.3, was
5 that SAEs which weren't SAEs should positively be
6 excluded from the information supplied to DSMB.

7 Alternatively, you say, that at least there was an
8 obligation on the defendant, if they weren't getting
9 that, to explain to the DSMB that they hadn't, and you
10 say that they should have in terms said, and didn't,
11 that they were not taking into account and reconciling
12 the information from the SAEs, that they were not
13 carrying out a full cleaning process. The fact that
14 they said some wasn't clean didn't give the full
15 picture, and, thirdly, that the amendment of the
16 protocol -- sorry, not the protocol, the procedure to
17 exclude the soft lock procedure, either was done
18 inappropriately without consulting you or, at the least,
19 should have been informed to the DSMB so that they would
20 realise that the soft lock procedure hadn't been
21 operated, and therefore that even if ordinarily under
22 the soft lock procedure there would have been at least
23 some cleaning and reconciling, that was not now
24 necessarily to be expected.

25 So that, if I've understood your case, is where the

1 thrust of the case goes. Of course, the answer to that
2 from the defendants, is, firstly, that you have
3 misunderstood those obligations. Secondly, that the
4 DSMB knew -- and this is part and parcel of what Mr Bear
5 and I were discussing earlier -- knew that the SAE
6 information was not included, indeed didn't want it, and
7 if that's right, then that's not the defendant's fault,
8 if they positively weren't obliged to supply it, and
9 that in any event it wouldn't have made any difference.

10 Now, that's an interesting area and I shall need to
11 understand that. Can you terminate a contract for
12 a breach which is of no materiality because it makes no
13 difference?

14 They say, first of all, that it's apparent that --
15 and indeed supported by Dr Sandercock -- it wouldn't
16 have helped at all to know that there were more SAEs or
17 less SAEs. SAEs are to be expected when people have
18 serious brain injuries. People do die and have strokes
19 and that kind of thing, even if they aren't having any
20 treatment at all, and what was important was to see the
21 distinction between the number of SAEs in the drug group
22 and in the placebo, and that would be unaffected by the
23 overall total, being either too many or too small.

24 Secondly, that in any event, the Sandercock/DSMB
25 decision was double banked and that the test would have

1 been suspended, if suspended it was, in any event, by
2 virtue of the second round of the decision of the
3 1st November, namely the outcomes round, if anything
4 more important than the first round.

5 That seems to be the battleground. I can understand
6 in general terms the position on both sides. I shall
7 need them developed, but that's where I see there being
8 a real issue in the case, but not, subject to your
9 persuasiveness, in relation to any of the matters up to
10 and including that issue.

11 And, indeed, nor in relation to your fall-back
12 argument under 9.2 as to which a great deal of effort
13 has been expended as a result of the orders that I made
14 in the last few weeks, so far as more general
15 allegations about failure to -- failures of data
16 collection and processing where I have to say at the
17 moment I share Mr Bear's puzzlement as to what your case
18 is, even with the benefit of your expert's report. You
19 are of course having to some extent ride a rather unruly
20 horse of either deciding that you do want to support the
21 audit report or that you don't, and you've attempted to
22 bring back in the earlier audit report as to which the
23 defendant's case is that that is complete irrelevance,
24 not least because most of it was complied with long
25 before, and, as I say, at the moment, I'm finding it

1 very difficult to grasp what your case is and I'm sure
2 it's my fault, but I can't see the strength of it.

3 Once we get to that, then -- at the moment I assume
4 that you are either going to win or not on the basis of
5 the non-reconciliation/non-cleaning point, and if you
6 are successful in showing that you were entitled to
7 terminate the contract under clause 9.2 on that basis,
8 then I shall need some persuading by Mr Bear that, if
9 you are contractually entitled to terminate it, that the
10 contract can for some other reason not be terminated. I
11 shall listen with interest to Mr Bear.

12 If you are not entitled to terminate, then all the
13 points he makes about the involvement of all the various
14 committees, the needs for publication, the protocol
15 needing to be overriding the contract, and all these
16 other points are splendid reasons why I should be slow
17 to conclude that the contract has been terminated, but
18 I will be equally slow to think that if you are
19 otherwise entitled to terminate the contract -- I'm not
20 talking about Pageguide or any of these authorities
21 about, of course I can grant an injunction subject to
22 what you may say -- to keep unwilling bed fellows
23 together unless it involves the kind of services which
24 unwilling bed fellows are reluctant to give to each
25 other.

1 But it's not that. It's simply that I don't see why
2 or how, if there is a mechanism for termination which
3 you have successfully operated, the parties should be
4 other than sent on their ways.

5 But that is a long way away at the moment. I need
6 some considerable persuading that you have succeeded in
7 terminating the contract.

8 As for the counterclaim, that seems to me to stand
9 or fall with the claim. If you were entitled to
10 terminate, most of what you've done was consistent with
11 your case that it was properly terminated. If you
12 weren't, then you've been, for commercial reasons,
13 struggling to get out of this contract for months and
14 have failed to do so. It may be a ground for my not
15 simply refusing you relief, but granting an injunction
16 to stop you doing it again. That may be appropriate.
17 At the moment, I can't see any independent life for the
18 allegations on the counterclaim.

19 So that's where I've got to. I hope that may help
20 in the way that you open the case to me, both of you,
21 shortly, just to give me -- either put me right or give
22 me comfort depending on which way you want.

23 Opening Submissions by MR NASH

24 MR NASH: Yes, thank you, my Lord.

25 Your Lordship has summarised really the shape of the

1 case very fully in those opening comments.

2 What I intended to do by way of an opening, it being
3 a short opening, was to give what Mr Justice Langley
4 used to call a mission statement to show your Lordship
5 how we see the case at a fairly high level of
6 generality. We'll need to descend to some of the detail
7 and then get straight into the evidence.

8 So let me do it that way.

9 This is of course a trial of certain of the issues,
10 and they're identified in the list of issues which
11 I hope your Lordship has seen and --

12 MR JUSTICE BURTON: Yes, have I summarised them all?

13 I mean, I have left out, of course, the fees issue,
14 whether it's cost plus or fixed fee and such like.

15 That's nothing to do with it. Other than that all the
16 major issues are in play, aren't they?

17 MR NASH: Yes, absolutely, my Lord. There is some
18 disagreement about the wording, I think, of two of the
19 issues, but your Lordship, we suggest, has summarised it
20 exactly right. On the question of performance of the
21 data processing, the question is whether or not the SAEs
22 were being properly reconciled and whether or not the
23 data was being cleaned "timeously", I think is one of
24 the words used in the experts' reports.

25 Our view of the case is this: Xytis is in the

1 business of seeking to identify safe and effective
2 treatments for disease. Its shareholders and those who
3 run it have very substantial experience in that business
4 and in particular they have extensive experience of
5 operating in this heavily regulated environment of
6 clinical trials.

7 There is an important distinction that is picked up
8 in Ms Charnley Nickols' report on page 10 of the
9 45 pages of that report, between interventional and
10 non-interventional trials. The distinction -- your
11 Lordship will perhaps have seen it -- is between a trial
12 in which you are introducing a new treatment to see
13 whether it's first safe and second effective -- that's
14 an interventional trial -- and a trial in which you are
15 investigating the effectiveness of an existing
16 treatment.

17 There's no doubt that the school has vast experience
18 in non-interventional trials. It's a matter for
19 cross-examination the extent to which the relevant
20 individuals at the school -- and we hear referring
21 particularly to Dr Shakur -- has experience of
22 interventional trials. That is trials involving the
23 testing of a new product for a commercial sponsor with
24 a view, ultimately, to obtaining approval for that
25 product.

1 My Lord, there's no dispute between the parties as
2 to the relevant regulations, the 2004 regulations in the
3 UK, and there's also agreement generally that good
4 clinical practice, GCP, applies to this trial.

5 There seems to be some dispute as to whether or not
6 GCP is relevant to the complaints made about data
7 handling. You may have picked up the reference in
8 Mr Bear's skeleton, paragraph 50.6(c), in which I think
9 it's suggested that the GCP has no direct application to
10 our complaints about data handling.

11 We say that it obviously does. Perhaps we could
12 look very briefly at GCP in --

13 MR JUSTICE BURTON: Yes, shall I look first of all at
14 50.6(c)?

15 MR NASH: Yes, it's page 19 of the document.

16 MR JUSTICE BURTON: Yes. All he says is:

17 "If, which is not the case, it applies ..."

18 He hasn't explained why. Yes, now you want to take
19 me to it?

20 MR NASH: If you go to the first of the expert bundles
21 behind tab 1 and then sub-tab 3, you will see ICH topic
22 E6:

23 "Guideline for clinical practice."

24 MR JUSTICE BURTON: Yes.

25 MR NASH: Within that, in particular, if you go to paragraph

1 part 2 of it at the 9th page of 58 --

2 MR JUSTICE BURTON: Just a second. How does this relate
3 to -- just so that I know -- the document which is in
4 bundle -- experts' bundle 2 at tab 3 behind
5 Ms Charnley Nickols' report? What is the status of
6 that?

7 MR NASH: That is a guideline. I don't believe that this
8 has statutory authority.

9 I will have to clarify that, my Lord.

10 MR JUSTICE BURTON: It's a great fat wedge of stuff and the
11 only page that appeared to me to be relevant in that
12 bundle, page 190, was what it was said had to happen
13 before data lock:

14 "Verify that all queries have been returned and
15 integrated into the database correctly. A QC process
16 should be in place. Ensure reconciliation has been
17 performed on all events. Ensure that all expected SAE
18 information has been received", et cetera.

19 MR NASH: Yes.

20 MR JUSTICE BURTON: To which, as I understand it, the
21 defendant's answer would be, assuming they accept this
22 applies, that would be so, but of course with the
23 amendment of the practice, or whatever it was called,
24 the DMP, soft lock was no longer mandatory in relation
25 to what happened in November.

1 But before we get there, I would like to know what
2 the status is of this guideline. It's obviously less
3 significant than the one that you're just about to show
4 me, and the defendants don't even accept the validity or
5 relevance of the one you are about to show me.

6 I'd just like to know about, when you're telling me
7 about, on your case, what the status is of the one
8 you're about to show me, don't forget to tell me what,
9 if anything, is the relevance of the other one.

10 MR NASH: I won't forget, my Lord. I'm just --

11 MR JUSTICE BURTON: I don't think Ms Charnley Nickols
12 specifically explains why she's exhibited it, but I may
13 be wrong.

14 MR NASH: That may be right, my Lord, but we'll get to the
15 bottom of that. My Lord, GCP.

16 MR JUSTICE BURTON: Yes?

17 MR NASH: Principles of GCP practice, paragraph 2, 958.

18 And reference is made to 2.2:

19 "Before a trial is initiated, foreseeable risks and
20 inconveniences should be weighed against the anticipated
21 benefit for the individual trial subject and society",
22 et cetera.

23 Then 2.10 is important:

24 "All clinical trial information should be recorded,
25 handled and stored in a way that allows as accurate

1 reporting, interpretation and verification."

2 And 2.13:

3 "Systems with procedures that assure the quality of
4 every aspect of the trial should be implemented."

5 So your Lordship --

6 MR JUSTICE BURTON: It's all very nice general stuff, that,
7 where does that take us?

8 MR NASH: Well, Miss Charnley Nickols says that guided by
9 those principles it can be seen that the failings which
10 she identifies in the data management within the school
11 amount to breaches of GCP.

12 MR JUSTICE BURTON: Are we talking about what I consider to
13 be the main issue or to the subsidiary issue?

14 MR NASH: The main issue.

15 MR JUSTICE BURTON: Well, now, on the main issue, assume
16 that there's no issue between you that they should be
17 recorded, handled and stored in a way that allows its
18 accurate reporting, et cetera, if they are right that
19 this was a conscious and sensible decision to exclude
20 the SAE forms from the DSMB's consideration, then there
21 wouldn't be a breach of these principles, would there?

22 MR NASH: My Lord, Miss Charnley Nickols's criticism of what
23 happened is not focused simply on the information that
24 was submitted to the DSMB. Her case, and the case which
25 indeed your Lordship I think has been describing, is

1 that by the time the DSMB meeting came around, there was
2 a failure within the school to process and reconcile the
3 information which it was receiving up from the local
4 sites, timeously, so that the information which was
5 presented to the DSMB, instead of being a package of
6 cleaned data which had gone through the reconciliation
7 processes which were supposed to have been gone through,
8 it was presented with a mix of partly cleaned data, data
9 which had not been cleaned at all, and fully cleaned
10 data.

11 MR JUSTICE BURTON: When you say "not cleaned", do you mean
12 not reconciled as against the SAE forms or not cleaned
13 in some other way? Because if you mean the latter,
14 I haven't understood it.

15 MR NASH: We mean not cleaned -- not cleaned in another way,
16 my Lord, to use your Lordship's phrase. The cleansing
17 process -- I think this will become clear as I develop
18 the opening -- the cleaning process is not simply
19 a matter of comparing the CRF forms with the HPM/SAE
20 forms. The cleaning process involving checking that the
21 CRF forms and the entries which have been made by the
22 local sites through the electronic connection are (a)
23 accurate, they don't contain obvious mistakes and
24 omissions, and (b) that the trial criteria which is set
25 out in the protocol, has been correctly followed.

1 MR JUSTICE BURTON: Is there any other way in which you
2 suggest a breach of that other than by not having
3 checked them against the SAE form?

4 MR NASH: Yes, we say that they were, by October of 2007, so
5 far behind in their checking processes that they were
6 compelled to present to the DSMB this wedge of uncleaned
7 data. They had to lift the data lock in order to be
8 able to supply the DSMB with a population of 100
9 patients, because they had fallen so far behind in their
10 processes, that they had, by that stage, a mix of
11 information which had not been cleaned within the
12 timeframe in which it should have been cleaned.

13 MR JUSTICE BURTON: Yes, I see, right.

14 MR NASH: That's how we put it. The relevance of GCP in
15 those passages I've just shown you, my Lord, as
16 explained in Miss Charnley Nickols's report is that
17 there is an obligation, a guideline -- a GCP obligation
18 to ensure that you have processes in place which enable
19 accurate reporting to be given.

20 MR JUSTICE BURTON: Now, you were going to tell me why it is
21 that this is binding, contrary to the non-admission of
22 the defendants.

23 MR NASH: We say that once it is accepted -- and I think it
24 is common ground that this trial was bound to be
25 performed in accordance with ICH-GCP --

1 MR JUSTICE BURTON: But that seems to be non-accepted, so
2 just show me why it is that this trial was to be
3 governed by the ICH-GCP. Do you accept it was?

4 MR BEAR: The trial as a whole has to be governed by
5 ICH-GCP because that's what the regulations say. The
6 question is about whether ICH-GCP govern the stage at
7 which data is submitted to a DSMB. That's the point,
8 and we say that ICH-GCP merely creates a data safety
9 monitoring board or data monitoring committee, as it's
10 called there, as an option and having done that -- this
11 is what Professor Gray, our independent expert, says --
12 is thereafter silent as to what should or should not be
13 done.

14 MR JUSTICE BURTON: So this is something that's got to be
15 done at all material times and by the end of the trial,
16 is that it?

17 MR BEAR: That implicitly is the claimant's case, that
18 everything needs to be cleaned throughout, and we say
19 that's not so, and that there's nothing in GCP that says
20 that. GCP is not directed towards setting a standard
21 for the work that needs to be done when you prepare data
22 or hand over data for analysis by a DSMB.

23 MR JUSTICE BURTON: Thank you.

24 MR NASH: My Lord, just to make it clear, it's not just
25 a question of regulation. You will recall that

1 article 2.2 of the CTSA says, in terms, that the
2 provider, which is the school, shall provide the
3 services, which is the trial, in accordance with
4 regulations and guidance governing the conduct of
5 clinical research including the ICH guideline. So this
6 is clearly a contractual standard. It's tab 2 of the
7 first core bundle, 2.2.

8 MR JUSTICE BURTON: Thank you.

9 MR NASH: The importance of the regulations in GCP and the
10 reasons why it's in the contract, is firstly, if the
11 trial is not conducted in accordance with the
12 regulations, its output may not be acceptable for
13 regulatory purposes. That means, in the present
14 context, that Xytis might not get permission to move on
15 to a phase 3 trial, which is the efficacy test, and
16 secondly, of course, if it can't get permission to move
17 on to phase 3, or if there's doubt about that, Xytis
18 will not be able to obtain funding from its investors to
19 move on to that stage.

20 MR JUSTICE BURTON: Who gives the permission to go on to
21 phase 3?

22 MR NASH: Within the UK, it would be the MHRA, I believe,
23 who also gave the regulatory approval for this phase 2
24 trial.

25 MR JUSTICE BURTON: I see, so when you've -- if you get this

1 trial desuspended, in your phraseology, whether with the
2 defendant or whether with your chosen replacement, you
3 go to the end of phase 2 and then you present the
4 results to the MHRA, is this right, and they then decide
5 whether to allow you to go on to phase 3?

6 MR NASH: Yes, I think that's right. Whether you present
7 the results at the end of this trial or whether you
8 present the results to MHRA as part of an application
9 for approval to go on to phase 3, I'm not sure, but
10 either way --

11 MR JUSTICE BURTON: It comes to the same thing, yes.

12 MR NASH: -- the performance of this trial, and whether it
13 conforms with ICH will have a direct bearing on whether
14 we can move on to phase 3.

15 MR JUSTICE BURTON: Yes.

16 MR NASH: Our second point in relation to this is that the
17 regulations and GCP are there to protect patients. The
18 point is made by the school that the two are not
19 synonymous, in other words protection of patients and
20 GCP are not the same thing. To some extent GCP deals
21 with other matters as well. And we agree that's of
22 course right so far as it goes.

23 But where, as here, there's been a serious breach of
24 GCP in that the data was not being recorded and handled
25 in such a way that allows us accurate reporting,

1 interpretation, verification, we say that patient safety
2 was compromised and Xytis --

3 MR JUSTICE BURTON: But it wouldn't be an automatic
4 conclusion: you are in breach of the GCP, therefore you
5 have compromised the patient's safety. I would have to
6 decide, wouldn't I, that the particular manner in which
7 they have breached GCP was a manner which offended
8 against patient safety? I mean, they are two different
9 questions.

10 I can entirely understand that GCP is set up with
11 patient safety in mind, but if you breach some rule of
12 the GCP which is mainly aimed at acquiring some
13 procedural method which has nothing to do with patient
14 safety, then the breach of the one doesn't automatically
15 mean the breach of the other, does it?

16 MR NASH: That's obviously right, my Lord. Our point -- and
17 this, I think, ties in with your comments on our patient
18 safety case -- the decision for your Lordship is whether
19 Xytis concluded, within its sole discretion, that
20 patient safety was being compromised by the conduct of
21 this trial.

22 MR JUSTICE BURTON: I see that, but, I mean, if the only
23 issue is whether they gave the information now, that is
24 before 1st November, and the fact that they didn't has
25 caused you problems because the trial may have been

1 suspended when it may not have needed to be, but
2 nevertheless it would all have been done properly by the
3 end of the trial. Surely patient safety is not only put
4 at risk, but it's positively enhanced by holding up
5 trials, holding up recruitment, in the meanwhile.

6 MR NASH: Yes.

7 MR JUSTICE BURTON: It's only if the system they introduced
8 was itself detrimental to patients' safety, wouldn't it
9 be that I would conclude this was a breach which also
10 offended against that principle.

11 MR NASH: I see my learned friend has very effectively
12 directed your Lordship's thinking down a particular road
13 in relation to patient safety, and I must try and direct
14 you off that road, my Lord.

15 MR JUSTICE BURTON: Yes.

16 MR NASH: Our point about patient safety is not the
17 suspension of the trial.

18 MR JUSTICE BURTON: No.

19 MR NASH: They suggest that there can't have been an issue
20 because the trial was suspended and the regulatory
21 authorities were, et cetera.

22 MR JUSTICE BURTON: They can't pull themselves up by their
23 own boot straps.

24 MR NASH: Exactly.

25 MR JUSTICE BURTON: If they were doing so badly that they

1 had to stop the trial, then the fact that patients are
2 miraculously saved from disaster by no longer being
3 recruited wouldn't help, and I quite agree.

4 But their case isn't as simplistic as that, I don't
5 think. They are saying, of course they're doing the
6 right thing. If they hadn't done it all by
7 1st November, that doesn't put patient safety at risk.

8 MR NASH: Exactly, my Lord. In a sense, the case is as
9 simplistic as that, because the answer to our patient
10 safety concern comes back. The trial was suspended, and
11 the regulatory authorities were informed. You didn't
12 rush off to the regulatory authorities as soon as the
13 suspension took place, where is the case in patient
14 safety?

15 The answer to that is, my Lord, if we concluded that
16 the data management which was going on in September
17 and October --

18 MR JUSTICE BURTON: Had been so detrimental to patient
19 safety, while being done, then that will --

20 MR NASH: Yes.

21 MR JUSTICE BURTON: That's all I'm saying. I think it just
22 needs to be -- it's a separate question: was there
23 a breach of GCP -- were the breaches of GCP such as to
24 put at risk patient safety?

25 MR NASH: Yes, exactly.

1 MR JUSTICE BURTON: That's all I put to you, the two
2 questions. If the system was that they didn't even have
3 a system, never mind not look at it, for reporting or
4 processing SAE forms, well, then, that would be probably
5 something that would affect patient safety. If they're
6 simply saying, yes, we had them, but we weren't going to
7 reconcile them yet, your case may be that shows they had
8 a system which didn't put at risk patient safety, but
9 it's not an obvious one. I'm just saying you've got to
10 prove both.

11 MR NASH: It's not simply a question of the system. Put it
12 this way: if the data collection was being operated in
13 a way that wholly inaccurate material was coming up from
14 the sites, reports on the condition of patients, in
15 a way which disguised what effect this treatment was
16 having on the patients, while the trial was ongoing,
17 that endangers patient safety.

18 It happens that the results which were put before
19 the DSMB led them to conclude: safety first, let's halt
20 the trial, suspend the trial. But data errors could
21 equally well have disguised adverse trends in the
22 performance of this drug and led the DSMB to say: we'll
23 continue.

24 MR JUSTICE BURTON: That is system, isn't it? If their
25 system is such as not to be able to pick up the kind of

1 problem you are indicating, then their system would put
2 at risk patient safety. All I'm saying is I'm not sure
3 that's -- if it is the difference between you, that's
4 fine, but I think the difference between you at the
5 moment on the facts I've seen is: they're saying no, it
6 isn't that we didn't have that system, it's just that we
7 shelved it in order to get the information quickly to
8 the DSMB but we would have done it after 1st November.

9 MR NASH: But the system, my Lord, the system involves
10 checking this material, both reconciling with the SAEs,
11 but also checking with the local site.

12 MR JUSTICE BURTON: Have you got some case -- if so
13 I haven't seen it -- that the system which was required
14 whereby CRAs would double-check the CRFs was not being
15 operated properly? I thought your case was: of course,
16 that's fine, that's all going on, but, look, you've got
17 a whole series of SAEs, why didn't you marry the two
18 together? I can see that case, but are you further
19 saying that even leaving aside the SAEs what was being
20 done as between the -- vis-a-vis the checking of the
21 CRFs through the CRAs was not being done properly.

22 MR NASH: My Lord, I think I need to take a step back and
23 just explain the process so that we're all clear about
24 this.

25 MR JUSTICE BURTON: Yes.

1 MR NASH: A patient receives treatment or placebo at a local
2 site from a local doctor. The CRA obligation at the
3 local site is to check that the CRF is filled in
4 correctly. That process of filling in involves firstly
5 data entry through a remote terminal, which takes it
6 back to the school, and then, when the treatment is
7 finished, a paper CRF which contains the same
8 information is sent to the school.

9 MR JUSTICE BURTON: And that will be double-checked?

10 MR NASH: And that is then within the school double-checked.
11 There is what's called a second entry at the school,
12 into the database.

13 MR JUSTICE BURTON: Yes.

14 MR NASH: Then a process of checking commences.

15 MR JUSTICE BURTON: Yes.

16 MR NASH: That checking involves not simply checking that
17 obvious mistakes, numbers, ages, dates and so on, have
18 not crept into the CRF, but checking also that the trial
19 criteria is being followed correctly and that there are
20 no omissions in the CRF.

21 MR JUSTICE BURTON: Yes, yes.

22 MR NASH: So if you have a CRF which comes in and it is
23 apparent that an SAE has occurred to a patient which is
24 not married up with an SAE form, that will generate
25 a query back to the local site: where is your SAE form?

1 But there's also the sort of query that arises when
2 a CRF comes in, and it is apparent that the local site
3 has classified an event as an SAE for the purposes of
4 the trial.

5 This trial had a particular criteria that an SAE --
6 paragraph 8 of the protocol, your Lordship referred to
7 it -- an SAE is an untoward occurrence. That is an
8 occurrence which is not expected in the normal course of
9 TBI.

10 The local site of course would be required to make
11 a judgment as to whether any particular occurrence is
12 untoward or not. One of the queries which has been
13 generated at the school, the central database, was:
14 I look at the CRF, I see there's an event there which
15 I regard, the school regards, as not an untoward event
16 for the purposes of TBI. So they go back to the site
17 and say: this is surely just part of the normal course
18 of the disease? The local site may or may not agree
19 with that, and the local site has the final word on that
20 question.

21 But the whole business of processing the CRF is
22 designed to ensure both accuracy and consistency in the
23 way the results are assembled for the purposes of the
24 trial.

25 MR JUSTICE BURTON: Yes. You say that can't be done without

1 filtering in the SAE forms?

2 MR NASH: The SAE forms are part of the process, my Lord,
3 yes, but it's not -- the story doesn't begin and end
4 with the SAEs.

5 MR JUSTICE BURTON: No, no. But is there any evidence that
6 they weren't doing their job other than by not paying
7 any attention to the SAE forms?

8 MR NASH: Yes, Miss Charnley Nickols gives extensive
9 evidence about what she says is the failings to process
10 the CRFs and to eliminate queries timeously.

11 MR JUSTICE BURTON: Quite independently of not
12 cross-checking the SAEs?

13 MR NASH: Yes.

14 MR JUSTICE BURTON: Right.

15 MR NASH: That's why there is a patient safety issue in
16 relation to this?

17 MR JUSTICE BURTON: Yes.

18 MR NASH: Because, if that's not done, then, as I say,
19 adverse events --

20 MR JUSTICE BURTON: Just jumping forward for a moment,
21 I entirely see that if you can establish those breaches
22 by reference to Miss Charnley Nickols' expert's report,
23 that will help you on your 9.2 second argument, and
24 indeed it may support your 9.2 main argument which is
25 that the SAE forms, non-reconciliation is only a part of

1 a general failure to do a good job.

2 But does it help you on your 9.3 form given that
3 when you terminated on the patient protection ground, if
4 you did, you didn't have any of Charnley Nickols' points
5 in mind? You couldn't have had, because you didn't know
6 about them.

7 MR NASH: We didn't know the detail of it, my Lord, but the
8 evidence will be -- and this is from Mr Simmon -- that
9 we were concerned that the data handling at the school
10 had reached such a pitch of delay and defectiveness,
11 that there was a patient safety concern.

12 MR JUSTICE BURTON: You don't say any of that. I have a
13 subject to your explaining away to me the letters
14 of August and September, I say explaining away,
15 explaining more fully the August and September letters.

16 It just doesn't read like that at all.

17 MR NASH: There is an August letter in which data
18 reconciliation --

19 MR JUSTICE BURTON: 30th August.

20 MR NASH: -- real-time data reconciliation is raised as
21 a specific point.

22 MR JUSTICE BURTON: I have understood about the
23 reconciliation point, but I can't see anything else in
24 that correspondence. No doubt there is. We'll come to
25 it.

1 MR NASH: Mr Simmon will deal with that and no doubt he will
2 be asked questions about that.

3 MR JUSTICE BURTON: He has dealt with this whole 9.3 patient
4 protection decision, assuming it was his, very concisely
5 in one paragraph of his witness statement. It doesn't
6 shiver the timbers as it should have done:

7 "I can't stand any more of this, you are making
8 a complete mess of this, you've got to go ..."

9 It doesn't read like that.

10 MR NASH: We will see what he says about that. But I was
11 anxious your Lordship should understand at least the way
12 we put it.

13 MR JUSTICE BURTON: No, what I understand is -- I'm glad you
14 have done -- that the breaches you allege of the
15 GCP which go more broadly than the allegation of
16 non-filtering in of the SAE forms -- although that's
17 a very good indicator and probably the best example of
18 the failure -- are important because they carry with
19 them patient safety implications. That I've understood.

20 But to amount to a separate ground for termination
21 on notice number 1 under 9.3(v), that I'm not satisfied
22 about, at least at the moment. But there we are.

23 MR NASH: Thank you.

24 MR JUSTICE BURTON: Thank you.

25 MR NASH: My Lord, those who run Xytis have no illusions

1 about the difficulties of the business. They know it
2 requires heavy front-end investment and that many drugs
3 in the end are not effective, and they accept that as
4 part of the business.

5 The suggestion put forward by Professor Roberts that
6 Xytis was concerned to convert this phase 2 trial into
7 a mini phase 3 trial is, we suggest, absurd.

8 Xytis, and indeed Mr Simmon, know perfectly well
9 that that simply cannot be done. It was always a phase
10 2 trial. There are, however --

11 MR JUSTICE BURTON: He wanted to amend the protocol in some
12 way or other I haven't understood, in order to include
13 something -- I've not got my mind round it not least
14 because I'm not sure it's been fully concentrated on.

15 MR NASH: We sought an amendment, it's amendment number 3 to
16 the protocol in I think October 2007 for two things: to
17 increase the follow-up period and to increase the number
18 of patients within the trial, but the school --

19 MR JUSTICE BURTON: Is that not part of converting phase 2
20 into phase 3?

21 MR NASH: No, it's still within phase 2.

22 MR JUSTICE BURTON: Of course, but I mean they say that
23 shows that what you were trying to do was to gain some
24 information from phase 2 which would ordinarily not have
25 been obtained until phase 3.

1 MR NASH: Well, part of phase 2, in addition to safety
2 testing -- I'll show you the document in relation to
3 this -- was also, so far as it could be obtained, to get
4 some efficacy information to see if the drug worked or
5 not.

6 MR JUSTICE BURTON: Yes, because they say phase 3 stuff.

7 MR NASH: To test efficacy properly is phase 3, and to do it
8 with sufficient statistical power to convince regulators
9 that this drug is something that should be allowed into
10 the market would require a much larger study. We
11 understand this, and there was no question of the
12 phase 2 becoming a phase 3.

13 MR JUSTICE BURTON: Well, there it is. It may be that this
14 was all part of the commercial reasons for the falling
15 out between you. But we'll come to that.

16 The shorthand writers want a short break which we
17 shall give them, but just let me see, if we can, before
18 we break, where we are going.

19 I'm finding all this very helpful. I don't want to
20 waste any time and don't want to cut you back from
21 explaining the case so that -- after all I've got to
22 decide the case, I need to understand it.

23 How much longer are you going to be? Another half
24 an hour?

25 MR NASH: Yes, half an hour, no more than that.

1 MR JUSTICE BURTON: Right. So that will be 12.30. Then how
2 long will you want?

3 MR BEAR: I'll try to be half an hour or less because --

4 MR JUSTICE BURTON: I don't want a guillotine. If it runs
5 over not least because of my asking questions then it
6 must run over. But if we can try and start evidence, if
7 not at 2.00, shortly thereafter, and then -- but before
8 we do, we'll have a final discussion about timetable.

9 I am not saying that -- I'm conscious of the
10 expense. On the other hand, I'm equally conscious of
11 the importance of the issues. I'm not saying we've got
12 to finish this in seven days, which is what's allowed
13 for. So, if it goes over a bit, subject to counsel's
14 convenience and the witnesses' convenience, then it runs
15 over. If necessary, we can have all of next week.

16 MR NASH: Thank you.

17 MR BEAR: My Lord, thank you.

18 (11.50 am)

19 (A short break)

20 (11.55 am)

21 MR JUSTICE BURTON: Yes?

22 MR NASH: My Lord, continuing from where I was just before
23 the break, it's worth remembering at this stage two
24 things.

25 Firstly, the purpose of the trial was stated from

1 the outset ultimately to obtain regulatory approval for
2 Anatibant and that appears in the initial agreement
3 which predated the CTSA.

4 Can I show that you briefly?

5 MR JUSTICE BURTON: Thank you.

6 MR NASH: Core bundle 1, tab 1, and at page 327, first page
7 of the document.

8 Although this is a restated agreement -- in other
9 words it was made again in August of 2006 -- it was
10 originally made in December of 2005, you see that date
11 in the first paragraph?

12 MR JUSTICE BURTON: Yes. Now, what's the status of this
13 document? Is it overtaken by the CTSA?

14 MR NASH: It's incorporated in the CTSA.

15 MR JUSTICE BURTON: But not all the recitals, is that the
16 point? Is that why you're showing it to me?

17 MR NASH: No, this is a document that was incorporated. So
18 you have the CTSA which incorporates this as well.
19 Broadly speaking, this governs the design and setting up
20 of the trial.

21 MR JUSTICE BURTON: I see.

22 MR NASH: And the CTSA governs the performance of the trial.
23 So you'll see on the first page:

24 "The objective of the trial is stated to be to
25 obtain international regulatory approval for the

1 Anatibant drug in TBI with clinical trials that comply
2 with international regulatory standards and guidelines."

3 Perhaps also if you go over the page to 328, you'll
4 see the clause dealing with the setting up of
5 committees:

6 "Three committees to be formed: protocol committee,
7 trial steering committee and DSMB. Define their own
8 organisation and operating rules," et cetera, and I draw
9 particular attention to the middle paragraph:

10 "The protocol committee will be established in order
11 to assist the sponsor in defining the clinical trial
12 design and statistical plan in accordance with
13 international regulatory standards."

14 And:

15 "The protocol committee is to draft, review and
16 finalise the clinical trial protocol."

17 Then if one goes to item 3 on the same page:

18 "There's to be an independent protocol review
19 process and sign-off procedure to be established by the
20 sponsor."

21 Finally, over the page, clause 5, page 329:

22 "It is the sponsor's sole responsibility to accept
23 and approve the final CTP ...", which is the protocol
24 and CRFs.

25 MR JUSTICE BURTON: What's the status of the -- let me get

1 it right, the DMP. Is it the DMP?

2 MR NASH: The data management plan?

3 MR JUSTICE BURTON: Yes, that's right, what's the status of
4 that?

5 MR NASH: That's what --

6 MR JUSTICE BURTON: Just so that I've got in mind your case,
7 which is that -- you made it just before the break --
8 that they had to amend the DMP in order to eliminate the
9 mandatory requirements as to what had to be done before
10 the soft lock, or as part of the soft lock, because they
11 were behind, and there's some suggestion by
12 Miss Charnley Nickols that this was naughty.

13 Who did the power to amend the data management plan?

14 MR NASH: It's a standard operating procedure, the data
15 management plan. It defines one of the things which
16 they are doing in the conduct of the trial, and we say
17 that that -- whether or not Dr Shakur as trial manager
18 was entitled to amend it, it was an amendment of such
19 significance that it should have been reported both to
20 the TSC, the trial steering committee, which has
21 supervision of the trial, and advised to us, Xytis.

22 MR JUSTICE BURTON: Now, why?

23 And, of course, you also say "reported to DSMB"
24 because if -- in case the DSMB was expecting that the
25 soft lock procedure had been complied with before

1 information arrived.

2 MR NASH: Yes.

3 MR JUSTICE BURTON: That I can see is nothing to do with
4 a constitutional requirement but what you would say is
5 good sense. But is there a constitutional requirement
6 to report an amendment to the TSC or to the sponsor?

7 MR NASH: Well, the protocol requires that the trial be
8 conducted in accordance with the trial design. The
9 trial design is fixed by a whole series of standard
10 operating procedures, of which the DMP is one.

11 So, if you make a significant change to the DMP,
12 you're making a significant change to the conduct of the
13 trial.

14 The TSC is charged, on our behalf, with supervision
15 of the trial. It follows that if you're going to change
16 the trial design, the TSC needs to know about it, and
17 they are obliged under the CTSA --

18 MR JUSTICE BURTON: Who establishes -- can you show me who
19 establishes the standard operating procedures and the --
20 you say the DMP is simply one of the standard operating
21 procedures. Can you give me a family tree or
22 a legislative structure for all these documents, because
23 I haven't got that in my mind at all.

24 MR NASH: Well, we need, I think, first, then, to go --

25 MR JUSTICE BURTON: Do we start with the protocol?

1 MR NASH: The protocol, my Lord, yes.

2 MR JUSTICE BURTON: If I'm doing a family tree, what is it,
3 what comes at the top?

4 MR NASH: The protocol comes at the top.

5 MR JUSTICE BURTON: The protocol at the top. Then where do
6 the standard operating procedures come from and where do
7 the DMPs come from?

8 MR NASH: The standard operating procedures is a class of
9 documents. That comes in a line below the protocol.

10 MR JUSTICE BURTON: Right.

11 MR NASH: And then --

12 MR JUSTICE BURTON: Does that mean it's established by the
13 protocol committee?

14 MR NASH: It's established --

15 MR JUSTICE BURTON: I mean, who drafts the SOP, or is it the
16 defendant?

17 MR NASH: My Lord, the easiest way to deal with this is
18 perhaps to go to the protocol at tab 3 of core bundle 1.

19 MR JUSTICE BURTON: Thank you.

20 MR NASH: If you go firstly, just so you note, at page 282
21 within that document, the trial is sponsored by Xytis.
22 Some of the sponsor's responsibilities will be delegated
23 to the trial coordinating centre based at the London
24 School of Hygiene and Tropical Medicine, et cetera.
25 There's then a definition of the DSMB and the trial

1 steering committee, and you'll see towards the bottom of
2 the page:

3 "The role of the TSC is to provide overall
4 supervision of the trial on behalf of the sponsor. In
5 particular, the TSC will concentrate on the progress of
6 the trial, adherence to protocol patient safety and
7 consideration ..."

8 And this is important, my Lord:

9 "The TSC, in the development of this protocol and
10 throughout the trial, will take responsibility for major
11 decisions such as a need to change the protocol for any
12 reason, monitoring and supervision ..."

13 And then finally:

14 "... considering recommendations from the DSMB and
15 informing and advising the sponsor on all aspects of the
16 trial."

17 MR JUSTICE BURTON: Yes, but what it doesn't say anything
18 about is anything about the SOPs or the DMP.

19 MR NASH: If your Lordship would then go to page 316 within
20 that document, part of the protocol says, 10.1, "Data
21 management":

22 "Data management will be performed under the
23 responsibility of the trial coordinating centre and
24 according to its SOP."

25 MR JUSTICE BURTON: Its SOP. That suggests it's the

1 defendant's SOP and the defendant drafts its own, does
2 it?

3 MR NASH: Yes, the TCC is entitled to develop its own SOP.

4 MR JUSTICE BURTON: Hold on, not the TCP, the defendant?

5 MR NASH: Yes, I'm sorry, the TCC is a synonym for the
6 school.

7 MR JUSTICE BURTON: I was muddling it with the TSC. Let's
8 call them the defendant, yes, the school, LSHTM, yes.
9 So they have their own SOPs, and they do, do they?

10 MR NASH: Yes, they do.

11 MR JUSTICE BURTON: So how is the SOP born? We've got the
12 SOP or at least part of it in the other bundle, have we,
13 tab 14?

14 MR NASH: Yes.

15 MR JUSTICE BURTON: No, that's HPM's standard operating --
16 tab 15.

17 MR NASH: No, this is one of the SOPs, my Lord, we have
18 many.

19 MR JUSTICE BURTON: We haven't got them all, I'm delighted
20 not to have them all, at least I have got them
21 somewhere. But the defendant drafts its SOPs which are
22 dedicated to this trial or no doubt based on previous
23 formats.

24 MR NASH: Yes.

25 MR JUSTICE BURTON: Is that approved by someone?

1 MR NASH: Well, the data management plan, for example --

2 MR JUSTICE BURTON: I haven't got to the data management.

3 Let's just talk about the SOPs. The SOPs, and you say

4 there were a number of them, are you simply saying that

5 the data management plan is one of the SOPs?

6 MR NASH: Yes.

7 MR JUSTICE BURTON: Then we can talk about DMPs. So all the

8 SOPs including the DMP are drafted by the defendant, but

9 do they have to be approved by them?

10 MR NASH: I'm just trying to recall whether the documents

11 evidence any approval at TSC level. They are certainly

12 circulated to various people within the trial. I'm not

13 sure -- I'd better just check, if I may, for a moment.

14 My Lord, can I park that and come back to you on

15 that?

16 MR JUSTICE BURTON: You can. What's your case on the SOPs?

17 MR BEAR: They are internal documents which need to be in

18 place.

19 MR JUSTICE BURTON: Oh, yes, of course.

20 MR BEAR: They need to be there, but other than that it's up

21 to the defendant to change. When we look at the DMP, as

22 I'll sure we will be, we'll see that it starts off by

23 saying it can be updated as necessary, and that's why

24 Professor Gray, our independent expert, says there was

25 no difficulty at all in amending it in order to meet the

1 requirements of the DSMB for its second meeting.

2 MR JUSTICE BURTON: You can deal with it in your opening,
3 but the requirements of the DSMB were simply to have 100
4 patients by the second meeting. It was your clients who
5 said: ooh lord, we can't possibly comply with that
6 without amending the DMP to remove the mandatory
7 requirement which there would otherwise be before we
8 could deliver those 100.

9 MR BEAR: With great respect it's not quite right that the
10 requirement was simply to look at the data. What the
11 DSMB said is: we want to look at it as soon as possible.

12 MR JUSTICE BURTON: Oh, certainly.

13 MR BEAR: Yes, but that's the key point.

14 MR JUSTICE BURTON: I see it's a key point, but it didn't
15 automatically -- I mean, the DSMB didn't say: we want it
16 and of course we recognise you will have to amend your
17 DMP.

18 MR BEAR: Yes, they did. What they did was to say: you
19 won't be able to clean the data and put a soft lock on.
20 I'll show you the evidence.

21 MR JUSTICE BURTON: Right, okay, thank you. At any rate,
22 you say that this was a particularly important
23 amendment.

24 MR NASH: Yes.

25 MR JUSTICE BURTON: But in general terms, subject to having

1 parked it for the moment, you're not able at the moment
2 to say that SOPs and DMP are not in the sole discretion
3 of the defendants to draft, and you simply say that in
4 practice they were circulated before -- at an early
5 stage, all the SOPs, so your client saw them at some
6 stage. Presumably, therefore, also saw -- well, by
7 definition, therefore, saw DMP plan or version 1.0.

8 MR NASH: Yes.

9 MR JUSTICE BURTON: Albeit didn't approve it, saw it. Now,
10 did you see -- that was the 21st March -- did you see
11 version 1.01 which isn't in the core bundle?

12 MR NASH: The amendment, no we didn't see that, I think,
13 until January of this year.

14 MR JUSTICE BURTON: There is a version 1.02 which I've got
15 in the core bundle.

16 MR NASH: I'm sorry, I meant the amendment which removed the
17 soft lock?

18 MR JUSTICE BURTON: That was 1.02.

19 MR NASH: Yes.

20 MR JUSTICE BURTON: I was asking you about whether you saw
21 version 1.01, which I haven't got in the core bundle,
22 and which presumably, therefore, is not material. It
23 did amount to some kind of amendment.

24 MR NASH: 1.01, I think, is the amendment whereby the DSMB
25 ask for an additional table or an additional --

1 a variation in the tables, and I don't think that that
2 is said to be material by either side.

3 MR JUSTICE BURTON: Did you see it?

4 MR NASH: I'm not sure, I don't think --

5 MR JUSTICE BURTON: It would be significant if you saw every
6 single thing but not this one. You're saying: if it's
7 a minor amendment, you don't expect to see it. If it's
8 of significance, then of course you should have been
9 consulted.

10 MR NASH: Well, the first step is that the TSC should be
11 consulted. The TSC is charged for supervising --

12 MR JUSTICE BURTON: When I say you I meant the TSC. Yes,
13 I see that, because you are represented on the TSC, so
14 you'll soon find out about it.

15 MR NASH: Yes.

16 MR JUSTICE BURTON: Can I just look at 1.02? Is there
17 a special bundle of DMPs?

18 MR NASH: There is. There's not a special bundle of DMPs,
19 but there's a special bundle of SOPs.

20 MR JUSTICE BURTON: Yes, sir, I've got that. Where is DMP
21 version 1.01?

22 MR NASH: Bundle 2, tab 24, my Lord.

23 MR JUSTICE BURTON: Sorry? At some stage over an
24 adjournment, it would be very kind if someone would do
25 what I haven't done, which is to slot the -- could I ask

1 you to do this -- slot the indexes into the front of all
2 the bundles. Thank you. They're sitting here.

3 MR NASH: It's page 317 of SOP volume 2.

4 MR JUSTICE BURTON: Thank you. Yes?

5 MR NASH: This is 1701:
6 "Changes to DSMB data requirements."
7 And --

8 MR JUSTICE BURTON: Right, and it's 1/09/2007 I assume,
9 1st September 2007, the review date, it says, by error,
10 2009, but I assume it's the same date but a wrong year.

11 MR NASH: Yes.

12 MR JUSTICE BURTON: That's an unimportant -- it doesn't
13 matter to me, but do you know whether that was
14 circulated?

15 MR NASH: I don't believe it was circulated to us.

16 MR JUSTICE BURTON: To the TSC, is what I'm interested in.

17 MR NASH: I can't answer that.

18 MR JUSTICE BURTON: Thank you for that. So the
19 constitutional arrangement is that the obligation under
20 the protocol to prepare SOPs is that of the defendant,
21 and there is no constitutional requirement on them to
22 get permission, approval, or even give notice of any
23 amendments to those SOPs?

24 MR NASH: There's no rule that we can point to that says
25 that must have happened, yes.

1 MR JUSTICE BURTON: Right. So it just comes back to your
2 point that this was an important change, and it
3 wasn't -- do you say this: it wasn't a necessary result
4 of the request by the DSMBs for 100 patients?

5 MR NASH: Yes.

6 MR JUSTICE BURTON: Or do you say it?

7 MR NASH: We say in relation to that, my Lord -- it's
8 a matter obviously we'll have to deal with with
9 Dr Shakur -- is when the DSMB make this request to have
10 information for the 100 patients, and even if they
11 accept at that stage, well, we understand that you won't
12 be able to operate the soft lock for that particular
13 meeting, that was not a wholesale instruction that the
14 soft lock requirement to the DMP should be amended for
15 all future DSMB meetings. You will have seen the
16 amendment, I think, and it is changing the way the soft
17 lock was to be operated thenceforth.

18 MR JUSTICE BURTON: It was only by not making it mandatory,
19 wasn't it -- wasn't that all?

20 MR NASH: Yes.

21 MR JUSTICE BURTON: That change would have to be made in
22 order to accommodate the 1st November, and there's no
23 indication -- perhaps there is, I don't know, it will
24 have to be explored in evidence -- that this was going
25 to be taken advantage of for future occasions.

1 MR NASH: Well --

2 MR JUSTICE BURTON: There would be no point in amending
3 a DMP just to say: (except for the meeting of
4 1st November).

5 MR NASH: Sorry, my Lord, I obviously haven't made the point
6 correctly. It's the other way round. There's
7 a difference between saying: we understand for this
8 meeting you just need to comply with that rule --

9 MR JUSTICE BURTON: Except the DMP would need to be amended
10 for that purpose, wouldn't it? Just like they had
11 amended it to deal with what tables needed to be
12 required. Even if it was just for one meeting, the DMP
13 would have to be amended, wouldn't it?

14 MR NASH: My Lord, I don't think it would be for one
15 meeting. If it was a question simply -- if it was
16 simply waiving that rule, waiving that requirement for
17 that meeting, that's one thing. But that's different
18 obviously from saying we're now going to change the data
19 management rules henceforth for this trial.

20 MR JUSTICE BURTON: Right. Your case, which will need to be
21 explored is, it wasn't just because they asked for the
22 100 patients; it was because they knew they weren't
23 coping that they changed the rules with a view to giving
24 themselves more leeway.

25 MR NASH: Yes. I don't know whether your Lordship has

1 focused on the detail of the soft lock very much at this
2 stage, but you will appreciate that the way the soft
3 lock operates, or should have operated, is that six
4 weeks before the DSMB meeting, a population of patients
5 is isolated as being the population of patients in
6 respect of whom clean data will be submitted to the
7 DSMB.

8 MR JUSTICE BURTON: Yes.

9 MR NASH: What happened in September, as far as we can
10 determine, is that the population of clean data patients
11 that was presented to the DSMB was a markedly smaller
12 population of the total population of patients in
13 treatment at that time than there should have been, and
14 the DSMB --

15 MR JUSTICE BURTON: You mean because they had 227 patients?

16 MR NASH: Because they had been recruiting very quickly
17 in July and August.

18 MR JUSTICE BURTON: The DSMB only asked for 100.

19 MR NASH: In September, my Lord, but at the first -- at the
20 meeting in September, we think -- and it will be
21 explored in evidence -- that the DSMB concluded that
22 they weren't seeing enough data from the population of
23 patients as a whole so they said: we want to see the
24 data from 100 patients as soon as possible.

25 MR JUSTICE BURTON: Yes.

1 MR NASH: Because the population has expanded so much.

2 MR JUSTICE BURTON: Yes.

3 MR NASH: Now, in order to achieve that, there was -- or

4 it's said there's some discussion about removing the

5 soft lock. But it doesn't follow from that, that

6 discussion, that the DSMB were saying that: when we meet

7 in late October or November that we expect to receive

8 uncleaned data in relation to the patients. All that we

9 are saying is that you don't need to isolate your

10 population six weeks ahead of the meeting.

11 MR JUSTICE BURTON: Right.

12 MR NASH: So that's the point on the soft lock.

13 MR JUSTICE BURTON: That's your case. Of course, a lot will

14 depend upon what Dr Sandercock says.

15 MR NASH: Professor Sandercock, yes.

16 MR JUSTICE BURTON: Yes.

17 MR NASH: My Lord, I showed you the initial agreement. I'd

18 like to show you also, please, the CTSA, which is the

19 operative agreement for the conduct of the trial at core

20 bundle 2. I'm sorry, it's core bundle 1, tab 2.

21 MR JUSTICE BURTON: Yes.

22 MR NASH: On the first page, 304, within the recitals,

23 there's a reference to the initial agreement and then:

24 "Xytis now wishes to entrust the provider with the

25 performance of services in connection with the

1 organisation and management ..."

2 We emphasise that, my Lord, because despite the
3 overlay of regulations and so forth, this is essentially
4 a contract for services to be provided to us by the
5 school.

6 Then going through the articles, article 1 deals
7 again with the committees. Article 1.1 is important.
8 It states that the committees are to remain in place for
9 the purposes of this agreement, and that's our point on
10 when the agreement comes to an end, the committees come
11 to an end.

12 MR JUSTICE BURTON: Yes.

13 MR NASH: The form of the protocol committee is then defined
14 in 1.2, and then the role and responsibility of the TSC
15 is to provide overall supervision of safety and quality
16 of trial on behalf of the sponsor. So they are there
17 acting for us. One of their obligations is to ensure
18 adherence to the protocol, patient safety and so on, and
19 the responsibilities track what is in the initial
20 agreement.

21 My Lord, as far as contractual standard of
22 performance is concerned, one sees that at 2.2.

23 MR JUSTICE BURTON: Yes.

24 MR NASH: In accordance with the protocol, et cetera, and
25 GCP, and compliance with the ICH-GCP.

1 MR JUSTICE BURTON: Did you communicate any written
2 instructions, (i)?

3 MR NASH: I don't think we rely on any written instructions,
4 no, in relation to the issues in this case.

5 MR JUSTICE BURTON: Right.

6 MR NASH: Then 2.3(g) is the information clause.

7 MR JUSTICE BURTON: Just going back to the written
8 instructions which you could have but didn't
9 communicate, would it have made a difference to this
10 case or at all if you had given an instruction to the
11 provider that they must reconcile and pass on to the
12 DSMB the contents of the SAE forms?

13 MR NASH: I suspect, if we had given that instruction, we
14 would have met with resistance from the school probably
15 along the lines of: the DMP is a matter for us to deal
16 with.

17 MR JUSTICE BURTON: Then at least you could have said:
18 right, we want to know that the DSMB doesn't want the
19 information.

20 MR NASH: Yes, I can see that.

21 MR JUSTICE BURTON: At any rate, you didn't give such
22 instructions. I suppose -- I don't know -- did you know
23 that the SAE forms weren't being analysed and reconciled
24 and supplied?

25 MR NASH: Well, again, we didn't know that particular point

1 until after, as it were, the balloon went up on
2 1st November.

3 MR JUSTICE BURTON: Yes.

4 MR NASH: Then you know there's a great deal of
5 correspondence about the HPM database, what the DSMB had
6 seen, and so forth.

7 MR JUSTICE BURTON: Yes. But at any rate, prior to the
8 1st November, the TSC on which you were represented
9 didn't know that SAE forms were not being -- the
10 information from the SAE forms were not being supplied
11 to the DSMB.

12 MR NASH: One of the matters I want to explore in the
13 evidence, my Lord, is the extent to which Dr Shakur, who
14 had immediate daily management of the trial, was
15 reporting difficulties up the line.

16 MR JUSTICE BURTON: Right.

17 MR NASH: So, my Lord, there's clause 2.2.
18 2.3(g) is the information clause, which of course
19 you understand is part of the termination.

20 MR JUSTICE BURTON: Yes, I'm familiar with that.

21 MR NASH: I think we can then move through to covenants on
22 page 9, and 7.2 is a covenant that the services will be
23 performed in a professional manner in accordance with
24 the highest standards of the profession expected in the
25 performance of the services.

1 MR JUSTICE BURTON: Yes.

2 MR NASH: And again a reference to ICH-GCP at (ii).

3 MR JUSTICE BURTON: Yes.

4 MR NASH: And termination at article 9, I'm sure your
5 Lordship has worked through that.

6 MR JUSTICE BURTON: No reference to that other document,
7 whatever it's called, in your expert's report?

8 MR NASH: The large document in Charnley Nickols, no.
9 There's article 9, the termination provisions, which
10 your Lordship knows about.

11 MR JUSTICE BURTON: Yes.

12 MR NASH: Perhaps at the bottom of page 315 your Lordship
13 should keep in mind the obligation, if there is
14 termination, to deliver up, and that's one of the
15 remedies that we're seeking.

16 MR JUSTICE BURTON: Yes.

17 MR NASH: Then 10.6 may be relevant, the question of waiver.
18 So that's the contractual question with which we're
19 concerned.

20 Now, there's no doubt, my Lord, that the
21 relationship between the parties had soured considerably
22 before the decision of the DSMB on 1st November, and it
23 may not be necessary to decide in the end where the
24 fault lies in relation to that.

25 MR JUSTICE BURTON: Well, except for the purposes of the

1 defendant's counterclaim.

2 MR NASH: Yes, yes, possibly, my Lord, yes. Yes.

3 MR JUSTICE BURTON: Which, as I say, at the moment, although

4 I permitted it to go forward, I don't see it, for
5 reasons I've given, as having an independent life.

6 I can see -- indeed I've just done a trial last week,
7 which all hang on a defendant in that case putting
8 forward reasons for terminating the contract when in
9 fact they had real reasons which could be -- which
10 showed that the reasons they put forward were not
11 supportable. So I can see that it's going to be a part
12 of whether you really had these reasons that you say you
13 had in clause 9.2 and 9.3. So there's that as well, the
14 souring of the relationship, the desire to bring in the
15 alternative provider who popped up in October. It may
16 be earlier, but certainly the sign of Technostat --

17 MR NASH: Technostat, yes.

18 MR JUSTICE BURTON: -- the sign of them in October. So your
19 clients will be cross-examined on the basis, I assume,
20 that this is all a rouse to find a way out of the
21 contract.

22 But, from your point of view, it's not important.

23 From your point of view, you need to establish that you
24 had reasons in November and December and February.

25 MR NASH: Yes, yes.

1 MR JUSTICE BURTON: Yes.

2 MR NASH: If necessary, we will say that the difficulties
3 arose by reason of the school's resentment and rejection
4 of any proposal to amend the protocol so as to increase
5 the population or the follow-up period. They took the
6 view that it was indefensible on scientific grounds.
7 I must make it absolutely clear, my Lord, that in taking
8 that position, there was no question of Xytis tainting
9 the work which had already been done, ie skewing the
10 science up to then. There were problems, or there were
11 anticipated difficulties, according to the school, in
12 simply the resource to follow up patients at an extended
13 period.

14 This trial was intended to be a 15 day direct
15 observation period, I think with a follow-up over the
16 following four weeks, and to increase that period to
17 follow up patients at a later stage they considered
18 would involve too much work and too much expense.

19 MR JUSTICE BURTON: Were Technostat prepared to go in on the
20 basis of an amended protocol? Is that one of their
21 charms?

22 MR NASH: I beg your pardon?

23 MR JUSTICE BURTON: Is one of the charms of Technostat as an
24 alternative provider that they were prepared to do
25 a larger number of patients and to amend the protocol?

1 It wouldn't have been the same protocol.

2 MR NASH: I don't know whether they were prepared to amend
3 the protocol, but --

4 MR JUSTICE BURTON: It would have been a different protocol
5 anyway, but --

6 MR NASH: -- they are certainly persuaded that it is
7 necessary to seek more data than this present trial is
8 seeking.

9 MR JUSTICE BURTON: So that's one of the commercial
10 advantages that would be gained, not only having
11 a provider who you would feel more comfortable with, but
12 also a provider who will do that which this provider was
13 not willing to do in August, September, October.

14 MR NASH: Well, yes, save that I don't think it ever got to
15 a moment where the TSC refused to allow an amendment,
16 because matters were overtaken by the 1st November
17 meeting and the difficulties that arose from that. But
18 certainly there was resistance in correspondence or
19 email between Professor Roberts and Mr Simmon.

20 MR JUSTICE BURTON: You say that -- I don't know, but you
21 never put it before the TSC. You seem to have accepted
22 the refusal by Professor Roberts.

23 MR NASH: There was a draft amendment, quite a full
24 amendment, to the protocol, draft number 3.

25 MR JUSTICE BURTON: Yes, which Professor Roberts wouldn't

1 have --

2 MR NASH: Yes.

3 MR JUSTICE BURTON: -- and that was it.

4 MR NASH: Well, then the next stage, I suppose, would have

5 been to go to the TSC, but, as I say --

6 MR JUSTICE BURTON: How long before 1st November did the

7 amendment of the protocol get rejected?

8 MR NASH: I think the amendment --

9 MR JUSTICE BURTON: Beginning of October, wasn't it?

10 MR NASH: I think it's October. Whether it's the

11 beginning -- it's certainly October. Whether it's the

12 beginning or not --

13 MR BEAR: We will be looking at this in Mr Simmon's

14 cross-examination, but it is first advanced to the

15 school on 17th August, and it's rejected by

16 Professor Roberts about two weeks after that.

17 MR JUSTICE BURTON: Yes, I follow.

18 MR BEAR: Then there's further correspondence in which the

19 point is --

20 MR JUSTICE BURTON: So it was off the agenda by September,

21 which is no doubt why the claimants were by then

22 thinking of their alternatives.

23 MR BEAR: That's our case, yes.

24 MR JUSTICE BURTON: Yes.

25 MR NASH: I am told it was going to go to the TSC, but it's

1 never actually been looked at by the TSC.

2 MR JUSTICE BURTON: Yes.

3 MR NASH: Yes.

4 In any event, notwithstanding those issues, Xytis
5 had perfectly legitimate concerns about the quality of
6 data collection and processing, and we, I think,
7 discussed that earlier this morning.

8 There's no doubt that data collection for this trial
9 was complex and challenging.

10 MR JUSTICE BURTON: Just dealing with that -- you are about
11 to deal with it, but at the moment I rather share
12 Mr Bear's concerns about precisely how it's put, both by
13 reference to Miss Charnley Nickols' report and even in
14 the light of the agreed document from the weekend, and
15 certainly in the light of the rather lengthy February
16 notice, and if you were able, just as you've been able
17 to formulate the main case in relation to a failure to
18 reconcile, failure to clean, misusing the amendment by
19 way of the soft lock, falling behind on cleansing
20 generally, et cetera, et cetera, that's your main case
21 and you put that very concisely.

22 If you are able, at least, to summarise at some
23 point on a piece of paper, in perhaps 15 lines or so, or
24 a number of subheadings, what your case is on this
25 fall-back case, because at the moment I can't get my

1 mind around it, the data collection and management case,
2 save insofar as it relies upon what we've just been
3 discussing.

4 It's a very diffuse series of criticisms.

5 MR NASH: We'll look at that, my Lord. I had hoped that the
6 Charnley Nickols notice in February, if nothing else, or
7 the notice based on --

8 MR JUSTICE BURTON: It's a page and a half as far as
9 I remember, isn't it?

10 MR NASH: There's a schedule to it.

11 MR JUSTICE BURTON: Yes, exactly. I don't blame you,
12 because you needed to put the kitchen sink in in order
13 to safeguard yourself. The case has come on so quickly.

14 MR NASH: Sure.

15 MR JUSTICE BURTON: Reports were being prepared, et cetera,
16 et cetera. If you are now able to at least tell me what
17 your main criticisms are under this head, even if it's
18 four or five major criticisms, it would help, because
19 I've got to get my mind around it.

20 At the moment, it just feels like a general grumble.

21 MR NASH: We'll produce a document, my Lord.

22 MR JUSTICE BURTON: Thank you.

23 MR NASH: I was about to agree with Professor Roberts, who
24 says in his statement that data monitoring is one of the
25 most methodologically challenging aspects of conducting

1 a trial of this sort. The problem is readily apparent
2 from the multitude of queries which data reporting gave
3 rise to, which we have in two files called the AE files,
4 the adverse events files.

5 My Lord, and again, I think this is what I touched
6 on this morning, reference has been made to errors in
7 the data, and I think certainly Professor Sandercock
8 says in particular that that's a misnomer, and we agree
9 to some extent. We're not talking just about simple
10 mistakes; we're talking also about misunderstandings of
11 the trial criteria and in particular the key criteria of
12 what counts as an adverse event or not.

13 Misunderstandings at local level which give rise to
14 inaccurate data, ie data which does not conform with the
15 protocol definition, being reported up to the TSC.

16 MR JUSTICE BURTON: If you were able to show -- I don't know
17 whether you are -- some kind of picture in which there
18 were so many errors coming up from the reporting
19 officers which were checked by the defendant and found
20 not really to be SAEs, something perhaps along the lines
21 of this spreadsheet once it's explained, then that might
22 strengthen your case that they really ought to have
23 double-checked them against the SAE form. By I haven't
24 got a picture of numerous errors being picked up which
25 should have led them to realise that things were going

1 wrong.

2 We can't blame the defendants for errors made by the
3 CRAs or a fortiori by the doctor.

4 MR NASH: We certainly can't blame -- well, subject to
5 points about training and so forth, we can't blame them
6 for errors at the site, but they had a separate
7 obligation to clean the data.

8 MR JUSTICE BURTON: Yes.

9 MR NASH: To check and clean.

10 MR JUSTICE BURTON: Is there any evidence that apart from
11 not reconciling them against the SAE forms, they were
12 not doing that?

13 MR NASH: Yes, my Lord, it's the Charnley Nickols report and
14 the --

15 MR JUSTICE BURTON: Give me a reference in it. I won't ask
16 you to read it to me now, but which section or sections
17 of Charnley Nickols? Of course I have read the report,
18 but clearly without the benefit of your education.

19 MR NASH: My Lord, it's particularly focused on in her
20 question: has the data been adequately cleaned? That
21 begins at page 17. If your Lordship finds --

22 MR JUSTICE BURTON: Yes, I have noted down that page.
23 I remember it as being significant. I thought -- again,
24 I was tying it into the absence of the SAE forms. You
25 say it's more general than that?

1 MR NASH: That section through to page 22 --

2 MR JUSTICE BURTON: Well, I'll read it again. But, as
3 I say, I had read that -- apart, of course, from the
4 reference on page 22 to the spreadsheet which I couldn't
5 appreciate then because I didn't have it and I still
6 don't appreciate now having got it, but that's obviously
7 a matter of importance, reported AEs that were not real
8 AEs, if it was known by Sealed Envelope and the
9 defendant that matters that had been reported as an AE
10 wasn't a real AE and yet were still reported as an AE to
11 the DSMB, I understand that's an important case which is
12 only tickled at on page 22.

13 But apart from that, I had only read 17 to 21 as
14 relating to your main point about, the perfect way of
15 reconciliation would have been to have brought in the
16 SAE forms and they should have done it, et cetera,
17 et cetera. But leaving aside the failure to reconcile
18 the SAE forms, and for the moment leaving aside the
19 spreadsheet, do you have evidence of a failure to clean
20 and a failure to reconcile by reference to the AEs? If
21 you do, it's just in these pages, is this it?

22 MR NASH: It's in the Charnley Nickols report.

23 MR JUSTICE BURTON: 17 to 21?

24 MR NASH: 17 to 21, and the underlying material that I will
25 be cross-examining on are the AE files, of which there

1 are two. So your Lordship knows what are in the AE
2 files --

3 MR BEAR: Can I just pause here? They weren't in the index
4 proposed for the agreed trial bundles. They appeared at
5 the start of last week. We objected to them saying they
6 weren't agreed. That request was not dealt with
7 expressly, until a letter I think either late last night
8 or tomorrow morning which asserts that they go to
9 a "central issue in this trial".

10 MR JUSTICE BURTON: I'm missing you?

11 MR BEAR: Forgive me, my voice is also suffering from what
12 you had, I think we've probably shared the same
13 underlying condition so to speak. A letter from
14 Messrs Dechert either yesterday evening, late, or first
15 thing tomorrow morning, says that these bundles which
16 we've objected to, which weren't in the proposed index,
17 are bundles which go to a "central issue in the trial".

18 That's as far as it's got.

19 MR JUSTICE BURTON: We're about to learn it.

20 MR BEAR: I'm just putting down a marker, that we haven't
21 agreed --

22 MR JUSTICE BURTON: They're documents which emanate from one
23 side or the other. They're not new documents.

24 MR BEAR: They're not new documents, I assume, although
25 I don't know -- Mr Nash will tell me if this is wrong --

1 that they have been pooled off a mirror copy of the
2 database which your Lordship ordered, which must
3 contain, no doubt, tens of thousands of pages.

4 MR JUSTICE BURTON: It does mean that you're going to need
5 to have some kind of understanding of what case is going
6 to be made based on it.

7 MR BEAR: If there's now to be a new systemic case and we
8 say obviously they haven't begun to lay the ground for
9 it, that's another distraction.

10 MR JUSTICE BURTON: That does make some sense, Mr Nash. My
11 lack of understanding is obviously not simply my
12 ignorance; it seems to be shared by Mr Bear and his
13 solicitors, and if you're going to be using this bundle
14 as a basis of cross-examination then I think we ought to
15 understand what it is that's coming to you.

16 Is this a subset of the main case, namely it's
17 illustrating the significance of the necessity of
18 reconciling SAEs and, therefore, bringing in the SAE
19 forms, or is it part of a separate case which is lousy
20 operation of the database?

21 MR NASH: It's not lousy operation of the database, my Lord.
22 It is whether, as we pleaded, the CRFs were being
23 cleaned properly at the school.

24 So your Lordship knows what's in the AE bundle, it
25 is the 92 adverse claims, in other words SAEs, that were

1 presented to the DSMB.

2 MR JUSTICE BURTON: Which you say should have been 57?

3 MR NASH: Yes, I think 57 is the right number. Anyway, 56

4 or 57. They're divided up to show the SAE and the

5 queries that were being generated by the school in

6 relation to those SAEs, and if one goes through that,

7 one sees, firstly, the difficulties that the school were

8 facing in chasing up queries and the extent of delay

9 which was becoming pressing, we say, by October, in

10 relation to resolving queries on those SAEs.

11 MR JUSTICE BURTON: You see, I'd thought up till now that

12 the answer to that was -- either an answer or your real

13 case, which is: if only you had filtered in the SAE

14 forms, that would have resolved the questions, or

15 resolved the queries. But you seem to be making a quite

16 separate case in addition, namely that really, even if

17 you had brought the SAE forms in, it would only have

18 added to the puzzlement because you just weren't doing

19 your job of cleaning quickly or efficiently enough.

20 MR NASH: It is part of the pleaded case -- and it's part of

21 the case to which Dr Shakur and indeed Professor Roberts

22 have given evidence. So I can't really conceive that

23 it's caused surprise. Dr Shakur in particular gives

24 evidence about the difficulties in chasing up queries.

25 Professor Roberts gives quite a lot of evidence --

1 MR JUSTICE BURTON: I have understood it. If Mr Bear wants
2 any more information, he'll ask for it.

3 In general terms, you are saying that it's only part
4 of your complaint that the SAE forms were set on one
5 side. That would have been a helpful way of bringing it
6 in to the checking or reconciling system. But there was
7 just no timeous or efficient operation of a checking of
8 the SAEs, even as provided from the CRF forms.

9 MR NASH: Yes, yes.

10 MR JUSTICE BURTON: Right. All that, of course, is answered
11 by saying: well, the DSMB knew that we hadn't cleansed.
12 I had understood your answer to that by saying: ah, but
13 they didn't know -- but perhaps they do -- that the SAE
14 forms weren't being looked at at all. But insofar as
15 you are saying, well, this is a very poor cleansing
16 exercise being done, they did know that it wasn't being
17 cleansed, you say they didn't know the extent of a lack
18 of cleaning.

19 MR NASH: Yes, exactly. It's a matter to be explored with
20 Professor Sandercock exactly what they understood they
21 were getting on 1st November.

22 MR JUSTICE BURTON: If your case is: there was a very
23 substantial failure to clean -- and I can show it by
24 cross-examination -- by reference to the SAE forms, and
25 I'm not going to stop you, subject to what Mr Bear may

1 say, that is going to take a bit of time, isn't it, in
2 cross-examination?

3 MR NASH: I'm not going to go through every single SAE form
4 I'm going to --

5 MR JUSTICE BURTON: But have got to show -- because they're
6 going to say, a few errors here and there, this is what
7 you expect, it would be cleaned up by the end. You've
8 got to show me that this is really a monumental failure,
9 haven't you. I'll not going to put a limit on it, but
10 I would have thought you've got to show at least 30
11 badly followed up or incorrectly assessed SAEs, haven't
12 you, by reference to the SAE files?

13 MR NASH: I think we need to try and establish the extent to
14 which the data remained in an unclean state.

15 MR JUSTICE BURTON: I understand that, but their case is: of
16 course it was unclean. The DSMB knew it was, it was
17 bound to be with the speed that they were insisting on,
18 the rapid expansion of the recruitment, et cetera,
19 et cetera. It's only because this is a DSMB requirement
20 that this arises at all. The DSMB is an optional extra.
21 Our obligations are that by the end of the trial
22 everything's got to be cleaned and reconciled, and it
23 would have been.

24 In order to meet that case, haven't you got to show
25 that you were just doing this very badly from beginning

1 to end. You might have sorted it all out by the end,
2 but you are in breach of your obligation, not simply by
3 virtue of the imposition of the request from the DSMB
4 for 1st November, but generally.

5 Now, to do that, you've got to show me more than
6 a few errors here and there, because there are bound to
7 be errors.

8 MR NASH: We accept that there are bound to be errors,
9 my Lord, but it's wrong to suggest that the whole issue
10 of cleaning is postponed until the end of the trial.
11 Cleaning is going on throughout the trial. The DSMB is
12 not an optional extra in the sense that once you have
13 decided you're going to have a DSMB, the DSMB is
14 performing the primary safety function on this trial,
15 which is there to monitor the safety of the product at
16 trial.

17 MR JUSTICE BURTON: Maybe I am just putting down a marker
18 that I am not going to be impressed by two or three
19 failures, which why you have got to show me quite a lot
20 of failures, in which case it is going to take quite
21 a bit of time.

22 MR NASH: I think Dr Shakur's cross-examination is likely to
23 take a little bit of time.

24 MR JUSTICE BURTON: Yes, that's why -- all I'm doing,
25 really, is highlighting what we discussed briefly

1 earlier, that two days, whatever it was, for factual
2 witnesses is not going to be enough.

3 MR NASH: Understood. My Lord, I've already used much more
4 than --

5 MR JUSTICE BURTON: Don't worry, you carry on, I'm
6 interrupting a lot. Take up till lunch.

7 MR NASH: Okay. The difficulties were perhaps exacerbated
8 by confusion arising from a feature in the protocol, the
9 paragraph 8.3.1 feature, which excluded AEs which were
10 expected in the course of TBI, and that appears to have
11 caused real confusion amongst the researchers at local
12 level, and we know, because we've seen the emails, that
13 by 19th October, Dr Shakur had prepared a spreadsheet of
14 reported AEs which were not real AEs, and we think --
15 although, again, it's a matter for cross-examination --
16 that that comprises AEs where the local doctors are
17 thought to have misunderstood the trial criteria.

18 MR JUSTICE BURTON: Is it your understanding that
19 notwithstanding the characterisation of those events as
20 not real AEs that they were nevertheless reported as AEs
21 without qualification to the DSMB?

22 MR NASH: That's our understanding.

23 MR JUSTICE BURTON: That's part of your criticism.

24 MR NASH: Yes. I've made the point that the cleaning of
25 data is not about eliminating simple errors, but also

1 testing for mistakes as to trial criteria and
2 inconsistency across the network, and it's obviously, we
3 suggest, a vital part of obtaining scientifically
4 objective data on which decisions about safety as well
5 as efficacy can be made.

6 My Lord, there's no fixed timetable within which
7 data must be cleaned. The GCP requires procedures to be
8 in place to ensure that the data is accurate for
9 reporting purposes. We've seen the paragraph earlier
10 today.

11 The SAE SOP, standard operating practice, required
12 the local trial centres to report separately SAEs within
13 24 hours to the school and for the school to pass them
14 on to HPM, the pharmacovigilance people, within
15 a further 24 hours.

16 There's also reference in the DMP to a period of
17 five days for second entry of data at the school, ie
18 five days from receipt of the CRF at the school, has got
19 to be second entered there.

20 Otherwise, the data has to be cleaned as an ongoing
21 process. But we say that the statements to the effect
22 that nobody expects the data to be 100 per cent
23 accurate, or the data is only clean when the trial is
24 finished --

25 MR JUSTICE BURTON: You say that the SAE SOP makes certain

1 requirements of which -- because the defendant's answer
2 is: that was regulatory. Do you say it is sufficiently
3 interrelated, even in the SOPs, that it should have been
4 apparent that it should have not been regarded as
5 a separate exercise to report it to the
6 pharmacovigilance people, that it should have been part
7 of the main CRF entries?

8 MR NASH: No, as far as the separate reporting up to
9 pharmacovigilance, that's governed by the SAE SOP, and
10 we don't seek to interlink the two. It's a separate
11 exercise.

12 We do say -- this is a point that comes out of some
13 of the things said in the witness statements -- that
14 it's wrong to regard HPM as simply performing
15 a regulatory exercise. It is part -- HPM is part of the
16 safety overview in this trial.

17 MR JUSTICE BURTON: But the SOPs do not interlink the two at
18 all. The SOPs do not produce any inference that in the,
19 for example, second entry of the CRF forms regard should
20 be paid to the SAE forms, there's nothing of that kind?

21 MR NASH: There's no statement to that effect, no.

22 MR JUSTICE BURTON: Right.

23 MR NASH: Now, my Lord, we accept that the catalyst for this
24 litigation was the decision of the DSMB to suspend
25 recruitment and treatment on 1st November last year.

1 It's proper that Xytis was concerned to understand the
2 basis for that decision, but we make it clear, again --
3 although it's said in the skeleton -- that it's no part
4 of our case that the DSMB made a wrong decision in
5 suspending the trial. It was a case of safety first.

6 Our complaint is a different one. It's that by the
7 time of the DSMB meeting, the data collection and
8 cleaning had fallen so far behind, it was so defective,
9 as to amount to a breach of GCP -- see the
10 Charnley Nickols report -- and therefore a breach of
11 contract, and also in our view -- and it was a matter
12 for to us reach a view on -- to endanger patient safety.

13 Putting it shortly, we say that the TCC, or the
14 school -- to get away from the acronym-- had lost its
15 grip on the data. This had the consequence that the
16 data presented to the DSMB was unclean, we say
17 substantially unclean, although the precise level of
18 uncleanliness is impossible to establish, I think, on
19 the documents.

20 It's a matter for cross-examination to determine the
21 extent to which the DSMB appreciated the uncleanliness
22 of the data.

23 It so happens that the data appeared to reveal
24 adverse trends so the trial was suspended, but Xytis's
25 point is that it could just have easily disguised

1 adverse trends leading to the continuation of the trial
2 when this was inappropriate and dangerous for patients.

3 MR JUSTICE BURTON: It could have done, but on the facts
4 you're not saying that they underestimated SAEs, so as
5 far as conclusion number 2 is concerned, that remains --
6 in the 1st November notice, that remains unaffected by
7 your case, doesn't it?

8 MR NASH: It goes to the question of patient safety,
9 I think, my Lord, because it's been suggested that
10 because the trial was suspended there could be no issue
11 as to that.

12 MR JUSTICE BURTON: Yes.

13 MR NASH: But if one has problems with the data --

14 MR JUSTICE BURTON: Data safety by virtue of your complaint
15 about the system, but given that -- all I'm enquiring at
16 the moment about, given that the only way in which your
17 criticisms go is that in fact they overstated the SAEs,
18 it can't affect, can it, the DSMB's decision to suspend
19 the trial, if that's what it was, on their second
20 ground.

21 Let me quickly look at that, the wording of the
22 second ground. As I say, I'm not sure how far this
23 goes, but it may go to the fundamentality of the breach.

24 The 1st November notice is -- which tab is it? 22
25 is it?

1 MR NASH: The 1st November notice?

2 MR JUSTICE BURTON: Of course, yes, it was the TSC.

3 MR NASH: The DSMB recommendation?

4 MR JUSTICE BURTON: Yes, that's right. I've got it at

5 tab 45:

6 "The efficacy results at day 15 provided no evidence

7 of benefit and there were adverse trends in all three

8 outcome measures."

9 Now that's unaffected, isn't it, by all your

10 criticisms?

11 MR NASH: That's right, my Lord. I'm not going to

12 cross-examine along the lines that the HIREOS scale, for

13 example, has been wrongly entered.

14 MR JUSTICE BURTON: Yes, so on that basis, the -- we'll have

15 to hear what Professor Sandercock says, but if he says

16 they would have suspended recruitment on the basis of

17 (b) anyway, that doesn't result from any failure by the

18 defendant?

19 MR NASH: You're absolutely right, my Lord, that's a matter

20 for cross-examination of Professor Sandercock.

21 MR JUSTICE BURTON: Yes, thank you.

22 MR NASH: My Lord, our position on the issues very swiftly,

23 then.

24 As far as the first notice is concerned, it's

25 largely a question of construction, the meaning of

1 "administrative" and "ministerial" and "suspension" and
2 so forth, and we will deal with that at the end.

3 MR JUSTICE BURTON: Yes, it didn't seem to me Mr Bear had,
4 in his pleading, set out as clearly as he does in his
5 skeleton, that he doesn't just rely on the
6 administrative/ministerial point -- and I find it a more
7 persuasive case than the administrative/ministerial --
8 I'm not saying I don't find administrative/ministerial
9 persuasive also -- but I found the suspension point,
10 that it isn't in fact a suspension, a much clearer
11 point. You're not saying you are prejudiced by that not
12 being sufficiently pleaded.

13 MR NASH: I'm here to argue that point, my Lord.

14 MR JUSTICE BURTON: That seems to be a point which has
15 emerged in its full glory only in his skeleton.

16 MR NASH: It's an expedited trial, my Lord, so we're all
17 running to catch up to some extent.

18 There's the issue of the decision was genuinely
19 motivated by patient safety, and that will turn on your
20 Lordship's assessment, I think largely of Mr Simmon and
21 Mr Furcha's evidence.

22 MR JUSTICE BURTON: Yes. Do you accept that the decision
23 has got to be non-capricious? Using the words in
24 Clark v Nomura?

25 MR NASH: The way we put it is, it's got to be a decision

1 made in good faith.

2 MR JUSTICE BURTON: Yes, but Mr Bear says: in addition to

3 good faith, it's also got to be one which -- it was

4 almost the administrative law test, ie not one made on

5 reasonable grounds, that puts the case too high. It

6 clearly can't be that given that it's in your sole

7 discretion, but it's got to be one which -- not one

8 which no reasonable employer --

9 MR NASH: Wednesbury reasonableness, yes.

10 MR JUSTICE BURTON: -- in the case of Clark v Nomura, no

11 reasonable contracting party could have taken. It puts

12 it very high, which is why I use the word "capricious",

13 but there is that element, isn't there: it's got to be

14 actually made in good faith and not one which is

15 capricious, not one which is without reason.

16 MR NASH: We don't accept the third element, my Lord.

17 MR JUSTICE BURTON: I understand that. I say I understand,

18 I've asked that. You don't accept that?

19 MR NASH: We don't accept that.

20 MR JUSTICE BURTON: You say that it could be capricious.

21 I am citing you for not wearing a green sweater, but in

22 fact you have never been known to wear a green sweater.

23 I just assume you come in wearing green sweaters and in

24 good faith, because I'm sure you must have worn a green

25 sweater on one day or another, but I've got absolutely

1 no reason to know whether you didn't, but I'm sacking
2 you for that reason.

3 I genuinely believe that, but I've never taken any
4 steps to find out whether you even wore a sweater at
5 all, never mind what colour it was. That would be okay,
6 would it?

7 MR NASH: I see the way your Lordship puts it. But we will
8 deal with that --

9 MR JUSTICE BURTON: It's just worth looking at
10 Clark v Nomura, which is there. It doesn't make it the
11 same as -- that was a bonus case, and I notice other
12 authorities in the bundle. It doesn't make the same as,
13 you've got to show you have reasonable grounds.

14 MR NASH: Quite.

15 MR JUSTICE BURTON: What you'd have to show is that there
16 was a ground, it's not one which no reasonable person
17 could have made.

18 MR NASH: That's that.

19 MR JUSTICE BURTON: Yes.

20 MR NASH: We rely as far as information is concerned, or
21 failure to provide information, on the notices given or
22 the demands for information on the 2nd and 8th November.

23 MR JUSTICE BURTON: Yes.

24 MR NASH: We say we were entitled to seek, albeit in
25 unblinded form, the data which went to --

1 MR JUSTICE BURTON: Will you just tell me in two sentences
2 what it is of an unblinded nature that you didn't get
3 pursuant to that request which they could reasonably
4 have provided?

5 MR NASH: We wanted, in blinded form -- to protect the
6 blinding -- the information which went to the DSMB on
7 1st November.

8 MR JUSTICE BURTON: Didn't you get that on 14th November?

9 MR NASH: We say we didn't get it in the data dump, because
10 the data dump was firstly a mass of raw data which isn't
11 sorted in any particular way.

12 MR JUSTICE BURTON: But isn't that what went to the DSMB?

13 MR NASH: No, that went to Sealed Envelope who then cast it
14 into the tables that went up to the DSMB.

15 MR JUSTICE BURTON: And did Sealed Envelope provide it in
16 unblinded form? I didn't think they did. I thought
17 DSMB's -- sorry, blinded form. I thought Sealed
18 Envelope provide it in unblinded form.

19 MR NASH: Yes, the tables are unblinded.

20 MR JUSTICE BURTON: How can you see that?

21 MR NASH: There would have had to be protection of those
22 tables. Either the blinding we were suggesting was to
23 use simply A, B, C, D for the groups.

24 MR JUSTICE BURTON: Well, let me understand this. You got
25 what was supplied to Sealed Envelope, which was in

1 blinded form.

2 MR NASH: Yes.

3 MR JUSTICE BURTON: You wanted to see what Sealed Envelope
4 provided to DSMB, but you couldn't because that was
5 unblinded. So you wanted an exercise carried out which
6 would have amounted to the blinding of the unblinded
7 information supplied by Sealed Envelope?

8 MR NASH: Yes. That's one element of it, my Lord. The
9 other two elements, or the other two points to make in
10 relation to that, is that the data dump, as we
11 understand it, was not broken up into the forms which
12 you get in the shell tables which went up to the DSMB.
13 It is just a mass of data as it appears on the school's
14 database.

15 So we would have wanted (a) anonymised, blinded
16 tables, but the same tables that the DSMB got.
17 Alternatively -- and we were open to suggestions -- the
18 data from the data dump broken up into the various
19 tables which were supplied to the DSMB, but in a way
20 which didn't distinguish between the treatment groups,
21 and --

22 MR JUSTICE BURTON: That's a whole lot of extra work.

23 MR NASH: And finally, and in any event, the data dump, when
24 it arrived on 14th November, we weren't able to read
25 without access to, firstly, the MYSQL software and even

1 when we got the MYSQL software we weren't able to read
2 it as effectively as ultimately we've been able to read
3 it through provision of the --

4 MR JUSTICE BURTON: There it is, that's your case under 9.3
5 which requires to be reasonable and give enough time to
6 comply with it, and requires to take account of the fact
7 that the information has got to be blinded.

8 MR NASH: Yes.

9 MR JUSTICE BURTON: Yes?

10 MR NASH: And finally, my Lord, we have the notices of which
11 the latest version is in February based on the
12 Charnley Nickols report, but the earlier version is also
13 based on breach in relation to data handling, and
14 I think we have discussed that at some length already
15 this morning.

16 MR JUSTICE BURTON: Subject to your giving me this extra
17 document relating to your fall-back, I call it
18 fall-back, your alternative case, the nub of the case it
19 seems to me to revolve around the SAEs and SAE forms,
20 the duty to reconcile, the duty to clean in relation to
21 SAEs, and the consequence of the undisclosed amendments
22 of the DMP.

23 MR NASH: Yes.

24 MR JUSTICE BURTON: I can see how your cross-examination on
25 what they got up to, insofar as cleansing is concerned,

1 feeds into the overriding point on the SAE form.

2 As to anything else, all this training, and this
3 that and the other, and reliance on the audit reports
4 and triggers and all that, how far any of that survives
5 as an alternative case I shall need persuading of, and
6 certainly that's what I need putting on a piece of
7 paper.

8 MR NASH: I understand, my Lord.

9 My Lord, those were the points I wanted to make in
10 opening, and I think it takes us to 1.00.

11 MR JUSTICE BURTON: Thank you very much. I look forward to
12 hearing you at 2.00. Thank you.

13 (1.00 pm)

14 (The short adjournment)

15 (2.00 pm)

16 MR NASH: My Lord, one very short follow-up from this
17 morning, and it's in answer to your Lordship's question
18 about what we should have got in response to our notices
19 on the 2nd and 8th November. You said, well, you've got
20 the data dump. The answer is, what we should have been
21 given is quite straightforwardly a list of the 94 SAEs
22 which had been submitted to the DSMB. That could have
23 been given in an entirely blinded form in the sense that
24 it did not need to distinguish between --

25 MR JUSTICE BURTON: Is that what you asked for?

1 MR NASH: Well, we asked for, in unblinded form, the data
2 which went to the DSMB.

3 MR JUSTICE BURTON: Yes.

4 MR NASH: And a response to that, a sensible response to
5 that, would have been: the list of the 94. The data
6 dump which we got later on, apart from the difficulties
7 with the data dump, contained both the SAEs which had
8 gone to the DSMB and the separate part of the database
9 which included the SAE forms which had been received for
10 transmission on to HPM.

11 MR JUSTICE BURTON: Which had not gone to the DSMB?

12 MR NASH: Which had not gone to DSMB and we were not told
13 when we received -- we were not told at that stage which
14 of the two groups had been the basis of the DSMB
15 decision. In fact we say -- although this is in
16 dispute -- that we were told that the DSMB had had
17 a look at the -- I call it HMP, I think it's HPM
18 information. So that's a short answer to the notice
19 point.

20 MR JUSTICE BURTON: Thank you very much. Yes?

21 Opening Submissions by MR BEAR

22 MR BEAR: If your Lordship would take the authorities bundle
23 and go to divider 1, which is the regulations you will
24 see at page 69 of the print-out, part 2 of schedule 1,
25 at the foot of the page:

1 "Conditions and principles which apply to all
2 clinical trials."

3 Over the page, the first principle with the number
4 at the bottom of page 69 is stated as follows:

5 "The rights, safety and well being of the trial
6 subjects shall prevail over the interests of science and
7 society."

8 Then paragraph 10 dropping down says that:

9 "Before the trial is initiated, foreseeable risks
10 and inconveniences have been weighed against the
11 anticipated benefit for the individual trial subjects
12 and other present and future patients."

13 Then this:

14 "A trial should be initiated and continued only if
15 the anticipated benefits justify the risks."

16 Then finally paragraph 6 in the middle of the page
17 is a reference to the Declaration of Helsinki. Your
18 Lordship doesn't have that yet in the bundle, but it's
19 also referred to in the protocol.

20 Can I hand that up and perhaps we can put it at the
21 beginning or end of this divider if that's convenient.

22 I'll give you the cross-reference for the protocol
23 which incorporates the Declaration of Helsinki in
24 a moment.

25 If we can just look at it, it's a declaration dating

1 originally from 1964 and amended since, from the World
2 Medical Association, the WMA.

3 Paragraph 1:

4 "The association has developed the Declaration of
5 Helsinki as a statement of ethical principles to provide
6 guidance to physicians and other participants in medical
7 research involving human subjects."

8 Number 2:

9 "It is the duty of the physician to promote and
10 safeguard the health of the people. The physician's
11 knowledge and conscience are dedicated to the fulfilment
12 of this duty."

13 Number 3:

14 "The Declaration of Geneva of the World Medical
15 Association binds the physician with the words: the
16 health of my patient will be my first consideration.
17 The International Code of Medical Ethics declares
18 a physician shall act only in the patient's interest
19 when providing medical care", et cetera.

20 Then dropping down to 5:

21 "In medical research on human subjects,
22 considerations related to the well being of the human
23 subject should take precedence over the interests of
24 science and society."

25 So that fairly ringing endorsement chimes with what

1 one saw in paragraphs 1 and 10 of schedule 1, part 2,
2 which is very firmly putting patient interests and
3 patient safety at the centre of any trial.

4 MR JUSTICE BURTON: Well, there's no issue between the two
5 of you.

6 MR BEAR: There's no issue between us about that as
7 a principle, but it's quite important in terms of how it
8 affected what was done, and we say properly done, in
9 this case.

10 I mentioned earlier to you the evidence of
11 Professor Sandercock, and perhaps I can just briefly
12 take you to his statement in bundle 1, tab 6.

13 MR JUSTICE BURTON: I gather there was some concern in the
14 lunch hour when whoever put the indexes in -- and I was
15 very grateful for it -- noted or thought that I didn't
16 have witness statement 8A, but I have got it, but I've
17 put it in after 1. So it's -- because it's much easier
18 to have it in after Mr Simmon, so it's there. Yes?

19 MR BEAR: If that's Mr Simmon's seventh statement, I don't
20 think it's going to play any part in the trial itself.

21 MR JUSTICE BURTON: You want me to go to Professor
22 Sandercock?

23 MR BEAR: I do, please, to page 15 of his statement.

24 MR JUSTICE BURTON: Yes?

25 MR BEAR: Paragraph 45:

1 "At their meeting by teleconference on
2 13th September ..."

3 So that was their first meeting which actually
4 looked at data.

5 "... we observed patterns in the data and concluded
6 that the next meeting should be scheduled relatively
7 soon when data were available from at least 100 patients
8 with CRFs on the database with a target date of
9 22nd October 2007. The submission of the data to the
10 DSMB's statistician ..."

11 Pausing there, this was at a time of -- and this
12 isn't disputed -- rapid recruitment into the trial.

13 MR JUSTICE BURTON: Yes.

14 MR BEAR: So Professor Sandercock says, or will say, they
15 saw patterns, and they concluded that the next meeting
16 should be scheduled relatively soon, and he goes on to
17 say:

18 "It was self-evident that this request would require
19 the defendant to complete the collation of the data only
20 a short time before it was sent to the DSMB's
21 statistician for entry into the shell tables. The
22 members of the DSMB considered that the application of
23 soft lock some weeks before the analysis was neither
24 practicable nor desirable."

25 MR JUSTICE BURTON: So this means that they pass this

1 message on?

2 MR BEAR: Shall we go on and then we'll see what he says.

3 MR JUSTICE BURTON: Yes.

4 MR BEAR: The first thing is just to note what he says the
5 members of the DSMB thought.

6 MR JUSTICE BURTON: Indeed. So if they had been told:
7 there's been a formal amendment to make it
8 non-mandatory, they would have said: good, quite right,
9 that's what we expected.

10 MR BEAR: That's the logic of it, yes. But underlying even
11 that is the -- and the reason I wearied you with the
12 Declaration of Helsinki, is the scientific basis from
13 why exactly this approach is important, bearing in mind
14 that which I know you're well aware of, which is that
15 the DSMB is there not to provide final rulings on what
16 this study shows, but as a safety -- as a risk avoidance
17 device, monitoring the trial as it goes along.

18 MR JUSTICE BURTON: Yes. On the other hand, it's quite
19 plain that they have considerable power, because
20 although of course they needed the TSC to ratify what
21 they said, the likelihood of the TSC not following their
22 recommendation --

23 MR BEAR: I'm not suggesting they don't have power. It must
24 be almost inconceivable that the recommendations of
25 a DSMB, even if it wasn't as eminent as this one, would

1 not be followed. Different point, I was simply making
2 the even more fundamental point. The nature of their
3 exercise is about risk avoidance. It's during a trial,
4 keeping a handle on the data as it comes in.

5 They say or he says, rather, that:

6 "The soft lock was considerably less important than
7 having information on the largest number of subject
8 patients ..."

9 MR JUSTICE BURTON: Yes.

10 MR BEAR: " ... in the full knowledge that the data we would
11 be reviewing had not been cleaned. This point was
12 discussed between the DSMB and Professor Roberts and
13 Haleema Shakur at the end of the ..."

14 MR JUSTICE BURTON: Yes, strangely, and it's quite a tribute
15 to the honesty of your witnesses, they don't remember
16 that conversation.

17 MR BEAR: Well, it certainly is a tribute to their honesty,
18 but it's perhaps not that strange, because -- although
19 this will be a matter for comment at the end -- we say
20 it's just self-evident that that is what would be
21 required and that's what the DSMB were doing and would
22 expect. So, in a sense, it would chime with what any
23 informed person would expect, and, therefore, he might
24 not remember.

25 MR JUSTICE BURTON: There's this worry that lies behind what

1 Mr Nash said this morning, namely that the amendment of
2 the DSMB -- of the DMP, because it was in such
3 unconditional terms, would, in effect, downgrade the
4 soft lock on a permanent basis. It's perhaps
5 unfortunate that, if it was intended only to put it on
6 ice for this occasion, it didn't say so.

7 MR BEAR: The way it was amended -- perhaps we should look
8 at it --

9 MR JUSTICE BURTON: The way it was amended was to say it
10 wasn't mandatory, which would apply in future as well.

11 MR BEAR: Indeed. It was amended in quite a specific way.
12 If you look at core bundle 2, tab 17, page 354 at the
13 foot of the page.

14 MR JUSTICE BURTON: Yes, I've got it.

15 MR BEAR: Thank you. 14.1:
16 "Soft lock will take place six weeks before a DSMB
17 if time between meetings will allow. Not mandatory for
18 it to be done for every DSMB review ..."

19 MR JUSTICE BURTON: That's right, whereas the old words just
20 said: it will take six weeks before. Finish. All I'm
21 pointing out -- and I think what you've shown me doesn't
22 undermine that -- is that Mr Nash is saying on the face
23 of it this is going to allow you to have a no soft lock
24 for any meeting.

25 MR BEAR: It's going to allow it if that is --

1 MR JUSTICE BURTON: Time doesn't allow?

2 MR BEAR: -- what's required by timing between the meetings.
3 That's the sense of it.

4 MR JUSTICE BURTON: That's fine.

5 "Soft lock will take place if time between meetings
6 will allow."

7 If it had stopped there, that would have been one
8 thing. It then says it's "not mandatory" for a soft
9 lock to be done for every DSMB review. So that was an
10 additional amendment. If it had just been the first
11 sentence, it would have been a bit different, ie time --
12 if time wouldn't allow it, then you wouldn't have to do
13 it, but it's now actually said it's not mandatory for it
14 ever to be done before a review.

15 MR BEAR: As I interpret that document, if you had in the
16 future -- it doesn't matter, and we're not with great
17 respect looking at --

18 MR JUSTICE BURTON: No, they say it was a cover for your --

19 MR BEAR: Oh yes, of course.

20 MR JUSTICE BURTON: -- your default.

21 MR BEAR: That's right.

22 MR JUSTICE BURTON: You knew you were so far behind you were
23 never going to be able to get back on top again, and,
24 therefore, while you were at it, you were covering your
25 back for the future.

1 MR BEAR: That's what they say.

2 MR JUSTICE BURTON: Yes.

3 MR BEAR: That's what they say.

4 MR JUSTICE BURTON: That's why it would have been -- I don't
5 know whether it would have been safer to have had
6 perhaps just the first sentence and not the second.

7 MR BEAR: Well, the two sentences, in my submission, one
8 perhaps needs to be a little bit careful about reading
9 this as if it was an Act of Parliament.

10 MR JUSTICE BURTON: Yes.

11 MR BEAR: But they're going to the underlying functional
12 point, and this is what I'm on --

13 MR JUSTICE BURTON: At any rate, this was done on
14 14th October, and either this was a natural result of
15 what had happened at the meeting or it was positively as
16 a result of an express suggestion from Dr Sandercock --
17 from Professor Sandercock.

18 MR BEAR: I was just going to take you back to
19 Professor Sandercock.

20 MR JUSTICE BURTON: Yes.

21 MR BEAR: I appreciate you've read this, but it is important
22 to look at what underpins what he says, not merely his
23 assertions, but also the reasoning.

24 MR JUSTICE BURTON: Professor Roberts doesn't deal with
25 this, I don't think. It's only Mrs Shakur who deals

1 with it at paragraph 86 when she says she can't
2 expressly remember the conversation, and
3 Professor Roberts doesn't even say that.

4 MR BEAR: I'll check exactly what he says. He certainly
5 deals with the general point about the quantum of data
6 subjects, and that being more important to the cleaning
7 of the data.

8 MR JUSTICE BURTON: Oh yes.

9 MR BEAR: Just coming back to 46, Professor Sandercock says:
10 "Our approach reflected the essential statistical
11 point that any collection of data is no more and no less
12 than an estimate of truth. When one is considering
13 information on a patient population, the more patients
14 for whom data is available the less susceptible are the
15 results to the play of chance."

16 That's a phrase which seems to be used quite a lot
17 by those who are expert in this field: the play of
18 chance. The obvious underlying point is that human
19 beings vary enormously in their physical make-up. When
20 you look at a number of people and see how a particular
21 treatment affects them or doesn't affect them, all sorts
22 of random variables come in.

23 The best way, Professor Sandercock says, that he and
24 his colleagues thought -- and it's backed up by a lot of
25 other evidence in the case -- the best way to reduce the

1 play of chance is to get more numbers in. That's the
2 single most important tool.

3 MR JUSTICE BURTON: Is this in any way relevant to the
4 suggestion that was being made in August which your
5 client didn't like, as to increasing the number of
6 patients to 400? Is it that they didn't like 400, or
7 they didn't like other things about the proposed
8 amendment?

9 MR BEAR: What my client didn't like was the way in which
10 the increase which was from 400 to 500 was going to be
11 used, because essentially it was going to be used to go
12 out into the market and put a spin on the efficacy
13 results from the phase 2 trial.

14 MR JUSTICE BURTON: But it wasn't the increase to 500.
15 Because consistently this -- no harm in having 500.

16 MR BEAR: No, and that's what my clients said at the time,
17 and indeed they had originally -- and this is
18 documented -- proposed 500 themselves --

19 MR JUSTICE BURTON: I follow.

20 MR BEAR: -- and had been beaten down to 400 on cost
21 grounds, and as we'll see, had in fact vigorously
22 resisted a last minute attempt just before the contract
23 was entered into to take it down to 320.

24 MR JUSTICE BURTON: I see.

25 MR BEAR: But having said that, the difference, so

1 Professor Roberts said at the time -- I am now talking
2 about August/September -- between 400 and 500
3 statistically is not that great.

4 MR JUSTICE BURTON: No.

5 MR BEAR: What has been made here is just the general point,
6 and just to carry on with what Professor Sandercock
7 says:

8 "... data on a smaller number of patients, even if
9 it had been cleaned."

10 MR JUSTICE BURTON: I can see that. If you've got something
11 completely new which you are trying out on patients who
12 are not terribly ill, then you may be able to do it on
13 a small number. But if people are going to drop dead
14 anyway from the underlying injury, have strokes, heart
15 attacks, whatever it may be, then you do need a larger
16 quotient.

17 MR BEAR: Exactly. This is what those who are expert in
18 actually running these trials who look at this
19 biostatistical data, take the view as the correct way to
20 deal with it.

21 MR JUSTICE BURTON: Again, there may be no difference
22 between the two of you on this. What is said,
23 I suppose, is that you could have coped with this if
24 only you'd been up to snuff on your cleaning, or your
25 reconciling.

1 MR BEAR: Yes, but Professor Sandercock goes on to say:
2 "The qualitative difference between cleaned and
3 uncleaned data is likely to be marginal" --
4 MR JUSTICE BURTON: That's of course your central point on
5 "wouldn't have made any difference".
6 MR BEAR: Yes, but it isn't just "wouldn't have made any
7 difference", but why it was correct for the DSMB to ask
8 for data and why it was correct for my clients to
9 provide them with data through the statistician.
10 MR JUSTICE BURTON: No doubt at all the DSMB were entitled
11 to have that view. Equally, if they realised what they
12 were getting was uncleaned, then that's fine.
13 What Mr Nash is saying is that that would be no
14 reason for your clients to slacken their efforts at
15 cleansing.
16 MR BEAR: It's not quite as simple as Mr Nash just being
17 able to say that. His case -- although we say that the
18 precise point of cleaning which needs to be carried out
19 isn't something they've been able to identify at all,
20 let alone by reference to any objective norms coming
21 from a body of professional opinion, which is what they
22 need -- his case is that in some unspecified way we've
23 fallen short of some unspecified norm of cleaningness,
24 if I can put it that way.
25 MR JUSTICE BURTON: We'll have to hear, but if he

1 establishes in cross-examination my suggested number of
2 30 erroneous results, that there are SAEs reported in
3 relation to 30 people, where had your clients only done
4 a bit more work they would have been shown to be not
5 SAEs, possibly not even AEs, then subject to the expert
6 opinion, it may be said to evidence a sloppy cleaning
7 process. It may, on the other hand, be the kind of
8 thing that happens every day.

9 MR BEAR: Well, we say it wouldn't evidence anything of the
10 sort. The whole point of what Professor Sandercock is
11 saying here, and what we say -- supported by all of the
12 other evidence that we're going to present -- is that it
13 was not the appropriate task for LSHTM to set about
14 especially cleaning this data. The key thing was to get
15 it to the DSMB as soon as possible.

16 MR JUSTICE BURTON: I understand that entirely. You clearly
17 are not -- couldn't be expected -- and DSMB didn't
18 expect you to specially speed up the cleaning on the 100
19 that you were going to produce to me.

20 What I would be interested about is whether,
21 although you got on with the 100, nevertheless the
22 cleaning that you were doing anyway was being done
23 properly.

24 Of course, it may be that you will say: we had to
25 put that on the backburner while we hurried to get the

1 100 together. If that is it then that's your answer.

2 MR BEAR: Can I just make one point absolutely plain,
3 because this is a weakness, we say, of the claimant's
4 case.

5 When one talks about data being cleaned, obviously
6 for the purposes of this trial, on the case they want to
7 bring, they focus on adverse events, and in particular
8 on serious adverse events. That of course is a focus
9 which they bring not only instrumentally to further
10 their case, but with hindsight, because that is the way
11 in which the data have turned out to be, they say, of
12 concern to them.

13 The underlying position though is a rather different
14 one, which is that the data that was collected fell into
15 all sorts of categories, of which adverse events, or
16 serious adverse events, were only one part.

17 Let me give you another example, which I know you're
18 well aware of: efficacy measures, outcome measures. But
19 there are all sorts of others. The baseline data, on
20 the blood, on toxicity, on a whole range of other
21 functions.

22 Now, the flaw in the claimant's case is that they
23 come along now and say: ah well, you should have focused
24 your efforts on trying to resolve queries on this
25 particular subset of the data which now, after the

1 event, we say is open to some sort of further analysis
2 and further process of reconciliation.

3 Scientifically, and under proper principles of
4 clinical and statistical practice, you can't do that.
5 You can't, in advance, decide what it is that you're
6 going to focus on. You've got to treat all the data
7 equally, and my clients would have had absolutely no
8 logical basis, or ethical basis, come to that, for
9 seeking to zero in on what the claimant now says,
10 opportunistically, we say, should have been the subject
11 of their attention, which is whether they could whittle
12 down the number of serious adverse events, because out
13 there there was a collection of forms which might well
14 have been smaller in number than the adverse events
15 recorded on the case report form.

16 MR JUSTICE BURTON: What do you say about this apparent
17 obligation under 8.3 to leave out of your reports
18 adverse events which weren't adverse events?

19 MR BEAR: The way it starts is that in the first place, the
20 data is collected according to a systematic and proper
21 process which my clients designed and supervised, which
22 was to give investigators a case report form and require
23 them to say, based on the protocol and on the case
24 report form, whether a particular event had occurred.

25 MR JUSTICE BURTON: Yes.

1 MR BEAR: So the starting point in fact is not what actually
2 happened; it's what the investigator reports.

3 MR JUSTICE BURTON: Certainly.

4 MR BEAR: So what you have is data then coming in, and it's
5 being collected equally from every patient in the trial
6 on that basis and, as a starting point, you can't assume
7 that the data is being unequally collected as between
8 any one patient or another, or any different treatment
9 group. You've got a local doctor who is reporting, if
10 it be the case, that he considers there's an adverse
11 event, and if there is one, he then decides whether it
12 was serious or not, and if so, what sort of seriousness.

13 MR JUSTICE BURTON: Yes.

14 MR BEAR: So the starting point is quite simply that, that
15 you have what those doctors report and that is, we say,
16 obviously accurately held on the database, there are
17 mechanisms for ensuring that it's accurately
18 transposed --

19 MR JUSTICE BURTON: Well, I shall wait to hear, but I don't
20 think any suggestion is made that that was inaccurately
21 transcribed, that the CRF forms have not been --

22 MR BEAR: No.

23 MR JUSTICE BURTON: But what about this:

24 "The definition of an AE excludes all medical
25 occurrences which are expected in the course of the

1 natural history of the TBI."

2 In your list of agreed and non-agreed items from the
3 experts, there is a disagreement as to whether that was
4 an unusual paragraph. I don't know who was on which
5 side of this.

6 MR BEAR: I suspect this relates to a comment which I think
7 Mrs Nickols makes in her report, to say that it was
8 unusual. We say a number of things about that, one of
9 which is that she doesn't, with respect, remotely have
10 the expertise to make that sort of observation, and I am
11 going to be commenting on that, but we also say: it's
12 totally irrelevant. This is the protocol. This is the
13 way it's drawn up. But whether it's usual or unusual --

14 MR JUSTICE BURTON: I don't see it's relevant, whether it's
15 usual or unusual, but the fact is it was there. Does
16 that impose any extra obligation on your clients to make
17 sure that the AEs -- well, I suppose it comes back to
18 this mysterious spreadsheet which someone's got to help
19 me to understand at some stage, which is Mrs Shakur's
20 comments about AEs which are not real AEs. Can you help
21 me on that?

22 MR BEAR: Yes, I can help you straightaway on that. That's
23 nothing whatever to do with definitions in the protocol;
24 this was simply a list of adverse events, whether they
25 were serious or not, by the way, which had originally

1 been reported as adverse events, and which had been
2 queried, where the local doctor had agreed that they
3 were not in fact adverse events --

4 MR JUSTICE BURTON: Good.

5 MR BEAR: -- and thereafter they had been delisted.

6 MR JUSTICE BURTON: That's fundamental, because Mr Nash's
7 belief, in his submission this morning, was that he
8 wasn't sure about it, but that they remained part of the
9 92.

10 MR BEAR: Of the 94.

11 MR JUSTICE BURTON: 94.

12 MR BEAR: No, that's certainly not going to be our evidence,
13 and as far as we know there's no evidence from the other
14 side to --

15 MR JUSTICE BURTON: So you're going to say that those items
16 on that spreadsheet did not form part of the 94?

17 MR BEAR: No.

18 MR JUSTICE BURTON: That's quite easy of resolution, and it
19 might take a bit of the sting out of the case.

20 MR BEAR: If we're correct, then this is, if I may say --

21 MR JUSTICE BURTON: It supports your case if you are
22 correct.

23 MR BEAR: Of course it does. It's a pure red herring. It's
24 just a document in the disclosure.

25 MR JUSTICE BURTON: No, on the face of it it's unexplained

1 by anyone. Unfortunately it was picked up by their
2 side, not by yours in the witness statement. Mrs Shakur
3 doesn't deal with it, not surprisingly, because she
4 didn't think there's anything wrong with it. The answer
5 is, they have lit on this -- it wasn't in the core
6 bundle -- and they say -- at least I think implicitly
7 they say: there you are, that shows that there's some
8 kind of conspiracy, some kind of breach, whatever it is.

9 They knew there were AEs which weren't AEs and they
10 still shoved them up before the DSMB.

11 MR BEAR: Yes, exactly.

12 MR JUSTICE BURTON: That's a strong case. It forms part of
13 their expert's propositions, and it supports their case,
14 but if it's wrong, not only is that point gone, but it
15 positively supports your case that you were doing your
16 job properly.

17 MR BEAR: Of course, absolutely. It's an example, with
18 great respect, of the opportunistic way, and I say this
19 deliberately, the slipshod way --

20 MR JUSTICE BURTON: If that pops up on disclosure it's not
21 surprising that it's relied upon.

22 MR BEAR: What would be a proper way to deal with it would
23 be to try to investigate what it means, rather than run
24 a reading of the document --

25 MR JUSTICE BURTON: Well, there was shortage of time and the

1 answer is, of course Mrs Charnley Nickols, giving her
2 evidence on the basis that she was assuming -- and of
3 course that's a matter of cross-examination -- that they
4 formed part of the 92, and that is still Mr Nash's
5 understanding.

6 MR BEAR: Exactly. We'll come back later to whether it's
7 a --

8 MR JUSTICE BURTON: Of course, that will have to be
9 explored.

10 MR BEAR: Exactly.

11 MR JUSTICE BURTON: But it isn't an irrelevance. It is,
12 however, a rather central point, but potentially very
13 helpful to you if you are right.

14 MR BEAR: Absolutely. I just observe this, that it's one
15 thing to alight on a document in disclosure and to say,
16 well, we don't have a lot of time, there's an expedited
17 trial. I have to say there's been no shortage of
18 resources here, no shortage of intersolicitor
19 correspondence, expert meetings, et cetera, huge amounts
20 of work done. So there would have been time to raise
21 this document.

22 MR JUSTICE BURTON: I suppose there was this meeting between
23 experts, and given that it formed part of
24 Mrs Charnley Nickols's reports, your witness
25 Professor Gray could have made some explorations into

1 whether she was right or not.

2 No doubt he has by now.

3 MR BEAR: No doubt. If one stands back just a little and
4 says: what conceivable reason would the defendant have
5 for including -- the defendant which is the
6 investigator, the chief investigator in this trial. It
7 doesn't want the trial to fail. What conceivable reason
8 would it have for including a lot of false negative
9 signals in the data? It defies belief.

10 MR JUSTICE BURTON: But if it's right that it answers my
11 question, which is: of course when you discovered it
12 wasn't an AE, you took it out, and I suppose all that is
13 left, then, against you, assuming you did that, would
14 have been, it would have given you a much better chance
15 of carrying on that splendid work if you had only looked
16 at the SAE forms.

17 MR BEAR: What is suggested is that the SAE forms should
18 have been used, not as the sole source, that's no
19 longer --

20 MR JUSTICE BURTON: No.

21 MR BEAR: Let's be clear though, your Lordship is quite
22 right to say "no", but that was, as I shall be seeking
23 to --

24 MR JUSTICE BURTON: During the interlocutory stage, it was
25 certainly -- that was the case, as I understood it.

1 MR BEAR: That was the case that Mr Simmon was putting
2 forward very forcibly.

3 MR JUSTICE BURTON: I know, it isn't any longer.

4 MR BEAR: No, it doesn't seem to be any longer. What is
5 said is there should have been some sort of cross-check
6 that should be run --

7 MR JUSTICE BURTON: That's right.

8 MR BEAR: -- and the point I was addressing you was that
9 among many other problems with that criticism is the
10 totally hindsight based nature of it, which is that it
11 ignores the fact that, in reality, as you go through the
12 work, what you've got is data on dozens if not hundreds
13 of various data points, not just adverse events, but
14 also all sorts of other things, and there is absolutely
15 no basis for saying in advance one should be zeroing in
16 on one particular potential facet of that data in trying
17 to --

18 MR JUSTICE BURTON: Except that they've got the database
19 sitting there, the HSM database, not the end of the
20 world just to do a bit of cross-referencing.

21 MR BEAR: But the only way it could help would be if you
22 then go back to the local sites and you then pursue it
23 all.

24 MR JUSTICE BURTON: Yes.

25 MR BEAR: And the difficulty again is you would be

1 prioritising, by definition, that part of it. Now, if
2 the claimant was serious about it, let's just stand back
3 again for a moment, if I can ask you to, and just say
4 let's assume that the claimant was seriously interested
5 in a case, that somehow there hadn't been a proper
6 exercise of preparation for the Data Safety Monitoring
7 Board. What would be the most important thing? In my
8 submission, it's this: the most important thing a DSMB
9 should be doing is stopping the trial, if there is
10 reason, or halting it if there is reason to do so,
11 because risk avoidance is at the heart and protecting
12 patients is the single most important principle.

13 So the most important thing, if one had to try to
14 look at it a priori and say: should we be focusing in --
15 and my clients say that's an entirely wrong approach --
16 but if one were to do it, if the claimants were at all
17 genuine about this, what you would be doing is not
18 trying to whittle down the number of SAEs. What you
19 would be doing is you would be looking at adverse events
20 that had been reported, but that had not been coded as
21 serious, because when a doctor makes a report of an
22 adverse event, he can report it as serious or he can
23 report it as not being serious.

24 MR JUSTICE BURTON: Yes.

25 MR BEAR: It can still be something which is adverse for the

1 patient, it might make the patient feel pretty bad, but
2 not be considered serious. One might have thought
3 a priori that if there were a genuine concern for parent
4 safety, it's that category which is the one that the
5 claimant would be saying should have been particularly
6 looked at because, if there were any underreporting of
7 adverse events as serious, if they were being wrongly
8 coded by the local doctors as not serious, then that
9 could have an important impact. The DSMB, in theory,
10 might find itself deprived of information which could be
11 pointing towards a risk on the trial.

12 MR JUSTICE BURTON: Well, you're not going to find Xytis
13 alleging a failure in that regard.

14 MR BEAR: No, of course we're not because their only
15 interest --

16 MR JUSTICE BURTON: Of course.

17 MR BEAR: But if we're looking at the matter --

18 MR JUSTICE BURTON: Their interest is, provided that the
19 patients are safeguarded, so far as they know, and
20 provided that they've got all these vast array of
21 professionals who they are paying for, their interest is
22 getting the trial successful.

23 MR BEAR: Yes, and that's a shared interest although my
24 clients don't have a financial interest in the outcome,
25 but they also want to see, as they have said,

1 hopefully --

2 MR JUSTICE BURTON: Your clients might get reputation from
3 being very careful overseers of trials. I'm not
4 suggesting in any way that you were out to stop the
5 trial, but you don't come out as badly from an aborted
6 trial as the sponsor.

7 MR BEAR: No, you don't, because of course your reputation
8 is running it according to proper scientific principles.

9 MR JUSTICE BURTON: That's right.

10 MR BEAR: That's undoubtedly where their reputation lies.

11 MR JUSTICE BURTON: I now understand paragraph 120 of
12 Professor Roberts's statement, because I was unclear why
13 he was knocking down what I thought to be an Aunt Sally
14 when he said.

15 "Nor would it be scientifically correct to provide
16 the DSMB with both SAEs from the CRFs and SAEs derived
17 from the SAE forms ..."

18 It may be that he was dealing with an earlier
19 allegation.

20 As I understand it, it's not the suggestion being
21 made that you should have simply slung at Sealed
22 Envelope the undigested two lots of forms. The case
23 against is you that you should have, as part of your
24 pleading exercise, reconciled the contents of the two
25 forms. It clearly wouldn't have made any sense at all

1 to sling a whole load of forms at the DSMB. But that
2 seemed to me to be answering a non-point.

3 This is because he's still at an earlier stage of
4 argument, is that it, or what?

5 MR BEAR: Yes, what he is contemplating --

6 MR JUSTICE BURTON: We will have to hear what he has to say
7 in evidence, but now it's understood what the case is,
8 he would make the same point, would he, namely: you
9 don't even need to give the information in digested
10 form?

11 MR BEAR: That must be the logic of it, yes.

12 MR JUSTICE BURTON: Yes.

13 MR BEAR: If you've got -- what you have to do at the start
14 is decide what sort of data you're going to look at, and
15 that is what the DSMB did when they approved the shell
16 tables.

17 MR JUSTICE BURTON: Yes.

18 MR BEAR: Perhaps we can just take a quick look at the shell
19 tables.

20 MR JUSTICE BURTON: Yes, please.

21 MR BEAR: In fact, if we're in the witness statement
22 bundle --

23 MR JUSTICE BURTON: There is an example in the core bundle,
24 I think.

25 MR BEAR: There is one, but I just want to show you the

1 shell table first of all.

2 MR JUSTICE BURTON: Was there not -- I'm happy to go to the
3 witness statement, but is there not a shell table in the
4 core bundle? I think there is.

5 MR BEAR: I think there is as well, yes.

6 MR JUSTICE BURTON: If it's the same, I don't mind where
7 I look at it.

8 MR BEAR: Tab 8.

9 MR JUSTICE BURTON: Thank you. Yes, I haven't looked at
10 this at all.

11 MR BEAR: Why don't we look at page 1428 at the bottom.

12 Table 5:

13 "Adverse events by intention to treat."

14 You may or may not need to know, "intention to
15 treat" is the all-out group of patients who were brought
16 to the trial whom there was an intention to treat, and
17 there's a slightly different subset which you can see at
18 the top of the next page which is by per protocol,
19 that's if they actually were treated in accordance with
20 the protocol which requires doses to be given at
21 a certain frequency over the four or five days at the
22 start. It doesn't matter, but that's all it goes to.

23 So let's look at 5. So one starts off:

24 "Number of patients, randomised."

25 Then in each of the four groups: high dose, medium

1 dose, low dose, and then obviously all of those
2 combining, finally placebo. That's the number, which of
3 course you can only get --

4 MR JUSTICE BURTON: So there are four groups?

5 MR BEAR: Four groups and the penultimate column is just the
6 combination of the first three.

7 MR JUSTICE BURTON: Yes.

8 MR BEAR: Then it starts off by saying look at the number of
9 patients with no adverse events. For that, of course,
10 you need to go from the trial database, because only
11 that will tell you what the total number of patients is
12 in each group, and whether they have no adverse events.

13 MR JUSTICE BURTON: Yes.

14 MR BEAR: Second row, number, percentage of patients, with
15 at least one adverse event.

16 MR JUSTICE BURTON: So all three of the -- the first three
17 you can only get that information from the CRF forms?

18 MR BEAR: Yes, you can only get it from the CRF.

19 MR JUSTICE BURTON: Yes.

20 MR BEAR: Now, the next one, with at least one serious
21 adverse event, in theory you could choose, at that
22 point, to depart from the CRFs, and you could look at
23 a separate set of data coming in which is the SAE report
24 forms, but, if you did that, then you wouldn't be
25 looking at it consistently.

1 MR JUSTICE BURTON: No.

2 MR BEAR: That's the problem. And that's why this,
3 therefore, means that the DSMB necessarily --

4 MR JUSTICE BURTON: I see that entirely, but it doesn't mean
5 to say that you are prevented in completing this
6 particular form -- at least on what I've seen so far --
7 from using the CRFs as your base but double-checking
8 them against the SAEs.

9 MR BEAR: It doesn't stop you perhaps from checking, but at
10 the end of the day you have to go by what's on the CRF.
11 If you check --

12 MR JUSTICE BURTON: You have to go on what's on the CRFs,
13 unless you go back to the CRAs, who go back to the
14 doctor.

15 MR BEAR: Yes, exactly. I was just about to say if you go
16 back to the doctor and you say we've looked at this --

17 MR JUSTICE BURTON: And we noticed you didn't put in an SAE
18 form although you originally said it was an SAE, what's
19 your explanation?

20 MR BEAR: That's right. Well, or however interrogative one
21 was, but: do you consider that this is an adverse event
22 which is serious, or whatever.

23 MR JUSTICE BURTON: There are possibilities. One is you
24 forgot to fill in the SAE form. One is you made
25 a decision later that it was serious having not thought

1 it was originally or vice versa. The other is you
2 changed your mind. Or another is that something has
3 happened subsequently.

4 But at any rate you've got to go back, via the CRA,
5 to the doctor.

6 MR BEAR: Yes, and then having gone back to the doctor, what
7 you then do, if he says, "All right, I want to change
8 what I initially recorded", then he has to change it.

9 MR JUSTICE BURTON: Yes.

10 MR BEAR: The protocol, and indeed GCP, specifically
11 required that there should be a physical process of
12 careful crossing out, not obscuring the data,
13 initialling the change.

14 MR JUSTICE BURTON: Given that the -- I forget which
15 document it is, it's the DMP 12, says that you've got to
16 do all this by the end of the trial -- let me just
17 remind myself.

18 MR BEAR: It's the data management plan.

19 MR JUSTICE BURTON: Yes, tab 6.

20 MR BEAR: Yes, tab 6.

21 MR JUSTICE BURTON: Was it tab 6? Sorry, tab 16, core
22 bundle 2.

23 MR BEAR: Yes.

24 MR JUSTICE BURTON: Yes, so that says you'll do it at the
25 end of the trial.

1 Now, that formed part of the DMP from the beginning.

2 MR BEAR: Yes, it did.

3 MR JUSTICE BURTON: So that was not dissented from by

4 anybody, this having been seen. So that's your job.

5 Does the DSMB know that or, do they see the DMP? They

6 probably don't.

7 MR BEAR: I'm not aware of evidence as to whether they do or

8 not.

9 MR JUSTICE BURTON: At any rate, the general understanding

10 is that you'll reconcile the SAEs against the SAE forms

11 at the end of the trial?

12 MR BEAR: At the end of the trial, yes, as a result of which

13 it may be necessary to generate lots more SAE forms.

14 One can't say in advance.

15 MR JUSTICE BURTON: But it will be sensible to do it before

16 the end because, really, you don't want to find in the

17 last week of the trial suddenly you have got to go back

18 to 25 different CRAs. But the obligation is to do it at

19 the end of the trial.

20 MR BEAR: Yes.

21 MR JUSTICE BURTON: That's irrespective of the fact that the

22 DSMB is calling for information from time to time.

23 MR BEAR: That's right. It's because the DSMB -- precisely

24 because the DSMB is looking at the information that's

25 flowing through from the case report forms, which may or

1 may not have been amended according to the ongoing
2 process of gradually checking the data as it comes in,
3 and the DSMB gets its snapshot of that trial database at
4 any time, and it takes its view based on that.

5 MR JUSTICE BURTON: What does Professor Gray say about
6 item 12, because I suppose Miss Charnley Nickols has to
7 be regarded as being critical of that provision.

8 She has to say, I assume, that's inconsistent with
9 proper practice, and it should never have -- it's
10 obviously relied upon by you heavily, and it shouldn't
11 be there, I suppose, she has to say. Does
12 Professor Gray say that's okay?

13 MR BEAR: Professor Gray says what was done was --

14 MR JUSTICE BURTON: It was done on the basis of a provision
15 and is the provision an acceptable provision, that you
16 don't reconcile the SAE forms until the end? Or at any
17 rate you're not obliged to reconcile the SAE forms until
18 the end?

19 MR BEAR: The overall gist of what Professor Gray says is
20 that you would expect checking to occur as you go on
21 during the trial.

22 MR JUSTICE BURTON: Yes.

23 MR BEAR: And that the DSMB is not needed to look at data
24 which in some way has been fully cleaned up --

25 MR JUSTICE BURTON: Given that then all sides would accept

1 that what you're supposed to do is go on cleaning and
2 reconciling as you go, which may well include looking at
3 the SAE forms, if you've got time, what's the impact of
4 that on a provision in the procedure which governed you,
5 not the subject of any disagreement at the time, that
6 said you didn't have to do it until the end?

7 MR BEAR: None at all, in my submission. The procedure
8 contemplates that there will be a final reconciliation.

9 MR JUSTICE BURTON: Yes, but were you looking at the -- this
10 is the point. Were you looking at SAE forms or did you
11 say to yourselves, pursuant to paragraph 12 of the DMP:
12 we don't need to look at the SAE forms until the end?
13 What was the factual position?

14 MR BEAR: As I understand the position, there are regular
15 checks which occur in the fullness of time on every
16 report that comes in, which include looking at the
17 adverse events and whether or not they are, on the face
18 of it, properly reported, or whether there might be
19 queries which could be posed.

20 MR JUSTICE BURTON: Plainly, that schedule about "these
21 aren't real AEs" was compiled, but did that involve
22 looking at the SAE forms as part of the exercise?

23 MR BEAR: That I don't know.

24 MR JUSTICE BURTON: There are heads nodding behind you.

25 MR BEAR: If there are heads nodding, then your Lordship can

1 read it better than I can.

2 MR JUSTICE BURTON: Obviously you can develop it in due
3 course with the evidence, but I think it's important for
4 me to understand whether you are saying: well, look,
5 there it is, paragraph 12 allows us not to look at the
6 SAE forms at all until the end, and unless somebody can
7 knock paragraph 12 down as being an inappropriate
8 procedural requirement showing negligence of itself,
9 that's the end of it.

10 Alternatively, you can say although that was the
11 well understood parameters, we understood that we needed
12 to -- so far as we could, given the pressures of time,
13 the new requirements of the DSMB, to do some reconciling
14 and we did, and that reconciling did include, although
15 not as a priority, looking at the SAE forms.

16 As far as I understand it, it's the latter.

17 MR BEAR: Let's take it in stages.

18 First of all, the document is perfectly plain, that
19 you don't need to reconcile until the end, so that's the
20 starting point, that there's nothing in terms of any of
21 the written procedures for the trial that requires this
22 exercise of reconciliation to take place beforehand.

23 MR JUSTICE BURTON: On the other hand, if you are cleaning
24 as you go along, so you can say to yourself, "Ah,
25 wonderful, that's 50 of them done. Now have we got time

1 to do any more before the next meeting?", if that's the
2 attitude, 50 of them done should include, surely, having
3 done, admittedly in advance of your obligation,
4 reconciling the SAE forms?

5 MR BEAR: Well, again, one mustn't fall into the trap, with
6 great respect, of assuming that somehow reconciling one
7 particular piece of the data against one alternative
8 data source is somehow a priority or should be given
9 additional attention, but --

10 MR JUSTICE BURTON: No, I understand that, but if you are
11 saying to yourself, "We are cleaning as we go along
12 insofar as we can, insofar as there's time for it,
13 et cetera, et cetera, it will all be done by the end",
14 all I really wanted to know -- it may be you can't
15 answer it and the witnesses will need to answer it --
16 but my question is: when you do your reconciliation and
17 you manage to clean, to your own satisfaction, 25 files,
18 and you go back to the CRAs if necessary, that, I would
19 have thought, would include looking at the SAE forms at
20 that stage.

21 Otherwise you're doubling your work, because you're
22 doing your cleansing as it goes, and then you're adding
23 in an extra factor, at the end of the trial, of already
24 cleansed files being reconciled against the SAE forms.

25 MR BEAR: I don't have to speculate too much about what the

1 witnesses are going to say, because there is some
2 correspondence between the parties in August
3 and September of 2007 which touched on this. You've
4 probably seen it.

5 MR JUSTICE BURTON: Discrepancies.

6 MR BEAR: Well, putting it in a nutshell, because again I'll
7 be going through it with Mr Simmon, but Mr Simmon sent
8 a letter -- and let's not worry about the reasons for
9 the letter for the moment -- but he sent a letter in
10 which he set out a number of desiderata, and one of the
11 points he mentioned was the differences between the HPM
12 database and the trial database. So he acknowledged
13 that there were differences and said:

14 "We'd like to see these cleaned up as quickly as
15 possible."

16 Professor Roberts, again just to give you a summary,
17 very briefly, of it -- you have obviously read it --
18 comes back and says: look, we can't do this in
19 real-time.

20 MR JUSTICE BURTON: Yes.

21 MR BEAR: And there are always going to be discrepancies and
22 they will be finally cleared up at the end of the trial.

23 Then you get Mr Simmon returning to the fray and
24 saying: we don't want to have a long delay at the end of
25 the trial -- in other words when they're hoping to sell

1 the product on to another investor, perfectly legitimate
2 no doubt -- we don't want to have a long delay while you
3 clean up this and then add other bits of data, so we
4 want to know that it's ongoing quickly and finally it
5 ends up with Professor Roberts saying:

6 "Well, I can't commit to any particular schedule,
7 but I can assure you we'll make every effort."

8 That's where it gets to.

9 So the parties' expectations, I would submit not
10 anything that has any defined contractual basis, but
11 just their understanding of what was going to happen in
12 practice, was touched on in that correspondence.

13 MR JUSTICE BURTON: Your general answer to my question, did
14 they simply rely on paragraph 12, do other cleaning and
15 reconciling, but not reconcile the SAE forms, and put
16 them aside and say we'll look at them at the end, your
17 answer to that is: no.

18 MR BEAR: No in practice, it is a matter of contractual
19 obligation --

20 MR JUSTICE BURTON: They regarded, albeit there wasn't time
21 to do it all by 1st November, they regarded the cleaning
22 process as including -- which would involve going back
23 to CRAs if necessary -- as including reconciling with
24 the SAE forms?

25 MR BEAR: Cleaning is cleaning. It's something you do on an

1 ongoing basis, and this particular facet is one part of
2 the overall mosaic of the cleaning exercise.

3 MR JUSTICE BURTON: It's just that my interest -- I suppose
4 we all like to get things done -- out of the in-tray --
5 my interest would be whether they regarded files as
6 cleansed for good and all, or whether they would have to
7 go back for more cleansing when they'd looked at the SAE
8 forms. The former must be much more sensible. Just do
9 it once and for all, and then you either say: no, well,
10 it's not fully cleansed, because I haven't yet checked
11 the SAE form. Or to say: no, no, it is cleansed.

12 MR BEAR: Again, I come back, I'm labouring the point
13 perhaps, but the -- one simply cannot assume in advance
14 that this is the area that needs to be focused on.

15 MR JUSTICE BURTON: Yes.

16 MR BEAR: Now, as I said, just as important is looking for
17 adverse events that have not been coded as serious in
18 the first place. HPM of course would never know about
19 those. You'd only pick it up if you looked at it and
20 you thought: well, the doctor has recorded this adverse
21 event, you know, the patient had a severe seizure, but
22 he's given it a coding of zero, indicating that it's not
23 serious, or whatever the code is, I can't remember.
24 That doesn't look right to us. So we will get in touch
25 with him.

1 MR JUSTICE BURTON: But my underlying question really is:
2 presumably you try only to go back to the CRA once?
3 It's an awful nuisance to go back to Colombia more than
4 once.
5 MR BEAR: I think it is also an ongoing process.
6 MR JUSTICE BURTON: Is it?
7 MR BEAR: That's something you'll have to explore with the
8 witnesses.
9 MR JUSTICE BURTON: Very good. Yes?
10 MR BEAR: So we were looking at the shell table. I think
11 your Lordship has our point on that.
12 MR JUSTICE BURTON: I've closed it. We'd got down to
13 a certain stage, and -- let me see. We'd got down to
14 a certain stage. All you're saying about this is not
15 that it forecloses looking at SAE forms, but that it
16 assumes that the one form -- and you're going to be
17 consistent with one form -- the one form to use which
18 gives you all these answers, albeit may need to be
19 checked, double-checked, cleansed, cross-cleansed,
20 reconciled, is the CRF form.
21 MR BEAR: Yes.
22 MR JUSTICE BURTON: But it doesn't anywhere say answers must
23 be given by reference to the CRF form?
24 MR BEAR: No, it doesn't say that in terms, but it is
25 necessarily consistent only with that, and Professor

1 Sandercock from page 10 onwards also gives detailed
2 evidence that that is what he wanted, and that's what he
3 would have expected.

4 MR JUSTICE BURTON: Yes.

5 MR BEAR: So everything is marching, we say, entirely in
6 step and in the proper way.

7 MR JUSTICE BURTON: Right.

8 MR BEAR: Then just to come back to page 16 where we broke
9 off, again coming back to this issue of cleansing:

10 "In my opinion [paragraph 47] the DSMB would have
11 failed ..."

12 MR JUSTICE BURTON: Hold on, sorry, I've closed it up.

13 MR BEAR: Page 16 of tab 6.

14 MR JUSTICE BURTON: Yes.

15 MR BEAR: "... the DSMB would have failed to discharge its
16 duties if it had waited for the soft lock procedures to
17 be applied before it conducted a further review of the
18 trial data ... fast recruitment ... should review as
19 much as up-to-date data as possible at the soonest
20 opportunity. The DSMB viewed the application of a soft
21 lock as a luxury that it could not afford."

22 So he's perfectly clear in his statement, at any
23 rate, that a soft lock wasn't only not expected; it
24 would actually have been wrong because, by going through
25 the process of cleaning, you delay, and what's going on

1 during the delay? More patients are being recruited.
2 50, 60 more per month, perhaps an even greater rate.

3 That's why I took you to the underlying principle,
4 because underneath the statistical language and
5 discussion of objective standards of cleaning and so on
6 is the simple fact, which I make no apology for
7 emphasising, that patients are coming into the trial,
8 and if there is data, even if it is open to some further
9 process of cleaning and refinement, which in its current
10 state, as it's currently got on to the trial database in
11 the first place, which once underlined it suggests
12 disparate adverse effects or lack of beneficial outcomes
13 in the study drug groups, then you've just got to act on
14 that data, you've got to work quickly and not wait for
15 several weeks while more people come on and get the
16 drug, and that's the simple point he makes.

17 MR JUSTICE BURTON: So the obligation in the charter on the
18 DSMB -- tab 6 of the core bundle, page 1391 -- to carry
19 out a secondary analysis of the numbers of SAEs in
20 combined treatment and placebo groups, the primary
21 analysis is to compare the proportions of patients with
22 one or more SAEs, secondary analysis of the numbers of
23 SAEs, can the DSMB fulfil their two obligations on the
24 basis of the kind of information which
25 Professor Sandercock says he needed or he expected in

1 those paragraphs you've just been reading to me?

2 MR BEAR: Yes, they can. There's absolutely nothing in the
3 DSMB charter.

4 MR JUSTICE BURTON: It doesn't have to be perfect
5 information?

6 MR BEAR: One starts off from the point, information is
7 collected -- once you've got your CRFs for a patient
8 who's been through the trial, you will have the data
9 about adverse events and about serious adverse events.

10 MR JUSTICE BURTON: Yes.

11 MR BEAR: There's no suggestion in the DSMB charter that you
12 must look outside the trial database to the SAE report
13 forms. It doesn't prescribe SAE data as being, if you
14 like, the supplementary stream of information that may
15 or may not occur if the doctor remembers to complete the
16 form.

17 MR JUSTICE BURTON: By implication, it's the secondary
18 analysis of the numbers of SAEs as then appearing, or
19 something of that kind. If they know that it's not
20 perfect, that's all that's necessary for them to know.

21 MR BEAR: As I interpret it, the primary analysis is
22 a comparison of the proportions of patients who have
23 SAEs. So what you're doing, if we just remind ourselves
24 of the shell table at 5 in tab 8, page 1428, if you look
25 at the fourth or fifth line, fifth row, rather, number

1 of patients --

2 MR JUSTICE BURTON: Yes, that's primary.

3 MR BEAR: Yes, so that's -- indeed, so are the -- so to some
4 extent are the previous ones, and then a secondary
5 analysis, which is the --

6 MR JUSTICE BURTON: Hold on, one or more -- no, I think it's
7 only because the primary analysis is one or more SAEs,
8 so it's only that fifth one which is of significance,
9 isn't it, for the primary analysis, because the first
10 three have no SAEs.

11 MR BEAR: Yes, but that would be true if you assumed --
12 which the DSMB don't -- that you should only look at
13 what's actually been reported as an adverse event that's
14 been coded as serious, whereas in fact what they want to
15 do is look at -- as if you like corroborative or
16 surrounding evidence -- all adverse events because they
17 recognise that there may be boundaries or border lines
18 which a doctor may not be absolutely sure about, or
19 there could be random errors if you like, the play of
20 chance.

21 So in order to arrive at your assessment of the
22 proportions of patients with one or more SAEs, you also
23 need to look at what's going on just with AEs generally.

24 MR JUSTICE BURTON: All right, and then the secondary
25 analysis. Now, which columns deal with the --

1 MR BEAR: That is the seventh and eighth, I think,
2 underneath the little blank line about two-thirds of the
3 way down the table: number of non-serious adverse
4 events, mean number of patient, number of the serious
5 adverse events.

6 MR JUSTICE BURTON: Sorry, the seventh, on the assumption
7 that the primary is number 5, then number 6?

8 MR BEAR: Then it's 8 and 9, I'm sorry. Can you see a blank
9 line, under that?

10 MR JUSTICE BURTON: Yes, that's 9. It's just underneath
11 there, and then 10. Which ones go to the number of SAEs
12 in the combined treatment and placebo groups, yes. It's
13 number 10, isn't it?

14 MR BEAR: Yes, number 10, and then number 9 as, if you like,
15 circumstantial evidence around it.

16 MR JUSTICE BURTON: Yes. But primarily, number 5 is primary
17 and number 10 is secondary?

18 MR BEAR: Yes.

19 MR JUSTICE BURTON: Thank you.

20 MR BEAR: So the distinction there is, as your Lordship
21 sees, between comparing number of patients who have at
22 least one -- that's the primary analysis. So a patient
23 who has one or a patient who has ten, it doesn't matter.
24 You're looking at the difference in the proportions of
25 patients who have at least one. That's the primary

1 analysis. The secondary analysis is to look at the
2 number of events.

3 MR JUSTICE BURTON: Yes.

4 MR BEAR: I think I've really covered this point that your
5 Lordship identifies -- we say correctly -- as the main
6 issue that's still standing, the points I wanted to make
7 in opening, unless there's anything else that I can help
8 you with?

9 I should just say on the DMP amendment, so far as
10 that is concerned we say it's a matter for the defendant
11 and the claimant is unable to identify any objective
12 legal principle which would support a conclusion that
13 it -- the claimant -- or indeed the trial steering
14 committee should have been involved. There simply isn't
15 one. It's just trying to get to its desired result but
16 has no --

17 MR JUSTICE BURTON: So unless he can get something off the
18 ground with his cross-examination of Professor Roberts,
19 that you are really doing -- or Mrs Shakur -- you are
20 really doing a lousy job in cleansing generally, as
21 evidenced by a large number of errors which were not
22 picked up or should have been picked up or were picked
23 up but were not disclosed, then if the case is simply
24 resting on your failure to reconcile the SAEs by
25 reference to the SAE forms, you said, well, insofar as

1 you did a cleansing exercise you were doing it, which
2 would include: reconciliation of the SAE forms even
3 though you didn't need to do it till the end; your
4 classification of SAEs was done diligently, witness your
5 spreadsheet; and it was limited by the time which the
6 priority of the DSMB imposed upon you.

7 MR BEAR: Yes, and can I just say this, although it's
8 obviously not for me to direct my learned friend how to
9 pursue his case, but I want to just lay down a marker
10 now. We say: they haven't begun to lay the positive
11 basis as they should have done for any sort of systemic
12 case that there wasn't an adequate ongoing process of
13 data cleaning.

14 Now, what one would need for this -- and what is
15 conspicuously lacking in their evidence, whether factual
16 or expert -- is, first of all, some sort of definition
17 of what the objective standards would be for timely
18 querying and timely cleaning up of data.

19 MR JUSTICE BURTON: Yes.

20 MR BEAR: Secondly, defining or surveying, rather, the whole
21 of the operations that had been done under the trial in
22 order to see how, just as a matter of fact, data was
23 being collected, how it was being picked up on,
24 reviewed, how queries were being processed, and thirdly,
25 to some sort of attempt at a definition at where

1 a breach, if there was one, had emerged by comparison of
2 stages 1 and 2. Take --

3 MR JUSTICE BURTON: Well unless the macro point succeeds,
4 they are going to have great difficulty with the micro
5 point, the macro point being by reference to their SAE
6 forms. If they don't succeed on that, then the micro is
7 both insufficiently articulated, you say, and in any
8 event going to fail?

9 MR BEAR: That's right. So even if -- it's up to my learned
10 friend if he wants to spend days poking around over some
11 adverse event forms, but --

12 MR JUSTICE BURTON: So you put them at risk in relation to
13 costs in relation to that?

14 MR BEAR: Absolutely. We think it is a misconceived
15 exercise and perhaps Xytis's final throw of the dice.
16 Who knows, maybe that's optimistic.

17 MR JUSTICE BURTON: We will make sure, well it's clear from
18 the transcript how much of the hearing will be taken on
19 that, which is bound to be quite some time.

20 MR BEAR: Well, my Lord --

21 MR JUSTICE BURTON: You were optimistic of getting the
22 factual evidence through, but that's going to be a large
23 chunk of time.

24 MR BEAR: We could be here for days poring over the fine
25 details without even an expert report from some

1 statistician or biostatistician or trial manager,
2 someone who's got an experience which Mrs Nickols
3 doesn't have, which is actually running a trial, sitting
4 on a committee, things which she conspicuously lacks.
5 An expert report, it would be a long and perhaps far
6 from enthralling document which would tabulate the whole
7 thing, Scott Schedules, rather like a construction case
8 in the TCC, our TCC I mean, and we just don't begin to
9 have that.

10 MR JUSTICE BURTON: The only error I've seen is the one
11 which Mrs Wells picks up on and is all historic anyway,
12 but that's not Mrs Charnley Nickols.

13 MR BEAR: No, that was one point which didn't work on day
14 one and was corrected thereafter.

15 MR JUSTICE BURTON: Yes.

16 MR BEAR: And I think Mrs Wells -- I think I'm right in
17 saying that's one of the points she now accepts, once
18 she's seen the documents, that she can't pursue, but no
19 doubt we'll find out when we get my learned friend's
20 document.

21 So, my Lord, could I then just very briefly comment
22 on another two or three aspects of the case, moving on
23 from these issues of clinical practice, if you like, or
24 trial conduct practice.

25 First of all, the information request.

1 What was surprising about the requests that were
2 made in this period -- the first two weeks of November,
3 although they were advanced with great vim in the
4 correspondence by my learned friend's solicitors -- was
5 in the first place a complete failure to recognise that
6 the defendant did not have the tables that had gone to
7 the DSMB, and it couldn't, because, by definition, they
8 are unblinded.

9 MR JUSTICE BURTON: Well, let's just look quickly at what
10 your obligation was when you were asked.

11 MR BEAR: It's 2.3(g), I think.

12 MR JUSTICE BURTON: Thank you.

13 "On Xytis's request, provide Xytis with any
14 information, results and statistics reports reasonably
15 requested."

16 It doesn't actually say it has to be in your
17 possession.

18 MR BEAR: No, it doesn't actually say that, but it's got to
19 be "reasonably requested".

20 MR JUSTICE BURTON: It would plainly impinge upon the
21 reasonableness of the request and the timing within
22 which the request should be performed prior to the
23 notice seeking to terminate the contract.

24 But if they had said to you: we recognise that you
25 don't have -- or we now learn that you don't have the

1 unblinded information from which you could then
2 construct some blinded information, tell us how long you
3 need, or whatever, and this is precisely what we want,
4 will you now set about doing it for us in order to
5 enable us to monitor or audit the trial by specific
6 reference to -- the Simmon's table, I suppose, our
7 dissatisfaction with the apparent over-reporting of
8 SAEs.

9 MR BEAR: May I make a number of points in relation to that?

10 MR JUSTICE BURTON: Yes.

11 MR BEAR: The first one, and one of the striking features in
12 relation to this period of pre-action as it turned out
13 to be correspondence, is that Mr Simmon and Xytis's
14 solicitors were very reluctant to come off the fence and
15 actually say what alleged discrepancies they had
16 observed. Extraordinary if they were interested in
17 actually finding out but they didn't do that.

18 But secondly, as a matter of the contract, we say: a
19 request, when it's framed, must fall within the
20 requirements of reasonableness and other requirements of
21 purpose, so that you can't carve out of an unreasonable
22 request one that's reasonable.

23 MR JUSTICE BURTON: There's nowhere a letter which specifies
24 precisely what it is they want, whether in the terms
25 that Mr Nash put it this afternoon, or at all.

1 MR BEAR: No. Well, that's absolutely right. There was
2 just a sort of, if I can put it this way, a very
3 aggressive stream of demands for information, most of
4 which seemed to be predicated on a denial of the fact,
5 which we say was obvious, but which my instructing
6 solicitors manfully endeavoured to explain to Xytis, no
7 recognition of the fact that the tables were not only
8 not in our possession, they were not in our possession
9 because they were unblinded and only made sense as
10 tables divided up by categories of treatment group.

11 So you can't begin to construct these tables which
12 is what the DSMB actually saw.

13 MR JUSTICE BURTON: Let us assume that you had been given
14 sufficient time and you had had properly described what
15 it is they wanted, namely a blinded version of the
16 tables which were prepared by Sealed Envelope to send to
17 DSMB, not being the information you had supplied to
18 Sealed Envelope, but the information Sealed Envelope had
19 derived from your information and unblinded, now blinded
20 again, how long would that have taken?

21 MR BEAR: Well, could I start just by asking you to look at
22 core bundle 2, tab 18? These are the unblinded tables,
23 so this is subject to --

24 MR JUSTICE BURTON: I didn't look at these either, thank
25 you.

1 MR BEAR: This is subject to the order that your Lordship
2 has indicated in principle you will make.

3 MR JUSTICE BURTON: These are unblinded --

4 MR BEAR: Unblinded, yes, so I'm --

5 MR JUSTICE BURTON: So this must form the basis of any order
6 that I'm invited to make?

7 MR BEAR: Yes.

8 MR JUSTICE BURTON: Have you had the opportunity of
9 discussing an agreed order?

10 MR NASH: My Lord, there are two points here. There's the
11 question of general confidentiality vis-a-vis the world
12 at large and there's the question of blinding.

13 These tables have not been shown to Dr Simmon,
14 because they contain blinded information. Dr Simmon is
15 in court, of course, about to give evidence, so if we're
16 going to go into the detail of these, we need to
17 consider this whole question of blinding.

18 Our position is that if Dr Simmon sees this
19 information, it is not going to affect the unblinded
20 status of this trial, and he wishes to see this
21 information because, of course, at the moment he feels
22 that certain witnesses have access to material which he
23 hasn't seen. But that's a matter which --

24 MR JUSTICE BURTON: How are we dealing with this, because
25 I obviously can't make any orders other than by consent,

1 I don't think, can I?

2 I can make orders vis-a-vis the outside world, but
3 how am I going to deal with this vexed question of: as
4 between the two of you what's blinded and what isn't
5 blinded?

6 MR BEAR: I was going to suggest that you could at least
7 deal with it by stages. First of all, for the immediate
8 present, I was just going to refer to the columns,
9 without reading out any figures, explain what, in my
10 submission, is the difficulty or impossibility of going
11 down the road that Xytis --

12 MR JUSTICE BURTON: Let's do that for the moment and see
13 where we go. I think we'll finish your opening and then
14 before we start the witness, we'll deal with this
15 question in a discrete form.

16 The point you want to make to me, I was asking you
17 how would you have set about -- how long would it have
18 taken you to set about, assuming you could have done it,
19 what Mr Nash now says you should have supplied?

20 MR BEAR: Yes, I was going to start off by saying that in
21 fact it is just not possible to try and produce the
22 information. It is, with respect, a meaningless
23 concept.

24 If one looks at this, just take the first table,
25 number of adverse events per patient, and you'll see

1 you've got the treatment groups: high dose, medium dose,
2 low dose, placebo.

3 MR JUSTICE BURTON: Yes.

4 MR BEAR: Then, if you look at the row marked "total",
5 you'll see figures there, which are the total number of
6 persons in each group --

7 MR JUSTICE BURTON: Yes.

8 MR BEAR: -- and then that's broken down above it depending
9 on how many of that total --

10 MR JUSTICE BURTON: Does that deblind?

11 MR BEAR: Yes. That is unblinded because what it does is it
12 links groups of patients to the treatment they're
13 getting, and this is all -- all the information the DSMB
14 saw was in this form. It categorises the patients by
15 their treatment group and then by the event which has
16 happened to them, in this case --

17 MR JUSTICE BURTON: So this is a total answer to the point.
18 Leave aside the unreasonableness and non-timeousness of
19 the request and the lack of particularity, all these
20 other points that you make.

21 This is a complete answer, because you couldn't have
22 produced the information in unblinded form, and
23 therefore you aren't in breach of the obligation given
24 that -- what's the words -- you have to bear in mind
25 that the unblinded status of the data it is to be

1 maintained.

2 MR BEAR: Exactly. Now, what was said in correspondence at
3 the time was: ah well, instead of having high dose,
4 medium, low dose and placebo, you've got A, B, C, D.
5 There are a number of perhaps rather obvious objections
6 to that. The first is: just in order to construct this
7 kind of table, however you label the groups, you need to
8 know who belongs to which group, and to do that you need
9 the randomisation code, the unblinding code. My clients
10 don't have that, because, of course, once you get that,
11 you can unblind the information. So they can't even
12 produce the table.

13 Secondly, it would be an obviously ineffective
14 device to conceal the significance of the information,
15 because what was known -- and inevitably so -- and what
16 was known to the world generally, was that there was
17 a disparate relationship of adverse events and also of
18 outcome measures between the treatment -- between the
19 Anatibant groups on the one hand and placebo on the
20 other. That information had to be made public. That
21 was released by the DSMB to the TSC and released by the
22 TSC -- because there has to be some explanation for why
23 you're stopping the trial.

24 MR JUSTICE BURTON: Without giving me any answer which gives
25 away the numbers in each group, are you able to tell me

1 what the conclusion is that can be drawn from that table
2 vis-a-vis placebo versus drug?

3 MR BEAR: I'm not sure I can do it without --

4 MR JUSTICE BURTON: Ie does it show that people who are
5 using the placebo are better off? What is it? The
6 worry is that people who take the drug are either no
7 better off than -- or more likely to have adverse events
8 than those who are taking the placebo, or, at any rate,
9 equally likely. What does it show in that regard?

10 MR BEAR: What this particular sub-table shows, if you look
11 at the one or more row, is that the percentage who have
12 one or more, on the whole, is what it is compared to the
13 placebo percentage. And then if you look over the page,
14 for example, at the top table, if you look at the top
15 table, patients with at least one serious adverse event,
16 then if you look at the row marked "yes" --

17 MR JUSTICE BURTON: I follow.

18 MR BEAR: Yes. Now, the interpretation of the statistical
19 significance of that is something Professor Sandercock
20 deals with in a schedule to his witness statement which
21 we ask be treated in the same way as this information,
22 because it's a commentary on it.

23 MR JUSTICE BURTON: Yes, I've got the point.

24 MR BEAR: Can I say, we are sympathetic from a litigation
25 procedural point of view to Dr Simmon's desire to see

1 this. The difficulty and reason that we don't feel able
2 to consent is because there is a statement in the
3 protocol which has regulatory force under regulation 29,
4 I think it is, (a) that participants in the trial should
5 be blinded, and the chief executive of the sponsor is,
6 as we see it, a participant in the trial.

7 MR JUSTICE BURTON: Yes, now, Dr whatever his name is, who
8 is the claimant's representative on the TSC --

9 MR BEAR: He's seen this.

10 MR JUSTICE BURTON: He has seen it, but of course he is
11 under an oath of confidence which you say he's broken.

12 MR BEAR: Regardless of whether he's strayed outside that,
13 he can discuss it in the witness-box.

14 MR JUSTICE BURTON: Yes.

15 MR BEAR: He's Xytis's representative, and so Xytis, we say,
16 are not in fact disadvantaged.

17 Now, the problem is that if your Lordship were to
18 make an order allowing Dr Simmon to see it, that would
19 constitute an unblinding, and that's the problem for
20 you.

21 MR JUSTICE BURTON: The consequence of that would be it is
22 a breach of regulation.

23 MR BEAR: It would be a breach of regulation.

24 MR JUSTICE BURTON: And what's the impact of that?

25 MR BEAR: It's impossible to say. That's not something

1 which --

2 MR JUSTICE BURTON: If they want to carry on with the

3 project, a fortiori with a new -- whatever it's

4 called -- provider, the less breaches of regulations

5 there are the better?

6 MR BEAR: They would be much better advised to keep their

7 noses clean, but from the position of the courts, it's

8 difficult to see that -- I don't want to suggest your

9 Lordship has no jurisdiction, but it would be a strong

10 matter to put in place a situation which appeared to

11 constitute a breach of the regulations.

12 Now, if Mr Nash thinks that's not so, then of course

13 we should hear, and your Lordship has indicated you will

14 do that at the end of my opening.

15 That's the problem we face.

16 MR JUSTICE BURTON: Right. As for the other matter, which

17 is how we deal with the outside world, we'll come to

18 that at the end of your opening.

19 MR BEAR: Yes.

20 MR JUSTICE BURTON: Yes, anything else you want to say?

21 MR BEAR: My Lord, the outside world doesn't seem to be

22 flocking in here at the moment.

23 MR JUSTICE BURTON: That's the documents. Patient

24 protection?

25 MR BEAR: Patient protection in terms of 9.3(v).

1 MR JUSTICE BURTON: Both.

2 MR BEAR: Yes. Your Lordship has our submissions on that.

3 We say that this wasn't a decision which was motivated

4 by patient protection. I was going to show you just

5 briefly -- although it's in opening -- an authority that

6 you may or may not have come across called

7 Abu Dhabi v Product Star.

8 MR JUSTICE BURTON: I had a very quick look at it, yes.

9 I hadn't seen it before.

10 MR BEAR: No, I had the impression that it may not have been

11 cited in Clark v Nomura.

12 MR JUSTICE BURTON: It wasn't -- it may have been.

13 MR BEAR: Ultimately in Clark the parties didn't appear to

14 be in dispute about the legal principles.

15 MR JUSTICE BURTON: Oh, I think they were, I think they

16 were.

17 MR BEAR: It may be I've misread your Lordship's judgment.

18 At any rate, this is a Court of Appeal case from 1992,

19 [1993] 1 Lloyd's Reports, 397.

20 Looking at the headnote, first column, it was

21 a charterparty, so in effect --

22 MR JUSTICE BURTON: Arbitrarily, capriciously or

23 unreasonably.

24 MR BEAR: That's right.

25 MR JUSTICE BURTON: What was the wording of the sole

1 discretion clause?

2 MR BEAR: If you look at column 1 of the headnote, 40(ii):

3 "If (a) any port of loading or discharge ...(Reading
4 to the words)... charter be blockaded or (b) owing to
5 any more ...(Reading to the words)... entry to any such
6 port or the loading or discharging of cargo, any such
7 port be considered by the master or owner in his or
8 their discretion dangerous."

9 MR JUSTICE BURTON: Yes.

10 MR BEAR: Then similar wording for reaching the port of
11 loading.

12 MR JUSTICE BURTON: So it's 404, is it?

13 MR BEAR: Yes, it's 404 in Lord Justice Leggatt's judgment.

14 He cites at the top of the page a case called Government
15 of the Republic of Spain v North of England. This is
16 the first citation:

17 "No mala fides is suggested, but it is said, and
18 I think with truth, that discretion must not be
19 exercised in an arbitrary and unreasonable manner. In
20 this case, there was really no exercise of discretion at
21 all as the matter was not considered or no full or
22 sufficient enquiry was made."

23 Then dropping down to the last break on the page,
24 reference to judicial review, those principles are
25 cited, Lord Justice Leggatt says:

1 "You should apply it with caution", but he goes on
2 to nonetheless arrive at a similar conclusion.

3 "The essential question always is whether the
4 relevant power has been abused, where A and B contract
5 with each other to confer a discretion on A ..."

6 MR JUSTICE BURTON: It's similar to the conclusion I reached
7 in Clark v Nomura, isn't it? It may be I wasn't given
8 the benefited of that Court of Appeal decision, but
9 that's --

10 MR BEAR: I wanted to read on a little more. It is
11 certainly similar.

12 MR JUSTICE BURTON: Yes.

13 MR BEAR: What Lord Justice Leggatt says is:

14 "The discretion not only exercised honestly and in
15 good faith, but having regard to the provisions ..."

16 MR JUSTICE BURTON: I've read that about arbitrarily or
17 capriciously unreasonable.

18 MR BEAR: The next sentence:

19 "Proper consideration of the matter after making any
20 necessary enquiries ..."

21 Then just to look at page 406, column 2 where the
22 judge's conclusions are summarised about halfway down,
23 or rather extracted:

24 "... impossible to accept from Mr Gallagher that
25 commercial considerations such as the dispute about

1 overage insurance had nothing to do with the owner's
2 refusal to proceed to the Gulf ..."

3 MR JUSTICE BURTON: Yes.

4 MR BEAR: Then looking down about three lines:

5 "The refusal was capricious because it was prompted
6 not by danger still less by increased danger proceeding
7 to the port but by the commercial dispute. Such danger
8 as there was afforded the occasion for the refusal, not
9 the courts."

10 So that that's the sort of enquiry that your
11 Lordship can make if we're correct on the legal nature
12 of this clause.

13 MR JUSTICE BURTON: As you say, although Lord Justice
14 Leggatt deprecated the comparison with judicial review,
15 that was actually the test he adopted in the end, or
16 something very close to it, which I think is the same
17 conclusion I reached in Clark v Nomura.

18 MR BEAR: That's right.

19 MR JUSTICE BURTON: It's not the same test as saying: was it
20 a reasonable decision?

21 MR BEAR: No. It's not the same --

22 MR JUSTICE BURTON: It's: was it a perverse decision, one
23 which no reasonable person to could come to?

24 MR BEAR: It's possibly a little higher than pure
25 perversity, because one looks to see whether it was made

1 after necessary enquiry and whether it was exaggerated
2 and so on and so forth.

3 MR JUSTICE BURTON: Yes.

4 MR BEAR: But these are matters of fine wording. Your
5 Lordship has the point.

6 MR JUSTICE BURTON: Perverse would include no consideration
7 of the evidence.

8 MR BEAR: Yes. My Lord, exactly. Anyway, as your Lordship
9 says, even if we are to proceed with the judicial review
10 analogy with caution, we seem to end up in a very
11 similar place to the administrative court in relation to
12 these clauses.

13 MR JUSTICE BURTON: Yes.

14 MR BEAR: So that's what we say on discretion, so we say
15 there wasn't an objective basis, even at the level that
16 was required for this clause, and obviously the
17 particular motives, we say, were essentially commercial
18 motives and Xytis was simply looking for a pretext.

19 MR JUSTICE BURTON: Yes.

20 MR BEAR: My Lord, I see that -- I'm sorry to dot about, but
21 I should have mentioned one small point on the
22 information request which was something which was
23 mentioned I believe just after the short adjournment by
24 Mr Nash.

25 He said that what they would have liked was a list

1 of SAEs.

2 We make two points about that. The first is that's

3 not what they asked for.

4 MR JUSTICE BURTON: No.

5 MR BEAR: And the second is that -- speaking for myself at

6 any rate -- I find that a surprising submission because

7 set out at page 15 of my skeleton, paragraph 43 --

8 MR JUSTICE BURTON: Hang on. Paragraph?

9 MR BEAR: 43. On 8th November, second line, a listing of

10 AEs was sent to HPM. I give you the references in the

11 footnote, and it was also sent to Xytis.

12 So we don't quite understand how it can be said that

13 this is something which Xytis --

14 MR JUSTICE BURTON: Sorry, I missed footnote 15. That was

15 where you gave me the reference to the 14th November,

16 thank you. But you say -- can I just look at these?

17 MR BEAR: Yes.

18 MR JUSTICE BURTON: It looks as though I may want to pull

19 them out and put them in the core bundle.

20 MR BEAR: Yes, chronological bundle 11.

21 MR JUSTICE BURTON: It looks as though I've pulled 3038 out

22 already. What about 3058?

23 MR BEAR: 3058 goes with 3059. It's an email string which

24 rather tediously records the attempts by my client to

25 send this particular file through Xytis's server, was

1 getting bounced back, they ended up asking --

2 MR JUSTICE BURTON: Is it identified in 3058, 3059, what it

3 is they're sending? Whereabouts do I find that?

4 MR BEAR: Well, you find it by the last one in the string,

5 which is the top of 3058.

6 MR JUSTICE BURTON: "Please could you try ..."

7 MR BEAR: "... sending the DSMB ..."

8 So this is writing to HPM, a Dr Geraldine Aubes.

9 MR JUSTICE BURTON: The DSMB line listing data file, that

10 was it, was it?

11 MR BEAR: Yes, that was what was referred to at 3038.

12 MR JUSTICE BURTON: Now I'd better track down 3038. I must

13 have put it in the bundle without realising what it was

14 I have already included it in the core bundle.

15 "Please, rather than send a line listing, I asked

16 Tony Brady to do a blinded list from the data he

17 received from the DSMB analysis ..."

18 MR BEAR: Pausing there, what he is saying is: I don't want

19 to send you something from the current status as at

20 8th November, because I know what you're interested is

21 what went to Brady which went to the DSMB.

22 MR JUSTICE BURTON: Yes.

23 MR BEAR: So she has asked him to effectively extract the

24 data.

25 MR JUSTICE BURTON: So you say this is exactly what they now

1 say they wanted?

2 MR BEAR: Well, it's exactly what they now say we should
3 have provided as a sensible response to their broader
4 request, even though they accept they didn't request it.
5 But even that last throw of the dice doesn't work,
6 because we did actually provide it.

7 MR JUSTICE BURTON: Yes, thank you.

8 MR BEAR: And seems to have been met with not a great deal
9 of interest at the time.

10 MR JUSTICE BURTON: Do you want to briefly deal with -- was
11 there anything else wanted to say? Do you want to
12 briefly deal with -- just to get my mind thinking the
13 right way -- as to the fall-back, which only arises, as
14 I understand it, if you fail, ie if the claimants are
15 right that there were breaches for which they were
16 entitled to terminate the contract?

17 MR BEAR: Yes.

18 MR JUSTICE BURTON: You say, notwithstanding that you are in
19 repudiatory breach of contract, on that assumption, or
20 at any rate a sufficient breach to have entitled them to
21 terminate, you can hang on in there because it would be
22 unlawful to terminate a contract which you yourself have
23 provided for termination of.

24 MR BEAR: Yes, what it does is it flows from the committee
25 structure and from what Xytis say about --

1 MR JUSTICE BURTON: Yes, but it makes a nonsense, doesn't
2 it, to have a specific contract saying how you terminate
3 it but then the guilty party can turn around afterwards
4 and say, well, even though you've acted exactly in
5 accordance with the contract, but we haven't, we've
6 broken the terms, you've terminated it successfully, yah
7 boo sucks, you're stuck with it.

8 MR BEAR: It's not saying that, it's saying that the
9 regulatory structure comes first and if there's an
10 inconsistency, if there is an inconsistency --

11 MR JUSTICE BURTON: So how do you terminate? It can't be
12 a non-terminable contract.

13 MR BEAR: You have to amend the protocol.

14 MR JUSTICE BURTON: You amend the protocol to delete you
15 from the protocol?

16 MR BEAR: To delete the committee, yes.

17 MR JUSTICE BURTON: And how is that done?

18 MR BEAR: An application would need to be made to the
19 licensing authority. Could I show you -- the way that
20 we look at it is to start on page 22 of Xytis's
21 skeleton.

22 MR JUSTICE BURTON: We'll have a short break for the
23 shorthand writer when you've finished your opening.

24 MR BEAR: Page 22 of Xytis's skeleton, paragraph 85.
25 So they say that the TSC ceases to have any

1 contractual foundation --

2 MR JUSTICE BURTON: Right.

3 MR BEAR: -- and, as we understand it, they are saying that
4 the TSC disappears once the contract is over.

5 MR JUSTICE BURTON: Right.

6 MR BEAR: If that's the case, then that means that the
7 termination of the CTSA, the contract, on its own, if it
8 were allowed to happen, would bring about the
9 termination of the TSC. The TSC would cease to exist.

10 The trouble with that problem -- and I appreciate of
11 course it would give the guilty party a sort of ability
12 to hang on in there, but the legal difficulty that it
13 gives rise to is this: first of all, the regulations
14 require that the protocol should be governing -- in
15 other words, they require that any trial should be
16 conducted according to the approved --

17 MR JUSTICE BURTON: How do we amend the protocol? I must be
18 frank, when you get an English divorce, that there's
19 a get to be got, in a Jewish divorce the English Court
20 nowadays as I understand it orders one side or other to
21 go and get the get. So that if I decided this contract
22 was terminated, then I would have thought the right step
23 for me to take would be to direct that whatever steps
24 were necessary to put that termination into effect
25 should be taken, and if some regulatory consent had to

1 be given, one side or other would have to cooperate in
2 obtaining it.

3 MR BEAR: Well, yes, but the --

4 MR JUSTICE BURTON: What I don't see is that it stops the
5 termination.

6 MR BEAR: I understand that. I don't want to spend too much
7 time on this, because obviously --

8 MR JUSTICE BURTON: It won't arise on your view.

9 MR BEAR: -- it's so far back on our case, I see your
10 Lordship doesn't either. The regulators approved a very
11 specific structure, under which there was a scientific
12 steering committee. Now, Xytis would have to propose
13 some alternative to that which might or might not be
14 acceptable to the regulators. It's one thing to have
15 a trial where the conduct of the trial is in the hands
16 of a body of scientists, and it's another to have
17 a trial where it's in the hands of the sponsor, for
18 example.

19 MR JUSTICE BURTON: No, but at the moment I see a difference
20 between the trial continuing, which is what they want
21 with their Technostat people. I can't give permission
22 for that. That's not up to me to do. If they want to
23 carry on the trial with another provider, that's up to
24 them to get all the regulatory requirements.

25 But surely there's a difference between them

1 carrying on the trial in some different form and for the
2 trial as presently constituted under your steering
3 committee coming to an end because the agreement has
4 come to an end. Why is there such a difference there?

5 MR BEAR: If the consequence of the agreement coming to an
6 end is that the committee would disappear, that then
7 means that the agreement, we say, can't come to an end
8 until the requirement for the committee, which is
9 contained in the protocol, has been replaced by
10 different approved regulatory requirements.

11 MR JUSTICE BURTON: Let's assume, Mr Bear, that -- it's not
12 the case, but let's assume that they simply want to
13 stop, they're fed up with you and they don't want to get
14 a new person in, this has cost them a fortune, they are
15 just not going to do the drug anymore.

16 MR BEAR: If they don't want to conduct the trial --

17 MR JUSTICE BURTON: In those circumstances they can
18 terminate the agreement with you and walk away.

19 MR BEAR: Yes.

20 MR JUSTICE BURTON: It only arises if they want to have
21 a new provider with a new trial.

22 MR BEAR: Yes.

23 MR JUSTICE BURTON: That, surely, is for a new arrangement
24 which has to be entered into, I can quite see that, but
25 surely it can't affect the termination with you?

1 MR BEAR: What we say is that they've got to continue with
2 a steering committee as per the protocol, and that if
3 the consequence either of terminating or of any
4 consequential orders they might seek would be to put the
5 steering committee out of business, then that would be
6 unlawful. That's the problem.

7 At the moment, the steering committee is there not
8 just as a sort of body of form; it actually has conduct
9 of the trial, that's its job.

10 MR JUSTICE BURTON: My present feeling, I must say, is that
11 I'm going to decide in this trial whether, but for all
12 these other points, there has been a breach of the
13 contract justifying termination, and if that's my
14 conclusion, there must be a way out here, and I will
15 hear argument on it separately. It doesn't need any
16 oral evidence --

17 MR BEAR: No.

18 MR JUSTICE BURTON: -- and either you can reach agreement
19 between the two of you as to the way out, ie my making
20 necessary orders, perhaps an injunction restraining them
21 from carrying on the trial with somebody else until
22 they've got the necessary regulatory permission, if
23 you're entitled to that, so be it.

24 But, on the other hand, more likely, directing you
25 as the guilty party to cooperate with them as the

1 innocent party, to obtain any necessary regulatory
2 permissions to allow the trial to go on if that's what
3 they decide. But whatever it is, it just doesn't seem
4 to me at the moment that it's something which prevents
5 the termination of a contract which both of you have
6 agreed can be terminated. The law doesn't like --
7 I remember a decision of Lord Denning who interpreted an
8 apparently non-terminable contract to say that it could
9 be terminated, if it was a licensing -- you're probably
10 familiar with one or two of these old cases, and the
11 courts don't like non-terminable contracts.

12 MR BEAR: They don't, it's the Staffordshire case that your
13 Lordship has in mind.

14 MR JUSTICE BURTON: That's right.

15 MR BEAR: I'm not suggesting that ultimately the contract
16 can't be terminated. That would be a most unattractive
17 result. What I'm suggesting is simply that -- and it
18 may be as much a matter of timing -- that if the
19 termination would involve deleting a committee which has
20 a place under the regulatory framework via the protocol,
21 then the termination has to be postponed, unless and
22 until some alternative regulatory --

23 MR JUSTICE BURTON: Yes.

24 MR BEAR: -- and that's all.

25 MR JUSTICE BURTON: So be it, but heads can be put together

1 on that, I'm sure, to find a way out.

2 MR BEAR: I would have thought we could.

3 MR JUSTICE BURTON: Obviously we'll postpone that until

4 later, and it may be it can be done by agreement. But

5 the main point, of course, is that you say that there's

6 no justification for termination. In those

7 circumstances, (a) that question is irrelevant, (b) my

8 next question, does it matter that they have been making

9 commercial efforts to get out of the contract but will

10 have failed? So far as your counterclaim is concerned,

11 where does that go?

12 MR BEAR: Well, the counterclaim in one sense has no

13 independent life because it is the counterclaim under

14 the contract. So by definition it assumes that your

15 Lordship will end up finding, if that's your conclusion,

16 that the contract is still in being.

17 MR JUSTICE BURTON: I can understand that. So if in fact my

18 conclusion is that the contract has terminated under one

19 or other of the notices --

20 MR BEAR: Exactly --

21 MR JUSTICE BURTON: -- the counterclaim falls away.

22 MR BEAR: That's an end to the counterclaim.

23 MR JUSTICE BURTON: Right, I understand that. If I don't --

24 if I find that the contract is still alive, then either

25 I say, claim fails, or I say claim fails and, because of

1 the efforts to get out of it, which indicate
2 untrustworthiness of some kind, I grant some injunctive
3 relief to prevent that happening again.

4 MR BEAR: Yes.

5 MR JUSTICE BURTON: But I don't see at the moment that your
6 counterclaim has any other separate life.

7 MR BEAR: No, we've not sought to suggest that it does.

8 MR JUSTICE BURTON: I don't know whether any damages flow
9 from it.

10 MR BEAR: Well, there would be -- if there were findings of
11 breach, then your Lordship might give us time to decide
12 whether we wanted to seek an enquiry as to damages, but
13 at the moment it's not the way the case is put.

14 MR JUSTICE BURTON: No, I don't see it. Unless you can tell
15 me now that some loss and damage has flowed, then,
16 obviously there will be some interest to be paid on your
17 fees, but I'm not dealing with fees, assuming there are
18 any unpaid fees and I don't even know if there are any
19 unpaid fees, but at the moment I can't see any damages
20 flowing, and if there are no damages flowing, I see this
21 counterclaim as simply part of your case that their
22 whole motivation has been to get out of this contract
23 one way or the other, right back to August, and they
24 will have failed to do so.

25 MR BEAR: Let me try and explain why the counterclaim is

1 there.

2 MR JUSTICE BURTON: Yes.

3 MR BEAR: If your Lordship finds, as we urge, that the
4 contract is still in being, we want to continue
5 performing it.

6 MR JUSTICE BURTON: Yes.

7 MR BEAR: But we feel a grave suspicion that Xytis will
8 continue to try and --

9 MR JUSTICE BURTON: That's why you need injunctive relief,
10 but that's all it goes to.

11 MR BEAR: It's aimed at protecting our performance interests
12 going forward.

13 Now, I have not given any thought, and it's been
14 agreed that issues of quantum and damages to be
15 postponed, it could be, for example, there might be
16 reputational damages. Xytis has been busy spraying
17 around the world allegations that my clients have done
18 a dreadful job, and there may be some general damages,
19 I don't know. And that's really not the main issue.

20 MR JUSTICE BURTON: I want you to think about that, because
21 it seems to me that for you -- you don't need to
22 establish a counterclaim for breach of contract in order
23 to put forward a sufficient evidential basis for saying:
24 not only should this claim fail but I'm sufficiently
25 worried about whether attempts to break it will carry on

1 that I ought not to grant an injunction to secure that
2 it will be properly performed in future.

3 That doesn't need findings of breach of contract.
4 That simply goes, in my discretion, to the relief that I
5 grant on dismissing the claim, assuming I do.

6 MR BEAR: True.

7 MR JUSTICE BURTON: But if you really are wanting me to make
8 specific findings that this letter was a breach, that
9 letter was a breach --

10 MR BEAR: I understand the point.

11 MR JUSTICE BURTON: -- this implied term was broken, then
12 because of the possibility of preserving some damages,
13 I think you'll need to let me know about it. At the
14 moment, I don't regard that as necessary.

15 MR BEAR: No, and we're not going to create unnecessary
16 work. I take the point.

17 MR JUSTICE BURTON: I did make this comment, of course, in
18 correspondence, that it's rather like one of those old
19 undefended divorces here. The claimants want out, free,
20 because you've been in breach of contract. You want to
21 stay on in, married, and carry on with the work.
22 Neither of you want a negotiated severance package, on
23 the face of the legal claim that's before me, and the
24 only way that can be done is by outside negotiation.
25 I can only say either that this contract is at an end

1 with no damages or that this contract continues and
2 these two people who no longer love each other must
3 remain together.

4 MR BEAR: It's a contested divorce.

5 MR JUSTICE BURTON: Very good, we'll have our short break
6 and we'll start with the first witness subject to
7 a prior discussion about confidentiality.

8 (3.40 pm)

9 (A short break)

10 (3.45 pm)

11 MR JUSTICE BURTON: Two matters of housekeeping. One is
12 confidentiality and the other is a rough idea as to
13 timescale of witnesses, it would be helpful just to
14 discuss that briefly.

15 Now, confidentiality.

16 Discussion re confidentiality

17 MR NASH: My learned friend a moment ago offered me a draft
18 order. The point about the draft order is that it seeks
19 to deal both with confidentiality against the world,
20 which we have no difficulty with, but also with this
21 issue of blinding.

22 I'd like to deal with that. I think the first
23 question is really not contentious. We're quite happy
24 that --

25 MR JUSTICE BURTON: Is there a draft I can look at even if

1 it's not -- it's not agreed, obviously, but I can see --
2 I can now see what we're talking about.

3 MR BEAR: This is the only copy. I hope it's legible.

4 MR JUSTICE BURTON: Thank you, because it may be we can make
5 the one against the world now and we can return to the
6 blinding point tomorrow.

7 "Notwithstanding CPR ... it is ordered ... that the
8 following documents may not be used or further disclosed
9 for any purpose other than for the purpose of these
10 proceedings, and the distribution of the documents or
11 their contents be limited ..."

12 Then the shell tables:

13 "... any witness statements referring to the
14 contents and any transcript of evidence specific to
15 referring to the contents."

16 Now, you say you're not unhappy with (a)?

17 MR NASH: I don't have the draft in front of me, my Lord.

18 MR JUSTICE BURTON: Of course, but it's distribution of the
19 documents -- limitation of distribution that you're
20 unhappy with, is that right? Can Mr Nash have a look at
21 that? Thank you very much.

22 MR NASH: We had to difficulty with the principle that the
23 fact that a document has been referred to in court
24 during the course of this trial should not thereby
25 release the implied undertaking given on disclosure that

1 documents will not be used generally, apart from the
2 purposes of the litigation. I have no difficulty with
3 that at all.

4 MR JUSTICE BURTON: Yes, and it also ought to deal with
5 publication, I suppose. It's not just non-user. It's
6 also publication. I don't know whether there's any
7 press in court. It ought to be wider than the non-user
8 of documents; it ought to be publication.

9 MR NASH: Again, no difficulty with that.

10 MR JUSTICE BURTON: Yes.

11 MR NASH: The blinding issue arises in this way:

12 Professor Sandercock in particular -- I think this may
13 go wider than simply him -- gives evidence about the
14 information that was contained in the shell tables that
15 went to -- in the first instance the DSMB, but
16 thereafter the limited tables that went to the TSC, the
17 steering committee, on which they formed their decision.

18 MR JUSTICE BURTON: Yes.

19 MR NASH: At the moment, as matters stand, Dr Simmon has not
20 been able to look at that material or comment on it at
21 all.

22 MR JUSTICE BURTON: No.

23 MR NASH: Because it's said that that will lead to an
24 unblinding of the trial.

25 MR JUSTICE BURTON: Would it not?

1 MR NASH: No, my Lord, we say it wouldn't. Our position is
2 that the mere fact that Dr Simmon, who is the chief
3 executive of Xytis, sees that material or indeed any
4 material, does not lead to an unblinding of the trial.

5 MR JUSTICE BURTON: My immediate reaction is that you are
6 the ones at risk because it's your trial, and you want
7 not only to carry on with this trial if you lose the
8 action, but if you win the action you want to carry on
9 with someone else, and you will therefore have to go
10 through the gamut of regulatory checks again before
11 Technostat can be approved, et cetera, et cetera, and
12 I would have thought it's in your interest to have no
13 suggestion of unnecessary unblinding.

14 But if, balanced against that, you prefer Dr Simmon
15 to see the evidence and have it said that the chief
16 executive of the sponsor has seen something he shouldn't
17 have seen, but in the course of litigation, I would have
18 thought it's a matter for you.

19 MR NASH: That's exactly our point, my Lord. The way it
20 works is this way: he's not unblinded. If he were, we'd
21 have to deal with it by way of an amendment to the
22 protocol for which we have to seek regulatory approval,
23 and if we fall at that hurdle, then it's our funeral.

24 So there's no real difficulty here. The converse
25 position is that Dr Simmon will have to either leave

1 court altogether when Professor Sandercock gives his
2 evidence or comes in and goes out again, something of
3 that sort --

4 MR JUSTICE BURTON: Is there anyone else who is in
5 Dr Simmon's position? You have a number of people
6 behind you. Who else is there?

7 MR NASH: There's Dr Furcha who is in the same position and
8 there's, of course, Dr Goedkoop who has seen some of the
9 information but not the whole of the information.

10 MR JUSTICE BURTON: Yes, some but not all.

11 MR NASH: Yes.

12 MR JUSTICE BURTON: So you'd need to have to have a decision
13 as to whether you say to yourselves, it's not so
14 essential for Dr Goedkoop to be in court, he can go,
15 but --

16 MR NASH: I think insofar as information is going to be
17 unblinded, as it were, or come into the public domain,
18 it's going to be the TSC information in particular which
19 Dr Goedkoop has seen in the same way as
20 Professor Roberts has seen.

21 MR JUSTICE BURTON: It's not going to be anything more than
22 has already gone to the TSC, is that right?

23 MR NASH: I don't think anyone is planning to put in the
24 entire DSMB tables.

25 MR JUSTICE BURTON: No, but everything that is in the

1 evidence so far has gone to the TSC and Dr Goedkoop has
2 seen, but in confidence?

3 MR NASH: Yes, exactly.

4 MR JUSTICE BURTON: Right, now what about Mrs Basch and
5 Mr Furcha?

6 MR NASH: They are in the Dr Simmon position, so they have
7 not seen this information.

8 MR JUSTICE BURTON: I know, but are they going to sit around
9 while they listen to it, are they going to be unblinded
10 as well, or are you going to have them out of court?

11 MR NASH: Both Mr Furcha and I think Ms Veronique Basch will
12 not be in court while that information is discussed.

13 MR JUSTICE BURTON: That does diminish your risk somewhat,
14 doesn't it?

15 MR NASH: Yes.

16 MR JUSTICE BURTON: So the position that you are telling
17 me -- I will hear Mr Bear in a moment -- you are telling
18 me and you are telling the providers, is that neither
19 I nor the providers need to worry about it, because you
20 are taking this risk upon yourself, and the risk is
21 pretty limited because it is limited to Dr Goedkoop who
22 already knows it anyway, and Dr Simmon who, for
23 litigation reasons, wanted to take that risk?

24 MR NASH: Exactly, my Lord.

25 MR JUSTICE BURTON: The others will not be in court so that

1 they're not going to be -- to have that problem, and the
2 public is going to have an order made against it anyway.

3 MR NASH: Yes. My Lord, can I just -- while I'm on my
4 feet -- deal with one or point on information and
5 access?

6 MR JUSTICE BURTON: Yes.

7 MR NASH: Dr Simmon would also want to look at the database
8 material that's been produced by the defendant, and no
9 blinding issue arises in relation to that, because
10 that's all unblinded -- that's all blinded anyway.

11 At the moment, we're not able to show him that
12 because we gave undertakings as to who would see that
13 material, and we haven't been able to persuade the
14 defendants to allow Dr Simmon to look at that. There's
15 some point been taken about proprietary software,
16 I think, or something of that sort, but in any event we
17 would like Dr Simmon to have access to that as well.

18 I am told the application is that Xytis should be
19 able to see it, so we don't limit it just to Dr Simmon;
20 we'd like to have all our witnesses --

21 MR JUSTICE BURTON: It's unblinded information? Sorry, it's
22 blinded information.

23 MR NASH: It's blinded information. The terminology gets
24 confusing. It's blinded information, yes, and we'd like
25 to have -- their witnesses of course had access to that

1 and some of them give evidence about it.

2 MR JUSTICE BURTON: There are two matters here. One is:

3 does it worry you that they may be putting themselves at

4 risk by having Dr Simmon seeing this limited

5 blinded/unblinded information?

6 MR BEAR: Can I try to make my client's position plain?

7 MR JUSTICE BURTON: Yes.

8 MR BEAR: I can understand why Mr Nash wants to show his

9 client's principal representative the material and

10 I would have exactly the same approach in his situation.

11 The reason my clients can't consent is not because of

12 any selfish desire.

13 MR JUSTICE BURTON: Of course not.

14 MR BEAR: But because they don't consider it's proper

15 practice.

16 MR JUSTICE BURTON: They don't want to participate in any

17 breach of the regulation.

18 MR BEAR: Exactly, exactly.

19 MR JUSTICE BURTON: You don't need to consent.

20 MR BEAR: We don't need to consent.

21 MR JUSTICE BURTON: You can simply listen and not oppose.

22 MR BEAR: Well, I do oppose it because it's not proper

23 practice, but I'm not going to suggest, because it is

24 not my client's position, that they have any, as it

25 were, personal or institutional interest.

1 MR JUSTICE BURTON: No.

2 MR BEAR: They simply want your Lordship to appreciate they
3 object because they consider it would involve a breach
4 of the regulations.

5 MR JUSTICE BURTON: I can't sanction any breach of
6 regulation if that's what it is, but I'm far from sure
7 it is going to be a breach of regulation and I'm told,
8 if it is, they'll ask for exemption from it.

9 MR BEAR: Yes.

10 MR JUSTICE BURTON: And to have so much money at stake on
11 a piece of litigation with your chief executive with one
12 arm behind his back is not sensible.

13 MR BEAR: My Lord, I see the force of all of that, if I may
14 say so.

15 MR JUSTICE BURTON: So I shan't make any order, but I shall
16 expect that Dr Simmon and Dr Goedkoop will remain in
17 court and that the other two won't.

18 MR BEAR: What I'd suggest is that you should make an
19 order -- and we can find the wording -- which recognises
20 that Dr Simmon should be allowed to see it. As far as
21 Dr Goedkoop is concerned, he was already carved out
22 because he is a member of the TSC.

23 MR JUSTICE BURTON: Oh yes.

24 MR BEAR: So no difficulty there.

25 MR JUSTICE BURTON: An order can be agreed along those

1 lines.

2 What about the other matter relating to the already
3 blinded data which surely ought to be made available to
4 the claimants, shouldn't it?

5 MR BEAR: Yes, and we don't have an objection in principle.

6 There is a pragmatic concern that I have which is this
7 is going to lead to lots of other material being put
8 forward into the course of the trial, but your Lordship
9 will have to deal with that.

10 MR JUSTICE BURTON: As far as I'm concerned this is not
11 intended to enlarge the trial. Your limitation on the
12 usage up to now hasn't been complained of, and it may
13 well have achieved that result, namely lots of
14 collateral points have been avoided. But the
15 information is now in, and it must be seen.

16 MR BEAR: My Lord, thank you. Could I say, again it may be
17 at least for the sake of form that it may be appropriate
18 to make a limited order against the world in general
19 under CPR 31.22 for the database because there are
20 proprietary codes and it belonged to Sealed Envelope.
21 I don't think it's of any interest to anybody, it's just
22 a case of a formal record.

23 MR JUSTICE BURTON: If you can agree an order, I will make
24 an order which restricts the public from -- or the press
25 from publishing the confidential information contained

1 in the database and in the unblinded information in
2 proper form, ie I'm not making -- not anything like as
3 widely as that. You will split it down, explain it
4 tomorrow in an order. But I want it to be said now in
5 open court, but what that is will be specified in an
6 order that I will make in terms tomorrow.

7 MR BEAR: Yes.

8 MR JUSTICE BURTON: And that will relate both to misuse of
9 but also publication of that information.

10 MR BEAR: Thank you very much.

11 MR JUSTICE BURTON: And you will reach -- I'm sure you can
12 agree an order which satisfies both sides in terms of
13 your not consenting to any breach of regulation if such
14 there be, but equally safeguards the position that they
15 are -- Dr Goedkoop and Dr Simmon -- are not going to be
16 subject to contempt of court. They must be exempted
17 from the effect of any order.

18 MR BEAR: Yes.

19 MR JUSTICE BURTON: Thank you very much.

20 Discussion re timetable

21 Now, timescales? We're going to start the first
22 witness today, which will -- which may or may not get
23 him through in-chief, I don't think it will.

24 Now, what are we going to do? What's the general
25 picture? Do you want to produce for tomorrow morning

1 a planned timescale indicating when witnesses are going
2 to be called? Is that the right course?

3 MR BEAR: If it would help your Lordship, at least to have
4 a sort of working document --

5 MR JUSTICE BURTON: Yes, I'm not going to keep you to it,
6 nor guillotine or anything of that kind. But I think it
7 will help everybody to have a rough idea.

8 In general terms, we've been talking about two days
9 for each side in terms of factual evidence, but that
10 looks as though it may need to be expanded by reference
11 to at least some of the witnesses. We'll effectively be
12 starting Dr Simmon tomorrow. I would have thought
13 Wednesday, Thursday, may be enough from your point of
14 view. It looks as though it's going to be your
15 witnesses who are going to take longer.

16 MR BEAR: Well, we're quite keen to have some sort of
17 parity, not in the abstract, but that's been agreed as
18 general principle.

19 MR JUSTICE BURTON: I'm thinking about this ploughing
20 through the AE bundle, which is not going to need to be
21 done by them in-chief, not least because you won't know
22 what it's all about. You may need to reserve your
23 parity, I suppose, by saying that you may need to recall
24 a witness depending on how this AE cross-examination
25 materialises.

1 MR BEAR: Quite, and I'm not particularly happy at witnesses
2 having to face a whole series of allegations without any
3 structure having been laid out beforehand.

4 MR JUSTICE BURTON: If they need time, we'll have to see how
5 it goes.

6 MR BEAR: We'll have to see whether we can.

7 MR JUSTICE BURTON: I'm not going to have you prejudiced,
8 but you may need to ask to recall some of their
9 witnesses depending on what happens.

10 MR BEAR: Indeed, that would be one way, although I'm not
11 going to cross-examine someone just to build up parity.

12 MR JUSTICE BURTON: No.

13 MR BEAR: What I would suggest is that, if your Lordship
14 were able to give an indication, because I think even
15 this afternoon when we are putting together the document
16 it would help us to have a rough idea of how long for
17 all the evidence in the case -- I appreciate your
18 Lordship has very kindly said there will be extra time,
19 but presumably at some point that runs out. My clients
20 obviously have only limited security for costs, so
21 they're a bit concerned about that as well.

22 MR JUSTICE BURTON: If you need to make another application
23 you will have to do so.

24 MR BEAR: I may have to. Hopefully we can do that.

25 MR JUSTICE BURTON: But in terms of a timescale, it would be

1 nice to finish by Thursday of next week, but if we
2 can't, then if we need Friday, I'll square the position
3 with the Commercial Court and we'll sit Friday, subject
4 to your convenience.

5 MR BEAR: Do you have a view about the length of time for
6 closing submissions?

7 MR JUSTICE BURTON: Well, I would have thought that it may
8 well be that your proposal is right that you need a day
9 each, but --

10 MR BEAR: I think based just on today's form, probably a day
11 each would be --

12 MR JUSTICE BURTON: I think, subject to this AE bundle,
13 I think it's right that there's much more a question of
14 submissions in this case than there is of factual
15 evidence, but we'll have to see how it goes.

16 MR BEAR: Yes.

17 MR JUSTICE BURTON: So equally, I'm not at all sure that the
18 experts -- the first lot of experts are going to take
19 any time at all. It's going to be the Gray/Nickols
20 experts who are going to take time, plainly.

21 MR BEAR: I think that is where the weight is going to be.
22 The other wrinkle is Dr Goedkoop, if I'm pronouncing
23 that right, has to give evidence tomorrow. He's only
24 available tomorrow.

25 MR JUSTICE BURTON: Dr Goedkoop is only available tomorrow?

1 MR NASH: There are two points, my Lord.

2 Professor Sandercock and Dr Goedkoop can only give
3 evidence tomorrow, as I understand it -- I think
4 Professor Sandercock can do Friday as well. But in any
5 event --

6 MR JUSTICE BURTON: Well, sort it out between you.

7 Certainly we can box and cox between claimant's
8 witnesses and defendant's witnesses, I've got sufficient
9 of the grasp, it's not going to throw me, as long as it
10 doesn't throw you, but I think we need -- for that
11 reason, we need to have a schedule, and clearly if
12 necessary, if Dr Simmon hasn't finished by lunchtime
13 tomorrow or so, then Dr Goedkoop will have to be
14 interposed.

15 MR NASH: My Lord, I was going to suggest, it's gone 4.00
16 now, Dr Simmon will want to look at these tables, and we
17 would want to discuss them with him. So I would suggest
18 that we don't swear him tonight, that he begins -- he
19 isn't embargoed overnight, we can begin tomorrow with
20 Dr Goedkoop, take him slightly out of order, but
21 nonetheless.

22 Professor Sandercock can go in after him if he
23 wishes to be sure of being away tomorrow, and then we've
24 cleared those out of the way, we can begin on Dr Simmon
25 probably shortly before lunch, I think I'll be about an

1 hour, maybe slightly more, with Professor Sandercock.
2 That's what I would propose.

3 MR JUSTICE BURTON: Yes, I see, so you think we can still
4 start Dr Simmon tomorrow?

5 MR NASH: Certainly, yes, unless my learned friend is going
6 to be very long with Dr Goedkoop.

7 MR BEAR: I'm not going to be very long with Dr Goedkoop.
8 Professor Sandercock isn't going to be here tomorrow
9 unless you want him. His days are Wednesday and Friday,
10 so seeing how it was going to --

11 MR JUSTICE BURTON: Let's do that. Let's have Goedkoop
12 followed by Sandercock, followed by Simmon.

13 MR BEAR: No, Sandercock won't be here tomorrow.

14 MR NASH: I think on that basis -- I thought he was, but if
15 he is coming on Friday I think that would work as well,
16 because we will have Simmon, Goedkoop --

17 MR JUSTICE BURTON: I think the answer is, if you ask -- do
18 you object to Mr Nash's suggestion?

19 MR BEAR: No, I think it's very sensible.

20 MR JUSTICE BURTON: Then can you spend the next 15 minutes
21 or so (a) hammering out the confidentiality order, but
22 also hammering out a timescale while your solicitors are
23 here and we all know availability of witnesses.

24 So in general terms, we've got factual evidence
25 tomorrow, Thursday, Friday, Monday, and experts possibly

1 Tuesday, Wednesday, Wednesday/Thursday, counsel's
2 closing submissions. So it may be we can finish by
3 Thursday night, but I'm not going to hold you to it, and
4 I'll make immediate enquiries now as to whether I can
5 sit on Friday.

6 The only other matter is this: given the fact that
7 it's come as a bit of a surprise to everybody, this
8 question of the AE files, if you are able at least to
9 indicate the documents about which -- I don't want to
10 make you give away any exciting secrets, but if you are
11 able to indicate which documents you're going to be
12 cross-examining on in the AE files to Mr Bear, that
13 would, I would have thought, be likely to at least save
14 some time.

15 Are you going to be in a position to do that?

16 MR NASH: Not right now, my Lord --

17 MR JUSTICE BURTON: No, of course not, but before his
18 witness on whom you will be cross-examining -- I mean,
19 who are you going to cross-examine?

20 MR NASH: It's going to be Mrs Shakur on these --
21 principally on these AE --

22 MR JUSTICE BURTON: Not Professor Roberts?

23 MR NASH: I may have one or two questions to him, but the
24 detail is going to be Mrs Shakur.

25 MR JUSTICE BURTON: The attack in relation to AE will be

1 Mrs Shakur?

2 MR NASH: Yes.

3 MR JUSTICE BURTON: So if you could, a day before Mrs Shakur
4 gives evidence, give a list of the documents in the AE
5 files which you are going to be asking about --

6 MR NASH: My Lord, with respect, I'm not prepared to do
7 that. It's a very unusual direction that counsel should
8 give a list of cross-examination documents to a witness.

9 MR JUSTICE BURTON: I'm certainly not going to order it if
10 you object to it, but it isn't unusual to be told -- and
11 certainly I've done it as counsel -- when one has
12 bundles with large numbers of documents, to give an
13 indication as to which documents are going to be
14 particularly used in the following days, it's quite
15 normal.

16 I certainly don't want you to give away the
17 questions, but it's not going to be possible for to you
18 say: I'm going to ask questions about the following
19 twenty or thirty files?

20 MR NASH: Well, my Lord, the AE files are two lever arch
21 files.

22 MR JUSTICE BURTON: Well, they are quite large.

23 MR NASH: Which contain --

24 MR JUSTICE BURTON: Are you going to ask questions about all
25 39 -- there are 39 of them, start?

1 MR NASH: Well, there are --

2 MR JUSTICE BURTON: You don't need to answer now.

3 MR NASH: There are 94 SAEs listed.

4 MR JUSTICE BURTON: Yes, but there are only 39 tabs.

5 MR NASH: There are 39 tabs, and I intend to ask questions
6 about a fair proportion of those tabs. Mrs Shakur --

7 MR JUSTICE BURTON: If there are any that you are not going
8 to ask questions about, perhaps you can at least
9 indicate that?

10 MR NASH: Well --

11 MR JUSTICE BURTON: Not now.

12 MR NASH: Not now, but I think if she proceeds on the basis
13 that she needs to be reasonably familiar with those two
14 files, then we won't waste time.

15 MR BEAR: Could I just lay down two markers, if I may?

16 MR JUSTICE BURTON: Yes.

17 MR BEAR: First of all, it's entirely a matter for my
18 learned friend whom he cross-examines, but if he's going
19 to make a criticism which on its true nature is
20 a systemic criticism, then that may have implications
21 for how he should cross-examine. I say no more than
22 that, I'm sure your Lordship --

23 MR JUSTICE BURTON: Vis-a-vis whether he's got to put it to
24 Professor Roberts.

25 MR BEAR: Exactly.

1 MR JUSTICE BURTON: I wonder whether Mrs Shakur ought to be
2 called before Professor Roberts.

3 MR BEAR: I would want to have Professor Roberts --

4 MR JUSTICE BURTON: I would be very reluctant to see
5 everything put twice just for the sake of it. If you've
6 had Mrs Shakur taken through the detail, then
7 Professor Roberts will have been in court and heard it
8 and he will be able to deal in-chief, if he wants to,
9 with any points he wants to make.

10 MR BEAR: We're in danger of the tail wagging the dog. I'm
11 quite keen to put the chief investigator, who's my
12 principal witness, first in the box, to explain -- to
13 give an overview and to explain the way in which the --
14 the principles on which the trial was organised and
15 run --

16 MR JUSTICE BURTON: I understand that. The whole attack on
17 Mrs Shakur, may fall away like a damp squib. Maybe the
18 answer is, as you aren't going to be familiar with what
19 it is, if you need to recall Professor Roberts after
20 Mrs Shakur's cross-examination, then you can do.

21 MR BEAR: Exactly. I was also making a point, though, that
22 it's up to Mr Nash whom he cross-examines, but
23 I wouldn't want it to be thought that I was accepting
24 that the only proper --

25 MR JUSTICE BURTON: No, you're right to make the point, but

1 I just don't think that I want to join in on any
2 suggestion that Mr Nash has to do his cross-examination
3 twice.

4 MR BEAR: I'm not --

5 MR JUSTICE BURTON: Your point is well taken. The detail
6 will be Mrs Shakur, but I think when we've heard the
7 detail, then there will be a conclusion to be drawn from
8 it: this was load of rubbish, wasn't it? From beginning
9 to end you've failed. That's a conclusion which can't
10 be put to Professor Roberts until we've heard the
11 details, but which could be put to him afterwards when
12 we've heard the details.

13 MR BEAR: My Lord, I was only laying down markers that
14 I didn't want Mr Nash to proceed --

15 MR JUSTICE BURTON: Do you agree with that, Mr Nash?
16 I think for you to -- you've got to put something to
17 Professor Roberts, but for to you put, "I suggest to
18 Professor Roberts that what I'm going to say to
19 Mrs Shakur is going to show that ...", that's not
20 acceptable.

21 Equally putting it all twice is not sensible. So
22 would it be sensible for you to have your bash at
23 Mrs Shakur and then have Professor Roberts recalled,
24 having heard all that, to say: well, there was nothing
25 in it, or whatever?

1 MR NASH: I certainly won't be bashing Mrs Shakur, my Lord,
2 but I think I have a clear idea of the distinction of
3 responsibilities between the two, and it may be I can
4 see the sense of cross-examining her first and then
5 asking --

6 MR JUSTICE BURTON: I understand that. However, I can see
7 Mr Bear's point that he doesn't want to mess his case
8 up, ie he wants to call Professor Roberts first. So all
9 I'm saying is in those circumstances Professor Roberts
10 could come back to deal with anything arising out of
11 Mrs Shakur.

12 MR NASH: Obviously, if that's necessary, then --

13 MR JUSTICE BURTON: If you feel able to cross-examine
14 Professor Roberts on the point sufficiently without
15 going into detail, ie so we don't have to either give
16 away your cross-examination to Mrs Shakur or repeat it
17 twice, fine, but if you -- I suspect you won't want to
18 do that. I would have thought you'd want to have your
19 attack on Mrs Shakur, in which case I think
20 Professor Roberts comes back afterwards.

21 MR NASH: Yes, yes.

22 MR BEAR: The second marker I was going to lay down is this:
23 that there is absolutely no proper objection that can be
24 taken by the claimant to identifying those instances,
25 those patients, where it says that a timeous querying

1 process was not carried out, and with great respect --

2 MR JUSTICE BURTON: In the normal course, that would have

3 been done in an expert's report.

4 MR BEAR: It would have been. For Mr Nash to complain about

5 what is in effect an indulgence that he's been offered

6 is a bit rich. We would like to see in advance and not

7 half an hour beforehand, properly in advance, actually

8 tying themselves down for once in this case, this

9 claimant coming off the fence and telling us which cases

10 it's concerned about and very briefly why, and if my

11 learned friend doesn't know that now, then his

12 cross-examination is just going to be a mere

13 exploration, but I don't believe that is the case, he

14 must have some idea. He should share it with us, it's

15 only fair.

16 MR JUSTICE BURTON: It is a problem, Mr Bear, isn't it,

17 because there may be a perfectly good answer -- sorry,

18 Mr Nash, I didn't realise you were up -- there may be

19 a perfectly good answer to some of the points you're

20 going to put which Mrs Shakur may need time to look

21 into.

22 MR NASH: If that is the answer in particular instances,

23 then that's an answer she can give.

24 MR JUSTICE BURTON: Yes, but wouldn't it be better to have

25 given advance notice of the points so that she can

1 prepare that answer in advance?

2 MR NASH: My Lord, I think we take the risk that if

3 Mrs Shakur says, there is an explanation that I need to
4 go back to the files to look at it, or something of that
5 sorted, on a particular issue, then so be it. But you
6 will appreciate this matter has come on very quickly,
7 it's an expedited trial, there aren't full pleadings and
8 we are resistant to the idea of trying, in the middle of
9 the trial, to start adding to the pleadings.

10 MR JUSTICE BURTON: Let me start by asking you to indicate
11 which tabs in volumes 1 and 2 you won't be asking about,
12 and that's what you said you thought you would be able
13 to do although not immediately. If it becomes apparent
14 that there are half of them which you won't be asking
15 about, then I suspect I'll leave it at that. If it
16 becomes apparent that you are asking about all of them,
17 then I think we will need to think again as to whether
18 we can't -- we mustn't find some way, Mrs Shakur, having
19 her attention directed to what it is you're going to ask
20 about.

21 MR NASH: Let's leave it at that and think about it

22 overnight and come forward with something tomorrow.

23 MR BEAR: I am sure my learned friend wouldn't want to be

24 unfair. I just invite him to consider this position:

25 Mrs Shakur, who undoubtedly does have a huge amount of

1 detailed knowledge -- obviously she's the trial
2 manager -- is going to be cross-examined and on the
3 current scenario all I will know in advance is which
4 cases are not to be the subject of cross-examination.

5 Let's say I wanted to exercise counsel's normal
6 prerogative of questions in re-examination. How am I to
7 do that when I've had no chance at all before this
8 examination to speak with the witness, I am not going to
9 speak to her during the examination.

10 MR JUSTICE BURTON: Well, it may mean that you will have to
11 be allowed to speak to your witness after
12 cross-examination.

13 MR BEAR: It may do. Wouldn't it, with great respect, be
14 simpler --

15 MR JUSTICE BURTON: I want Mr Nash to think about it.

16 MR BEAR: Absolutely.

17 MR JUSTICE BURTON: You're quite right, there is a balance
18 to be drawn between in some way prejudicing
19 a cross-examination on the one hand and allowing you to
20 prepare yourself for factual questions, and I think that
21 one's got to -- into the balance has got to come the
22 fact that it would at all have been surprising here if
23 there had been experts' reports indicating -- and
24 possibly even leading to a Scott Schedule with errors --
25 alleged errors in each of the various transactions.

1 That's not happened, and I want to try and balance
2 the allowing you some leeway in cross-examination; on
3 the other hand avoiding prejudice.

4 So can you have a think about this?

5 MR NASH: Yes, my Lord.

6 MR JUSTICE BURTON: Come back to it. The thing you're going
7 to do anyway is to say what you're not going to ask
8 about, but if you are able to indicate, having thought
9 about it -- not overnight, because you have other things
10 to do, but before Mrs Shakur, if you are able to
11 indicate the errors that you're going to ask her about
12 in these transactions, I would have thought it would be
13 much more sensible.

14 MR NASH: The only other matter, my Lord, is, I hadn't
15 intended to take Dr Simmon in-chief at any length.
16 I was simply going to tender him. Is there any matter
17 you --

18 MR JUSTICE BURTON: I thought it might be sensible, if you
19 wanted to, just to explain it to me, for him to deal
20 with his table insofar as he still stands by it.
21 I mean, there's some comment about whether Dr Simmon
22 still stands by his table, but if he does, he might like
23 to address me in-chief on what he makes of his table
24 having read what Professor Roberts and
25 Professor Sandercock say about his table, that's all I

1 would expect him to give in-chief.

2 MR NASH: Very well.

3 MR JUSTICE BURTON: If he wants to. If he doesn't, you
4 don't need to. I always think people like to have
5 a little bit of a go in-chief before they're
6 cross-examined. But it's up to you.

7 MR NASH: Thank you, my Lord.

8 MR JUSTICE BURTON: Thank you. 10.30.

9 (4.15 pm)

10 (The court adjourned until 10.30 am the following day)

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21
22
23
24
25

INDEX

PAGE

Questions from the Bench	3
Opening Submissions by MR NASH	32
Opening Submissions by MR BEAR	105
Discussion re confidentiality	183
Discussion re timetable	193

