THE INFECTED BLOOD INQUIRY

FURTHER SUBMISSIONS ON BEHALF OF THOSE REPRESENTED

BY MILNERS SOLICITORS

21 DECEMBER 2023

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1. These submissions are made in response to the disclosure of 1,483 documents ("the MULL Disclosure") in November 2023; the documents concern various litigation which has taken place in the United States of America concerning infected blood products.

2. These submissions are intended to build upon our closing submissions and take account of certain themes which run through the newly disclosed, MULL Disclosure. What follows is intended to compliment that which has already been said on our clients' behalf and particularly (though not exclusively) in relation to product licensing.

3. The primary position advanced on behalf of our clients remains that factor concentrates should never have been administered to hemophilia patients until they had been virally inactivated and that the requisite technology to do so existed prior to their introduction. On this point, the evidence of Frank Putnam in his affidavit of 10 May 1994[1] is conclusive:

   "…Prior to 1970, several classes of chemical agents had been determined to stabilize many different proteins against denaturation and loss of biologic activity.

   As of 1970, one or more of these known classes of chemical agents of protein stabilizers could have been used to develop specific stabilization processes for preserving the biologic activity of Factor VIII and Factor IX during viral heat inactivation (pasteurization).

   Had a series of systematic experiments been begun in 1970 using available knowledge and technology and conventional experimental techniques, it would have probably taken about three years or less to develop satisfactory processes for stabilizing Factor VIII and Factor IX for purposes of viral heat inactivation."

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[1] MULL0003421_0046

4. Nevertheless, having regard for the fact that haemophiliacs were in any event treated with concentrates which carried a universal viral risk, we submit that rather than taking all reasonable steps to mitigate such risk, fractionators instead employed practices which exacerbated that risk and did so with the acquiescence of the Food and Drug Administration ("FDA")[2].

The Relationship between the FDA and product manufacturers.

5. Hyland applied to the Division of Biologics Standards of the National Institute of Health (the forerunner to the FDA) for a licence for their Prothrombin Complex (FVIII) in 1968. On 19 June 1968[3], the regulator responded to the application noting, *inter alia*, that: *"We are deeply concerned over the risk of hepatitis with this product."* Albeit, the regulator did little about their concerns and a licence followed in any event. In our submission, this exchange between manufacturer and regulator at the advent of factor concentrates, 'set the tone' and is demonstrative of failed regulation in relation to concentrates from the very beginning.[4]

6. On 8 December 1988, J. Garrot Allen swore an affidavit in the case of *John Doe v Cutter Biological*[5]. Within that document, Dr Allen sets out, *inter-alia* that:

> *"Most regulators come from the industry itself. After they regulate they return to Industry. Thus there is no real regulation and the blood industry has become largely self-regulating over the years. This has lead* [sic] *to considerable abuse culminating in a disastrous epidemic which we know as AIDS. In my opinion, this was predictable as far back as 1975, when the American Blood Policy Act was not vigorously implemented by the blood industry. Then when the HB Core Test was not used this lead* [sic] *to the needless contamination of the blood supply with hepatitis B and NonA, NonB. Even more disastrous for the blood supply was the fact that high risk donors became the "order of the day" and FDA regulations were largely ignored."*

4. Dr Allen's evidence is borne out repeatedly through the MULL Disclosure; In our submission, Dr Allen's affidavit is the prism through which the MULL Disclosure should be considered. We will return to Dr Allen's statement throughout this submission but in the first instance:

    a) It is quite clear from the wealth of testimony offered amongst the MULL Disclosure that it was a frequent occurrence for deponents to have moved either from regulatory work at the FDA (in which we include the Office of Biologics and the

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[2] One obvious step which could have mitigated risk was to maintain haemophilia patients on cryoprecipitate per the Finnish example, discussed at length within our closing submission [SUBS0000055_0049].
[3] JEVA0000101
[4] It will be recalled that in Dr Craske's study, running from 1974-79, Baxter Hyland's Hemofil was found to be (by some margin) the most infective for both HBV and NANB Hepatitis – WITN1055191_0021 and brought to the attention of Baroness Andrews by Carol Grayson in 2003 [WITN1055101].
[5] MULL0000027

Bureau of Biologics) to a pharmaceutical company or vice versa, from industry to regulation.

b) A prime example of the incestuous relationship between the FDA and industry is set out in the deposition of Marietta (Penny) Carr; she sets out her involvement in regulation between 1956 and 1967 before then moving to being Head of Regulatory at Abbot and Alpha[6].

From page 53 of her deposition onwards, Ms Carr lists three other colleagues from her time as a regulator who moved into industry; at page 55 of her deposition, the following exchange takes place:

"Q. Are there others that come to mind who went from DBS to industry?

A. There were others before me and there were others than the ones I've given you but I can't remember all of them."

In short, the labour exchange between regulator and industry was considerable.

c) Dr Allen's charge, that the blood industry was responsible for the frustration of the 1975 Blood Policy Act and America's drive towards a voluntary donor system, is borne out in a letter from the Pharmaceutical Manufacturer's Association to the Assistant Secretary for Health[7]. Within that letter, an exemption for paid plasma is sought (and ultimately granted); the PMA makes abundantly clear that fractionators have no intention of moving to a voluntary donor system where it is concluded:

"Present regulation under both the Public Health Service Act and the Federal Food, Drug and Cosmetic Act is, in our view, sufficient to protect the public health. Imposing additional requirement for unpaid donors would serve to have far more adverse than beneficial effects on the public health."

d) Perhaps the most egregious example of ineffective regulation in the US comes in a letter from the Associate Chief Counsel for Enforcement of the Department of Health and Human Services dated 7 May 1982[8]. The letter is addressed to the Director of the FDA's Bureau of Biologics ("BoB") and implores the BoB to cease their practice of tipping off plasmapheresis centres about impending inspections. The author writes:-

"...I was startled to realize that the Bureau gives advance notice of some inspections of plasmapheresis centers. When I asked at the Bureau, I was told that this practice was long-established and the result of firm policy at the Bureau. This memo is to urge you to change that policy.

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[6] MUL0000146
[7] MULL0001251_016
[8] MULL0003336

The June 1980 inspections of both locations of Buffalo Plasma Centre reveal a pattern of systemic violations and intentional deception, including instructing employees how to change their procedures when inspectors appeared…

[…]

… But one cost is glaringly obvious: of the five past or potential criminal prosecutions of plasmapheresis centers of which I am aware – none was first detected as a serious violator as a result of an inspection, and all were brought to our attention through the fortuitous action of employee-informants or media reporting."

e) If there were any doubt as to the lack of effective oversight operated by the FDA in connection with plasma manufacturers, an internal memo from Cutter, written by their Regulatory Head, Steve Ojala, is illuminating. The memo concerns a meeting which took place between all of the US fractionators and Dr Meyer of the FDA between 22 and 24 May 1985.

Mr Ojala explains that *"Dr Harry Meyer called this special meeting of all producers of coagulation products to discuss the use/production/license of non-viral inactivated products"*

Then:

"Dr Meyer explained that the major manufacturers of coagulation products (AHF and PTC) had been approved for a viral inactivation process for some time, and the data demonstrated reasonable performance for eliminating HTLV-III virus from the final product. He questioned the utility for a non-treated process given the current situation and requested that we uniformly send letters to the FDA stating we would no longer produce or distribute non-heated product to preclude negative reaction from the medical community and general public […] *He explained that although the FDA could revoke these* [licences] *through the regulatory process, he did not want any attention paid to the fact that the FDA had allowed this situation to continue for so long, and he would like the issue quietly solved without alerting the Congress, the medical community and the public. Implicit in the discussion was the concern that the FDA felt that this action was long overdue.*

[original emphasis]

It is clear from this document that the oversight of the FDA was so feeble that licences to products, known to be lethally contaminated with HIV, were permitted to remain in place for approximately 18 months longer than should have been allowed.

f) Before moving away from the Cutter memo, the response of the pharmaceuticals is of particular interest; all expressed a reluctance to surrender their licences, and many did so on the grounds that their existing stock inventory was too large for them to be prohibited from selling it. All of these manufacturers knew the viral risk

posed by their unheated products, by May 1985, scores of haemophiliacs in the US had died of AIDS and yet the value of unheated stock was too luring to curb the manufacturer's desire to continue such sales.

To Mr Meyer's credit, it is recorded that he responded:-

"[He] *could sympathize with the difficulties but that did not remove the overriding concern that no one anywhere in the world should be allowed continued exposure to HTLV-III for any of the reasons mentioned."*

5. The regulatory position in the US is not of mere interest to the Inquiry's investigation, it is fundamental. The UK Licensing Authority ("LA") had ceded some of their own regulatory responsibility to the FDA in UK licences. A report by the Committee on the Safety of Medicines[9] demonstrates, by way of example, the degree of reliance which the licensing authority placed on US regulation; under the heading "Quality Control" within that document, it is said: *"Quality control will be exercised as required under the U.S. Food and Drug regulations."*

6. In our submission there is a dearth of transatlantic interaction between the LA and the Department of Health on the UK side and the FDA and Centres for Disease Control ("CDC") on the American side. Instead, the UK authorities appear mere passive observers and reporters of FDA activities.

7. In the area of public safety, the issues which show that regulation and industry grow too close and too often work in confederation is not confined to blood products. As the fire expert Professor Bisby [day 290: 117 /8-13] explained in his evidence before the Grenfell Tower Inquiry, those charged with invigilating the likes of Kingspan a cladding manufacturer were, in practice, colluding in their conduct: " *... somebody somewhere within this process of building regulation and oversight need to be the person who stands up and says, "No, this is not okay, we cannot be doing tests like this", and that didn't happen, and that's the issue. "*

Hepatitis B Anti-C testing ("anti-core testing")

8. We have been unable to pinpoint the precise point at which it became a US regulation that donors with a history of hepatitis must be excluded but in September 2017, the FDA removed this longstanding requirement and published guidance for industry[10]. In doing so, the FDA noted:

"The longstanding requirement to evaluate donors for a history of hepatitis was introduced in the 1950's before HBV and HCV were recognized and before specific laboratory tests became available to screen all donations. The regulations, in place until May 23, 2016, precluded donation by individuals with "a history of viral hepatitis after the 11th birthday" from Whole Blood and Source Plasma donation (21 CFR

[9] MHRA0000091_005
[10] RLIT0002226

640.3(c)(1) and 21 CFR 640.63(c)(11), respectively). The age-related exception was allowed because most cases of viral hepatitis that occurred in donors when they were younger than 11 years were attributed to hepatitis A virus (HAV). HAV would not have caused a chronic and therefore potentially transfusion-transmissible infection in the donor. The regulations persisted for many years because it was unknown if there were viruses other than HBV and HCV that could cause chronic posttransfusion hepatitis."

9. It must be noted that the regulation does not merely require that a person with a current hepatitis infection be deferred from a donor panel; it requires that where there is any evidence that a person ever had a hepatitis infection after their eleventh birthday, they must be excluded from donation.

10. That some regard for this regulation was had by fractionators is demonstrated in a Cutter quality assurance document dated 28 July 1983[11] where it is written:

    "Hepatitis (Disease or Contact) – Any history of hepatitis will prevent donor from entering the program. Clinical jaundice from an unproven cause is to be considered as indicative of a positive history of hepatitis. Contact with person who has hepatitis will cause donation to be deferred for 6 months without symptoms of hepatitis. Contact means cohabitation, routine use of the same eating and sanitary facilities."

11. In evidence in 1983 the position of a donor who had donated and subsequently found to have hepatitis was discussed[12] at the Blood Products Advisory Committee Meeting: Safety and Purity of Plasma Derivatives (19th July 1983):

    > *"The only action taken at this point in time is that the donor is rejected from further participation in plasma programs. No action is taken against any product that had been put into production or into distribution from that individuals plasma on the basis that the plasma itself was collected and processed in accordance with appropriate regulations....."*

12. It was noted in our closing submissions that in the UK, Dr Maycock had issued a directive to all Regional Transfusion Centres on 8 August 1952 to exclude any donor with a history of jaundice at any time, from donor panels[13].

13. The position then on both sides of the Atlantic, as at 1960 at the very latest, was that donors with a history of hepatitis were to be excluded from donor panels. The method for establishing the donor's history inevitably improved over time, with the advent of new technologies and new diagnostic tests.

14. Whilst those responsible for transfusion centres initially had to rely upon screening questions to identify a history of hepatitis, the discovery of Hepatitis B Surface Antigen

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[11] MULL0006107

[12] MULL0001202_092_0008 Minutes of meeting of the Department of Health and Human Services, FDA Blood Products Advisory Committee on Safety and Purity of Plasma Derivatives, held July 19, 1983, Chaired by William V. Miller at the Auditorium Lister Hill Center, National Institute of Health, Maryland

[13] DHSC0100011_222

("HBsAG") and the development of (several generations of) tests for that antigen improved the ability to exclude donors who had suffered HBV infection.

15. Nevertheless, the HBsAG tests had a fundamental limitation; they would only identify extant or recent infection; save in those who become chronically infected, HBsAG disappears from the blood of the infected person within months of recovery. Whilst HBsAG tests inevitably improved the safety of transfusion medicine to a degree, they did not establish definitively whether the donor had a history of hepatitis.

16. Returning to Garrot Allen's affidavit[14], Dr Allen notes that:-

"One of the reasons that the Act [Blood Policy Act 1975] *was subverted is the fact that the "paid for" sector and the "voluntary" sector had a common enemy emerge in 1975 that was much more significant than any squabble over turf in the blood industry. This "enemy" was the HB Core Antibody Test. This test had the ability to detect the Core to the HB Antigen. It was now possible to determine not only if someone was actively infectious for the HB surface Antigen, but also if a donor had ever been infected with hepatitis B. This meant that the means existed to eliminate, consistent with FDA regulations, all donors who were not "normal and healthy" to a much greater degree than ever before."*

17. HBV Anti-core appears to have first been reported by Hollinger et al in a New England Journal of Medicine paper titled *"A Prospective Study indicating that Double-Antibody Radioimmunoassay reduces the incidence of Post-Transfusion Hepatitis B"*[15]. Assuming that Dr Allan correctly attributes the development of an Anti-Core test to 1975 then from that point, the means to exclude all donors with a history of HBV infection existed.

18. In our submission, UK and US regulation required that (at all material times) reasonable steps be taken to eliminate donors from donor pools with a history of HBV infection. What constituted a 'reasonable step' was a moving goalpost which shifted with advances in science and technology. In the 1960s, a reasonable step would have been questioning donors as to whether they had a history of jaundice. By the early 1970s, a reasonable step was to test all donations for Australia or Hepatitis B surface antigen. With the advent of an anti-core test in or around 1975, testing all donations for HBV anti-core antibody was the reasonable step which must be taken to maintain compliance with the (UK and US) regulations that donors with a history of hepatitis must be excluded.

What actually happened,

21. Resistance to the logic behind core-testing was so strong as to compel a minority group paper to say[16]:

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[14] MULL0000027

[15] BAYP0000022_061

[16] MULL0001241_028_0002 Minority Position Paper Advocating the Implementation of Anti-Core Testing for Source and Recovered Plasma; January 1983

"Some studies suggest that between 5% and 16% of plasma donors would be positive for core antibody. It is this fact which is central to the controversy regarding the use of the test as a screening tool for high risk plasma. Notwithstanding that concern, a minority membership of this Task Force is of the opinion that until such time as a more specific test for high risk plasma is available, the use of the anti-core test would significantly reduce the likelihood that plasma from members of groups at increased risk of infectious diseases would be used to manufacture coagulation products. It is our belief that this would ultimately be beneficial to hemophiliacs as well as to the manufacturers of coagulation factors."

22. Armour in the UK argued[17] that:

"The high incidence of Hepatitis B infection in each of these groups suggests that testing for laboratory markers of this virus might be of value in screening potential AIDS victims. Testing of AIDS patients for antibody to Hepatitis B core antigen (anti-HBc) shows that over 85% of them are positive for this marker. However, extrapolation of these findings to a general screening programme in order to identify potential AIDS victims or carriers may not be practical. Information developed by various organisations shows that approximately 15% of the population also tests positive for anti-HBc, indicating that this would not be a specific test for AIDS."

23. Anti-core testing was only implemented by one US pharmaceutical and even then, not until 1983. John Hink of Cutter gave a deposition on 11 November 1998[18] Where he set out that Cutter investigated the implications of implementing anti-core testing and found that they did not need to enlarge their laboratories, that testing was feasible and that they would lose around 15% of their donors through implementing the testing. Mr Hink added:

"As a consequence it was a natural kind of a decision to go ahead and try in our minds to possibly improve the product and prevent some of the transmission of this agent [AIDS] *that was seemingly happening with hemophiliacs."*

24. Cutter's 1983 decision to implement anti-core testing was not followed by any other manufacturer and came eight years after the development of an anti-core test. Their anti-core testing was promptly ceased once Cutter was satisfied that their heat-treatment technique was effective.

25. Throughout the 1970s and early 1980s, manufacturers had, instead of employing the best means to eliminate viral danger from their products, cultivated donor pools in some of the most (infectiously) dangerous areas of American society:

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[17] Letter dated 19th May 1983 from KW Fitch, Chairman and Managing Director Armour Pharmaceutical Company Limited to all Haemophilia Centre Directors ARMO0000250

[18] MULL0000025_002

a) A Cutter memo from June 1982[19] records the inspection of Arizona State Prison with a view to operating a plasmapheresis centre from the grounds; the author notes *"This is a great opportunity for us to produce some low cost plasma."*

b) A deposition was given on 4 August 1998[20] by an inmate of Wade Prison and Louisiana State Penitentiary who described the utter disregard for regulation which occurred in the prison plasma programs of which he participated; he notes that the programs were operated by inmates who would pre-fill screening questionnaires to ensure that no donation was excluded.

c) Plasmapheresis centres were established in areas known to be popular with urban gay men; their plasma was sought for the specific reason that gay men were commonly infected with HBV and their donations aided the manufacture of HBV immunoglobulin. Advertisements were placed in gay publications in an attempt to draw gay men into those plasma centres; this was widespread practice, not confined to a single manufacturer – we have seen adverts placed by Alpha[21], Hyland[22], and a myriad of other private plasma centres who supplied the manufacturers generally[23]

d) William Hartin, an Alpha employee, was deposed on 24 April 1989 and discussed desirable locations for plasma centres, he said:-

"When you're dealing with paid donors the likelihood of people from the lower socioeconomic bracket becoming donors is much greater than from the higher socioeconomic bracket. And so, yes, to locate our centers in areas where there is – the income is lower is important."[24]

26. These practices had long been known in the UK and ought reasonably to have been known to the UK Licensing Authority. We dealt with this point extensively in our closing submissions and refer back to, amongst other things, Professor Arie Zuckerman's 1975 World in Action documentary[25] prompted by Dr Craske's investigation of the Bournemouth hepatitis outbreak resulting from the use of Hemofil[26].

27. In any event, no complaint could be made of these 'high titre' plasma sources if the donations had been confined to the production of immunoglobulins which had been shown not to transmit disease. This was not the case however:-

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[19] MULL0000913_017
[20] MULL0000531
[21] CGRA0000204_018
[22] CGRA0000294_053
[23] A Relativity search for the term "advert" returns 60 documents with a CGRA reference, all of which are adverts in gay publications.
[24] MULL0000282_0184
[25] MDIA0000113 & MDIA0000114
[26] SUBS0000055_0113

a) In submissions made on behalf of Cutter, their attorney, Duncan Barr, said: *"…if there were donors that had been – 1983 – '82 – if there were donors that had been targeted specifically because they had high antibodies to hepatitis B, that that plasma not be utilized in concentrates. And the record of the Cutter memos is very clear that after July or August of 1982, it was not utilized."*

The obvious implication here is that prior to August 1982, it had been utilised in the manufacture of concentrates.

b) In a deposition on 10 July 1995[27], Armour's Mike Rodell said:

"First, the testing of units of plasma for antibody to HBc and the elimination of those units of plasma from a plasma pool would have two potentially detrimental effects: Units of plasma that are positive for anti-HBc, predominant number or the great majority of those units are also going to be positive for antibody to hepatitis B surface antigen, anti-HBs, which is a protective antibody.

It's protective for at least two products: It's protective and helpful in the production of coagulation factor concentrates because the presence of excess antibody to HBs enables complexation of a good amount of residual hepatitis B surface antigen that escapes the third-generation sensitivity testing capabilities. So that you, by removing units of plasma and depleting the plasma pool of circulating anti-HBs, you run the risk of preparing units of coagulation factor concentrate that are going to have a higher level, detectable level of antigen, which could – maybe even a non-detectable level of antigen, but which could increase its potential for transmitting hepatitis B.

Secondly, another product that comes out of the plasma pool is immune globulin. One of the characteristics of immune globulin is that it has a relatively high titer of antibody to hepatitis B surface antigen, anti-HBs, even if it's obtained from a normal donor pool population…"

Here then, Mr Rodell not only confirms that high titre plasma was used in the same pools used to manufacture immune globulin, but finds himself in the somewhat perverse position of arguing that it was desirable (in spite of regulation to the contrary) to include donors with an obvious history of hepatitis, in pools used for the manufacture of AHF concentrates.

c) For Baxter Highland, William Srigley was deposed on 1 May 1995[28] and the following exchange took place:

"Q. And you needed those donors [high titer anti-HBs] *in order to make immune globulins; isn't that true?*

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[27] MULL0000035
[28] MULL0000036

A. You needed those donors in order to make immune globulins with antibodies against hepatitis, yes.

Q. Okay. So if you made immune globulins and Factor VIII and Factor IX out of the same plasma pool, you would have to have some of those types of donors in the plasma pool; isn't that correct?

A. If I understand your question correctly, yes."

d) It is clear from this sample of the evidence contained in the MULL Disclosure that most, if not all of the manufacturers who produced both concentrates and immune globulins, manufactured the two products from the same pool, necessarily meaning that concentrates were routinely (if not universally) manufactured from the plasma of donors with a history of hepatitis.

e) For the avoidance of any and all doubt, our submission is not that pools were manufactured using surface antigen positive (and therefore HBV infective) plasma (although this seems a likely if not inevitable occurrence from the practices employed) but rather that the very fact that surface antibody positive plasma was used demonstrates the inclusion of plasma from donors with a history of hepatitis.

27. On 19 October 1999, Don Francis (formerly of the CDC) swore an affidavit[29] in which he explained some of the reasoning behind excluding any donors with a history of hepatitis, he said: *"Persons with a history of viral Hepatitis B were excluded not only because of the risk of transmitting Hepatitis B, but because such a history indicated a lifestyle or previous behavior of the prospective donor which carried the risk of transmitting other viruses in addition to Hepatitis."*

28. He goes on to say that the failure of the FDA to mandate the use of the HBc test by 1978 was evidence of a *"collaborative rather than regulatory"* relationship between the FDA and the blood industry *"which was allowed to develop over the years and contributed to the needless deaths of thousands of transfusion and blood product recipients from AIDS, Hepatitis and other viruses."*

29. Elsewhere within the same affidavit, Mr Francis recalls a meeting between the CDC and manufacturers on 4 January 1983 where the CDC presented statistics demonstrating that *"90% of definite AIDS cases were positive for anti-HBc* [...] *it was recommended that any donor anti-HBc positive be excluded from donating plasma."*

Contemporaneous evidence of the CDC's thoughts in this regard exists in a CDC memo of the 4 January meeting, dated 12 January 1983.[30]

30. Still, in light of information from the CDC that anti-core testing would eliminate 90% of donors with HIV, the manufacturers (with the exception of Cutter) resisted. A

[29] MULL0000554
[30] MULL0000913_005

position paper[31] (which we have taken to be drafted by a working group of the ABRA[32]) sets out the oppositions raised to anti-core testing. The paper lists, *inter-alia,* the following objections:-

i. A lack of specificity in the anti-core tests' ability to eliminate AIDS donors;

ii. A significant number of otherwise healthy donors would be lost which could substantially affect the availability of blood products for patients;

iii. That plasma pools may be more dangerous for the lack of HBV antibody; and

iv. The substantial cost of implementing testing outweighs any benefit that might be derived.

31. On any objective reading, the position paper sets up nothing more than a series of strawmen. The fundamental point is that those involved in plasma and blood collection ought to have been testing for HBV anti-core (and were, in our submission, obliged by regulation to do so) since the mid to late 1970s, they should not have still been looking to avoid using the test some eight or nine years later.

32. Moreover, the FDA could not reasonably or realistically have failed to have heard the CDC's calls for anti-core testing to be implemented. Whether they ignored the calls or whether they hoped rapid development of viral inactivation techniques would spare blushes from their abject failure to enforce regulation is unknown. What is clear however is that the FDA never mandated anti-core testing.

33. In our submission, it is a stunning failure of regulation that a regulator persistently and comprehensively failed to enforce regulations (re the elimination of donors with a history of hepatitis) even in the face of expert epidemiological advice from (amongst others) the CDC and Dr Garrot Allen. This failure betrays a lack of understanding as to the purpose of the regulation itself; as Don Francis set out, the regulation was intended to guard against the risk of the unknown as well as the known.

What should have happened?

34. It will be clear from our submission thus far that we consider that the FDA should have mandated and the manufacturers should have employed, anti-HBc testing from (absolutely no later than) 1978. Had this happened then it seems clear that the scale of HIV infection from American made concentrates would have been dramatically reduced.

35. We have addressed in previous submissions, the various failures which we say contributed to the scale of infection of people with bleeding disorders from blood products; these include the non-existent attempts to virally inactivate products before

[31] MULL0001245_035
[32] American Blood Resources Association

they were brought to market, the ever-increasing sizes of plasma pools in pursuit of greater profits and the pursuit of donors from the most (virally) dangerous parts of society. Added to those failures now is the laissez-faire regulatory approach of the FDA and, in turn, the UK Licensing Authority.

36. The question that stands to be answered is what the UK authorities could have done differently to better protect (as is their duty) UK haemophiliacs from infected blood products. Whilst we have already set out elsewhere that UK authorities should never have licensed American concentrates in their (then) current state, there is action that could have been taken which would have at least reduced the scale of infection in the UK. The example for such action is set by Germany.

37. Eugine Lindell was involved in regulatory affairs at Plasma Alliance, a sister company to Armour responsible for plasma collection; a summary of his deposition is included within the MULL Disclosure[33]. He recalls that Plasma Alliance did not just supply Armour with source plasma but also Alpha, Hyland, Merieux, Behringwerke and Abbott. Mr Lindell is noted as giving evidence that from July 1985, ALT testing was performed on all plasma destined for Germany as German regulators had demanded the test as a surrogate for NANB hepatitis. He recalls that he would receive instructions from Armour as to how much plasma needed to be tested each month and that the tests were only performed on plasma destined for Germany.

38. What effect this testing had on the levels of HCV infection in German haemophiliacs after 1985 is unknown to us, but the important point is that this episode clearly demonstrates that when a regulator imposed a condition, the manufacturers didn't merely cease supply, they adapted their practices to comply.

39. We noted in our closing submission[34], that the first two product licences for FVIII concentrates were granted in the spring of 1973; both licences were valid for a period of five years. Whilst it is abundantly clear from the evidence (or lack thereof) that the Committee on the Review of Medicines ("CRM") were 'asleep at the wheel' in relation to the ongoing monitoring of the safety of blood products, the CSM had opportunity from 1978 onwards to insist upon anti-core testing as and when licences came for renewal.

40. In our submission, their failure to do so was not only a reckless dereliction of duty, but it is also evidence of the over-reliance placed upon the regulation of the FDA, which, as we have set out, barely constituted regulation.

41. Moreover, and returning to the CSM report we referred to at the outset of this submission[35], it appears that the Licensing Authority, through its inaction, allowed concentrates to be sold which, by 1978, had inaccurate warning labels. Page three of the report sets out the warnings which must be affixed to the container and leaflet of Abbott's FVIII product:

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[33] MULL0000337
[34] SUBS0000055_0022
[35] MHRA0000091_005

"This product is prepared from units of human plasma which have been tested and found nonreactive for Hepatitis Associated Antigen. However, it is recognised that presently available methods are not sensitive enough to detect all units of potentially infectious plasma and the risk of transmitting hepatitis is still present."

42. The warning suggests that all possible that could be done, has been done to render the product free of hepatitis. The assumed continued presence of hepatitis is blamed on the lack of sensitivity in existing tests. With the development of anti-core testing, this warning became untrue; the means did exist to detect any donation from a donor with a history of Hepatitis B, the means were simply not employed.

43. Abbot were granted a license for a product bearing the cited warning in or around August 1974; they remained entitled to sell product bearing this warning until in or around August 1979, long after the establishment of anti-core testing. We have found no record of the Licensing Authority intervening to ensure that the warning label was updated; we know that the Licensing Authority never insisted on anti-core testing.

44. Had the Licensing Authority insisted upon anti-core testing (either through in-period licence review or through licence renewal), the German example suggests that the manufacturers would have acceded and performed the tests rather than lose their interest in the UK market.

45. Had this happened, the scale of infection with HIV in the UK would have been dramatically reduced as would the scale of the enormous attendant suffering of those infected and affected.

Conclusions

46. The Mull Disclosure goes some way to confirming our clients' suspicions about the worst excesses of the US' fractionators practices; the disclosure demonstrates the complete regulatory failure of the FDA and by extension, the UK Licensing Authority.

47. It is of particular note that disinterested parties such as the CDC – those with no financial interest, regulatory interest or medical dependency upon factor concentrates, are the first to recognise the danger posed by the novel virus that became known as HIV.

48. Dr Theodore Keorner says that there was a medical and scientific consensus by 27 July 1982 that there was an association of risk between the use of blood products and contracting AIDS[36]. Dr Bruce Evatt of the CDC gave evidence that by October 1982, it was the CDC's position that haemophilia patients should be warned of the risk of AIDS from concentrates; he went on to say:

[36] MULL0007726_0002

"In the early – in that mid part of 1982, a contagious agent that is capable of being spread person to person, that's – the group that it's attacked are associated with blood-borne diseases and then the sudden appearance in the haemophilia population, and its only risk factor it has in combination with the other groups is the fact it receives blood products, it – the – it doesn't take a rocket scientist to begin to make those – those associations that this is a blood borne disease."[37]

49. Yet all the while, the manufacturers obfuscated, refusing to accept that AIDS was caused by a blood borne virus, suggesting other causes for the emergence of AIDS in haemophiliacs such as 'protein overload' and refusing to take any step which they considered would be overly damaging to their profits or plasma sources.

50. The delays caused by the obstinance of the manufacturers and the lack of any meaningful regulation, cost any chance to mitigate the scale of the epidemic amongst haemophiliacs.

51. Had anti-core testing been implemented in the mid to late 1970s per regulation, the scale of HIV infection amongst haemophiliacs would have been dramatically reduced. In our submission, it was only not introduced, because the US plasma industry had cultivated donor panels comprised of individuals who they knew to have a history of hepatitis or who were amongst the demographics at the highest risk of hepatitis infection. The test risked reducing their panel sizes and therefore by extension, their profits.

52. The FDA acquiesced to the manufacturers' breach of regulation and the UK Licensing Authority blindly trusted in the FDA's regulation. These failures directly led to many UK haemophiliacs becoming infected with HIV.

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[37] MULL0000032