

Friday, 1 October 2021

(10.00 am)

**Presentation by Counsel to the Inquiry on
the Pharmaceutical Companies (continued)**

SIR BRIAN LANGSTAFF: Yes.

MR HILL: Sir, today we turn to Speywood, and it is important to begin by noting the differences between Speywood and the other companies that we have been. Speywood was a British company and was, throughout the period involved, a relatively small company. While it manufactured some blood products, these were not widely used in the UK market. It's fair to describe them as being somewhat peripheral products.

The company was also involved in a wide range of other activities, we will look at those as we go through. But there are three elements that of particular interest to the Inquiry. The first, and as we heard yesterday, is that Speywood imported Cutter product, Koate, and subsequently re-branded it as Humanate, and sold it in the UK.

The second aspect is the work that was done by Speywood on human Factor VIII fractionation through a process called polyelectrolyte fractionation. We will hear evidence about what that was in due course. The product subsequently came to be called

1

pre-empt that evidence. Her analysis of the documents may be different to mine, and ultimately, sir, it will be for you to decide what your analysis is.

The presentation, as with all of the presentations this week, will touch upon some of the documents. It's not exhaustive. It is not comprehensive. There are matters that we may have to return to later, if that would be of assistance to you. And as, again, with all of the presentations in the last couple of weeks, it is limited by the access that we have to the papers. We have a lot of material, but we have by no means all of the material that we would like to have in order to tell the full story.

Before turning to the products, it is helpful to have a look at the company structure and how that developed over time. A helpful way of doing that is by looking at a document IPSN00000027, please, Soumik.

We can see from the front page of this document that it is a report prepared by Deloitte, Haskins & Sells, a firm of accountants, a very eminent firm of accountants, and it is dated 9 December 1981, and the report is headed "Speywood Laboratories Limited".

The context of the report is that it was prepared ahead of a proposed joint investment in

3

Mono VIII:C, but is often referred to in the documents as the human Factor VIII product, or words to that effect. The product was never widely produced and never widely used, and we will explore why that was.

The techniques developed for Mono VIII:C were, however, very important in the origins of the recombinant Factor VIII story. We will look at that today as well.

The third element of interest to the Inquiry of Speywood's work was the production of porcine Factor VIII, again, through polyelectrolyte fractionation.

As the name suggests, porcine Factor VIII was produced from pig plasma. The product that was made using that technique was called Hyate:C. It was primarily used for treating patients with Factor VIII inhibitors, and was not in general used for haemophilia patients who did not have inhibitors, and we will examine why that was.

We will hear evidence later today from Sarah Middleton, who was, among other roles, the chief scientist at Speywood for a period during the early eighties, late seventies and early eighties. We will hear her evidence after this presentation. What I say in the presentation is not intended in any way to

2

Speywood by the National Enterprise Board, who was a Government body that's invested money in firms that were, it was hoped, going to go on and make a successful business within the UK, and also an investment by Prutec Limited, which was the investment arm of Prudential Insurance. We will return in due course to the context of that investment and what happened around it, but for present purposes, the report is a helpful way of us understanding the company and the way that it was structured as of 1981.

Could we have, please the second page.

We can see in the left-hand corner that the report is directed to DA Smart of Prutec Limited and I Burns of the National Enterprise Board. It says:

"Introduction:

"In accordance with the instructions contained in your letters of 26 October 1981, we have carried out an investigation into the affairs of Speywood Laboratories Limited and its present subsidiaries ('Speywood Group') in connection with a proposed joint investment of £4 million in Speywood Laboratories Limited ... by Prutec limited and the National Enterprise Board."

The report refers to Speywood throughout and I'm going to do the same throughout this presentation. If

4

we could go, please, to page 3. The "History and Business" section. The report says this:

"Speywood was incorporated on 19th November 1973. In 1974 the company purchased ethical drug products from S Maw and Sons, including animal plasma fractions for the treatment of haemophilia and Zonulysin, an enzyme for the removal of cataracts.

"By 1978, the main trading activity of the company was the sale of Koate (human Factor VIII imported from Cutter Laboratories). This distributorship was terminated by Cutter in 1980 although Speywood are still able to obtain the product through a US intermediary. Speywood continued to sell Koate in the UK under the name of Humanate, but stopped in June 1981 when the product licence was amended."

Pause there, sir, to tell you that these are all matters that, I will come on to in due course.

On to the next page:

"Over the years the company has been seeking to improve its animal plasma products. It has now developed a manufacturing process using polyelectrolytes developed by Monsanto. Porcine Factor VIII produced by this process and sold as

5

a 10,000 square foot factory on the Wrexham Industrial Estate leased from the Welsh Development Agency.

If we could go over, please, to page 7. This is a page containing details of a licensing agreement reached with the Monsanto Company. We will again come back to some details of this, but I don't intend to go through the fine detail of who had which rights. But you will see there, sir, that by 1981, there is a fairly detailed explanation of the relationship between Speywood and Monsanto. The crux of it is that Monsanto had licensed to Speywood the technique to use polyelectrolyte fractionation both in porcine and human plasma, and in return, Speywood had agreed to certain limitations on its rights use the products that resulted from them.

Although that version of the licensing agreement dates from 15 August 1981, there was a previous agreement as well.

If we could now, Soumik, please, go to page 30 of the document. Under the heading "Management and Staff" the report says:

"At the time of our review, Speywood employed 12 persons at Bingham [that's the Nottinghamshire site] and 21 at Wrexham."

So we can see, sir, a much smaller company from

7

Hyate C is now the company's main product."

The report then goes on to list subsidiaries and former subsidiaries, and we can see at various points there have been a variety of businesses: a dietary food business, a television projection and ancillary equipment business, a business entitled Vision Medical Limited. These had all either been sold off or had ceased trading, some with losses, some sold at a profit. Then the final one is Cardio Technology Limited, and we can see that that was sold with 85 per cent of the share capital to a Mr P Hammond, who went to become the Chancellor of the Exchequer.

If we could go over to the next page, please.

Some further businesses, retail pharmacies, and then a US company, Speywood Corporation, and a west German company, Speywood GmbH, which were intended to be outlets into those two markets. But, as the report says, the US company has never traded and the German company is intended to be used as an outlet that, at that stage, I don't think it was being used. These aren't companies that will trouble us today.

What is also clear from the report is that Speywood is based in two centres. There is an office in Nottingham, or Nottinghamshire, I should say, and, as we can see in the "Future Plans" section,

6

those that we have been dealing with in the recent days and weeks.

"The senior staff are:-

"D Heath -- Managing director

"P Lees -- Commercial director

"D Williams -- Marketing director"

And those names, David Heath, Peter Lees and David Williams will come up as we go through the presentation today.

Then, a few names down:

"Mrs S Middleton -- Chief Scientist"

That's Sarah Middleton who will be giving evidence later today.

If we could go back, please, Soumik to page 27 -- sorry, 26. The bottom half of that page, please, under the heading "Share Capital". The accountants set out the current position as of 1981 on the shares that were owned by the different equity holders in the company. I will use the adjusted figures, and we can see that an investment trust owns 32,000 shares, so that's about 40 per cent of the company.

A finance body owns a further 21,200 shares, so that's about 26.5 per cent of the company. Mr Heath owns 18,800 shares, that's 23.5 per cent. So that's

8

about roughly a quarter of the company. And Mr Lees and Mr Williams have about 5 per cent of the company each. So those are the equity holders.

I merely note that Sarah Middleton is not one of the equity holders. She was the chief scientist and hence an employee of the company.

Thank you, Soumik. We can take that down now.

The proposed investment of £4 million was in fact made in 1982 by Prutec and the National Enterprise Board. Both of those entities took 25 per cent of the equity of the company, meaning that the 50 per cent that was left remained in the hands of the original investors, presumably according to the same proportions.

After that investment, a new chairman, Mr Seymour, was appointed, and Mr James Mottram became the general manager in 1983. His brief, according to the documents that we have, was to, and I quote, "reorganise Speywood into a classical UK pharmaceutical company". The reference for that is IPSN0000166_019. Mr Heath and Mr Williams subsequently left the company and we will hear a little evidence about the circumstances in which that took place, and the disputes that gave rise to it.

9

documents that will help to answer the questions that we raised yesterday about the level of detail that was provided before the licence was granted, to what extent further information was provided about the source of plasma and the way in which donors were selected and indeed rejected. That is something we will continue to explore. We will seek to work with others within the Inquiry, as well, to see if they can shed any light on it. But, at present, I'm afraid, I can't take that story any further.

We know that there was some further correspondence about packaging and the hepatitis warning in October 1976, a reference is IPSN0000312_040. The warning itself -- and perhaps we could bring this up, Soumik -- is at IPSN0000329_001.

Here we can see the data sheet for Koate. The product licence is there on the left-hand side. The address of Speywood and, of note, sir, is that the address given is the Bingham address, the Nottingham address, and not the Wrexham address. There may be a significance to that as we go through.

If we could -- give me one second, Soumik.

If we could go to the second page, please, the "Contra-indications and warnings", it says:

"There are no known contra-indications to Koate.

11

In 1984, the company was acquired by Porton International. It was later acquired by Ipsen Biopharm Limited.

Just for your note, Ms Middleton, from whom we will hear later, left the company in 1984, just before it was acquired by Porton.

Turning then to the importation and sale of factor concentrates. As we heard yesterday, there was an agreement, a distribution agreement, between Speywood Laboratories and Cutter Laboratories, so that Speywood could import and sell within the UK the Factor VIII product, Koate. The agreement itself is at IPSN0000139_003. It ran for three years from June 1976.

I won't take you to the agreement, sir, but it is there for future consideration should that be necessary.

A product licence, PL 0370/0004, was granted to Speywood for Koate in August 1976. The reference I have for that is IPSN0000312_036. We know, and as we heard yesterday, that Cutter had originally submitted an application for Koate, but Speywood in effect took this on. There is correspondence to that effect, which is BAYP0000020_046.

Unfortunately, sir, we don't have at present the

10

"Hepatitis -- Koate is prepared from units of human plasma, each donation offer which has been found non-reactive for hepatitis B antigen ... when tested by radioimmunoassay. In addition, each batch has also been tested against hepatitis by radioimmunoassay. However, despite these tests and the precautions taken in selecting donors, the risk of transmitting serum hepatitis cannot be excluded."

Thank you, Soumik.

The product was on sale from Speywood from 1 November 1976. Reference for that is IPSN0000312_038.

We have some sales figures from November 1976 to October 1977, and please can we have this on screen, please, Soumik, IPSN0000146.

Very helpfully set out per haemophilia centre with a grand total at the bottom. We can see that we're not entirely comparing like with like because the -- some of the centres have been using the product for longer than others. Bristol has been using it for a full 12 months, compared to St Thomas's just using it for five.

More than 500,000 units, and I take that to mean international units, had been sold to Oxford. Then about just over 300,000 units to Liverpool.

12

1 If we go down to the bottom Soumik, we can see
2 that the total sales for that period, November '76 to
3 October '77, a 12-month period, is 2.7 million units.

4 Those sales, sir, were achieved despite not
5 tendering for the NHS central contract that we have
6 seen in some of the other presentations. We will
7 return to this matter and, indeed, the reasons why
8 Speywood didn't tender to that contract when we come
9 back to look at some of the evidence from civil
10 servants and Government ministers.

11 A reference, so that we have it for when we come
12 back, is DHSC0003719_098, which explains Speywood's
13 thinking at that time.

14 David Williams, the marketing director, one of
15 the names that we saw in the accountant's report, met
16 with leading haemophilia clinicians between
17 August 1978 and January 1979 to discuss their factor
18 concentrate usage, and the Inquiry has considered some
19 of the notes that he made of those meetings when
20 examining each of the centres, so I won't take you
21 through each one but they're helpful ways of getting
22 a snapshot of what the Centre was doing at the time.

23 I will, however, just highlight one, for present
24 purposes, which is IPSN0000334_019. We can see from
25 the file note that this is Mr Williams's meeting with

13

1 "He is not interested in the administration kits
2 but prefers to make his own up in the hospital.

3 "I offered Koate at 10p for 50,000 unit lots and
4 am reasonably confident that we will get some of the
5 business. Bloom always likes to keep two suppliers,
6 but is reluctant to make frequent changes.

7 "Bloom is obviously not an animal lover although
8 he is interested in our work."

9 Pause there, sir. A slightly cryptic reference,
10 I believe, to porcine Factor VIII.

11 "He is prepared to look at the new material when
12 available. He referred to Rizza's suggestion that use
13 of porcine increased the inhibitor level to human. He
14 also felt that the present material was too antigenic
15 and expressed doubts as to the likelihood of our
16 reducing this to a level which he would regard as
17 satisfactory. I think it important that we provide
18 him with clinical evidence as soon as possible.
19 Perhaps Jean Pierre could prepare some notes."

20 I pause there, sir, to say that we will be
21 coming back to this, but Professor Bloom's reaction to
22 the possible use of porcine Factor VIII is, I would
23 suggest, fairly typical of the view at that time in
24 1978, and we will come on to see how that view changed
25 or, indeed, whether it changed, in due course.

15

1 Professor Bloom at the University Hospital of Wales on
2 24 August 1978.

3 I'm going to read through all of this note, sir.
4 There will be some things that I focus on now, which
5 are to do with the product sales, and some things that
6 I will come back to in due course which in particular
7 concerns polyelectrolyte fractionation. The initials
8 "PE", as we will see on this note, refer to
9 polyelectrolyte fractionation.

10 What Mr Williams said in the note is this:

11 "There are 250 haemophiliacs attached to this
12 centre, of which 100 are regular attenders and 13
13 inhibitors. Until recently, human factor VIII
14 purchases have been split three ways, Hemofil,
15 Factorate and Elstree. They have now stopped using
16 Armour, following the hepatitis problem."

17 I just pause there to note that, although it's
18 not clear from this document, that may relate to
19 reports in 1977 and 1978 of adverse reactions and
20 hepatitis infection through the use of the Armour
21 product.

22 "Prices are: Hemofil 11p and Factorate 9.5p."

23 Factorate being the Armour product.

24 "Bloom used to favour Immuno, but as this is now
25 16p, he never buys.

14

1 "Bloom would like some PE to help with new
2 research project of his looking at the biochemistry of
3 human factor VIII. He has a research worker starting
4 January 1979, to work full time on this subject. We
5 could arrange to have first option on the results.

6 "PPF was at one time rationed in his area, but
7 is now issued on a first come, first served basis.
8 There is never enough available, partly because the
9 Health Service does not produce sufficient, partly
10 because of the high price. Bloom felt that there was
11 a place for commercial material, if it could be
12 produced more cheaply. We should obviously
13 investigate."

14 The date of the note is 31 August 1978 and we
15 can see at the bottom that it was copied to Mr Heath.

16 As I say, sir, there are a number of other
17 similar notes. I'm going to be give some references
18 for the transcript so that people have those in case
19 they are of use to them. I would point out that in
20 one of them, which concerns Dr Stewart at Birmingham,
21 he says that he hadn't heard about any hepatitis
22 problem in connection with the Armour product.
23 That is IPSN0000333_022.

24 The other references are IPSN0000332_021,
25 IPSN0000334_019, IPSN0000331_008, IPSN0000333_022,

16

IPSN0000338_011 and IPSN0000321_026.

The prices that were offered to the various clinicians varied. Some of that variation is due to different amounts of product being offered. As you observed the other day, sir, there is generally a discount for bulk. However, there is also an attempt to negotiate with individual clinicians to try to get their business, in essence.

As we've seen in that letter, 10p was offered to Professor Bloom; 9.5p for 1 million international units was offered to Dr Kernoff at the Royal Free in January 1979; 9p was offered in a draft letter, seemingly to the whole Haemophilia Centre Directors, dated 1980. The reference for that is IPSN0000325_001.

Dr Preston was offered 9.25p in August 1979 and 8.5p by May 1980. The reference is IPSN0000322_006, and the same stem, _003.

The pattern, which you will have observed, sir, is generally a falling one.

In December 1979, an issue arose about the potency claimed for Koate on its labelling.

What appears to have happen is that, when the product was tested by NIBSC and by the individual Haemophilia Centres, they found that their assays did

17

is of paramount importance. The other side of the coin is that we have two major and influential customers, Oxford and Newcastle, reluctant to trust our assay figures and insisting on their own check prior to acceptance."

He gives some further detail on each of the batches.

The first batch, C 1090, if we look back at the table we can see that its assigned potency was 1,100. Mr Williams, in his letter, says that C 1090 was:

"Not acceptable to NIBS unless we re-label at 900 my own view is that this should be returned to USA."

So NIBS has run its tests, found that the potency figure that they can obtain using their tests is around 900, and are insisting that the product is re-labelled to show that potency, if it is to be sold in the UK. This is an example, sir, of the stop orders that we have heard made reference to. The suggestion from Mr Williams is that that product should be sent back to Cutter and, presumably, Speywood would be compensated for the cost of it.

The second lot considered is NC 8610, which:

"... has been extensively used in Oxford and Newcastle and is the subject of an attached letter

19

not accord with the potency that was stated on the label. If we could go, please, Soumik, to IPSN0000575, we will see some of the correspondence about this. The date is 4 December 1979, and the letter is going from David Williams to Mr C Jones of Cutter Laboratories. As we will see it's not only raising the problem but also raising the point that Speywood would like compensation from Cutter for the difficulties and the financial difficulties that the problem had given rise to.

What Mr Williams says in the letter is that the: "... situation with respect to [as he terms them] 'suspect' batches of Koate is as follows ..."

We can see there four batches listed down, and we can see, in the second column, the assigned potency, which I take to mean the potency that was stated on the label.

You can also see the quantity received, the current stock and how much had been sold.

The paragraph below, Mr Williams says:

"As you will realise from the quantity involved, we have a major problem. On the one hand, we are desperately short of 'good' stock and, clearly, we dare not sell new batches without first obtaining NIBS clearance. So your urgent help with prompt despatches

18

from Rizza and Jones."

We don't have that letter.

"NIBS obtained 210 and cleared at 230. Repeat assays at Oxford indicate 185."

What I take that to mean, sir, is that when NIBS -- the assigned potency, as we can see from the table on the previous page, is 230. NIBS in their tests obtained 210, the units don't matter but a figure of 210 for the potency, so about 10 per cent below that which was claimed. I read that as meaning that NIBS were content to clear the product as saying that it had a potency of 230, presumably allowing some leeway for a potential difference in testing.

But when the product was then tested at Oxford, the potency was 185, which appears to have prompted a complaint to Speywood about the product.

Mr Williams goes on to say that:

"For the present, I have supplied replacement material free of charge to both centres. Probably the simple way out financially, is to give them units equivalent to their 'loss', say 20% or 126,000 units. Obviously we will be looking to Cutter for compensation."

So the fact that the product is not as potent as claimed means that more will have to be used, hence

20

1 that figure of 20 per cent. They will build up the
2 stockpile to replace that which these centres should
3 have had. And as is stated in terms there, Speywood
4 are looking to Cutter for compensation on that. So
5 Speywood very much seeing this as a problem of
6 Cutter's making.

7 "NC 8185

8 "This was cleared by NIBS at label declaration,
9 although their assay was around 10% low."

10 Again, sir, showing that there is a degree of
11 leeway allowed by NIBSC. But as we can see from
12 "NC 8184":

13 "NIBS again got 900 and will not clear without
14 re-label."

15 The claimed potency was 1130.

16 So the leeway only extends so far before NIBS,
17 using stop orders, say: you can't distribute this
18 product without re-labelling it.

19 What Mr Williams says about that product is:

20 "I originally stated that we would [re]sell to
21 France at label strength and in fact we have sold them
22 200,010 units. However, in view of total problem,
23 I feel it is not sensible to continue this policy."

24 I would say there is a further document, sir, at
25 IPSN0000291, which is dated 21 February 1980, which

21

1 the way in which the licensing system works its way
2 through at different levels.

3 Turning to the switch of products from Koate to
4 Humanate. The June 1976 distribution agreement
5 between Cutter and Speywood ran for three years, and
6 it appears that it was terminated at the end of 1979.
7 Cutter then began supplying Koate directly to the UK
8 market. We heard something about that yesterday.

9 The references are IPSN0000331_001, and
10 MHRA0036365_018.

11 In February 1980, Speywood obtained a variation
12 to their product licence allowing them to continue
13 selling Koate for up to one year, and also allowing
14 them to import unlicensed -- sorry, to import
15 unlabelled factor concentrate manufactured by Cutter
16 for relabelling and for sale under the name Humanate.

17 I'm afraid, sir, that we don't have the
18 documents that accompanied that licence variation
19 application, or at least we haven't identified them if
20 we do have them. Our information is taken from
21 a later licensing issue, which we will come on to.

22 The reference is MHRA0036365_018.

23 **MR HILL:** According to company records, the last Koate
24 batch imported by Speywood was released by the DHSS,
25 so that's released by NIBS, in February 1980. The

23

1 shows that, after further thought, Speywood had
2 decided not to sell product to France when NIBS has
3 said that it must be re-labelled. And one of the
4 reasons that is given for that policy is that Duncan
5 Thomas of NIBSC is in regular contact with his French
6 opposite number and it would be embarrassing for the
7 companies involved to be found to be selling with one
8 label in one country and one label in the other
9 country. Although I should add that it's important to
10 note that in his letter of 21 February 1980,
11 Mr Williams also refers to a basic moral issue that is
12 involved as well. So it is not just a cynical attempt
13 to avoid being caught.

14 The further point made by Mr Williams in his
15 letter of 4 December 1979, a little further down the
16 page, please -- thank you Soumik -- is:

17 "Of course, any recommendations on these batches
18 could change if your technical people can resolve the
19 matter with NIBS. I do hope you can achieve an
20 agreement quickly."

21 So there is some thought that this may be
22 a technical issue perhaps about how the different
23 tests work.

24 Thank you, Soumik. We can take that down.

25 I leave that there, sir. It is an example of

22

1 reference is IPSN0000139_022. That product, of
2 course, would have had a longer shelf life. The last
3 time that a Speywood sale under the licensing
4 agreement seems to have been cleared by NIBS was
5 February 1980.

6 The way in which Speywood began to sell Humanate
7 can be shown by a letter that was sent to Dr Aronstam
8 at Treloar's Centre by Mr Williams on 30 July 1980.
9 The reference is IPSN0000331_001.

10 Again, sir, I'm going to read all of the letter
11 through. There are matters that we will come back to
12 later, but I think it is important to show how the
13 different strands of Speywood's work: the human
14 Factor VIII, the porcine Factor VIII, and the sale of
15 imported products, all work together. Although we're
16 going to be looking at them individually for purposes
17 of analysis, they are running alongside each other all
18 the time.

19 What Mr Williams said is this, and I quote:

20 "Dear Tony,

21 "As you are aware, Speywood are the only British
22 owned company researching new blood fractionation
23 techniques and the isolation of highly purified plasma
24 proteins for clinical use.

25 "The first successful result of our research

24

programme, is the availability of a preparation of porcine Factor VIII:C, Hyate:C, for the treatment of inhibitor patients. This product has now been used for the first time in man. We are delighted to report that the treatment, in a life-threatening situation, was entirely problem-free. Thrombocytopenia was completely absent and there were no antigenic reactions. It would therefore appear that the criteria for the use of porcine material can be relaxed."

I will come back to that later.

"We are now working hard to produce human VIII:C and a vWF [von Willebrand's fraction] concentrate. Initial clinical samples will be ready by the end of this summer.

"Financing this research has been a major difficulty for such a small company as ours. For the first four years, we relied on our profits from sales of Cutter's Koate to provide the cash. Cutter are now selling direct and, to fill the gap, we have arranged the supply of a high quality freeze-dried Factor VIII product under our own trade mark, Humanate.

"Humanate is not an intermediate product and has a specific activity of approximately one AHF unit per milligram of protein. It is readily soluble and ideal

25

the specific activity is approximately one AHF unit per milligram, which perhaps explains the slightly odd wording of Humanate being "not an intermediate product" but it is not claimed that it is a high purity product.

Soumik, can we have on screen, please, BAYP0000021_023, at the top right-hand corner, please.

This appears to be a data sheet for Humanate and, in the top right-hand corner -- I'm afraid it's a very poor copy -- we can see that it's written:

"Humanate is prepared from human ..."

SIR BRIAN LANGSTAFF: It looks like "venous".

MR HILL: "... venous plasma"? Yes, it looks like "venous plasma".

"Each unit of donor plasma has been tested for Hepatitis B Surface Antigen by a radioimmunoassay technique and found non-reactive. However, this test does not necessarily preclude the presence of Hepatitis Virus."

That appeared to be the warning that accompanied Humanate as of circa 1980.

Two things are clear from other documents. The first is that Humanate was Koate being sold under a different name. We saw reference to that in the accountant's report that we looked at earlier, and

27

for home treatment. A leaflet and data sheet giving further information are enclosed. Pack sizes are nominal 250, 500 and 1,000 units.

"Our price for Humanate is 7.5p per unit, delivered, regardless of quantity, which we hope will give you some saving over current prices.

"Administration kits are available free of charge, if required. We can normally guarantee delivery within 24 hours.

"I do hope you will be able to give us some support and use Humanate for part of your treatment programme."

He says that he is sending a copy of this letter to Brian Grundy in Southampton.

One point that I would pick up from the letter, sir, is the reference to Humanate being, and I quote "not an intermediate product". You've heard evidence about the distinctions drawn between intermediate purity and high purity product and it was Dr Kingdon's evidence in his witness statement, CBLA0000011_005 at paragraph 31, he's referring to the 1970s but this letter is 30 July 1980. His evidence was that high purity was between 1 and 2 international units per milligram.

What is claimed for the product Humanate is that

26

a further reference, should it be needed, is BAYP0000021_063.

Second, the product was not obtained directly from Cutter but through an independent company called Parlier Medical Support. Sorry, Parlier Medical Supply Company, which was based in San Francisco, the reference for that is MHRA0036365_018.

On the first of these points, can we have on screen, please, IPSN0000338_001, a letter dated 31 October 1980, a few months after the letter that we looked at a moment ago, and sent from Mr Williams to Dr Evans of the Royal Manchester Children's Hospital. The section that I'd like to look at now is the second and third paragraphs. What Mr Williams says is, and I quote:

"Humanate is manufactured for us by Cutter Laboratories, so is identical to the product which we have previously sold as their agent [that's Koate].

"I will be grateful if you can keep this information confidential."

SIR BRIAN LANGSTAFF: So what you've just told me means that that's a lie, does it?

MR HILL: No, sir.

SIR BRIAN LANGSTAFF: "Manufactured for us", because it was bought from an intermediary, not direct.

28

1 **MR HILL:** It was bought with the knowledge, I believe, of
 2 Cutter, so --
 3 **SIR BRIAN LANGSTAFF:** So Cutter manufactured it for
 4 Speywood and sold it through an intermediary?
 5 **MR HILL:** As I understand it the position to be, yes, sir.
 6 **SIR BRIAN LANGSTAFF:** I see, so it was manufactured for
 7 them?
 8 **MR HILL:** So far as I can ascertain from the documents.
 9 It was certainly manufactured with -- well, it was
 10 within Cutter's knowledge that Speywood were doing
 11 this.
 12 **SIR BRIAN LANGSTAFF:** Well, that's a different issue. You
 13 may know that somebody is manufacturing or selling
 14 something that you actually made but you may not want
 15 them to do it.
 16 **MR HILL:** You may not, I don't know, but I've seen no
 17 evidence to suggest that Cutter didn't want them to do
 18 it, and Cutter could have entered into an arrangement
 19 with the Parlier Medical Supply Company to ensure that
 20 they didn't do it, and that, at least at this stage,
 21 does not appear to have been --
 22 **SIR BRIAN LANGSTAFF:** At some stage they used the word
 23 "pirate product", Cutter.
 24 **MR HILL:** There is a tension which develops, and we saw
 25 some of that in some of the documents yesterday.

29

1 where the product was from but then asks Dr Evans to
 2 keep that information confidential.
 3 We will come back to this letter about the
 4 porcine product in due course.
 5 If we could go forward, sir, just a few months,
 6 this is a document we did see yesterday
 7 BAYP0000021_063, please, Soumik.
 8 This is the board meeting of Cutter Laboratories
 9 Limited, the UK-based company, held on Tuesday
 10 16 December 1980. As I say, Ms Richards showed us
 11 this yesterday. If we could go down, please, to the
 12 central paragraph under the heading "Koate", it says:
 13 "It was agreed that the Managing Director,
 14 Mr BA Dyos, would put together a full situation report
 15 regarding Koate and also the Speywood parallel product
 16 known as Humanate which was in fact Koate marketed
 17 under a different label. It was agreed that this
 18 situation report was important and should receive full
 19 priority."
 20 A little further on there's a discussion about
 21 sales, and if we pick it up three lines from the
 22 bottom, it was said:
 23 "... it should be possible to price Humanate out
 24 of the market coupled with the fact that NIBSAC and
 25 Doctor Duncan Thomas were very concerned regarding

31

1 The --
 2 **SIR BRIAN LANGSTAFF:** That's not yet this stage?
 3 **MR HILL:** So far as I can tell, that's not yet this stage.
 4 But there is a tension which does develop, and we will
 5 see, shortly, that there is also a tension with
 6 licensing position --
 7 **SIR BRIAN LANGSTAFF:** Yes.
 8 **MR HILL:** -- with Speywood.
 9 What I take from this document, though, is that
 10 Mr Williams is prepared to answer what appears to have
 11 been a question from Dr Evans, and say, "This is Koate
 12 and it's made by Cutter", but, as we have seen from
 13 a previous letter from Dr Aronstam, there was an
 14 opaqueness, if I may put it that way, as to what the
 15 product was. It was certainly not said to Dr Aronstam
 16 that, "This is Koate", and it was not said, indeed,
 17 that it was a Cutter product -- no, sorry, it was said
 18 that it was a Cutter product. It says -- no, sorry
 19 I apologise. It was not. It said:
 20 "We have arranged for supply of a high quality
 21 freeze-dried Factor VIII product under our own
 22 trademark Humanate."
 23 So no further information given there about the
 24 source of that product, but, seemingly in response to
 25 a request from Dr Evans, Mr Williams does explain

30

1 Humanate and the impossibility of tracing its
 2 manufacture back to its source."
 3 So concerns within Cutter Laboratories Limited
 4 about the market position, if I may put it that way,
 5 of Koate in respect of this other product, and
 6 a desire to price it out of the market. And also an
 7 indication that the Licensing Authority was concerned.
 8 And that is the second element that I'll pick up now:
 9 the significance of the use of Parlier Medical Supply
 10 Company.
 11 The concerns flagged there in the minutes, the
 12 specific reference to Dr Thomas, led in fact to
 13 a variation of the licence that had been granted to
 14 Speywood for Humanate, and it's helpful to examine
 15 that process in a little detail, again because it
 16 assists us with our understanding of the way the
 17 licensing process worked.
 18 If we could have on screen, please, Soumik
 19 MHRA0036365_001.
 20 We can see that these are the minutes of the
 21 Committee on Safety of Medicines, that's the main
 22 committee, a meeting held on the Thursday,
 23 22 January 1981. So the first meeting of 1981, and
 24 just a month or so after the previous document that we
 25 looked at.

32

1 There's a list of attendees. I note in passing
2 that Dr J Smith, Dr Joseph Smith, is there, from whom
3 we've heard evidence. And among the committee
4 secretariat, for hearing 2 only, are Dr Fowler and
5 Dr Holgate. Hearing 2, as we will see, concerns
6 Speywood and Humanate.

7 If we could turn, please, Soumik, to page 3 of
8 that document. Under the heading "Hearings" it says:

9 "Humanate ... Speywood Laboratories.

10 "8.2. A record of the Committee's findings in
11 respect of the above is included at appendices B and C
12 to these minutes."

13 And it is appendix C to which we will turn,
14 because that's records a discussion on Humanate.

15 That is at MHRA0036365_018.

16 You can see, top right-hand corner:

17 "Appendix C ...

18 "CSM/81/1st Meeting

19 "Hearing 2"

20 Medical assessor is Dr Fowler and the product is
21 Humanate.

22 We're going to go through this document in
23 a little detail, partly because this is the
24 information that we have about the original variation
25 that allowed Humanate to be sold in the UK. We don't

33

1 licence holder to supply samples and protocols of
2 tests above on every batch of product and not to sell
3 or supply material from a batch until a certificate of
4 clearance for it had been granted by the licensing
5 authority. Speywood had complied with this
6 requirement for Koate by supplying samples and
7 protocols obtained from Cutter, to the National
8 Institute of Biological Standards and Control."

9 I pause there, sir. That is why we had that
10 exchange about the potency of the products and
11 re-labelling.

12 Paragraph 1.5.

13 "The protocols supplied to NIBSC by Speywood for
14 their first batch of Humanate has provided results of
15 tests done on the finished product by a British
16 contract laboratory. These had followed very closely
17 those done by Cutter for Koate, but the protocol had
18 omitted material included in the Koate protocol
19 concerning the Bulk Active Substance Used for
20 Formulation, Formulation and Filling. The Koate
21 protocol had also contained Cutter's statement that
22 the product had been manufactured by them at their
23 plant in Berkeley, California. Although the tests
24 done on the finished product were satisfactory, the
25 protocol had been deemed inadequate, as it was

35

1 have further papers, or at least we haven't found
2 further papers. We will continue to look for them,
3 because it will be interesting to see how the original
4 variation was granted.

5 "Background

6 "1.1. Since 1976, Speywood Laboratories Limited
7 has sold anti-haemophilic globulin (Factor VIII)
8 manufactured by Cutter Laboratories under the name
9 Koate in the United Kingdom. This arrangement had
10 been terminated by Cutter at the end of 1979.

11 "1.2. In February 1980, Speywood had obtained
12 a variation to their product licence which had
13 permitted them to:-

14 "a. continue selling their remaining stocks of
15 Koate for up to one year.

16 "b. import, in bulk, unlabelled vials of
17 anti-haemophilic globulin manufactured by Cutter for
18 relabelling and sale under the name Humanate.

19 "1.3. The material for sale as Humanate was not
20 obtained from Cutter, but through an independent
21 company called Parlier Medical Supply Company of
22 San Francisco, California.

23 "1.4. At the time of granting the Speywood
24 Product Licence for Koate in 1976, a full 'stop order'
25 had been routinely applied. This had required the

34

1 impossible to assess the safety of a blood product by
2 reference to finished product-testing alone. Speywood
3 have repeatedly said that they now had no contact with
4 Cutter, and thus had no access to information relating
5 to the manufacture of the product they were selling."

6 Over the page.

7 "Moreover the Product Licence granted to
8 Speywood had obliged the company to ensure that all
9 batches of the product continued to conform to the
10 various specifications contained in the original
11 application. While Speywood had acted as distributors
12 for Cutter they had been able to do this. Now that
13 they had no contact with Cutter they were no longer in
14 a position to guarantee that the product sold as
15 Humanate conformed to its Product Licence
16 specification. If in fact Cutter were the original
17 manufacturers of Humanate as claimed by Speywood they
18 could have changed the source, place or method of
19 manufacture of the product and Speywood would have
20 been unaware of this and unable to communicate such
21 changes to the Licensing Authority.

22 "The scientists at the National Institute for
23 Biological Standards and Control ... frequently had to
24 refer back to the company for clarification or further
25 information concerning the manufacture of the product.

36

Where the Licence Holder was the manufacturer or his authorised distributor, this posed no problem. Where the Licence Holder had no communication with the manufacturer, as in Speywood's case, such a dialogue was impossible.

"As a matter of routine, the additional conditions contained in the Schedule to the Product Licence issued to Speywood referred to protocols but no mention was made therein to the contents required in respect of such protocols. This lack of information was unsatisfactory, particularly in regard to biological products of the type in question. So as to remedy the situation, it had been proposed under Section 29(1) using powers conferred under Section 28(3)(g) of the Medicines Act 1968, compulsorily to vary Speywood's Product Licence in order to require the protocols to include evidence of the source and date of collection of the donor blood from which the product was prepared, the date of manufacture and the results of tests done during and on completion of manufacture. This would have put beyond doubt the nature of the evidence required when the term protocol was used and would have served to bring Speywood into line with the current practice of other manufacturers of anti-haemophilic globulin."

37

Committee giving notice that they intended to avail themselves of the opportunity to appear before the Committee to ensure that their position was fully understood.

So this the working through of the Medicines Act 1968. The Licensing Authority is proposing to vary, the company has an opportunity to put its case and this report from Dr Fowler is part of the process that then follows.

Paragraph 2, or section 2, "Additional information":

"The Company had submitted a paper giving the background to their case and why the variation to the licence should not be imposed.

"On the day of the hearing, the Company handed in a copy of the a notarised statement from Parlier Medical Supply Company which certified that bulk unlabelled antihaemophilic factor (human) shipped to Speywood was:

"(i) manufactured and sold by Cutter Laboratories,

"(ii) approved and released for general sale in the USA by the FDA (Bureau of Biologics division)

"(iii) derived from human plasma collected in plasmapheresis centres licensed by and conforming to

39

I pause there, sir, to summarise what I understand the position to be, that the use of the intermediary company meant that NIBSC were unable to satisfy themselves that there was a chain that they could follow all of the way back to the manufacturers of the product in order to understand how the product was manufactured and the -- (overspeaking) --

SIR BRIAN LANGSTAFF: Way I understand it is that, leave aside the intermediary, there was no direct link between Cutter and Speywood any more --

MR HILL: Yes.

SIR BRIAN LANGSTAFF: -- so Speywood didn't have the information.

MR HILL: Yes.

SIR BRIAN LANGSTAFF: It begs the question, going back to what I raised earlier in the letter to Evans, how one could say that Cutter was making it for Speywood.

MR HILL: Yes. I will jump, if I may, to paragraph 1.10, which records that:

"The Licensing Authority [wrote] to the company on 27 November 1980 stating their proposal to vary the product licence ..."

The wording is given, which I won't go through now, because it will come up again.

On 30 July 1980, the company had written to the

38

the regulations of the US Bureau of Biologics.

"Preliminary discussion

"The following points emerged from the preliminary discussion:

"(i) that 4% of the batches supplied for testing in 1980 came from Speywood

"(ii) that of 50% of the batches from US sources, there had been need to refer back to the manufacturers."

We understand that to mean that in 50 per cent of the cases where batches of factor concentrates are tested, there's a need to go back to the manufacturer to ask of them some questions, which shows the importance of having that chain going all the way back.

"(iii) that Speywood were merely being asked to give information which was routinely supplied by all manufacturers of anti-haemophilic globulin sold in the UK."

Section 4, the "Hearing":

"The representatives of the Company were as follows ..."

Mr Williams, the spokesman and Dr Jones, from Newcastle.

"The Company's representatives were welcomed by

40

1 the Chairman, who introduced the Committee, the
2 secretariat, and the DHSS officials present. The
3 representatives had no objection to the presence of
4 any officials.

5 "Mr Williams referred to the affidavit from
6 Parlier Medical Supply Company which had been
7 furnished and with the aid of slides explained that
8 the Cutter material was subject to Cutter in-house
9 quality control, before submission to the FDA/BOB for
10 clearance. The material was purchased after clearance
11 and thus its integrity was in his view guaranteed.
12 Following delivery to Parlier Medical Supply Company,
13 all packaging was removed and the product shipped
14 intact to the UK. On arrival in the UK, the
15 (unlabelled) material was subject to quality control,
16 carried out in the laboratories of Toxicol and the
17 Oxford Haemophilia Centre. Samples were then
18 submitted to NIBSC together with protocols and
19 following approval, the material was repackaged as
20 Humanate.

21 "He considered that all Factor VIII products
22 carried a risk of Non-A, Non-B hepatitis, but that the
23 risk was minimised by the monitoring of donors by the
24 FDA.

25 "Mr Williams felt that any additional data could

41

1 "The Committee found that there was insufficient
2 evidence of any firm arrangement which would enable
3 Speywood to obtain the data specified in
4 [paragraph] 1.9."

5 **SIR BRIAN LANGSTAFF:** Sorry, now, that's not coming up on
6 my screen at the moment.

7 **MR HILL:** Section 5 of page 4 of the document.

8 **SIR BRIAN LANGSTAFF:** Yes.

9 **MR HILL:** "The Committee found that there was insufficient
10 evidence of any firm arrangement which would enable
11 Speywood to obtain the data specified in ... 1.9."

12 If we can go back now, please, Soumik to page 2
13 and to 1.9, and I'll read out what that data is.

14 What paragraph 1.9 says is:

15 "Following the Licensing Authority proposals
16 a letter had been sent to the Company on 29 July 1980
17 in accordance with Sections 28 and 29 and Schedule 2
18 of the Medicines Act 1968. It had informed the
19 Company in accordance with paragraph 2 of Schedule 2
20 that the committee had had reason to think that they
21 might have to advise the Licensing Authority to vary
22 the Product Licence for this product" --

23 **SIR BRIAN LANGSTAFF:** The information is the last five
24 lines, six lines, is it?

25 **MR HILL:** Yes, so it is proposing varying the product so

43

1 be obtained from the FDA possibly by NIBSC, under the
2 US Freedom of Information Act.

3 "He explained that his objective in appearing
4 before the Committee was to seek an extension of the
5 present arrangements to enable the company to make
6 other arrangements if possible for the purchase of
7 Factor VIII and eventually to remove the Company's
8 financial dependence on this imported Factor VIII.

9 "Dr Jones then explained that he had come to the
10 hearing as an independent consultant (unpaid) to
11 advise the Committee that in his capacity as director
12 of a Haemophilia Centre, he had satisfactorily treated
13 patients with Humanate.

14 "In reply to questions Mr Williams stated that
15 he thought that, if necessary, donors of blood might
16 be traced from Cutter's records by means of the
17 Freedom of Information Act.

18 "He had accepted that the batches he imported
19 (unlabelled) were consistent with Cutter batches,
20 because of the assurances given by Parlier Medical
21 Supply.

22 "Mr Williams said that he did not know of any
23 other manufacturer who was asked to provide the
24 information required.

25 "Findings

42

1 that the information -- so that it contains --

2 "... the licence holder should on request
3 furnish the Licensing Authority from every batch of
4 a product" --

5 **SIR BRIAN LANGSTAFF:** -- (overspeaking) --

6 **MR HILL:** -- "a sample of such amount as the Authority
7 considered adequate for any examination ... the
8 licence holder should if required by the Licensing
9 Authority, furnish evidence of a source and date(s) of
10 collection of the donor blood from which the product
11 was prepared, the date of manufacture of the product,
12 and an outline of manufacturing methods, protocols and
13 results of tests done, on the donor blood, during
14 manufacture and on the finished product."

15 So that's the information that the Committee
16 accepted was necessary, and they accepted the point
17 made to them by the Licensing Authority that there was
18 no way that Speywood could obtain that data.

19 The advice that the Committee then gave, and
20 it's important to remember that the Committee is not
21 the decision-making body, the Licensing Authority is
22 the decision-making body, but, under these
23 circumstances, it must consult the Committee. The
24 advice that the Committee gave was to vary the product
25 licence --

44

1 **SIR BRIAN LANGSTAFF:** Well, let's have a look at that
 2 because we're still back on paragraph 1.10.
 3 **MR HILL:** Yes.
 4 **SIR BRIAN LANGSTAFF:** We need to go to paragraph 6, don't
 5 we?
 6 **MR HILL:** Page 5, please, Soumik.
 7 **SIR BRIAN LANGSTAFF:** Shall we go back to the previous
 8 page?
 9 **MR HILL:** Page 4, please, Soumik.
 10 **SIR BRIAN LANGSTAFF:** "Advice", at the bottom of the page.
 11 **MR HILL:** The advice that has been given is to vary the
 12 licence to "include the following words", and that's
 13 on page 5. I quote:
 14 "The Licence Holder shall on request furnish to
 15 the Licensing Authority from every batch of the
 16 product, or from such batch or batches as the
 17 Licensing Authority may from time to time specify,
 18 a sample of such amount as the Authority may consider
 19 adequate for any examination required to be made; and
 20 the licence holder shall, if required by the Licensing
 21 Authority, furnish evidence of the source and date(s)
 22 of collection of the donor blood from which the
 23 product is prepared, the date of manufacture of the
 24 product, an outline of manufacturing methods,
 25 protocols and results of the tests done, on the donor

45

1 this consideration, which is taking place in
 2 January 1981, and the ceasing of the sales of Koate in
 3 June 1981. We don't have the --
 4 **SIR BRIAN LANGSTAFF:** What was it, sales of Koate?
 5 **MR HILL:** Sorry, of Humanate. It's fair to say that the
 6 accountant's report doesn't cite the resources that
 7 it's using, and nor was this its principal focus. So
 8 I'm afraid we simply don't know why there is that
 9 seeming gap -- of the significance, if any, of it.
 10 I'm going to turn very briefly, sir, if I may
 11 before the break -- because I've nearly finished the
 12 section on Humanate and Koate -- there were a number
 13 of adverse incidents in the use of Humanate.
 14 Glasgow Royal Infirmary reported possible NANB
 15 infection in three patients in a letter to Speywood in
 16 January 1981, and later, in March 1981, expressed
 17 their view that it was "highly probable" -- those were
 18 the words they used -- that Humanate was responsible
 19 for that infection. The references are
 20 IPSN0000336_005 and IPSN0000336_002.
 21 There were also reports from Treloar's and
 22 Bournemouth of apparent allergic reactions to Humanate
 23 in February 1981. IPSN0000323_002 and
 24 IPSN0000323_003.
 25 It may be that these concerns prompted the

47

1 blood, during manufacture and on the finished
 2 product."
 3 So it's accepting the argument that had been
 4 made by the Licensing Authority as to the information
 5 that was required.
 6 The reasons for the advice, if we can go back,
 7 please, Soumik:
 8 "That, because of the risk to patients arising
 9 from lack of evidence as to the origins and provenance
 10 of the donor blood, the Committee were not satisfied
 11 as to the safety [underlined] of the product."
 12 That was the advice given by the Committee.
 13 I don't have a document for you, sir, showing the
 14 decision of the Licensing Authority, but it is clear
 15 that there was a product variation, and that, as
 16 a result of that product variation, Speywood ceased to
 17 sell Humanate.
 18 **SIR BRIAN LANGSTAFF:** You mean licence variation?
 19 **MR HILL:** Sorry, licence variation, yes. The accountant's
 20 report that we looked at earlier, IPSN0000027, page 3,
 21 says in terms:
 22 "Speywood continued to sell Koate in the UK
 23 under the name of Humanate but stopped in June 1981
 24 when the product licence was amended."
 25 I don't know, sir, why there is a gap between

46

1 following letter which was sent by Professor Bloom in
 2 March 1981. It's DHSC0001191.
 3 I'm afraid it's a very poor copy. It is dated
 4 10 March 1981. It is sent to Dr Holgate at the DHSS.
 5 I will try my best to read from it.
 6 Dr Bloom says at the start that he is writing in
 7 his official capacity as Chairman of the Haemophilia
 8 Centre Directors of the UK. And he is referring to,
 9 he says, the problem of --
 10 **SIR BRIAN LANGSTAFF:** "At a ... meeting of Reference
 11 Centre Directors the problem of [something]
 12 impurities ..."
 13 **MR HILL:** It is for something I'm afraid I can't assist
 14 with, but it is referring to impurities in Factor VIII
 15 concentrates, and in particular, Humanate.
 16 If we go to the second paragraph, the first
 17 legible sentence of it:
 18 "... the first concerns the preparation of
 19 Humanate, about which there was some adverse publicity
 20 in the National Press recently. My colleagues and
 21 I would like to be reassured that this material has
 22 been cleared for use and has passed the normal control
 23 processes for the UK. We would like to be reassured
 24 that it is possible from the protocol to trace actual
 25 batches to source in the event of an outbreak of

48

hepatitis etc attributable to it. Most of us are aware of rumours that this material originates with an American Company and is sold through brokerage or other means to Speywood Laboratories Ltd where it is relabelled. This seems to us to be somewhat irregular and would greatly appreciate your advice on its current status."

If we could go to the final paragraph:

"The Haemophilia Reference Centre Directors have expressed disquiet at these developments although we are aware that by virtue of plasma [brokerages] ... in the USA it may be difficult sometimes to be sure of the exact origin of plasma used in any of the currently available concentrates. These problems highlight the importance of developing a UK potential within the Health Service to supply all the needs of the British haemophiliacs. I would be very grateful for your advice."

So that is the concern that is being raised in March 1981 with Dr Holgate.

His reply is at BPLL0001351_039, dated 23 March 1981. Dr Holgate wrote:

"Dear Professor Bloom,

"Thank you for your letter of 10th March drawing our attention to the recent disturbing press reports

49

concerning Factor VIII concentrate and enclosing a copy of a letter given to you by Dr Savidge.

"As I am sure you are aware, one of the cornerstones of our philosophy for the licensing of 'biological' products is to have detailed knowledge of and control over early stages of manufacturing and in-process control -- this including source material. I am particularly delighted to have your clearly expressed support for this attitude.

"With regard to Humanate and Speywood Laboratories Ltd I can say no more at this stage as the matter is being dealt with at the present time."

This may reflect the strict confidentiality that surrounded the meetings of the Committee on Safety of Medicines. We can see that as of 23 March 1981, at least according to Dr Holgate's letter, the matter is still being dealt with, the process is still running. But as we know, they were aware of concerns pre-dating Professor Bloom's letter and had proposed a variation of the licence as a result.

SIR BRIAN LANGSTAFF: Well, Professor Bloom was referring to some press comment, I think, wasn't he?

MR HILL: He was.

SIR BRIAN LANGSTAFF: So the matter was out in -- at least allegations were out in the open.

50

MR HILL: Yes. What we don't know is what the adverse publicity in the press was, whether it was just that there had been a hepatitis outbreak or whether it was the more detailed point about the ability to trace back. But it's interesting to note that Professor Bloom, the director of Haemophilia Centre Directors -- sorry, the chairman of the Haemophilia Centre Directors -- referred in his letter only to rumours about the origins of Humanate. He does not appear to have known the exact process by which Speywood imported the product.

SIR BRIAN LANGSTAFF: If you write to someone like Mr Evans and say, "Well, you've pressed me, so I'll tell you this is really Koate manufactured -- which we buy from a broker and put a label on it, well, they make it for us, but please keep it quiet", it's bound to be at the level of rumours, I would have thought.

MR HILL: Yes. Save for the fact that Dr Evans asked and was given an answer.

SIR BRIAN LANGSTAFF: Yes.

MR HILL: Sir, the only other point I would make in respect of the importation of products is that no product licence was obtained for Konyne, which is the Factor IX product, and the Inquiry has found no evidence that Speywood sold Konyne in the UK.

51

Reference, should one be needed, IPSN0000139_022. I note the time, sir.

SIR BRIAN LANGSTAFF: Right, well, we will take a break now until ten to 12. Ten to 12.

(11.22 am)

(A short break)

(11.50 am)

MR HILL: Sir, I'm turning now to Speywood and polyelectrolyte fractionation. I'm going to attempt to give a very brief layperson's guide to polyelectrolyte fractionation but I'm conscious that Ms Middleton will be able to give us far more detail, no doubt more accurate detail, in due course.

My understanding is that it is a process that involves the use of a polymer, a large molecule, that when used in fractionation can act as an absorbent, meaning that it causes the adhesion, the sticking of certain protein factors, such as Factor VIII, to separate it out from other molecules, particularly lower weight molecules. It is a different method of fractionation when compared to the traditional methods based on the work of Cohn and others.

There were two potential advantages which were of particular significance to this Inquiry, sir. The first is that it could allow for a higher purity of

52

Factor VIII to be obtained. The second is that there was a line of thinking, and we will see how far that developed, that while Factor VIII would adhere to the polyelectrolyte, the lower weight viruses would not, which means that the two could be separated out. So it would work as a form of viral inactivation.

SIR BRIAN LANGSTAFF: Yes. I will stand to be corrected in due course, as you are, by Ms Middleton and what she has to tell us, but my understanding is that there are two steps. One is the adherence or adsorption of the protein of interest onto a substrate, which is basically a form of polymer, and the second is applying a solvent to release it from the polymer. So it gets separated out by the process of adsorption and then released by the process of -- well, it's eluted, to use the words of the scientist.

MR HILL: Yes, that's my understanding, sir.

SIR BRIAN LANGSTAFF: Right. Well, we may both be wrong.

MR HILL: Ms Middleton will mark our homework in due course.

Speywood had begun its work on polyelectrolyte fractionation of porcine Factor VIII by 1978, before Ms Middleton's arrival. I won't go to the document but we can see that from documents including IPSN0000334_019.

53

link between blood products and hepatitis. Palmer Research in North Wales were making the polyelectrolyte under licence for Speywood, but further development work was needed on the fractionation process, and this work was being undertaken by Dr Johnson in New York. The potential market for the porcine product could not be met from production at their Wrexham plant and they were looking at an advance factory in Wales. £200-250K expenditure on sterile areas etc, was envisaged. About 80-90% of the £4-5m turnover from the factory would be exported. They hoped to occupy the factory in November or December 1979 and be ready for production by April 1980.

"Human blood fractionation using polyelectrolytes was a more problematic undertaking because of the implications of using human blood for commercial purposes. Speywood envisaged taking out patents and licensing overseas producers, and supplying the polyelectrolyte for the NHS to undertake their own fractionation. Dr Lane of the BPL was working on the fractionation process."

Then there are references to the other lines of business that Speywood were pursuing at the time, sets and disposable accessories and blood bags.

55

On 7 May 1979, Speywood met with representatives of the DHSS to discuss the possibility of Government financial assistance. The minutes help to explain the position at that time, and if we could have them on screen, please. DHSC0003936_082, please.

We can see this is a meeting that was held on 7 May. Present were Mr Heath and Mr Lees of Speywood, and Mr Weston and Mr Buck of DHSS. The minutes record this:

"The meeting had been arranged to discuss the possibility of government financial assistance for the company."

It talks about its establishment and its specialisation of porcine blood fractionation.

The minutes go on to say that:

"The company had 3 projects under consideration."

1 is -- I'm afraid, the first word is --

SIR BRIAN LANGSTAFF: "To use", I think.

MR HILL: Yes.

"1. To use polyelectrolytes for a new blood fractionation process. The process had been developed and patented by Monsanto, who had licensed it to Speywood in March 1979 because they were concerned about their corporate image in view of the possible

54

What the meetings record is that:

"Speywood sought assistance [this is the final paragraph] specifically with the first project."

So that's polyelectrolyte fractionation of both porcine and human Factor VIII.

"This was a new product area with considerable commercial potential but the company would have to proceed slowly and cautiously unless government support was available. The Department said that the PPDS assistance appeared to be the appropriate, and offered to consider an application, with support from STB."

PPDS is the Department of Industry's Product and Process Development Scheme. So the company Speywood are being invited to consider an application under that scheme, with some assistance from the Department. I will leave that document there, sir.

An application was made to the scheme on 12 October 1979. Can we have, please, on screen, Soumik, IPSN0000165_077.

You can see there, sir, the application title page, "PPDS Application", by Speywood. On page 3, please, Soumik. You can see the date, 12 October 1979.

If we can turn, please, Soumik to page 5.

56

1 This application gives us a picture of what
2 Speywood was doing at that time, and what it intended
3 to do, as of October 1979, whilst seeking a degree of
4 financial assistance from the Government to do it.

5 Under the heading "Introduction":

6 "For over two years Speywood Laboratories
7 Limited has been researching into the fractionation
8 and purification of animal (porcine) and human blood
9 fractions using polyelectrolytes. The initial work
10 which has concentrated on Factor VIII has been very
11 successful. Moreover, the laboratory results show
12 that polyelectrolytes can be used for a total blood
13 fractionation process producing purer fractions with
14 better yields at lower capital and labour costs than
15 can be obtained with a traditional Cohn process. This
16 discovery could have a significant impact on the
17 Department of Health's plasma fractionation costs, it
18 will generate substantial foreign exchange earnings
19 from exports and licence fees, and it will increase
20 employment. This introduction explains the process
21 and programme required to turn a laboratory discovery
22 into commercially producible licensed products."

23 If we could go over to the next page, please,
24 Soumik. This is under the heading "The Process".
25 I won't go through every word, but you can see the

57

1 outlined in Appendix B.

2 "At Stage 2 [small scale production] all the
3 work is drawn together at Speywood."

4 Sir, we can see there the plan is to use
5 external laboratories as part of the research stage
6 before bringing things back to Speywood once you get
7 to scale matters up to production.

8 "The Programme", section 2:

9 "The Company's intention is to develop the
10 existing polyelectrolyte fractionation process to a
11 point where the Company can produce itself a range of
12 animal fractions and can licence others to produce
13 human fractions. The fractions envisaged and their
14 stages of development are as follows ..."

15 If we could turn over, please, to the next page.
16 I won't go through all of these, sir, but the point is
17 that although Factor VIII:C is the first of the
18 factions mentioned, there is an intention or a hope
19 that the process can also be used to produce other
20 products: fibronogen, albumin, animal globulins,
21 et cetera. I won't go through the detailed plan as to
22 how that might be achieved.

23 If we could turn, please, to page 10, Soumik.

24 This is entitled "Capital Investment", and it
25 talks about the figures that are going to be involved.

59

1 different stages involved: the first is production
2 research, the second is small scale production, and
3 the third is pilot plant production.

4 If we could go to the paragraph that follows.

5 It goes on to say:

6 "Because of the size of the Company, its
7 personnel, laboratory equipment and research
8 facilities, much of the work in Stage 1 is either
9 sub-contracted to outside laboratories, or is carried
10 out by Speywood's staff in outside laboratories. Two
11 laboratories are of particular importance to us:

12 "- Dr Alan Johnson's laboratory in New York.

13 Dr Johnson was the first man to realise the possible
14 potential of polyelectrolyte fractionation.

15 "- Dr Jean-Pierre Allain's haemostasis and
16 coagulation laboratory at the CNTS in Paris."

17 And you will recall, sir, that there was
18 a reference we looked at before the break to getting
19 some data from Jean-Pierre. That is Jean-Pierre Alan.

20 "Other laboratories where specific parts of the
21 work will probably be carried out include

22 Dr Richard Lane's laboratory at the Lister Institute,

23 Prof Arthur Bloom's laboratory in Cardiff and

24 Dr Preston's laboratory in Sheffield. Proposed

25 programmes of work in these various laboratories are

58

1 I won't take you to each one of them, sir, but the
2 document reveals that the anticipated capital costs
3 are £298,000 to June 1980, £354,700 of management
4 costs to July 1981, and £142,660 of external research
5 costs. There are also further costs for clinical
6 trial and licensing stages. So we can see, sir, that
7 these are considerable sums of money.

8 That was the application, sir. It was discussed
9 within the DHSS. I'm not going to take you to all of
10 the documentation about those discussions, but there
11 is one helpful summary at DHSC0003936_049, please,
12 Soumik.

13 This is a memorandum on 30 October 1979 from
14 D Weston, copied to colleagues within the DHSS, about
15 the application, and it is sent to Dr Walford.

16 Picking it up from the second paragraph, this
17 refers back to some of the other correspondence that
18 has been going on in the DHSS at that time.

19 "Dr Waiter's earlier comments, and those
20 received from Dr Wintersgill and Mr Sloggem, suggest
21 that DHSS should support the application on
22 medical/technical grounds and there are also sound
23 commercial reasons which hinge on the prospects for
24 import substitute and export earnings. The main
25 problem was, and still is, that the project is

60

extremely ambitious for a relatively small company of limited financial and technological resources and with the first application it seemed that neither the company nor the project could be regarded as being financially viable. Some of the earlier doubts about supplementary sources of funding have been lifted a little and it is possible that once one body makes a firm offer others may follow suit. But the fact remains that this is a project not far short of £1M in value and even with grants and loans which [may] be expected to amount to something in excess of £1M the company will be hard pressed to fund the operation even allowing for the substantial sales it expects to obtain. Cash flow problems are likely to loom larger in view of the level of expenditure expected especially during the first nine months of the project.

"I have discussed the application for funds with Department of Industry and they have are prepared to consider a case for financial assistance: under the PPDS this may take the form of a cash grant of up to 25% of approved project costs but if we considered the development to be of outstanding significance and importance, 50% funding with provision for a return on sales might be recommended."

61

completed to production clinical scale for porcine factor VIII:C and, to pilot scale for human factor VIII:C. The feasibility of the process is thus confirmed.

"Speywood lack facilities for the scale-up of human blood processing to the next stage. That is, the finalisation of the production scale process for human factor VIII:C and the extension of the technology to the separation of albumin, immune serum globulins, etc.

"This initial proposal is confined to the factor VIII:C aspect."

Then it goes on to talk about the "Objectives of the joint programme":

"Finalisation of a production scale process ...

"Determination of the purity and yield parameters ..."

On to the next page, please, Soumik:

"Initial UK clinical trials ...

"The preparation, acceptance and approval of a UK product licence ..."

Moving to the "Benefits envisaged":

"1. A product consisting primarily of factor VIII:C purified 500 to 1000 times over plasma."

It talks about the total removal of A/B

63

I will leave that document there, sir.

On 14 April 1980, the Department of Industry did offer a PPDS grant of up to £186,820 which represented 25 per cent of net eligible costs. So, as we have seen from Mr Weston's memorandum, that is approval for the application but at the 25 per cent level rather than the 50 per cent level which could have been given for a development of outstanding significance and importance.

Separately from the application for financial assistance from the Department of Industry, an agreement was reached between Speywood and BPL for a joint programme in developing polyelectrolyte fractionation of human blood, according to -- stress that this is human rather than porcine.

Could we have, please, Soumik, on screen BPLL0016008_151.

This is the proposal for that joint development. I will read through it. The "Background":

"Speywood Laboratories Limited, a privately owned British company, had developed unique and beneficial technology for the processing of animal and human plasma.

"The first stage of the development programme, the production of high quality coagulation factors, is

62

isoagglutinins, negligible fibrinogen, negligible von Willebrand's factor and Factor VIII:RAg.

"2. Improved yield, via plasma

"3. Considerably greater clinical acceptability."

The first point raised there is reduced hepatitis risk. The other points are lower incidence of protein shock, reduced liver damage and reduced injection volume.

Fourth point:

"Simpler processing procedure, requiring considerably less time."

So that is what it is hoped this method of fractionation will lead to.

The "Staff/facility requirements":

"1. Speywood Chief Scientist, Mrs Sarah Middleton, to work at Elstree."

We'll come back to that with Ms Middleton's evidence later.

"2. [Technical] assistant is to be provided by BPL.

"3. Speywood to provide all equipment, with the possible exception of [a] centrifuge.

"4. BPL are to provide cryoprecipitate ..."

So that is the proposal. Speywood would provide

64

1 the solid phase polyelectrolyte, which is said to be
 2 the key to the process.
 3 **SIR BRIAN LANGSTAFF:** We're missing that, I think.
 4 **MR HILL:** On to the next page, please, Soumik. Point 5.
 5 My fault, sorry.
 6 Then reference to the space requirement.
 7 **SIR BRIAN LANGSTAFF:** Can you assist with this, I've just
 8 noticed the date of this, 31 July 1979 --
 9 **MR HILL:** Yes, sir.
 10 **SIR BRIAN LANGSTAFF:** -- and the application for the PPDS
 11 scheme was made in October '79.
 12 **MR HILL:** Yes.
 13 **SIR BRIAN LANGSTAFF:** In that, it was said that there were
 14 three stages. It wasn't suggested that they were
 15 already at and had completed, stage 2?
 16 **MR HILL:** No.
 17 **SIR BRIAN LANGSTAFF:** But they are suggesting that in this
 18 document, aren't they?
 19 **MR HILL:** There does -- the wording between the two
 20 documents is not precise, but this document certainly
 21 suggests that they are further down that route. Yes.
 22 **SIR BRIAN LANGSTAFF:** It says, "We're ready to roll it out
 23 commercially", as I read it.
 24 **MR HILL:** I don't think it's quite saying that. It is
 25 saying that they need to finalise a scaling up of the

65

1 **MR HILL:** -- to these areas, and --
 2 **SIR BRIAN LANGSTAFF:** But the importation business was
 3 ending?
 4 **MR HILL:** The agreement with Cutter was ending and there
 5 was then an attempt to --
 6 **SIR BRIAN LANGSTAFF:** I see. So the importation business
 7 is separate, the one where they secure it from the
 8 intermediary?
 9 **MR HILL:** Yes. So looked at from the outside, there would
 10 continue to be an importation process which would
 11 allow for sales which would allow for money to keep
 12 coming in to the company which could then fund the
 13 research that they were undertaking.
 14 As we will see, in due course, when that supply
 15 of money ceases, there is a need to find funding from
 16 elsewhere. That's when we get on to the National
 17 Enterprise Board and Prutec.
 18 I won't go through the commercial arrangements,
 19 sir, at heading E, but they are there should they be
 20 of relevance later. But there is -- this, it should
 21 be remembered, is the proposal.
 22 The agreement, which I won't take you through,
 23 is BPLL0016007_013. The agreement was formally for
 24 a 6-month period but, as we will see, it continued in
 25 practice into 1981. Reference for that is

67

1 process.
 2 **SIR BRIAN LANGSTAFF:** Yes. So they've done the first two
 3 steps?
 4 **MR HILL:** They have done the production of high-quality
 5 coagulation factors, completed to production clinical
 6 scale for porcine and to pilot scale for human.
 7 There has been some production, according to
 8 this document, of human Factor VIII but, in contrast
 9 to the document that is to come, which says that there
 10 will be a -- Speywood will bring in to house future
 11 production. This proposal is actually saying that
 12 Speywood don't have the facilities to do that and,
 13 hence, that has to be done with the assistance of BPL.
 14 **SIR BRIAN LANGSTAFF:** The date of their suggesting this
 15 agreement, was this at about the time that the sales
 16 agreement with Koate ended?
 17 **MR HILL:** The sales agreement with Koate ends a little
 18 later, at the end of 1979.
 19 **SIR BRIAN LANGSTAFF:** Yes. So it's '79?
 20 **MR HILL:** Yes, but there is, from the documents that we --
 21 the letter that we saw earlier, the way that Speywood
 22 explained the position to clinicians was that they
 23 were using the importation business to finance their
 24 research --
 25 **SIR BRIAN LANGSTAFF:** Yes.

66

1 DHSC00003936_005.
 2 Jumping forward about nine months to one year,
 3 we have some optimistic predictions of the future
 4 which come from Mr Heath. The reference, please, is
 5 IPSN0000257_059.
 6 This document is called "Polyelectrolyte plasma
 7 fractionation 10 years on", and it is signed by
 8 Mr Heath and dated August 1980 in the bottom
 9 right-hand corner. The purpose of this document isn't
 10 clear, but it shows what Mr Heath was saying as of
 11 August 1980.
 12 Sir, he's projecting ten years into the future
 13 and saying what the situation will be.
 14 "By 1990 the Cohn and cryoprecipitate
 15 fractionation techniques will have been replaced by
 16 polyelectrolyte ion-exchange process.
 17 "The effect on the plasma donation programme,
 18 the plasma fractionation industry and clinical
 19 application will be dramatic.
 20 "Extra high yields of the coagulation factors
 21 will enable the donor programme to keep pace with the
 22 increasing demand with only a minimal increase in
 23 plasma collection. The imbalance between the
 24 requirements for Factor VIII and the other plasma
 25 proteins will vanish. Donor centres will be

68

responsible for the first stage of the fractionation adsorbing the labile fractions directly onto the polyelectrolytes.

"Elution and further processing will be completed by a local fractionation unit, which, due to the simple, low cost nature of the polyelectrolyte process, will be viable for a much smaller plasma throughput. This spread of technology coupled with the increased yields will allow most countries to conform with the WHO ideal of 'self-sufficiency' in plasma products. Paid donor collection will decrease rapidly in the United States when export demand declines.

"There will be no risk of hepatitis infection from polyelectrolyte fractionated materials, prophylactic treatments will increase and new fractions will provide a wider range of therapeutic treatments probably via the intramuscular route."

That's his vision of the future, as it were. I stress, sir, now, that we are dealing here with a businessman who is talking about a product and a process that his business is promoting. This is a very different thing from looking at data sheets containing detailed information about individual products.

69

research and scale up we can now report that polyelectrolytes do indeed offer a viable alternative to conventional processes, giving extremely pure fractions at high yield."

I note, sir, that the "5 years" is where we get the date of 1981, because the date isn't on the document itself.

If we could just expand out, please, Soumik, we can see that there are references to slides, which don't help us because we don't have the slides, but what I will do is take you to page 2 of this document, please.

Towards the bottom of that page, Dr Tuddenham says:

"The operation has significant advantages over current fractionation methodology.

"1) Higher yields -- 35% from cryo, 50% from plasma."

That is referring to the source material that is used in the polyelectrolyte fractionation. So if you use cryoprecipitate, your yield is 35 per cent. If you use plasma, it's 50 per cent.

"2) Ultra high purity fractions."

Not just high purity, but ultra high purity.

"3) Simple process, less labour, energy and

71

I will trace through in some documents the development of polyelectrolyte fractionation, a topic that we will return to with Ms Middleton later. Some of the documents can helpfully be introduced now.

By November 1980, Dr Edward Tuddenham, at the Royal Free, had begun work on a clinical sample of human and porcine Factor VIII provided as a result of the BPL/Speywood/Monsanto collaboration. Reference is BPLL0016008_125, and IPSN0000156_034.

At some point in 1981 he gave a lecture in Toronto on his initial laboratory results. It is a document that Ms Richards took Professor Tuddenham to when he gave his evidence in October last year. I won't go through it all, but I will just bring it up and refer to certain sections of it.

IPSN0000156_101, please.

The lecture begins:

"It was at the 1976 World Federation of Haemophilia Conference in Kyoto that Dr Alan Johnson of [New York] University first outlined a new fractionation process using solid-phase ion exchange resins known as polyelectrolytes".

So that's where the technology dates from.

Professor Tuddenham goes on to say:

"After almost 5 years of further intensive

70

capital required."

Go on to the next page, please, Soumik.

"4) Operates at room temperature.

"5) Can be performed at small scale, 1 Kilo cryo or 1 litre plasma.

"It is thus an entirely feasible process for individual blood centres or small Governmental fractionation units."

Some more detail is given in the page that follows. I will just pick out the point that the specific activity of human Factor VIII is ten units per milligram. We were talking earlier about high purity being between 1 and 2 units, as defined by Dr Kingdon. So this is what is meant by ultra high purity.

The final paragraph of that page, please, Soumik.

"Both products [so that's the human Factor VIII and the porcine Factor VIII] have now been used clinically and some of the results have been presented here and in Toronto. Half-life is of the same order as present [Factor]VIII products, ranging between 8 and 16 hours, depending on individual patient response."

Go over to the next page. I won't read the

72

section about porcine Factor VIII. We will come back to that. The paragraph starting "In vitro tests", I understand this is about human Factor VIII:

"In vitro tests have demonstrated that Hepatitis B surface particles do not bind to the E5 polyelectrolyte under the conditions used for the production of FVIII:C.

"In trials, using heavily infected cryo, simple washing of the polymer reduced hepatitis B below detectable levels, leaving the Factor VIII:C intact. There is the encouraging possibility of concentrates with a reduced risk of hepatitis transmittal. It has also been hypothesised that the immunogenic character of [polyelectrolyte] [Factor] VIII:C may differ from that of the conventional [Factor] VIII agglomerate. Antibody response may be changed.

"Only further clinical experience will prove or disprove the latter points but, despite this, we feel that a higher purity Factor VIII concentrate at a yield significantly above the conventional, offers excellent prospects for the treatment of haemophilia in the 1980s."

So an optimistic assessment but, as that final paragraph shows, the need for clinical experience being required to test whether or not these laboratory

73

electronically of the document, "Introduction:

"Over the past seven years Speywood Laboratories have spent large sums of money researching and developing new protein fractionation techniques. Approximately two-thirds of the funds have been expended on animal plasma fractionation, the remaining third on human plasma processes. In the last few years a new technique, the 'polyelectrolyte process', has emerged as a practical and exciting alternative to the 40 year old Cohn process.

"Whilst the polyelectrolyte animal fractions have far less eventual potential than the human fractions, they are unique to Speywood and offer an ideal base for a small, highly specialised business. To maximise on their potential, Speywood have committed to a new 10,000 [square foot] facility for production and research purposes, and a comprehensive and costly development programme for the next five years. This plan does not allow for any major expenditure in the human fractionation area.

"The human polyelectrolyte process has not been practised on the same scale as the animal process. However, recent production yields, clinical trials and hepatitis tests have adequately demonstrated that the major protein, Factor VIII:C, can be produced

75

results will be replicated.

Dr Tuddenham was also the author on a paper considering response of patients to infusions of polyelectrolyte Factor VIII. Ms Middleton was the co-author, so I will ask her about that in due course. There is a further paper from October 1983 from Ms Middleton on the clearance of hepatitis B surface antigen during polyelectrolyte fractionation and, again, I will ask her about that in due course.

As I mentioned earlier, alongside these developments, there was thought being given to the need for further investment in the company, no doubt in part prompted by the disappearance of the importation business, as a result of the variation of the product licence.

I won't go through all of the documents, but I will take you to one which is of significance from July 1981. It is DHSC0003936_019, please, Soumik. Again, from the front page we can see the Speywood group's title. On the second page, please, Soumik, "Human Protein Plans", the title of the document, and the date -- sorry, Soumik, if we could just go back one page, bottom right-hand corner, and handwritten on "July 1981".

If we could turn, please, to the third page

74

economically, is very efficacious and is most probably free of hepatitis infectivity. Other human proteins, which have a vast therapeutic potential and cannot be produced via the classical Cohn fractionation process, have also been successfully isolated. To exploit these developments Speywood originally planned to license this technology and the products thereof to a major American plasma fractionator. In the light of these recent findings and in view of a new EXCLUSIVE licence from Monsanto, Speywood now proposes to raise the necessary finance to fund the advance of 'human proteins' through a new venture."

Go over to page 2, please, Soumik. We can see the "Outline plan" for that new venture, which is:

"To form a new division adequately financed to undertake the following:

"1) The establishment of a new manufacturing unit for the production of human biologicals, using polyelectrolyte fractionation technology and continuous centrifugal electrophoresis.

"2) A research and development programme aimed at providing further therapeutic proteins from plasma and servicing the development of fractionation/purification skills.

"3) An external research and development

76

programme, designed to investigate the viability of producing therapeutically proven proteins via the recombinant DNA route.

"This highly specialised company will have a base of products from the outset. It should become one of the leading protein fractionation companies in Europe with unique technology that can be applied to natural or synthesised product separation. The research and development plan is intended to provide a second generation of products which do not rely on the finite source -- plasma.

"Financial Support:

"£4-5 [million] will be required to fund MBL through the first 4 years."

That's Molecular Biology Limited, which is the proposed name of the new company:

"The National Enterprise Board, Prutec and Celltech [an American firm and we will come back to their role later] are evaluating Speywood's proposals with a view to providing this requirement in the form of equity and loans."

Turning to page 3, I won't read through all of this, but we can see that the manufacturing unit is proposed for Wrexham and, by the end of the year, it's proposed that this will employ 61 people. The section

77

effort to scale up to commercial production scale."

If we turn to page 5, we can see various programmes set out, but the first is research and development programme. Then item 3, the genetic engineering programme, which talks about the need to have academic institute studies and then scale up, and the pilot plant and then industrial production. That, as I understand it, is a reference to recombinant.

On page 6, you can see the academic institute studies that have been instigated by that stage, so there's a team in Oxford, and a group at the Royal Free Hospital and the Hallamshire Hospital. The objective is:

"Investigational studies to produce the gene clones and the laboratory expression of the following proteins", which includes Factor VIII:C.

Thank you, Soumik, we can take that off the screen.

As of July 1981, that appears to be the Speywood plan.

This plan seems to have prompted considerable concern at BPL, who, at that stage, were still collaborating with Speywood on their work. We see correspondence from BPL to Dr Tuddenham, urging him to take steps to protect intellectual property. I won't

79

headed "Raw materials", if we look at the second paragraph of that:

"A supply of cryoprecipitate has been arranged direct with a United States plasma collection company, on a long term contract. Each shipment will have full donor information and the plasmapheresis centres will be open to inspection by the UK Medicines Inspectorate."

So this, sir, just so that we are clear, it's not about importing finished Factor VIII product but the raw material that will be used in polyelectrolyte fractionation.

If we go over to page 4, please, "The products".

"Factor VIII:C

"For the treatment of haemophilia A.

"-- 20 times purer than any competitive product.

"-- Substantially free of hepatitis."

Various other claims made including a greater yield than conventional Factor VIII.

Then he goes through the other products that is intended to produce a von Willebrand's factor, fibronectin and fibrinogen. Then it says:

"The Factor VIII:C and [von Willebrand's factor] are fully developed products. The Fibronectin and Fibrinogen still require considerable development

78

take you to those letters, sir, but they're at BPLL0016008_075, and the same stem _066.

There are minutes from a meeting on 12 July 1981 between BPL, the DHSS and Speywood, concerning the ongoing collaboration and the future of the collaboration. That is at DHSC0003936_005. That's a need there, to formalise what other arrangements are going forward and it is revealed at that meeting that BPL had entered its own talks with Monsanto, which created a further layer of complexity and tension.

Those minutes also record that a lead time of three years is estimated for a product licence.

I am going to take you to two documents though, which show the nature of BPL's concerns and the terms in which it is expressed.

Could we have, please, BPLL0016008_068, please, Soumik.

This is a letter from Dr Lane to Dr Walford. It's dated 17 August 1981. From the context of the letter, we can tell that Dr Lane is referring back to the human protein plans document that we have just looked at. What Dr Lane says is this:

"Dear Diana,

"I am sure you have seen this document [that's the human protein plans] which has presumably been

80

presented to NEB, Prutec and Celltech among others, including DHSS. On page 4, I hope the attention has been drawn to these organisations of the highly spurious nature of the claims made on three of their principle four products. I have coloured these in.

"The claims are either without substance, ie 'At greater yield than conventional factor VIII', or meaningless, for example, 'Substantially free of hepatitis'. There are also substantial contradictions as in 'Fibronectin for the treatment of traumatic septic shock' followed by 'A fibronectin therapeutic concentrate has never been produced before' ...

"I am well aware of Speywood's enormous needs to generate funds for their operation but I would be disturbed if financial backers in this country were so ill-advised that they could not see some defects in the claims that are being made in this document. I would be pleased to have your comments.

"Our experience of polyelectrolyte indicates that its development has not reached the point set out in the attached document and is not appropriate for onward process of the fresh plasma into immunoglobulin, albumin and other fractions which are needed to make the overall economies."

Dr Walford's reply is at BPLL0016008_064.

81

are safeguarded. He sets out the reasons, or the safeguard that he requires.

Point (d) is:

"a firm understanding that BPL is not a training ground for Speywood employees. I will have Sarah Middleton in CF Department [I understand that to mean cold fractionation department] for the 'cryo' part of the work, and no one else, on present evidence."

So we can see Dr Smith there deeply disturbed by the human protein plans.

A further document to which I will give a reference but not go is BPLL0016008_072. This is a more technical minute in which Dr Smith expresses his reservations about the technical challenges involved in scaling up polyelectrolyte fractionation, echoing some of Dr Lane's concerns that the document is presenting too optimistic a picture.

Despite those reservations of BPL, in December 1981 a £4 million-pound investment was announced into Speywood. The reference is BPLL0016007_048.

I won't take you to the document sir, but I will read one quote from Mr Heath, which is a press release, and Mr Heath is quoted as saying:

83

I won't take you to it, sir. Suffice to say that

Dr Walford thinks that those involved in potentially backing this project have got sufficient information and sufficient expertise to be able to make their own -- form their own judgements. But she acknowledges Dr Lane's concerns.

One further document, BPLL0016008_065, please, Soumik.

This is dated 26 August 1981, and it is from Dr Smith in BPL, who is writing this memo to Dr Lane and Dr Harvey.

He makes explicit reference to the human protein plans, and he says these confirm:

"... ambitions which had been reported to me by third parties but denied by employees of Speywood. These intentions are incompatible with BPL's aims, the national interest, and my interpretation of our contract. They are entirely compatible with my assessment of Speywood's reliability as partners. It is obvious that if Speywood's interpretation of our current contract is taken with this document, BPL lose control of the main issues."

And he goes on to say that he is unwilling to proceed with the next stages of preparation for polyelectrolyte for clinical trial until the interests

82

"Not only will this extra investment create new jobs but it will add momentum to our existing lead in fractionation technology and bring nearer the exciting possibility of producing valuable blood proteins through genetic engineering. If this becomes reality, as I have every confidence it will, then by the year 2001 we may never need to collect plasma from donors again."

So Mr Heath, at that stage, is emphasising the prospect of recombinant technology. And although, as we will see, events didn't transpire as Mr Heath would have hoped, you may feel, sir, that there is some prescience in that statement.

In the same month in which the £4 million investment was announced -- and as we know that's from Prutec and the National Enterprise Board -- the cooperation between Speywood and BPL effectively ended. The reference is BPLL0016008_053. And although there is some contact going forward, there is an end to the previous arrangements that had been made between Speywood and BPL.

If we jump forward to 24 April 1982, the document is BPLL0016008_034.

We can see this is a minute from Dr Smith to Dr Lane, an internal minute from BPL concerning

84

1 a Speywood meeting at Uberlingen on 24 April 1982.
 2 Dr Smith said that:
 3 "The meeting seemed to be designed to present
 4 the merits of porcine factor VIII to influential
 5 German clinicians, and to associate the PE technology
 6 for porcine factor VIII with projected production of
 7 human factor VIII."

8 The first page concerns porcine product. I'm
 9 going to take us to the second page, if I may.
 10 I won't go through everything that was said but it is
 11 perhaps captured by the third paragraph down.

12 "Pending the millennium (which incidentally
 13 sounds like a marketing nightmare), Speywood hope to
 14 make human factor VIII pay the bills. It is therefore
 15 very disappointing to find how little progress has
 16 been made since we parted company.

17 "Speywood would appear to have abandoned the
 18 plasma route ..."

19 He gives the reasons for that. So it is no
 20 longer, in Dr Smith's understanding, trying to use
 21 polyelectrolyte fractionation on plasma, but it is
 22 instead using it on cryoprecipitate.

23 He goes on to discuss further down the document
 24 how Speywood are:

25 "... concentrating on a commercial (probably US

85

1 It should also, however, be noted that this is
 2 an internal BPL document, Dr Smith reporting to his
 3 colleagues.

4 I won't take you to these documents but
 5 correspondence from Mr Heath in May 1982 confirms the
 6 impression of progress being slower than anticipated.
 7 The reference is IPSN0000402 and IPSN0000232_001.

8 Studies were ongoing to demonstrate that the
 9 product was "free from hepatitis infectivity", but
 10 these were in vitro studies, in the laboratory, and
 11 Mr Heath, in a letter dated 2 April 1982 to the
 12 Reverend Tanner, accepted that only a full year's
 13 clinical trial in what he described as patients with
 14 clean livers would provide proof that the product was
 15 indeed hepatitis-free.

16 The reference is IPSN0000252_001. There is some
 17 evidence that a research project was being designed by
 18 Dr Howard Thomas at the Royal Free at this time.

19 Can we go, please, Soumik, to IPSN0000249.

20 This is a letter sent by Mr Heath, dated
 21 7 July 1982, to the British Technology Group, which,
 22 as I understand it, the National Enterprise Board had
 23 been absorbed into, so it's to one of the financial
 24 backers and, indeed, equity holders of Speywood.

25 If we look at the third paragraph down, what

87

1 frozen cryo source. JP Allain ... and JJ Morganthaler
 2 ... are the only people working along similar lines to
 3 Speywood, if one neglects Alan Johnson's contribution
 4 which always seems to be difficult to substantiate.
 5 The following problems continue to plague this
 6 work ..."

7 He goes through those problems: the frozen cryo
 8 is difficult to redissolve; the yields are low; the
 9 polyelectrolytes "is accused of being variable";
 10 Morganthaler has not produced a non-pyrogenic batch
 11 yet and has filtration problems, which echoed by BPL's
 12 experience. And:

13 "(e) the lack of hard results after more than
 14 a year underlines the lack of professional control
 15 over Speywood's multi-centre efforts."

16 He goes on to say:

17 "The low yield remains the most important
 18 feature of the method."

19 I will leave that document there, sir, but
 20 Dr Smith's view, as of April 1982, is that very slow
 21 progress is being made and very large problems remain.
 22 It should be noted, of course, that Dr Smith is not
 23 a dispassionate observer and has some hostility
 24 towards Speywood, as we have seen from the other
 25 documents.

86

1 Mr Heath says is this:

2 "Producing 'Pure Factor VIII:C' for clinical
 3 use, is not going to be a commercially viable
 4 proposition and therefore will probably never generate
 5 any monies for the inventors, but, we feel it will be
 6 a useful factor in the patent protection built around
 7 biosynthetic factor VIII production."

8 What I interpret those words to mean is that the
 9 focus is now on the recombinant product, and the
 10 polyelectrolyte fractionation of Factor VIII is no
 11 longer being considered as a commercially viable
 12 proposition in the long term, but it's being done for
 13 reasons of patent protection in respect of recombinant
 14 product.

15 **SIR BRIAN LANGSTAFF:** This is from Heath?

16 **MR HILL:** This is from Heath. 7 July 1982.

17 I am a little wary, sir, that I may be reading
 18 too much into one paragraph of one letter, but it does
 19 seem part of a picture that, during 1982, there is
 20 a more pessimistic view of the prospects of the
 21 polyelectrolyte fractionation of Factor VIII.

22 **SIR BRIAN LANGSTAFF:** Well, it's gone from being
 23 a Europe-beater to being a commercial failure.

24 **MR HILL:** Yes.

25 **SIR BRIAN LANGSTAFF:** In the space of how long?

88

1 **MR HILL:** The --
 2 **SIR BRIAN LANGSTAFF:** About a year?
 3 **MR HILL:** -- protein plans was July 1981. This is
 4 July 1982.
 5 **SIR BRIAN LANGSTAFF:** Yes. And what is now the enthusiasm
 6 is the recombinant, the biosynthetic.
 7 **MR HILL:** Yes. Now that was always part of the protein
 8 plans.
 9 **SIR BRIAN LANGSTAFF:** Yes.
 10 **MR HILL:** But the emphasis has shifted to the recombinant
 11 product.
 12 There was an application made for a clinical
 13 trial certificate for the Factor VIII product produced
 14 as a result of polyelectrolyte fractionation. That
 15 product is now known by the name of Mono C. It's not
 16 entirely clear when that trial certificate was applied
 17 for, but there is a report on the second quarter of
 18 1982 made by Mr Heath, which says that a submission
 19 had been made at that stage. That's IPSN0000232_001.
 20 We have other documents to indicate that the
 21 trial was intended to be established at Lord Mayor
 22 Treloar School and at the Royal Free. IPSN0000398,
 23 for those.
 24 Can we go now, please, Soumik, to IPSN0000230.
 25 This is a letter dated 26 November 1982. It is

89

1 jeopardised Speywood's prospects of -- in the
 2 licensing process. But we can't really work out what
 3 that conversation was.
 4 But this is a letter from Mr Heath reassuring
 5 Mr Seymour that's not the case. And he has spoken --
 6 Mr Heath has spoken to Dr Keith Fowler at the DHSS.
 7 Mr Heath reports that:
 8 "Dr Fowler concluded our conversation by
 9 assuring me that the Mono VIII:C application which was
 10 on his desk would go on the fast track as soon as the
 11 Alpha cryo application was received."
 12 I pause there to say this I take to be
 13 a reference to the clinical trial application. So by
 14 26 November 1982, that application was on Dr Thomas's
 15 desk, but he was awaiting what is described as the
 16 Alpha cryo application, and I understand that to be
 17 a further application that the cryoprecipitate from
 18 Alpha be allowed into the country so that it can be
 19 used as the raw material for the production of the
 20 Mono C (*sic*) polyelectrolyte fractionated Factor VIII.
 21 **SIR BRIAN LANGSTAFF:** Thank you.
 22 **MR HILL:** I add this now for future reference:
 23 "However, he also added that we were doing
 24 entirely the right thing to go for a full product
 25 licence for Hyate-C."

91

1 from Mr Heath and it is to Mr Seymour, who has been
 2 appointed as the chair. If we could -- sorry,
 3 Soumik -- if we could just take that off the screen,
 4 please.
 5 Could we just go down a little further, please,
 6 Soumik? Thank you, yeah, we'll take it off screen.
 7 Sir, I note there was an address that was left
 8 on that document which should not have been left on
 9 that document.
 10 **SIR BRIAN LANGSTAFF:** I see.
 11 **MR HILL:** I will ask in due course for a restriction order
 12 to be made.
 13 **SIR BRIAN LANGSTAFF:** Yes, well, no one should reveal
 14 the -- any details which have come from looking at
 15 that letter online.
 16 **MR HILL:** I'm grateful, sir. Thank you.
 17 I will read from the letter rather than --
 18 **SIR BRIAN LANGSTAFF:** Please.
 19 **MR HILL:** -- show it, as a result of that.
 20 The context of this letter, I'm afraid I cannot
 21 fathom. But the relevant section for the current
 22 purposes is this, it refers to concerns that
 23 Mr Seymour either has or has reported about how some
 24 form of conversation between somebody representing
 25 Speywood and somebody representing the DHSS may have

90

1 That's the porcine product.
 2 **SIR BRIAN LANGSTAFF:** Yes.
 3 **MR HILL:** So clinical trial for the human product, full
 4 product licence for the porcine product.
 5 Mr Heath goes on to say:
 6 "On reflection, I think it was entirely wrong of
 7 me to condone Paul's request to speak to the DHSS."
 8 That's a reference to Paul Joaquim or --
 9 **SIR BRIAN LANGSTAFF:** -- Joaquim. We have a statement,
 10 have we not, from his wife?
 11 **MR HILL:** That's right, which contains an extract from
 12 what appears to be a memoir, from Mr Joaquim. He was
 13 a director of Speywood and he was on the board at the
 14 behest of the British Technology Group:
 15 "I feel that the Medicines Inspectorate in
 16 particular are anxious to be truly independent of any
 17 outside pressures, either governmental or
 18 business-wise. If anything, Speywood will get a hard
 19 ride because the BTG owns 25% equity."
 20 I will leave that document there, sir.
 21 The CSM main committee considered the clinical
 22 trial application on 24 March 1983, and it was
 23 rejected. If we could have, please, DHSC0003950_016.
 24 We can see that this is the minute of the main
 25 Committee of the Committee on Safety of Medicines. It

92

is dated 24 March 1983. So some four or five months after the previous correspondence:

"The advice that the main Committee gave was, on the evidence before them, the Committee had reasons to think that on grounds relating to safety and quality it would be unable to advise the grant of a clinical trial certificate, the preparation ... and directed the secretary to notify the applicant in accordance with the Act."

That product, as we can see, is Mono VIII:C. So a rejection of clinical trial certificate. The reasons are given. I won't go through them all. The first six relate to the use of bulk cryoprecipitate, which is obtained, as we can see, from Alpha Therapeutics. The following five reasons relate to the technical details of the product Mono VIII:C.

Remarks on page 2, please, Soumik.

"By product licence stage:

"1. Evidence should be provided to show that the manufacturing process yields a consistent product.

"2. Evidence should be provided concerning the long termed toxicity of a product and its possible contaminants.

"3. Evidence of clinical pharmacology of a product would be required."

93

certificate was ever granted. That's something we will pick up with Ms Middleton, but I note that we are getting towards the end of her time with the company as well, so we're not sure how far we will be able to take that.

In 1983, Speywood underwent a significant change of direction. By April of that year, Mr Heath had become the non-executive deputy chairman, Mr Williams had lost his seat on the board, IPSN0000260_024. Mr Heath resigned from Speywood in September 1983, reference for that is IPSN0000442_042.

There was a significant change in business plan. If we could have, please, Soumik, IPSN0000021. You can see this is a corporate plan for 1983 to 1985. It is produced by Mr Seymour, who is the new chairman. He may also be chairman and managing director, I'm afraid I'm not entirely sure of all of his titles. It is dated 19 April 1983.

If we could turn over, please, to the next page. It sets out the original plan of the company and then, in the second paragraph, some fairly harsh words, and I quote:

"The majority of the Board now recognise that the original plans were unrealistic and that the rate of sales growth projected was unattainable whilst the

95

So, that is what it's saying in the remarks to give the company further information about where it should be going.

It also, I note, at paragraph 12, just above that -- this is among the reasons for rejecting the certificate -- it says:

"In the event of a clinical trial certificate being issued the study should be limited to ten patients and to no more than one bleeding episode in each patient."

Which is, as I understand it, a more confined trial than the one that had been proposed.

So no clinical trial certificate. There was a meeting on 2 June 1983 between the DHSS and representatives of Speywood, as we have seen, this is fairly common after licensing rejections, an opportunity for the company to speak to those involved in the licensing process to understand what they have to do.

It is a meeting that was attended by Ms Middleton, as a result I will come back to that later.

It's not clear from the documents that I have seen whether a further application for a clinical trial certificate was made or whether a clinical trial

94

resources required to establish production, technical support and marketing were underestimated. In 1982 management priorities were poorly selected with funds being diverted to prestige projects, whilst inadequate attention was devoted to the necessities of technical support [data, I think] for Product Licences, essential product plant and facilities.

"During the first quarter of 1983 priority has been given to correcting the matters indicated above. A reappraisal has also been undertaken to ascertain whether the original plan for Speywood is still viable but on an extended timetable, or whether the company must change its direction and concept in order to ensure future profitability.

"There is little doubt that with standard management practice a radical improvement can be achieved so that a loss in 1982 approaching £1.5 million need not reoccur."

I won't take you through all of the plans, sir, but if we could go to page 6, please, Soumik. We have a comment -- sorry, electronic page 7, internal page 6. My fault.

A section on the production of human material. Mr Seymour says this:

"The fundamental reason for Speywood failing to

96

1 achieve a breakeven in the next 12 months is the
 2 absence of any revenue from products resulting from
 3 the processing of human cryoprecipitate.
 4 "Such products are considered to be uneconomical
 5 due to a high price of imported cryoprecipitate, and
 6 impracticable due to the inevitable licensing problems
 7 that would arise in employing USA plasma raw
 8 materials, and their association with viral diseases.
 9 "Experience to date has also indicated that the
 10 [Factor] VIII content of this material and the yield
 11 achieved after this processing is so variable that no
 12 reliable commercial forecasts are possible."
 13 In short, a commercially unviable proposition.
 14 I will leave that section there, just to note
 15 the door wasn't being closed completely on
 16 polyelectrolyte human factor concentrate, but severe
 17 doubt being cast upon it.
 18 **SIR BRIAN LANGSTAFF:** Well, it goes on to make
 19 observations doesn't it, at the bottom of the page --
 20 **MR HILL:** Yes, I will read through if that would help,
 21 sir.
 22 **SIR BRIAN LANGSTAFF:** -- which suggests that "Well, it
 23 might be possible to do it but not the way we were
 24 trying".
 25 **MR HILL:** Yes, yes. If we go over to the next page, as

97

1 be unable to fund university research at a seven
 2 figure level as was originally projected. An interest
 3 can be maintained in genetically engineered [Factor]
 4 VIII:C however, providing this is progressed as
 5 a co-operative venture."
 6 That is the recombinant product, sir.
 7 I will come back to the recombinant product
 8 after lunch, but I will just say this now, sir. There
 9 is a dispute that then generates between the original
 10 management of the company, Mr Heath and Mr Williams,
 11 and those who are now in control, Mr Seymour and his
 12 colleagues. It's played out in a New Scientist
 13 article in March 1983, IPSN000426_036. There's an
 14 article in Business Magazine, IPSN0000442_042.
 15 There are questions in Parliament, RLIT0001486
 16 and 1487 and 1488, and private correspondence,
 17 IPSN0000260_024.
 18 I won't go through all of those documents but
 19 the fundamental battle lines, as it were, are between
 20 Mr Heath and Mr Williams, who saw a lack of investment
 21 in research and a prioritisation of short-term profits
 22 leading to a failure to exploit the technological
 23 advances made, and in particular, a failure to exploit
 24 work in recombinant technologies which later comes to
 25 fruition. Mr Heath from the Business Magazine article

99

1 well, please, Soumik.
 2 It talks about some of the possibilities
 3 considered, including a contract processing human
 4 plasma or cryoprecipitate from third parties, but that
 5 also appeared to be uneconomical. It notes the DHSS's
 6 concern about the risk of AIDS, and they are now no
 7 longer prepared to permit a multi-function plant. So
 8 you can't have a plant which is doing both porcine and
 9 human Factor VIII. Then it says:
 10 "No firm proposals are made at this time, but
 11 obviously the Board of Speywood must consider the
 12 future handling of human blood products most
 13 carefully."
 14 So the door isn't shut but nor is there much
 15 optimism.
 16 If we could go, please, Soumik, to page --
 17 electronic page 12, internal page 11, of the document.
 18 The section "Final summary and conclusion", I will
 19 pick it up from the second paragraph there, and
 20 I quote:
 21 "The company that evolves from the proposed
 22 re-organisation will, however, fall short of the
 23 aspirations of the original management. It is
 24 unlikely to have a significant role in the supply of
 25 high purity Human [Factor] VIII:C and certainly will

98

1 said:
 2 "It's a tragedy, a disillusioning ten years of
 3 my life went into Speywood, wasted because the British
 4 didn't get the best out of it."
 5 In contrast to that, and we can see it from the
 6 business plan we've just looked at, is the view of
 7 Mr Seymour and his colleagues which is in essence that
 8 the previous management were too ambitious, too
 9 disparate, lacking focus in their funding, and not
 10 sufficiently orientated on running a conventional
 11 pharmaceutical business. That had led to the problems
 12 that Speywood had in 1983. I don't seek to resolve
 13 that argument there. I just draw out the outlines
 14 of it for you.
 15 I note that Speywood was acquired by Porton
 16 International Limited in July 1984.
 17 I will come back, sir, to recombinant porcine
 18 Factor VIII after lunch, and we will also hear from
 19 Ms Middleton then. I am conscious that whereas I can
 20 continue the presentation on Tuesday if necessary,
 21 Ms Middleton must give her evidence today and I --
 22 **SIR BRIAN LANGSTAFF:** Well, yes, we will obviously want to
 23 hear Ms Middleton in full, without any pressure of
 24 time, on her or on you.
 25 **MR HILL:** Sir, I suggest, then, that I -- directly after

100

1 lunch, I introduce just a couple of very quick
2 documents about recombinants, and then we hear from
3 Ms Middleton, and then I return to porcine Factor VIII
4 at a later stage.

5 **SIR BRIAN LANGSTAFF:** Yes, well, let's take a break now,
6 shall we, until five past two, and expect to hear from
7 Ms Middleton sometime around about quarter past two.

8 **MR HILL:** I'm grateful, sir. Thank you.

9 (1.07 pm)

10 (The luncheon adjournment)

11 (2.06 pm)

12 **MR HILL:** Sir, after further thought, it may make sense to
13 call Ms Middleton straight away, just to avoid the
14 difficulties of moving equipment around between
15 presentation and witness evidence.

16 **SIR BRIAN LANGSTAFF:** Let's do that.

17 Ms Middleton, would you like to come forward and
18 Lauren will swear you in.

19 **MS SARAH MIDDLETON (affirmed)**

20 **Examination-in-chief by MR HILL**

21 **SIR BRIAN LANGSTAFF:** And it is, I think, Ms Middleton?

22 **THE WITNESS:** Yes, thank you.

23 **MR HILL:** Ms Middleton, you provided the Inquiry with
24 a statement dated 14 April 2021. I'd just like to ask
25 you one or two things about your qualifications and

101

1 your early career. If we could have on screen,
2 please, WITN5666001, please, Soumik.

3 We can see from the statement that you did a BSc
4 in biochemistry at the University of Saint Andrews
5 between 1966 and 1969; is that right?

6 **A.** Yes.

7 **Q.** Then if we go over to the second page, please, Soumik.

8 The outline of your career, I'll come back to fill in
9 some more detail on this in due course, but from 1969
10 to 1976 you were at the Protein Fractionation Centre
11 in Edinburgh as a biochemist; is that right?

12 **A.** Yes.

13 **Q.** So was that your first job after university?

14 **A.** That was my first job, yes.

15 **Q.** 1976 to 1979, you were at the Department of Medicine
16 University of Glasgow, again as a biochemist?

17 **A.** Yes.

18 **Q.** Then 1979 to 1987 it says here, "Speywood Laboratories
19 Ltd: Chief Scientist"?

20 **A.** Yes.

21 **Q.** Is the 1987 date correct?

22 **A.** I think that includes consultancy work that I did
23 subsequently.

24 **Q.** I understand. 1987 to 1996, another firm, Delta
25 Biotechnology Limited?

102

1 **A.** Yes.

2 **Q.** Working on recombinant human albumin in yeast?

3 **A.** Yes.

4 **Q.** 1986 to 2001, "Andaris Ltd: Director of Targeted
5 Therapeutics"?

6 **A.** Yes.

7 **Q.** Then 2001 to 2016, you founded Haemostatix Ltd, as CEO
8 and CTO; is that right?

9 **A.** Yes.

10 **Q.** You haven't, as I understand it, given evidence
11 previously to any Inquiry about the infected blood?

12 **A.** No.

13 **Q.** But you were interviewed with respect to a US class
14 action. Without giving away any confidences that you
15 can't give away, what were the circumstances of that
16 interview?

17 **A.** I have very little recollection, actually. I was
18 called to London, and interviewed by American
19 attorneys, and I thought that is a class action on
20 behalf of haemophiliacs in the United States. And
21 I was interviewed twice, but nothing ever came of it,
22 and there were no written papers or anything.

23 **Q.** Do you know on whose behalf the attorneys were acting?

24 **A.** I suspect they were acting on behalf of the
25 haemophiliacs.

103

1 **Q.** Plaintiffs in the action?

2 **A.** Yes, the plaintiffs.

3 **Q.** Thank you. I'd like to begin, if I may, by asking you
4 a few questions about the protein fractionation centre
5 in Edinburgh, and your time there.

6 **A.** Yes.

7 **Q.** As we have seen, you joined in 1969, directly after
8 university?

9 **A.** Yes.

10 **Q.** Who was your line manager, if such a thing --

11 **A.** Jim Smith. Dr Smith.

12 **Q.** Which department were you in?

13 **A.** Well, we were one big department, or one little
14 department, in the bowels of the Royal Infirmary in
15 Edinburgh, and we were just -- there were a group of
16 us, about 15 of us, I guess, fractionating, learning
17 to fractionate blood.

18 **Q.** Under the guidance of Dr Smith?

19 **A.** Yes. Well, Dr Smith was my immediate boss. The
20 organisation was run by Mr John Watt, who was a vet.

21 **Q.** How --

22 **A.** And then he was, I suppose, reporting to -- it wasn't
23 John Cash, it was the predecessor. I'm sorry, I can't
24 remember his name.

25 **Q.** I understand.

104

1 A. Head of Blood Transfusion Service.
 2 Q. You say there were about 15 of you?
 3 A. Approximately.
 4 Q. What kind of gradations were there in terms of the
 5 different work that was being done, in terms of the
 6 seniority of --
 7 A. Well, I was first employed as a technician, and was
 8 promoted to biochemist, but mostly we were
 9 technicians. They were technicians.
 10 Q. When you say you were promoted to biochemist from
 11 a technician, can you recall when that happened?
 12 A. After about a year, I think, about a year.
 13 Q. Should I understand from what you said there that you
 14 weren't in any policy formulating at that time?
 15 A. No, no. I was doing what I was told.
 16 Q. By Dr Smith?
 17 A. By Dr Smith.
 18 Q. Thank you. So we are clear, that's the same
 19 Dr Jim Smith --
 20 A. Yes.
 21 Q. -- who later moves to BPL and with whom you --
 22 A. Yes.
 23 Q. -- worked at BPL?
 24 A. Yes.
 25 Q. And if we could have page 1 of your witness statement

105

1 clean, and didn't appear to activate clotting factors,
 2 as some concentrates did. So it was a very --
 3 regarded as very safe.
 4 Q. Is this a forerunner of the products that became
 5 Defix?
 6 A. No, that is Defix.
 7 Q. It is Defix?
 8 A. Yes.
 9 Q. So the first bullet point there we should understand
 10 to be working on the production of --
 11 A. Defix, yes.
 12 Q. And was that the first time that it was being
 13 produced?
 14 A. Yes.
 15 Q. 1969 time?
 16 A. Yes, it was.
 17 Q. Could we have onscreen, please, Soumik, PRSE0003648,
 18 please.
 19 This is a document that we provided you with.
 20 We have provided two sets of documents, it's in the
 21 second set.
 22 A. Yes.
 23 Q. And it is an article from Vox Sang, volume 24,
 24 pages 441 to 456, from 1973, entitled "A Therapeutic
 25 Concentrate of Coagulation Factors II, IX and X from

107

1 back onscreen, please -- sorry, page 2 of your witness
 2 statement back onscreen.
 3 The description that you give of the different
 4 processes involved, if I could just ask you to expand
 5 a little and explain, in layperson's terms, insofar as
 6 is able, the different elements of your work there,
 7 the first being:
 8 "Purification of Factor IX, for human
 9 plasma ..."
 10 A. Yes.
 11 Q. "... using ion exchange resin."
 12 A. Yes.
 13 Q. Could you explain what you were doing, when you were
 14 doing it and what the product was?
 15 A. The purification took the supernatant from
 16 cryoprecipitate, which was cryosupernatant, and was
 17 then diluted and passed over an exchange resin in
 18 order to prepare a concentrate of factor II, IX and X.
 19 There was no Factor VII, which was in some
 20 concentrates.
 21 The issue for Factor IX is that it can be
 22 thrombogenic, in other words it can actually promote
 23 clotting outside of the action of Factor IX, so you
 24 want it to be controlled and not produce clots when
 25 you're not expecting it. And this Factor IX was very

106

1 Citrated Factor VIII-Depleted Plasma?"
 2 A. Yes.
 3 Q. And you're listed as the lead author there.
 4 A. Yes.
 5 Q. With Ida Bennett and JK Smith, presumably Dr Smith?
 6 A. Yes.
 7 Q. If we could look at the abstract, please, Soumik:
 8 "Abstract. A simple procedure is described for
 9 large-scale absorption on to DEAE-cellulose of
 10 coagulation factors II, IX and X from citrated,
 11 factor VIII-depleted plasma. The coagulation factors
 12 are eluted frontally from the exchanger in a high
 13 yield and in a form suitable for therapeutic use,
 14 without further fractionation. The lyophilised
 15 concentrate is very stable without the addition of
 16 heparin and, when redissolved to iso-osmolar solution
 17 ..."
 18 Forgive my repeated butchering of pronunciations
 19 as we go through!
 20 "... contains approximately 30 U/ml factors II,
 21 IX and X, 250-300 times purified from the starting
 22 plasma. The effectiveness of the concentrate in the
 23 treatment of haemophilia B is discussed."
 24 A. Yes.
 25 Q. So that's the abstract of the article. Should I take

108

1 it that this article is describing the process that
 2 you have just described to us?
 3 **A.** Yes.
 4 **Q.** This is the formulation of Def --
 5 **A.** Yes.
 6 **Q.** To the best of your knowledge, was this article from
 7 1973 the first publication of the Defix product?
 8 **A.** Yes.
 9 **Q.** If we just look at the introduction section, there are
 10 a couple of points to pick out from it:
 11 "Until 1967, only fresh-frozen plasma could be
 12 offered in Scotland for correcting deficiencies of
 13 coagulation factors II, VII, IX and X. Such treatment
 14 was frequently inadequate to maintain haemostatic
 15 levels of factor IX in patients with severe
 16 haemophilia B during major bleeding episodes or
 17 surgery."
 18 **A.** Yes.
 19 **Q.** "Since 1967 the Protein Fractionation Centre has made
 20 approximately 1,100 doses of 'PPSB' from blood
 21 collected in EDTA, by the method published by
 22 Soulier ..."
 23 What was PPSB?
 24 **A.** That was a full factor concentrate which contained
 25 Factor VII in addition to factor II, IX and X.

109

1 procuring batches of tricalcium phosphate with the
 2 appropriate absorbent properties."
 3 If I just pause there for a moment, am I right
 4 in understanding that to mean that your work in trying
 5 to create Defix was a response to the need for more
 6 product and concerns about running short of the
 7 existing product?
 8 **A.** More product, and more efficient use of blood.
 9 **Q.** Going back to the article:
 10 "This report describes the absorption of factors
 11 II, IX and X from large batches of citrated Cohn
 12 supernatant ... on DEAE-cellulose, and their selective
 13 elution in a form suitable for freeze-drying and
 14 administration to patients without further
 15 purification or stabilisation."
 16 **A.** Yes.
 17 **SIR BRIAN LANGSTAFF:** That's "supernatant I", I think it
 18 is said there, isn't it?
 19 **A.** Yes, Cohn supernatant.
 20 **MR HILL:** Sorry, my printed version is not --
 21 **A.** It's actually cryosupernatant.
 22 **Q.** I'm not going to go through the technical detail of
 23 the article but, if we could please go to electronic
 24 page 11, which is internal page 451, the section
 25 dealing with "Transmission of serum hepatitis". What

111

1 Now, I can't actually remember how PPSB was
 2 made, but obviously it started off in blood collected
 3 in EDTA, which is rather different because none of the
 4 other fractions can be collected from that blood.
 5 **Q.** Could you just explain EDTA to us?
 6 **A.** Ethylenediaminetetraacetic acid.
 7 **Q.** I won't try and repeat that!
 8 Going back to the article:
 9 "This product represented an important advance
 10 in the treatment of haemophilia B, and its use has
 11 been extended to a number of other deficiencies of the
 12 prothrombin complex of coagulation factors. The
 13 demand for PPSB for use, eg, in liver disease and the
 14 reverse of anticoagulant therapy, at times threatened
 15 to exhaust the stocks required for emergency treatment
 16 of haemophilia B, and prompted us to look for new
 17 methods of recovering factor IX or prothrombin complex
 18 from normal citrated plasma. A large increase in the
 19 production of PPSB was considered uneconomical of
 20 limited fresh blood resources, because cellular
 21 components and factor VIII are not readily recovered
 22 from blood collected in EDTA. It was hoped that an
 23 alternative method could be devised to improve the
 24 yield of factor IX (only about 30% in large scale
 25 production of PPSB) and end our dependence on

110

1 is written is this:
 2 "More than 20 batches, each made from 200 to 600
 3 donations of plasma, have been used since May 1970.
 4 In Scotland the screening of all donations of blood
 5 for Australia antigen by immunodiffusion or
 6 immunoelectrophoresis became routine during 1971.
 7 Using such methods, which detect probably less than
 8 50% of Australia antigen carriers, the incidence of
 9 antigenaemia among blood donors in Scotland has found
 10 to be about 0.07%. All batches of the factor II, IX
 11 and X concentrate have been tested for Australia
 12 antigen by the methods used for donor plasma, usually
 13 in five-fold concentration. Australia antigen has not
 14 been found in any batch, nor has any recipient
 15 developed hepatitis or Australian antigenaemia
 16 following treatment with the concentrate alone.
 17 "Since the methods used to detect the agent
 18 causing serum hepatitis were very insensitive and
 19 since no systematic attempt has been made to assess
 20 the incidence of sub-clinical hepatitis among the
 21 recipients, it would be prudent to assume that the
 22 concentrate could be infective if made from infective
 23 plasma, but it seems likely that the concentration of
 24 the infective agent is substantially reduced by the
 25 preparative procedure."

112

1 A couple of things to pick up from there. First
 2 of all, the batch size that is cited there, which is
 3 200 to 600 donations of plasma, am I right to
 4 understand that that was -- those were the batch sizes
 5 that were used in the work that you were doing at that
 6 time?
 7 A. Yes.
 8 Q. Do you know why there was such a variation between 200
 9 and 600 donations?
 10 A. Well, I suspect that, at the time, we were -- well,
 11 I'm fairly sure we were -- we were making it and
 12 scaling up as we went along.
 13 Q. Scaling up to use --
 14 A. Scaling up to use more plasma and bigger columns.
 15 Q. Do you know how the batch size developed in terms of
 16 the Factor IX product produced at PFC, during the
 17 remainder of your time there -- to 1976?
 18 A. Err ... I'm actually not sure what size it went up to.
 19 Q. Do you recall what discussions were taking place
 20 within PFC about batch size around this time?
 21 A. No.
 22 Q. The article here clearly demonstrates an awareness of
 23 the risk of what is described as Australia antigen --
 24 A. Yeah.
 25 Q. -- serum hepatitis, at the time.

113

1 did actually have a technician in the Blood
 2 Transfusion Service who did have an accident with
 3 a positively -- a positive hepatitis B donation, and
 4 she subsequently died. So there was definitely
 5 an awareness.
 6 Q. Are you able to say approximately when that occurred?
 7 A. Well, it was probably in the first couple of years,
 8 I think, that I was there. Maybe a bit longer.
 9 Q. Early 1970s?
 10 A. Yeah, early '70s.
 11 Q. Are you able to -- this is a very difficult question
 12 thinking back all these years -- are you able to
 13 recall what kind of journals and learning that you
 14 would have been keeping up to date with at that time?
 15 A. Well, obviously Vox Sanguinis was one of them, Blood,
 16 Thrombosis and Haemostasis, those are the ones I sort
 17 of remember. Vox Sanguinis was very much the one to
 18 do with fractionation. Obviously Blood. No virology
 19 journal specifically, but hepatitis would have been
 20 discussed in some of those -- in those other ones that
 21 I've mentioned.
 22 Q. Were they made available to you at the PFC or did you
 23 have to find them off your own back?
 24 A. No, they were available.
 25 Q. I'd like to just again pick up a couple of more things

115

1 A. Yeah.
 2 Q. Do you know whether there was discussion, recognition,
 3 of whether or not that risk increased with a larger
 4 batch size?
 5 A. No, I don't know whether there was. But it's likely,
 6 isn't it, that it would have been?
 7 Q. Do you think you would have been involved in those
 8 discussions?
 9 A. I was only a lowly technician at the time. I wasn't
 10 involved in those discussions.
 11 Q. Those would have been matters for whom?
 12 A. Er ... probably Jim Smith, um ... and/or the director
 13 of the Blood Transfusion Service, whoever that was.
 14 I don't think it was John Cash. It was --
 15 Q. The predecessor --
 16 A. The predecessor.
 17 Q. Do you remember what information you were given, what
 18 training you were given, about the risk of hepatitis
 19 from such products at this time?
 20 A. We were -- yes. We were aware of hepatitis as
 21 a potential problem but, I have to say, I don't think
 22 we took a great deal of precautions for it, at the
 23 time. We weren't that aware of it. I suspect
 24 Scottish plasma was thought to be a fairly clean
 25 plasma, so I can't really answer that question, but we

114

1 from that section. There's a reference to the testing
 2 that became routine during 1971. Should we understand
 3 that, before that, there was no routine testing for
 4 hepatitis?
 5 A. Possibly not. The assays, as they say, were rather
 6 insensitive at the time.
 7 Q. That's what I was going to ask next.
 8 A. Yeah.
 9 Q. There's a figure of probably less than 50 per cent
 10 given.
 11 A. Yes.
 12 Q. An awareness, then, that testing wasn't going to catch
 13 everybody?
 14 A. Yes.
 15 Q. The figure that is given about the blood donors in
 16 Scotland being found to be about 0.07 per cent --
 17 SIR BRIAN LANGSTAFF: I think we've lost it on the screen.
 18 A. Yes -- (overspeaking) -- on the screen.
 19 MR HILL: Apologies. If we could highlight the middle
 20 paragraph, "Transmission of Serum Hepatitis". Thank
 21 you.
 22 A. Yes.
 23 Q. Sir, we can see that figure there given of
 24 0.07 per cent --
 25 A. Yeah.

116

1 Q. -- for instance, among blood donors in Scotland. How
 2 much faith should we put in that figure, given the
 3 limited sensitivity of testing at the time?
 4 A. I can't answer that question. I won't answer that
 5 question.
 6 Something just in, sort of, qualification of all
 7 of this. There was insufficient Factor IX available,
 8 and very much the emphasis with everything I did at
 9 PFC, and subsequently, really, was with the aim of
 10 getting a product out there to treat haemophilia
 11 because there were problems, obviously, for
 12 haemophiliacs who didn't get treatment. So bleeding
 13 was regarded as the first problem.
 14 Q. The question of the risk and benefit of those
 15 products, was that a question for you to consider as
 16 biochemist and previously a technician, or is that for
 17 others?
 18 A. That was more for others, I think. But it was
 19 definitely very important.
 20 Q. The conclusion of that sentence says:
 21 "... it would be prudent to assume that the
 22 concentrate could be infective if made from infective
 23 plasma, but it seems likely that the concentration of
 24 the infective agent is substantially reduced by the
 25 preparative procedure."

117

1 the same, positively charged resins, and getting full
 2 factor concentrates.
 3 At the end of the day, the difference between
 4 the resins and the products made was going to be
 5 probably the amount of activation of clotting factors
 6 that you got between the different products, and that
 7 was really the difference between them.
 8 MR HILL: Do I understand the start of that answer to be
 9 that this idea --
 10 A. Yes.
 11 Q. -- insofar as it was exploited in PFC --
 12 A. Yes.
 13 Q. -- was that of Dr Smith?
 14 A. Yes, that of Dr Smith within PFC, but it was being
 15 used in other places, other facilities.
 16 SIR BRIAN LANGSTAFF: So the inspiration, the basic idea,
 17 scientifically, was somebody else's in Europe, you
 18 think --
 19 A. I think it came from somebody else in Europe --
 20 SIR BRIAN LANGSTAFF: -- and roughly --
 21 A. -- because it's quite common, people were using
 22 cellulose or sepharose, I think. One was more highly
 23 charged than the other, and Oxford, the Haemophilia
 24 Centre, they, I think, were using the sepharose
 25 product, but I might be wrong, the full factor.

119

1 A. Yes.
 2 Q. Do you know the reasons why it was thought that the
 3 procedure --
 4 A. Well, the agent -- the factors II, IX and X clotting
 5 factors were absorbed to the resin. It was very
 6 likely that the infective agent wouldn't be absorbed,
 7 would remain in the supernatant and, therefore, it
 8 could be concluded, possibly, that there would be
 9 a reduction, in any event, of virus.
 10 Q. What was the basis for thinking that the virus --
 11 A. Well, the virus is very big and I don't think --
 12 I think it wouldn't -- it subsequently turned out to
 13 be the case -- it wouldn't absorb or be bound to
 14 a positively charged resin.
 15 Q. That is, you think, the reason for that final clause
 16 in the final sentence?
 17 A. Yes, yes.
 18 SIR BRIAN LANGSTAFF: May I just ask, who was it who first
 19 had the idea of using electrically charged resin to
 20 attract certain proteins and not others?
 21 A. Well, it was Jim Smith's, the method. The method
 22 actually did come, I think, from the Dutch -- I think
 23 it the Dutch, or was it the Swiss? Somebody in
 24 Europe, who was already using this cellulose method.
 25 Other manufacturers were using similar resins but not

118

1 SIR BRIAN LANGSTAFF: Yes.
 2 A. So it was fairly well known to use a positively
 3 charged resin.
 4 SIR BRIAN LANGSTAFF: Thank you.
 5 MR HILL: If I could go, please, to electronic page 15 of
 6 the document, internal page 455. This may follow from
 7 the answers you've given already, if we look at the
 8 second paragraph there, it is stated -- this is in the
 9 concluding section:
 10 "There is no reason to believe that the
 11 concentrate cannot transmit serum hepatitis; however
 12 it is probably better in this respect than alternative
 13 sources of factor IX, including plasma."
 14 Do I understand from your previous answer that
 15 the reason for that is the technique that was used was
 16 thought to have a degree of viral inactivation?
 17 A. Yes, well, viral separation.
 18 Q. I'm going to take you to another article now, if
 19 I may. It is again, one of yours. If we could have
 20 PRSE0003799.
 21 A. Oh, right, yes.
 22 Q. This is the Journal of Laboratory and Clinical
 23 Medicine from 1976 --
 24 A. Yeah.
 25 Q. -- volume 88, pages 91 to 101, "Removal of hepatitis B

120

1 surface antigen ... from plasma fractions".
 2 A. Yes.
 3 Q. We can see the authors are Dr Johnson and his
 4 colleagues from New York, and you and Jim Smith from
 5 Edinburgh.
 6 A. Yes, yes.
 7 Q. You refer in your statement, the second of your bullet
 8 points was -- sorry, third your bullet points -- was
 9 "Clearance of Hepatitis B from Factor IX concentrate
 10 using polyethylene glycol precipitation".
 11 A. Yes.
 12 Q. Am I right in thinking that this article covers that
 13 aspect of your work?
 14 A. Yes. Yes, it does.
 15 Q. Before we delve into it, could I ask you again for
 16 a quick potted guide of what polyethylene glycol
 17 precipitation is?
 18 A. Polyethylene glycol is a large, molecular weight
 19 polymer and you can add it to solutions of protein
 20 when it would cause precipitation of proteins in
 21 a selective way, depending on their charge. And you
 22 can, by adjusting the pH of the solution, adding the
 23 polyethylene glycol, you can get selective
 24 precipitation of certain proteins. So size and
 25 charge.

121

1 investigators feel that use of the more sensitive
 2 radioimmunoassay ... has reduced it by about 50 per
 3 cent. However, pretesting has failed to achieve
 4 further reduction because of possible contamination of
 5 the blood by infectious agents capable of causing
 6 non-A, non-B hepatitis, and insufficient sensitivity
 7 of the assay."
 8 Just pausing there for a moment, two factors
 9 mentioned. One is the same as with the previous
 10 article, there's a lack of sensitivity in the testing,
 11 and the second is a reference here in this article
 12 from 1976 to non-A, non-B hepatitis.
 13 A. Yes.
 14 Q. So plainly you were aware, at that stage, of non-A,
 15 non-B hepatitis?
 16 A. Yes, which is now hepatitis C.
 17 Q. Yes. Can you recall how serious non-A, non-B was
 18 considered to be, as a risk to potential patients at
 19 that time?
 20 A. Well, once again, at this time, the overall objective
 21 was to stop the patients from bleeding. And while we
 22 were doing this work, obviously to try to improve the
 23 situation as far as the hepatitis was concerned,
 24 that's all I was, sort of, aware of. Obviously, we
 25 were aware of hepatitis. We had the agent -- we

123

1 Q. Size and charge. If we could look at the abstract,
 2 please:
 3 "Endogenous or deliberately added hepatitis B
 4 antigen was removed and concentrated for assay from
 5 albumin, and from coagulation factor II, VII, IX and X
 6 concentrates as model plasma fractions. The
 7 concentrates carry considerable risk of causing
 8 hepatitis in transfused patients. The amount of
 9 antigen remaining in the fraction was estimated to be
 10 less than 1/10,000 of that detectable by the Ausria II
 11 radioimmunoassay and 1/100 of that found to be
 12 infectious when highly contaminated human sera were
 13 diluted and injected in chimpanzees. Batch
 14 fractionation methods with polyethylene glycol were
 15 used. The yield of albumin was 96 per cent and of the
 16 coagulation factors about 90 per cent."
 17 That's an overview there of the article.
 18 Going to the first paragraph, it says:
 19 "The high incidence of hepatitis from the
 20 administration of blood and plasma fractions remains
 21 a serious problem despite governmental requirements to
 22 pretest donors for the hepatitis B antigen ... Use of
 23 the counterelectrophoresis (CEP) assay for screening
 24 donors has reduced the overall incident of serum
 25 hepatitis by nearly 30 per cent, and most

122

1 developed these agents to try to stop bleeding first.
 2 Second, we wanted to try and address the hepatitis
 3 problem.
 4 Q. So that everybody is clear, your role as a biochemist
 5 was to work on those projects --
 6 A. Yes.
 7 Q. -- not to decide whether or not the treatment that
 8 resulted from it should be given to a patient?
 9 A. No. I mean yes.
 10 Q. You agree with the proposition?
 11 A. Yes. [Laughs]
 12 Q. Do you recall what discussions were taking place at
 13 around that time about other pathogens or potential
 14 pathogens in blood products?
 15 A. In the 1970s?
 16 Q. Yes.
 17 A. No.
 18 Q. If I could turn, please, to electronic page 7 of the
 19 article. Forgive me, I think I miscounted.
 20 Electronic page 8, please, internal page 98. This is
 21 in the "Discussion" section. In the second paragraph
 22 down, it says:
 23 "Our purpose has been to reduce the antigen
 24 level in selected model plasma fractions, albumin, and
 25 factor II, (VII), IX and X concentrates, to 105 or 104

124

1 particles per millilitre and then inject the material
 2 in chimpanzees to determine its infectivity."
 3 Am I right in saying this was a spiked sample
 4 that would then be inserted into the chimpanzees?
 5 **A.** Yes.
 6 **Q.** It goes on:
 7 "Albumin is normally heated to 60°C to prevent
 8 hepatitis, but since this temperature would cause
 9 inactivation, and factor II, (VII), IX and X
 10 concentrates, they cannot be heated and carry a strong
 11 risk of causing hepatitis in recipients."
 12 So albumin, it was known at that time, could be
 13 subjected to a heat treatment at 60 degrees C.
 14 **A.** Yes.
 15 **Q.** But, according to this article Factor IX and the other
 16 factors couldn't be?
 17 **A.** That's what was considered at the time: they couldn't
 18 be.
 19 **Q.** Do you know why that was considered so?
 20 **A.** Well, they were both -- they're all quite labile
 21 proteins, which is subject to denaturation, whereas
 22 albumin is known to be a very robust protein and can
 23 be heated, and it was heated at 60 degrees for
 24 10 hours, originally to remove bacteria.
 25 **Q.** Do you know if any work was going on within PFC at

125

1 "... and contained at least 1011 antigen
 2 particles per millilitre prior to PEG fractionation."
 3 That's polyethylene.
 4 **A.** Yes --
 5 **Q.** -- glycol fractionation.
 6 "But these concentrates were prepared by an
 7 earlier version of the PEG procedure, which" --
 8 I am afraid I can't --
 9 **SIR BRIAN LANGSTAFF:** "Utilised", I think.
 10 **A.** "... which utilised 0.15 M [sodium chloride] and could
 11 not quantitatively remove the HBsAg below levels of
 12 ..."
 13 10 to the 8th.
 14 **SIR BRIAN LANGSTAFF:** 5th, I think.
 15 **A.** It couldn't, anyway.
 16 **MR HILL:** 105.
 17 **A.** Yes, they didn't get a very good result.
 18 **Q.** It says:
 19 "... one of the two injected animals" --
 20 **A.** Yes, "became infected".
 21 **Q.** -- "while the other did not ..."
 22 **A.** Yeah.
 23 **Q.** Could you just talk us through that aspect and the
 24 significance, both of the previous method being used
 25 and the fact that one of the chimpanzees became

127

1 that time about heat treatment --
 2 **A.** No.
 3 **Q.** -- of those factors?
 4 **A.** Not in those, no. Not at that time.
 5 **Q.** No, the work wasn't going on, or, no, you don't --
 6 **A.** No, the work was not going on. I'm not even sure
 7 that -- in those days, we all believed what is said
 8 here, that they can't be heat treated, and that was
 9 what was believed at the time.
 10 **Q.** Received wisdom, as it were?
 11 **A.** Sort of received wisdom from what we knew about those
 12 proteins.
 13 **Q.** But were there any discussions, as far as you recall,
 14 about the --
 15 **A.** It was --
 16 **Q.** -- possible --
 17 **A.** It was dismissed at the time as being unlikely to be
 18 possible, which is why we looked at this precipitation
 19 method.
 20 **Q.** If we could go on to the next paragraph.
 21 "In collaborative studies with Dr Hoofnagle, two
 22 chimpanzees were injected with PEG-fractionated II,
 23 (VII), IX and X concentrates which were known to be
 24 infectious ..."
 25 I'm afraid the copy isn't good here:

126

1 infected?
 2 **A.** Actually, I can't, because I'm not quite sure what
 3 this actually meant, now, going back 40 years.
 4 I apologise for that. I'm not quite sure what the
 5 procedure was that was different.
 6 **Q.** But you say they didn't get a very good result,
 7 whatever that procedure was?
 8 **A.** Was, it didn't seem to work.
 9 **Q.** Hadn't inactivated -- separated the --
 10 **A.** No, it hadn't separated it out.
 11 **Q.** I am just going to take you to see if we could perhaps
 12 get some assistance from Peter Foster's evidence to
 13 the Penrose Inquiry.
 14 **A.** Yes.
 15 **Q.** You're aware of Dr Foster?
 16 **A.** Yes.
 17 **Q.** He became a colleague of yours --
 18 **A.** Yes, he did.
 19 **Q.** -- in due course.
 20 **A.** Yes.
 21 **Q.** If we could have on screen, please, Soumik,
 22 PRSE0003349, this is one of the documents that you
 23 were provided with. If we could have page 3 -- sorry,
 24 just leave it there for one second, we can see this is
 25 the witness statement of Peter Foster to the Penrose

128

1 Inquiry, or one of his witness statements.
 2 If we could turn to page 3 of that, please, and
 3 paragraph (f). It says -- Dr Foster said this:
 4 "Factor IX preparing experimentally in the USA
 5 by this procedure, from plasma known to contain
 6 hepatitis B infectivity, was tested by Dr Johnson in
 7 chimpanzees. The chimpanzees developed hepatitis B,
 8 demonstrating that hepatitis B infectivity had not
 9 been fully removed ..."
 10 Then there is citation to the article which we
 11 have just seen.
 12 A. Yes.
 13 Q. So, leaving aside the reference to whether or not it
 14 was one chimpanzee or two chimpanzees, it became
 15 infected. Dr Foster's take from the paper, as it
 16 were, is that the process hadn't been successful?
 17 A. Yes.
 18 Q. Or I should say wholly successful?
 19 A. Well --
 20 Q. It may have reduced --
 21 A. Not really successful -- it wasn't successful.
 22 Q. Yes, and that's a conclusion you would agree with?
 23 A. I would agree with that.
 24 Q. If we could just go to (g), then:
 25 "Dr Johnson's subsequently refined for

129

1 the product was more concentrated than established
 2 Factor IX concentrates."
 3 Were you aware of or involved in the Cash work
 4 which led to the production of that article?
 5 A. Yes. We supplied the concentrates for it. Actually,
 6 I was surprised because I didn't recall -- and I have
 7 read Peter's submission -- but I was surprised because
 8 I -- it could have been because it was a very high
 9 dose of Factor IX that was administered. That's all
 10 I can conclude from that.
 11 Q. Yes.
 12 A. And that -- because a lot of Factor IX, a lot of
 13 Factor II, a lot of Factor X, that could be the result
 14 of -- that could be resulting in this thrombogenicity
 15 that I referred to.
 16 Q. Yes, yes.
 17 A. But that was the Defix.
 18 Q. That was the Defix that you supplied Dr Cash --
 19 A. Yes.
 20 Q. -- for that article --
 21 A. Yes, yes.
 22 Q. So a slightly different stream of work?
 23 A. No, that was Defix. And what -- well, I think it
 24 was -- I think that's what he's referring to. If you
 25 go back to the page before, can you just ...

131

1 precipitation parameters (the revised method being
 2 known as the mark II method) to remain greater removal
 3 of the hepatitis B virus. However, he told me that
 4 his application for funding for another chimpanzee
 5 study, to discover if the removal of hepatitis B
 6 infectivity had been successful, was rejected by the
 7 USA National Institute of Health (NIH) because they
 8 considered that [and he quotes] 'hepatitis is no
 9 longer a problem'.
 10 A. Oh, that's interesting.
 11 Q. Is that something you were aware of or can assist us
 12 with?
 13 A. No, I wasn't.
 14 Q. We will leave that for Dr Foster, then.
 15 If we could continue on as we are here, to:
 16 "h). Another issue that arose with factor IX
 17 prepared by the first (mark I) version of the method
 18 was a thrombogenic reaction in dogs [Dr Cash is cited]
 19 suggesting that the product might be harmful to
 20 patients. Alternatively, this may have been
 21 a consequence of the very high dose of factor IX ..."
 22 SIR BRIAN LANGSTAFF: Sorry.
 23 MR HILL: Sorry.
 24 "... consequence of the very high dose of
 25 factor IX that had been administered in this study, as

130

1 Oh, I'm apologising, sorry. He wasn't referring
 2 to Defix.
 3 Q. We will pick this up with Dr Foster in due course.
 4 A. Yes, because when we went on to use the polyethylene
 5 glycol process that Dr Johnson had developed, we did
 6 a parallel, not -- we did it with no, obviously,
 7 hepatitis added in, we did it just to look at the
 8 fractionation of Factor IX, through this polyethylene
 9 glycol process. We actually got a reduction in
 10 thrombogenic material by tests that were introduced
 11 later, which was again one of those publications that
 12 we had.
 13 Q. I am just going to take you back to the 1976 article
 14 of which you were a co-author.
 15 If we could have on the screen, please, Soumik,
 16 PRSE0003799, internal page 99.
 17 So I think page 8 of the electronic version.
 18 I'm afraid I don't have a marked copy. Sorry, page 9.
 19 A. That's 98.
 20 Q. Thank you. I just want to take you to the final
 21 paragraph:
 22 "Although the clinical value of the PEG method
 23 for removing [hepatitis B] must be confirmed by
 24 further studies in chimpanzees, we fully expect that
 25 its application to selected, clinically useful blood

132

1 fractions will reduce or even eliminate
 2 post-transfusion hepatitis due to hepatitis B antigen
 3 contained in these administered fractions."
 4 Could you just explain the basis for that
 5 thinking?
 6 **A.** Um ... well, I think ... there was only two
 7 chimpanzees. The method was refined, and I think he
 8 felt that the use of a precipitation method to
 9 precipitate out the virus, which is obviously very big
 10 and very heavy, it -- theoretically, it would be
 11 a good method.
 12 **Q.** Shall we read this as being that although there has
 13 been infectivity with the mark I method --
 14 **A.** Yeah.
 15 **Q.** -- Dr Johnson is already thinking about the mark II
 16 methods and is optimistic for the results that may be
 17 obtained?
 18 **A.** Yes, yes.
 19 **Q.** We see an express reference to the need for further
 20 chimpanzee studies.
 21 **A.** Yes.
 22 **Q.** We can tie that back to what Dr Foster said in --
 23 **A.** Mm.
 24 **Q.** -- and pick that up with him in due course. Thank
 25 you.

133

1 briefly explain what that involved, please.
 2 **A.** Well, it was well known and was used, single donor
 3 cryoprecipitate, which means that plasma was thawed
 4 very slowly to not more than 5 degrees, and the
 5 precipitate that was Factor VIII and fibrinogen, in
 6 large proteins, was recovered.
 7 This is a very slow process but it was single
 8 donor, which was the advantage from the hepatitis
 9 point of view. But it was very slow, and if a patient
 10 was bleeding, it was not a particularly useful thing
 11 to do. So what I did, again with Dr Smith, was to
 12 make bulk preparations of cryoprecipitate, which
 13 essentially involved taking large amounts of plasma,
 14 thawing it out very slowly, with mixing, to get
 15 a cryoprecipitate which would then be dissolved and --
 16 essentially dissolved and formulated to make a bulk
 17 product, which could be freeze-dried.
 18 And that was the first Factor VIII to be made by
 19 that method at -- in Scotland.
 20 **Q.** Very difficult question but can you remember the
 21 time span in which you were engaged in that work, and
 22 particularly when it came to -- (overspeaking) --
 23 **A.** Well, I did it almost when I first started my first --
 24 in the first couple of years.
 25 **SIR BRIAN LANGSTAFF:** From 1969 to 1971?

135

1 One further article from your time at PFC -- or,
 2 published after your time, but referring back to while
 3 you were there.
 4 If we could have, please, WITN2235010. The
 5 second page of this, please.
 6 An article from British Journal of Haematology
 7 in 1981, volume 47, pages 91-104, an article by
 8 Dr Prowse and Dr Cash:
 9 "The Use of Factor IX Concentrates In Man:
 10 a 9-Year Experience of Scottish Concentrates in the
 11 South-East of Scotland."
 12 You are not an author of this paper.
 13 **A.** No.
 14 **Q.** It is published after you have left the PFC but would
 15 include periods that you were at the PFC if it's
 16 a nine-year study; is that fair?
 17 **A.** Yes.
 18 **Q.** Did you have any role in the study to which this
 19 article refers?
 20 **A.** No.
 21 **Q.** I will leave it there.
 22 Returning to your witness statement, you also
 23 say that while you were at the PFC, you were involved
 24 in purification of Factor VIII from human blood using
 25 purified cryoprecipitate fraction. Could you just

134

1 **A.** Yes, I guess so. Yeah.
 2 **MR HILL:** How -- may I ask a broad question: how
 3 successful was the product that was created?
 4 **A.** Quite successful.
 5 **Q.** Was it used by clinicians in the --
 6 **A.** Oh, yes.
 7 **Q.** -- (overspeaking) --
 8 **A.** Yes, it was. In fact, after I left PFC, which was for
 9 reasons of -- I had a husband who moved to the West
 10 Coast of Scotland, and I went to Glasgow and worked
 11 with a haemophilia director there, and was involved in
 12 some of the treatment of patients -- for the first
 13 time, really.
 14 And they were using some of that concentrate,
 15 and it just made such a difference to -- for the
 16 patients to be able to have a freeze-dried concentrate
 17 used immediately out of the fridge for immediate use.
 18 **Q.** This concentrate, shall we understand that it was
 19 essentially a freeze-dried cryoprecipitate?
 20 **A.** Yes.
 21 **Q.** Rather than what became known as freeze-dried factor
 22 concentrates at a later stage, rather than pooled
 23 plasma?
 24 **A.** It was -- I'm not sure I understand your question.
 25 **Q.** I'm sorry.

136

1 A. It was a freeze-dried -- it was freeze-dried
 2 cryoprecipitate, but made in bulk. So you got several
 3 hundred vials from a batch.
 4 Q. I see.
 5 A. That were freeze-dried.
 6 Q. So what was the pool size of the cryoprecipitate?
 7 A. Well, I know initially it was about 20 litres but
 8 I can't remember how many units that -- how much that
 9 made, but ...
 10 Q. Obviously obtained from more than one donor at that
 11 size?
 12 A. Yes, it was.
 13 Q. You said initially. Do you remember about --
 14 A. I don't know how high because it was being done in
 15 a small facility, and using small scale equipment, and
 16 therefore we were somewhat limited to about 20 litres.
 17 Now, I'm sure it went up to about 100 litres,
 18 subsequently, about that's what I recall doing.
 19 SIR BRIAN LANGSTAFF: Can I just tell you, the -- we've
 20 had a conversion factor used in the course of the last
 21 week or so of somewhere around 600 ml a litre of whole
 22 blood is plasma.
 23 A. Yeah.
 24 SIR BRIAN LANGSTAFF: So if that is so --
 25 A. Yes.

137

1 explanation earlier, could I ask for your explanation
 2 of what polyelectrolyte fractionation is, please?
 3 A. Well, essentially it was just a novel polymer,
 4 positively charged polymer, that was -- I can't
 5 remember its original use from Monsanto but it was
 6 being evaluated for plasma fractionation. And there
 7 were variations on the degree of positive charge that
 8 could be introduced into it.
 9 So there was one called E100, which was a 100
 10 per cent substitute with positive charge, which was
 11 used -- potentially which was developed to purify
 12 albumin and gamma globulin away from each other. And
 13 then there was -- the one that -- when I first
 14 evaluated those polyelectrolytes, I went to New York.
 15 There was no -- from my recollection, and I think this
 16 was true, there was no polyelectrolyte at that point
 17 that was very useful for Factor VIII. I don't know
 18 whether it was because the Factor VIII wouldn't come
 19 off the polyelectrolyte. I suspect that was the case.
 20 But at that time, there wasn't one.
 21 So I ended up -- from PFC, I went over and
 22 learnt about albumin and gamma globulin.
 23 Q. Was that at Dr Johnson's --
 24 A. That was in Dr Johnson's lab.
 25 Q. You mentioned Monsanto.

139

1 SIR BRIAN LANGSTAFF: -- then a donation of plasma is
 2 about 600 ml?
 3 A. Yes.
 4 SIR BRIAN LANGSTAFF: So 20 litres would give you
 5 somewhere between 35 and 40 donors.
 6 A. Yes, yes.
 7 SIR BRIAN LANGSTAFF: Or donations, I should say, because
 8 they might be the same donor giving a couple of pints.
 9 A. Most likely single at that point. Yes. That would be
 10 right.
 11 SIR BRIAN LANGSTAFF: That would be right?
 12 A. Yes.
 13 MR HILL: Same question as earlier. Were you involved in
 14 any discussions about the potential risk of --
 15 A. No.
 16 Q. -- increasing the donor size?
 17 A. No.
 18 Q. Again, a decision made at a higher level?
 19 A. Yes.
 20 Q. The final bullet point you gave through PFC is the:
 21 "Evaluation of Plasma Fractionation using solid
 22 phase polyelectrolyte based on Ethylene Maleic
 23 anhydride (EMA PE)."
 24 A. Yes.
 25 Q. Now with some trepidation, given that I attempted an

138

1 A. Yes.
 2 Q. That was the company providing the polyelectrolyte?
 3 A. Yes.
 4 Q. Yes. And that's the same company as later provided --
 5 A. Yes.
 6 Q. Well, even at this time as was providing Speywood, and
 7 you would --
 8 A. Yes. Yes.
 9 Q. Other than those areas that we've discussed, were you
 10 involved in any other viral separation or viral
 11 inactivation work in PFC at that time?
 12 A. Um ... no, only the creation of Supernine, which we've
 13 talked about, the PEG precipitated.
 14 Q. We will come back to Supernine perhaps with Dr Foster
 15 or with others.
 16 A. And I did actually -- yes. I did actually look at
 17 separation of viruses with polyelectrolyte with immune
 18 globulins. But that's not -- that was never
 19 published, so I am not quite sure -- but there
 20 obviously was an awareness there of ...
 21 Q. Who was directing the areas in which R&D would be
 22 aimed, in the PFC at that time?
 23 A. Um, Jim Smith. Dr Smith.
 24 Q. What resources were available to him?
 25 A. Plasma.

140

1 Q. As in laboratory and human resources?
 2 A. In PFC?
 3 Q. Yes.
 4 A. Um ... we had laboratory, we had equipment. We had
 5 plasma.
 6 Q. How many people?
 7 A. Doing research, or doing this development work?
 8 Q. Doing research.
 9 A. Well, there was me and I guess there was a couple of
 10 others, but it was mostly me doing coagulation
 11 factors.
 12 Q. Fair to say then that there had to be a fair degree of
 13 prioritisation on the work which you were doing?
 14 A. Mm.
 15 Q. We know that in 1981, after you had left, some
 16 five years after you had left, the Medicines
 17 Inspectorate gave a critical report of the PFC.
 18 In your experience, up until 1976, did the PFC
 19 meet the standards that you would have expected of
 20 a laboratory and fractionation centre.
 21 A. Well, I didn't know any better. They -- we were --
 22 well, we were obviously trying to work as cleanly as
 23 possible. The Medicines Act had only just really come
 24 into play in 1969, so I think we were sort of -- it
 25 sounds terrible but it isn't meant to -- making it up

141

1 said something of it originally, but what kind of
 2 interaction, if any, did you have with haemophilia
 3 patients?
 4 A. Well, I, having moved to Glasgow, I was involved
 5 with -- we were collecting blood samples from patients
 6 to check on their Factor VIII levels after treatment,
 7 and looking at things like half lives and those sorts
 8 of things.
 9 Q. The half life of a Factor VIII product that they'd
 10 been given?
 11 A. Yes, yes.
 12 Q. Did you conduct any other routine blood tests on those
 13 patients at that time?
 14 A. No. Just factor assays.
 15 Q. Would you actually draw the blood yourself?
 16 A. No, no, it was drawn by a nurse or a doctor.
 17 Q. And are you able to assist at all with what the
 18 consenting process was that the patient went through
 19 before giving that blood?
 20 A. There wasn't -- as I recall, there was no consenting
 21 process.
 22 Q. So the blood would be taken from the patient without
 23 the patient being told what the blood was going to be
 24 used for?
 25 A. It might have been. It might have been.

143

1 as we went along. We had to keep out bacteria, we had
 2 to keep out pyrogen in particular, and these were the
 3 things that drove us to work as cleanly as possible
 4 and that's what we did.
 5 But the facilities in PFC at the time -- and
 6 this is before it moved into its new facility out at
 7 Liberton -- we were in the bowels of the Royal
 8 Infirmary in Edinburgh, and in fact -- which was not
 9 a particularly desirable place to be making clean
 10 blood products, but it was all we had.
 11 Q. How did it compare with your later experience of
 12 Speywood?
 13 A. When I first went to Speywood the conditions were not
 14 great. We were working in a Portakabin -- and
 15 a garage, actually. So I got used to that sort of
 16 thing, and, amazingly, made pyrogen-free products out
 17 of -- in some of these facilities.
 18 Q. Is it fair to say that then both your initial work in
 19 Speywood and the work that you did at the PFC, your
 20 burdens were added to by the need to work hard to make
 21 pyrogen-free product in the --
 22 A. Yes, it adds quite a lot of problems, and cleaning
 23 equipment, and water quality, and those sorts of
 24 things. So yes.
 25 Q. Moving to your time in Glasgow in 1976 to '79, you

142

1 Q. You personally weren't involved in those
 2 discussions --
 3 A. No -- no.
 4 Q. -- with the patient?
 5 A. No. I can't tell you if there were bits of paper
 6 signed or whatever was done. It wasn't that apparent,
 7 because the number of patients within a haemophilia
 8 unit -- the whole haemophilia unit is very much sort
 9 of like a family. And patients were coming in all the
 10 time to get their treatment and knew the haemophilia
 11 directors and the nurses intimately, because they were
 12 there quite often, and I don't think -- I don't know
 13 what consenting processes would have been involved.
 14 Q. What, other than checking the blood for the effect of
 15 the Factor VIII products, what other roles did you
 16 undertake at Glasgow at that time?
 17 A. Well, I actually looked at the Factor IX concentrate
 18 that -- the Defix Factor IX concentrate, and the
 19 Supernine concentrate, and looked at using different
 20 assays to look at that thrombogenicity.
 21 Q. That was research work that you were doing --
 22 A. Yes.
 23 Q. -- on the products rather than -- (overspeaking) --
 24 the patients?
 25 A. Yes, on the products, yes. While I was there.

144

1 I also did things to do with Factor VIII assays,
 2 recoveries after exercise and various other things.
 3 I worked with who is now Professor Lowe at the time
 4 and we did some work with recovery of Factor VIII with
 5 exercise, and things like that, physiological effects.
 6 **Q.** What links did you have at that stage with your former
 7 colleagues at the PFC?
 8 **A.** Well, I was still working -- Peter Foster was there at
 9 that time. I suspect Jim Smith had left, I think.
 10 And he knew what I was doing, because we subsequently
 11 wrote the paper about Supernine and PEG concentrate.
 12 So he knew what I was doing.
 13 **Q.** Did you have any links with pharmaceutical companies
 14 at that stage, while you were at Glasgow?
 15 **A.** No, the only reason -- the only pharmaceutical company
 16 that happened while I was in Glasgow was that
 17 David Heath, who you've heard mentioned, came into the
 18 lab while I was working to speak to my boss,
 19 Dr Prentice, who was the haemophilia director, and
 20 started to talk about polyelectrolytes. Within my
 21 hearing. So that's how it came about that I ended up
 22 working for Speywood.
 23 **Q.** You've pre-empted my next question.
 24 **A.** Right.
 25 **Q.** It was how you were recruited to Speywood in 1979.

145

1 **A.** Yes.
 2 **Q.** What did that role entail?
 3 **A.** Well, I sometimes thought it was because I was the
 4 only scientist. At the time.
 5 It involved -- my going there was primarily to
 6 develop porcine Factor VIII. There was a problem with
 7 the current product, which was not soluble, and
 8 couldn't be used. I subsequently sorted that problem
 9 out -- actually, quite quickly -- then went over to
 10 the States to pick up the polyelectrolyte, which
 11 seemed to have been now working for Factor VIII. So
 12 that's the way it went. I then came back and scaled
 13 the polyelectrolyte method up to produce Hyate:C.
 14 **Q.** That's the porcine product?
 15 **A.** The porcine product.
 16 **Q.** But when you say you went over to the States, should
 17 we understand that to be literally --
 18 **A.** -- (overspeaking) -- Dr Johnson's lab.
 19 **Q.** Did you stay there for long and conduct research or
 20 was it literally to pick up the polyelectrolyte --
 21 **A.** Well, I stayed there -- I think I stayed there three
 22 or four weeks, just to make sure that the method
 23 worked, and to -- because I didn't -- because it
 24 previously hadn't, for Factor VIII, but it did work.
 25 So I then picked up the polyelectrolyte, brought it

147

1 Was it from that --
 2 **A.** Essentially I heard that conversation about
 3 polyelectrolyte. I also -- and -- yes, I wrote to
 4 David and said -- because I wanted to actually get
 5 back to something more production-orientated, and
 6 explained my experience, and I got a letter by return
 7 of post saying: Yes, when are you going to start?
 8 So that's what happened.
 9 **Q.** You then moved to Speywood. Physically, where were
 10 you based when you were working for Speywood?
 11 **A.** Wrexham.
 12 **Q.** In Wrexham?
 13 **A.** Yes.
 14 **Q.** Did you have anything to do with the office in
 15 Nottinghamshire?
 16 **A.** Not really. We occasionally -- we went over there
 17 occasionally. Myself and the production, I guess you
 18 mean the production director, Dr Costello, (?) **
 19 and -- he was in charge of the Wrexham site. We
 20 occasionally went over there, but just to talk about
 21 progress with porcine Factor VIII.
 22 **Q.** So you're essentially going there for meetings, but
 23 never being based there; is that right?
 24 **A.** No, never been based there.
 25 **Q.** Your title was chief scientist?

146

1 back to Wales, which is where we were, to Wrexham.
 2 **Q.** So that we are clear, this is for polyelectrolyte that
 3 was being licensed from Monsanto?
 4 **A.** Yes, it was.
 5 **Q.** The accountant's report from 1981 that we looked at
 6 earlier -- and I know you were in the room when we
 7 were going through the presentation earlier -- it
 8 referred to there being 21 staff in Wrexham. I am not
 9 going to ask you for what each one of them did, as of
 10 1981, but what kind of roles were those people doing?
 11 What were people doing in --
 12 **A.** Initially, there were not 21 but there was --
 13 initially, there was a technician in the lab who was
 14 doing Factor VIII assays, mostly, and there were
 15 a collection of three or four or maybe five
 16 individuals who were responsible for collecting the
 17 blood on the abattoir.
 18 **Q.** The pig blood?
 19 **A.** Yeah, collecting and separating it.
 20 **Q.** Then there was you, as chief/sole scientist?
 21 **A.** Yes. And then there was Dr Costello (?) ** who,
 22 actually, was a botanist but he was obviously
 23 a scientist, as well. But he was in overall charge of
 24 the site, and the personnel.
 25 **Q.** Who gave you directions about what it was that you

148

1 should be doing?

2 A. Me.

3 Q. We heard in the presentation about the importation of

4 Koate and Humanate --

5 A. Yes.

6 Q. -- and its sale within the United Kingdom. What role,

7 if any, did you have in the importation and sale of

8 Koate and Humanate?

9 A. I had no -- very little knowledge of it. I certainly

10 had no input at all.

11 Q. We saw from the data sheet that it was -- the address

12 given was the Nottingham address.

13 A. Yeah.

14 Q. So far as you're aware, was the Koate and Humanate

15 business run from Nottingham --

16 A. Yes.

17 Q. -- or from Wrexham?

18 A. No, from Nottingham.

19 Q. Were you ever involved in the processes of seeking

20 product licences or dealing with the DHSS, insofar as

21 it related to Koate and Humanate?

22 A. No.

23 Q. I'm going to quickly ask you, before we have a break,

24 about porcine Factor VIII and Hyate:C. You said --

25 you've explained how you went and you picked up

149

1 Factor VIII assays are particularly difficult to

2 standardise, and we did have a problem with porcine

3 Factor VIII because the kinetics of the production of

4 porcine Factor VIII are different between human and

5 pigs. And there was a pig standard which was supplied

6 by a commercial company, which turned out to be wrong

7 because of the way it was -- had been assayed. So

8 yes, I had quite a lot of input into that. It's an

9 interesting topic, the kinetics of blood clotting in

10 pigs versus human. Sorry.

11 Q. I won't go into too much detail about that, and you'll

12 forgive me. But were you involved in any of the

13 applications for product licences for Hyate:C?

14 A. Somebody else wrote them, because I wasn't there at

15 the time.

16 Q. But you left the company by that stage?

17 A. I was either -- I may not have left. I might have

18 been somewhere else, like at Elstree or in Paris, or

19 I also worked on deficient plasmas and various other

20 things. So I was away from, sometimes away from

21 Speywood, and I don't think that licence was applied

22 for until the facility, the manufacturing facility,

23 had been built. And so I was -- I'm not -- I did --

24 don't think -- I might have done. I don't remember

25 whether I did or not.

151

1 a polyelectrolyte and understood that it now worked in

2 respect of Factor VIII, and then you solved the

3 problem that they had been having with it. In your

4 statement, I won't take you to it, but at paragraph 14

5 you say:

6 "I developed a production scale process to

7 recover porcine Factor VIII."

8 A. Yeah.

9 Q. Then at paragraph 37 you say that you had little

10 involvement in porcine Factor VIII thereafter.

11 A. I had -- after scaling up, yes, I showed the method to

12 others, the other people, and they were perfectly

13 capable of handling it. It was a very easy process,

14 really. The difficulty with any Factor VIII or

15 Factor IX concentrate, it's not so much making it,

16 it's knowing you've got the right thing at the end of

17 it, in terms of assays, and analytical work, and

18 knowing that there's no potential for clotting when

19 you don't want clotting. So thrombogenicity, as we

20 call it.

21 Q. Did you have any role in that aspect of the work in

22 terms of Hyate:C?

23 A. The assay?

24 Q. The assay and the checking, the quality control and --

25 A. Yes, to an extent, because I had experience of --

150

1 Q. I haven't found many papers with your name on in

2 connection with the Hyate:C --

3 A. The product. The product licensing or --

4 Q. And indeed the product licensing.

5 A. Yes, well, okay, in that case I didn't.

6 Q. We haven't looked at this in the presentations and we

7 will come back to that at a later date, but we know

8 that the application for the product licence was made

9 on 29 November 1983 --

10 A. Oh, right. Okay.

11 Q. -- and the licence was granted on 3 December 1984.

12 A. Right.

13 Q. Would you have still been working at Wrexham for

14 Speywood at that time?

15 A. Um ... well, no, I don't -- now you come to mention it

16 I actually don't know, because I did have a very --

17 I didn't really work full time at Wrexham, for a long

18 time before -- a long time after -- after I went and

19 worked down at the -- at Elstree.

20 Q. At BPL?

21 A. At BPL. And I don't know -- if you ask where I was,

22 I know I was doing work at the Royal Free on depleted

23 plasmas, for example, and I just was working in other

24 people's labs, I think.

25 Q. Is it fair to say, then that, certainly from your

152

1 current recollection, you didn't have a great deal of
 2 input into the finalisation of the product Hyate:C?
 3 **A.** No, I don't think I did.
 4 Well, in the sense that I did formulate it, and
 5 I did run -- develop assays, and various other things,
 6 and I did have an interaction with NIBSC, N-I-B-S-C,
 7 about the assay, because that caused us all a lot of
 8 confusion at one stage. So I was doing that.
 9 **Q.** Were you involved in, for example, directing the
 10 thinking about where this product should be used, and
 11 which cohort of patients it should be used with?
 12 **A.** Not really. It was inhibitor patients, as far as
 13 I was concerned.
 14 **Q.** That's where my question is leading to. When the
 15 product licence went in, we'll look at this in due
 16 course, it is very expressly said to be for inhibitor
 17 patients.
 18 **A.** Yeah.
 19 **Q.** One question that the Chair may wish to consider, in
 20 due course, is why porcine Factor VIII, in the
 21 mid-1980s at a time of risk of both hepatitis and
 22 AIDS, was directed towards inhibitor patients rather
 23 than the wider population of --
 24 **A.** Of patients without an inhibitor?
 25 **Q.** Yes, exactly, without inhibitors.

153

1 seen in the past, with much more -- much less pure
 2 products, so I don't think people wanted to use it.
 3 **Q.** We will come back to that, sir, as I say, in due
 4 course, when we look at some further papers. I am
 5 going to move on from porcine Factor VIII to human
 6 Factor VIII, so I wonder if now might be a convenient
 7 moment?
 8 **SIR BRIAN LANGSTAFF:** Well, how much longer do you think
 9 you might be?
 10 **MR HILL:** Probably, sir, about another half an hour or so.
 11 **SIR BRIAN LANGSTAFF:** Because I am concerned that we need
 12 plenty of time for you to pick up questions from those
 13 Core Participants who might want to ask them. Yes, so
 14 we'll take 25 minutes, and come back, therefore, at
 15 ten to four.
 16 **MR HILL:** Thank you, sir.
 17 (3.23 pm)
 18 (A short break)
 19 (3.50 pm)
 20 **MR HILL:** Ms Middleton, I'd like to turn now to the
 21 fractionation of human Factor VIII, by the
 22 polyelectrolyte method. I won't take you to your
 23 statement but you say in it that shortly after,
 24 relatively shortly after joining Speywood, you were
 25 seconded to BPL, and you subsequently spent some time

155

1 **A.** Yeah.
 2 **Q.** Are you able to give any insight into that question
 3 from your perspective?
 4 **A.** Well, from what I knew, first of all, porcine --
 5 original porcine Factor VIII had a shocking
 6 reputation. This is before Hyate:C. It was a really
 7 toxic product. It produced thrombocytopenia, platelet
 8 reduction because of this so-called platelet
 9 activating factor, which was thought to cause this
 10 problem. They had allergic reactions to the protein,
 11 et cetera. When it came to Hyate:C, it was much more
 12 highly purified and actually was very well tolerated
 13 by patients. But there was the concern that it would,
 14 potentially, in non-inhibitor patients, produce
 15 a cross-reacting inhibitor to human Factor VIII.
 16 **Q.** It follows from that, that by taking this product,
 17 they would then render themselves incapable of taking
 18 a human --
 19 **A.** Yes.
 20 **Q.** -- Factor VIII plasma product in the future?
 21 **A.** Yes, and that was the big unknown concern.
 22 **Q.** Were there any other reasons, you think, that --
 23 **A.** Well, I think you were going to be giving pig protein
 24 to people and, again, that might be a risk of creating
 25 allergic reactions to the pig protein, which had been

154

1 in Paris as well at the CNTS lab.
 2 **A.** Yes.
 3 **Q.** I think that was in April, from April 1981.
 4 We heard in the presentation about how there was
 5 some optimism about the product in 1981, which gave
 6 way fairly quickly to a more pessimistic view of the
 7 prospects of the product.
 8 **A.** Mm.
 9 **Q.** Can I ask, you have said in your statement that yields
 10 were variable, and that problems soon became apparent
 11 with the product. Could you explain what those
 12 problems were, and how quickly they became apparent to
 13 you, and to others?
 14 **A.** Well, as you probably know, blood clotting is
 15 a very -- it's quite a complex process. It's
 16 a cascade. That's to make the blood clot. There are
 17 also a lot of mechanisms in there to stop blood
 18 clotting when it's not supposed to. So it's quite
 19 a complex system to deal with. And if you are making
 20 Factor VIII, purifying it, depending on the starting
 21 material, you, have plasma which is in various -- once
 22 you collect plasma or blood from the body, it's
 23 immediately not as stable as it was when it was in the
 24 body, because you've exposed it to surfaces, you've
 25 generally exposed it to the air and you've generally

156

changed the profile of it. And the inhibitors to blood clotting and the procoagulant. So, particularly with the polyelectrolyte, the Factor VIII, it proved to be very difficult to control the clotting, if you like, because the Factor VIII became -- was probably becoming activated during the process. And how activated it became depended on the quality of the starting material, quite often.

But it did result with -- with huge variability, trying to control the process, and it proved, in my hands anyway, very difficult to control it with any of the sort of different parameters that I tried.

So you absorb onto the polyelectrolyte and then you wash off. That's essentially what you have to do. By controlling -- the way you absorb it, or the things you add to it to try to keep it stable, the way you elute it off, can all affect what happens in terms of the stability of the final product, and what it proved to be -- relatively easy, you could elute things off, and you could measure a Factor VIII level that seemingly was high, remembering that the assays themselves could sometimes not discriminate as to whether you'd got an activated system or not, and then, as you stored it, let it stand, the activity dropped off because the Factor VIII was becoming

157

the reference is HSOC0022968. And he is describing how he worked with you and with others in order to try to purify Factor VIII that he can then go on to use in gene sequencing which would then give rise to recombinant products?

And he said that by 1982 he had devised a multi-step procedure, which had -- which led to that -- in cooperation with others, I should emphasise.

A. Mm.

Q. And he said:

"The bulk processing capacity of polyelectrolyte, combined with the exquisite specificity of monoclonal antibodies, overcame all remaining problems, although Frances Rotblat and Don O'Brian (?) ** in my laboratory found that they needed to use large amounts of highly poisonous nerve gas type enzyme inhibitors to keep the Factor VIII stable."

A. Yes.

Q. So that is what you were referring to a moment ago?

A. Yes.

Q. I don't think it needs to be stated why using a nerve agent --

A. Yes.

159

activated and lost.

So it proved very difficult to control and that in essence was confirmed, because when we made Factor VIII sequencing, that was Professor Tuddenham's project, he had to use a very serious anti-proteolytic agent -- it was actually nerve gas -- to stop the clotting factors prevent activation of the clotting cascade, in order to get pure Factor VIII at the end of it.

Q. If I can just interject there, a couple of things arise from that. The variability of the product.

A. Yes.

Q. Does that make it hard to translate from a laboratory-based product on which you can do your experiments and test the potential, into a mass produced product which could actually be marketed?

A. Yes, the main thing you have to remember when you're producing any product is quality, safety, and efficacy. If you're getting variability yields and you don't know why, then you don't have the quality. And not the safety, either.

Q. The process you were talking about with Dr Tuddenham there -- I'm going to come on to recombinant shortly, but there's an article that he's written that I know that you have seen. I'm not going to bring it up, but

158

Q. -- as part of a product --

A. Not suitable for a therapeutic product, no.

Q. Thinking back now, are you able to put a timescale on when you became aware that these problems were going to be insurmountable in terms of bringing a product to market?

A. Well, I think I became aware of it when I was actually at Elstree.

Q. This is 1980 to 1981?

A. Yes. If that's when it was, yes. And I spent a couple of months after that in Orsay, in Paris, and we had the same problems. We couldn't get the thing to be stable. You know, one day, we got something that we thought was 75% yield, then if you left it on the bench, it had gone down to 25 per cent. So it was really not looking very viable at this stage in Elstree.

Q. You were in Paris from April 1981, according to paragraph 17 of your statement, for a few months?

A. Yes, for a few months, yes.

Q. By that stage do you think you were aware that this wasn't really going to be --

A. Well, it did just never seemed to -- no, I ...

Q. I am just going to ask from a document to be brought up on the screen. It's BPLL00016007_018, please,

160

1 Soumik. BPLL0016007_018. This a letter which is
 2 written to Mr Heath from Dr Allain in Paris.
 3 A. Mm.
 4 Q. I know you have seen this in the files we provided you
 5 with. He says:
 6 "Dear David.
 7 "I enclose a summary of the results of PE5
 8 phase 1 which has worked out very well.
 9 "We are presently doing some additional
 10 experiments on filtration and freeze drying that looks
 11 very promising. The loss in yield seems quite
 12 reasonable.
 13 "I have done all the background work for the
 14 next step and the raw material is now being prepared.
 15 I am confident that step 2 will be as successful as
 16 step 1."
 17 So that's Dr Allain's view in this letter on
 18 27 May 1981.
 19 A. Yes.
 20 Q. I'm cautious about reading too much into one letter in
 21 a snapshot in time, but around that time, had you
 22 already doubts developing in your mind?
 23 A. I did. And obviously Jean-Pierre Allain and I worked
 24 together on the preparation in stage -- I think it was
 25 step 2, in Paris, and, we had the same problems as I'd

161

1 collected -- in fact I think it was almost fresh --
 2 cryoprecipitate, from very good quality --
 3 specifically for those clinical trials, because it was
 4 done on four patients, I think, three haemophiliacs
 5 and one von Willebrand.
 6 Q. Yes.
 7 A. Yes. And specifically for that. It was made in the
 8 clean room at BPL, and -- specifically for that
 9 experiment. And that showed that the Factor VIII that
 10 we got was good recovery, which suggests it was quite
 11 good Factor VIII, and that it didn't work in
 12 von Willebrand's disease, which is what we might have
 13 expected because of the nature of the protein at that
 14 point.
 15 Q. So an example of how, when it is done in very closely
 16 controlled circumstances, it could work, but that --
 17 A. Yes, and that was probably due to the fact that the
 18 cryoprecipitate was very good quality. The stuff --
 19 the product I was working with at BPL was mostly
 20 freeze-dried product that had failed quality control
 21 for some reason. Mostly due to pyrogenal bacteria, or
 22 pyrogen really, or something of that order. So
 23 I worked on that, which had been freeze-dried and was
 24 not terribly good quality.
 25 The stuff that probably -- the cryo that I

163

1 had at BPL. So I think his letter was optimistic.
 2 Q. This letter, of course, is referring to him at the end
 3 of step 1.
 4 A. Yes.
 5 Q. You subsequently worked with step 2 --
 6 A. Yes.
 7 Q. -- and it was disappointing?
 8 A. Yes. And we never really went to step 3, I don't
 9 think.
 10 Q. We heard earlier, I believe you were in the room for
 11 it, about Dr Tuddenham's lecture from some point in
 12 1981 in which he expressed some optimism.
 13 A. Mm.
 14 Q. There is also a paper -- I won't bring it up, but
 15 BPLL0016007_026 -- the authors are Tuddenham, Lane,
 16 Rotblatt, Johnson, Snape, you and Kernoff, "Response
 17 to infusions of polyelectrolyte fractionated human
 18 factor VIII concentrate ..."
 19 A. Yes.
 20 Q. "... in human haemophilia A and von Willebrand's
 21 disease.
 22 A. Yes.
 23 Q. Both of those -- both the lecture and the paper --
 24 express some hope for the method?
 25 A. Yes. We made a batch at BPL with carefully

162

1 worked with on this -- on that product, was possibly
 2 fresh and probably never been even frozen. It was
 3 probably made straight from that. So if you had
 4 perfectly good quality cryo, then maybe it would work.
 5 Q. You also wrote a short paper on viral inactivation
 6 which is dated October 1983.
 7 A. Yes.
 8 Q. I won't bring it up, but it's ISPN0000409_009.
 9 A. Viral separation.
 10 Q. Sorry, viral separation, my error.
 11 If I may summarise the paper, it's that the
 12 in vitro experiment that you did showed viral
 13 separation.
 14 A. Yeah.
 15 Q. But as per Dr Tuddenham's lecture, there was a need to
 16 look at that in clinical trials if that were to be
 17 proved to be safe and efficacious?
 18 A. Yes, we showed that in Professor Thomas's lab. We
 19 added hepatitis to the concentrate and then worked it
 20 over the polyelectrolyte, and that showed that there
 21 was no absorption of the virus to the ion-exchange
 22 resin.
 23 Q. Meaning that the ultimate product would be free --
 24 A. Yes.
 25 Q. -- of hep B?

164

1 A. Would be separated from it, yes.
 2 Q. Was there any expectation that it would also clear
 3 NANB hepatitis?
 4 A. Possibly for the same reason.
 5 Q. You say "possibly" but that, of course, couldn't be
 6 tested for at the time?
 7 A. No, no.
 8 Q. Hence the need for clinical trials. We will come back
 9 to the clinical trial in a second. Before I do, we
 10 know that you developed your concerns about how viable
 11 this was going to be as a product. Did you share
 12 those concerns with Mr Heath?
 13 A. Yes.
 14 Q. We've seen some of the things that he was saying in
 15 1981. To give you just one example from July 1981,
 16 the human protein plan. He said:
 17 "Recent production yields, clinical trials and
 18 hepatitis tests have adequately demonstrated that the
 19 major protein, Factor VIII:C, can be produced
 20 economically, is very efficacious and is most probably
 21 free from hepatitis activity."
 22 That is from July 1981. In your view, was that
 23 a claim that was justified?
 24 A. Err ... I think it was optimistic at that point.
 25 Q. This was at a point in time when Mr Heath and Speywood

165

1 some of the things they did and that was a shame. And
 2 he also ended up -- he could very easily, because he
 3 was the way he was, put people's backs up, and that
 4 was certainly the case with the bio products
 5 laboratory, because of the different cultures. Bio
 6 products was there to make blood products, and get as
 7 much as possible out for the population.

8 David was constantly looking into the future,
 9 and trying to raise money, in those days, was
 10 difficult, and therefore you tend to overpromise, or
 11 he was over-promising.

12 The porcine Factor VIII was working very well,
 13 mainly because I think a lot of the clotting that
 14 happened and the problems with clotting happened
 15 before the plasma ever got from the abattoir to what
 16 we were working with, and we were left and the yields
 17 were probably pretty dreadful from porcine blood, but
 18 it was easier, in that sense, because we had -- but
 19 with Factor VIII you were so totally dependent on
 20 fresh frozen good quality human plasma, human blood
 21 that you had to be so careful about the yield.

22 So he had -- he was optimistic because the
 23 porcine was going well. He maybe thought that the
 24 human should be going well because the porcine was,
 25 and that was his -- probably his reasons for doing it.

167

1 was seeking a £4 to 5 million investment, half of
 2 which was coming from public funds. In that context,
 3 do you think that that claim was one that could
 4 reasonably have been made?
 5 A. Um ... with hindsight, it was perhaps a bit economical
 6 with the truth.
 7 Q. Were you involved in any way in the --
 8 A. No, no.
 9 Q. If you had been involved, what would you have said to
 10 Mr Heath about it at the time?
 11 A. Well, I would have said -- I would have suggested that
 12 he moderated his language.
 13 Q. Sorry --
 14 A. Well, I think I should say something about David,
 15 because he was very entrepreneurial, and he was
 16 entrepreneurial from very early -- he took on
 17 a porcine Factor VIII; why on earth would he do that?
 18 He was a pharmacist. It was a very strange thing to
 19 do. But he saw the potential in it. He took on the
 20 polyelectrolyte fractionation to improve that porcine
 21 Factor VIII, which, again, was very entrepreneurial.
 22 And obviously the recombinant Factor VIII came from
 23 him and he worked on it.
 24 But the trouble was that he was very -- not very
 25 good at man management, and people let him down in

166

1 Q. But by July 1981 he was aware, was he, of your
 2 reservations?
 3 A. He knew but he probably thought I was just being, you
 4 know, slightly negative on the subject, quite likely.
 5 Q. You were the chief scientist of Speywood, and he was
 6 a pharmacist by trade, as I understand it?
 7 A. Yes, he was.
 8 Q. The clinical trial of Mono C, (sic) the Factor VIII
 9 product. Were you involved in putting the application
 10 for the clinical trial together?
 11 A. Well, I must have been but I don't remember doing it.
 12 But we must have done it.
 13 Q. We know that it went in at some point in 1982, and we
 14 also know that progress on the product had slowed by
 15 that stage. What was the purpose of having a clinical
 16 trial in those circumstances?
 17 A. I think it was to -- well, basically to check to see
 18 whether it was safe and whether the concept of
 19 Factor VIII:C, which is what it was, the clotting
 20 activity, as opposed to the complex, which circulates
 21 in plasma with the von Willebrand factor sort of
 22 attached to it, or that's what was thought, whether it
 23 would survive like that in the circulation.
 24 Q. Was there any feasible prospect, as of 1982, of
 25 bringing this to a product that could be placed on the

168

1 market?

2 **A.** At the time of clinical trial?

3 **Q.** Yes.

4 **A.** Um ... maybe in some -- I don't -- I don't know how to

5 answer that question.

6 **Q.** Let me --

7 **SIR BRIAN LANGSTAFF:** As best you can.

8 **A.** As best I can. Um ... because the question is: why

9 did you do a clinical trial?

10 **MR HILL:** No smoke and mirrors here, that's the --

11 **A.** That's the question.

12 **Q.** If you're in the circumstances where it is unlikely

13 that this will ever be made into a --

14 **A.** Well, it was made at the bio products laboratory, that

15 product. So they must have thought something positive

16 about it at that stage, in spite of the difficulties

17 that we had with it. So maybe they thought that they

18 should check that it would work, because it was

19 a different entity. So, maybe, you know, things

20 might -- things might work out. Maybe I was being too

21 negative about it. Maybe it was possible to make it

22 work.

23 But the other question that needed to be

24 answered is would it actually work in the circulation?

25 Never mind whether the -- you know, because if you can

169

1 **Q.** So this is a meeting on 2 June 1983.

2 **A.** Yeah.

3 **Q.** The subject "Clinical trials certificate for

4 Mono VIII:C".

5 **A.** Yes.

6 **Q.** Then "source of cryoprecipitate"?

7 **A.** Which was this Alpha cryoprecipitate, which was being

8 bought in 100-kilo lots -- was it 100-kilo lots -- in

9 large lots, as a frozen cryoprecipitate, to make -- to

10 try to make Mono Factor VIII:C out of. It wasn't that

11 material that went into the patients. The product

12 that went into patients came from Elstree.

13 **Q.** Yes, I think we're at slightly cross purposes.

14 **A.** Oh right, okay.

15 **Q.** So the paper I referred you to earlier, which you

16 co-wrote with Dr Lane, et cetera, et cetera, and

17 Dr Tuddenham, that was a product that was made in

18 Elstree --

19 **A.** In Elstree, yes.

20 **Q.** -- and that was used, as you said, on three

21 patients --

22 **A.** And one von Willebrand's.

23 **Q.** -- with haemophilia A and one von Willebrand's

24 patient.

25 **A.** Yes.

171

1 get the production process to work, which I couldn't,

2 but other people might have got it to work, would

3 Factor VIII:C on its own last in the circulation? And

4 yes, it did.

5 **Q.** Do I take it from your answer that you were trying now

6 to help us by looking back and thinking what the

7 thinking might have been, but you weren't actually --

8 you're not able to say what you yourself thought at

9 the time?

10 **A.** Yes.

11 **Q.** I should say, out of fairness, that we looked at the

12 1983-1985 business plan and, as we discussed during

13 the presentation, the door was not being closed

14 absolutely on Factor VIII through polyelectrolyte

15 fractionation, although there were concerns about how

16 feasible it was going to be.

17 **A.** Mm.

18 **Q.** We know that the initial application was turned down,

19 and I referred to a meeting that you attended on

20 2 June 1983. If we could have that on screen, please,

21 Soumik. It's IPS --

22 **A.** That wasn't the same product.

23 **Q.** Ah. If we bring it up on screen, perhaps you can

24 assist us with it. IPSN0000165_109, please.

25 **A.** Yeah.

170

1 **Q.** This is different. This is the application for the

2 clinical trial --

3 **A.** Yes.

4 **Q.** -- which was made at some point in 1982?

5 **A.** Yes.

6 **Q.** That was what I was discussing with you a moment ago?

7 **A.** Yes, yes.

8 **Q.** Why it was that there was an attempt to have

9 a clinical trial at that stage.

10 **A.** Oh, from this -- yes.

11 **Q.** Does that alter your assessment, any of your answers,

12 now that we're clear about what we're talking about?

13 **SIR BRIAN LANGSTAFF:** I don't see why it should alter your

14 answers, but just that we now know you're talking

15 about -- we're quite clear which trial you're now

16 talking about.

17 **A.** Yes. I can't ... I recall this and, as you know in

18 the plans, there was the idea of building a facility

19 to make human Factor VIII from this frozen

20 cryoprecipitate. I wasn't certain about it at all.

21 But I'm not sure why we applied for a clinical trial

22 certificate using this material.

23 **MR HILL:** The idea was that the material -- the

24 cryoprecipitate would come up in from Alpha, and then

25 you would fractionate it --

172

1 A. It was a frozen paste that you re-suspended. We
 2 did -- I did do some work with it. It was a frozen
 3 paste that was re-suspended and then put over the
 4 polyelectrolyte.
 5 Q. I'd like to just look at what was said at this
 6 meeting. There was you and Anne Walton from Speywood?
 7 A. Yes.
 8 Q. The note is by -- the initials are EAW. Is that Anne
 9 Walton?
 10 A. Yes.
 11 Q. Who was Anne Walton?
 12 A. She was -- she did some marketing but she also focused
 13 in on regulatory affairs.
 14 Q. Was she a scientist?
 15 A. Yes.
 16 Q. The participants from the DHSS, a Dr Fowler and
 17 Dr Purves.
 18 A. Yes.
 19 Q. And if we could just look at the note and I'll read it
 20 through to you.
 21 "1. Dr Fowler was of the opinion that, despite
 22 the controversy surrounding US imports as a result of
 23 AIDS, our application will not be judged prejudicially
 24 by the CSM if we pursue it with Alpha cryo cited as
 25 source material. There have been suggestions in

173

1 A couple of points about that. Paragraph 1, the
 2 discussion of the potential ban on US blood products,
 3 and the recognition that that was impractical. Are
 4 you able to help us with who was saying that it would
 5 be impractical to ban US blood products?
 6 A. No.
 7 Q. Would you or Anne Walton have been in a position to
 8 make that observation? Do you think it's more likely
 9 to have come from the DHSS officials?
 10 A. I think it's more likely to have come from the DHSS
 11 officials.
 12 Q. But the references to the source material choice being
 13 "based on commercial and scientific grounds", as
 14 opposed to what other grounds?
 15 A. Um ... as opposed, presumably, to citing the source of
 16 the raw material. So in other words, it's coming from
 17 the US. I don't know what else.
 18 Q. Are you able to assist us any further now about the
 19 contents of that meeting and what was discussed at it?
 20 Can you remember it at all?
 21 A. I can't remember it. I can't remember it very well at
 22 all, no.
 23 Q. Do you know why it was that you were asked to go from
 24 Speywood?
 25 A. Well, Anne would have set it up, and I would have gone

175

1 certain quarters about the banning of importation of
 2 all US blood products but the impracticality of this
 3 is recognised by those who were well informed in this
 4 area and a ban does not, therefore seem likely. An
 5 application based on Alpha cryo would (or should) be
 6 judged solely on its scientific merit.

7 "2. The possibility of leaving an application
 8 open-ended with respect to source material was
 9 discussed and dismissed as unacceptable.

10 "3. We were advised that if a change in source
 11 material is desired, the application might proceed
 12 more easily if the licensing of the import or the cryo
 13 were included in the CTC application. The
 14 responsibility wore the quality of the raw material
 15 would then be entirely Speywood's and in addition, the
 16 cryo would then be licensed for importation only for
 17 the purpose covered by the CTC."

18 If we go over to the next page, the possible
 19 courses of action are discussed. I won't go thorough
 20 that, but it says:

21 "In conclusion it appears that the use of US
 22 cryo will not prejudice our case with the licensing
 23 authorities and therefore our choice of source
 24 material can be based on commercial and scientific
 25 grounds."

174

1 along because of being -- whenever that meeting was,
 2 still being chief scientist of Speywood. The most
 3 experienced for the human Factor VIII.
 4 Q. Can you help us with whether or not a further
 5 application was made for a clinical trial certificate
 6 on that product?
 7 A. I don't think it was.
 8 Q. Do you know why it wasn't pursued?
 9 A. No -- well, yes, I probably do, because I don't think
 10 there was anywhere to make it.
 11 Q. The facility that had been planned wasn't built?
 12 A. No. And I think at one stage it might even have been
 13 thought you could share the facility with porcine, but
 14 that became a no-goer when -- because of virus
 15 concerns, and it had to be separate.
 16 Q. That is something we saw with the business plan about
 17 the DHSS no longer allowing a multi-purpose site.
 18 A. Yes.
 19 Q. Looking back on human Factor VIII and polyelectrolyte
 20 fractionation, was this always a project that was
 21 ultimately bound to fail, given the knowledge and
 22 equipment and availability of material in the early
 23 1980s, or were there any missed opportunities to have
 24 developed it further?
 25 A. Sorry, do you mean with respect to human Factor VIII?

176

1 Q. Yes.
 2 A. I don't think it was going to fly. It worked very
 3 nicely for porcine Factor VIII.
 4 Q. But not for human?
 5 A. But not for human.
 6 Q. On recombinants -- I'm going to take this very
 7 briefly, if I may -- your role was important but
 8 limited in helping to provide the purified -- the
 9 first step of the purification process?
 10 A. Yes.
 11 Q. And then passing that on to Dr Tuddenham and his team
 12 to work on thereafter?
 13 A. Yes.
 14 Q. Mr Heath's view that we heard earlier was that this
 15 was something of a tragic failure by the UK to
 16 capitalise upon the work that was done, because the --
 17 ultimately the work was taken forward by Genentech,
 18 an American company, and subsequently by other
 19 American pharmaceutical companies as well?
 20 A. Yes.
 21 Q. Could I ask for your opinion on that view from
 22 Mr Heath, and in particular upon the question of
 23 whether, if other steps had been taken, it would have
 24 led to a quicker development of recombinant products
 25 or just a development by a British firm as opposed to

177

1 it was never going to be a bacteria. And the Oxford
 2 people, who were working on the project, were working
 3 in yeast, which was not terribly much better for a big
 4 protein like Factor VIII. There was not much known
 5 about the structure either.

6 I do recall that after some had been purified,
 7 it was sent to ICRF, but Mike Waterfield, who was
 8 going to do some sequencing, couldn't get time on the
 9 sequencer.

10 So when it went over to Genentech, they had
 11 a whole department with several people, sequences
 12 dedicated to the project. It was just completely
 13 different.

14 So going back to your original question, which
 15 I've probably not answered, I don't know, but it came
 16 down to the fact that I think the funding from Prutec
 17 and BTG was not used in a very constructive way, and
 18 that goes back to what I said originally about David,
 19 that he gave responsibility to people for doing
 20 things, and the person that stood out was Ted
 21 Tuddenham. The rest of them didn't really have the
 22 technology to do it. And Prutec and BTG got a bit
 23 upset about that, and that's when the trouble came,
 24 and David was removed and put to one side.

25 He wasn't terribly popular with a lot of people

179

1 an American firm?
 2 A. I think what happened with the recombinant Factor VIII
 3 was that, as I understood it, the -- there was
 4 a certain amount of money brought forward by Prutec
 5 and BTG, and that was sort of -- that money was
 6 dispersed around various Oxford facilities to try to
 7 clone the gene, to sequence it -- sequence it first,
 8 purify it, et cetera -- and none of that programme
 9 really worked out. The only bit of that programme
 10 that worked out was Ted Tuddenham's purification.
 11 The UK didn't really have the technology at the
 12 time. In a paper that Ted wrote, Ted Tuddenham wrote,
 13 he said that they had, and I recall that they did,
 14 they interviewed Genentech, Genetics Institute,
 15 with -- another American company, and Celltech in this
 16 country, after Ted had presented his work on
 17 purification. And Celltech in this country was at the
 18 stage of making protein -- I think it was rennet -- in
 19 bacteria. Factor VIII was a big protein. Nobody knew
 20 what the structure was. It needed to be done in
 21 mammalian cells.

22 David had actually written into the original
 23 agreement that if it was mammalian cells then the UK
 24 manufacturing rights would stay here. So he was
 25 astute enough to realise that, and they realised that

178

1 because of his, sort of, rather -- what shall we
 2 say -- his sort of -- his energetic sort of -- I can't
 3 think of the right word, but he wanted -- he was
 4 passionate about what he wanted, but that passion
 5 tended to make him promise too much and achieve -- not
 6 achieve it, and I don't think that made him a very
 7 good source for somebody to invest in. I don't think
 8 they were very happy with it.

9 MR HILL: Thank you. Those are the questions I have for
 10 you.

11 Sir, may I suggest a few minutes break while we
 12 allow the Core Participants -- I don't anticipate
 13 there will be many questions from them -- I received
 14 a great deal of assistance in advance,
 15 Ms Middleton's --

16 SIR BRIAN LANGSTAFF: Well, we will see, because the
 17 question may have prompted some questions. What we'd
 18 always do, I don't know if you've watched any of the
 19 Inquiry at all before you came, but what we always do
 20 is we take a break when a witness has finished the
 21 evidence which the Inquiry counsel has to ask to allow
 22 the Core Participants -- they come from all different
 23 perspectives -- to ask questions through counsel of
 24 the witness and, that way, we make sure that we try to
 25 collect as many different questions, answering

180

1 different viewpoints, as there may be.
 2 It does mean you've got to wait a little bit
 3 longer. I can't promise you how long but we'll say 15
 4 minutes and come back at quarter to five, and we will
 5 see then what questions there are, if there are any.

6 A. Okay.

7 **SIR BRIAN LANGSTAFF:** So quarter to five.

8 **THE WITNESS:** Right.

9 (4.27 pm)

10 (A short break)

11 (4.45 pm)

12 Questions from CORE PARTICIPANTS

13 **MR HILL:** Ms Middleton, a few questions from some of the
 14 Core Participants that I've been invited to ask you.

15 This means we're going to jump rather from one topic
 16 to another.

17 A. Yes, okay.

18 Q. Starting with your time still in Scotland, and the
 19 reference that you made to a colleague sadly dying of
 20 hepatitis B, were any changes made to the way you
 21 operated in response to that death?

22 A. Um ... immediately, yes, we did become much more
 23 aware, I think, of the potential problems with the
 24 plasma we were dealing with. The person that had the
 25 accident, it was a known infected patient that caused

181

1 Q. I am going to -- this is a document that you haven't
 2 seen and I don't think is on our system, so I'm just
 3 going to read a short passage to you. It comes from
 4 a meeting in May 1985, a meeting in Scotland of the
 5 Scottish National Blood Transfusion Service. And it
 6 refers to a request that has come from you to the
 7 SNBTS -- and forgive me, I've just lost my place
 8 temporarily.

9 What is recorded in the minutes is this you have
 10 asked:

11 "... to obtain from the SNBTS about 50 litres
 12 per annum of fresh frozen plasma from which to
 13 developed a range of reagent biodepleted plasmas."

14 You had approached SNBTS because of "concern
 15 that the haemophilic plasma substates in use at
 16 present might be contaminated with HTLV-III or
 17 hepatitis".

18 A. Yes.

19 Q. First of all, do you have any recollection of making
 20 such a request?

21 A. I don't, but I do remember the project, so ...

22 Q. Could you explain what that project was?

23 A. The project was to use monoclonal antibodies, the ones
 24 developed at the Royal Free, to make
 25 a Factor VIII-deficient plasma. Factor VIII-deficient

183

1 the problem there. And that was in a lab, which was a
 2 separate lab, where they were doing studies with the
 3 hepatitis virus.

4 But as far as PFC was concerned, obviously we --
 5 I suppose we did become much more aware of the
 6 potential.

7 Q. Do I understand from that answer that the colleague
 8 was somebody who worked within the Edinburgh Royal
 9 Infirmary rather than within the PFC?

10 A. Yes, she wasn't in the PFC, she was in the Royal
 11 Infirmary. But in the same sort of department, blood
 12 transfusion.

13 Q. Do you know if the accident and the death was notified
 14 to any public health body?

15 A. I'm sure it was. It was a prick. It was an
 16 accidental prick with a needle, which was, you know,
 17 tiny, but yeah, that's what happened.

18 Q. Staying with your time in Scotland, and moving to
 19 Glasgow, do you recall if the blood that you were
 20 dealing with, which was taken from patients with
 21 haemophilia, was marked as being high risk?

22 A. I don't think it was.

23 Q. Do you remember if any particular procedures were in
 24 place for how you dealt with and handled that blood?

25 A. No, I don't think so.

182

1 plasmas from haemophiliacs were used as reagents to
 2 test for the potency of a Factor VIII concentrate. So
 3 rather than use -- these obviously became much more
 4 potentially risky -- that was thought to be the case,
 5 as reagents. And therefore, we decided to use normal
 6 plasma, and deplete it of Factor VIII using monoclonal
 7 antibody column to deplete it.

8 Q. In order to create assays?

9 A. To use for assays.

10 Q. So everybody has the reference, it's PRSE0004075, and
 11 the minutes record that it was considered not
 12 appropriate to provide the material because there was
 13 no surplus at the time.

14 A. Right.

15 Q. Do you know if you were able to obtain an equivalent
 16 material from elsewhere?

17 A. I did get some from somewhere. I bought some from
 18 somewhere. But it wasn't the United States. I'm not
 19 quite sure. It can't have been English, British --
 20 I don't know where it -- (overspeaking) --

21 Q. Because it was commercial?

22 A. It must have been commercial.

23 Q. And your desire was to avoid the material coming from
 24 the United States because of perceived risk of
 25 HTLV-III?

184

1 A. Well, it was to come from -- there was no point in
 2 doing it unless it came from a clean source. And
 3 I can't recall now where it did come from, but we did
 4 use that technology, and subsequently it was -- the
 5 assay was developed and was sold commercially by an
 6 organisation called Diagnostic Reagents who were based
 7 in Oxford and who supplied -- probably still do --
 8 reagents for coagulation factors.

9 Q. Moving on to a different topic, was there any
 10 discussion about proposed research concerning AIDS,
 11 HIV, HTLV-III, at Speywood during your time there?

12 A. Not AIDS, no. I think AIDS and HIV were only really
 13 identified -- started to be identified in '82, '83.

14 Q. But Speywood wasn't involved in any --

15 A. No.

16 Q. Specific projects that tried to address the risk of --

17 A. No.

18 Q. -- HIV, HTLV-III, et cetera?

19 A. No.

20 Q. Further question. How much of your work, either at
 21 the PFC or at Speywood, informed by a knowledge of the
 22 different severities of haemophilia in patients, mild,
 23 moderate and severe haemophilia?

24 A. Um, I'm not sure I understand the question. We were
 25 making concentrates to treat haemophilia, whatever the

185

1 A. (Witness nodded)

2 SIR BRIAN LANGSTAFF: But you moved to Liberton --

3 A. Yes.

4 SIR BRIAN LANGSTAFF: -- did you? That would be about
 5 1973, I think.

6 A. Possibly, yes.

7 SIR BRIAN LANGSTAFF: What was life like there?

8 A. Oh, well, that was very different, because it was
 9 purpose-built facility.

10 SIR BRIAN LANGSTAFF: So you had a purpose-built facility
 11 there.

12 A. Yes.

13 SIR BRIAN LANGSTAFF: Then when you moved down south to
 14 Wrexham, you found yourself in a Portakabin in --

15 A. And a garage.

16 SIR BRIAN LANGSTAFF: A garage?

17 A. Yes. I only did the research work in the garage, I
 18 should say.

19 SIR BRIAN LANGSTAFF: [Laughs]. So I -- would I be right
 20 in thinking that David Heath, whose enthusiasm had
 21 recruited you to post --

22 A. Yes.

23 SIR BRIAN LANGSTAFF: -- he would have had some schemes
 24 and dreams for improving those facilities.

25 A. Well, he did, ultimately. They did improve that

187

1 level, however severe or mild it was.

2 Q. But were you aware of the distinctions between --

3 A. Yes.

4 Q. -- mild, moderate and severe?

5 A. Yes.

6 Q. Does it come back to the fact that your role as
 7 a scientist was to seek to make the product --

8 A. Yes.

9 Q. -- and not to decide how it should be used by the
 10 clinician --

11 A. Yes.

12 Q. -- and the patient?

13 A. Yes, yes. Although in discussions with the
 14 clinicians -- because we were very close to the
 15 clinical use, particularly in the UK -- we did get to
 16 learn about what people were doing, what clinicians
 17 were doing for treatment, et cetera.

18 MR HILL: Those are, sir, the questions that we have had
 19 from the CPs. I turn to you now, sir, if you have
 20 anything further.

Questions from SIR BRIAN LANGSTAFF

22 SIR BRIAN LANGSTAFF: I just have a couple of questions.
 23 You've described life in the basement in the old
 24 Royal Infirmary in Lauriston Place, which I can
 25 imagine was like working in a basement.

186

1 facility and they had a purpose-built production
 2 facility for Hyate:C, on the Wrexham estate.

3 SIR BRIAN LANGSTAFF: So you did eventually get the
 4 facilities you wanted, for research as well?

5 A. Well, it didn't happen until -- um, I'm not even sure
 6 of the timing of it, but it was '82/'83. I mean, it
 7 was later than I was -- my -- all my work was done in
 8 the garage, and the -- and the Portakabin, under
 9 laminar flow, I should say. We did clean up the
 10 Portakabin.

11 SIR BRIAN LANGSTAFF: Did you know -- this is a second
 12 topic -- anything about the Speywood's continuing to
 13 market Koate without, it may be thought, telling Koate
 14 they were doing it by buying it and sourcing it --

15 A. No, I didn't.

16 SIR BRIAN LANGSTAFF: -- from an intermediary.

17 A. No, I didn't.

18 SIR BRIAN LANGSTAFF: Is that the sort of thing that David
 19 Heath might do, as you would see him?

20 A. Well, I suppose -- I guess, I guess he might have
 21 done. I'm sorry to say.

22 SIR BRIAN LANGSTAFF: Well, you have a slightly,
 23 I suspect, a slightly ambivalent attitude towards him.

24 A. Well, he was a -- he was the sort of person -- I had
 25 two mentors. One was Jim Smith and one was David

188

1 Heath, really, on the business side. But I didn't --
 2 but only in the sense that -- it was all his ideas and
 3 everything else that I admired. But when it came to
 4 doing -- he did do certain things that I thought were
 5 a little bit, a bit near the edge, and I didn't
 6 really -- it wasn't my style at all and I didn't
 7 really like it, and it was very unfortunate, because
 8 it caused problems with BPL, which I could see why.
 9 And my two mentors didn't get on at all. Jim Smith
 10 and -- because they were opposite ends of the
 11 spectrum.

12 So it caused difficulties.

13 **SIR BRIAN LANGSTAFF:** Yes. And --

14 **A.** Sir, I'm afraid it was the downside, the upside being
 15 he had these amazing ideas, and some of the ideas like
 16 putting polyelectrolyte into a donor centre to collect
 17 plasma straight from the donor on to the
 18 polyelectrolyte and then fractionating it on site, as
 19 it were, I mean that's a very interesting idea. But
 20 obviously fractionation, plasma fractionation was not
 21 going to carry on in the same way it, you know, it was
 22 never going to happen in the future, but had plasma
 23 fractionation gone on for, you know -- had recombinant
 24 technology not started to take over, then it would
 25 have -- it was a really good idea.

189

1 us. And can I just tell you, that's very much
 2 appreciated. And thank you for coming the way you
 3 have down here, and I hope you have a good trip back
 4 tonight.

5 **THE WITNESS:** Thank you.

6 **SIR BRIAN LANGSTAFF:** Mr Hill, what does next week hold in
 7 store for us?

8 **MR HILL:** On Tuesday, sir, we will return to the
 9 presentations. We will complete the presentation on
 10 Speywood, and then we will move on to the last of the
 11 current set of presentations on pharmaceutical
 12 companies, which is on Alpha and associated companies.
 13 Then later in the week we will move on to some
 14 presentations about Haemophilia Centres.

15 **SIR BRIAN LANGSTAFF:** Very well. So ten o'clock on
 16 Monday. Ten o'clock.

17 **MR HILL:** Sir, Tuesday.

18 **SIR BRIAN LANGSTAFF:** I've done it again, sorry! I do
 19 apologise. It will be ten o'clock for me, or before
 20 ten o'clock for me on Monday, but for you, ten o'clock
 21 on Tuesday -- for us, ten o'clock on Tuesday.

22 (5.00 pm)

23 (The hearing adjourned until 10.00 am on Tuesday,
 24 5th October 2021)

25

191

1 So he did have very good ideas. But sometimes
 2 bringing them to fruition was not quite so good.

3 **SIR BRIAN LANGSTAFF:** Yes, it was a case of the next big
 4 thing, as it were.

5 **A.** A little bit. Yes, I'm afraid so.

6 **SIR BRIAN LANGSTAFF:** Yes, well, thank you. That's all
 7 that I have to ask.

8 **A.** Okay.

9 **MR HILL:** Ms Middleton, with all of our witnesses, we ask
 10 at the end if there is anything else that you wish to
 11 say in your evidence.

12 **A.** Um, no, I don't think so. Thank you.

13 **MR HILL:** Thank you, sir.

14 **SIR BRIAN LANGSTAFF:** Well, we have asked you a number of
 15 difficult questions this afternoon, and detained you
 16 I think for an hour longer than you might have hoped
 17 this afternoon. I'm sorry about that.

18 **THE WITNESS:** That's all right.

19 **SIR BRIAN LANGSTAFF:** But I'm very grateful. And you've
 20 done two, in particular, difficult things it seems to
 21 me. You've explained to us how the polyelectrolyte
 22 system works in terms which I think I can understand,
 23 and those around me will, and you've answered
 24 questions which you didn't really want to have to
 25 answer, but have done so, and done so in order to help

190

1 INDEX	
2 Presentation by Counsel to the	1
3 Inquiry on the Pharmaceutical	
4 Companies (continued)	
4 MS SARAH MIDDLETON (affirmed)	101
5 Examination-in-chief by MR HILL	101
6 Questions from CORE PARTICIPANTS	181
7 Questions from SIR BRIAN LANGSTAFF	186

8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

192

MR HILL: [83] 1/6 23/23 27/13 28/23 29/1 29/5 29/8 29/16 29/24 30/3 30/8 38/11 38/14 38/18 43/7 43/9 43/25 44/6 45/3 45/6 45/9 45/11 46/19 47/5 48/13 50/23 51/1 51/18 51/21 52/8 53/17 53/19 54/20 65/4 65/9 65/12 65/16 65/19 65/24 66/4 66/17 66/20 67/1 67/4 67/9 88/16 88/24 89/1 89/3 89/7 89/10 90/11 90/16 90/19 91/22 92/3 92/11 97/20 97/25 100/25 101/8 101/12 101/23 111/20 116/19 119/8 120/5 127/16 130/23 136/2 138/13 155/10 155/16 155/20 169/10 172/23 180/9 181/13 186/18 190/9 190/13 191/8 191/17 SIR BRIAN LANGSTAFF: [107] 1/5 27/12 28/21 28/24 29/3 29/6 29/12 29/22 30/2 30/7 38/8 38/12 38/15 43/5 43/8 43/23 44/5 45/1 45/4 45/7 45/10 46/18 47/4 48/10 50/21 50/24 51/12 51/20 52/3 53/7 53/18 54/19 65/3 65/7 65/10 65/13 65/17 65/22 66/2 66/14 66/19 66/25 67/2 67/6 88/15 88/22 88/25 89/2 89/5 89/9 90/10 90/13 90/18 91/21 92/2 92/9 97/18 97/22 100/22 101/5 101/16 101/21 111/17 116/17 118/18 119/16 119/20 120/1 120/4 127/9 127/14 130/22 135/25 137/19 137/24 138/1 138/4 138/7 138/11 155/8 155/11 169/7 172/13 180/16 181/7 186/22 187/2 187/4 187/7 187/10 187/13 187/16 187/19 187/23 188/3 188/11 188/16 188/18 188/22 189/13 190/3 190/6 190/14 190/19 191/6 191/15	191/18 THE WITNESS: [4] 101/22 181/8 190/18 191/5 ' '70s [1] 115/10 '76 [1] 13/2 '77 [1] 13/3 '79 [3] 65/11 66/19 142/25 '82 [2] 185/13 188/6 '82/'83 [1] 188/6 '83 [2] 185/13 188/6 'A [1] 81/11 'A fibronectin [1] 81/11 'At [1] 81/6 'biological' [1] 50/5 'cryo' [1] 83/7 'Fibronectin [1] 81/10 'good' [1] 18/23 'hepatitis [1] 130/8 'human [1] 76/11 'loss' [1] 20/21 'polyelectrolyte [1] 75/8 'PPSB' [1] 109/20 'Pure [1] 88/2 'self [1] 69/10 'self-sufficiency' [1] 69/10 'Speywood [1] 4/20 'stop [1] 34/24 'Substantially [1] 81/8 'suspect' [1] 18/13 -- -- increasing [1] 138/16 -- worked [1] 105/23 0 0.07 [2] 112/10 116/16 0.07 per cent [1] 116/24 0.15 [1] 127/10 0004 [1] 10/18 001 [9] 11/15 17/15 23/9 24/9 28/9 32/19 87/7 87/16 89/19 002 [2] 47/20 47/23 003 [3] 10/13 17/18 47/24 005 [4] 26/20 47/20 68/1 80/6 006 [1] 17/17 008 [1] 16/25 009 [1] 164/8 011 [1] 17/1 013 [1] 67/23 016 [1] 92/23	018 [6] 23/10 23/22 28/7 33/15 160/25 161/1 019 [5] 9/21 13/24 16/25 53/25 74/18 021 [1] 16/24 022 [4] 16/23 16/25 24/1 52/1 023 [1] 27/7 024 [2] 95/9 99/17 026 [2] 17/1 162/15 034 [2] 70/9 84/23 036 [2] 10/20 99/13 038 [1] 12/12 039 [1] 49/21 040 [1] 11/14 042 [2] 95/11 99/14 046 [1] 10/24 048 [1] 83/22 049 [1] 60/11 053 [1] 84/18 059 [1] 68/5 063 [2] 28/2 31/7 064 [1] 81/25 065 [1] 82/7 066 [1] 80/2 068 [1] 80/16 072 [1] 83/13 075 [1] 80/2 077 [1] 56/20 082 [1] 54/5 098 [1] 13/12 1 1 litre [1] 72/5 1 million [1] 17/10 1 November 1976 [1] 12/11 1 October 2021 [1] 1/1 1,000 [1] 26/3 1,100 [2] 19/9 109/20 1.07 [1] 101/9 1.1 [1] 34/6 1.10 [2] 38/18 45/2 1.2 [1] 34/11 1.3 [1] 34/19 1.4 [1] 34/23 1.5 [1] 35/12 1.5 million [1] 96/18 1.9 [4] 43/4 43/11 43/13 43/14 1/10,000 [1] 122/10 1/100 [1] 122/11 10 [4] 20/9 21/9 59/23 127/13 10 hours [1] 125/24 10 March 1981 [1] 48/4 10 years [1] 68/7 10,000 [2] 75/16 122/10	10.00 [2] 1/2 191/23 100 [3] 14/12 122/11 139/9 100 litres [1] 137/17 100-kilo [2] 171/8 171/8 1000 [1] 63/24 101 [2] 70/16 120/25 1011 [1] 127/1 104 [2] 124/25 134/7 105 [2] 124/25 127/16 109 [1] 170/24 1090 [2] 19/8 19/10 10p [2] 15/3 17/9 10th March [1] 49/24 11 [2] 98/17 111/24 11.22 [1] 52/5 11.50 [1] 52/7 1130 [1] 21/15 11p [1] 14/22 12 [7] 12/21 52/4 52/4 56/23 94/4 97/1 98/17 12 July 1981 [1] 80/3 12 October 1979 [1] 56/19 12 persons [1] 7/23 125 [1] 70/9 126,000 [1] 20/21 13 [1] 14/12 14 [2] 101/24 150/4 14 April 1980 [1] 62/2 142,660 [1] 60/4 1487 [1] 99/16 1488 [1] 99/16 15 [4] 104/16 105/2 120/5 181/3 15 August 1981 [1] 7/17 151 [1] 62/17 16 December 1980 [1] 31/10 16 hours [1] 72/23 16p [1] 14/25 17 [1] 160/19 17 August 1981 [1] 80/19 18,800 shares [1] 8/25 185 [2] 20/4 20/15 186,820 [1] 62/3 19 April 1983 [1] 95/18 1966 [1] 102/5 1967 [2] 109/11 109/19 1968 [3] 37/15 39/6 43/18 1969 [6] 102/5 102/9 104/7 107/15 135/25 141/24 1970 [1] 112/3 1970s [3] 26/21 115/9	124/15 1971 [3] 112/6 116/2 135/25 1973 [4] 5/4 107/24 109/7 187/5 1974 [1] 5/4 1976 [17] 10/14 10/19 11/13 12/11 12/13 23/4 34/6 34/24 70/18 102/10 102/15 113/17 120/23 123/12 132/13 141/18 142/25 1977 [2] 12/14 14/19 1978 [7] 5/9 13/17 14/2 14/19 15/24 16/14 53/22 1979 [21] 13/17 16/4 17/12 17/16 17/21 18/4 22/15 23/6 34/10 54/1 54/24 55/13 56/19 56/24 57/3 60/13 65/8 66/18 102/15 102/18 145/25 1980 [25] 5/12 17/14 17/17 21/25 22/10 23/11 23/25 24/5 24/8 26/22 27/21 28/10 31/10 34/11 38/21 38/25 40/6 43/16 55/14 60/3 62/2 68/8 68/11 70/5 160/9 1980s [3] 73/22 153/21 176/23 1981 [46] 3/22 4/10 4/17 5/16 7/8 7/17 8/17 32/23 32/23 46/23 47/2 47/3 47/16 47/16 47/23 48/2 48/4 49/20 49/22 50/15 60/4 67/25 70/10 71/6 74/18 74/24 79/19 80/3 80/19 82/9 83/20 89/3 134/7 141/15 148/5 148/10 156/3 156/5 160/9 160/18 161/18 162/12 165/15 165/15 165/22 168/1 1982 [19] 9/9 84/22 85/1 86/20 87/5 87/11 87/21 88/16 88/19 89/4 89/18 89/25 91/14 96/2 96/17 159/6 168/13 168/24 172/4 1983 [16] 9/17 74/6 92/22 93/1 94/14 95/6 95/10 95/14 95/18 96/8 99/13 100/12 152/9 164/6 170/20 171/1 1983-1985 [1] 170/12 1984 [4] 10/1 10/5	100/16 152/11 1985 [3] 95/14 170/12 183/4 1986 [1] 103/4 1987 [3] 102/18 102/21 102/24 1990 [1] 68/14 1996 [1] 102/24 19th November 1973 [1] 5/4 1M [2] 61/9 61/11 1st [1] 33/18 2 2 April 1982 [1] 87/11 2 June 1983 [3] 94/14 170/20 171/1 2.06 [1] 101/11 2.7 [1] 13/3 20 [4] 20/21 21/1 78/16 112/2 20 litres [3] 137/7 137/16 138/4 200 [3] 112/2 113/3 113/8 200,010 [1] 21/22 200-250K [1] 55/9 2001 [3] 84/7 103/4 103/7 2016 [1] 103/7 2021 [3] 1/1 101/24 191/24 21 [3] 7/24 148/8 148/12 21 February 1980 [2] 21/25 22/10 21,200 [1] 8/23 210 [3] 20/3 20/8 20/9 22 January 1981 [1] 32/23 23 March 1981 [2] 49/22 50/15 23.5 [1] 8/25 230 [3] 20/3 20/7 20/12 24 [3] 84/22 85/1 107/23 24 August 1978 [1] 14/2 24 hours [1] 26/9 24 March 1983 [2] 92/22 93/1 25 [6] 9/10 61/22 62/4 62/6 92/19 155/14 25 per cent [1] 160/15 250 [2] 14/11 26/3 250-300 [1] 108/21 250K [1] 55/9 26 [1] 8/15 26 August 1981 [1] 82/9 26 November 1982 [2] 89/25 91/14
--	--	---	--	--	---

2 26 October 1981 [1] 4/17 26.5 [1] 8/24 27 [1] 8/15 27 May 1981 [1] 161/18 27 November 1980 [1] 38/21 28 [2] 37/15 43/17 29 [2] 37/14 43/17 29 July 1980 [1] 43/16 29 November 1983 [1] 152/9 298,000 [1] 60/3	47 [1] 134/7 5 5 degrees [1] 135/4 5 million [1] 166/1 5 years [1] 70/25 5.00 [1] 191/22 50 [10] 9/11 40/7 40/10 61/24 62/7 71/17 71/22 112/8 116/9 123/2 50 litres [1] 183/11 50,000 [1] 15/3 500 [2] 26/3 63/24 500,000 [1] 12/23 5m [1] 55/11 5th [1] 127/14 5th October 2021 [1] 191/24 6 60 [1] 125/7 60 degrees [2] 125/13 125/23 600 [3] 112/2 113/3 113/9 600 ml [2] 137/21 138/2 61 [1] 77/25 7 7 July [1] 88/16 7 July 1982 [1] 87/21 7 May [1] 54/7 7 May 1979 [1] 54/1 7.5p [1] 26/4 75% yield [1] 160/14 8 8.2 [1] 33/10 8.5p [1] 17/17 80-90 [1] 55/11 8184 [1] 21/12 8185 [1] 21/7 85 [1] 6/10 8610 [1] 19/23 88 [1] 120/25 8th [1] 127/13 9 9 December 1981 [1] 3/22 9.25p [1] 17/16 9.5p [2] 14/22 17/10 90 [2] 55/11 122/16 900 [3] 19/12 19/16 21/13 91 [1] 120/25 96 [1] 122/15 98 [2] 124/20 132/19 99 [1] 132/16 9p [1] 17/12	A A, [1] 123/17 abandoned [1] 85/17 abattoir [2] 148/17 167/15 ability [1] 51/4 able [18] 5/13 26/10 36/12 52/12 82/4 95/4 106/6 115/6 115/11 115/12 136/16 143/17 154/2 160/3 170/8 175/4 175/18 184/15 about [130] 1/24 8/21 8/24 9/1 9/2 9/23 11/2 11/4 11/12 12/25 16/21 17/21 18/4 20/9 20/16 21/19 22/22 23/8 26/18 30/23 31/3 31/20 32/4 33/24 35/10 48/19 51/4 51/9 54/13 54/25 55/11 59/25 60/10 60/14 61/5 63/13 63/25 66/15 68/2 69/21 69/24 72/12 73/1 73/3 74/5 74/9 78/10 79/5 83/15 89/2 90/23 94/2 98/2 98/6 101/2 101/7 101/25 103/11 104/4 104/16 105/2 105/12 105/12 110/24 111/6 112/10 113/20 114/18 116/15 116/16 122/16 123/2 124/13 126/1 126/11 126/14 133/15 137/7 137/13 137/16 137/17 137/18 138/2 138/14 139/22 140/13 145/11 145/20 145/21 146/2 146/20 148/25 149/3 149/24 151/11 153/7 153/10 155/10 156/4 156/5 158/22 161/20 162/11 165/10 166/10 166/14 167/21 169/16 169/21 170/15 172/12 172/12 172/15 172/16 172/20 174/1 175/1 175/18 176/16 179/5 179/18 179/23 180/4 183/11 185/10 186/16 187/4 188/12 190/17 191/14 above [5] 33/11 35/2 73/20 94/4 96/9 absence [1] 97/2 absent [1] 25/7 absolutely [1] 170/14 absorb [3] 118/13 157/13 157/15 absorbed [3] 87/23	118/5 118/6 absorbent [1] 52/16 absorbitive [1] 111/2 absorption [3] 108/9 111/10 164/21 abstract [4] 108/7 108/8 108/25 122/1 academic [2] 79/6 79/9 acceptability [1] 64/5 acceptable [1] 19/11 acceptance [2] 19/5 63/20 accepted [4] 42/18 44/16 44/16 87/12 accepting [1] 46/3 access [2] 3/10 36/4 accessories [1] 55/25 accident [3] 115/2 181/25 182/13 accidental [1] 182/16 accompanied [2] 23/18 27/20 accord [1] 18/1 accordance [4] 4/16 43/17 43/19 93/8 according [8] 9/13 9/17 23/23 50/16 62/14 66/7 125/15 160/18 accountant's [5] 13/15 27/25 46/19 47/6 148/5 accountants [3] 3/21 3/22 8/17 accurate [1] 52/13 accused [1] 86/9 achieve [5] 22/19 97/1 123/3 180/5 180/6 achieved [4] 13/4 59/22 96/17 97/11 acid [1] 110/6 acknowledges [1] 82/6 acquired [4] 10/1 10/2 10/6 100/15 act [8] 37/15 39/6 42/2 42/17 43/18 52/16 93/9 141/23 Act 1968 [1] 39/6 acted [1] 36/11 acting [2] 103/23 103/24 action [5] 103/14 103/19 104/1 106/23 174/19 activate [1] 107/1 activated [4] 157/6 157/7 157/23 158/1 activating [1] 154/9 activation [2] 119/5	158/7 Active [1] 35/19 activities [1] 1/15 activity [7] 5/9 25/24 27/1 72/11 157/24 165/21 168/20 actual [1] 48/24 actually [29] 29/14 66/11 103/17 106/22 110/1 111/21 113/18 115/1 118/22 128/2 128/3 131/5 132/9 140/16 140/16 142/15 143/15 144/17 146/4 147/9 148/22 152/16 154/12 158/6 158/16 160/7 169/24 170/7 178/22 add [5] 22/9 84/2 91/22 121/19 157/16 added [5] 91/23 122/3 132/7 142/20 164/19 adding [1] 121/22 addition [4] 12/4 108/15 109/25 174/15 additional [4] 37/6 39/10 41/25 161/9 address [10] 11/18 11/19 11/19 11/20 11/20 90/7 124/2 149/11 149/12 185/16 adds [1] 142/22 adequate [2] 44/7 45/19 adequately [3] 75/24 76/15 165/18 adhere [1] 53/3 adherence [1] 53/10 adhesion [1] 52/17 adjourned [1] 191/23 adjournment [1] 101/10 adjusted [1] 8/19 adjusting [1] 121/22 administered [3] 130/25 131/9 133/3 administration [4] 15/1 26/7 111/14 122/20 admired [1] 189/3 adsorbing [1] 69/2 adsorption [2] 53/10 53/14 advance [4] 55/9 76/11 110/9 180/14 advances [1] 99/23 advantage [1] 135/8 advantages [2] 52/23 71/15 adverse [4] 14/19 47/13 48/19 51/1 advice [9] 44/19	44/24 45/10 45/11 46/6 46/12 49/6 49/18 93/3 advise [3] 42/11 43/21 93/6 advised [2] 81/16 174/10 affairs [2] 4/18 173/13 affect [1] 157/17 affidavit [1] 41/5 affirmed [2] 101/19 192/4 afraid [14] 11/9 23/17 27/9 47/8 48/3 48/13 54/18 90/20 95/17 126/25 127/8 132/18 189/14 190/5 after [33] 2/24 9/15 22/1 28/10 32/24 41/10 70/25 86/13 93/2 94/16 97/11 99/8 100/18 100/25 101/12 102/13 104/7 105/12 134/2 134/14 136/8 141/15 141/16 143/6 145/2 150/11 152/18 152/18 155/23 155/24 160/11 178/16 179/6 afternoon [2] 190/15 190/17 again [22] 2/11 3/9 7/5 21/10 21/13 24/10 32/15 38/24 74/9 74/19 84/8 102/16 115/25 120/19 121/15 123/20 132/11 135/11 138/18 154/24 166/21 191/18 against [1] 12/5 Agency [1] 7/2 agent [9] 28/18 112/17 112/24 117/24 118/4 118/6 123/25 158/6 159/24 agents [2] 123/5 124/1 agglomerate [1] 73/15 ago [3] 28/11 159/21 172/6 agree [3] 124/10 129/22 129/23 agreed [3] 7/13 31/13 31/17 agreement [18] 7/4 7/16 7/18 10/9 10/9 10/12 10/15 22/20 23/4 24/4 62/12 66/15 66/16 66/17 67/4 67/22 67/23 178/23 Ah [1] 170/23 ahead [1] 3/25
---	--	---	--	--	--

A	172/24 173/24 174/5 191/12 already [5] 65/15 118/24 120/7 133/15 161/22 also [42] 1/14 4/4 6/22 12/4 15/14 17/6 18/7 18/18 22/11 23/13 30/5 31/15 32/6 35/21 47/21 59/19 60/5 60/22 73/13 74/2 76/5 80/11 81/9 87/1 91/23 94/4 95/16 96/10 97/9 98/5 100/18 134/22 145/1 146/3 151/19 156/17 162/14 164/5 165/2 167/2 168/14 173/12 alter [2] 172/11 172/13 alternative [4] 71/2 75/9 110/23 120/12 Alternatively [1] 130/20 although [17] 5/13 7/16 14/17 15/7 21/9 22/9 24/15 35/23 49/10 59/17 84/10 84/19 132/22 133/12 159/15 170/15 186/13 always [6] 15/5 86/4 89/7 176/20 180/18 180/19 am [26] 1/2 15/4 50/3 50/8 52/5 52/7 80/13 80/24 81/13 88/17 100/19 111/3 113/3 121/12 125/3 127/8 128/11 132/13 140/19 148/8 155/4 155/11 160/24 161/15 183/1 191/23 amazing [1] 189/15 amazingly [1] 142/16 ambitions [1] 82/14 ambitious [2] 61/1 100/8 ambivalent [1] 188/23 amended [2] 5/17 46/24 American [8] 49/3 76/8 77/18 103/18 177/18 177/19 178/1 178/15 among [7] 2/21 33/3 81/1 94/5 112/9 112/20 117/1 amount [6] 44/6 45/18 61/11 119/5 122/8 178/4 amounts [3] 17/4 135/13 159/17	an accident [1] 115/2 an activated [1] 157/23 an American [1] 177/18 an answer [1] 51/19 an attached [1] 19/25 an attempt [2] 17/7 172/8 an awareness [2] 113/22 115/5 an example [1] 19/18 an extended [1] 96/12 an extension [1] 42/4 an extent [1] 150/25 an extract [1] 92/11 an hour [1] 155/10 an independent [1] 28/4 an interaction [1] 153/6 an intermediary [2] 28/25 29/4 an intermediate [3] 25/23 26/17 27/3 an issue [1] 17/21 an opportunity [1] 94/17 an optimistic [1] 73/23 an outline [1] 44/12 analysis [3] 3/1 3/3 24/17 analytical [1] 150/17 ancillary [1] 6/5 Andaris [1] 103/4 Andrews [1] 102/4 anhydride [1] 138/23 animal [10] 5/6 5/22 15/7 57/8 59/12 59/20 62/22 75/6 75/11 75/22 animals [1] 127/19 Anne [5] 173/6 173/8 173/11 175/7 175/25 announced [2] 83/21 84/15 annum [1] 183/12 another [7] 102/24 120/18 130/4 130/16 155/10 178/15 181/16 answer [12] 11/1 30/10 51/19 114/25 117/4 117/4 119/8 120/14 169/5 170/5 182/7 190/25 answered [3] 169/24 179/15 190/23 answering [1] 180/25 answers [3] 120/7 172/11 172/14 anti [5] 34/7 34/17	37/25 40/18 158/5 anti-haemophilic [4] 34/7 34/17 37/25 40/18 anti-proteolytic [1] 158/5 antibodies [2] 159/14 183/23 antibody [2] 73/16 184/7 anticipate [1] 180/12 anticipated [2] 60/2 87/6 anticoagulant [1] 110/14 antigen [15] 12/3 27/16 74/8 112/5 112/8 112/12 112/13 113/23 121/1 122/4 122/9 122/22 124/23 127/1 133/2 antigenaemia [2] 112/9 112/15 antigenic [2] 15/14 25/7 antihaemophilic [1] 39/18 anxious [1] 92/16 any [59] 2/25 11/9 11/10 16/21 22/17 38/10 41/4 41/25 42/22 43/2 43/10 44/7 45/19 47/9 49/13 75/19 78/16 88/5 90/14 92/16 97/2 100/23 103/11 103/14 105/14 112/14 112/14 118/9 125/25 126/13 134/18 138/14 140/10 141/21 143/2 143/12 145/13 149/7 150/14 150/21 151/12 154/2 154/22 157/11 158/18 165/2 166/7 168/24 172/11 175/18 176/23 180/18 181/5 181/20 182/14 182/23 183/19 185/9 185/14 anything [6] 92/18 103/22 146/14 186/20 188/12 190/10 anyway [2] 127/15 157/11 anywhere [1] 176/10 Apologies [1] 116/19 apologise [3] 30/19 128/4 191/19 apologising [1] 132/1 apparent [4] 47/22 144/6 156/10 156/12 appear [6] 25/8 29/21 39/2 51/10 85/17	107/1 appeared [3] 27/20 56/10 98/5 appearing [1] 42/3 appears [8] 17/23 20/15 23/6 27/8 30/10 79/19 92/12 174/21 appendices [1] 33/11 appendix [3] 33/13 33/17 59/1 applicant [1] 93/8 application [39] 10/22 23/19 36/11 56/11 56/15 56/18 56/21 56/22 57/1 60/8 60/15 60/21 61/3 61/18 62/6 62/10 65/10 68/19 89/12 91/9 91/11 91/13 91/14 91/16 91/17 92/22 94/24 130/4 132/25 152/8 168/9 170/18 172/1 173/23 174/5 174/7 174/11 174/13 176/5 applications [1] 151/13 applied [5] 34/25 77/7 89/16 151/21 172/21 applying [1] 53/13 appointed [2] 9/16 90/2 appreciate [1] 49/6 appreciated [1] 191/2 approached [1] 183/14 approaching [1] 96/17 appropriate [4] 56/10 81/21 111/2 184/12 approval [3] 41/19 62/5 63/20 approved [2] 39/22 61/22 approximately [7] 25/24 27/1 75/5 105/3 108/20 109/20 115/6 April [12] 55/14 62/2 84/22 85/1 86/20 87/11 95/7 95/18 101/24 156/3 156/3 160/18 April 1980 [1] 55/14 April 1981 [2] 156/3 160/18 April 1982 [3] 84/22 85/1 86/20 April 2021 [1] 101/24 are [113] 1/16 3/7 5/13 5/18 8/3 9/3 11/25 14/5 14/11 14/12 14/22 16/16 16/19 16/24 18/22	19/16 21/4 23/9 24/11 24/17 24/21 24/21 25/4 25/12 25/19 26/2 26/2 26/7 27/22 32/20 33/4 40/11 47/19 49/1 49/11 50/3 53/8 53/10 55/23 56/15 58/11 58/25 59/14 59/25 60/3 60/5 60/7 60/22 61/14 61/19 64/7 64/24 65/17 65/21 67/19 69/20 71/9 75/13 77/19 78/9 78/24 80/3 80/7 81/6 81/9 81/17 81/23 82/16 82/18 83/1 85/24 86/2 86/8 92/16 93/12 95/2 97/4 97/12 98/6 98/10 99/11 99/15 99/19 105/18 108/12 109/9 110/21 115/6 115/11 115/12 115/16 121/3 130/15 134/12 143/17 146/7 148/2 151/1 151/4 154/2 156/16 156/19 160/3 161/9 162/15 173/8 174/19 175/3 175/18 180/9 181/5 181/5 186/18 area [4] 16/6 56/6 75/20 174/4 areas [4] 55/10 67/1 140/9 140/21 aren't [2] 6/21 65/18 argument [2] 46/3 100/13 arise [2] 97/7 158/11 arising [1] 46/8 arm [1] 4/6 Armour [4] 14/16 14/20 14/23 16/22 Aronstam [3] 24/7 30/13 30/15 arose [2] 17/21 130/16 around [12] 4/8 19/16 21/9 88/6 101/7 101/14 113/20 124/13 137/21 161/21 178/6 190/23 arrange [1] 16/5 arranged [4] 25/20 30/20 54/10 78/3 arrangement [4] 29/18 34/9 43/2 43/10 arrangements [5] 42/5 42/6 67/18 80/7 84/20 arrival [2] 41/14 53/23 Arthur [1] 58/23 article [27] 99/13
----------	---	---	--	---	---

A	associate [1] 85/5 associated [1] 191/12 association [1] 97/8 assume [2] 112/21 117/21 assurances [1] 42/20 assuring [1] 91/9 astute [1] 178/25 attached [4] 14/11 19/25 81/21 168/22 attempt [6] 17/7 22/12 52/9 67/5 112/19 172/8 attempted [1] 138/25 attended [2] 94/20 170/19 attendees [1] 33/1 attenders [1] 14/12 attention [3] 49/25 81/2 96/5 attitude [2] 50/9 188/23 attorneys [2] 103/19 103/23 attract [1] 118/20 attributable [1] 49/1 August [10] 7/17 10/19 13/17 14/2 16/14 17/16 68/8 68/11 80/19 82/9 August 1976 [1] 10/19 August 1978 [1] 13/17 August 1979 [1] 17/16 August 1980 [2] 68/8 68/11 Ausria [1] 122/10 Ausria II [1] 122/10 Australia [5] 112/5 112/8 112/11 112/13 113/23 Australian [1] 112/15 author [5] 74/2 74/5 108/3 132/14 134/12 authorised [1] 37/2 authorities [1] 174/23 authority [18] 32/7 35/5 36/21 38/20 39/6 43/15 43/21 44/3 44/6 44/9 44/17 44/21 45/15 45/17 45/18 45/21 46/4 46/14 authors [2] 121/3 162/15 avail [1] 39/1 availability [2] 25/1 176/22 available [9] 15/12 16/8 26/7 49/14 56/9 115/22 115/24 117/7	140/24 avoid [3] 22/13 101/13 184/23 awaiting [1] 91/15 aware [22] 24/21 49/2 49/11 50/3 50/18 81/13 114/20 114/23 123/14 123/24 123/25 128/15 130/11 131/3 149/14 160/4 160/7 160/21 168/1 181/23 182/5 186/2 awareness [4] 113/22 115/5 116/12 140/20 away [6] 101/13 103/14 103/15 139/12 151/20 151/20	B BA [1] 31/14 back [61] 7/6 8/14 13/9 13/12 14/6 15/21 19/8 19/21 24/11 25/11 31/3 32/2 36/24 38/5 38/15 40/8 40/12 40/15 43/12 45/2 45/7 46/6 51/5 59/6 60/17 64/18 73/1 74/22 77/18 80/20 94/21 99/7 100/17 102/8 106/1 106/2 110/8 111/9 115/12 115/23 128/3 131/25 132/13 133/22 134/2 140/14 146/5 147/12 148/1 152/7 155/3 155/14 160/3 165/8 170/6 176/19 179/14 179/18 181/4 186/6 191/3 backers [2] 81/15 87/24 background [4] 34/5 39/13 62/19 161/13 backing [1] 82/3 backs [1] 167/3 bacteria [5] 125/24 142/1 163/21 178/19 179/1 bags [1] 55/25 ban [3] 174/4 175/2 175/5 banning [1] 174/1 base [2] 75/14 77/5 based [13] 6/23 28/6 31/9 52/22 138/22 146/10 146/23 146/24 158/14 174/5 174/24 175/13 185/6 basement [2] 186/23 186/25 basic [2] 22/11 119/16	basically [2] 53/12 168/17 basis [3] 16/7 118/10 133/4 batch [19] 12/4 19/8 23/24 35/2 35/3 35/14 44/3 45/15 45/16 86/10 112/14 113/2 113/4 113/15 113/20 114/4 122/13 137/3 162/25 batches [17] 18/13 18/14 18/24 19/7 22/17 36/9 40/5 40/7 40/11 42/18 42/19 45/16 48/25 111/1 111/11 112/2 112/10 battle [1] 99/19 battle lines [1] 99/19 BAYP0000020 [1] 10/24 BAYP0000021 [3] 27/7 28/2 31/7 be [234] beater [1] 88/23 became [17] 9/16 107/4 112/6 116/2 127/20 127/25 128/17 129/14 136/21 156/10 156/12 157/5 157/7 160/4 160/7 176/14 184/3 because [80] 12/18 16/8 16/10 28/24 32/15 33/14 33/23 34/3 38/24 42/20 45/2 46/8 47/11 54/24 55/17 58/6 71/6 71/10 92/19 100/3 110/3 110/20 117/11 119/21 123/4 128/2 130/7 131/6 131/7 131/8 131/12 132/4 137/14 138/7 139/18 144/7 144/11 145/10 146/4 147/3 147/23 147/23 150/25 151/3 151/7 151/14 152/16 153/7 154/8 155/11 156/24 157/5 157/25 158/3 163/3 163/13 166/15 167/2 167/5 167/13 167/18 167/22 167/24 169/8 169/18 169/25 176/1 176/9 176/14 177/16 180/1 180/16 183/14 184/12 184/21 184/24 186/14 187/8 189/7 189/10 become [5] 6/12 77/5 95/8 181/22 182/5 becomes [1] 84/5	becoming [2] 157/6 157/25 been [110] 1/8 5/21 6/4 6/7 8/1 12/2 12/5 12/19 12/20 12/24 14/14 18/19 19/24 24/4 25/3 25/16 27/15 29/21 30/11 32/13 34/10 34/25 35/4 35/22 35/25 36/12 36/20 37/13 40/8 41/6 43/16 45/11 46/3 48/22 51/3 54/10 54/22 57/7 57/10 60/18 61/6 62/7 66/7 68/15 72/19 72/20 73/13 75/5 75/21 76/5 78/3 79/10 80/25 81/3 81/12 82/14 84/20 85/16 87/23 89/19 90/1 90/8 94/12 96/9 96/10 110/11 112/3 112/11 112/14 112/19 114/6 114/7 114/11 115/14 115/19 124/23 129/9 129/16 130/6 130/20 130/25 131/8 133/13 143/10 143/25 143/25 144/13 146/24 147/11 150/3 151/7 151/18 151/23 152/13 154/25 163/23 164/2 166/4 166/9 168/11 170/7 173/25 175/7 176/11 176/12 177/23 179/6 181/14 184/19 184/22 before [24] 3/15 10/5 11/3 21/16 39/2 41/9 42/4 47/11 53/22 58/18 59/6 93/4 116/3 121/15 131/25 142/6 143/19 149/23 152/18 154/6 165/9 167/15 180/19 191/19 before' [1] 81/12 began [2] 23/7 24/6 begin [2] 1/7 104/3 begins [1] 70/17 begs [1] 38/15 begun [2] 53/21 70/6 behalf [3] 103/20 103/23 103/24 behest [1] 92/14 being [56] 1/13 6/20 14/23 17/4 22/13 26/16 27/3 27/23 40/16 49/19 50/12 50/17 55/5 56/15 61/4 72/13 73/25 74/11 81/17 86/9 86/21 87/6 87/17 88/11 88/12	88/22 88/23 94/8 96/4 97/15 97/17 105/5 106/7 107/12 116/16 119/14 126/17 127/24 130/1 133/12 137/14 139/6 143/23 146/23 148/3 148/8 161/14 168/3 169/20 170/13 171/7 175/12 176/1 176/2 182/21 189/14 believe [4] 15/10 29/1 120/10 162/10 believed [2] 126/7 126/9 below [4] 18/20 20/10 73/9 127/11 bench [1] 160/15 beneficial [1] 62/22 benefit [1] 117/14 Benefits [1] 63/22 Bennett [1] 108/5 Berkeley [1] 35/23 best [5] 48/5 100/4 109/6 169/7 169/8 better [4] 57/14 120/12 141/21 179/3 between [31] 1/7 7/10 10/9 13/16 23/5 26/18 26/23 38/10 46/25 55/1 62/12 65/19 68/23 72/13 72/22 80/4 84/17 84/21 90/24 94/14 99/9 99/19 101/14 102/5 113/8 119/3 119/6 119/7 138/5 151/4 186/2 beyond [1] 37/22 big [7] 104/13 118/11 133/9 154/21 178/19 179/3 190/3 bigger [1] 113/14 bills [1] 85/14 bind [1] 73/5 Bingham [2] 7/23 11/19 bio [3] 167/4 167/5 169/14 biochemist [6] 102/11 102/16 105/8 105/10 117/16 124/4 biochemistry [2] 16/2 102/4 biodepleted [1] 183/13 biological [3] 35/8 36/23 37/12 biologicals [1] 76/18 Biologics [2] 39/23 40/1 Biology [1] 77/15 Biopharm [1] 10/3
----------	--	---	---	---	--	--

B	12/17 13/1 16/15 31/22 45/10 68/8 71/13 74/23 97/19 bought [4] 28/25 29/1 171/8 184/17 bound [3] 51/16 118/13 176/21 Bournemouth [1] 47/22 bowels [2] 104/14 142/7 BPL [28] 55/21 62/12 64/21 64/24 66/13 70/8 79/22 79/24 80/4 80/9 82/10 82/21 83/4 83/19 84/17 84/21 84/25 87/2 105/21 105/23 152/20 152/21 155/25 162/1 162/25 163/8 163/19 189/8 BPL's [3] 80/14 82/16 86/11 BPL/Speywood/Mons anto [1] 70/8 BPLL0001351 [1] 49/21 BPLL00016007 [1] 160/25 BPLL0016007 [4] 67/23 83/22 161/1 162/15 BPLL0016008 [9] 62/17 70/9 80/2 80/16 81/25 82/7 83/13 84/18 84/23 branded [1] 1/19 break [10] 47/11 52/3 52/6 58/18 101/5 149/23 155/18 180/11 180/20 181/10 breakeven [1] 97/1 Brian [3] 26/14 186/21 192/7 brief [2] 9/17 52/10 briefly [3] 47/10 135/1 177/7 bring [9] 11/15 37/24 66/10 70/14 84/3 158/25 162/14 164/8 170/23 bringing [4] 59/6 160/5 168/25 190/2 Bristol [1] 12/20 British [11] 1/9 24/21 35/15 49/17 62/21 87/21 92/14 100/3 134/6 177/25 184/19 broad [1] 136/2 broker [1] 51/15 brokerage [1] 49/3 brokerages [1] 49/11 brought [3] 147/25	160/24 178/4 BSc [1] 102/3 BTG [4] 92/19 178/5 179/17 179/22 Buck [1] 54/8 build [1] 21/1 building [1] 172/18 built [6] 88/6 151/23 176/11 187/9 187/10 188/1 bulk [9] 17/6 34/16 35/19 39/17 93/13 135/12 135/16 137/2 159/12 bullet [4] 107/9 121/7 121/8 138/20 burdens [1] 142/20 Bureau [2] 39/23 40/1 Burns [1] 4/14 business [24] 4/4 5/2 6/5 6/6 6/6 15/5 17/8 55/24 66/23 67/2 67/6 69/22 74/14 75/14 92/18 95/12 99/14 99/25 100/6 100/11 149/15 170/12 176/16 189/1 business-wise [1] 92/18 businesses [2] 6/4 6/14 businessman [1] 69/21 but [212] butchering [1] 108/18 buy [1] 51/15 buying [1] 188/14 buys [1] 14/25 by [165] 1/3 1/7 1/21 3/10 3/12 3/18 3/20 4/1 4/5 4/22 5/9 5/12 5/24 5/25 7/8 8/18 9/9 10/1 10/2 10/6 12/4 12/5 17/17 17/24 17/24 21/8 21/11 22/14 23/15 23/24 23/24 23/25 24/4 24/7 24/8 25/14 27/16 28/16 30/12 34/8 34/10 34/17 35/4 35/6 35/13 35/15 35/17 35/22 36/1 36/17 39/20 39/23 39/25 40/17 40/25 41/23 41/23 42/1 42/16 42/20 44/8 44/17 45/20 46/4 46/12 48/1 49/11 50/2 51/10 53/8 53/14 53/15 53/22 54/23 55/6 55/14 56/22 58/10 64/20 68/7 68/14 68/15 69/5	70/5 72/13 72/14 74/13 77/24 78/7 79/10 81/11 82/14 82/15 83/10 84/6 85/11 86/11 87/17 87/20 89/15 89/18 91/8 91/13 93/18 94/20 95/7 95/15 100/15 101/20 103/18 104/3 104/20 105/16 105/17 109/21 109/21 112/5 112/12 112/24 117/24 121/22 122/10 122/25 123/2 123/5 127/6 129/5 129/6 130/6 130/17 132/10 132/23 134/7 135/18 136/5 142/20 143/16 146/6 151/6 151/16 154/13 154/16 155/21 157/15 159/6 160/21 168/1 168/6 168/14 170/6 173/8 173/24 174/3 174/17 177/15 177/17 177/18 177/25 178/4 185/5 185/21 186/9 188/14 192/2 192/5	71/9 72/4 74/19 75/25 76/13 77/7 77/23 79/2 79/9 79/17 80/20 83/10 84/24 87/19 89/24 91/18 92/24 93/10 93/14 95/14 96/16 99/3 100/5 100/19 102/3 105/11 106/21 106/22 110/4 116/23 121/3 121/19 121/22 121/23 123/17 125/22 128/24 130/11 131/10 131/25 133/22 135/20 137/19 156/9 157/17 158/10 158/14 159/3 165/19 169/7 169/8 169/25 170/23 174/24 175/20 176/4 186/24 190/22 191/1 can't [23] 11/10 21/17 48/13 91/2 98/8 103/15 104/23 110/1 114/25 117/4 126/8 127/8 128/2 137/8 139/4 144/5 172/17 175/21 175/21 180/2 181/3 184/19 185/3 cannot [5] 12/8 76/3 90/20 120/11 125/10 capable [2] 123/5 150/13 capacity [3] 42/11 48/7 159/12 capital [6] 6/11 8/16 57/14 59/24 60/2 72/1 capitalise [1] 177/16 captured [1] 85/11 Cardiff [1] 58/23 Cardio [1] 6/9 career [2] 102/1 102/8 careful [1] 167/21 carefully [2] 98/13 162/25 carried [5] 4/17 41/16 41/22 58/9 58/21 carriers [1] 112/8 carry [3] 122/7 125/10 189/21 cascade [2] 156/16 158/8 case [13] 16/18 37/4 39/7 39/13 61/20 91/5 118/13 139/19 152/5 167/4 174/22 184/4 190/3 cases [1] 40/11 cash [9] 25/19 61/14 61/21 104/23 114/14 130/18 131/3 131/18 134/8 Cash flow [1] 61/14 cast [1] 97/17	cataracts [1] 5/8 catch [1] 116/12 caught [1] 22/13 cause [3] 121/20 125/8 154/9 caused [4] 153/7 181/25 189/8 189/12 causes [1] 52/17 causing [4] 112/18 122/7 123/5 125/11 cautious [1] 161/20 cautiously [1] 56/8 CBLA0000011 [1] 26/20 ceased [2] 6/8 46/16 ceases [1] 67/15 ceasing [1] 47/2 cells [2] 178/21 178/23 Celltech [4] 77/18 81/1 178/15 178/17 cellular [1] 110/20 cellulose [4] 108/9 111/12 118/24 119/22 cent [24] 6/11 8/21 8/24 8/25 9/2 9/11 9/12 20/9 21/1 40/10 62/4 62/6 62/7 71/21 71/22 116/9 116/16 116/24 122/15 122/16 122/25 123/3 139/10 160/15 central [2] 13/5 31/12 centre [19] 12/16 13/22 14/12 17/13 24/8 41/17 42/12 48/8 48/11 49/9 51/6 51/8 86/15 102/10 104/4 109/19 119/24 141/20 189/16 centres [11] 6/23 12/19 13/20 17/25 20/19 21/2 39/25 68/25 72/7 78/6 191/14 centrifugal [1] 76/20 centrifuge [1] 64/23 CEO [1] 103/7 CEP [1] 122/23 certain [9] 7/14 52/18 70/15 118/20 121/24 172/20 174/1 178/4 189/4 certainly [7] 29/9 30/15 65/20 98/25 149/9 152/25 167/4 certificate [13] 35/3 89/13 89/16 93/7 93/11 94/6 94/7 94/13 94/25 95/1 171/3 172/22 176/5 certified [1] 39/17
----------	---	--	--	--	--

(53) biosynthetic - certified

C	108/10 110/18 111/11	clots [1] 106/24	172/24 175/9 175/10	96/12 98/21 99/10	79/22 98/6 154/13
cetera [7] 59/21	civil [1] 13/9	clotting [16] 106/23	180/22 181/4 183/6	140/2 140/4 145/15	154/21 183/14
154/11 171/16 171/16	claim [2] 165/23	107/1 118/4 119/5	185/1 185/3 186/6	151/6 151/16 177/18	concerned [7] 31/25
178/8 185/18 186/17	166/3	150/18 150/19 151/9	comes [2] 99/24	178/15	32/7 54/24 123/23
CF [1] 83/6	claimed [7] 17/22	156/14 156/18 157/2	183/3	company's [4] 6/1	153/13 155/11 182/4
chain [2] 38/4 40/14	20/10 20/25 21/15	157/4 158/7 158/7	coming [8] 15/21 43/5	40/25 42/7 59/9	concerning [7] 35/19
chair [2] 90/2 153/19	26/25 27/4 36/17	167/13 167/14 168/19	67/12 144/9 166/2	compare [1] 142/11	36/25 50/1 80/4 84/25
chairman [7] 9/15	claims [4] 78/18 81/4	CNTS [2] 58/16 156/1	175/16 184/23 191/2	compared [2] 12/21	93/21 185/10
41/1 48/7 51/7 95/8	81/6 81/17	co [4] 74/5 99/5	comment [2] 50/22	52/21	concerns [18] 14/7
95/15 95/16	clarification [1] 36/24	132/14 171/16	96/21	comparing [1] 12/18	16/20 32/3 32/11 33/5
challenges [1] 83/15	class [2] 103/13	co-author [1] 74/5	comments [2] 60/19	compatible [1] 82/18	47/25 48/18 50/18
Chancellor [1] 6/12	103/19	co-wrote [1] 171/16	81/18	compensated [1]	80/14 82/6 83/17 85/8
change [5] 22/18 95/6	classical [2] 9/19 76/4	coagulation [13]	commercial [15] 8/5	19/22	90/22 111/6 165/10
95/12 96/13 174/10	clause [1] 118/15	58/16 62/25 66/5	16/11 55/18 56/7	compensation [3]	165/12 170/15 176/15
changed [5] 15/24	clean [7] 87/14 107/1	68/20 107/25 108/10	60/23 67/18 79/1	18/8 20/23 21/4	conclude [1] 131/10
15/25 36/18 73/16	114/24 142/9 163/8	108/11 109/13 110/12	85/25 88/23 97/12	competitive [1] 78/16	concluded [2] 91/8
157/1	185/2 188/9	122/5 122/16 141/10	151/6 174/24 175/13	complaint [1] 20/16	118/8
changes [3] 15/6	cleaning [1] 142/22	185/8	184/21 184/22	complete [1] 191/9	concluding [1] 120/9
36/21 181/20	cleanly [2] 141/22	Coast [1] 136/10	commercially [6]	completed [4] 63/1	conclusion [4] 98/18
character [1] 73/13	142/3	Cohn [7] 52/22 57/15	57/22 65/23 88/3	65/15 66/5 69/5	117/20 129/22 174/21
charge [9] 20/19 26/8	clear [16] 6/22 14/18	68/14 75/10 76/4	88/11 97/13 185/5	completely [3] 25/7	conditions [3] 37/7
121/21 121/25 122/1	20/11 21/13 27/22	111/11 111/19	committed [1] 75/16	97/15 179/12	73/6 142/13
139/7 139/10 146/19	46/14 68/10 78/9	cohort [1] 153/11	committee [24] 32/21	completion [1] 37/21	condone [1] 92/7
148/23	89/16 94/23 105/18	coin [1] 19/2	32/22 33/3 39/1 39/3	complex [5] 110/12	conduct [2] 143/12
charged [6] 118/14	124/4 148/2 165/2	cold [1] 83/7	41/1 42/4 42/11 43/1	110/17 156/15 156/19	147/19
118/19 119/1 119/23	172/12 172/15	collaborating [1]	43/9 43/20 44/15	168/20	Conference [1] 70/19
120/3 139/4	clearance [6] 18/25	79/23	44/19 44/20 44/23	complexity [1] 80/10	conferred [1] 37/14
cheaply [1] 16/12	35/4 41/10 41/10 74/7	collaboration [3] 70/8	44/24 46/10 46/12	complied [1] 35/5	confidence [1] 84/6
check [4] 19/4 143/6	121/9	80/5 80/6	50/14 92/21 92/25	components [1]	confidences [1]
168/17 169/18	cleared [4] 20/3 21/8	collaborative [1]	92/25 93/3 93/4	110/21	103/14
checking [2] 144/14	24/4 48/22	126/21	Committee's [1]	comprehensive [2]	confident [2] 15/4
150/24	clearly [3] 18/23 50/8	colleague [3] 128/17	33/10	3/7 75/17	161/15
chief [11] 2/21 8/11	113/22	181/19 182/7	common [2] 94/16	compulsorily [1]	confidential [2] 28/20
9/5 64/16 101/20	clinical [46] 15/18	colleagues [7] 48/20	119/21	37/16	31/2
102/19 146/25 148/20	24/24 25/14 60/5 63/1	60/14 87/3 99/12	communicate [1]	concentrate [29]	confidentiality [1]
168/5 176/2 192/5	63/19 64/4 66/5 68/18	100/7 121/4 145/7	36/20	13/18 23/15 25/13	50/13
chief/sole [1] 148/20	70/6 73/17 73/24	collect [4] 84/7	communication [1]	50/1 73/19 81/12	confined [2] 63/11
Children's [1] 28/12	75/23 82/25 87/13	156/22 180/25 189/16	37/3	97/16 106/18 107/25	94/11
chimpanzee [3]	88/2 89/12 91/13 92/3	collected [6] 39/24	companies [10] 1/4	108/15 108/22 109/24	confirm [1] 82/13
129/14 130/4 133/20	92/21 93/6 93/11	109/21 110/2 110/4	1/8 6/21 22/7 77/6	112/11 112/16 112/22	confirmed [3] 63/4
chimpanzees [10]	93/24 94/7 94/13	110/22 163/1	145/13 177/19 191/12	117/22 120/11 121/9	132/23 158/3
122/13 125/2 125/4	94/24 94/25 112/20	collecting [3] 143/5	191/12 192/3	136/14 136/16 136/18	confirms [1] 87/5
126/22 127/25 129/7	120/22 132/22 163/3	148/16 148/19	company [81] 1/9	144/17 144/18 144/19	conform [2] 36/9
129/7 129/14 132/24	164/16 165/8 165/9	collection [7] 37/18	1/10 1/14 3/16 4/10	145/11 150/15 162/18	69/10
133/7	165/17 168/8 168/10	44/10 45/22 68/23	5/4 5/10 5/21 6/15	164/19 184/2	conformed [1] 36/15
chloride [1] 127/10	168/15 169/2 169/9	69/11 78/4 148/15	6/16 6/18 6/19 7/5	concentrated [3]	conforming [1] 39/25
choice [2] 174/23	171/3 172/2 172/9	coloured [1] 81/5	7/25 8/19 8/22 8/24	57/10 122/4 131/1	confusion [1] 153/8
175/12	172/21 176/5 186/15	column [2] 18/15	9/1 9/2 9/6 9/11 9/20	concentrates [20]	connection [3] 4/20
circa [1] 27/21	clinically [2] 72/20	184/7	9/22 10/1 10/5 23/23	10/8 40/11 48/15	16/22 152/2
circulates [1] 168/20	132/25	columns [1] 113/14	24/22 25/17 28/4 28/6	49/14 73/11 106/20	conscious [2] 52/11
circulation [3] 168/23	clinician [1] 186/10	combined [1] 159/13	29/19 31/9 32/10	107/2 119/2 122/6	100/19
169/24 170/3	clinicians [8] 13/16	come [44] 5/19 7/5	34/21 34/21 36/8	122/7 124/25 125/10	consenting [3] 143/18
circumstances [6]	17/3 17/7 66/22 85/5	8/8 13/8 13/11 14/6	36/24 38/3 38/20	126/23 127/6 131/2	143/20 144/13
9/23 44/23 103/15	136/5 186/14 186/16	15/24 16/7 23/21	38/25 39/7 39/12	131/5 134/9 134/10	consequence [2]
163/16 168/16 169/12	clone [1] 178/7	24/11 25/11 31/3	39/15 39/17 40/21	136/22 185/25	130/21 130/24
citation [1] 129/10	clones [1] 79/15	38/24 42/9 64/18 66/9	41/6 41/12 42/5 43/16	concentrating [1]	consider [7] 45/18
cite [1] 47/6	close [1] 186/14	68/4 73/1 77/18 90/14	43/19 49/3 54/12	85/25	56/11 56/15 61/20
cited [3] 113/2 130/18	closed [2] 97/15	94/21 99/7 100/17	54/16 56/7 56/14 58/6	concentration [3]	98/11 117/15 153/19
173/24	170/13	101/17 102/8 118/22	59/11 61/1 61/4 61/12	112/13 112/23 117/23	considerable [5] 56/6
citing [1] 175/15	closely [2] 35/16	139/18 140/14 141/23	62/21 67/12 74/12	concept [2] 96/13	60/7 78/25 79/21
citrated [4] 108/1	163/15	152/7 152/15 155/3	77/4 77/16 78/4 85/16	168/18	122/7
	clot [1] 156/16	155/14 158/23 165/8	94/2 94/17 95/3 95/20	concern [6] 49/19	considerably [2] 64/4

(54) cetera - considerably

C	81/9 contrast [2] 66/8 100/5 contribution [1] 86/3 control [16] 35/8 36/23 41/9 41/15 48/22 50/6 50/7 82/22 86/14 99/11 150/24 157/4 157/10 157/11 158/2 163/20 controlled [2] 106/24 163/16 controlling [1] 157/15 controversy [1] 173/22 convenient [1] 155/6 conventional [6] 71/3 73/15 73/20 78/19 81/7 100/10 conversation [4] 90/24 91/3 91/8 146/2 conversion [1] 137/20 cooperation [2] 84/17 159/8 copied [2] 16/15 60/14 copy [7] 26/13 27/10 39/16 48/3 50/2 126/25 132/18 Core [6] 155/13 180/12 180/22 181/12 181/14 192/6 corner [6] 4/12 27/7 27/9 33/16 68/9 74/23 cornerstones [1] 50/4 corporate [2] 54/25 95/14 Corporation [1] 6/15 correct [1] 102/21 corrected [1] 53/7 correcting [2] 96/9 109/12 correspondence [8] 10/23 11/12 18/3 60/17 79/24 87/5 93/2 99/16 cost [2] 19/22 69/6 Costello [2] 146/18 148/21 costly [1] 75/18 costs [8] 57/14 57/17 60/2 60/4 60/5 60/5 61/22 62/4 could [106] 4/11 5/1 6/13 7/3 7/19 8/14 10/11 11/15 11/22 11/23 15/19 16/5 16/11 18/2 22/18 29/18 31/5 31/11 32/18 33/7 36/18 38/5 38/17 41/25 44/18 49/8 52/25 53/5 54/4	55/7 57/16 57/23 58/4 59/15 59/23 61/4 62/7 62/16 67/12 71/8 74/22 74/25 80/16 81/16 90/2 90/3 90/5 92/23 95/13 95/19 96/20 98/16 102/1 105/25 106/4 106/13 107/17 108/7 109/11 110/5 110/23 111/23 112/22 116/19 117/22 118/8 120/5 120/19 121/15 122/1 124/18 125/12 126/20 127/10 127/23 128/11 128/21 128/23 129/2 129/24 130/15 131/8 131/13 131/14 132/15 133/4 134/4 134/25 135/17 139/1 139/8 156/11 157/19 157/20 157/22 158/16 163/16 166/3 167/2 168/25 170/20 173/19 176/13 177/21 183/22 189/8 couldn't [8] 125/16 125/17 127/15 147/8 160/12 165/5 170/1 179/8 counsel [4] 1/3 180/21 180/23 192/2 counterelectrophoresis [1] 122/23 countries [1] 69/9 country [6] 22/8 22/9 81/15 91/18 178/16 178/17 couple [13] 3/10 101/1 109/10 113/1 115/7 115/25 135/24 138/8 141/9 158/10 160/11 175/1 186/22 coupled [2] 31/24 69/8 course [26] 1/24 4/7 5/19 14/6 15/25 22/17 24/2 31/4 52/13 53/8 53/20 67/14 74/5 74/9 86/22 90/11 102/9 128/19 132/3 133/24 137/20 153/16 153/20 155/4 162/2 165/5 courses [1] 174/19 covered [1] 174/17 covers [1] 121/12 CPs [1] 186/19 create [3] 84/1 111/5 184/8 created [2] 80/10 136/3 creating [1] 154/24 creation [1] 140/12	criteria [1] 25/9 critical [1] 141/17 cross [2] 154/15 171/13 crux [1] 7/10 cryo [14] 71/17 72/4 73/8 86/1 86/7 91/11 91/16 163/25 164/4 173/24 174/5 174/12 174/16 174/22 cryoprecipitate [25] 64/24 68/14 71/21 78/3 85/22 91/17 93/13 97/3 97/5 98/4 106/16 134/25 135/3 135/12 135/15 136/19 137/2 137/6 163/2 163/18 171/6 171/7 171/9 172/20 172/24 cryosupernatant [2] 106/16 111/21 cryptic [1] 15/9 CSM [3] 33/18 92/21 173/24 CSM/81/1st [1] 33/18 CTC [2] 174/13 174/17 CTO [1] 103/8 cultures [1] 167/5 current [11] 8/17 18/19 26/6 37/24 49/7 71/16 82/21 90/21 147/7 153/1 191/11 currently [1] 49/14 customers [1] 19/3 Cutter [43] 1/18 5/11 5/12 10/10 10/21 18/6 18/8 19/21 20/22 21/4 23/5 23/7 23/15 25/19 28/4 28/16 29/2 29/3 29/17 29/18 29/23 30/12 30/17 30/18 31/8 32/3 34/8 34/10 34/17 34/20 35/7 35/17 36/4 36/12 36/13 36/16 38/10 38/17 39/20 41/8 41/8 42/19 67/4 Cutter's [5] 21/6 25/19 29/10 35/21 42/16 cynical [1] 22/12	69/23 96/6 149/11 date [18] 16/14 18/4 37/18 37/19 44/9 44/11 45/21 45/23 56/23 65/8 66/14 71/6 71/6 74/22 97/9 102/21 115/14 152/7 dated [16] 3/22 17/14 21/25 28/9 48/3 49/21 68/8 80/19 82/9 87/11 87/20 89/25 93/1 95/18 101/24 164/6 dates [2] 7/17 70/23 dating [1] 50/18 David [15] 8/7 8/8 13/14 18/5 145/17 146/4 161/6 166/14 167/8 178/22 179/18 179/24 187/20 188/18 188/25 David Heath [1] 145/17 day [4] 17/5 39/15 119/3 160/13 days [3] 8/2 126/7 167/9 DEAE [2] 108/9 111/12 DEAE-cellulose [2] 108/9 111/12 deal [4] 114/22 153/1 156/19 180/14 dealing [6] 8/1 69/20 111/25 149/20 181/24 182/20 dealt [3] 50/12 50/17 182/24 Dear [4] 24/20 49/23 80/23 161/6 death [2] 181/21 182/13 December [8] 3/22 17/21 18/4 22/15 31/10 55/13 83/20 152/11 December 1979 [1] 17/21 December 1981 [1] 83/20 decide [3] 3/3 124/7 186/9 decided [2] 22/2 184/5 decision [4] 44/21 44/22 46/14 138/18 decision-making [2] 44/21 44/22 declaration [1] 21/8 declines [1] 69/13 decrease [1] 69/11 dedicated [1] 179/12 deemed [1] 35/25	deeply [1] 83/10 Def [1] 109/4 defects [1] 81/16 deficiencies [2] 109/12 110/11 deficient [3] 151/19 183/25 183/25 defined [1] 72/13 definitely [2] 115/4 117/19 Defix [11] 107/5 107/6 107/7 107/11 109/7 111/5 131/17 131/18 131/23 132/2 144/18 degree [5] 21/10 57/3 120/16 139/7 141/12 degrees [3] 125/13 125/23 135/4 deliberately [1] 122/3 delighted [2] 25/4 50/8 delivered [1] 26/5 delivery [2] 26/9 41/12 Deloitte [1] 3/20 Delta [1] 102/24 delve [1] 121/15 demand [3] 68/22 69/12 110/13 demonstrate [1] 87/8 demonstrated [3] 73/4 75/24 165/18 demonstrates [1] 113/22 demonstrating [1] 129/8 denaturation [1] 125/21 denied [1] 82/15 department [15] 56/9 56/13 56/16 57/17 61/19 62/2 62/11 83/6 83/7 102/15 104/12 104/13 104/14 179/11 182/11 depended [1] 157/7 dependence [2] 42/8 110/25 dependent [1] 167/19 depending [3] 72/23 121/21 156/20 deplete [2] 184/6 184/7 depleted [3] 108/1 108/11 152/22 deputy [1] 95/8 derived [1] 39/24 describe [1] 1/12 described [6] 87/13 91/15 108/8 109/2 113/23 186/23 describes [1] 111/10
----------	--	---	--	--	---

(55) considerably... - describes

D	DHSC0003936 [4] 54/5 60/11 74/18 80/6 DHSC0003950 [1] 92/23 DHSS [20] 23/24 41/2 48/4 54/2 54/8 60/9 60/14 60/18 60/21 80/4 81/2 90/25 91/6 92/7 94/14 149/20 173/16 175/9 175/10 176/17 DHSS's [1] 98/5 Diagnostic [1] 185/6 dialogue [1] 37/4 Diana [1] 80/23 did [76] 2/18 17/25 31/6 42/22 62/2 102/3 102/22 107/2 115/1 115/2 115/22 117/8 118/22 127/21 128/18 132/5 132/6 132/7 134/18 135/11 135/23 140/16 140/16 141/18 142/4 142/11 142/19 143/2 143/12 144/15 145/1 145/4 145/6 145/13 146/14 147/2 147/19 147/24 148/9 149/7 150/21 151/2 151/23 151/25 152/16 153/3 153/4 153/5 153/6 157/9 160/23 161/23 164/12 165/11 167/1 169/9 170/4 173/2 173/2 173/12 178/13 181/22 182/5 184/17 185/3 185/3 186/15 187/4 187/17 187/25 187/25 188/3 188/9 188/11 189/4 190/1 didn't [28] 13/8 29/17 29/20 38/12 84/11 100/4 107/1 117/12 127/17 128/6 128/8 131/6 141/21 147/23 152/5 152/17 153/1 163/11 178/11 179/21 188/5 188/15 188/17 189/1 189/5 189/6 189/9 190/24 died [1] 115/4 dietary [1] 6/4 differ [1] 73/14 difference [4] 20/13 119/3 119/7 136/15 differences [1] 1/7 different [32] 3/2 8/18 17/4 22/22 23/2 24/13 27/24 29/12 31/17 52/20 58/1 69/23 105/5 106/3 106/6	110/3 119/6 128/5 131/22 144/19 151/4 157/12 167/5 169/19 172/1 179/13 180/22 180/25 181/1 185/9 185/22 187/8 difficult [12] 49/12 86/4 86/8 115/11 135/20 151/1 157/4 157/11 158/2 167/10 190/15 190/20 difficulties [5] 18/9 18/9 101/14 169/16 189/12 difficulty [2] 25/17 150/14 diluted [2] 106/17 122/13 direct [4] 25/20 28/25 38/9 78/4 directed [3] 4/13 93/7 153/22 directing [2] 140/21 153/9 direction [2] 95/7 96/13 directions [1] 148/25 directly [5] 23/7 28/3 69/2 100/25 104/7 director [14] 8/4 8/5 8/6 13/14 31/13 42/11 51/6 92/13 95/16 103/4 114/12 136/11 145/19 146/18 directors [7] 17/13 48/8 48/11 49/9 51/7 51/8 144/11 disappearance [1] 74/13 disappointing [2] 85/15 162/7 discount [1] 17/6 discover [1] 130/5 discovery [2] 57/16 57/21 discriminate [1] 157/22 discuss [4] 13/17 54/2 54/10 85/23 discussed [9] 60/8 61/18 108/23 115/20 140/9 170/12 174/9 174/19 175/19 discussing [1] 172/6 discussion [8] 31/20 33/14 40/2 40/4 114/2 124/21 175/2 185/10 discussions [9] 60/10 113/19 114/8 114/10 124/12 126/13 138/14 144/2 186/13 disease [3] 110/13	162/21 163/12 diseases [1] 97/8 disillusioning [1] 100/2 dismissed [2] 126/17 174/9 disparate [1] 100/9 dispassionate [1] 86/23 dispersed [1] 178/6 disposable [1] 55/25 disprove [1] 73/18 dispute [1] 99/9 disputes [1] 9/24 disquiet [1] 49/10 dissolved [2] 135/15 135/16 distinctions [2] 26/18 186/2 distribute [1] 21/17 distribution [2] 10/9 23/4 distributor [1] 37/2 distributors [1] 36/11 distributorship [1] 5/12 disturbed [2] 81/15 83/10 disturbing [1] 49/25 diverted [1] 96/4 division [2] 39/23 76/15 DNA [1] 77/3 do [69] 4/25 14/5 22/19 23/20 26/10 29/15 29/17 29/20 36/12 57/3 57/4 66/12 71/2 71/11 73/5 77/10 94/19 97/23 101/16 103/23 113/8 113/15 113/19 114/2 114/7 114/17 115/18 118/2 119/8 120/14 124/12 125/19 125/25 135/11 137/13 145/1 146/14 155/8 157/14 158/14 160/21 165/9 166/3 166/17 166/19 169/9 170/5 173/2 175/8 175/23 176/8 176/9 176/25 179/6 179/8 179/22 180/18 180/19 182/7 182/13 182/19 182/23 183/19 183/21 184/15 185/7 188/19 189/4 191/18 doctor [2] 31/25 143/16 Doctor Duncan Thomas [1] 31/25 document [48] 3/18 3/19 7/20 14/18 21/24	30/9 31/6 32/24 33/8 33/22 43/7 46/13 53/23 56/17 60/2 62/1 65/18 65/20 66/8 66/9 68/6 68/9 70/12 71/7 71/11 74/21 75/1 80/21 80/24 81/17 81/21 82/7 82/21 83/12 83/17 83/23 84/23 85/23 86/19 87/2 90/8 90/9 92/20 98/17 107/19 120/6 160/24 183/1 documentation [1] 60/10 documents [24] 2/1 3/1 3/6 9/18 11/1 23/18 27/22 29/8 29/25 53/24 65/20 66/20 70/1 70/4 74/16 80/13 86/25 87/4 89/20 94/23 99/18 101/2 107/20 128/22 does [17] 16/9 27/18 28/22 29/21 30/4 30/25 51/9 65/19 75/19 88/18 121/14 158/13 172/11 174/4 181/2 186/6 191/6 does it [1] 28/22 doesn't [2] 47/6 97/19 dogs [1] 130/18 doing [36] 3/17 13/22 29/10 57/2 91/23 98/8 105/15 106/13 106/14 113/5 123/22 137/18 141/7 141/7 141/8 141/10 141/13 144/21 145/10 145/12 148/10 148/11 148/14 149/1 152/22 153/8 161/9 167/25 168/11 179/19 182/2 185/2 186/16 186/17 188/14 189/4 Don [1] 159/15 don't [61] 6/20 7/6 10/25 20/2 20/8 23/17 29/16 33/25 45/4 46/13 46/25 47/3 47/8 51/1 65/24 66/12 71/10 71/10 100/12 114/5 114/14 114/21 118/11 126/5 132/18 137/14 139/17 144/12 144/12 150/19 151/21 151/24 151/24 152/15 152/16 152/21 153/3 155/2 158/20 158/20 159/23 162/8 168/11 169/4 169/4 172/13 175/17 176/7 176/9 177/2 179/15 180/6	180/7 180/12 180/18 182/22 182/25 183/2 183/21 184/20 190/12 donation [4] 12/2 68/17 115/3 138/1 donations [5] 112/3 112/4 113/3 113/9 138/7 done [27] 1/21 35/15 35/17 35/24 37/20 44/13 45/25 66/2 66/4 66/13 88/12 105/5 137/14 144/6 151/24 161/13 163/4 163/15 168/12 177/16 178/20 188/7 188/21 190/20 190/25 190/25 191/18 donor [19] 27/15 37/18 44/10 44/13 45/22 45/25 46/10 68/21 68/25 69/11 78/6 112/12 135/2 135/8 137/10 138/8 138/16 189/16 189/17 donors [11] 11/5 12/7 41/23 42/15 84/7 112/9 116/15 117/1 122/22 122/24 138/5 door [3] 97/15 98/14 170/13 dose [3] 130/21 130/24 131/9 doses [1] 109/20 doubt [5] 37/22 52/13 74/12 96/15 97/17 doubts [3] 15/15 61/5 161/22 down [20] 8/10 9/7 13/1 18/14 22/15 22/24 31/11 65/21 85/11 85/23 87/25 90/5 124/22 152/19 160/15 166/25 170/18 179/16 187/13 191/3 downside [1] 189/14 Dr [112] 16/20 17/11 17/16 24/7 26/19 28/12 30/11 30/13 30/15 30/25 31/1 32/12 33/2 33/2 33/4 33/5 33/20 39/8 40/23 42/9 48/4 48/6 49/20 49/22 50/2 50/16 51/18 55/6 55/21 58/12 58/13 58/15 58/22 58/24 60/15 60/19 60/20 70/5 70/19 71/13 72/14 74/2 79/24 80/18 80/18 80/20 80/22 81/25 82/2 82/6 82/10 82/10 82/11 83/10
----------	--	--	--	---	--

(56) describing - Dr

D	Dr Joseph Smith [1] 33/2 Dr Keith Fowler [1] 91/6 Dr Kernoff [1] 17/11 Dr Kingdon [1] 72/14 Dr Kingdon's [1] 26/19 Dr Lane [7] 55/21 80/18 80/20 80/22 82/10 84/25 171/16 Dr Lane's [1] 82/6 Dr Lane's's [1] 83/17 Dr Prentice [1] 145/19 Dr Preston [1] 17/16 Dr Preston's [1] 58/24 Dr Prowse [1] 134/8 Dr Purves [1] 173/17 Dr Richard Lane's [1] 58/22 Dr Savidge [1] 50/2 Dr Smith [15] 82/10 83/10 83/14 84/24 85/2 86/22 87/2 104/19 105/16 105/17 108/5 119/13 119/14 135/11 140/23 Dr Smith's [2] 85/20 86/20 Dr Stewart [1] 16/20 Dr Thomas [1] 32/12 Dr Thomas's [1] 91/14 Dr Tuddenham [6] 71/13 74/2 79/24 158/22 171/17 177/11 Dr Tuddenham's [2] 162/11 164/15 Dr Waiter's [1] 60/19 Dr Walford [3] 60/15 80/18 82/2 Dr Walford's [1] 81/25 Dr Wintersgill [1] 60/20 draft [1] 17/12 dramatic [1] 68/19 draw [2] 100/13 143/15 drawing [1] 49/24 drawn [4] 26/18 59/3 81/3 143/16 dreadful [1] 167/17 dreams [1] 187/24 dried [11] 25/21 30/21 135/17 136/16 136/19 136/21 137/1 137/1 137/5 163/20 163/23 dropped [1] 157/25 drove [1] 142/3 drug [1] 5/5 drying [2] 111/13 161/10	due [27] 1/24 4/6 5/19 14/6 15/25 17/3 31/4 52/13 53/8 53/19 67/14 69/5 74/5 74/9 90/11 97/5 97/6 102/9 128/19 132/3 133/2 133/24 153/15 153/20 155/3 163/17 163/21 Duncan [2] 22/4 31/25 during [15] 2/22 37/20 44/13 46/1 61/16 74/8 88/19 96/8 109/16 112/6 113/16 116/2 157/6 170/12 185/11 Dutch [2] 118/22 118/23 dying [1] 181/19 Dyos [1] 31/14	E E100 [1] 139/9 E5 [1] 73/5 each [14] 9/3 12/2 12/4 13/20 13/21 19/6 24/17 27/15 60/1 78/5 94/10 112/2 139/12 148/9 earlier [16] 27/25 38/16 46/20 60/19 61/5 66/21 72/12 74/10 127/7 138/13 139/1 148/6 148/7 162/10 171/15 177/14 early [8] 2/22 2/23 50/6 102/1 115/9 115/10 166/16 176/22 earnings [2] 57/18 60/24 earth [1] 166/17 easier [1] 167/18 easily [2] 167/2 174/12 East [1] 134/11 easy [2] 150/13 157/19 EAW [1] 173/8 echoed [1] 86/11 echoing [1] 83/17 economical [1] 166/5 economically [2] 76/1 165/20 economies [1] 81/24 edge [1] 189/5 Edinburgh [6] 102/11 104/5 104/15 121/5 142/8 182/8 EDTA [4] 109/21 110/3 110/5 110/22 Edward [1] 70/5 effect [5] 2/3 10/23 10/24 68/17 144/14 effectively [1] 84/17	effectiveness [1] 108/22 effects [1] 145/5 efficacious [3] 76/1 164/17 165/20 efficacy [1] 158/19 efficient [1] 111/8 effort [1] 79/1 efforts [1] 86/15 eg [1] 110/13 eighties [2] 2/23 2/23 either [9] 6/7 58/8 81/6 90/23 92/17 151/17 158/21 179/5 185/20 electrically [1] 118/19 electronic [7] 96/21 98/17 111/23 120/5 124/18 124/20 132/17 electronically [1] 75/1 electrophoresis [1] 76/20 element [2] 2/9 32/8 elements [2] 1/16 106/6 eligible [1] 62/4 eliminate [1] 133/1 else [7] 83/8 119/19 151/14 151/18 175/17 189/3 190/10 else's [1] 119/17 elsewhere [2] 67/16 184/16 Elstree [9] 14/15 64/17 151/18 152/19 160/8 160/17 171/12 171/18 171/19 elute [2] 157/17 157/19 eluted [2] 53/15 108/12 elution [2] 69/4 111/13 EMA [1] 138/23 embarrassing [1] 22/6 emerged [2] 40/3 75/9 emergency [1] 110/15 eminent [1] 3/21 emphasis [2] 89/10 117/8 emphasise [1] 159/9 emphasising [1] 84/9 employ [1] 77/25 employed [2] 7/22 105/7 employee [1] 9/6 employees [2] 82/15 83/5 employing [1] 97/7 employment [1] 57/20 empt [1] 3/1	empted [1] 145/23 enable [4] 42/5 43/2 43/10 68/21 enclose [1] 161/7 enclosed [1] 26/2 enclosing [1] 50/1 encouraging [1] 73/11 end [13] 23/6 25/14 34/10 66/18 77/24 84/20 95/3 110/25 119/3 150/16 158/8 162/2 190/10 ended [6] 66/16 84/18 139/21 145/21 167/2 174/8 ending [2] 67/3 67/4 Endogenous [1] 122/3 ends [2] 66/17 189/10 energetic [1] 180/2 energy [1] 71/25 engaged [1] 135/21 engineered [1] 99/3 engineering [2] 79/5 84/5 English [1] 184/19 enormous [1] 81/13 enough [2] 16/8 178/25 ensure [4] 29/19 36/8 39/3 96/14 entail [1] 147/2 entered [2] 29/18 80/9 Enterprise [8] 4/1 4/14 4/23 9/10 67/17 77/17 84/16 87/22 enthusiasm [2] 89/5 187/20 entirely [9] 12/18 25/6 72/6 82/18 89/16 91/24 92/6 95/17 174/15 entities [1] 9/10 entitled [3] 6/6 59/24 107/24 entity [1] 169/19 entrepreneurial [3] 166/15 166/16 166/21 envisaged [4] 55/10 55/18 59/13 63/22 enzyme [2] 5/7 159/18 episode [1] 94/9 episodes [1] 109/16 equipment [8] 6/6 58/7 64/22 101/14 137/15 141/4 142/23 176/22 equity [7] 8/18 9/3 9/5 9/11 77/21 87/24 92/19 equivalent [2] 20/21	184/15 Er [1] 114/12 Err [2] 113/18 165/24 error [1] 164/10 especially [1] 61/16 essence [3] 17/8 100/7 158/3 essential [1] 96/7 essentially [7] 135/13 135/16 136/19 139/3 146/2 146/22 157/14 establish [1] 96/1 established [2] 89/21 131/1 establishment [2] 54/13 76/17 estate [2] 7/2 188/2 estimated [2] 80/12 122/9 et [7] 59/21 154/11 171/16 171/16 178/8 185/18 186/17 et cetera [5] 59/21 154/11 178/8 185/18 186/17 etc [3] 49/1 55/10 63/10 ethical [1] 5/5 Ethylene [1] 138/22 Ethylenediaminetetra acetic [1] 110/6 Europe [5] 77/7 88/23 118/24 119/17 119/19 evaluated [2] 139/6 139/14 evaluating [1] 77/19 Evaluation [1] 138/21 Evans [7] 28/12 30/11 30/25 31/1 38/16 51/13 51/18 even [8] 61/10 61/13 126/6 133/1 140/6 164/2 176/12 188/5 event [3] 48/25 94/7 118/9 events [1] 84/11 eventual [1] 75/12 eventually [2] 42/7 188/3 ever [5] 95/1 103/21 149/19 167/15 169/13 every [5] 35/2 44/3 45/15 57/25 84/6 everybody [3] 116/13 124/4 184/10 everything [3] 85/10 117/8 189/3 evidence [35] 1/24 2/20 2/24 3/1 8/13 9/23 13/9 15/18 26/17 26/20 26/22 29/17 33/3 37/17 37/22 43/2
----------	---	--	--	---	--	--

E	106/5 106/13 110/5 133/4 135/1 156/11 183/22 explained [7] 41/7 42/3 42/9 66/22 146/6 149/25 190/21 explains [3] 13/12 27/2 57/20 explanation [3] 7/9 139/1 139/1 explicit [1] 82/12 exploit [3] 76/5 99/22 99/23 exploited [1] 119/11 explore [2] 2/4 11/7 export [2] 60/24 69/12 exported [1] 55/12 exports [1] 57/19 exposed [2] 156/24 156/25 express [2] 133/19 162/24 expressed [6] 15/15 47/16 49/10 50/9 80/15 162/12 expresses [1] 83/14 expression [1] 79/15 expressly [1] 153/16 exquisite [1] 159/13 extended [2] 96/12 110/11 extends [1] 21/16 extension [2] 42/4 63/8 extensively [1] 19/24 extent [2] 11/4 150/25 external [3] 59/5 60/4 76/25 extra [2] 68/20 84/1 extract [1] 92/11 extremely [2] 61/1 71/3	factor IX [25] 51/24 106/8 106/21 106/23 106/25 109/15 110/17 110/24 113/16 117/7 120/13 121/9 125/15 129/4 130/16 130/21 130/25 131/2 131/9 131/12 132/8 134/9 144/17 144/18 150/15 Factor VII [2] 106/19 109/25 factor VIII [106] 1/22 2/2 2/7 2/11 2/13 2/16 5/10 5/25 10/12 14/13 15/10 15/22 16/3 24/14 24/14 25/21 30/21 34/7 41/21 42/7 42/8 48/14 50/1 52/18 53/1 53/3 53/22 56/5 57/10 66/8 68/24 70/7 72/11 72/18 72/19 73/1 73/3 73/19 78/10 78/19 85/4 85/6 85/7 85/14 88/7 88/10 88/21 89/13 91/20 98/9 100/18 101/3 110/21 134/24 135/5 135/18 139/18 143/6 144/15 145/1 145/4 146/21 147/6 147/24 148/14 149/24 150/2 150/7 150/10 150/14 151/1 151/3 151/4 153/20 154/5 154/15 154/20 155/5 155/6 155/21 156/20 157/3 157/5 157/25 158/4 158/8 159/3 159/18 163/9 163/11 166/17 166/21 166/22 167/12 167/19 168/8 170/14 172/19 176/3 176/19 176/25 177/3 178/2 178/19 179/4 184/6 factor VIII' [1] 81/7 Factor VIII-deficient [1] 183/25 factor VIII-depleted [2] 108/1 108/11 factor VIII:C [14] 25/2 59/17 63/2 63/3 63/8 63/12 63/24 73/10 75/25 78/14 78/23 79/16 168/19 170/3 Factor VIII:C' [1] 88/2 Factor VIII:RAg [1] 64/2 Factor X [1] 131/13 Factorate [3] 14/15 14/22 14/23 factors [22] 52/18 62/25 66/5 68/20	107/1 107/25 108/10 108/11 108/20 109/13 110/12 111/10 118/4 118/5 119/5 122/16 123/8 125/16 126/3 141/11 158/7 185/8 factory [4] 7/1 55/9 55/11 55/12 fail [1] 176/21 failed [2] 123/3 163/20 failing [1] 96/25 failure [4] 88/23 99/22 99/23 177/15 fair [7] 1/12 47/5 134/16 141/12 141/12 142/18 152/25 fairly [8] 7/9 15/23 94/16 95/21 113/11 114/24 120/2 156/6 fairness [1] 170/11 faith [1] 117/2 fall [1] 98/22 falling [1] 17/20 family [1] 144/9 far [13] 21/16 29/8 30/3 52/12 53/2 61/9 75/12 95/4 123/23 126/13 149/14 153/12 182/4 fast [1] 91/10 fathom [1] 90/21 fault [2] 65/5 96/22 favour [1] 14/24 FDA [4] 39/23 41/9 41/24 42/1 FDA/BOB [1] 41/9 feasibility [1] 63/3 feasible [3] 72/6 168/24 170/16 feature [1] 86/18 February [7] 21/25 22/10 23/11 23/25 24/5 34/11 47/23 February 1980 [4] 23/11 23/25 24/5 34/11 February 1981 [1] 47/23 Federation [1] 70/18 feel [6] 21/23 73/18 84/12 88/5 92/15 123/1 fees [1] 57/19 felt [4] 15/14 16/10 41/25 133/8 few [9] 8/10 28/10 31/5 75/7 104/4 160/19 160/20 180/11 181/13 fibrinogen [3] 78/22 78/25 135/5	fibronectin [3] 78/22 78/24 81/11 fibronogen [2] 59/20 64/1 figure [8] 19/15 20/9 21/1 99/2 116/9 116/15 116/23 117/2 figures [4] 8/20 12/13 19/4 59/25 file [1] 13/25 files [1] 161/4 fill [2] 25/20 102/8 Filling [1] 35/20 filtration [2] 86/11 161/10 final [11] 6/9 49/8 56/2 72/16 73/23 98/18 118/15 118/16 132/20 138/20 157/18 finalisation [3] 63/7 63/15 153/2 finalise [1] 65/25 finance [3] 8/23 66/23 76/11 financed [1] 76/15 financial [11] 18/9 42/8 54/3 54/11 57/4 61/2 61/20 62/10 77/12 81/15 87/23 financially [2] 20/20 61/5 Financing [1] 25/16 find [3] 67/15 85/15 115/23 findings [3] 33/10 42/25 76/9 fine [1] 7/7 finished [8] 35/15 35/24 36/2 44/14 46/1 47/11 78/10 180/20 finite [1] 77/11 firm [11] 3/21 3/21 43/2 43/10 61/8 77/18 83/4 98/10 102/24 177/25 178/1 firms [1] 4/2 first [58] 1/17 16/5 16/7 16/7 18/24 19/8 24/25 25/4 25/18 27/23 28/8 32/23 35/14 48/16 48/18 52/25 54/18 56/3 58/1 58/13 59/17 61/3 61/16 62/24 64/6 66/2 69/1 70/20 77/14 79/3 85/8 93/13 96/8 102/13 102/14 105/7 106/7 107/9 107/12 109/7 113/1 115/7 117/13 118/18 122/18 124/1 130/17 135/18 135/23 135/23 135/24	136/12 139/13 142/13 154/4 177/9 178/7 183/19 five [11] 12/22 43/23 75/19 93/1 93/15 101/6 112/13 141/16 148/15 181/4 181/7 five years [2] 75/19 141/16 five-fold [1] 112/13 flagged [1] 32/11 flow [2] 61/14 188/9 fly [1] 177/2 focus [4] 14/4 47/7 88/9 100/9 focused [1] 173/12 fold [1] 112/13 follow [3] 38/5 61/8 120/6 followed [2] 35/16 81/11 following [12] 14/16 40/3 41/12 41/19 43/15 45/12 48/1 76/16 79/15 86/5 93/15 112/16 follows [7] 18/13 39/9 40/22 58/4 59/14 72/10 154/16 food [1] 6/5 foot [2] 7/1 75/16 forecasts [1] 97/12 foreign [1] 57/18 forerunner [1] 107/4 forgive [4] 108/18 124/19 151/12 183/7 form [9] 53/6 53/12 61/21 76/15 77/20 82/5 90/24 108/13 111/13 formalise [1] 80/7 formally [1] 67/23 former [2] 6/3 145/6 formulate [1] 153/4 formulated [1] 135/16 formulating [1] 105/14 formulation [3] 35/20 35/20 109/4 forward [8] 31/5 68/2 80/8 84/19 84/22 101/17 177/17 178/4 Foster [8] 128/15 128/25 129/3 130/14 132/3 133/22 140/14 145/8 Foster's [2] 128/12 129/15 found [16] 12/2 17/25 19/14 22/7 27/17 34/1 43/1 43/9 51/24 112/9 112/14 116/16 122/11
----------	--	---	--	--	---

(58) evidence... - found

F	142/16 142/21 152/22 164/23 165/21 183/24 Freedom [2] 42/2 42/17 freeze [13] 25/21 30/21 111/13 135/17 136/16 136/19 136/21 137/1 137/1 137/5 161/10 163/20 163/23 freeze-dried [8] 25/21 30/21 135/17 136/21 137/1 137/5 163/20 163/23 freeze-drying [1] 111/13 French [1] 22/5 frequent [1] 15/6 frequently [2] 36/23 109/14 fresh [7] 81/22 109/11 110/20 163/1 164/2 167/20 183/12 fresh-frozen [1] 109/11 Friday [1] 1/1 fridge [1] 136/17 from [269] from British [1] 134/6 front [2] 3/19 74/19 frontally [1] 108/12 frozen [10] 86/1 86/7 109/11 164/2 167/20 171/9 172/19 173/1 173/2 183/12 fruition [2] 99/25 190/2 full [15] 3/13 12/21 16/4 31/14 31/18 34/24 78/5 87/12 91/24 92/3 100/23 109/24 119/1 119/25 152/17 fully [4] 39/3 78/24 129/9 132/24 function [1] 98/7 fund [5] 61/12 67/12 76/11 77/13 99/1 fundamental [2] 96/25 99/19 funding [6] 61/6 61/24 67/15 100/9 130/4 179/16 funds [5] 61/18 75/5 81/14 96/3 166/2 furnish [4] 44/3 44/9 45/14 45/21 furnished [1] 41/7 further [47] 6/14 8/23 11/4 11/10 11/11 19/6 21/24 22/1 22/14 22/15 26/2 28/1 30/23 31/20 34/1 34/2 36/24	55/4 60/5 65/21 69/4 70/25 73/17 74/6 74/12 76/22 80/10 82/7 83/12 85/23 90/5 91/17 94/2 94/24 101/12 108/14 111/14 123/4 132/24 133/19 134/1 155/4 175/18 176/4 176/24 185/20 186/20 future [13] 6/25 10/16 66/10 68/3 68/12 69/19 80/5 91/22 96/14 98/12 154/20 167/8 189/22 FVIII:C [1] 73/7	G gamma [2] 139/12 139/22 gap [3] 25/20 46/25 47/9 garage [5] 142/15 187/15 187/16 187/17 188/8 gas [2] 158/6 159/17 gave [11] 9/24 44/19 44/24 70/10 70/13 93/3 138/20 141/17 148/25 156/5 179/19 gene [3] 79/14 159/4 178/7 Genentech [3] 177/17 178/14 179/10 general [3] 2/17 9/17 39/22 generally [4] 17/5 17/20 156/25 156/25 generate [3] 57/18 81/14 88/4 generates [1] 99/9 generation [1] 77/10 genetic [2] 79/4 84/5 genetically [1] 99/3 Genetics [1] 178/14 German [3] 6/16 6/18 85/5 get [24] 15/4 17/8 59/6 67/16 71/5 92/18 100/4 117/12 121/23 127/17 128/6 128/12 135/14 144/10 146/4 158/8 160/12 167/6 170/1 179/8 184/17 186/15 188/3 189/9 gets [1] 53/14 getting [6] 13/21 58/18 95/3 117/10 119/1 158/19 give [17] 11/22 16/17 20/20 26/6 26/10 40/17 52/10 52/12	83/12 94/2 100/21 103/15 106/3 138/4 154/2 159/4 165/15 given [28] 11/19 18/10 22/4 30/23 38/23 42/20 45/11 46/12 50/2 51/19 62/7 72/9 74/11 93/12 96/9 103/10 114/17 114/18 116/10 116/15 116/23 117/2 120/7 124/8 138/25 143/10 149/12 176/21 gives [3] 19/6 57/1 85/19 giving [9] 8/12 26/1 39/1 39/12 71/3 103/14 138/8 143/19 154/23 Glasgow [9] 47/14 102/16 136/10 142/25 143/4 144/16 145/14 145/16 182/19 globulin [6] 34/7 34/17 37/25 40/18 139/12 139/22 globulins [3] 59/20 63/10 140/18 glycol [8] 121/10 121/16 121/18 121/23 122/14 127/5 132/5 132/9 GmbH [1] 6/16 go [64] 1/15 4/3 5/1 6/13 7/3 7/6 7/19 8/8 8/14 11/21 11/23 13/1 18/2 31/5 31/11 33/22 38/23 40/12 43/12 45/4 45/7 46/6 48/16 49/8 53/23 54/15 57/23 57/25 58/4 59/16 59/21 67/18 70/14 72/2 72/25 74/16 74/22 76/13 78/13 83/13 85/10 87/19 89/24 90/5 91/10 91/24 93/12 96/20 97/25 98/16 99/18 102/7 108/19 111/22 111/23 120/5 126/20 129/24 131/25 151/11 159/3 174/18 174/19 175/23 goer [1] 176/14 goes [14] 6/2 20/17 58/5 63/13 70/24 78/20 82/23 85/23 86/7 86/16 92/5 97/18 125/6 179/18 going [63] 4/3 4/25 14/3 16/17 18/5 24/10 24/16 33/22 38/15	40/14 47/10 52/9 59/25 60/9 60/18 80/8 80/13 84/19 85/9 88/3 94/3 110/8 111/9 111/22 116/7 116/12 119/4 120/18 122/18 125/25 126/5 126/6 128/3 128/11 132/13 143/23 146/7 146/22 147/5 148/7 148/9 149/23 154/23 155/5 158/23 158/25 160/4 160/22 160/24 165/11 167/23 167/24 170/16 177/2 177/6 179/1 179/8 179/14 181/15 183/1 183/3 189/21 189/22 gone [4] 88/22 160/15 175/25 189/23 good [17] 126/25 127/17 128/6 133/11 163/2 163/10 163/11 163/18 163/24 164/4 166/25 167/20 180/7 189/25 190/1 190/2 191/3 got [15] 21/13 82/3 119/6 132/9 137/2 142/15 146/6 150/16 157/23 160/13 163/10 167/15 170/2 179/22 181/2 government [6] 4/2 13/10 54/2 54/11 56/8 57/4 governmental [3] 72/7 92/17 122/21 gradations [1] 105/4 grand [1] 12/17 grant [3] 61/21 62/3 93/6 granted [8] 10/18 11/3 32/13 34/4 35/4 36/7 95/1 152/11 granting [1] 34/23 grants [1] 61/10 grateful [5] 28/19 49/17 90/16 101/8 190/19 great [4] 114/22 142/14 153/1 180/14 greater [4] 64/4 78/18 81/7 130/2 greatly [1] 49/6 ground [1] 83/5 grounds [5] 60/22 93/5 174/25 175/13 175/14 group [4] 79/11 87/21 92/14 104/15 Group [1] 4/20	group's [1] 74/20 growth [1] 95/25 Grundy [1] 26/14 guarantee [2] 26/8 36/14 guaranteed [1] 41/11 guess [6] 104/16 136/1 141/9 146/17 188/20 188/20 guidance [1] 104/18 guide [2] 52/10 121/16
	H had [138] 6/7 6/7 7/7 7/11 7/13 10/21 12/24 18/10 18/19 20/12 21/3 22/1 24/2 32/13 34/9 34/11 34/12 34/25 34/25 35/4 35/5 35/9 35/16 35/17 35/21 35/22 35/25 36/3 36/4 36/8 36/11 36/12 36/13 36/23 37/3 37/13 38/25 39/12 40/8 41/3 41/6 42/9 42/12 42/18 43/16 43/18 43/20 43/20 46/3 50/19 51/3 53/21 54/10 54/16 54/22 54/23 62/21 65/15 70/6 80/9 82/14 84/20 87/22 89/19 93/4 94/12 95/7 95/9 100/11 100/12 118/19 123/25 129/8 130/6 130/25 132/5 132/12 136/9 137/20 141/4 141/4 141/4 141/12 141/15 141/16 141/23 142/1 142/1 142/10 145/9 149/9 149/10 150/3 150/9 150/11 150/25 151/7 151/8 151/23 154/5 154/10 154/25 158/5 159/6 159/7 160/12 160/15 161/21 161/25 162/1 163/20 163/23 164/3 166/9 167/18 167/21 167/22 168/14 169/17 176/11 176/15 177/23 178/13 178/16 178/22 179/6 179/10 181/24 183/14 186/18 187/10 187/20 187/23 188/1 188/24 189/15 189/22 189/23 hadn't [5] 16/21 128/9 128/10 129/16 147/24 Haematology [1] 134/6					

H	19/24 22/2 25/3 25/16 25/23 27/15 34/7 35/14 39/7 45/11 48/21 48/22 51/24 53/9 57/7 57/10 57/10 60/18 66/7 66/13 71/15 73/12 75/9 75/21 78/3 80/25 81/2 81/12 81/20 85/15 86/10 86/11 86/23 89/10 90/1 90/23 90/23 91/5 91/6 96/8 96/10 97/9 109/19 110/10 112/9 112/13 112/14 112/19 122/24 123/2 123/3 124/23 133/12 161/8 180/20 180/21 183/6 184/10 Haskins [1] 3/20 have [228] haven't [6] 23/19 34/1 103/10 152/1 152/6 183/1 having [4] 40/14 143/4 150/3 168/15 HBsAg [1] 127/11 he [111] 13/19 14/25 15/1 15/8 15/11 15/12 15/13 15/16 16/3 16/21 16/21 18/12 19/6 26/13 26/13 41/21 42/3 42/9 42/12 42/15 42/18 42/18 42/22 48/6 48/8 48/9 50/22 50/23 51/9 70/10 70/13 78/20 82/12 82/13 82/23 82/23 83/1 83/2 85/19 85/23 86/7 86/16 87/13 91/5 91/15 91/23 92/12 92/13 95/16 104/22 128/17 128/18 130/3 130/8 132/1 133/7 145/10 145/12 146/19 148/22 148/23 158/5 159/1 159/2 159/3 159/6 159/6 159/11 161/5 162/12 165/14 165/16 166/12 166/15 166/15 166/16 166/17 166/18 166/19 166/19 166/23 166/24 167/2 167/2 167/2 167/3 167/11 167/22 167/22 167/23 168/1 168/1 168/3 168/3 168/5 168/7 178/13 178/24 179/19 179/25 180/3 180/3 180/4 187/23 187/25 188/20 188/24 188/24 189/4 189/15 190/1	he's [4] 26/21 68/12 131/24 158/24 Head [1] 105/1 headed [2] 3/23 78/1 heading [7] 7/20 8/16 31/12 33/8 57/5 57/24 67/19 health [5] 16/9 49/16 68/10 130/7 182/14 Health's [1] 57/17 hear [9] 1/24 2/20 2/24 9/22 10/5 100/18 100/23 101/2 101/6 heard [14] 1/18 10/8 10/21 16/21 19/19 23/8 26/17 33/3 145/17 146/2 149/3 156/4 162/10 177/14 hearing [8] 33/4 33/5 33/19 39/15 40/20 42/10 145/21 191/23 Hearings [1] 33/8 heat [3] 125/13 126/1 126/8 heated [4] 125/7 125/10 125/23 125/23 Heath [38] 8/4 8/7 8/24 9/21 16/15 54/7 68/4 68/8 83/24 83/25 84/9 84/11 87/5 87/11 87/20 88/1 88/15 88/16 89/18 90/1 91/4 91/6 91/7 92/5 95/7 95/10 99/10 99/20 99/25 145/17 161/2 165/12 165/25 166/10 177/22 187/20 188/19 189/1 Heath's [1] 177/14 heavily [1] 73/8 heavy [1] 133/10 held [3] 31/9 32/22 54/6 help [10] 11/1 16/1 18/25 54/3 71/10 97/20 170/6 175/4 176/4 190/25 helpful [6] 3/15 3/17 4/9 13/21 32/14 60/11 helpfully [2] 12/16 70/4 helping [1] 177/8 Hemofil [2] 14/14 14/22 hence [4] 9/6 20/25 66/13 165/8 hep [1] 164/25 hep B [1] 164/25 heparin [1] 108/16 hepatitis [71] 11/12 12/1 12/3 12/5 12/8 14/16 14/20 16/21	27/16 27/19 41/22 49/1 51/3 55/1 64/7 69/14 73/5 73/9 73/12 74/7 75/24 76/2 78/17 87/9 87/15 111/25 112/15 112/18 112/20 113/25 114/18 114/20 115/3 115/19 116/4 116/20 120/11 120/25 121/9 122/3 122/8 122/19 122/22 122/25 123/6 123/12 123/15 123/16 123/23 123/25 124/2 125/8 125/11 129/6 129/7 129/8 130/3 130/5 132/7 132/23 133/2 133/2 135/8 153/21 164/19 165/3 165/18 165/21 181/20 182/3 183/17 hepatitis B [17] 12/3 73/5 73/9 74/7 115/3 120/25 121/9 122/3 122/22 129/6 129/7 129/8 130/3 130/5 132/23 133/2 181/20 hepatitis C [1] 123/16 hepatitis' [1] 81/9 hepatitis-free [1] 87/15 her [7] 2/24 3/1 74/5 74/9 95/3 100/21 100/24 here [12] 11/16 69/20 72/21 102/18 113/22 123/11 126/8 126/25 130/15 169/10 178/24 191/3 high [25] 16/10 25/21 26/19 26/22 27/4 30/20 62/25 66/4 68/20 71/4 71/23 71/24 71/24 72/12 72/14 97/5 98/25 108/12 122/19 130/21 130/24 131/8 137/14 157/21 182/21 high-quality [1] 66/4 higher [4] 52/25 71/17 73/19 138/18 highlight [3] 13/23 49/15 116/19 highly [9] 24/23 47/17 75/14 77/4 81/3 119/22 122/12 154/12 159/17 HILL [3] 101/20 191/6 192/5 him [11] 15/18 79/24 133/24 140/24 162/2 166/23 166/25 180/5 180/6 188/19 188/23	hindsight [1] 166/5 hinge [1] 60/23 his [43] 9/17 15/2 16/2 16/6 19/10 22/5 22/10 22/14 26/20 26/22 37/1 41/11 42/3 42/11 48/7 49/21 51/8 69/19 69/22 70/11 70/13 83/15 87/2 91/10 92/10 95/9 95/17 99/11 100/7 104/24 121/3 129/1 130/4 162/1 166/12 167/25 167/25 177/11 178/16 180/1 180/2 180/2 189/2 History [1] 5/1 HIV [3] 185/11 185/12 185/18 hold [1] 191/6 holder [7] 35/1 37/1 37/3 44/2 44/8 45/14 45/20 holders [4] 8/19 9/3 9/5 87/24 Holgate [4] 33/5 48/4 49/20 49/22 Holgate's [1] 50/16 home [1] 26/1 homework [1] 53/19 Hoofnagle [1] 126/21 hope [8] 22/19 26/5 26/10 59/18 81/2 85/13 162/24 191/3 hoped [6] 4/3 55/12 64/13 84/12 110/22 190/16 hospital [5] 14/1 15/2 28/12 79/12 79/12 hostility [1] 86/23 hour [2] 155/10 190/16 hours [3] 26/9 72/23 125/24 house [2] 41/8 66/10 how [44] 3/16 15/24 18/19 22/22 24/12 34/3 38/6 38/16 53/2 59/22 85/15 85/24 88/25 90/23 95/4 104/21 110/1 113/15 117/1 123/17 136/2 136/2 137/8 137/8 137/14 141/6 142/11 145/21 145/25 149/25 155/8 156/4 156/12 157/6 159/2 163/15 165/10 169/4 170/15 181/3 182/24 185/20 186/9 190/21 Howard [1] 87/18 however [15] 2/6 12/6	13/23 17/6 21/22 27/17 75/23 87/1 91/23 98/22 99/4 120/11 123/3 130/3 186/1 HSOC0022968 [1] 159/1 HTLV [4] 183/16 184/25 185/11 185/18 HTLV-III [4] 183/16 184/25 185/11 185/18 huge [1] 157/9 human [74] 1/22 2/2 5/10 7/13 12/2 14/13 15/13 16/3 24/13 25/12 27/11 39/18 39/24 55/15 55/17 56/5 57/8 59/13 62/14 62/15 62/23 63/2 63/6 63/8 66/6 66/8 70/7 72/11 72/18 73/3 74/21 75/7 75/12 75/20 75/21 76/2 76/18 80/21 80/25 82/12 83/11 85/7 85/14 92/3 96/23 97/3 97/16 98/3 98/9 98/12 98/25 103/2 106/8 122/12 134/24 141/1 151/4 151/10 154/15 154/18 155/5 155/21 162/17 162/20 165/16 167/20 167/20 167/24 172/19 176/3 176/19 176/25 177/4 177/5 Humanate [49] 1/20 5/15 23/4 23/16 24/6 25/22 25/23 26/4 26/11 26/16 26/25 27/3 27/8 27/11 27/21 27/23 28/16 30/22 31/16 31/23 32/1 32/14 33/6 33/9 33/14 33/21 33/25 34/18 34/19 35/14 36/15 36/17 41/20 42/13 46/17 46/23 47/5 47/12 47/13 47/18 47/22 48/15 48/19 50/10 51/9 149/4 149/8 149/14 149/21 hundred [1] 137/3 husband [1] 136/9 Hyate [2] 6/1 91/25 Hyate C [1] 6/1 Hyate-C [1] 91/25 Hyate:C [11] 2/15 25/2 147/13 149/24 150/22 151/13 152/2 153/2 154/6 154/11 188/2 hypothesised [1]
----------	--	---	---	---	--

H	155/2 159/23 162/8 168/11 169/4 169/4 172/13 175/17 176/7 176/9 177/2 179/15 180/6 180/7 180/12 180/18 182/22 182/25 183/2 183/21 184/20 190/12	I raised [1] 38/16 I read [2] 20/10 65/23 I recall [4] 137/18 143/20 172/17 178/13 I referred [2] 170/19 171/15 I return [1] 101/3 I right [4] 111/3 113/3 121/12 125/3 I said [1] 179/18 I say [4] 2/24 16/16 31/10 155/3 I see [4] 29/6 67/6 90/10 137/4 I should [5] 22/9 129/18 138/7 166/14 170/11 I showed [1] 150/11 I sometimes [1] 147/3 I sort [1] 115/16 I spent [1] 160/10 I stayed [2] 147/21 147/21 I stress [1] 69/20 I subsequently [1] 147/8 I suggest [2] 100/25 180/11 I suppose [3] 104/22 182/5 188/20 I suspect [6] 103/24 113/10 114/23 139/19 145/9 188/23 I take [7] 12/23 18/16 20/5 30/9 91/12 108/25 170/5 I then [2] 147/12 147/25 I think [53] 15/17 24/12 50/22 54/19 65/3 92/6 96/6 101/21 102/22 105/12 115/8 116/17 117/18 118/12 118/22 119/19 119/22 119/24 124/19 127/9 127/14 131/23 131/24 132/17 133/6 133/7 139/15 141/24 145/9 147/21 152/24 154/23 156/3 160/7 161/24 162/1 163/1 163/4 165/24 166/14 167/13 168/17 171/13 175/10 176/12 178/2 178/18 179/16 181/23 185/12 187/5 190/16 190/22 I thought [1] 103/19 I turn [1] 186/19 I understand [12] 38/2 73/3 83/6 91/16 102/24 104/25 105/13 119/8 120/14 136/24	182/7 185/24 I understand it [1] 38/8 I understood [1] 178/3 I wanted [1] 146/4 I was [31] 103/17 103/21 105/7 105/15 105/15 114/9 116/7 123/24 131/6 131/7 143/4 144/25 145/8 145/10 145/12 145/16 145/18 147/3 151/17 151/20 151/23 152/21 152/22 153/8 153/13 160/7 163/19 168/3 169/20 172/6 188/7 I wasn't [3] 114/9 151/14 172/20 I went [4] 136/10 139/14 139/21 152/18 I will [30] 8/19 13/23 14/6 25/11 28/19 38/18 48/5 53/7 56/17 62/1 62/19 70/1 70/14 71/11 72/10 74/5 74/9 74/17 83/5 83/12 83/23 86/19 90/11 94/21 97/14 98/18 99/7 99/8 100/17 134/21 I won't [29] 10/15 13/20 38/23 53/23 57/25 59/16 59/21 60/1 67/18 67/22 70/14 72/25 74/16 77/22 79/25 82/1 83/23 85/10 87/4 93/12 96/19 99/18 117/4 150/4 151/11 155/22 162/14 164/8 174/19 I wonder [1] 155/6 I worked [3] 145/3 161/23 163/23 I would [12] 15/22 16/19 21/24 48/21 49/17 51/17 51/21 81/14 129/23 166/11 166/11 175/25 I wrote [1] 146/3 I'd [7] 28/13 101/24 104/3 115/25 155/20 161/25 173/5 I'll [5] 32/8 43/13 51/13 102/8 173/19 I'm [53] 4/24 11/9 14/3 16/17 23/17 24/10 27/9 47/8 47/10 48/3 48/13 52/8 52/9 52/11 54/18 60/9 85/8 90/16 90/20 95/16 95/17	101/8 104/23 111/22 113/11 113/18 120/18 126/6 126/25 128/2 128/4 132/1 132/18 136/24 136/25 137/17 149/23 151/23 158/23 158/25 161/20 172/21 177/6 182/15 183/2 184/18 185/24 188/5 188/21 189/14 190/5 190/17 190/19 I've [8] 29/16 47/11 65/7 115/21 179/15 181/14 183/7 191/18 I, [1] 143/4 I, having [1] 143/4 ICRF [1] 179/7 Ida [1] 108/5 Ida Bennett [1] 108/5 idea [7] 118/19 119/9 119/16 172/18 172/23 189/19 189/25 ideal [3] 25/25 69/10 75/14 ideas [4] 189/2 189/15 189/15 190/1 identical [1] 28/17 identified [3] 23/19 185/13 185/13 ie [1] 81/6 if [140] 3/8 4/25 6/13 7/3 7/19 8/14 11/8 11/22 11/23 13/1 16/11 18/2 19/8 19/17 22/18 23/19 26/8 28/19 30/14 31/5 31/11 31/21 32/4 32/18 33/7 36/16 38/18 42/6 42/15 43/12 44/8 45/20 46/6 47/9 47/10 48/16 49/8 51/12 54/4 56/25 57/23 58/4 59/15 59/23 61/22 71/8 71/20 71/21 74/22 74/25 78/1 78/13 79/2 81/15 82/20 84/5 84/22 85/9 86/3 87/25 90/2 90/3 92/18 92/23 95/13 95/19 96/20 97/20 97/25 98/16 100/20 102/1 102/7 104/3 104/10 105/25 106/4 108/7 109/9 111/3 111/23 112/22 116/19 117/22 120/5 120/7 120/18 120/19 122/1 124/18 125/25 126/20 128/11 128/21 128/23 129/2 129/24 130/5 130/15 131/24 132/15 134/4 134/15	135/9 137/24 143/2 144/5 149/7 152/21 155/6 156/19 157/4 158/10 158/19 160/10 160/14 164/3 164/11 164/16 166/9 169/12 169/25 170/20 170/23 173/19 173/24 174/10 174/12 174/18 177/7 177/23 178/23 180/18 181/5 182/13 182/19 182/23 184/15 186/19 190/10 ii [19] 39/22 40/7 106/18 107/25 108/10 108/20 109/13 109/25 111/11 112/10 118/4 122/5 122/10 124/25 125/9 126/22 130/2 131/13 133/15 iii [6] 39/24 40/16 183/16 184/25 185/11 185/18 ill [1] 81/16 ill-advised [1] 81/16 image [1] 54/25 imagine [1] 186/25 imbalance [1] 68/23 immediate [2] 104/19 136/17 immediately [3] 136/17 156/23 181/22 immune [2] 63/9 140/17 Immuno [1] 14/24 immunodiffusion [1] 112/5 immunoelectroosmop heresis [1] 112/6 immunogenic [1] 73/13 immunoglobulin [1] 81/23 impact [1] 57/16 implications [1] 55/17 import [6] 10/11 23/14 23/14 34/16 60/24 174/12 importance [6] 19/1 40/14 49/15 58/11 61/24 62/9 important [11] 1/7 2/6 15/17 22/9 24/12 31/18 44/20 86/17 110/9 117/19 177/7 importation [11] 10/7 51/22 66/23 67/2 67/6 67/10 74/14 149/3 149/7 174/1 174/16 imported [8] 1/18 5/11 23/24 24/15 42/8 42/18 51/11 97/5
----------	--	---	--	--	--

(61) hypothesised... - imported

importing [1] 78/10 imports [1] 173/22 imposed [1] 39/14 impossibility [1] 32/1 impossible [2] 36/1 37/5 impracticable [1] 97/6 impractical [2] 175/3 175/5 impracticality [1] 174/2 impression [1] 87/6 improve [5] 5/22 110/23 123/22 166/20 187/25 Improved [1] 64/3 improvement [1] 96/16 improving [1] 187/24 impurities [2] 48/12 48/14 inactivated [1] 128/9 inactivation [5] 53/6 120/16 125/9 140/11 164/5 inadequate [3] 35/25 96/4 109/14 incapable [1] 154/17 incidence [4] 64/7 112/8 112/20 122/19 incident [1] 122/24 incidentally [1] 85/12 incidents [1] 47/13 include [4] 37/17 45/12 58/21 134/15 included [3] 33/11 35/18 174/13 includes [2] 79/16 102/22 including [7] 5/5 50/7 53/24 78/18 81/2 98/3 120/13 incompatible [1] 82/16 incorporated [1] 5/3 increase [4] 57/19 68/22 69/16 110/18 increased [3] 15/13 69/9 114/3 increasing [2] 68/22 138/16 indeed [8] 11/6 13/7 15/25 30/16 71/2 87/15 87/24 152/4 independent [4] 28/4 34/20 42/10 92/16 indicate [2] 20/4 89/20 indicated [2] 96/9 97/9	indicates [1] 81/19 indication [1] 32/7 indications [2] 11/24 11/25 individual [5] 17/7 17/24 69/24 72/7 72/23 individually [1] 24/16 individuals [1] 148/16 industrial [2] 7/1 79/7 industry [4] 61/19 62/2 62/11 68/18 Industry's [1] 56/13 inevitable [1] 97/6 infected [6] 73/8 103/11 127/20 128/1 129/15 181/25 infection [4] 14/20 47/15 47/19 69/14 infectious [3] 122/12 123/5 126/24 infective [7] 112/22 112/22 112/24 117/22 117/22 117/24 118/6 infectivity [7] 76/2 87/9 125/2 129/6 129/8 130/6 133/13 Infirmary [6] 47/14 104/14 142/8 182/9 182/11 186/24 influential [2] 19/2 85/4 information [25] 11/4 23/20 26/2 28/20 30/23 31/2 33/24 36/4 36/25 37/11 38/13 39/11 40/17 42/2 42/17 42/24 43/23 44/1 44/15 46/4 69/24 78/6 82/3 94/2 114/17 informed [3] 43/18 174/3 185/21 infusions [2] 74/3 162/17 inhibitor [8] 15/13 25/3 153/12 153/16 153/22 153/24 154/14 154/15 inhibitors [6] 2/17 2/18 14/13 153/25 157/1 159/18 initial [7] 25/14 57/9 63/11 63/19 70/11 142/18 170/18 initially [4] 137/7 137/13 148/12 148/13 initials [2] 14/7 173/8 inject [1] 125/1 injected [3] 122/13 126/22 127/19 injection [1] 64/9 input [3] 149/10 151/8	153/2 Inquiry [14] 1/3 1/17 2/9 11/8 13/18 51/24 52/24 101/23 103/11 128/13 129/1 180/19 180/21 192/2 insensitive [2] 112/18 116/6 inserted [1] 125/4 insight [1] 154/2 insisting [2] 19/4 19/16 insofar [3] 106/5 119/11 149/20 inspection [1] 78/7 Inspectorate [3] 78/8 92/15 141/17 inspiration [1] 119/16 instance [1] 117/1 instead [1] 85/22 instigated [1] 79/10 institute [7] 35/8 36/22 58/22 79/6 79/9 130/7 178/14 instructions [1] 4/16 insufficient [4] 43/1 43/9 117/7 123/6 Insurance [1] 4/6 insurmountable [1] 160/5 intact [2] 41/14 73/10 integrity [1] 41/11 intellectual [1] 79/25 intend [1] 7/6 intended [8] 2/25 6/16 6/19 39/1 57/2 77/9 78/21 89/21 intensive [1] 70/25 intention [2] 59/9 59/18 intentions [1] 82/16 interaction [2] 143/2 153/6 interest [5] 1/17 2/9 53/11 82/17 99/2 interested [2] 15/1 15/8 interesting [5] 34/3 51/5 130/10 151/9 189/19 interests [1] 82/25 interject [1] 158/10 intermediary [7] 5/14 28/25 29/4 38/3 38/9 67/8 188/16 intermediate [4] 25/23 26/17 26/18 27/3 internal [8] 84/25 87/2 96/21 98/17 111/24 120/6 124/20 132/16 international [5] 10/2	12/24 17/10 26/23 100/16 interpret [1] 88/8 interpretation [2] 82/17 82/20 interview [1] 103/16 interviewed [4] 103/13 103/18 103/21 178/14 intimately [1] 144/11 into [33] 4/18 6/17 9/19 29/18 37/24 57/7 57/22 67/25 68/12 81/22 83/21 87/23 88/18 91/18 100/3 121/15 125/4 139/8 141/24 142/6 145/17 151/8 151/11 153/2 154/2 158/15 161/20 167/8 169/13 171/11 171/12 178/22 189/16 intramuscular [1] 69/18 introduce [1] 101/1 introduced [4] 41/1 70/4 132/10 139/8 introduction [5] 4/15 57/5 57/20 75/1 109/9 inventors [1] 88/5 invest [1] 180/7 invested [1] 4/2 investigate [2] 16/13 77/1 investigation [1] 4/18 Investigational [1] 79/14 investigators [1] 123/1 investment [15] 3/25 4/5 4/5 4/7 4/21 8/20 9/8 9/15 59/24 74/12 83/20 84/1 84/15 99/20 166/1 investors [1] 9/13 invited [2] 56/15 181/14 involved [31] 1/10 1/14 18/21 22/7 22/12 58/1 59/25 82/2 83/16 94/18 106/4 114/7 114/10 131/3 134/23 135/1 135/13 136/11 138/13 140/10 143/4 144/1 144/13 147/5 149/19 151/12 153/9 166/7 166/9 168/9 185/14 involvement [1] 150/10 involves [1] 52/15 ion [4] 68/16 70/21 106/11 164/21	ion-exchange [2] 68/16 164/21 IPS [1] 170/21 lpsen [1] 10/3 lpsen Biopharm [1] 10/3 IPSN00000027 [1] 3/18 IPSN00000021 [1] 95/13 IPSN00000027 [1] 46/20 IPSN0000139 [3] 10/13 24/1 52/1 IPSN0000146 [1] 12/15 IPSN0000156 [2] 70/9 70/16 IPSN0000165 [2] 56/20 170/24 IPSN0000166 [1] 9/21 IPSN0000230 [1] 89/24 IPSN0000232 [2] 87/7 89/19 IPSN0000249 [1] 87/19 IPSN0000252 [1] 87/16 IPSN0000257 [1] 68/5 IPSN0000260 [2] 95/9 99/17 IPSN0000291 [1] 21/25 IPSN0000312 [3] 10/20 11/14 12/12 IPSN0000321 [1] 17/1 IPSN0000322 [1] 17/17 IPSN0000323 [2] 47/23 47/24 IPSN0000325 [1] 17/15 IPSN0000329 [1] 11/15 IPSN0000331 [3] 16/25 23/9 24/9 IPSN0000332 [1] 16/24 IPSN0000333 [2] 16/23 16/25 IPSN0000334 [3] 13/24 16/25 53/25 IPSN0000336 [2] 47/20 47/20 IPSN0000338 [2] 17/1 28/9 IPSN0000398 [1] 89/22 IPSN0000402 [1] 87/7 IPSN0000442 [2] 95/11 99/14	IPSN0000575 [1] 18/3 IPSN000426 [1] 99/13 irregular [1] 49/5 isn't [7] 68/9 71/6 98/14 111/18 114/6 126/25 141/25 iso [1] 108/16 iso-osmolar [1] 108/16 isoagglutinins [1] 64/1 isolated [1] 76/5 isolation [1] 24/23 ISPN0000409 [1] 164/8 issue [7] 17/21 22/11 22/22 23/21 29/12 106/21 130/16 issued [3] 16/7 37/8 94/8 issues [1] 82/22 it's [53] 1/12 3/6 14/17 18/6 22/9 27/9 27/10 30/12 32/14 44/20 46/3 47/5 47/7 48/2 48/3 51/5 51/16 53/15 65/24 66/19 71/22 77/24 78/9 80/19 87/23 88/12 88/22 89/15 94/1 94/23 99/12 100/2 107/20 111/21 114/5 119/21 134/15 150/15 150/16 151/8 156/15 156/15 156/18 156/18 156/22 160/25 164/8 164/11 170/21 175/8 175/10 175/16 184/10 item [1] 79/4 its [30] 4/19 5/22 7/14 17/22 19/9 19/14 23/1 32/1 32/2 36/15 39/7 41/11 47/7 49/6 53/21 54/13 54/13 58/6 80/9 81/20 93/22 96/13 110/10 125/2 132/25 139/5 142/6 149/6 170/3 174/6 itself [4] 10/12 11/14 59/11 71/7 IX [38] 51/24 106/8 106/18 106/21 106/23 106/25 107/25 108/10 108/21 109/13 109/15 109/25 110/17 110/24 111/11 112/10 113/16 117/7 118/4 120/13 121/9 122/5 124/25 125/9 125/15 126/23 129/4 130/16 130/21 130/25 131/2 131/9 131/12 132/8 134/9
---	--	--	---	--	--

I	165/22 168/1	Kingdon's [1] 26/19	22/3	Lauriston [1] 186/24	162/2
IX... [3] 144/17 144/18 150/15	July 1981 [7] 60/4 74/18 74/24 79/19 89/3 165/15 168/1	kits [2] 15/1 26/7	labelling [3] 17/22 21/18 35/11	layer [1] 80/10	letters [2] 4/17 80/1
J	July 1982 [1] 89/4	knew [7] 126/11	labile [2] 69/2 125/20	layperson's [2] 52/10 106/5	level [12] 11/2 15/13 15/16 51/17 61/15 62/6 62/7 99/2 124/24 138/18 157/20 186/1
James [1] 9/16	July 1984 [1] 100/16	know [56] 10/20 11/11 29/13 29/16 42/22 46/25 47/8 50/18 51/1 84/15 103/23 113/8 113/15 114/2 114/5 118/2 125/19 125/25 137/7 137/14 139/17 141/15 141/21 144/12 148/6 152/7 152/16 152/21 152/22 156/14 158/20 158/24 160/13 161/4 165/10 168/4 168/13 168/14 169/4 169/19 169/25 170/18 172/14 172/17 175/17 175/23 176/8 179/15 180/18 182/13 182/16 184/15 184/20 188/11 189/21 189/23	laboratories [27] 3/23 4/19 4/21 5/11 10/10 10/10 18/6 28/17 31/8 32/3 33/9 34/6 34/8 39/21 41/16 49/4 50/11 57/6 58/9 58/10 58/11 58/20 58/25 59/5 62/20 75/2 102/18	lead [4] 64/14 80/11 84/2 108/3	levels [5] 23/2 73/10 109/15 127/11 143/6
January [6] 13/17 16/4 17/12 32/23 47/2 47/16	jump [3] 38/18 84/22 181/15	knowing [2] 150/16 150/18	laboratory [21] 35/16 57/11 57/21 58/7 58/12 58/16 58/22 58/23 58/24 70/11 73/25 79/15 87/10 120/22 141/1 141/4 141/20 158/14 159/16 167/5 169/14	leading [4] 13/16 77/6 99/22 153/14	Liberton [2] 142/7 187/2
January 1979 [3] 13/17 16/4 17/12	June [9] 5/16 10/14 23/4 46/23 47/3 60/3 94/14 170/20 171/1	knowledge [7] 29/1 29/10 50/5 109/6 149/9 176/21 185/21	Laboratories Ltd [1] 50/11	leaflet [1] 26/1	licence [44] 5/16 10/18 11/3 11/17 23/12 23/18 32/13 34/12 34/24 35/1 36/7 36/15 37/1 37/3 37/8 37/16 38/22 39/14 43/22 44/2 44/8 44/25 45/12 45/14 45/20 46/18 46/19 46/24 50/20 51/23 55/3 57/19 59/12 63/21 74/15 76/10 80/12 91/25 92/4 93/18 151/21 152/8 152/11 153/15
January 1981 [2] 47/2 47/16	June 1976 [2] 10/14 23/4	known [15] 11/25 31/16 51/10 70/22 89/15 120/2 125/12 125/22 126/23 129/5 130/2 135/2 136/21 179/4 181/25	labour [2] 57/14 71/25	learn [1] 186/16	licences [3] 96/6 149/20 151/13
Jean [5] 15/19 58/15 58/19 58/19 161/23	June 1980 [1] 60/3	Koate [45] 1/19 5/10 5/15 10/12 10/19 10/22 11/16 11/25 12/1 15/3 17/22 18/13 23/3 23/7 23/13 23/23 25/19 27/23 28/18 30/11 30/16 31/12 31/15 31/16 32/5 34/9 34/15 34/24 35/6 35/17 35/18 35/20 46/22 47/2 47/4 47/12 51/14 66/16 66/17 149/4 149/8 149/14 149/21 188/13 188/13	labs [1] 152/24	learning [2] 104/16 115/13	licensed [6] 7/11 39/25 54/23 57/22 148/3 174/16
Jean-Pierre [3] 58/15 58/19 58/19	June 1981 [3] 5/16 46/23 47/3	known [15] 11/25 31/16 51/10 70/22 89/15 120/2 125/12 125/22 126/23 129/5 130/2 135/2 136/21 179/4 181/25	lack [7] 37/10 46/9 63/5 86/13 86/14 99/20 123/10	learnt [1] 139/22	licensing [34] 7/4 7/16 23/1 23/21 24/3 30/6 32/7 32/17 35/4 36/21 38/20 39/6 43/15 43/21 44/3 44/8 44/17 44/21 45/15 45/17 45/20 46/4 46/14 50/4 55/19 60/6 91/2 94/16 94/18 97/6 152/3 152/4 174/12 174/22
Jean-Pierre Allain [1] 161/23	just [72] 10/4 10/5 12/21 12/25 13/23 14/17 22/12 28/21 31/5 32/24 51/2 65/7 70/14 71/8 71/24 72/10 74/22 78/9 80/21 90/3 90/5 94/4 97/14 99/8 100/6 100/13 101/1 101/13 101/24 104/15 106/4 109/2 109/9 110/5 111/3 115/25 117/6 118/18 123/8 127/23 128/11 128/24 129/11 129/24 131/25 132/7 132/13 132/20 133/4 134/25 136/15 137/19 139/3 141/23 143/14 146/20 147/22 152/23 158/10 160/23 160/24 165/15 168/3 172/14 173/5 173/19 177/25 179/12 183/2 183/7 186/22 191/1	known [15] 11/25 31/16 51/10 70/22 89/15 120/2 125/12 125/22 126/23 129/5 130/2 135/2 136/21 179/4 181/25	lacks [1] 100/9	least [6] 23/19 29/20 34/1 50/16 50/24 127/1	lie [1] 28/22
jeopardised [1] 91/1	just [72] 10/4 10/5 12/21 12/25 13/23 14/17 22/12 28/21 31/5 32/24 51/2 65/7 70/14 71/8 71/24 72/10 74/22 78/9 80/21 90/3 90/5 94/4 97/14 99/8 100/6 100/13 101/1 101/13 101/24 104/15 106/4 109/2 109/9 110/5 111/3 115/25 117/6 118/18 123/8 127/23 128/11 128/24 129/11 129/24 131/25 132/7 132/13 132/20 133/4 134/25 136/15 137/19 139/3 141/23 143/14 146/20 147/22 152/23 158/10 160/23 160/24 165/15 168/3 172/14 173/5 173/19 177/25 179/12 183/2 183/7 186/22 191/1	known [15] 11/25 31/16 51/10 70/22 89/15 120/2 125/12 125/22 126/23 129/5 130/2 135/2 136/21 179/4 181/25	laminar [1] 188/9	leave [10] 22/25 38/8 56/17 62/1 86/19 92/20 97/14 128/24 130/14 134/21	life [7] 24/2 25/5 72/21 100/3 143/9 186/23 187/7
Jim [9] 104/11 105/19 114/12 118/21 121/4 140/23 145/9 188/25 189/9	justified [1] 165/23	known [15] 11/25 31/16 51/10 70/22 89/15 120/2 125/12 125/22 126/23 129/5 130/2 135/2 136/21 179/4 181/25	labors [1] 152/24	leaving [3] 73/10 129/13 174/7	lifted [1] 61/6
Jim Smith [3] 145/9 188/25 189/9	K	known [15] 11/25 31/16 51/10 70/22 89/15 120/2 125/12 125/22 126/23 129/5 130/2 135/2 136/21 179/4 181/25	lack [7] 37/10 46/9 63/5 86/13 86/14 99/20 123/10	lecture [5] 70/10 70/17 162/11 162/23 164/15	light [2] 11/9 76/8
JJ [1] 86/1	keep [10] 15/5 28/19 31/2 51/16 67/11 68/21 142/1 142/2 157/16 159/18	known [15] 11/25 31/16 51/10 70/22 89/15 120/2 125/12 125/22 126/23 129/5 130/2 135/2 136/21 179/4 181/25	lacking [1] 100/9	led [5] 32/12 100/11 131/4 159/7 177/24	like [29] 3/13 12/18 12/18 16/1 18/8 27/12 27/13 28/13 48/21 48/23 51/12 85/13 101/17 101/24 104/3 115/25 143/7 144/9 145/5 151/18 155/20 157/5 168/23 173/5 179/4 186/25 187/7 189/7 189/15
JK [1] 108/5	keeping [1] 115/14	known [15] 11/25 31/16 51/10 70/22 89/15 120/2 125/12 125/22 126/23 129/5 130/2 135/2 136/21 179/4 181/25	laminar [1] 188/9	Lees [4] 8/5 8/7 9/1 54/7	likelihood [1] 15/15
JK Smith [1] 108/5	Keith [1] 91/6	known [15] 11/25 31/16 51/10 70/22 89/15 120/2 125/12 125/22 126/23 129/5 130/2 135/2 136/21 179/4 181/25	Lane [8] 55/21 80/18 80/20 80/22 82/10 84/25 162/15 171/16	leeway [3] 20/13 21/11 21/16	likely [10] 61/14 112/23 114/5 117/23 118/6 138/9 168/4
Joaquim [3] 92/8 92/9 92/12	Kernoff [2] 17/11 162/16	known [15] 11/25 31/16 51/10 70/22 89/15 120/2 125/12 125/22 126/23 129/5 130/2 135/2 136/21 179/4 181/25	Lane's [2] 58/22 82/6	left [16] 4/12 9/12 9/22 10/5 11/17 90/7 90/8 134/14 136/8 141/15 141/16 145/9 151/16 151/17 160/14 167/16	
job [2] 102/13 102/14	key [1] 65/2	known [15] 11/25 31/16 51/10 70/22 89/15 120/2 125/12 125/22 126/23 129/5 130/2 135/2 136/21 179/4 181/25	Lane's's [1] 83/17	left-hand [2] 4/12 11/17	
jobs [1] 84/2	kilo [3] 72/4 171/8 171/8	known [15] 11/25 31/16 51/10 70/22 89/15 120/2 125/12 125/22 126/23 129/5 130/2 135/2 136/21 179/4 181/25	LANGSTAFF [2] 186/21 192/7	legible [1] 48/17	
John [3] 104/20 104/23 114/14	king [4] 105/4 115/13 143/1 148/10	known [15] 11/25 31/16 51/10 70/22 89/15 120/2 125/12 125/22 126/23 129/5 130/2 135/2 136/21 179/4 181/25	language [1] 166/12	less [7] 64/12 71/25 75/12 112/7 116/9 122/10 155/1	
Johnson [8] 55/6 58/13 70/19 121/3 129/6 132/5 133/15 162/16	kinetics [2] 151/3 151/9	known [15] 11/25 31/16 51/10 70/22 89/15 120/2 125/12 125/22 126/23 129/5 130/2 135/2 136/21 179/4 181/25	large [12] 52/15 75/3 86/21 108/9 110/18 110/24 111/11 121/18 135/6 135/13 159/17 171/9	let [3] 157/24 166/25 169/6	
Johnson's [6] 58/12 86/3 129/25 139/23 139/24 147/18	Kingdom [2] 34/9 149/6	known [15] 11/25 31/16 51/10 70/22 89/15 120/2 125/12 125/22 126/23 129/5 130/2 135/2 136/21 179/4 181/25	large-scale [1] 108/9	let's [3] 45/1 101/5 101/16	
joined [1] 104/7	Kingdon [1] 72/14	known [15] 11/25 31/16 51/10 70/22 89/15 120/2 125/12 125/22 126/23 129/5 130/2 135/2 136/21 179/4 181/25	larger [2] 61/14 114/3	letter [44] 17/9 17/12 18/5 18/11 19/10 19/25 20/2 22/10 22/15 24/7 24/10 26/13 26/15 26/22 28/9 28/10 30/13 31/3 38/16 43/16 47/15 48/1 49/24 50/2 50/16 50/19 51/8 66/21 80/18 80/20 87/11 87/20 88/18 89/25 90/15 90/17 90/20 91/4 146/6 161/1 161/17 161/20 162/1	
joining [1] 155/24		known [15] 11/25 31/16 51/10 70/22 89/15 120/2 125/12 125/22 126/23 129/5 130/2 135/2 136/21 179/4 181/25	last [9] 3/10 23/23 24/2 43/23 70/13 75/7 137/20 170/3 191/10		
joint [5] 3/25 4/20 62/13 62/18 63/14		known [15] 11/25 31/16 51/10 70/22 89/15 120/2 125/12 125/22 126/23 129/5 130/2 135/2 136/21 179/4 181/25	late [1] 2/23		
Jones [4] 18/5 20/1 40/23 42/9		known [15] 11/25 31/16 51/10 70/22 89/15 120/2 125/12 125/22 126/23 129/5 130/2 135/2 136/21 179/4 181/25	later [25] 2/20 3/8 8/13 10/2 10/5 23/21 24/12 25/11 47/16 64/19 66/18 67/20 70/3 77/19 94/22 99/24 101/4 105/21 132/11 136/22 140/4 142/11 152/7 188/7 191/13		
Joseph [1] 33/2		known [15] 11/25 31/16 51/10 70/22 89/15 120/2 125/12 125/22 126/23 129/5 130/2 135/2 136/21 179/4 181/25	latter [1] 73/18		
journal [3] 115/19 120/22 134/6		known [15] 11/25 31/16 51/10 70/22 89/15 120/2 125/12 125/22 126/23 129/5 130/2 135/2 136/21 179/4 181/25	Laughs [2] 124/11 187/19		
journals [1] 115/13		known [15] 11/25 31/16 51/10 70/22 89/15 120/2 125/12 125/22 126/23 129/5 130/2 135/2 136/21 179/4 181/25	Lauren [1] 101/18		
JP [1] 86/1		known [15] 11/25 31/16 51/10 70/22 89/15 120/2 125/12 125/22 126/23 129/5 130/2 135/2 136/21 179/4 181/25			
judged [2] 173/23 174/6		known [15] 11/25 31/16 51/10 70/22 89/15 120/2 125/12 125/22 126/23 129/5 130/2 135/2 136/21 179/4 181/25			
judgements [1] 82/5		known [15] 11/25 31/16 51/10 70/22 89/15 120/2 125/12 125/22 126/23 129/5 130/2 135/2 136/21 179/4 181/25			
July [18] 24/8 26/22 38/25 43/16 60/4 65/8 74/18 74/24 79/19 80/3 87/21 88/16 89/3 89/4 100/16 165/15		known [15] 11/25 31/16 51/10 70/22 89/15 120/2 125/12 125/22 126/23 129/5 130/2 135/2 136/21 179/4 181/25			

L	144/19 148/5 152/6 170/11 likely... [3] 174/4 175/8 175/10 likes [1] 15/5 limitations [1] 7/14 limited [24] 3/10 3/23 4/5 4/13 4/19 4/22 4/22 6/7 6/10 10/3 31/9 32/3 34/6 57/7 61/2 62/20 77/15 94/8 100/16 102/25 110/20 117/3 137/16 177/8 line [3] 37/24 53/2 104/10 lines [6] 31/21 43/24 43/24 55/23 86/2 99/19 link [2] 38/9 55/1 links [2] 145/6 145/13 list [2] 6/2 33/1 listed [2] 18/14 108/3 Lister [1] 58/22 literally [2] 147/17 147/20 litre [2] 72/5 137/21 litres [5] 137/7 137/16 137/17 138/4 183/11 little [19] 9/23 22/15 31/20 32/15 33/23 61/7 66/17 85/15 88/17 90/5 96/15 103/17 104/13 106/5 149/9 150/9 181/2 189/5 190/5 liver [2] 64/8 110/13 Liverpool [1] 12/25 livers [1] 87/14 lives [1] 143/7 loans [2] 61/10 77/21 local [1] 69/5 London [1] 103/18 long [8] 78/5 88/12 88/25 93/22 147/19 152/17 152/18 181/3 longer [12] 12/20 24/2 36/13 85/20 88/11 98/7 115/8 130/9 155/8 176/17 181/3 190/16 look [24] 1/15 2/7 3/16 13/9 15/11 19/8 28/13 34/2 45/1 78/1 87/25 108/7 109/9 110/16 120/7 122/1 132/7 140/16 144/20 153/15 155/4 164/16 173/5 173/19 looked [14] 27/25 28/11 32/25 46/20 58/18 67/9 80/22 100/6 126/18 144/17	244/19 148/5 152/6 170/11 looked at [9] 28/11 32/25 46/20 58/18 67/9 100/6 144/17 144/19 152/6 looking [13] 3/18 16/2 20/22 21/4 24/16 55/9 69/23 90/14 143/7 160/16 167/8 170/6 176/19 looks [3] 27/12 27/13 161/10 loom [1] 61/14 Lord [1] 89/21 lose [1] 82/21 loss [2] 96/17 161/11 losses [1] 6/8 lost [4] 95/9 116/17 158/1 183/7 lot [11] 3/11 19/23 131/12 131/12 131/13 142/22 151/8 153/7 156/17 167/13 179/25 lots [4] 15/3 171/8 171/8 171/9 lover [1] 15/7 low [4] 21/9 69/6 86/8 86/17 Lowe [1] 145/3 lower [4] 52/20 53/4 57/14 64/7 lowly [1] 114/9 Ltd [4] 49/4 50/11 103/4 103/7 Ltd: [1] 102/19 Ltd: Chief [1] 102/19 lunch [3] 99/8 100/18 101/1 luncheon [1] 101/10 lyophilised [1] 108/14	Magazine [2] 99/14 99/25 main [9] 5/9 6/1 32/21 60/24 82/22 92/21 92/24 93/3 158/17 mainly [1] 167/13 maintain [1] 109/14 maintained [1] 99/3 major [8] 18/22 19/2 25/16 75/19 75/25 76/8 109/16 165/19 majority [1] 95/23 make [28] 4/3 15/2 15/6 42/5 51/16 51/21 81/24 82/4 85/14 97/18 101/12 135/12 135/16 142/20 147/22 156/16 158/13 167/6 169/21 171/9 171/10 172/19 175/8 176/10 180/5 180/24 183/24 186/7 makes [2] 61/7 82/12 making [13] 21/6 38/17 44/21 44/22 55/2 113/11 141/25 142/9 150/15 156/19 178/18 183/19 185/25 Maleic [1] 138/22 mammalian [2] 178/21 178/23 man [4] 25/4 58/13 134/9 166/25 management [8] 7/20 60/3 96/3 96/16 98/23 99/10 100/8 166/25 manager [2] 9/17 104/10 managing [3] 8/4 31/13 95/16 Manchester [1] 28/12 manufacture [10] 32/2 36/5 36/19 36/25 37/20 37/21 44/11 44/14 45/23 46/1 1/11 23/15 28/16 28/24 29/3 29/6 29/9 34/8 34/17 35/22 38/7 39/20 51/14 manufacturer [4] 37/1 37/4 40/12 42/23 manufacturers [6] 36/17 37/25 38/5 40/9 40/18 118/25 manufacturing [10] 5/23 29/13 44/12 45/24 50/6 76/17 77/23 93/20 151/22 178/24 many [5] 137/8 141/6 152/1 180/13 180/25	March [11] 47/16 48/2 48/4 49/20 49/22 49/24 50/15 54/24 92/22 93/1 99/13 March 1979 [1] 54/24 March 1981 [3] 47/16 48/2 49/20 March 1983 [1] 99/13 mark [6] 25/22 53/19 130/2 130/17 133/13 133/15 mark II [2] 130/2 133/15 marked [2] 132/18 182/21 market [9] 1/12 23/8 31/24 32/4 32/6 55/7 160/6 169/1 188/13 marketed [2] 31/16 158/16 marketing [5] 8/6 13/14 85/13 96/2 173/12 markets [1] 6/17 mass [1] 158/15 material [41] 3/12 3/12 15/11 15/14 16/11 20/19 25/9 34/19 35/3 35/18 41/8 41/10 41/15 41/19 48/21 49/2 50/7 71/19 78/11 91/19 96/23 97/10 125/1 132/10 156/21 157/8 161/14 171/11 172/22 172/23 173/25 174/8 174/11 174/14 174/24 175/12 175/16 176/22 184/12 184/16 184/23 materials [3] 69/15 78/1 97/8 matter [7] 13/7 20/8 22/19 37/6 50/12 50/16 50/24 matters [6] 3/7 5/19 24/11 59/7 96/9 114/11 Maw [1] 5/5 maximise [1] 75/15 may [53] 3/2 3/7 11/20 14/18 17/17 22/21 29/13 29/14 29/16 30/14 32/4 38/18 45/17 45/18 47/10 47/25 49/12 50/13 53/18 54/1 54/7 61/8 61/10 61/21 73/14 73/16 84/7 84/12 85/9 87/5 88/17 90/25 95/16 101/12 104/3 112/3 118/18 120/6 120/19 129/20	130/20 133/16 136/2 151/17 153/19 161/18 164/11 177/7 180/11 180/17 181/1 183/4 188/13 May 1970 [1] 112/3 May 1980 [1] 17/17 May 1982 [1] 87/5 May 1985 [1] 183/4 maybe [9] 115/8 148/15 164/4 167/23 169/4 169/17 169/19 169/20 169/21 Mayor [1] 89/21 MBL [1] 77/13 me [18] 11/22 28/21 51/13 82/14 91/9 92/7 124/19 130/3 141/9 141/10 149/2 151/12 169/6 183/7 190/21 190/23 191/19 191/20 mean [14] 12/23 18/16 20/5 40/10 46/18 83/7 88/8 111/4 124/9 146/18 176/25 181/2 188/6 189/19 meaning [4] 9/11 20/10 52/17 164/23 meaningless [1] 81/8 means [8] 3/12 20/25 28/21 42/16 49/4 53/5 135/3 181/15 meant [4] 38/3 72/14 128/3 141/25 measure [1] 157/20 mechanisms [1] 156/17 medical [12] 6/6 28/5 28/5 29/19 32/9 33/20 34/21 39/17 41/6 41/12 42/20 60/22 medical/technical [1] 60/22 Medicine [2] 102/15 120/23 Medicines [10] 32/21 37/15 39/5 43/18 50/15 78/7 92/15 92/25 141/16 141/23 meet [1] 141/19 meeting [21] 13/25 31/8 32/22 32/23 33/18 48/10 54/6 54/10 80/3 80/8 85/1 85/3 94/14 94/20 170/19 171/1 173/6 175/19 176/1 183/4 183/4 meetings [4] 13/19 50/14 56/1 146/22 memo [1] 82/10 memoir [1] 92/12	memorandum [2] 60/13 62/5 mention [2] 37/9 152/15 mentioned [6] 59/18 74/10 115/21 123/9 139/25 145/17 mentors [2] 188/25 189/9 merely [2] 9/4 40/16 merit [1] 174/6 merits [1] 85/4 met [3] 13/15 54/1 55/7 method [25] 36/18 52/20 64/13 86/18 109/21 110/23 118/21 118/21 118/24 126/19 127/24 130/1 130/2 130/17 132/22 133/7 133/8 133/11 133/13 135/19 147/13 147/22 150/11 155/22 162/24 methodology [1] 71/16 methods [9] 44/12 45/24 52/21 110/17 112/17 112/12 112/17 122/14 133/16 MHRA0036365 [5] 23/10 23/22 28/7 32/19 33/15 mid [1] 153/21 mid-1980s [1] 153/21 middle [1] 116/19 Middleton [29] 2/21 8/11 8/12 9/4 10/4 52/12 53/8 53/19 64/17 70/3 74/4 74/7 83/6 94/21 95/2 100/19 100/21 100/23 101/3 101/7 101/13 101/17 101/19 101/21 101/23 155/20 181/13 190/9 192/4 Middleton's [3] 53/23 64/18 180/15 might [27] 42/15 43/21 59/22 61/25 97/23 119/25 130/19 138/8 143/25 143/25 151/17 151/24 154/24 155/6 155/9 155/13 163/12 169/20 169/20 170/2 170/7 174/11 176/12 183/16 188/19 188/20 190/16 Mike [1] 179/7 mild [3] 185/22 186/1 186/4 millennium [1] 85/12 milligram [4] 25/25
----------	---	---	---	--	---	---

M	2/5 91/9 93/10 93/16 171/4	83/25 84/9 84/11 87/5 87/11 87/20 88/1	101/13 101/17 101/19 101/21 101/23 155/20	80/14 81/4 163/13 NC [3] 19/23 21/7	97/1 97/25 116/7 126/20 145/23 161/14
milligram... [3] 26/24 27/2 72/12	monoclonal [3] 159/14 183/23 184/6	89/18 90/1 90/1 90/23 91/4 91/5 91/6 91/7	180/15 181/13 190/9 192/4	21/12 NC 8184 [1] 21/12	NHS [2] 13/5 55/20
millilitre [2] 125/1 127/2	Monsanto [11] 5/24 7/5 7/10 7/11 54/23	92/5 92/12 95/7 95/8 95/10 95/15 96/24	Ms Middleton [21] 10/4 52/12 53/8 53/19	NC 8185 [1] 21/7 NC 8610 [1] 19/23	NIBS [14] 18/24 19/11 19/14 20/3 20/6 20/7
million [9] 4/21 9/8 13/3 17/10 77/13	70/8 76/10 80/9 139/5 139/25 148/3	99/10 99/10 99/11 99/20 99/20 99/25	70/3 74/4 74/7 94/21 95/2 100/19 100/21	near [1] 189/5 nearer [1] 84/3	20/11 21/8 21/13 21/16 22/2 22/19
83/20 84/14 96/18 166/1	month [4] 13/3 32/24 67/24 84/14	100/7 101/20 104/20 161/2 165/12 165/25	100/23 101/3 101/7 101/13 101/17 101/21	nearly [2] 47/11 122/25	23/25 24/4 NIBSAC [1] 31/24
mind [2] 161/22 169/25	months [10] 12/21 28/10 31/5 61/16 68/2	166/10 177/14 177/22 191/6 192/5	101/23 155/20 181/13 190/9	NEB [1] 81/1 necessarily [1] 27/18	NIBSC [8] 17/24 21/11 22/5 35/13 38/3 41/18
mine [1] 3/2 minimal [1] 68/22	93/1 97/1 160/11 160/19 160/20	Mr BA Dyos [1] 31/14 Mr Buck [1] 54/8	Ms Middleton's [3] 53/23 64/18 180/15	necessary [5] 10/17 42/15 44/16 76/11	42/1 153/6 nicely [1] 177/3
minimised [1] 41/23 ministers [1] 13/10	moral [1] 22/11 more [38] 12/23 16/12	Mr C Jones [1] 18/5 Mr Evans [1] 51/13	Ms Richards [2] 31/10 70/12	100/20 necessities [1] 96/5	nightmare [1] 85/13 NIH [1] 130/7
minute [4] 83/14 84/24 84/25 92/24	20/25 38/10 50/11 51/4 52/12 52/13	Mr Health [1] 68/10 Mr Heath [30] 8/24	much [28] 7/25 18/19 21/5 58/8 69/7 88/18	need [17] 40/8 40/12 45/4 65/25 67/15	nine [3] 61/16 68/2 134/16
minutes [13] 32/11 32/20 33/12 54/3 54/8	55/16 72/9 83/14 86/13 88/20 94/9	9/21 16/15 54/7 68/4 68/8 83/24 83/25 84/9	98/14 115/17 117/2 117/8 137/8 144/8	73/24 74/12 79/5 80/7 84/7 96/18 111/5	no [106] 3/12 11/25 25/7 28/23 29/16
54/15 80/3 80/11 155/14 180/11 181/4	94/11 102/9 111/5 111/8 111/8 112/2	84/11 87/5 87/11 87/20 88/1 89/18 90/1	150/15 151/11 154/11 155/1 155/1 155/8	133/19 142/20 155/11 164/15 165/8	30/17 30/18 30/23 36/3 36/4 36/13 36/13
183/9 184/11 mirrors [1] 169/10	113/14 115/25 117/18 119/22 123/1 131/1	91/4 91/6 91/7 92/5 95/7 95/10 99/10	161/20 167/7 179/3 179/4 180/5 181/22	needed [7] 28/1 52/1 55/4 81/24 159/16	37/2 37/3 37/9 38/9 41/3 44/18 50/11
miscounted [1] 124/19	135/4 137/10 146/5 154/11 155/1 156/6	99/20 99/25 161/2 165/12 165/25 166/10	182/5 184/3 185/20 191/1	169/23 178/20 needle [1] 182/16	51/22 51/24 52/13 65/16 69/14 74/12
missed [1] 176/23 missing [1] 65/3	174/12 175/8 175/10 181/22 182/5 184/3	177/22 Mr Heath's [1] 177/14	multi [4] 86/15 98/7 159/7 176/17	needs [3] 49/16 81/13 159/23	83/8 85/19 88/10 90/13 94/9 94/13
mixing [1] 135/14 ml [3] 108/20 137/21	Moreover [2] 36/7 57/11	MR HILL [3] 101/20 191/6 192/5	multi-centre [1] 86/15 must [10] 22/3 44/23	169/23 negative [2] 168/4	97/11 98/6 98/10 103/12 103/22 105/15
138/2 Mm [7] 133/23 141/14	Morganthaler [2] 86/1 86/10	Mr James [1] 9/16 Mr Joaquim [1] 92/12	96/13 98/11 100/21 132/23 168/11 168/12	169/21 neglects [1] 86/3	105/15 106/19 107/6 112/19 113/21 114/5
156/8 159/10 161/3 162/13 170/17	most [9] 49/1 69/9 76/1 86/17 98/12	Mr John Watt [1] 104/20	169/15 184/22 my [32] 19/12 43/6	64/1 negligible [2] 64/1	115/18 115/24 116/3 120/10 124/9 124/17
model [2] 122/6 124/24	122/25 138/9 165/20 176/2	Mr Lees [2] 9/1 54/7 Mr P Hammond [1] 6/11	48/5 48/20 52/14 53/9 53/17 65/5 82/17	negotiate [1] 17/7 neither [1] 61/3	126/2 126/4 126/5 126/5 126/6 128/10
moderate [2] 185/23 186/4	mostly [5] 105/8 141/10 148/14 163/19	Mr Seymour [8] 9/16 90/1 90/23 91/5 95/15	82/18 96/22 100/3 102/14 104/19 108/18	nerve [3] 158/6 159/17 159/23	130/8 130/13 131/23 132/6 134/13 134/20
moderated [1] 166/12 molecular [2] 77/15	163/21 Mottram [1] 9/16	96/24 99/11 100/7 Mr Sloggem [1] 60/20	111/20 135/23 139/15 145/18 145/20 145/23	net [1] 62/4 never [17] 2/3 2/4	138/15 138/17 139/15 139/16 140/12 143/14
121/18 molecule [1] 52/15	move [3] 155/5 191/10 191/13	96/24 99/11 100/7 Mr Weston [1] 54/8	146/6 147/5 153/14 157/10 159/16 164/10	6/18 14/25 16/8 81/12 84/7 88/4 140/18	143/16 143/16 143/20 144/3 144/3 144/5
molecules [2] 52/19 52/20	moved [6] 136/9 142/6 143/4 146/9	Mr Weston's [1] 62/5 Mr Williams [25] 9/2	183/7 188/7 188/7 189/6 189/9	146/23 146/24 160/23 162/8 164/2 169/25	145/15 146/24 149/9 149/10 149/18 149/22
moment [7] 28/11 43/6 111/3 123/8	187/2 187/13 moves [1] 105/21	9/21 14/10 18/11 18/20 19/10 19/20	Myself [1] 146/17	179/1 189/22 new [28] 9/15 15/11	150/18 152/15 153/3 160/2 160/23 164/21
155/7 159/21 172/6 momentum [1] 84/2	moving [5] 63/22 101/14 142/25 182/18	20/17 21/19 22/11 22/14 24/8 24/19	N	16/1 18/24 24/22 54/21 55/6 56/6 58/12	165/7 165/7 166/8 166/8 169/10 175/6
Monday [2] 191/16 191/20	185/9 Mr [82] 6/11 8/24 9/1	28/11 28/14 30/10 30/25 40/23 41/5	N-I-B-S-C [1] 153/6 name [11] 2/13 5/15	69/16 70/20 70/20 75/4 75/8 75/16 76/9	175/22 176/9 176/12 176/14 176/17 182/25
money [8] 4/2 60/7 67/11 67/15 75/3	9/2 9/16 9/16 9/21 9/21 13/25 14/10	41/25 42/14 42/22 95/8 99/10 99/20	23/16 27/24 34/8 34/18 46/23 77/16	76/12 76/14 76/15 76/17 77/16 84/1	184/13 185/1 185/12 185/15 185/17 185/19
167/9 178/4 178/5 monies [1] 88/5	16/15 18/5 18/11 18/20 19/10 19/20	Mr Williams's [1] 13/25	89/15 104/24 152/1 names [3] 8/7 8/10	95/15 99/12 110/16 121/4 139/14 142/6	188/15 188/17 190/12 Nobody [1] 178/19
monitoring [1] 41/23 Mono [10] 2/1 2/5	20/17 21/19 22/11 22/14 24/8 24/19	Mrs [2] 8/11 64/16 Mrs S [1] 8/11	13/15 NANB [2] 47/14 165/3	121/4 139/14 Newcastle [3] 19/3	nodded [1] 187/1 nominal [1] 26/3
89/15 91/9 91/20 93/10 93/16 168/8	28/11 28/14 30/10 30/25 31/14 40/23	Ms [28] 10/4 31/10 52/12 53/8 53/19	4/22 9/9 35/7 36/22 48/20 67/16 77/17	19/25 40/24 next [21] 5/20 6/13	non [15] 12/3 27/17 41/22 41/22 86/10
171/4 171/10 Mono Factor [1] 171/10	41/5 41/25 42/14 42/22 51/13 54/7 54/7	53/23 64/18 70/3 70/12 74/4 74/7 94/21	82/17 84/16 87/22 130/7 183/5	57/23 59/15 63/6 63/18 65/4 72/2 72/25	95/8 123/6 123/6 123/12 123/12 123/14
Mono VIII:C [6] 2/1	54/8 54/8 60/20 62/5 68/4 68/8 68/10 83/24	95/2 100/19 100/21 100/23 101/3 101/7	natural [1] 77/8 nature [5] 37/22 69/6	75/18 82/24 95/19	123/15 123/17 123/17 154/14

(65) milligram... - non

<p>N</p> <p>non-A [4] 41/22 123/6 123/12 123/14</p> <p>non-A, non-B [1] 123/17</p> <p>non-B [4] 41/22 123/6 123/12 123/15</p> <p>non-executive [1] 95/8</p> <p>non-inhibitor [1] 154/14</p> <p>non-reactive [2] 12/3 27/17</p> <p>none [2] 110/3 178/8</p> <p>nor [4] 47/7 61/4 98/14 112/14</p> <p>normal [3] 48/22 110/18 184/5</p> <p>normally [2] 26/8 125/7</p> <p>North [1] 55/2</p> <p>not [152] 1/11 2/17 2/18 2/25 3/6 3/6 9/4 11/20 12/18 13/4 14/18 15/1 15/7 16/9 18/1 18/6 18/24 19/11 20/24 21/13 21/23 22/2 22/12 25/23 26/17 27/3 27/4 27/18 28/3 28/25 29/14 29/16 29/21 30/2 30/3 30/15 30/16 30/19 34/19 35/2 39/14 42/22 43/5 44/20 46/10 51/9 53/4 55/7 60/9 61/9 65/20 71/24 73/5 73/25 75/19 75/21 77/10 78/10 81/16 81/20 81/21 83/4 83/13 84/1 86/10 86/22 88/3 89/15 90/8 91/5 92/10 94/23 95/4 95/17 96/18 97/23 100/9 106/24 106/25 110/21 111/20 111/22 112/13 113/18 114/3 116/5 118/20 118/25 124/7 124/7 126/4 126/4 126/6 126/6 127/11 127/21 128/2 128/4 129/8 129/13 129/21 132/6 134/12 135/4 135/10 136/24 140/18 140/19 142/8 142/13 146/16 147/7 148/8 148/12 150/15 151/17 151/23 151/25 153/12 156/18 156/23 157/22 157/23 158/21 158/25 160/2 160/16 163/24 166/24 170/8</p>	<p>170/13 172/21 173/23 174/4 174/22 176/4 177/4 177/5 179/3 179/4 179/15 179/17 180/5 184/11 184/18 185/12 185/24 186/9 188/5 189/20 189/24 190/2</p> <p>notarised [1] 39/16</p> <p>note [21] 9/4 10/4 11/18 13/25 14/3 14/8 14/10 14/17 16/14 22/10 33/1 51/5 52/2 71/5 90/7 94/4 95/2 97/14 100/15 173/8 173/19</p> <p>noted [2] 86/22 87/1</p> <p>notes [4] 13/19 15/19 16/17 98/5</p> <p>nothing [1] 103/21</p> <p>notice [1] 39/1</p> <p>noticed [1] 65/8</p> <p>notified [1] 182/13</p> <p>notify [1] 93/8</p> <p>noting [1] 1/7</p> <p>Nottingham [5] 6/24 11/19 149/12 149/15 149/18</p> <p>Nottinghamshire [3] 6/24 7/23 146/15</p> <p>novel [1] 139/3</p> <p>November [10] 5/4 12/11 12/13 13/2 38/21 55/13 70/5 89/25 91/14 152/9</p> <p>November '76 [1] 13/2</p> <p>November 1976 [1] 12/13</p> <p>now [57] 5/22 6/1 7/19 9/7 14/4 14/15 14/24 16/7 25/3 25/12 25/19 28/13 32/8 36/3 36/12 38/24 43/5 43/12 52/4 52/8 69/20 70/4 71/1 72/19 76/10 88/9 89/5 89/7 89/15 89/24 91/22 95/23 98/6 99/8 99/11 101/5 110/1 120/18 123/16 128/3 137/17 138/25 145/3 147/11 150/1 152/15 155/6 155/20 160/3 161/14 170/5 172/12 172/14 172/15 175/18 185/3 186/19</p> <p>number [6] 16/16 22/6 47/12 110/11 144/7 190/14</p> <p>nurse [1] 143/16</p> <p>nurses [1] 144/11</p>	<p>O</p> <p>O'Brian [1] 159/16</p> <p>o'clock [6] 191/15 191/16 191/19 191/20 191/20 191/21</p> <p>objection [1] 41/3</p> <p>objective [3] 42/3 79/13 123/20</p> <p>Objectives [1] 63/13</p> <p>obliged [1] 36/8</p> <p>observation [1] 175/8</p> <p>observations [1] 97/19</p> <p>observed [2] 17/5 17/19</p> <p>observer [1] 86/23</p> <p>obtain [8] 5/13 19/15 43/3 43/11 44/18 61/14 183/11 184/15</p> <p>obtained [14] 20/3 20/8 23/11 28/3 34/11 34/20 35/7 42/1 51/23 53/1 57/15 93/14 133/17 137/10</p> <p>obtaining [1] 18/24</p> <p>obvious [1] 82/20</p> <p>obviously [22] 15/7 16/12 20/22 98/11 100/22 110/2 115/15 115/18 117/11 123/22 123/24 132/6 133/9 137/10 140/20 141/22 148/22 161/23 166/22 182/4 184/3 189/20</p> <p>occasionally [3] 146/16 146/17 146/20</p> <p>occupy [1] 55/12</p> <p>occurred [1] 115/6</p> <p>October [15] 1/1 4/17 11/13 12/14 13/3 28/10 56/19 56/24 57/3 60/13 65/11 70/13 74/6 164/6 191/24</p> <p>October '77 [1] 13/3</p> <p>October '79 [1] 65/11</p> <p>October 1976 [1] 11/13</p> <p>October 1977 [1] 12/14</p> <p>October 1979 [2] 56/24 57/3</p> <p>October 1983 [2] 74/6 164/6</p> <p>odd [1] 27/2</p> <p>off [11] 6/7 79/17 90/3 90/6 110/2 115/23 139/19 157/14 157/17 157/19 157/25</p> <p>offer [5] 12/2 61/8 62/3 71/2 75/13</p>	<p>offered [9] 15/3 17/2 17/4 17/9 17/11 17/12 17/16 56/11 109/12</p> <p>offers [1] 73/20</p> <p>office [2] 6/23 146/14</p> <p>official [1] 48/7</p> <p>officials [4] 41/2 41/4 175/9 175/11</p> <p>often [3] 2/1 144/12 157/8</p> <p>Oh [8] 120/21 130/10 132/1 136/6 152/10 171/14 172/10 187/8</p> <p>okay [6] 152/5 152/10 171/14 181/6 181/17 190/8</p> <p>old [2] 75/10 186/23</p> <p>omitted [1] 35/18</p> <p>once [4] 59/6 61/7 123/20 156/21</p> <p>one [76] 6/9 9/4 11/22 13/14 13/21 13/23 16/6 16/20 17/20 18/22 22/3 22/7 22/8 22/8 23/13 25/24 26/15 27/1 34/15 38/16 50/3 52/1 53/10 60/1 60/11 61/7 67/7 68/2 74/17 74/23 77/6 82/7 83/8 83/24 86/3 87/23 88/18 88/18 90/13 94/9 94/12 101/25 104/13 104/13 115/15 115/17 119/22 120/19 123/9 127/19 127/25 128/22 128/24 129/1 129/14 132/11 134/1 137/10 139/9 139/13 139/20 148/9 153/8 153/19 160/13 161/20 163/5 165/15 166/3 171/22 171/23 176/12 179/24 181/15 188/25 188/25</p> <p>ones [3] 115/16 115/20 183/23</p> <p>ongoing [2] 80/5 87/8</p> <p>online [1] 90/15</p> <p>only [25] 18/6 21/16 24/21 33/4 51/8 51/21 68/22 73/17 84/1 86/2 87/12 109/11 110/24 114/9 133/6 140/12 141/23 145/15 145/15 147/4 174/16 178/9 185/12 187/17 189/2</p> <p>onscreen [3] 106/1 106/2 107/17</p> <p>onto [3] 53/11 69/2 157/13</p> <p>onward [1] 81/22</p> <p>opaqueness [1] 30/14</p>	<p>open [3] 50/25 78/7 174/8</p> <p>open-ended [1] 174/8</p> <p>operated [1] 181/21</p> <p>Operates [1] 72/3</p> <p>operation [3] 61/12 71/15 81/14</p> <p>operative [1] 99/5</p> <p>opinion [2] 173/21 177/21</p> <p>opportunities [1] 176/23</p> <p>opportunity [3] 39/2 39/7 94/17</p> <p>opposed [4] 168/20 175/14 175/15 177/25</p> <p>opposite [2] 22/6 189/10</p> <p>optimism [3] 98/15 156/5 162/12</p> <p>optimistic [7] 68/3 73/23 83/18 133/16 162/1 165/24 167/22</p> <p>option [1] 16/5</p> <p>or [101] 2/2 6/7 6/24 15/25 20/21 23/19 29/13 32/24 34/1 35/3 36/18 36/24 37/1 39/10 45/16 45/16 49/3 51/3 53/10 55/13 58/9 59/18 72/5 72/7 73/17 73/25 77/8 81/7 83/1 90/23 92/8 92/17 93/1 94/25 96/12 98/4 100/24 101/25 103/22 104/13 109/16 110/17 111/15 112/5 112/15 114/3 114/12 115/22 117/16 118/13 118/23 119/22 122/3 124/7 124/13 124/25 126/5 129/1 129/13 129/14 129/18 130/11 131/3 133/1 134/1 137/21 138/7 140/10 140/15 141/7 143/16 144/6 147/19 147/22 148/15 148/15 149/17 149/20 150/14 151/18 151/18 151/25 152/3 155/10 156/22 157/15 157/23 163/21 163/22 167/10 168/22 174/5 174/12 175/7 176/4 176/23 177/25 183/16 185/21 186/1 191/19</p> <p>order [12] 3/13 37/17 38/6 72/21 90/11 96/13 106/18 158/8 159/2 163/22 184/8 190/25</p> <p>order' [1] 34/24</p>	<p>orders [2] 19/19 21/17</p> <p>organisation [3] 98/22 104/20 185/6</p> <p>organisations [1] 81/3</p> <p>orientated [2] 100/10 146/5</p> <p>origin [1] 49/13</p> <p>original [14] 9/13 33/24 34/3 36/10 36/16 95/20 95/24 96/11 98/23 99/9 139/5 154/5 178/22 179/14</p> <p>originally [7] 10/21 21/20 76/6 99/2 125/24 143/1 179/18</p> <p>originates [1] 49/2</p> <p>origins [3] 2/6 46/9 51/9</p> <p>Orsay [1] 160/11</p> <p>osmolar [1] 108/16</p> <p>other [60] 1/8 1/15 2/21 13/6 16/16 16/24 17/5 19/1 22/8 24/17 27/22 32/5 37/25 42/6 42/23 49/4 51/21 52/19 55/23 58/20 59/19 60/17 64/7 68/24 76/2 78/18 78/20 80/7 81/23 86/24 89/20 106/22 110/4 110/11 115/20 118/25 119/15 119/15 119/23 124/13 125/15 127/21 139/12 140/9 140/10 143/12 144/14 144/15 145/2 150/12 151/19 152/23 153/5 154/22 169/23 170/2 175/14 175/16 177/18 177/23</p> <p>others [15] 11/8 12/20 52/22 59/12 61/8 81/1 117/17 117/18 118/20 140/15 141/10 150/12 156/13 159/2 159/8</p> <p>our [26] 7/22 15/8 15/15 19/4 23/20 24/25 25/18 25/22 26/4 30/21 32/16 49/25 50/4 53/19 81/19 82/17 82/20 84/2 91/8 110/25 124/23 173/23 174/22 174/23 183/2 190/9</p> <p>ours [1] 25/17</p> <p>out [49] 4/18 8/17 12/16 16/19 20/20 31/23 32/6 41/16 43/13 50/24 50/25 52/19 53/5 53/14</p>
---	---	--	---	---	--

O	41/17 79/11 119/23 178/6 179/1 185/7	120/25 134/7 pages 441 [1] 107/24 pages 91 [1] 120/25 pages 91-104 [1] 134/7 Paid [1] 69/11 Palmer [1] 55/1 paper [13] 39/12 74/2 74/6 129/15 134/12 144/5 145/11 162/14 162/23 164/5 164/11 171/15 178/12 papers [6] 3/11 34/1 34/2 103/22 152/1 155/4 paragraph [37] 18/20 26/21 31/12 35/12 38/18 39/10 43/4 43/14 43/19 45/2 45/4 48/16 49/8 56/3 58/4 60/16 72/16 73/2 73/24 78/2 85/11 87/25 88/18 94/4 95/21 98/19 116/20 120/8 122/18 124/21 126/20 129/3 132/21 150/4 150/9 160/19 175/1 Paragraph 1 [1] 175/1 paragraph 1.10 [2] 38/18 45/2 Paragraph 1.5 [1] 35/12 paragraph 1.9 [1] 43/14 paragraph 12 [1] 94/4 paragraph 14 [1] 150/4 paragraph 17 [1] 160/19 paragraph 2 [2] 39/10 43/19 paragraph 31 [1] 26/21 paragraph 37 [1] 150/9 paragraph 6 [1] 45/4 paragraphs [1] 28/14 parallel [2] 31/15 132/6 parameters [3] 63/17 130/1 157/12 paramount [1] 19/1 Paris [7] 58/16 151/18 156/1 160/11 160/18 161/2 161/25 Parliament [1] 99/15 Parlier [9] 28/5 28/5 29/19 32/9 34/21 39/16 41/6 41/12 42/20 part [8] 26/11 39/8	59/5 74/13 83/8 88/19 89/7 160/1 parted [1] 85/16 participants [7] 155/13 173/16 180/12 180/22 181/12 181/14 192/6 particles [3] 73/5 125/1 127/2 particular [11] 1/17 14/6 48/15 52/24 58/11 92/16 99/23 142/2 177/22 182/23 190/20 particularly [9] 37/11 50/8 52/19 135/10 135/22 142/9 151/1 157/2 186/15 parties [2] 82/15 98/4 partly [3] 16/8 16/9 33/23 partners [1] 82/19 parts [1] 58/20 passage [1] 183/3 passed [2] 48/22 106/17 passing [2] 33/1 177/11 passion [1] 180/4 passionate [1] 180/4 past [4] 75/2 101/6 101/7 155/1 paste [2] 173/1 173/3 patent [2] 88/6 88/13 patented [1] 54/23 patents [1] 55/19 pathogens [2] 124/13 124/14 patient [11] 72/23 94/10 124/8 135/9 143/18 143/22 143/23 144/4 171/24 181/25 186/12 patients [36] 2/16 2/18 25/3 42/13 46/8 47/15 74/3 87/13 94/9 109/15 111/14 122/8 123/18 123/21 130/20 136/12 136/16 143/3 143/5 143/13 144/7 144/9 144/24 153/11 153/12 153/17 153/22 153/24 154/13 154/14 163/4 171/11 171/12 171/21 182/20 185/22 pattern [1] 17/19 Paul [1] 92/8 Paul's [1] 92/7 pause [8] 5/18 14/17 15/9 15/20 35/9 38/1 91/12 111/3 pausing [1] 123/8	pay [1] 85/14 PE [4] 14/8 16/1 85/5 138/23 PE5 [1] 161/7 PEG [6] 126/22 127/2 127/7 132/22 140/13 145/11 PEG-fractionated [1] 126/22 Pending [1] 85/12 Penrose [2] 128/13 128/25 people [18] 16/18 22/18 77/25 86/2 119/21 141/6 148/10 148/11 150/12 154/24 155/2 166/25 170/2 179/2 179/11 179/19 179/25 186/16 people's [2] 152/24 167/3 per [34] 6/10 8/21 8/24 8/25 9/2 9/10 9/12 12/16 20/9 21/1 25/24 26/4 26/23 27/2 40/10 62/4 62/6 62/7 71/21 71/22 72/12 116/9 116/16 116/24 122/15 122/16 122/25 123/2 125/1 127/2 139/10 160/15 164/15 183/12 per annum [1] 183/12 perceived [1] 184/24 perfectly [2] 150/12 164/4 performed [1] 72/4 perhaps [9] 11/14 15/19 22/22 27/2 85/11 128/11 140/14 166/5 170/23 period [5] 1/10 2/22 13/2 13/3 67/24 periods [1] 134/15 peripheral [1] 1/13 permit [1] 98/7 permitted [1] 34/13 person [3] 179/20 181/24 188/24 personally [1] 144/1 personnel [2] 58/7 148/24 persons [1] 7/23 perspective [1] 154/3 perspectives [1] 180/23 pessimistic [2] 88/20 156/6 Peter [4] 8/7 128/12 128/25 145/8 Peter's [1] 131/7 PFC [26] 113/16	113/20 115/22 117/9 119/11 119/14 125/25 134/1 134/14 134/15 134/23 136/8 138/20 139/21 140/11 140/22 141/2 141/17 141/18 142/5 142/19 145/7 182/4 182/9 182/10 185/21 pH [1] 121/22 pharmaceutical [8] 1/4 9/20 100/11 145/13 145/15 177/19 191/11 192/2 pharmacies [1] 6/14 pharmacist [2] 166/18 168/6 pharmacology [1] 93/24 phase [4] 65/1 70/21 138/22 161/8 phase 1 [1] 161/8 philosophy [1] 50/4 phosphate [1] 111/1 Physically [1] 146/9 physiological [1] 145/5 pick [14] 26/15 31/21 32/8 72/10 95/2 98/19 109/10 113/1 115/25 132/3 133/24 147/10 147/20 155/12 picked [2] 147/25 149/25 Picking [1] 60/16 picture [3] 57/1 83/18 88/19 Pierre [5] 15/19 58/15 58/19 58/19 161/23 pig [5] 2/14 148/18 151/5 154/23 154/25 pigs [2] 151/5 151/10 pilot [4] 58/3 63/2 66/6 79/7 pints [1] 138/8 pirate [1] 29/23 PL [1] 10/18 PL 0370/0004 [1] 10/18 place [10] 9/24 16/11 36/18 47/1 113/19 124/12 142/9 182/24 183/7 186/24 placed [1] 168/25 places [1] 119/15 plague [1] 86/5 plainly [1] 123/14 plaintiffs [2] 104/1 104/2 plan [15] 59/4 59/21 75/19 76/14 77/9 79/20 79/21 95/12
----------	---	---	--	---	--

(67) out... - plan

P	80/16 82/7 87/19 89/24 90/4 90/5 90/18 92/23 93/17 95/13 95/19 96/20 98/1 98/16 102/2 102/2 102/7 106/1 107/17 107/18 108/7 111/23 120/5 122/2 124/18 124/20 128/21 129/2 132/15 134/4 134/5 135/1 139/2 160/25 170/20 170/24 pleased [1] 81/18 plenty [1] 155/12 pm [7] 101/9 101/11 155/17 155/19 181/9 181/11 191/22 point [28] 16/19 18/7 22/14 26/15 44/16 51/4 51/21 59/11 59/16 64/6 64/10 65/4 70/10 72/10 81/20 83/3 107/9 135/9 138/9 138/20 139/16 162/11 163/14 165/24 165/25 168/13 172/4 185/1 points [9] 6/3 28/8 40/3 64/7 73/18 109/10 121/8 121/8 175/1 poisonous [1] 159/17 policy [3] 21/23 22/4 105/14 polyelectrolyte [65] 1/23 2/11 7/12 14/7 14/9 52/9 52/11 53/4 53/21 55/3 55/20 56/4 58/14 59/10 62/13 65/1 68/6 68/16 69/6 69/15 70/2 71/20 73/6 73/14 74/4 74/8 75/11 75/21 76/19 78/11 81/19 82/25 83/16 85/21 88/10 88/21 89/14 91/20 97/16 138/22 139/2 139/16 139/19 140/2 140/17 146/3 147/10 147/13 147/20 147/25 148/2 150/1 155/22 157/3 157/13 159/13 162/17 164/20 166/20 170/14 173/4 176/19 189/16 189/18 190/21 polyelectrolytes [11] 5/24 54/21 55/16 57/9 57/12 69/3 70/22 71/2 86/9 139/14 145/20 polyethylene [8] 121/10 121/16 121/18 121/23 122/14 127/3	132/4 132/8 polymer [7] 52/15 53/12 53/13 73/9 121/19 139/3 139/4 pool [1] 137/6 pooled [1] 136/22 poor [2] 27/10 48/3 poorly [1] 96/3 popular [1] 179/25 population [2] 153/23 167/7 porcine [51] 2/10 2/13 5/24 7/12 15/10 15/13 15/22 24/14 25/2 25/9 31/4 53/22 54/14 55/7 56/5 57/8 62/15 63/1 66/6 70/7 72/19 73/1 85/4 85/6 85/8 92/1 92/4 98/8 100/17 101/3 146/21 147/6 147/14 147/15 149/24 150/7 150/10 151/2 151/4 153/20 154/4 154/5 155/5 166/17 166/20 167/12 167/17 167/23 167/24 176/13 177/3 Portakabin [4] 142/14 187/14 188/8 188/10 Porton [3] 10/1 10/6 100/15 posed [1] 37/2 position [10] 8/17 29/5 30/6 32/4 36/14 38/2 39/3 54/4 66/22 175/7 positive [4] 115/3 139/7 139/10 169/15 positively [5] 115/3 118/14 119/1 120/2 139/4 possibilities [1] 98/2 possibility [5] 54/2 54/11 73/11 84/4 174/7 possible [21] 15/18 15/22 31/23 42/6 47/14 48/24 54/25 58/13 61/7 64/23 93/22 97/12 97/23 123/4 126/16 126/18 141/23 142/3 167/7 169/21 174/18 possibly [7] 42/1 116/5 118/8 164/1 165/4 165/5 187/6 post [3] 133/2 146/7 187/21 post-transfusion [1] 133/2 potency [14] 17/22 18/1 18/16 18/16 19/9	19/15 19/17 20/6 20/9 20/12 20/15 21/15 35/10 184/2 potent [1] 20/24 potential [19] 20/13 49/15 52/23 55/6 56/7 58/14 75/12 75/15 76/3 114/21 123/18 124/13 138/14 150/18 158/15 166/19 175/2 181/23 182/6 potentially [4] 82/2 139/11 154/14 184/4 potted [1] 121/16 pound [1] 83/20 powers [1] 37/14 PPDS [6] 56/10 56/13 56/22 61/21 62/3 65/10 PPF [1] 16/6 PPSB [5] 109/23 110/1 110/13 110/19 110/25 practical [1] 75/9 practice [3] 37/24 67/25 96/16 practised [1] 75/22 pre [3] 3/1 50/18 145/23 pre-dating [1] 50/18 pre-empt [1] 3/1 pre-empted [1] 145/23 precautions [2] 12/6 114/22 precipitate [2] 133/9 135/5 precipitated [1] 140/13 precipitation [7] 121/10 121/17 121/20 121/24 126/18 130/1 133/8 precise [1] 65/20 preclude [1] 27/18 predecessor [3] 104/23 114/15 114/16 predictions [1] 68/3 prefers [1] 15/2 prejudice [1] 174/22 prejudicially [1] 173/23 preliminary [2] 40/2 40/4 Prentice [1] 145/19 preparation [6] 25/1 48/18 63/20 82/24 93/7 161/24 preparations [1] 135/12 preparative [2] 112/25 117/25	prepare [2] 15/19 106/18 prepared [14] 3/20 3/25 12/1 15/11 27/11 30/10 37/19 44/11 45/23 61/19 98/7 127/6 130/17 161/14 preparing [1] 129/4 prescience [1] 84/13 presence [2] 27/18 41/3 present [15] 4/8 4/19 10/25 11/9 13/23 15/14 20/18 41/2 42/5 50/12 54/7 72/22 83/8 85/3 183/16 presentation [14] 1/3 2/24 2/25 3/4 4/25 8/9 100/20 101/15 148/7 149/3 156/4 170/13 191/9 192/2 presentations [7] 3/5 3/9 13/6 152/6 191/9 191/11 191/14 presented [3] 72/20 81/1 178/16 presenting [1] 83/18 presently [1] 161/9 press [5] 48/20 49/25 50/22 51/2 83/24 pressed [2] 51/13 61/12 pressure [1] 100/23 pressures [1] 92/17 prestige [1] 96/4 Preston [1] 17/16 Preston's [1] 58/24 presumably [6] 9/13 19/21 20/12 80/25 108/5 175/15 pretest [1] 122/22 pretesting [1] 123/3 pretty [1] 167/17 prevent [2] 125/7 158/7 previous [11] 7/17 20/7 30/13 32/24 45/7 84/20 93/2 100/8 120/14 123/9 127/24 previously [4] 28/18 103/11 117/16 147/24 price [5] 16/10 26/4 31/23 32/6 97/5 prices [3] 14/22 17/2 26/6 prick [2] 182/15 182/16 primarily [3] 2/16 63/23 147/5 principal [1] 47/7 principle [1] 81/5 printed [1] 111/20	prior [2] 19/5 127/2 priorities [1] 96/3 prioritisation [2] 99/21 141/13 priority [2] 31/19 96/8 private [1] 99/16 privately [1] 62/20 probable [1] 47/17 probably [26] 20/19 58/21 69/18 76/1 85/25 88/4 112/7 114/12 115/7 116/9 119/5 120/12 155/10 156/14 157/5 163/17 163/25 164/2 164/3 165/20 167/17 167/25 168/3 176/9 179/15 185/7 problem [22] 14/16 16/22 18/7 18/10 18/22 21/5 21/22 25/6 37/2 48/9 48/11 60/25 114/21 117/13 122/21 124/3 147/6 147/8 150/3 151/2 154/10 182/1 problem' [1] 130/9 problem-free [1] 25/6 problematic [1] 55/16 problems [18] 49/14 61/14 86/5 86/11 86/21 97/6 100/11 117/11 142/22 156/10 156/12 159/15 160/4 160/12 161/25 167/14 181/23 189/8 problems: [1] 86/7 problems: the [1] 86/7 procedure [10] 64/11 108/8 112/25 117/25 118/3 127/7 128/5 128/7 129/5 159/7 procedures [1] 182/23 proceed [3] 56/8 82/24 174/11 process [58] 1/23 5/23 5/25 32/15 32/17 39/8 50/7 50/17 51/10 52/14 53/14 53/15 54/22 54/22 55/5 55/22 56/14 57/13 57/15 57/20 57/24 59/10 59/19 63/3 63/7 63/15 65/2 66/1 67/10 68/16 69/7 69/22 70/21 71/25 72/6 75/10 75/21 75/22 76/4 81/22 91/2 93/20 94/18 109/1 129/16 132/5 132/9 135/7
----------	---	---	--	---	---

<p>P</p> <p>process... [10] 143/18 143/21 150/6 150/13 156/15 157/6 157/10 158/22 170/1 177/9</p> <p>process' [1] 75/8</p> <p>processes [6] 48/23 71/3 75/7 106/4 144/13 149/19</p> <p>processing [8] 62/22 63/6 64/11 69/4 97/3 97/11 98/3 159/12</p> <p>procoagulant [1] 157/2</p> <p>procuring [1] 111/1</p> <p>produce [10] 16/9 25/12 59/11 59/12 59/19 78/21 79/14 106/24 147/13 154/14</p> <p>produced [15] 2/3 2/14 5/25 16/12 75/25 76/4 81/12 86/10 89/13 95/15 107/13 113/16 154/7 158/16 165/19</p> <p>producers [1] 55/19</p> <p>producible [1] 57/22</p> <p>producing [5] 57/13 77/2 84/4 88/2 158/18</p> <p>product [181] 1/19 1/25 2/2 2/3 2/14 5/13 5/16 6/1 10/12 10/18 11/17 12/10 12/19 14/5 14/21 14/23 16/22 17/4 17/24 19/16 19/20 20/11 20/14 20/16 20/24 21/18 21/19 22/2 23/12 24/1 25/3 25/22 25/23 26/17 26/19 26/25 27/4 27/5 28/3 28/17 29/23 30/15 30/17 30/18 30/21 30/24 31/1 31/4 31/15 32/5 33/20 34/12 34/24 35/2 35/15 35/22 35/24 36/1 36/2 36/5 36/7 36/9 36/14 36/15 36/19 36/25 37/7 37/16 37/19 38/6 38/6 38/22 41/13 43/22 43/22 43/25 44/4 44/10 44/11 44/14 44/24 45/16 45/23 45/24 46/2 46/11 46/15 46/16 46/24 51/11 51/23 51/24 55/7 56/6 56/13 63/21 63/23 69/21 74/15 77/8 78/10 78/16 80/12 85/8 87/9</p>	<p>87/14 88/9 88/14 89/11 89/13 89/15 91/24 92/1 92/3 92/4 92/4 93/10 93/16 93/18 93/20 93/22 93/25 96/6 96/7 99/6 99/7 106/14 109/7 110/9 111/6 111/7 111/8 113/16 117/10 119/25 130/19 131/1 135/17 136/3 142/21 143/9 147/7 147/14 147/15 149/20 151/13 152/3 152/3 152/4 152/8 153/2 153/10 153/15 154/7 154/16 154/20 156/5 156/7 156/11 157/18 158/11 158/14 158/16 158/18 160/1 160/2 160/5 163/19 163/20 164/1 164/23 165/11 168/9 168/14 168/25 169/15 170/22 171/11 171/17 176/6 186/7</p> <p>product-testing [1] 36/2</p> <p>production [39] 2/10 55/8 55/14 58/1 58/2 58/3 59/2 59/7 62/25 63/1 63/7 63/15 66/4 66/5 66/7 66/11 73/7 75/17 75/23 76/18 79/1 79/7 85/6 88/7 91/19 96/1 96/23 107/10 110/19 110/25 131/4 146/5 146/17 146/18 150/6 151/3 165/17 170/1 188/1</p> <p>production-orientated [1] 146/5</p> <p>products [51] 1/11 1/13 3/15 5/5 5/22 7/14 23/3 24/15 35/10 37/12 41/21 50/5 51/22 55/1 57/22 59/20 69/11 69/25 72/18 72/22 76/7 77/5 77/10 78/13 78/20 78/24 81/5 97/2 97/4 98/12 107/4 114/19 117/15 119/4 119/6 124/14 142/10 142/16 144/15 144/23 144/25 155/2 159/5 167/4 167/6 167/6 169/14 174/2 175/2 175/5 177/24</p> <p>Prof [1] 58/23</p> <p>Prof Arthur [1] 58/23</p> <p>professional [1] 86/14</p>	<p>Professor [13] 14/1 15/21 17/10 48/1 49/23 50/19 50/21 51/6 70/12 70/24 145/3 158/4 164/18</p> <p>Professor Bloom [6] 14/1 17/10 48/1 49/23 50/21 51/6</p> <p>Professor Bloom's [2] 15/21 50/19</p> <p>Professor Lowe [1] 145/3</p> <p>Professor Thomas's [1] 164/18</p> <p>Professor Tuddenham [2] 70/12 70/24</p> <p>Professor Tuddenham's [1] 158/4</p> <p>profile [1] 157/1</p> <p>profit [1] 6/9</p> <p>profitability [1] 96/14</p> <p>profits [2] 25/18 99/21</p> <p>programme [16] 25/1 26/12 57/21 59/8 62/13 62/24 63/14 68/17 68/21 75/18 76/21 77/1 79/4 79/5 178/8 178/9</p> <p>programmes [2] 58/25 79/3</p> <p>progress [5] 85/15 86/21 87/6 146/21 168/14</p> <p>progressed [1] 99/4</p> <p>project [16] 16/2 56/3 60/25 61/4 61/9 61/17 61/22 82/3 87/17 158/5 176/20 179/2 179/12 183/21 183/22 183/23</p> <p>projected [3] 85/6 95/25 99/2</p> <p>projecting [1] 68/12</p> <p>projection [1] 6/5</p> <p>projects [4] 54/16 96/4 124/5 185/16</p> <p>promise [2] 180/5 181/3</p> <p>promising [2] 161/11 167/11</p> <p>promote [1] 106/22</p> <p>promoted [2] 105/8 105/10</p> <p>promoting [1] 69/22</p> <p>prompt [1] 18/25</p> <p>prompted [6] 20/15 47/25 74/13 79/21 110/16 180/17</p> <p>pronunciations [1] 108/18</p>	<p>proof [1] 87/14</p> <p>properties [1] 111/2</p> <p>property [1] 79/25</p> <p>prophylactic [1] 69/16</p> <p>proportions [1] 9/14</p> <p>proposal [6] 38/21 62/18 63/11 64/25 66/11 67/21</p> <p>proposals [3] 43/15 77/19 98/10</p> <p>proposed [12] 3/25 4/20 9/8 37/13 50/19 58/24 77/16 77/24 77/25 94/12 98/21 185/10</p> <p>proposed a [1] 50/19</p> <p>proposes [1] 76/10</p> <p>proposing [2] 39/6 43/25</p> <p>proposition [4] 88/4 88/12 97/13 124/10</p> <p>prospect [2] 84/10 168/24</p> <p>prospects [5] 60/23 73/21 88/20 91/1 156/7</p> <p>protect [1] 79/25</p> <p>protection [2] 88/6 88/13</p> <p>protein [28] 25/25 52/18 53/11 64/8 74/21 75/4 75/25 77/6 80/21 80/25 82/12 83/11 89/3 89/7 102/10 104/4 109/19 121/19 125/22 154/10 154/23 154/25 163/13 165/16 165/19 178/18 178/19 179/4</p> <p>proteins [13] 24/24 68/25 76/2 76/22 77/2 79/16 84/4 118/20 121/20 121/24 125/21 126/12 135/6</p> <p>proteins' [1] 76/12</p> <p>proteolytic [1] 158/5</p> <p>prothrombin [2] 110/12 110/17</p> <p>protocol [6] 35/17 35/18 35/21 35/25 37/23 48/24</p> <p>protocols [9] 35/1 35/7 35/13 37/8 37/10 37/17 41/18 44/12 45/25</p> <p>prove [1] 73/17</p> <p>proved [5] 157/3 157/10 157/18 158/2 164/17</p> <p>proven [1] 77/2</p> <p>provenance [1] 46/9</p>	<p>provide [11] 15/17 25/19 42/23 64/22 64/24 64/25 69/17 77/9 87/14 177/8 184/12</p> <p>provided [13] 11/3 11/4 35/14 64/20 70/7 93/19 93/21 101/23 107/19 107/20 128/23 140/4 161/4</p> <p>providing [5] 76/22 77/20 99/4 140/2 140/6</p> <p>provision [1] 61/24</p> <p>Prowse [1] 134/8</p> <p>PRSE0003349 [1] 128/22</p> <p>PRSE0003648 [1] 107/17</p> <p>PRSE0003799 [2] 120/20 132/16</p> <p>PRSE0004075 [1] 184/10</p> <p>prudent [2] 112/21 117/21</p> <p>Prudential [1] 4/6</p> <p>Prutec [11] 4/5 4/13 4/22 9/9 67/17 77/17 81/1 84/16 178/4 179/16 179/22</p> <p>Prutec Limited [2] 4/5 4/13</p> <p>public [2] 166/2 182/14</p> <p>publication [1] 109/7</p> <p>publications [1] 132/11</p> <p>publicity [2] 48/19 51/2</p> <p>published [4] 109/21 134/2 134/14 140/19</p> <p>purchase [1] 42/6</p> <p>purchased [2] 5/4 41/10</p> <p>purchases [1] 14/14</p> <p>pure [3] 71/3 155/1 158/8</p> <p>purifier [2] 57/13 78/16</p> <p>purification [9] 57/8 76/24 106/8 106/15 111/15 134/24 177/9 178/10 178/17</p> <p>purified [7] 24/23 63/24 108/21 134/25 154/12 177/8 179/6</p> <p>purify [3] 139/11 159/3 178/8</p> <p>purifying [1] 156/20</p> <p>purity [13] 26/19 26/19 26/23 27/5 52/25 63/16 71/23 71/24 71/24 72/13</p>	<p>72/15 73/19 98/25</p> <p>purpose [8] 68/9 124/23 168/15 174/17 176/17 187/9 187/10 188/1</p> <p>purpose-built [1] 187/9</p> <p>purposes [7] 4/8 13/24 24/16 55/18 75/17 90/22 171/13</p> <p>pursue [1] 173/24</p> <p>pursued [1] 176/8</p> <p>pursuing [1] 55/24</p> <p>Purves [1] 173/17</p> <p>put [11] 30/14 31/14 32/4 37/21 39/7 51/15 117/2 160/3 167/3 173/3 179/24</p> <p>putting [2] 168/9 189/16</p> <p>pyrogen [4] 142/2 142/16 142/21 163/22</p> <p>pyrogen-free [2] 142/16 142/21</p> <p>pyrogenal [1] 163/21</p> <p>pyrogenic [1] 86/10</p> <p>Q</p> <p>qualification [1] 117/6</p> <p>qualifications [1] 101/25</p> <p>quality [19] 25/21 30/20 41/9 41/15 62/25 66/4 93/5 142/23 150/24 157/7 158/18 158/20 163/2 163/18 163/20 163/24 164/4 167/20 174/14</p> <p>quantitatively [1] 127/11</p> <p>quantity [3] 18/18 18/21 26/5</p> <p>quarter [6] 9/1 89/17 96/8 101/7 181/4 181/7</p> <p>quarters [1] 174/1</p> <p>question [26] 30/11 37/12 38/15 114/25 115/11 117/4 117/5 117/14 117/15 135/20 136/2 136/24 138/13 145/23 153/14 153/19 154/2 169/5 169/8 169/11 169/23 177/22 179/14 180/17 185/20 185/24</p> <p>questions [21] 11/1 40/13 42/14 99/15 104/4 155/12 180/9 180/13 180/17 180/23 180/25 181/5 181/12 181/13 186/18 186/21</p>
---	--	--	---	--	--

Q	98/22 re-suspended [2] 173/1 173/3 reached [3] 7/5 62/12 81/20 reacting [1] 154/15 reaction [2] 15/21 130/18 reactions [5] 14/19 25/8 47/22 154/10 154/25 reactive [2] 12/3 27/17 read [16] 14/3 20/10 24/10 43/13 48/5 62/19 65/23 72/25 77/22 83/24 90/17 97/20 131/7 133/12 173/19 183/3 readily [2] 25/25 110/21 reading [2] 88/17 161/20 ready [3] 25/14 55/13 65/22 reagent [1] 183/13 reagents [4] 184/1 184/5 185/6 185/8 realise [3] 18/21 58/13 178/25 realised [1] 178/25 reality [1] 84/5 really [26] 51/14 91/2 114/25 117/9 119/7 129/21 136/13 141/23 146/16 150/14 152/17 153/12 154/6 160/16 160/22 162/8 163/22 178/9 178/11 179/21 185/12 189/1 189/6 189/7 189/25 190/24 reappraisal [1] 96/10 reason [8] 43/20 96/25 118/15 120/10 120/15 145/15 163/21 165/4 reasonable [1] 161/12 reasonably [2] 15/4 166/4 reasons [15] 13/7 22/4 46/6 60/23 83/1 85/19 88/13 93/4 93/12 93/15 94/5 118/2 136/9 154/22 167/25 reassured [2] 48/21 48/23 reassuring [1] 91/4 recall [15] 58/17 105/11 113/19 115/13 123/17 124/12 126/13 131/6 137/18 143/20	172/17 178/13 179/6 182/19 185/3 receive [1] 31/18 received [6] 18/18 60/20 91/11 126/10 126/11 180/13 recent [5] 8/1 49/25 75/23 76/9 165/17 recently [2] 14/13 48/20 recipient [1] 112/14 recipients [2] 112/21 125/11 recognise [1] 95/23 recognised [1] 174/3 recognition [2] 114/2 175/3 recollection [4] 103/17 139/15 153/1 183/19 recombinant [19] 2/7 77/3 79/8 84/10 88/9 88/13 89/6 89/10 99/6 99/7 99/24 100/17 103/2 158/23 159/5 166/22 177/24 178/2 189/23 recombinants [2] 101/2 177/6 recommendations [1] 22/17 recommended [1] 61/25 record [5] 33/10 54/8 56/1 80/11 184/11 recorded [1] 183/9 records [4] 23/23 33/14 38/19 42/16 recover [1] 150/7 recovered [2] 110/21 135/6 recoveries [1] 145/2 recovering [1] 110/17 recovery [2] 145/4 163/10 recruited [2] 145/25 187/21 redissolve [1] 86/8 redissolved [1] 108/16 reduce [2] 124/23 133/1 reduced [10] 64/6 64/8 64/8 73/9 73/12 112/24 117/24 122/24 123/2 129/20 reducing [1] 15/16 reduction [4] 118/9 123/4 132/9 154/8 refer [5] 14/8 36/24 40/8 70/15 121/7 reference [44] 9/20	10/19 11/13 12/11 13/11 15/9 17/14 17/17 19/19 23/22 24/1 24/9 26/16 27/24 28/1 28/7 32/12 36/2 48/10 49/9 52/1 58/18 65/6 67/25 68/4 70/8 79/8 82/12 83/13 83/21 84/18 87/7 87/16 91/13 91/22 92/8 95/11 116/1 123/11 129/13 133/19 159/1 181/19 184/10 references [7] 16/17 16/24 23/9 47/19 55/23 71/9 175/12 referred [9] 2/1 15/12 37/8 41/5 51/8 131/15 148/8 170/19 171/15 referring [11] 26/21 48/8 48/14 50/21 71/19 80/20 131/24 132/1 134/2 159/21 162/2 refers [6] 4/24 22/11 60/17 90/22 134/19 183/6 refined [2] 129/25 133/7 reflect [1] 50/13 reflection [1] 92/6 regard [3] 15/16 37/11 50/10 regarded [3] 61/4 107/3 117/13 regarding [2] 31/15 31/25 regardless [1] 26/5 regular [2] 14/12 22/5 regulations [1] 40/1 regulatory [1] 173/13 rejected [3] 11/6 92/23 130/6 rejecting [1] 94/5 rejection [1] 93/11 rejections [1] 94/16 relabelled [1] 49/5 relabelling [2] 23/16 34/18 relate [3] 14/18 93/13 93/15 related [1] 149/21 relating [2] 36/4 93/5 relationship [1] 7/9 relatively [4] 1/10 61/1 155/24 157/19 relaxed [1] 25/10 release [2] 53/13 83/25 released [4] 23/24 23/25 39/22 53/15 relevance [1] 67/20	relevant [1] 90/21 reliability [1] 82/19 reliable [1] 97/12 relied [1] 25/18 reluctant [2] 15/6 19/3 rely [1] 77/10 remain [3] 86/21 118/7 130/2 remainder [1] 113/17 remained [1] 9/12 remaining [4] 34/14 75/6 122/9 159/15 remains [3] 61/9 86/17 122/20 remarks [2] 93/17 94/1 remedy [1] 37/13 remember [17] 44/20 104/24 110/1 114/17 115/17 135/20 137/8 137/13 139/5 151/24 158/17 168/11 175/20 175/21 175/21 182/23 183/21 remembered [1] 67/21 remembering [1] 157/21 removal [5] 5/7 63/25 120/25 130/2 130/5 remove [3] 42/7 125/24 127/11 removed [4] 41/13 122/4 129/9 179/24 removing [1] 132/23 render [1] 154/17 rennet [1] 178/18 reoccur [1] 96/18 reorganise [1] 9/19 repackaged [1] 41/19 repeat [2] 20/3 110/7 repeated [1] 108/18 repeatedly [1] 36/3 replace [1] 21/2 replaced [1] 68/15 replacement [1] 20/18 replicated [1] 74/1 reply [3] 42/14 49/21 81/25 report [24] 3/20 3/23 3/24 4/9 4/13 4/24 5/2 6/2 6/17 6/22 7/21 13/15 25/4 27/25 31/14 31/18 39/8 46/20 47/6 71/1 89/17 111/10 141/17 148/5 reported [3] 47/14 82/14 90/23 reporting [2] 87/2 104/22 reports [4] 14/19 47/21 49/25 91/7	representatives [5] 40/21 40/25 41/3 54/1 94/15 represented [2] 62/3 110/9 representing [2] 90/24 90/25 reputation [1] 154/6 request [6] 30/25 44/2 45/14 92/7 183/6 183/20 require [2] 37/17 78/25 required [16] 26/8 34/25 37/9 37/22 42/24 44/8 45/19 45/20 46/5 57/21 72/1 73/25 77/13 93/25 96/1 110/15 requirement [3] 35/6 65/6 77/20 requirements [3] 64/15 68/24 122/21 requires [1] 83/2 requiring [1] 64/11 research [27] 16/2 16/3 24/25 25/16 55/2 58/2 58/7 59/5 60/4 66/24 67/13 71/1 75/17 76/21 76/25 77/9 79/3 87/17 99/1 99/21 141/7 141/8 144/21 147/19 185/10 187/17 188/4 researching [3] 24/22 57/7 75/3 reservations [3] 83/15 83/19 168/2 resigned [1] 95/10 resin [7] 106/11 106/17 118/5 118/14 118/19 120/3 164/22 resins [4] 70/22 118/25 119/1 119/4 resolve [2] 22/18 100/12 resources [6] 47/6 61/2 96/1 110/20 140/24 141/1 respect [11] 18/12 32/5 33/11 37/10 51/22 88/13 103/13 120/12 150/2 174/8 176/25 response [7] 30/24 72/24 73/16 74/3 111/5 162/16 181/21 responsibility [2] 174/14 179/19 responsible [3] 47/18 69/1 148/16 rest [1] 179/21
----------	--	--	---	---	---

(70) questions... - rest

<p>R</p> <p>restriction [1] 90/11</p> <p>result [13] 24/25 46/16 50/20 70/7 74/14 89/14 90/19 94/21 127/17 128/6 131/13 157/9 173/22</p> <p>resulted [2] 7/15 124/8</p> <p>resulting [2] 97/2 131/14</p> <p>results [12] 16/5 35/14 37/20 44/13 45/25 57/11 70/11 72/20 74/1 86/13 133/16 161/7</p> <p>retail [1] 6/14</p> <p>return [9] 3/8 4/6 7/13 13/7 61/24 70/3 101/3 146/6 191/8</p> <p>returned [1] 19/12</p> <p>Returning [1] 134/22</p> <p>reveal [1] 90/13</p> <p>revealed [1] 80/8</p> <p>reveals [1] 60/2</p> <p>revenue [1] 97/2</p> <p>Reverend [1] 87/12</p> <p>Reverend Tanner [1] 87/12</p> <p>reverse [1] 110/14</p> <p>review [1] 7/22</p> <p>revised [1] 130/1</p> <p>Richard [1] 58/22</p> <p>Richards [2] 31/10 70/12</p> <p>ride [1] 92/19</p> <p>right [30] 27/7 27/9 33/16 52/3 53/18 68/9 74/23 91/24 92/11 102/5 102/11 103/8 111/3 113/3 120/21 121/12 125/3 138/10 138/11 145/24 146/23 150/16 152/10 152/12 171/14 180/3 181/8 184/14 187/19 190/18</p> <p>right-hand [4] 27/7 27/9 68/9 74/23</p> <p>rights [3] 7/7 7/14 178/24</p> <p>rise [3] 9/24 18/10 159/4</p> <p>risk [21] 12/7 41/22 41/23 46/8 64/7 69/14 73/12 98/6 113/23 114/3 114/18 117/14 122/7 123/18 125/11 138/14 153/21 154/24 182/21 184/24 185/16</p> <p>risky [1] 184/4</p> <p>Rizza [1] 20/1</p>	<p>Rizza's [1] 15/12</p> <p>RLIT0001486 [1] 99/15</p> <p>robust [1] 125/22</p> <p>role [9] 77/19 98/24 124/4 134/18 147/2 149/6 150/21 177/7 186/6</p> <p>roles [3] 2/21 144/15 148/10</p> <p>roll [1] 65/22</p> <p>room [4] 72/3 148/6 162/10 163/8</p> <p>Rotblat [1] 159/15</p> <p>Rotblatt [1] 162/16</p> <p>roughly [2] 9/1 119/20</p> <p>route [4] 65/21 69/18 77/3 85/18</p> <p>routine [5] 37/6 112/6 116/2 116/3 143/12</p> <p>routinely [2] 34/25 40/17</p> <p>Royal [14] 17/11 28/12 47/14 70/6 79/11 87/18 89/22 104/14 142/7 152/22 182/8 182/10 183/24 186/24</p> <p>Royal Free [6] 17/11 70/6 87/18 89/22 152/22 183/24</p> <p>rumours [3] 49/2 51/9 51/17</p> <p>run [4] 19/14 104/20 149/15 153/5</p> <p>running [4] 24/17 50/17 100/10 111/6</p> <p>S</p> <p>S Maw [1] 5/5</p> <p>sadly [1] 181/19</p> <p>safe [3] 107/3 164/17 168/18</p> <p>safeguard [1] 83/2</p> <p>safeguarded [1] 83/1</p> <p>safety [8] 32/21 36/1 46/11 50/14 92/25 93/5 158/18 158/21</p> <p>said [36] 14/10 22/3 24/19 30/15 30/16 30/17 30/19 31/22 36/3 42/22 56/9 65/1 65/13 85/2 85/10 100/1 105/13 111/18 126/7 129/3 133/22 137/13 143/1 146/4 149/24 153/16 156/9 159/6 159/11 165/16 166/9 166/11 171/20 173/5 178/13 179/18</p> <p>Saint [1] 102/4</p> <p>sale [11] 5/10 10/7</p>	<p>12/10 23/16 24/3 24/14 34/18 34/19 39/22 149/6 149/7</p> <p>sales [14] 12/13 13/2 13/4 14/5 25/18 31/21 47/2 47/4 61/13 61/25 66/15 66/17 67/11 95/25</p> <p>same [19] 4/25 9/13 17/18 72/21 75/22 80/2 84/14 105/18 119/1 123/9 138/8 138/13 140/4 160/12 161/25 165/4 170/22 182/11 189/21</p> <p>sample [4] 44/6 45/18 70/6 125/3</p> <p>samples [5] 25/14 35/1 35/6 41/17 143/5</p> <p>San [2] 28/6 34/22</p> <p>San Francisco [2] 28/6 34/22</p> <p>Sang [1] 107/23</p> <p>Sanguinis [2] 115/15 115/17</p> <p>Sarah [7] 2/21 8/12 9/4 64/17 83/6 101/19 192/4</p> <p>Sarah Middleton [4] 2/21 9/4 64/17 83/6</p> <p>satisfactorily [1] 42/12</p> <p>satisfactory [2] 15/17 35/24</p> <p>satisfied [1] 46/10</p> <p>satisfy [1] 38/4</p> <p>Save [1] 51/18</p> <p>Savidge [1] 50/2</p> <p>saving [1] 26/6</p> <p>saw [8] 13/15 27/24 29/24 66/21 99/20 149/11 166/19 176/16</p> <p>say [49] 2/24 6/24 15/20 16/16 20/17 20/21 21/24 30/11 31/10 38/17 47/5 50/11 51/13 54/15 58/5 70/24 82/1 82/23 86/16 91/12 92/5 99/8 105/2 105/10 114/21 115/6 116/5 128/6 129/18 134/23 138/7 141/12 142/18 147/16 150/5 150/9 152/25 155/3 155/23 165/5 166/14 170/8 170/11 180/2 181/3 187/18 188/9 188/21 190/11</p> <p>say: [1] 21/17</p> <p>say: you [1] 21/17</p> <p>saying [12] 20/11 65/24 65/25 66/11</p>	<p>68/10 68/13 83/25 94/1 125/3 146/7 165/14 175/4</p> <p>says [38] 4/14 5/2 6/18 7/21 11/24 16/21 18/11 18/20 19/10 21/19 26/13 28/14 30/18 31/12 33/8 43/14 46/21 48/6 48/9 65/22 66/9 71/14 78/22 80/22 82/13 88/1 89/18 94/6 96/24 98/9 102/18 117/20 122/18 124/22 127/18 129/3 161/5 174/20</p> <p>scale [20] 58/2 59/2 59/7 63/1 63/2 63/5 63/7 63/15 66/6 66/6 71/1 72/4 75/22 79/1 79/1 79/6 108/9 110/24 137/15 150/6</p> <p>scale up [1] 71/1</p> <p>scale-up [1] 63/5</p> <p>scaled [1] 147/12</p> <p>scaling [6] 65/25 83/16 113/12 113/13 113/14 150/11</p> <p>Schedule [3] 37/7 43/17 43/19</p> <p>Schedule 2 [1] 43/17</p> <p>scheme [4] 56/14 56/16 56/18 65/11</p> <p>schemes [1] 187/23</p> <p>School [1] 89/22</p> <p>scientific [3] 174/6 174/24 175/13</p> <p>scientifically [1] 119/17</p> <p>scientist [15] 2/22 8/11 9/5 53/16 64/16 99/12 102/19 146/25 147/4 148/20 148/23 168/5 173/14 176/2 186/7</p> <p>scientists [1] 36/22</p> <p>Scotland [11] 109/12 112/4 112/9 116/16 117/1 134/11 135/19 136/10 181/18 182/18 183/4</p> <p>Scottish [3] 114/24 134/10 183/5</p> <p>screen [19] 12/14 27/6 28/9 32/18 43/6 54/5 56/19 62/16 79/18 90/3 90/6 102/1 116/17 116/18 128/21 132/15 160/25 170/20 170/23</p> <p>screening [2] 112/4 122/23</p> <p>seat [1] 95/9</p>	<p>second [32] 1/21 4/11 11/22 11/23 18/15 19/23 28/3 28/13 32/8 48/16 53/1 53/12 58/2 60/16 74/20 77/10 78/1 85/9 89/17 95/21 98/19 102/7 107/21 120/8 121/7 123/11 124/2 124/21 128/24 134/5 165/9 188/11</p> <p>seconded [1] 155/25</p> <p>secretariat [2] 33/4 41/2</p> <p>secretary [1] 93/8</p> <p>section [21] 5/2 6/25 28/13 37/14 37/15 39/10 40/20 43/7 47/12 59/8 73/1 77/25 90/21 96/23 97/14 98/18 109/9 111/24 116/1 120/9 124/21</p> <p>section 2 [1] 39/10</p> <p>Section 28 [1] 37/15</p> <p>Section 29 [1] 37/14</p> <p>Section 5 [1] 43/7</p> <p>sections [2] 43/17 70/15</p> <p>secure [1] 67/7</p> <p>see [74] 3/19 4/12 6/3 6/10 6/25 7/8 7/25 8/20 11/8 11/16 12/17 13/1 13/24 14/8 15/24 16/15 18/3 18/6 18/14 18/15 18/18 19/9 20/6 21/11 27/10 29/6 30/5 31/6 32/20 33/5 33/16 34/3 50/15 53/2 53/24 54/6 56/21 56/23 57/25 59/4 60/6 67/6 67/14 67/24 71/9 74/19 76/13 77/23 79/2 79/9 79/23 81/16 83/10 84/11 84/24 90/10 92/24 93/10 93/14 95/14 100/5 102/3 116/23 121/3 128/11 128/24 133/19 137/4 168/17 172/13 180/16 181/5 188/19 189/8</p> <p>seeing [1] 21/5</p> <p>seek [4] 11/7 42/4 100/12 186/7</p> <p>seeking [4] 5/21 57/3 149/19 166/1</p> <p>seem [3] 88/19 128/8 174/4</p> <p>seemed [4] 61/3 85/3 147/11 160/23</p> <p>seeming [1] 47/9</p> <p>seemingly [3] 17/13 30/24 157/21</p>	<p>seems [8] 24/4 49/5 79/21 86/4 112/23 117/23 161/11 190/20</p> <p>seen [16] 13/6 17/9 29/16 30/12 62/5 80/24 86/24 94/15 94/24 104/7 129/11 155/1 158/25 161/4 165/14 183/2</p> <p>selected [4] 11/6 96/3 124/24 132/25</p> <p>selecting [1] 12/7</p> <p>selective [3] 111/12 121/21 121/23</p> <p>sell [9] 5/14 10/11 18/24 21/20 22/2 24/6 35/2 46/17 46/22</p> <p>selling [6] 22/7 23/13 25/20 29/13 34/14 36/5</p> <p>Sells [1] 3/21</p> <p>sending [1] 26/13</p> <p>senior [1] 8/3</p> <p>seniority [1] 105/6</p> <p>sense [4] 101/12 153/4 167/18 189/2</p> <p>sensible [1] 21/23</p> <p>sensitive [1] 123/1</p> <p>sensitivity [3] 117/3 123/6 123/10</p> <p>sent [9] 19/21 24/7 28/11 43/16 48/1 48/4 60/15 87/20 179/7</p> <p>sentence [3] 48/17 117/20 118/16</p> <p>separate [4] 52/19 67/7 176/15 182/2</p> <p>separated [5] 53/5 53/14 128/9 128/10 165/1</p> <p>Separately [1] 62/10</p> <p>separating [1] 148/19</p> <p>separation [8] 63/9 77/8 120/17 140/10 140/17 164/9 164/10 164/13</p> <p>sepharose [2] 119/22 119/24</p> <p>September [1] 95/10</p> <p>September 1983 [1] 95/10</p> <p>septic [1] 81/11</p> <p>sequence [2] 178/7 178/7</p> <p>sequencer [1] 179/9</p> <p>sequences [1] 179/11</p> <p>sequencing [3] 158/4 159/4 179/8</p> <p>sera [1] 122/12</p> <p>serious [3] 122/21 123/17 158/5</p> <p>serum [8] 12/7 63/9</p>
--	--	--	---	--	--

(71) restriction - serum

S	19/21 21/2 22/9 28/1 31/18 31/23 39/14 44/2 44/8 52/1 60/21 67/19 67/20 77/5 86/22 87/1 90/8 90/13 93/19 93/21 94/3 94/8 105/13 107/9 108/25 116/2 117/2 124/8 129/18 138/7 147/16 149/1 153/10 153/11 159/8 166/14 167/24 169/18 170/11 172/13 174/5 186/9 187/18 188/9 show [6] 19/17 24/12 57/11 80/14 90/19 93/19 showed [6] 31/10 150/11 163/9 164/12 164/18 164/20 showing [2] 21/10 46/13 shown [1] 24/7 shows [4] 22/1 40/13 68/10 73/24 shut [1] 98/14 sic [2] 91/20 168/8 side [4] 11/17 19/1 179/24 189/1 signed [2] 68/7 144/6 significance [8] 11/21 32/9 47/9 52/24 61/23 62/8 74/17 127/24 significant [5] 57/16 71/15 95/6 95/12 98/24 significantly [1] 73/20 similar [3] 16/17 86/2 118/25 simple [5] 20/20 69/6 71/25 73/8 108/8 Simpler [1] 64/11 simply [1] 47/8 since [7] 34/6 85/16 109/19 112/3 112/17 112/19 125/8 single [3] 135/2 135/7 138/9 sir [81] 1/6 3/2 5/18 7/8 7/25 10/15 10/25 11/18 13/4 14/3 15/9 15/20 16/16 17/5 17/19 19/18 20/5 21/10 21/24 22/25 23/17 24/10 26/16 28/23 29/5 31/5 35/9 38/1 46/13 46/25 47/10 51/21 52/2 52/8 52/24 53/17 56/17 56/21 58/17 59/4 59/16 60/1 60/6 60/8 62/1 65/9 67/19 68/12	69/20 71/5 78/9 80/1 82/1 83/23 84/12 86/19 88/17 90/7 90/16 92/20 96/19 97/21 99/6 99/8 100/17 100/25 101/8 101/12 116/23 155/3 155/10 155/16 180/11 186/18 186/19 186/21 189/14 190/13 191/8 191/17 192/7 site [5] 7/24 146/19 148/24 176/17 189/18 situation [7] 18/12 25/5 31/14 31/18 37/13 68/13 123/23 six [2] 43/24 93/13 size [11] 58/6 113/2 113/15 113/18 113/20 114/4 121/24 122/1 137/6 137/11 138/16 sizes [2] 26/2 113/4 skills [1] 76/24 slides [3] 41/7 71/9 71/10 slightly [7] 15/9 27/2 131/22 168/4 171/13 188/22 188/23 Sloggen [1] 60/20 slow [3] 86/20 135/7 135/9 slowed [1] 168/14 slower [1] 87/6 slowly [3] 56/8 135/4 135/14 small [10] 1/10 25/17 58/2 59/2 61/1 72/4 72/7 75/14 137/15 137/15 smaller [2] 7/25 69/7 Smart [1] 4/13 Smith [28] 33/2 33/2 82/10 83/10 83/14 84/24 85/2 86/22 87/2 104/11 104/11 104/18 104/19 105/16 105/17 105/19 108/5 108/5 114/12 119/13 119/14 121/4 135/11 140/23 140/23 145/9 188/25 189/9 Smith's [3] 85/20 86/20 118/21 smoke [1] 169/10 Snake [1] 162/16 snapshot [2] 13/22 161/21 SNBTS [3] 183/7 183/11 183/14 so [173] 7/25 8/21 8/23 8/25 9/3 10/10 13/11 13/20 16/18	18/25 19/14 20/9 20/24 21/4 21/16 21/16 22/12 22/21 23/25 28/17 28/21 29/2 29/3 29/6 29/8 30/3 30/23 32/3 32/23 32/24 37/12 38/12 39/5 43/25 43/25 44/1 44/15 46/3 47/7 49/19 50/24 51/13 53/5 53/13 56/4 56/14 60/6 62/4 64/13 64/25 66/2 66/19 67/6 67/9 70/23 71/20 72/14 72/18 73/23 74/5 78/9 78/9 79/10 81/15 83/10 84/9 85/19 87/23 91/13 91/18 92/3 93/1 93/10 94/1 94/13 95/4 96/17 97/11 98/7 98/14 102/13 105/18 106/23 107/2 107/9 108/25 114/25 115/4 117/12 119/16 120/2 121/24 123/14 124/4 125/12 125/19 129/13 131/22 132/17 135/11 136/1 137/2 137/6 137/21 137/24 137/24 138/4 139/9 139/21 140/19 141/24 142/15 142/24 143/22 145/12 145/21 146/8 146/22 147/11 147/25 148/2 149/14 150/15 150/19 151/7 151/20 151/23 153/8 154/8 155/2 155/6 155/10 155/13 156/18 157/2 157/13 158/2 159/21 160/15 161/17 162/1 163/15 163/22 164/3 167/19 167/21 167/22 169/15 169/17 169/19 171/1 171/15 175/16 178/24 179/10 179/14 181/7 182/25 183/2 183/21 184/2 184/10 187/10 187/19 188/3 189/12 190/1 190/2 190/5 190/12 190/25 190/25 191/15 so-called [1] 154/8 sodium [1] 127/10 sold [20] 1/20 5/25 6/7 6/8 6/10 12/24 18/19 19/17 21/21 27/23 28/18 29/4 33/25 34/7 36/14 39/20 40/18 49/3 51/25 185/5 sole [1] 148/20	solely [1] 174/6 solid [3] 65/1 70/21 138/21 solid-phase [1] 70/21 soluble [2] 25/25 147/7 solution [2] 108/16 121/22 solutions [1] 121/19 solved [1] 150/2 solvent [1] 53/13 some [87] 1/11 3/5 6/8 6/8 6/14 7/6 11/11 12/13 12/19 13/6 13/9 13/18 14/4 14/5 15/4 15/19 16/1 16/17 17/3 18/3 19/6 20/12 22/21 26/6 26/10 29/22 29/25 29/25 40/13 48/19 50/22 56/16 58/19 60/17 61/5 66/7 68/3 70/1 70/3 70/10 72/9 72/20 81/16 83/17 84/12 84/19 86/23 87/16 90/23 93/1 95/21 98/2 102/9 106/19 107/2 115/20 128/12 136/12 136/14 138/25 141/15 142/17 145/4 155/4 155/25 156/5 161/9 162/11 162/12 162/24 163/21 165/14 167/1 168/13 169/4 172/4 173/2 173/12 179/6 179/8 180/17 181/13 184/17 184/17 187/23 189/15 191/13 somebody [9] 29/13 90/24 90/25 118/23 119/17 119/19 151/14 180/7 182/8 someone [1] 51/12 something [17] 11/6 23/8 29/14 48/11 48/13 61/11 95/1 117/6 130/11 143/1 146/5 160/13 163/22 166/14 169/15 176/16 177/15 sometime [1] 101/7 sometimes [5] 49/12 147/3 151/20 157/22 190/1 somewhat [3] 1/13 49/5 137/16 somewhere [5] 137/21 138/5 151/18 184/17 184/18 Sons [1] 5/5 soon [3] 15/18 91/10 156/10	sorry [30] 8/15 23/14 28/5 30/17 30/18 43/5 46/19 47/5 51/7 65/5 74/22 90/2 96/21 104/23 106/1 111/20 121/8 128/23 130/22 130/23 132/1 132/18 136/25 151/10 164/10 166/13 176/25 188/21 190/17 191/18 sort [16] 115/16 117/6 123/24 126/11 141/24 142/15 144/8 157/12 168/21 178/5 180/1 180/2 180/2 182/11 188/18 188/24 sorted [1] 147/8 sorts [2] 142/23 143/7 sought [1] 56/2 Soulie [1] 109/22 Soumik [56] 3/18 7/19 8/14 9/7 11/15 11/22 12/9 12/15 13/1 18/2 22/16 22/24 27/6 31/7 32/18 33/7 43/12 45/6 45/9 46/7 56/20 56/23 56/25 57/24 59/23 60/12 62/16 63/18 65/4 71/8 72/2 72/17 74/18 74/20 74/22 76/13 79/17 80/17 82/8 87/19 89/24 90/3 90/6 93/17 95/13 96/20 98/1 98/16 102/2 102/7 107/17 108/7 128/21 132/15 161/1 170/21 sound [1] 60/22 sounds [2] 85/13 141/25 source [21] 11/5 30/24 32/2 36/18 37/18 44/9 45/21 48/25 50/7 71/19 77/11 86/1 171/6 173/25 174/8 174/10 174/23 175/12 175/15 180/7 185/2 sources [3] 40/8 61/6 120/13 sourcing [1] 188/14 south [2] 134/11 187/13 South-East [1] 134/11 Southampton [1] 26/14 space [2] 65/6 88/25 span [1] 135/21 speak [3] 92/7 94/17 145/18 specialisation [1] 54/14
----------	--	---	--	---	---

(72) serum... - specialisation

S	145/25 146/9 146/10 151/21 152/14 155/24 165/25 168/5 173/6 175/24 176/2 185/11 185/14 185/21 191/10 Speywood GmbH [1] 6/16 Speywood's [14] 2/10 13/12 24/13 37/4 37/16 58/10 77/19 81/13 82/19 82/20 86/15 91/1 174/15 188/12 spiked [1] 125/3 spite [1] 169/16 split [1] 14/14 spoken [2] 91/5 91/6 spokesman [1] 40/23 spread [1] 69/8 spurious [1] 81/4 square [2] 7/1 75/16 St [1] 12/21 stabilisation [1] 111/15 stability [1] 157/18 stable [5] 108/15 156/23 157/16 159/19 160/13 staff [5] 7/21 8/3 58/10 64/15 148/8 Staff/facility [1] 64/15 stage [33] 6/20 29/20 29/22 30/2 30/3 50/11 58/8 59/2 59/5 62/24 63/6 65/15 69/1 79/10 79/22 84/9 89/19 93/18 101/4 123/14 136/22 145/6 145/14 151/16 153/8 160/16 160/21 161/24 168/15 169/16 172/9 176/12 178/18 stages [6] 50/6 58/1 59/14 60/6 65/14 82/24 stand [2] 53/7 157/24 standard [2] 96/15 151/5 standardise [1] 151/2 standards [3] 35/8 36/23 141/19 start [3] 48/6 119/8 146/7 started [5] 110/2 135/23 145/20 185/13 189/24 starting [6] 16/3 73/2 108/21 156/20 157/8 181/18 stated [7] 18/1 18/17 21/3 21/20 42/14 120/8 159/23	statement [16] 26/20 35/21 39/16 84/13 92/9 101/24 102/3 105/25 106/2 121/7 128/25 134/22 150/4 155/23 156/9 160/19 statements [1] 129/1 States [7] 69/12 78/4 103/20 147/10 147/16 184/18 184/24 stating [1] 38/21 status [1] 49/7 stay [2] 147/19 178/24 stayed [2] 147/21 147/21 Staying [1] 182/18 STB [1] 56/12 stem [2] 17/18 80/2 step [9] 159/7 161/14 161/15 161/16 161/25 162/3 162/5 162/8 177/9 step 2 [1] 161/25 steps [4] 53/10 66/3 79/25 177/23 sterile [1] 55/10 Stewart [1] 16/20 sticking [1] 52/17 still [13] 5/13 45/2 50/17 50/17 60/25 78/25 79/22 96/11 145/8 152/13 176/2 181/18 185/7 stock [2] 18/19 18/23 stockpile [1] 21/2 stocks [2] 34/14 110/15 stood [1] 179/20 stop [6] 19/18 21/17 123/21 124/1 156/17 158/6 stopped [3] 5/16 14/15 46/23 store [1] 191/7 stored [1] 157/24 story [3] 2/7 3/14 11/10 straight [3] 101/13 164/3 189/17 strands [1] 24/13 strange [1] 166/18 stream [1] 131/22 strength [1] 21/21 stress [2] 62/14 69/20 strict [1] 50/13 strong [1] 125/10 structure [3] 3/16 178/20 179/5 structured [1] 4/10 studies [9] 79/6 79/10 79/14 87/8 87/10	126/21 132/24 133/20 182/2 study [5] 94/8 130/5 130/25 134/16 134/18 stuff [2] 163/18 163/25 style [1] 189/6 sub [2] 58/9 112/20 sub-clinical [1] 112/20 sub-contracted [1] 58/9 subject [7] 16/4 19/25 41/8 41/15 125/21 168/4 171/3 subjected [1] 125/13 submission [3] 41/9 89/18 131/7 submitted [3] 10/22 39/12 41/18 subsequently [15] 1/19 1/25 9/22 102/23 115/4 117/9 118/12 129/25 137/18 145/10 147/8 155/25 162/5 177/18 185/4 subsidiaries [3] 4/19 6/2 6/3 substance [2] 35/19 81/6 substantial [3] 57/18 61/13 81/9 substantially [3] 78/17 112/24 117/24 substantiate [1] 86/4 substates [1] 183/15 substitute [2] 60/24 139/10 substrate [1] 53/11 successful [11] 4/4 24/25 57/11 129/16 129/18 129/21 129/21 130/6 136/3 136/4 161/15 successfully [1] 76/5 such [16] 25/17 36/20 37/4 37/10 44/6 45/16 45/18 52/18 97/4 104/10 109/13 112/7 113/8 114/19 136/15 183/20 Suffice [1] 82/1 sufficiency [1] 69/10 sufficient [3] 16/9 82/3 82/4 sufficiently [1] 100/10 suggest [5] 15/23 29/17 60/20 100/25 180/11 suggested [2] 65/14 166/11 suggesting [3] 65/17	66/14 130/19 suggestion [2] 15/12 19/20 suggestions [1] 173/25 suggests [4] 2/13 65/21 97/22 163/10 suit [1] 61/8 suitable [3] 108/13 111/13 160/2 summarise [2] 38/1 164/11 summary [3] 60/11 98/18 161/7 summer [1] 25/15 sums [2] 60/7 75/3 supernatant [5] 106/15 111/12 111/17 111/19 118/7 Supernine [4] 140/12 140/14 144/19 145/11 supplementary [1] 61/6 supplied [8] 20/18 35/13 40/5 40/17 131/5 131/18 151/5 185/7 suppliers [1] 15/5 supply [16] 25/21 28/6 29/19 30/20 32/9 34/21 35/1 35/3 39/17 41/6 41/12 42/21 49/16 67/14 78/3 98/24 supplying [3] 23/7 35/6 55/20 support [9] 26/11 28/5 50/9 56/9 56/11 60/21 77/12 96/2 96/6 suppose [3] 104/22 182/5 188/20 supposed [1] 156/18 sure [20] 49/12 50/3 80/24 95/4 95/17 113/11 113/18 126/6 128/2 128/4 136/24 137/17 140/19 147/22 172/21 180/24 182/15 184/19 185/24 188/5 surface [4] 27/16 73/5 74/7 121/1 surfaces [1] 156/24 surgery [1] 109/17 surplus [1] 184/13 surprised [2] 131/6 131/7 surrounded [1] 50/14 surrounding [1] 173/22 survive [1] 168/23 suspect [6] 103/24 113/10 114/23 139/19	145/9 188/23 suspended [2] 173/1 173/3 swear [1] 101/18 Swiss [1] 118/23 switch [1] 23/3 synthesised [1] 77/8 system [5] 23/1 156/19 157/23 183/2 190/22 systematic [1] 112/19
T	table [2] 19/9 20/7 take [43] 9/7 10/15 11/10 12/23 13/20 18/16 20/5 22/24 30/9 52/3 60/1 60/9 61/21 67/22 71/11 74/17 79/17 79/25 80/1 80/13 82/1 83/23 85/9 87/4 90/3 90/6 91/12 95/5 96/19 101/5 108/25 120/18 128/11 129/15 132/13 132/20 150/4 155/14 155/22 170/5 177/6 180/20 189/24 taken [7] 12/6 23/20 82/21 143/22 177/17 177/23 182/20 taking [7] 47/1 55/18 113/19 124/12 135/13 154/16 154/17 talk [4] 63/13 127/23 145/20 146/20 talked [1] 140/13 talking [6] 69/21 72/12 158/22 172/12 172/14 172/16 talks [6] 54/13 59/25 63/25 79/5 80/9 98/2 Tanner [1] 87/12 Targeted [1] 103/4 team [2] 79/11 177/11 technical [10] 22/18 22/22 60/22 64/20 83/14 83/15 93/16 96/1 96/5 111/22 technician [6] 105/7 105/11 114/9 115/1 117/16 148/13 technicians [2] 105/9 105/9 technique [5] 2/15 7/11 27/17 75/8 120/15 techniques [4] 2/5 24/23 68/15 75/4 technological [2] 61/2 99/22 technologies [1]				

T	75/24 132/10 143/12 165/18	191/1	therapy [1] 110/14	27/22 59/6 101/25	115/16 115/20 115/20
technologies... [1] 99/24	than [33] 12/20 12/23 57/14 62/7 62/15	thawed [1] 135/3	there [217]	113/1 115/25 142/3	117/14 124/5 126/3
technology [17] 6/9 62/22 63/9 69/8 70/23	75/12 78/16 78/19	thawing [1] 135/14	there's [10] 31/20	142/24 143/7 143/8	126/4 126/7 126/11
76/7 76/19 77/7 84/3	81/7 86/13 87/6 90/17	their [37] 13/17 17/8	33/1 40/12 79/11	145/1 145/2 145/5	132/11 139/14 140/9
84/10 85/5 87/21	94/9 94/12 112/2	17/25 19/4 19/15 20/7	99/13 116/1 116/9	151/20 153/5 157/15	142/23 143/7 143/12
92/14 178/11 179/22	112/7 116/9 119/23	20/21 21/9 23/12	123/10 150/18 158/24	157/19 158/10 165/14	144/1 148/10 155/12
185/4 189/24	120/12 122/10 131/1	28/18 34/12 34/14	thereafter [2] 150/10	167/1 169/19 169/20	156/11 162/23 163/3
Ted [5] 178/10 178/12	135/4 136/21 136/22	35/14 35/22 38/21	177/12	179/20 189/4 190/20	165/12 167/9 168/16
178/12 178/16 179/20	137/10 140/9 144/14	39/3 39/13 47/17	therefore [10] 25/8	think [87] 6/20 15/17	174/3 180/9 186/18
television [1] 6/5	144/23 153/23 182/9	54/25 55/8 55/21	85/14 88/4 118/7	24/12 43/20 50/22	187/24 190/23
tell [9] 3/13 5/18 30/3	184/3 188/7 190/16	59/13 66/14 66/23	137/16 155/14 167/10	54/19 65/3 65/24 92/6	though [2] 30/9 80/13
51/14 53/9 80/20	thank [24] 9/7 12/9	75/15 77/19 79/23	174/4 174/23 184/5	93/5 96/6 101/21	thought [23] 22/1
137/19 144/5 191/1	22/16 22/24 49/24	81/4 81/14 82/4 82/5	therein [1] 37/9	102/22 105/12 111/17	22/21 42/15 51/17
telling [1] 188/13	79/17 90/6 90/16	97/8 100/9 111/12	thereof [1] 76/7	114/7 114/14 114/21	74/11 101/12 103/19
temperature [2] 72/3	91/21 101/8 101/22	121/21 143/6 144/10	these [38] 1/11 5/18	115/8 116/17 117/18	114/24 118/2 120/16
125/8	104/3 105/18 116/20	them [33] 1/13 7/15	6/7 6/20 12/6 21/2	118/11 118/12 118/15	147/3 154/9 160/14
temporarily [1] 183/8	120/4 132/20 133/24	16/19 16/20 18/13	22/17 28/8 32/20	118/22 118/22 119/18	167/23 168/3 168/22
ten [13] 52/4 52/4	155/16 180/9 190/6	20/20 21/21 23/12	33/12 35/16 44/22	119/19 119/22 119/24	169/15 169/17 170/8
68/12 72/11 94/8	190/12 190/13 191/2	23/14 23/19 23/20	47/25 49/10 49/14	124/19 127/9 127/14	176/13 184/4 188/13
100/2 155/15 191/15	191/5	24/16 29/7 29/15	58/25 59/16 60/7 67/1	131/23 131/24 132/17	189/4
191/16 191/19 191/20	that [903]	29/17 34/2 34/13	73/25 74/10 76/6 76/9	133/6 133/7 139/15	threatened [1] 110/14
191/20 191/21	that I [14] 14/4 26/15	35/22 40/13 44/17	81/3 81/5 82/13 82/16	141/24 144/12 145/9	threatening [1] 25/5
ten o'clock [6] 191/15	88/17 100/25 102/22	54/4 60/1 93/4 93/12	87/4 87/10 115/12	147/21 151/21 151/24	three [13] 1/16 10/13
191/16 191/19 191/20	115/8 131/15 145/21	115/15 115/23 119/7	124/1 127/6 133/3	152/24 153/3 154/22	14/14 23/5 31/21
191/20 191/21	153/4 157/12 158/24	148/9 151/14 155/13	142/2 142/17 160/4	154/23 155/2 155/8	47/15 65/14 80/12
ten years [2] 68/12	163/25 189/3 189/4	179/21 180/13 190/2	184/3 189/15	156/3 159/23 160/7	81/4 147/21 148/15
100/2	that is [31] 3/17 9/20	themselves [4] 38/4	they [81] 11/8 14/15	160/21 161/24 162/1	163/4 171/20
tend [1] 167/10	10/20 11/6 12/11	39/2 154/17 157/22	16/19 17/25 19/15	162/9 163/1 163/4	three years [2] 10/13
tended [1] 180/5	16/23 17/14 22/4	then [79] 6/2 6/9 6/15	21/1 24/17 29/20	165/24 166/3 166/14	23/5
tender [1] 13/8	22/11 32/8 33/15 35/9	8/10 10/7 12/24 20/14	29/22 36/3 36/5 36/12	167/13 168/17 171/13	thrombocytopenia [2]
tendering [1] 13/5	49/19 49/19 58/19	23/7 31/1 39/9 41/17	36/13 36/13 36/17	175/8 175/10 176/7	25/6 154/7
tension [4] 29/24 30/4	62/5 63/6 64/13 64/25	42/9 44/19 53/15	38/4 39/1 43/20 44/16	176/9 176/12 177/2	thrombogenic [3]
30/5 80/10	67/25 71/19 71/19	55/23 63/13 65/6 67/5	47/18 50/18 51/15	178/2 178/18 179/16	106/22 130/18 132/10
term [4] 37/23 78/5	94/1 99/6 103/19	67/12 78/20 78/22	54/24 55/8 55/12	180/3 180/6 180/7	thrombogenicity [3]
88/12 99/21	107/6 118/15 137/24	79/4 79/6 79/7 84/6	61/19 65/14 65/17	181/23 182/22 182/25	131/14 144/20 150/19
termed [1] 93/22	159/21 165/22 176/16	95/20 98/9 99/9	65/18 65/21 65/25	183/2 185/12 187/5	Thrombosis [1]
terminated [3] 5/12	that it [4] 22/3 107/12	100/19 100/25 101/2	66/4 66/22 67/7 67/13	190/12 190/16 190/22	115/16
23/6 34/10	114/6 175/4	101/3 102/7 102/18	67/19 67/19 75/13	thinking [12] 13/13	through [49] 1/16
terms [13] 18/12 21/3	that's [69] 4/2 7/23	103/7 104/22 106/17	81/16 82/18 94/19	53/2 115/12 118/10	1/22 2/11 5/14 7/7 8/8
46/21 80/14 105/4	8/12 8/21 8/24 8/25	116/12 125/1 125/4	98/6 103/24 105/9	121/12 133/5 133/15	11/21 13/21 14/3
105/5 106/5 113/15	8/25 23/25 28/18	129/10 129/24 130/14	115/22 115/24 116/5	153/10 160/3 170/6	14/20 23/2 24/11 28/4
150/17 150/22 157/17	28/22 29/12 30/2 30/3	135/15 138/1 139/13	119/24 125/10 125/17	170/7 187/20	29/4 33/22 34/20
160/5 190/22	32/21 33/14 43/5	141/12 142/18 146/9	125/20 126/8 127/17	thinks [1] 82/2	38/23 39/5 49/3 57/25
terrible [1] 141/25	44/15 45/12 53/17	147/9 147/12 147/25	128/6 130/7 136/14	third [10] 2/9 28/14	59/16 59/21 62/19
terribly [3] 163/24	56/4 67/16 69/19	148/20 148/21 150/2	138/8 141/21 144/11	58/3 74/25 75/7 82/15	67/18 67/22 70/1
179/3 179/25	70/23 72/18 77/15	150/9 152/25 154/17	150/3 150/12 154/10	85/11 87/25 98/4	70/14 74/16 76/12
test [4] 27/17 73/25	80/6 80/24 84/15	157/13 157/24 158/20	154/17 156/12 159/16	121/8	77/14 77/22 78/20
158/15 184/2	89/19 91/5 92/1 92/8	159/3 159/4 160/14	167/1 169/15 169/17	thirds [1] 75/5	84/5 85/10 86/7 93/12
tested [9] 12/3 12/5	92/11 95/1 105/18	164/4 164/19 171/6	169/17 178/13 178/13	this [249]	96/19 97/20 99/18
17/24 20/14 27/15	108/25 111/17 116/7	172/24 173/3 174/15	178/14 178/25 179/10	Thomas [4] 22/5	108/19 111/22 127/23
40/12 112/11 129/6	122/17 123/24 125/17	174/16 177/11 178/23	180/8 180/22 182/2	31/25 32/12 87/18	132/8 138/20 143/18
165/6	127/3 129/22 130/10	181/5 187/13 189/18	187/25 188/1 188/14	Thomas's [3] 12/21	148/7 170/14 173/20
testing [8] 20/13 36/2	131/9 131/24 132/19	189/24 191/10 191/13	189/10	91/14 164/18	180/23
40/5 116/1 116/3	137/18 140/4 140/18	theoretically [1]	they'd [1] 143/9	thorough [1] 174/19	throughout [3] 1/9
116/12 117/3 123/10	142/4 145/21 146/8	133/10	they're [3] 13/21 80/1	those [56] 1/15 6/17	4/24 4/25
tests [17] 12/6 19/14	147/12 147/14 153/14	therapeutic [7] 69/17	they've [1] 66/2	8/1 8/7 9/3 9/10 13/4	throughput [1] 69/8
19/15 20/8 22/23 35/2	156/16 157/14 160/10	76/3 76/22 81/11	thing [11] 69/23 91/24	13/19 16/18 35/17	Thursday [1] 32/22
35/15 35/23 37/20	161/17 168/22 169/10	107/24 108/13 160/2	104/10 135/10 142/16	47/17 60/10 60/19	thus [4] 36/4 41/11
44/13 45/25 73/2 73/4	169/11 179/23 182/17	therapeutically [1]	150/16 158/17 160/12	80/1 80/11 82/2 83/19	63/3 72/6
	189/19 190/6 190/18	77/2	166/18 188/18 190/4	86/7 88/8 89/23 94/17	tie [1] 133/22
		Therapeutics [2]	things [26] 14/4 14/5	99/11 99/18 113/4	time [87] 3/17 7/22
		93/15 103/5		114/7 114/10 114/11	13/13 13/22 15/23

(74) technologies... - time

T	topic [5] 70/2 151/9 181/15 185/9 188/12 Toronto [2] 70/11 72/21 total [5] 12/17 13/2 21/22 57/12 63/25 totally [1] 167/19 touch [1] 3/5 towards [5] 71/13 86/24 95/3 153/22 188/23 toxic [1] 154/7 toxicity [1] 93/22 Toxicol [1] 41/16 trace [3] 48/24 51/4 70/1 traced [1] 42/16 tracing [1] 32/1 track [1] 91/10 trade [2] 25/22 168/6 traded [1] 6/18 trademark [1] 30/22 trading [2] 5/9 6/8 traditional [2] 52/21 57/15 tragedy [1] 100/2 tragic [1] 177/15 training [2] 83/4 114/18 transcript [1] 16/18 transfused [1] 122/8 transfusion [6] 105/1 114/13 115/2 133/2 182/12 183/5 translate [1] 158/13 Transmission [2] 111/25 116/20 transmit [1] 120/11 transmittal [1] 73/12 transmitting [1] 12/7 transpire [1] 84/11 traumatic [1] 81/10 treat [2] 117/10 185/25 treated [2] 42/12 126/8 treating [1] 2/16 treatment [21] 5/6 25/2 25/5 26/1 26/11 73/21 78/15 81/10 108/23 109/13 110/10 110/15 112/16 117/12 124/7 125/13 126/1 136/12 143/6 144/10 186/17 treatments [2] 69/16 69/18 Treloar [1] 89/22 Treloar's [2] 24/8 47/21 trepidation [1] 138/25 trial [27] 60/6 82/25	87/13 89/13 89/16 89/21 91/13 92/3 92/22 93/7 93/11 94/7 94/12 94/13 94/25 94/25 165/9 168/8 168/10 168/16 169/2 169/9 172/2 172/9 172/15 172/21 176/5 trials [8] 63/19 73/8 75/23 163/3 164/16 165/8 165/17 171/3 tricalcium [1] 111/1 tried [2] 157/12 185/16 trip [1] 191/3 trouble [3] 6/21 166/24 179/23 true [1] 139/16 truly [1] 92/16 trust [2] 8/20 19/3 truth [1] 166/6 try [11] 17/8 48/5 110/7 123/22 124/1 124/2 157/16 159/2 171/10 178/6 180/24 trying [7] 85/20 97/24 111/4 141/22 157/10 167/9 170/5 Tuddenham [12] 70/5 70/12 70/24 71/13 74/2 79/24 158/22 162/15 171/17 177/11 178/12 179/21 Tuddenham's [4] 158/4 162/11 164/15 178/10 Tuesday [7] 31/9 100/20 191/8 191/17 191/21 191/21 191/23 turn [15] 1/6 33/7 33/13 47/10 56/25 57/21 59/15 59/23 74/25 79/2 95/19 124/18 129/2 155/20 186/19 turned [3] 118/12 151/6 170/18 turning [5] 3/15 10/7 23/3 52/8 77/22 turnover [1] 55/11 twice [1] 103/21 two [26] 6/17 6/23 15/5 19/2 27/22 52/23 53/5 53/10 57/6 58/10 65/19 66/2 75/5 80/13 101/6 101/7 101/25 107/20 123/8 126/21 127/19 129/14 133/6 188/25 189/9 190/20 two years [1] 57/6 two-thirds [1] 75/5 type [2] 37/12 159/18	typical [1] 15/23 U U/ml [1] 108/20 Uberlingen [1] 85/1 UK [25] 1/12 1/20 4/4 5/15 9/19 10/11 19/18 23/7 31/9 33/25 40/19 41/14 41/14 46/22 48/8 48/23 49/15 51/25 63/19 63/21 78/7 177/15 178/11 178/23 186/15 UK-based [1] 31/9 ultimate [1] 164/23 ultimately [4] 3/2 176/21 177/17 187/25 ultra [3] 71/23 71/24 72/14 um [14] 114/12 133/6 140/12 140/23 141/4 152/15 166/5 169/4 169/8 175/15 181/22 185/24 188/5 190/12 unable [4] 36/20 38/3 93/6 99/1 unacceptable [1] 174/9 unattainable [1] 95/25 unaware [1] 36/20 under [27] 5/15 7/20 8/16 23/16 24/3 25/22 27/23 30/21 31/12 31/17 33/8 34/8 34/18 37/13 37/14 42/1 44/22 46/23 54/16 55/3 56/15 57/5 57/24 61/20 73/6 104/18 188/8 underestimated [1] 96/2 underlined [1] 46/11 underlines [1] 86/14 understand [28] 29/5 38/2 38/6 38/8 40/10 73/3 79/8 83/6 87/22 91/16 94/11 94/18 102/24 103/10 104/25 105/13 107/9 113/4 116/2 119/8 120/14 136/18 136/24 147/17 168/6 182/7 185/24 190/22 understanding [8] 4/9 32/16 52/14 53/9 53/17 83/4 85/20 111/4 understood [3] 39/4 150/1 178/3 undertake [3] 55/20 76/16 144/16 undertaken [2] 55/6	96/10 undertaking [2] 55/16 67/13 underwent [1] 95/6 uneconomical [3] 97/4 98/5 110/19 unfortunate [1] 189/7 Unfortunately [1] 10/25 unique [3] 62/21 75/13 77/7 unit [10] 15/3 25/24 26/4 27/1 27/15 69/5 76/18 77/23 144/8 144/8 United [7] 34/9 69/12 78/4 103/20 149/6 184/18 184/24 United Kingdom [1] 149/6 United States [3] 103/20 184/18 184/24 units [16] 12/1 12/23 12/24 12/25 13/3 17/11 20/8 20/20 20/21 21/22 26/3 26/23 72/8 72/11 72/13 137/8 university [7] 14/1 70/20 99/1 102/4 102/13 102/16 104/8 unknown [1] 154/21 unlabelled [5] 23/15 34/16 39/18 41/15 42/19 unless [3] 19/11 56/8 185/2 unlicensed [1] 23/14 unlikely [3] 98/24 126/17 169/12 unpaid [1] 42/10 unrealistic [1] 95/24 unsatisfactory [1] 37/11 until [10] 14/13 35/3 52/4 82/25 101/6 109/11 141/18 151/22 188/5 191/23 unviable [1] 97/13 unwilling [1] 82/23 up [55] 8/8 11/15 15/2 21/1 23/13 26/15 31/21 32/8 34/15 38/24 43/5 59/7 60/16 61/21 62/3 63/5 65/25 70/14 71/1 79/1 79/6 83/16 95/2 98/19 113/1 113/12 113/13 113/14 113/18 115/14 115/25 132/3 133/24 137/17 139/21 141/18 141/25 145/21 147/10	147/13 147/20 147/25 149/25 150/11 155/12 158/25 160/25 162/14 164/8 167/2 167/3 170/23 172/24 175/25 188/9 upon [4] 3/5 97/17 177/16 177/22 upset [1] 179/23 upside [1] 189/14 urgent [1] 18/25 urging [1] 79/24 us [48] 4/9 5/14 6/15 6/18 6/21 26/10 28/16 28/24 31/10 32/16 40/1 40/7 42/2 49/1 49/5 51/16 52/12 53/9 57/1 58/11 71/10 85/9 85/25 103/13 104/16 104/16 109/2 110/5 110/16 127/23 130/11 142/3 153/7 170/6 170/24 173/22 174/2 174/21 175/2 175/4 175/5 175/17 175/18 176/4 190/21 191/1 191/7 191/21 USA [6] 19/13 39/23 49/12 97/7 129/4 130/7 usage [1] 13/18 use [50] 7/11 7/14 8/19 14/20 15/12 15/22 16/19 24/24 25/9 26/11 32/9 38/2 47/13 48/22 52/15 53/16 54/19 54/21 59/4 71/21 71/22 85/20 88/3 93/13 108/13 110/10 110/13 111/8 113/13 113/14 120/2 122/22 123/1 132/4 133/8 134/9 136/17 139/5 155/2 158/5 159/3 159/17 174/21 183/15 183/23 184/3 184/5 184/9 185/4 186/15 used [45] 1/12 2/4 2/16 2/17 6/19 6/20 14/24 19/24 20/25 25/3 29/22 35/19 37/23 47/18 49/13 52/16 57/12 59/19 71/20 72/19 73/6 78/11 91/19 112/3 112/12 112/17 113/5 119/15 120/15 122/15 127/24 135/2 136/5 136/17 137/20 139/11 142/15 143/24 147/8 153/10 153/11 171/20
----------	---	--	--	--	--

(75) time... - used

<p>U</p> <p>used... [3] 179/17 184/1 186/9</p> <p>useful [4] 88/6 132/25 135/10 139/17</p> <p>using [34] 2/15 5/23 12/19 12/20 12/21 14/15 19/15 21/17 37/14 47/7 55/15 55/17 57/9 66/23 70/21 73/8 76/18 85/22 106/11 112/7 118/19 118/24 118/25 119/21 119/24 121/10 134/24 136/14 137/15 138/21 144/19 159/23 172/22 184/6</p> <p>usually [1] 112/12</p> <p>utilised [2] 127/9 127/10</p> <hr/> <p>V</p> <p>valuable [1] 84/4</p> <p>value [2] 61/10 132/22</p> <p>vanish [1] 68/25</p> <p>variability [3] 157/9 158/11 158/19</p> <p>variable [3] 86/9 97/11 156/10</p> <p>variation [15] 17/3 23/11 23/18 32/13 33/24 34/4 34/12 39/13 46/15 46/16 46/18 46/19 50/19 74/14 113/8</p> <p>variations [1] 139/7</p> <p>varied [1] 17/3</p> <p>variety [1] 6/4</p> <p>various [11] 6/3 17/2 36/10 58/25 78/18 79/2 145/2 151/19 153/5 156/21 178/6</p> <p>vary [6] 37/16 38/21 39/7 43/21 44/24 45/11</p> <p>varying [1] 43/25</p> <p>vast [1] 76/3</p> <p>venous [3] 27/12 27/13 27/13</p> <p>venture [3] 76/12 76/14 99/5</p> <p>version [5] 7/16 111/20 127/7 130/17 132/17</p> <p>versus [1] 151/10</p> <p>very [84] 2/6 3/21 12/16 21/5 27/10 31/25 35/16 47/10 48/3 49/17 52/10 57/10 69/23 76/1</p>	<p>85/15 86/20 86/21 101/1 103/17 106/25 107/2 107/3 108/15 112/18 115/11 115/17 117/8 117/19 118/5 118/11 125/22 127/17 128/6 130/21 130/24 131/8 133/9 133/10 135/4 135/7 135/9 135/14 135/20 139/17 144/8 149/9 150/13 152/16 153/16 154/12 156/15 157/4 157/11 158/2 158/5 160/16 161/8 161/11 163/2 163/15 163/18 165/20 166/15 166/16 166/18 166/21 166/24 166/24 167/2 167/12 175/21 177/2 177/6 179/17 180/6 180/8 186/14 187/8 189/7 189/19 190/1 190/19 191/1 191/15</p> <p>vet [1] 104/20</p> <p>via [4] 64/3 69/18 76/4 77/2</p> <p>viability [1] 77/1</p> <p>viable [8] 61/5 69/7 71/2 88/3 88/11 96/11 160/16 165/10</p> <p>vials [2] 34/16 137/3</p> <p>view [19] 15/23 15/24 19/12 21/22 41/11 47/17 54/25 61/15 76/9 77/20 86/20 88/20 100/6 135/9 156/6 161/17 165/22 177/14 177/21</p> <p>viewpoints [1] 181/1</p> <p>VII [7] 106/19 109/13 109/25 122/5 124/25 125/9 126/23</p> <p>VIII [120] 1/22 2/2 2/7 2/11 2/13 2/16 5/10 5/25 10/12 14/13 15/10 15/22 16/3 24/14 24/14 25/21 30/21 34/7 41/21 42/7 42/8 48/14 50/1 52/18 53/1 53/3 53/22 56/5 57/10 66/8 68/24 70/7 72/11 72/18 72/19 72/22 73/1 73/3 73/15 73/19 74/4 78/10 78/19 85/4 85/6 85/7 85/14 88/7 88/10 88/21 89/13 91/20 97/10 98/9 100/18 101/3 108/1 108/11 110/21 134/24 135/5 135/18 139/17 139/18</p>	<p>143/6 143/9 144/15 145/1 145/4 146/21 147/6 147/11 147/24 148/14 149/24 150/2 150/7 150/10 150/14 151/1 151/3 151/4 153/20 154/5 154/15 154/20 155/5 155/6 155/21 156/20 157/3 157/5 157/20 157/25 158/4 158/8 159/3 159/18 162/18 163/9 163/11 166/17 166/21 166/22 167/12 167/19 168/8 170/14 172/19 176/3 176/19 176/25 177/3 178/2 178/19 179/4 183/25 183/25 184/2 184/6</p> <p>VIII [1] 81/7</p> <p>VIII:C [26] 2/1 2/5 25/2 25/12 59/17 63/2 63/3 63/8 63/12 63/24 73/10 73/14 75/25 78/14 78/23 79/16 91/9 93/10 93/16 98/25 99/4 165/19 168/19 170/3 171/4 171/10</p> <p>VIII:C' [1] 88/2</p> <p>VIII:RAg [1] 64/2</p> <p>viral [10] 53/6 97/8 120/16 120/17 140/10 140/10 164/5 164/9 164/10 164/12</p> <p>virology [1] 115/18</p> <p>virtue [1] 49/11</p> <p>virus [9] 27/19 118/9 118/10 118/11 130/3 133/9 164/21 176/14 182/3</p> <p>viruses [2] 53/4 140/17</p> <p>vision [2] 6/6 69/19</p> <p>vitro [4] 73/2 73/4 87/10 164/12</p> <p>volume [4] 64/9 107/23 120/25 134/7</p> <p>volume 24 [1] 107/23</p> <p>volume 47 [1] 134/7</p> <p>von [10] 25/13 64/2 78/21 78/23 162/20 163/5 163/12 168/21 171/22 171/23</p> <p>von Willebrand [2] 163/5 168/21</p> <p>von Willebrand's [6] 25/13 64/2 78/23 162/20 163/12 171/23</p> <p>Vox [3] 107/23 115/15 115/17</p> <p>vWF [1] 25/13</p>	<p>W</p> <p>wait [1] 181/2</p> <p>Waiter's [1] 60/19</p> <p>Wales [4] 14/1 55/2 55/9 148/1</p> <p>Walford [3] 60/15 80/18 82/2</p> <p>Walford's [1] 81/25</p> <p>Walton [4] 173/6 173/9 173/11 175/7</p> <p>want [8] 29/14 29/17 100/22 106/24 132/20 150/19 155/13 190/24</p> <p>wanted [6] 124/2 146/4 155/2 180/3 180/4 188/4</p> <p>warning [3] 11/13 11/14 27/20</p> <p>warnings [1] 11/24</p> <p>wary [1] 88/17</p> <p>was [623]</p> <p>was always [1] 89/7</p> <p>was announced [1] 84/15</p> <p>was hoped [1] 110/22</p> <p>wash [1] 157/14</p> <p>washing [1] 73/9</p> <p>wasn't [25] 50/22 65/14 97/15 104/22 114/9 116/12 126/5 129/21 130/13 132/1 139/20 143/20 144/6 151/14 160/22 170/22 171/10 172/20 176/8 176/11 179/25 182/10 184/18 185/14 189/6</p> <p>wasn't that [1] 171/10</p> <p>wasted [1] 100/3</p> <p>watched [1] 180/18</p> <p>water [1] 142/23</p> <p>Waterfield [1] 179/7</p> <p>Watt [1] 104/20</p> <p>way [31] 2/25 3/17 4/9 4/10 11/5 20/20 23/1 23/1 24/6 30/14 32/4 32/16 38/5 38/8 40/14 44/18 66/21 97/23 121/21 147/12 151/7 156/6 157/15 157/16 166/7 167/3 179/17 180/24 181/20 189/21 191/2</p> <p>ways [2] 13/21 14/14</p> <p>we [408]</p> <p>we'd [1] 180/17</p> <p>we'll [5] 64/18 90/6 153/15 155/14 181/3</p> <p>we're [12] 12/18 24/15 33/22 45/2 65/3 65/22 95/4 171/13 172/12 172/12 172/15 181/15</p>	<p>we've [8] 17/9 33/3 100/6 116/17 137/19 140/9 140/12 165/14</p> <p>week [4] 3/5 137/21 191/6 191/13</p> <p>weeks [3] 3/10 8/2 147/22</p> <p>weight [3] 52/20 53/4 121/18</p> <p>welcomed [1] 40/25</p> <p>well [91] 2/8 7/18 11/8 22/12 29/9 29/12 45/1 50/21 51/13 51/15 52/3 53/15 53/18 81/13 88/22 90/13 95/4 97/18 97/22 98/1 100/22 101/5 104/13 104/19 105/7 113/10 113/10 115/7 115/15 118/4 118/11 118/21 120/2 120/17 123/20 125/20 129/19 131/23 133/6 135/2 135/2 135/23 137/7 139/3 140/6 141/9 141/21 141/22 143/4 144/17 145/8 147/3 147/21 148/23 152/5 152/15 153/4 154/4 154/12 154/23 155/8 156/1 156/14 160/7 160/23 161/8 166/11 166/14 167/12 167/23 167/24 168/11 168/17 169/14 174/3 175/21 175/25 176/9 177/19 180/16 185/1 187/8 187/25 188/4 188/5 188/20 188/22 188/24 190/6 190/14 191/15</p> <p>Welsh [1] 7/2</p> <p>went [25] 6/11 100/3 113/12 113/18 132/4 136/10 137/17 139/14 139/21 142/1 142/13 143/18 146/16 146/20 147/9 147/12 147/16 149/25 152/18 153/15 162/8 168/13 171/11 171/12 179/10</p> <p>were [198]</p> <p>weren't [4] 105/14 114/23 144/1 170/7</p> <p>west [2] 6/15 136/9</p> <p>Weston [2] 54/8 60/14</p> <p>Weston's [1] 62/5</p> <p>what [132] 1/24 2/24 3/3 4/7 6/22 11/3 13/22 14/10 17/23 18/11 20/5 21/19 24/19 26/25 28/14 28/21 30/9 30/10</p>	<p>30/14 38/1 38/16 43/13 43/14 47/4 51/1 51/1 53/8 56/1 57/1 57/2 64/13 68/10 68/13 71/11 72/14 80/7 80/22 87/13 87/25 88/8 89/5 91/2 91/15 92/12 94/1 94/18 103/15 105/4 105/13 105/15 106/13 106/14 109/23 111/25 113/18 113/19 113/23 114/17 114/17 115/13 116/7 118/10 121/16 124/12 125/17 126/7 126/9 126/11 128/2 128/4 131/23 131/24 133/22 135/1 135/11 136/21 137/6 137/18 139/2 140/24 142/4 143/1 143/17 143/23 144/13 144/14 144/15 145/6 145/10 145/12 146/8 147/2 148/9 148/10 148/11 148/25 149/6 154/4 156/11 157/14 157/17 157/18 159/21 163/12 166/9 167/15 168/15 168/19 168/22 170/6 170/8 172/6 172/12 173/5 175/14 175/17 175/19 178/2 178/20 179/18 180/1 180/4 180/17 180/19 181/5 182/17 183/9 183/22 186/16 186/16 187/7 191/6</p> <p>whatever [3] 128/7 144/6 185/25</p> <p>when [55] 5/16 12/3 13/8 13/11 13/19 15/11 17/23 20/5 20/14 22/2 37/22 46/24 52/16 52/21 67/14 67/16 69/12 70/13 89/16 105/10 105/11 106/13 106/24 108/16 115/6 121/20 122/12 132/4 135/22 135/23 139/13 142/13 146/7 146/10 147/16 148/6 150/18 153/14 154/11 155/4 156/18 156/23 158/3 158/17 160/4 160/7 160/10 163/15 165/25 176/14 179/10 179/23 180/20 187/13 189/3</p> <p>whenever [1] 176/1</p> <p>where [20] 31/1 37/1 37/2 40/11 49/4 58/20 59/11 67/7 70/23 71/5</p>
--	---	--	---	---	--

W	159/7 159/7 161/1 161/8 162/12 163/10 163/12 163/23 164/6 166/2 166/21 168/19 168/20 170/1 171/7 171/7 171/15 172/4 172/15 179/3 179/14 180/21 182/1 182/16 182/20 183/12 186/24 189/8 190/22 190/24 191/12 while [12] 1/10 36/11 53/3 123/21 127/21 134/2 134/23 144/25 145/14 145/16 145/18 180/11 whilst [4] 57/3 75/11 95/25 96/4 who [43] 2/18 2/21 4/1 6/11 7/7 8/12 41/1 42/23 54/23 69/10 69/21 79/22 82/10 90/1 95/15 99/11 99/20 104/10 104/20 105/21 115/2 117/12 118/18 118/18 118/24 136/9 140/21 145/3 145/17 145/19 148/13 148/16 148/21 148/25 155/13 173/11 174/3 175/4 179/2 179/7 182/8 185/6 185/7 whoever [1] 114/13 whole [4] 17/13 137/21 144/8 179/11 wholly [1] 129/18 whom [4] 10/4 33/2 105/21 114/11 whose [2] 103/23 187/20 why [22] 2/4 2/19 13/7 35/9 39/13 46/25 47/8 113/8 118/2 125/19 126/18 153/20 158/20 159/23 166/17 169/8 172/8 172/13 172/21 175/23 176/8 189/8 wide [1] 1/14 widely [3] 1/12 2/3 2/4 wider [2] 69/17 153/23 wife [1] 92/10 will [152] 1/15 1/24 2/4 2/7 2/19 2/20 2/23 3/2 3/5 4/6 5/19 6/21 7/5 7/8 8/8 8/12 8/19 9/22 10/5 11/1 11/7 11/7 13/6 13/23 14/4 14/6 14/8 15/4 15/20 15/24 17/19 18/3 18/6 18/21 20/22 20/25 21/1 21/13 23/21	24/11 25/11 25/14 26/5 26/10 28/19 30/4 31/3 33/5 33/13 34/2 34/3 38/18 38/24 48/5 52/3 52/12 53/2 53/7 53/19 56/17 57/18 57/19 58/17 58/21 61/12 62/1 62/19 64/14 66/10 66/10 67/14 67/24 68/13 68/15 68/19 68/21 68/25 68/25 69/4 69/7 69/9 69/11 69/14 69/16 69/17 70/1 70/3 70/14 71/11 72/10 73/1 73/17 74/1 74/5 74/9 74/17 77/4 77/13 77/18 77/25 78/5 78/6 78/11 83/5 83/12 83/23 84/1 84/2 84/6 84/11 86/19 88/4 88/5 90/11 90/17 92/18 92/20 94/21 95/2 95/4 97/14 97/20 98/18 98/22 98/25 99/7 99/8 100/17 100/18 100/22 101/18 130/14 132/3 133/1 134/21 140/14 152/7 155/3 161/15 165/8 169/13 173/23 174/22 180/13 180/16 181/4 190/23 191/8 191/9 191/10 191/13 191/19 Willebrand [2] 163/5 168/21 Willebrand's [8] 25/13 64/2 78/21 78/23 162/20 163/12 171/22 171/23 Williams [29] 8/6 8/8 9/2 9/21 13/14 14/10 18/5 18/11 18/20 19/10 19/20 20/17 21/19 22/11 22/14 24/8 24/19 28/11 28/14 30/10 30/25 40/23 41/5 41/25 42/14 42/22 95/8 99/10 99/20 Williams's [1] 13/25 Wintersgill [1] 60/20 wisdom [2] 126/10 126/11 wise [1] 92/18 wish [2] 153/19 190/10 with [208] with it [1] 150/3 within [17] 4/4 10/11 11/8 26/9 29/10 32/3 49/16 60/9 60/14	113/20 119/14 125/25 144/7 145/20 149/6 182/8 182/9 without [13] 18/24 21/13 21/18 81/6 100/23 103/14 108/14 108/15 111/14 143/22 153/24 153/25 188/13 WITN2235010 [1] 134/4 WITN5666001 [1] 102/2 witness [10] 26/20 101/15 105/25 106/1 128/25 129/1 134/22 180/20 180/24 187/1 witnesses [1] 190/9 won't [30] 10/15 13/20 38/23 53/23 57/25 59/16 59/21 60/1 67/18 67/22 70/14 72/25 74/16 77/22 79/25 82/1 83/23 85/10 87/4 93/12 96/19 99/18 110/7 117/4 150/4 151/11 155/22 162/14 164/8 174/19 wonder [1] 155/6 word [4] 29/22 54/18 57/25 180/3 wording [3] 27/3 38/23 65/19 words [8] 2/2 45/12 47/18 53/16 88/8 95/21 106/22 175/16 wore [1] 174/14 work [73] 1/21 2/10 11/7 15/8 16/4 22/23 24/13 24/15 52/22 53/6 53/21 55/4 55/5 57/9 58/8 58/21 58/25 59/3 64/17 70/6 79/23 83/8 86/6 91/2 99/24 102/22 105/5 106/6 111/4 113/5 121/13 123/22 124/5 125/25 126/5 126/6 128/8 131/3 131/22 135/21 140/11 141/7 141/13 141/22 142/3 142/18 142/19 142/20 144/21 145/4 147/24 150/17 150/21 152/17 152/22 161/13 163/11 163/16 164/4 169/18 169/20 169/22 169/24 170/1 170/2 173/2 177/12 177/16 177/17 178/16 185/20 187/17 188/7 worked [20] 32/17 105/23 136/10 145/3	147/23 150/1 151/19 152/19 159/2 161/8 161/23 162/5 163/23 164/1 164/19 166/23 177/2 178/9 178/10 182/8 worker [1] 16/3 working [20] 25/12 39/5 55/22 86/2 103/2 107/10 142/14 145/8 145/18 145/22 146/10 147/11 152/13 152/23 163/19 167/12 167/16 179/2 179/2 186/25 works [2] 23/1 190/22 World [1] 70/18 would [104] 3/8 3/13 15/16 15/22 16/1 16/19 18/8 19/22 21/20 21/24 22/6 24/2 25/8 26/15 31/14 36/19 37/21 37/23 43/2 43/10 48/21 48/23 49/6 49/17 51/17 51/21 53/3 53/4 53/6 55/12 56/7 64/25 67/9 67/10 67/11 81/14 81/18 84/11 85/17 87/14 91/10 93/6 93/25 97/7 97/20 101/17 112/21 114/6 114/7 114/11 115/14 115/19 117/21 118/7 118/8 121/20 125/4 125/8 129/22 129/23 133/10 134/14 135/15 138/4 138/9 138/11 140/7 140/21 141/19 143/15 143/22 144/13 152/13 154/13 154/17 159/4 164/4 164/23 165/1 165/2 166/9 166/11 166/11 166/17 168/23 169/18 169/24 170/2 172/24 172/25 174/5 174/15 174/16 175/4 175/7 175/25 175/25 177/23 178/24 187/4 187/19 187/23 188/19 189/24 wouldn't [4] 118/6 118/12 118/13 139/18 Wrexham [15] 7/1 7/24 11/20 55/8 77/24 146/11 146/12 146/19 148/1 148/8 149/17 152/13 152/17 187/14 188/2 write [1] 51/12 writing [2] 48/6 82/10 written [7] 27/10 38/25 103/22 112/1	158/24 161/2 178/22 wrong [4] 53/18 92/6 119/25 151/6 wrote [9] 38/20 49/22 145/11 146/3 151/14 164/5 171/16 178/12 178/12	
	Y					
	yeah [20] 90/6 113/24 114/1 115/10 116/8 116/25 120/24 127/22 133/14 136/1 137/23 148/19 149/13 150/8 153/18 154/1 164/14 170/25 171/2 182/17 year [14] 23/13 34/15 68/2 70/13 75/10 77/24 84/6 86/14 89/2 95/7 105/12 105/12 134/10 134/16 year's [1] 87/12 years [20] 5/21 10/13 23/5 25/18 57/6 68/7 68/12 70/25 71/5 75/2 75/8 75/19 77/14 80/12 100/2 115/7 115/12 128/3 135/24 141/16 yeast [2] 103/2 179/3 yes [234] yesterday [8] 1/18 10/8 10/21 11/2 23/8 29/25 31/6 31/11 yet [3] 30/2 30/3 86/11 yield [15] 63/16 64/3 71/4 71/21 73/20 78/19 81/7 86/17 97/10 108/13 110/24 122/15 160/14 161/11 167/21 yields [11] 57/14 68/20 69/9 71/17 75/23 86/8 93/20 156/9 158/19 165/17 167/16 York [5] 55/6 58/12 70/20 121/4 139/14 you [374] you'd [1] 157/23 you'll [1] 151/11 you're [11] 106/25 108/3 128/15 146/22 149/14 158/17 158/19 169/12 170/8 172/14 172/15 you've [17] 26/17 28/21 51/13 120/7 145/17 145/23 149/25 150/16 156/24 156/24 156/25 180/18 181/2					

Y you've... [4] 186/23 190/19 190/21 190/23 your [69] 3/3 4/17 10/4 18/25 22/18 26/11 49/6 49/18 49/24 50/8 71/21 81/18 101/25 102/1 102/8 102/13 104/5 104/10 105/25 106/1 106/6 109/6 111/4 113/17 115/23 120/14 121/7 121/7 121/8 121/13 124/4 134/1 134/2 134/22 136/24 139/1 141/18 142/11 142/18 142/19 142/25 145/6 146/25 150/3 152/1 152/25 154/3 155/22 156/9 158/14 160/19 161/22 165/10 165/22 168/1 170/5 172/11 172/11 172/13 177/7 177/21 179/14 181/18 182/18 184/23 185/11 185/20 186/6 190/11 yours [2] 120/19 128/17 yourself [3] 143/15 170/8 187/14 Z Zonulysin [1] 5/7					
---	--	--	--	--	--