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Witness Name: GRO-B

Statement No: WITN3511002

Exhibits: Exhibit WITN3511003-4

Dated: February 2020

INFECTED BLOOD INQUIRY

SECOND WRITTEN STATEMENT OF

GRO-B

I, GRO-B, will say as follows:-

Section 1. Introduction

1. My name is GRO-B of GRO-B
GRO-B My date of birth is GRO-B 1952 and I am married.
2. I have Haemophilia B and I was infected with Hepatitis C and Hepatitis B as a result of receiving contaminated Factor IX concentrates.
3. **This statement has been prepared without the benefit of access to my medical records.**
4. I also produced a "First Written Statement" under Witness Number: **WITN3511001** in July 2019.
5. I now prepare this Second Written Statement to solely focus on gene therapy.

GENE THERAPY

6. My family and I have been searching for a cure for Haemophilia B since I was 18 months old. I really wanted to be cured before I died. It was initially thought that there could have been a cure prior to the introduction of gene therapy but this was

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not so. Therefore, when gene therapy came along and the medical professionals thought that this could potentially cure Haemophilia B I thought that the wish of being cured in my lifetime would be granted.

7. I have had gene therapy on my mind for the past 15 or so years and I always paid attention to anything I heard or found out about this subject matter. Historically, it has had a bit of a mixed success rate and I was aware of hearing in the news about someone dying from it, children getting cancer and reports of trials going wrong.
8. In or around November 2018 I found out that a gene therapy trial was going to take place for patients with Haemophilia B. I therefore discussed this with Professor Makris, Professor of Haemostasis and Thrombosis, at the Haemophilia Centre at the Royal Hallamshire Hospital in Sheffield. Historically, I had always discussed the prospects of gene therapy with Professor Makris and how it was progressing in terms of whether it could cure Haemophilia B. Professor Makris said he would put my name forward for the trial and that those organising the trial would consider my eligibility for the same and contact me in due course.
9. I did not hear anything until Spring 2019, when I received a Patient Information Sheet, from the GRO-D in London, entitled "A Phase I/II, Open label, Multicentre, Ascending Single Dose, Safety Study of a Novel Adeno-associated Viral Vector (FLT180a) in Patients With Haemophilia B". The sheet is undated and purports to consist of 18 pages but there were only 15. I attach this as **Exhibit WITN3511003**.
10. I believe that the Study Administrator also telephoned and wrote to me. I therefore duly made my way down to London in the Spring of 2019. I think I stayed overnight in a hotel and spent the best part of two days at the GRO-D while numerous tests were conducted. Following this I was told that I had met the criteria (despite the fact that there was an initial scare about a possible heart condition, which transpired to be a false alarm).
11. In terms of the trial, I was going to be given the Padua Gene. This gene was discovered in Italy and it is carried by a number of people who overproduce Factor IX.

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12. The trial was going to be split so that participants would be given one of three possible doses. I was going to be given the highest dose which I was really pleased about. This was because those on the lowest dose would still be haemophiliacs at the end of the trial, whereas those on the highest dose should have been cured. In terms of the levels, you are considered to be a haemophiliac if your level is at or below 49. Therefore if you had a level of 50 you would be cured. In my case, they told me they were aiming for a level of 60 which meant that I would definitely be cured.
13. I am particularly unhappy about the issues surrounding the obtaining of my consent for the trial. I believe that I completed the initial forms with Professor Makris and when I was in London at the [GRO-D]. Professor Makris went through what would happen after the trial. The [GRO-D] did all the consent for the trial. I would like to add that I have absolutely no complaints in respect of Professor Makris; I hold him in high regard. Before you gave your written consent for the trial, you had to meet with an "impartial" counsellor. I saw this person at the [GRO-D]. However, he was an ex-scientist so I would question the use of the word "impartial" in this regard. He had had a career in science and was used to a life of experimenting and dare I say he would have got a kick out of doing experiments. Therefore, as far as I was concerned, the "impartiality" went out of the window.
14. When I met with this counsellor I felt that I did not get satisfactory answers to my two main concerns which were firstly: What was the likely outcome going to be and if things went wrong what was the worst case scenario? It is correct that in the literature (see attached exhibit) they confirm that this could be death. However, the counsellor told me that the worst case scenario would be that I would remain as I currently was; which was a well managed haemophiliac. This was repeated by others too. Most of the people I met were a bit flippant and made me feel that my questions were superfluous, and not really worth asking.
15. My second question centred on animal testing because the consent form relied heavily on the safety of animal experiments to show how safe the trial was. I had read and researched this subject matter and was aware that literature existed confirming that only about 70 percent of things that worked on animals would also work on humans. I therefore raised this specific point with the counsellor and he just batted it off and said words to the effect "it has been thoroughly tested and it would not go ahead if it had not been". He made me feel like I was raising a trivial

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point and that the trial was going to be perfectly safe, easy and of no concern. It was sold on the basis that it was just one injection and then you would be monitored for 15 years because they wanted to measure the long term effects of the gene therapy in relation to curing Haemophilia B.

16. Later I learnt that other researchers in the same field had concerns about the validity of animal models, especially as there were some specific examples, in gene therapy for haemophiliacs that had worked in animals which had not been replicable in humans.
17. Despite the fact that my concerns had not been addressed, I felt that I was being unduly concerned about trivialities, it was stressed how easy and safe it was I felt I needed to show trust in these experts who had no concerns about the outcome, so I decided to sign the consent form and a duplicate of the same. One was sent to the Royal Hallamshire Hospital and the other to the GRO-D I did talk to some people, the study administrator, the nurse in charge too, June, who were organising the trial during the signing procedure but they were all so pro the trial and "Gung-Ho". Barely a cautionary word was uttered.
18. I duly commenced the trial at the end of Spring/beginning of Summer 2019. I received my injection, which was a small infusion lasting only thirty minutes. This took place at the GRO-D. I attended every day for tests. I was tested continuously throughout that first week. I was then sent back to my regional centre, which was the Royal Hallamshire Hospital, where I was tested three times per week for the first twelve weeks. This then reduced to twice per week for several weeks, then once per week and then once per fortnight. It is now February 2020 and I am tested once per month.
19. Initially those organising the trial were elated because I displayed the best results they had ever had. I think I jumped from 0 to 61 the day after the injection. Then my level reached 91 which surprised them and by the time I got back to the Royal Hallamshire Hospital I had reached 160 or 170 and you could immediately tell that the medical professionals at the Royal Hallamshire Hospital were concerned. Professor Makris, who was a superb doctor, was clearly under orders and he said to me "We definitely don't want your level going over 200". The average would be say 100 whereas a level of 150 would be exceptional. Studies have been carried out

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confirming that the risks, to include thrombosis, increase dramatically once the levels exceed 150.

20. The main difficulty and significance of it being so high is the risk of thrombosis; blood starts to clot at these higher levels. Furthermore, I believe that deaths from people at risk of thrombosis are three times higher from bleeding following an operation than from too much clotting problems.
21. It was abundantly clear that the medical professionals at the Royal Hallamshire Hospital were under orders from those at the GRO-D My levels became sky high in that I displayed the third highest level in the WORLD. The trial was set up to generate as big an expression as possible in terms of the Factor IX. Those running the trial had a script which they stuck to throughout. They had expected the level of expression to be under threat so they gave you drugs to protect the expression level and to prevent it from falling. Despite the fact that my levels were rising at an alarming and out of control rate, they kept pumping me with drugs to ensure that the level of expression was kept as high as possible. No one could justify treating me for prevention of loss of expression when it just went higher and higher. At no point during the first twelve weeks did anyone stop to consider the well being of the patient, which was me. This is contrary to what is stated in the attached exhibit. The trial had gone drastically wrong for me in that my level peaked at 584.
22. I was continuously asking them to stop giving me the drugs and to let my expression level drop. I think privately the doctors at the Royal Hallamshire Hospital all thought that it was crazy but I believe that they were being told by doctors at the GRO-D GRO-D that my levels would eventually drop so they were instructed to stick strictly to the trial proforma. One consultant, (whose name is known to me but I don't want to disclose it for fear of getting him into trouble because I don't think he should have told me what he did but he talked to me as a friend and not a patient) at the Royal Hallamshire Hospital told me that when my level had exceeded 500 he sent an email to those organising the trial, clinicians and the American Company who were sponsoring the trial, seeking advice in relation to my case. In fact, if I remember rightly he sent one email and it was copied and forwarded all over the place. He received about 100 emails in response and he said they were divided into three categories; those from individuals with a background in science/trial organisers were saying carry on and see if you can reach a level of 1000; those from clinicians were saying it is far too high and it must be brought down and the third voice was from the

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American company who were sponsoring the trial and they advocated that nothing must be changed and that the trial must continue with strict adherence to the set proforma.

23. Throughout the first twelve weeks I was being given very powerful anti-rejection drugs (the use of which were never mentioned to me prior to the commencement of the trial nor is this fact mentioned in the literature) together with huge doses of steroids. These drugs were the same type given to patients who had undergone heart or liver transplants.
24. I remember one of medical professionals (in fact it was the person administrating the trial, it was only later he told me he was not a doctor; I think his name was Chris) at the GRO-D, who was involved in the trial telling me, prior to me commencing the trial, that I would be "buzzing for three months". The reality was very different; I slept for around seventeen hours per day for those first twelve weeks. I used to sleep for twelve hours at night and then seven hours in the day and still had to be prodded to stay awake for the remainder of the day. It was only later that one of the sisters at the Royal Hallamshire Hospital said that the type of drugs I was being given over those twelve weeks were always going to turn me into a zombie and that it was very wrong of anyone to suggest otherwise.
25. I suffered from horrific side effects during the first twelve weeks, some of which lasted for months after the initial 12 week period and may be still ongoing. I could hardly walk, my speech was slurred and I used to almost fall over when I stood up. I suffered a suspected pulmonary embolism, chest pains, flare up of gall stones, pancreatitis and pneumonia. The anti-rejection drugs that were pumped into me eradicated my immune system.
26. In December 2019 I finally took a month's holiday to Cyprus, having had to cancel two holidays during that summer due to the side effects of the trial. Whilst I was on holiday I suffered a haemophiliac elbow bleed and therefore returned to the UK on 18th January 2020 and attended the Royal Hallamshire Hospital on 20th January 2020. The medical professionals were adamant that it was impossible for me to get such a bleed whilst registering levels in the 280s. I had reached a level of 584 in the Summer of 2019.

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27. When I attended both the **GRO-D** and the Royal Hallamshire Hospital they used to have the same discussion with me regarding the aims of the trial which was totally irrelevant to me and my health. They would always talk to me about the fact that people who have reached a level of 30 may experience a decline in that level over the next 15 years to drop to say 15 or 20. I am currently at a level of 284 and they still talk to me about a lifetime problem of dropping from 30 to say 15 or 20. It is so inappropriate as my levels are ridiculously high. It is like "trial talk" and the aims of the trial shall prevail over everything; to include common sense and a serious risk to a patient.

28. Possibly even more alarming is that when my levels rocketed, the medical professionals decided that they would utilise a new method of measuring these levels. For example, if my level had previously measured 380 it was now going to be, say, 150. The new method more than halved the old figures. I talked to one of the clinicians about this and he explained that the drugs companies had two ways of measuring and they used the one which best suited the outcome they were searching for. Therefore, in my case, the levels were too high so a new method was used to ensure that the figures were artificially lowered. However, historically they had always used the highest figures because the very aim of the trial had been to ensure that expression levels remained as high as possible.

29. The medical professionals were astounded by my case and were at a loss as to what to do. I was therefore placed on blood thinners to try to guard against the risk of thrombosis and a meeting took place to discuss my case. The outcome was that they did not know how to medicate me, the split 50/50 so, unbelievably, they left it up to me. I initially thought that I would come off the blood thinners but I was aware that Professor Makris had voiced his concerns with such an approach but still left it up to me. I did not know what to do, I therefore, somewhat tentatively, came off the blood thinners and after only two days I suffered a thrombosis. Things then went from bad to worse. The thrombosis occurred in an arteriovenous fistula (AVF) in my right arm which had been inserted because medical professionals had struggled to obtain blood from me (on one occasion I had 27 separate punctures with the outcome of no blood).

30. Only last week a medical professional told me that AVFs can promote thrombosis which was yet another problem and an additional worry. Why on earth had no one told me about this when I was already at such a high risk of thrombosis? I have an

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AVF in each arm; a failed one in the left and one that works in the right. I have now lost the fistula in my right arm which is now thrombosed and I have an extensive clot here. The medical professionals are currently in the process of dissolving this clot but the outcome will be a lost AVF and therefore the taking of blood from me in the future will be a near impossibility.

31. In conclusion, following commencement of the Gene Therapy Trial I have suffered with haemophiliac bleeds, thrombosis, loss of a fistula, been "as sick as a dog", a possible pulmonary embolism, chest pains, a flare up of gall stones, pancreatitis and pneumonia. I am currently stuck on a dangerously high level of 284 and have to take blood thinners to prevent thrombosis.
32. The medical professionals warned me that the blood clot in my fistula could break off at any time and if it went to my heart I would suffer a heart attack and if it went to my brain I would have a stroke. I have to endure the huge increase in anxiety and depression as a result of the failed trial. I have also been told that I am at an even greater risk of a thrombosis if I sit for more than two hours. Therefore, if I take a long car journey I am supposed to break it up and get out and walk around. This is just not possible for me given that I struggle to walk due to the unbearable pain in my joints at times.
33. I have been left very unwell, with no prospect or the hope of a recovery, as a result of a failed trial which was engineered to ensure the very highest levels of expression. Those running the trial could have stopped it any time yet they chose to continue pumping me full of drugs for the entire twelve week duration. They failed to take my seriously failing health into account and ploughed on regardless, all in the name of the research.
34. Even more frightening is that one of the consultants at the Royal Hallamshire let slip during the trial that participating in the same could well reactivate the Hepatitis C virus. My thoughts were "this is unbelievable and even more so that no one sought to advise me of the same".
35. The medical professionals do not have a clue as to how to treat me in the longer term or what is going to happen to me. Professor Makris told me that the only way to determine my real levels would be to continuously monitor me over the course of 5 or so years. The trial has gone disastrously wrong. I was advised that the worst

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case scenario, in terms of a negative trial outcome, would be that I would revert to being a well managed haemophiliac. If only this was the case.

36. The trial has been a nightmare for me and sadly my nightmare continues. They are still signing people up for the trial which both surprises and shocks me. I wrote a letter of complaint to them in or around 10th September 2019 and I attach a copy of my letter at **Exhibit WITN3511004**. In terms of the Factor IX levels, I confirm that I was initially the 3rd highest in the world but I then went to the second highest. The highest in the world has recurring thromboses. The now third highest (who was the then second highest) was a boy who I think had a level of 512 and he was the brother of the highest in the world. My worry was always that the family had evolved other ways of dealing with high levels. I had artificially acquired it, so had no such defences, maybe born out of my thrombosis.
37. In conclusion, I wanted to stress that there was a genuine sense of excitement and promise in the air. The company involved had just made a 200 million pound investment in a production facility. The hospital was going to get a brand new state of the art purpose built building and everyone was going to do well. Whatever the private reservations of the movers and shakers, down the chain.....the people I interacted with were all very gung ho. It was going to be great. It was so easy and there was no downside.
38. The industry is expected, in the next few years, to be worth 20 billion pounds. Using the Padua Gene means it is theoretically safer and cheaper. Several companies are vying to be first to the market. The first to get to market will take the lion's share. That's where the pressure comes from. An American drugs company and a UK private finance investment.
39. I was told initially when my level reached 91 that they wanted me to be the international face of the company, a pure success story on the cover of all their promotional brochures. They shot a video and told me they would arrange a meeting that week and promised to ring on a specific day. My levels went to 191 and they never spoke to or telephoned me ever again.

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Anonymity, disclosure and redaction

40. I wish to apply for anonymity and I do wish to give oral evidence to the Inquiry.

Statement of Truth

I believe that the facts stated in this witness statement are true.

Signed GRO-B

Dated 19/02/2020