Witness Name: Professor James Max Neuberger
Statement No.: WITN7306001
Exhibits: WITN7306002-WITN7306007
Dated: 29/09/2022

INFECTED BLOOD INQUIRY

FIRST WRITTEN STATEMENT OF PROFESSOR JAMES MAX NEUBERGER

Contents

Section 1: Introduction and opening comments

I, Professor James Max Neuberger, will say as follows: -

Introduction

1.1. My name is Professor James Max Neuberger, and my date of birth is GRO-C GRO-C 1949. My home address is GRO-C GRO-C Gloucestershire, GRO-C

1.2. I am providing this written statement in response to the Inquiry's Rule 9 request dated 2 September 2022.

Opening comments

1.3. This statement was written by myself, and the views expressed are my own. It should be noted that, in preparing this statement, I asked the lawyers at the Government Legal Department to review the statement and to advise me of any areas that are unclear, require clarification, or more detail.

Section 2: Professional history

Qualifications

2.1. My professional qualifications are as follows:

a. MA (Oxon), Physiology - 1974;

b. BM, BCh (Oxon), Medicine – 1974;

c. DM (Oxon), Medicine – 1982.

Employment history

2.2. After qualifying in medicine, my pre-registration posts were in London (1974 - 1975); this was followed by the Senior House Officer Rotation in Medicine in Leeds (1975 - 1977) and a medical registrar post at St James's University Hospital, Leeds (1977 - 1979).

2.3. I was then appointed Research Fellow at the Liver Unit, King's College Hospital (later the Institute for Liver Studies). I remained there until 1987, becoming a lecturer and later Senior Lecturer.

2.4. In 1987, I was appointed as Consultant Physician to the Queen Elizabeth Hospital, Birmingham which is now part of the University Hospitals Birmingham NHS Foundation Trust ("UHB NHSFT"). I worked primarily on the Liver Unit and my major interests were in liver disease, organ donation and transplantation. I have retained my contract with UHB NHSFT, where I now have an honorary Consultant contract.

2.5. I also worked as Associate Medical Director for Organ Donation and Transplantation at NHS Blood and Transplant (2009 - 2016).

2.6. I am registered with the General Medical Council as a specialist in General (Internal) Medicine and Gastroenterology.

2.7. I am a Fellow of the Royal College of Physicians of London.

2.8. I am currently the Chair of The Advisory Committee on the Safety of Blood, Tissues and Organs ("SaBTO") which I discuss further in section 2 below.

Memberships

1.1. Between 2016 and 2019, I was an Associate Medical Director for Organ Donation and Transplantation at NHS Blood and Transplant. I am a member of national and international liver, gastroenterology and transplant associations (including the British Society of Gastroenterology and British Association for the Study of Liver Disease).

Litigation history

2.9. I have not provided evidence or been involved in any other inquiry, investigation or litigation relevant to the Inquiry's Terms of Reference.

Section 2: Chair of the SaBTO

Role and responsibilities

2.1. SaBTO is an independent advisory committee that advises UK ministers and health departments on the '*safety of blood, cells, tissues and organs from transfusion/transplantation*' [JPAC0000230].

2.2. As Chair of SaBTO, I ensure that the advice and recommendations from SaBTO are relevant, timely, and appropriate. I also ensure, when accepted, that the recommendations are implemented and the relevant professionals,

patients and lay public are informed, not only as to the recommendations, but the evidence underlying the recommendations.

2.3. In helping to achieve these goals, I ensure that SaBTO is diverse in its membership and views and that it is aware of, and reviews, current relevant research, and has robust timely advice from any appropriate expert and lay members.

2.4. Additionally, I ensure that SaBTO works closely with the UK blood services and appropriate national and international bodies, and that it receives timely feedback regarding any adverse events from blood and its components. I also ensure SaBTO works in a similar manner in relation to other substances of human origin.

2.5. I ensure SaBTO reviews current guidance and is aware of any potential risks from new and emerging infections and that it considers mitigating any current and/or new risks. I also safeguard members by ensuring those attending feel empowered to speak freely and that SaBTO takes into account the diversity of stakeholders.

2.6. SaBTO is also aware that recommendations must take into account efficiency and cost effectiveness of implementing its recommendations.

Section 3: An explanation of haemovigilance

3.1. The Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee ("JPAC") describes haemovigilance as the ''*systematic surveillance of adverse reactions and adverse events related to transfusion*' *with the aim of improving transfusion safety*' [WITN7306002].

3.2. I would define haemovigilance as a set of surveillance procedures covering the entire blood transfusion process, including the assessment and selection of potential blood donors, the method of donating, the processing of blood and its components and its provision, transfusion, and follow-up with patients.

3.3. In regard to the blood donations and the processing and transfusion of the blood itself, the procedures include testing and monitoring donations, reporting any concerns, investigating those concerns, and analysing adverse events related

to the surveillance procedures referenced above, while informing the health care professionals, recipients of blood, and the public of any adverse events and taking steps to prevent the occurrence or recurrence of such adverse events.

Haemovigilance v pharmacovigilance

3.4. In my view, there is a clear parallel between haemovigilance and pharmacovigilance because both are a set of procedures based on legislation which, for blood, include the Blood and Safety Quality Regulations, with oversight from regulators such as the Medicines and Healthcare products Regulatory Agency ("MHRA") and the professional bodies such as the British Society of Haematology, with the goals of ensuring patient safety.

3.5. With that said, there are also some important differences between the two. For example, the starting point for pharmacological therapy is usually chemicals that are manufactured and then are purity and quality tested. The starting point in haemovigilance is blood from humans, where we know there are risks that the donations will include agents that might potentially transmit disease to recipients. Some of these risks can be identified, but there remains some concern about the potential for new and emerging infections to the donor pool. Such risks are mitigated primarily by a three-fold strategy: screening the donor, testing the donation prior to use of the donation and, in some cases, treating the donation such as by removing the white blood cells (leucodepletion). We know that, while the great majority of potential donors answer the screening questions honestly and accurately, a very small proportion will, for a variety of reasons, give inaccurate answers. Therefore, it is important to test the donation after screening by using a combination of blood tests for antigens and antibodies (antigens are part of the infectious agent and antibodies reflect the body's response to the infection) and other tests (such as nucleic acid technology ("NAT") testing part of the microbiological DNA or RNA).

3.6. We know that the tests will not always detect potentially infected blood because of the level of sensitivity of the assay. An assay tests for antibodies, antigens, DNA or RNA parts of the genes. The consequence of the limitation of the assays is known as the residual risk; this occurs mainly during the so-called

window period when the potential donor has become infected but remains asymptomatic. Although the donation may contain enough material (such as viral DNA or RNA) to enable disease transmission, it is at a concentration below the level of detection of the assay.

3.7. The level of residual risk and the risk tolerability is published and I have exhibited a summary on the risk tolerability working group where it outlines that '*SaBTO agreed to establish the working group in January 2020 to consider communication and public perception of risk, residual risk estimates for HBV, HCV and HIV and how these were calculated and published, and the safety framework used by SaBTO and UK blood services*' [WITN7306003] (4).

3.8. SaBTO has published guidelines to proclaim that *'[i]t is an accepted principle that a patient should give valid consent before receiving medical treatment, and this includes when they receive a transfusion of blood and blood components (such as fresh frozen plasma and platelets)*' [WITN7001044] (4). In 2021, I co-authored an article with Professor Michael F Murphy, Ms Andrea Harris entitled, '*Consent for blood transfusion: summary of recommendations from the Advisory Committee for the Safety of Blood, Tissues and Organs (SaBTO)*' which also acts as a guideline for supporting the advice from the General Medical Council ("GMC") and other professional bodies regarding consent [WITN7001045].

3.9. A further difference between pharmacovigilance and haemovigilance is the reporting of adverse events. There are significant differences between the processes for reporting of adverse events from medicines and from blood and its components, as discussed in paragraph 3.20 below.

3.10. The risks from medicines are largely a consequence of the inherent properties of the pharmacological agent (and the patient's response) whereas, the infectious risks from blood and its components relate to inherent risks because the starting point is a substance of human origin ("SoHO"). SoHO are likely to carry infectious agents, not all of which can be identified using current technologies, and so we can mitigate risk but not abolish it.

3.11. A further significant difference is that for medicines, the adverse consequences of any medication do not greatly vary over time (even if some adverse effects

may not be apparent for some time), whereas for blood, the risks are continuously changing. This change in risk occurs for a variety of reasons such as changes in behaviour (such as travel), changes in climate (allowing some infections not endemic in UK becoming endemic) and new and emerging infections (such as SARS-CoV-2). Thus, haemovigilance requires an on-going assessment of any new risks as well as changes in established risks.

Legislation, regulatory framework and guidelines

3.12. In relation to the relevant legislative and regulatory framework and guidelines, two EU Directives (2002/98/EC and 2004/33/EC) were transposed into UK law through the Blood Safety and Quality Regulations 2005 ("BSQR 2005") (Statutory Instruments 2005/50, 2005/1098 and 2006/2013). These regulations came into force on 8 February 2005, implemented on 8 November 2005 and an amendment to the regulations came into force on 8 April 2005. These regulations set standards for quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components, aspects of the regulations apply to blood establishments (establishments which collect, process and test human blood and blood components) and Hospital Blood Banks.

3.13. The Blood Safety and Quality (amendment) Regulations 2006/2013 further amend the BSQR 2005 (SI 2005/50) to make changes to the provisions governing the operation of blood establishments and hospital blood banks (hospital units which store, distribute, and perform compatibility tests on blood and blood components for use in hospitals). These changes relate specifically to traceability requirements and notification of adverse reactions and events and introduce community standards and specifications relating to a quality system for blood establishments. These have been superseded by The Blood Safety and Quality (Amendment) (EU Exit) Regulations 2019. This means that blood safety and quality is now devolved to the four UK nations rather than UK wide.

3.14. '*The Blood Safety and Quality Provisional Common Framework*' is a non-mandatory framework that '*relates to blood safety policy*) [WITN7306004]. *It encompasses elements of the Blood Directive (Directive 2002/98/EC) and the*

implementing acts which relate to the safety and quality of blood and blood components. This Framework sets out arrangements for co-operation between officials in the UK Government (UKG), Scottish Government (SG), Welsh Government (WG), and Northern Ireland Department of Health)' and tries to ensure the UK's policies remain aligned (although each of the four UK nations can now determine policy on blood safety independently) [WITN7306004] (5). Northern Ireland will remain linked to the EU Directives for as long as the Northern Ireland Protocol stands.

3.15. The MHRA is responsible for the controls and authorisations that apply to blood establishments including hospital blood banks and sites that collect, test and supply human blood or blood components intended for transfusion. Within this framework, SaBTO is an Expert Committee whose role is to provide high quality advice and recommendations on the most appropriate ways to ensure the safety of blood, cells, tissues and organs for transfusion or transplantation. The Committee is sponsored by the Department of Health and Social Care but provides its recommendations directly to Ministers and Health Departments.

3.16. The Committee works closely with other interested parties including JPAC. Its workings, reports and advice are available on its website: https://www.gov.uk/government/groups/advisory-committee-on-the-safety-of-blood-tissues-and-organs.

3.17. The UK Forum (Medical Directors and Chief Executives of the four UK Blood Services) agreed the terms of reference and lines of accountability for JPAC and its Standing Advisory Committees. The remit of JPAC is to prepare detailed service guidelines for the United Kingdom Blood Transfusion Services ("UK BTS") and to be an Advisory Committee to the UK BTS, normally by reporting to the Medical Directors of the individual Services who are themselves individually accountable to the Chief Executives of the Services. Decisions on policy and implementation would be vested in the individual Chief Executives and their service boards and, where appropriate, their respective health departments. SaBTO, unlike JPAC, reports directly to Ministers.

3.18. The World Health Organisation ("WHO") published a report in 2016 entitled, '*A guide to establishing a national haemovigilance system*' which contained a

number of recommendations the UK should fully implement. Within that report, they also identified the following characteristics of a successful haemovigilance system: -

'From an organization [sic] perspective:

- *an efficient, adequately resourced and sustainable national system, involving all relevant stakeholders;*
- *non-punitive environment and based on a learning culture;*
- *confidentiality (the source of submitted data being protected);*
- *an integral part of the quality system of health care establishments, encompassing the entire transfusion chain;*
- *traceability from the blood donor and blood unit to recipient and vice versa, allowing adverse events to be tracked and investigated, and corrective action to be implemented;*
- *standards and definitions in line with international recommendations;*
- *education and training;*
- *feedback reporting to the stakeholder community.*

From an operational perspective:

- *simple to use;*
- *clear and standardized [sic] reporting forms;*
- *written standard procedures to initiate, investigate and coordinate reports;*
- *timely reporting of trends with expert analysis and recommendations for improvement to minimize [sic] rates of occurrence or recurrence;*
- *mechanisms to monitor the implementation of corrective and preventive actions in a timely manner and to demonstrate improved safety and clinical outcomes'* [RLIT0000992] (10).

3.19. I believe that all the measures referred to in paragraph 3.18 above were in place in 2016. However, I do note that the systems which are currently in place are being constantly reviewed and improved. While I believe that the systems are robust, there is no room for complacency as it is inevitable that there is both under-recognition and under-reporting of adverse events, as discussed further in paragraph 3.20 below.

3.20. In my experience, I believe that in the UK, the implementation and best practice is adequate and on a par with other major jurisdictions, but there is a need for improvement (which is further discussed below).

3.21. There are several barriers to improvement which can be overcome. Some of these barriers stem from the fact that, while immediately apparent adverse events (such as transfusion-related lung injury or fluid overload) tend to be easily recognised, treated, reported and investigated; adverse events from disease transmission are less well recognised and reported. Such adverse events may occur weeks, months, years or even decades after the transfusion, and neither the health care practitioner nor patient may relate the infection to the transfusion. In addition, some infections are not recognised or diagnosed and some transfusion transmitted infections are attributed to other causes (such as travel, infection from food and so forth).

3.22. While my personal experience suggests that those involved in transfusion are alert to transfusion-related adverse events and the actions needed following a suspected adverse event, many other health care practitioners are not so attuned and do not appreciate that they should report possible transfusion-related illnesses or indeed know to report such adverse events.

3.23. Ideally, the reporting mechanisms would be included in the electronic patient record and the clinician or scientist would be able to access the reporting programmes directly and all relevant data downloaded automatically.

3.24. Multiple reporting programmes, in my experience, not only deter reporting adverse events but have the potential to lead to errors such as data entry errors. In my view, this situation can be best resolved by allowing reporting of adverse events directly from the electronic patient report, thus allowing all relevant bodies to be informed from a single report.

3.25. As patients may receive a transfusion in one of the four UK nations and have a transfusion transmitted infection ("TTI") diagnosed in another, I suggest that all four UK nations should maintain one unified system. I also suggest that consideration is given to reviewing the haemovigilance pathway as presently, many groups (and some statutory) are involved and there appears to be some duplication of roles.

3.26. The safety of blood and blood components (such as red cells and platelets) comes under different regulations from blood products; the safety of blood, tissues, organs and cells is also subject to different laws and regulations. A unified regulatory environment would allow simplification by defining responsibilities and reducing any confusion about where accountability lies.

3.27. There is an additional issue with regards to remuneration for committee members. Many of the committees and groups involved in maintaining the safety of blood are, like SaBTO, composed of leading experts who enthusiastically take on the work of these committees; without them or their employers getting any remuneration for their time or allowing a reduction in other responsibilities (so work done for SaBTO is usually an additional role). I note that several experts have had no option but to stop supporting SaBTO because their employers (e.g. NHS, academic or other) have advised them that they should not undertake additional and unpaid work, even though they recognise the national importance of the work. I must stress that the number of experts who have reported that they are under pressure is small. Contributions to national activities (such as SaBTO) are often recognised in schemes such as the National Clinical Impact Award ("NCIA") in England and Wales but these only apply to doctors.

3.28. Furthermore, national committees need adequate administrative support. SaBTO has been fortunate that the DHSC has provided high quality support.

Electronic identification system

3.29. The UK report on haemovigilance suggests that most errors associated with blood transfusion are related to non-infectious complications, especially procedural errors and errors related to transfusion decisions. Reports usually come from blood establishments, scientists and clinicians and are analysed by

a group of experts. These errors continue to be the most common causes of transfusion-related deaths in the UK. For example, delays in transfusion and pulmonary complications (mainly transfusion associated circulatory overload where the patients suffer because of the volume of fluid transfused places an excessive load on the heart) were the main causes of reported transfusion-related deaths in 2021 contributing to 77.1% (from the Annual Serious Hazards of Transfusion ("SHOT") 2021 report [SHOT0000032]. With respect to transfusion-transmitted infections, I am uncertain that an electronic identification system would significantly reduce errors.

3.30. I believe there is potential benefit in developing a system that links transfusion with potential infections and other adverse events associated with transfusion, as indicated in paragraph 3.44 below. However, I also believe that any such system should be integrated into current systems as clinicians and scientists are already faced with too many stand-alone systems that do not talk to each other and require the same data to be entered multiple times.

SHOT, the MHRA and SABRE

3.31. I believe there are links between SHOT, the MHRA and the Serious Adverse Blood Reactions and Events scheme ('SABRE') haemovigilance systems and that they do complement each other. SHOT published a guide entitled, a *'User guide for mandatory and professionally mandated haemovigilance reporting in the UK*' providing '*the legal framework for reporting all haemovigilance incidents in the UK and guides the reporter through the keys [sic] steps for reporting SABRE and the SHOT online reporting systems*' and which goes on to say:

'The MHRA and SHOT … have collaborated to improve haemovigilance reporting by producing an integrated single SHOT and MHRA incident reporting process by linking the SABRE and SHOT online reporting systems.

The main aims of this system are:

a. *A reporting system that avoids duplication of reporting, by the reporter, whilst maintaining the reporter's regulatory and professionally mandated obligations to report, as defined under the Blood Safety and Quality*

Regulations 2005 (as amended) (BSQR), to the competent authority and to SHOT.

b. *Maintain MHRA as the UK's competent authority (CA) for Serious adverse reaction (SAR) and Serious adverse event (SAE) reporting.*

c. *Provide a system that maximises the clinical scrutiny of reports, by SHOT, to ensure that they are correctly classified and imputability ratings identified as directed by BSQR.*

d. *Ensure that the data collected accurately reflect the number, type and imputability score of all UK SAR and SAE reports annually.*

e. *That both MHRA and SHOT have the appropriate access to the reporter for clarification of SAR and SAE data.*

f. *Maintain the legal requirement that ALL [sic] SARs and SAEs must be reported to the CA as soon as known'* [NHBT0203834] (4).

3.32. SaBTO is involved in the reporting system to a limited extent and does not take part in the working of SHOT and its committees. We are satisfied that the various stakeholders, such as the blood establishments, health care professionals, blood services and regulators, do work effectively together. However, '*[t]he main differences in reporting criteria are that the MHRA does not accept reports related to clinical errors, which account for a large proportion of SHOT-reportable incidents. SHOT only accept reports that involve a named patient for whom a blood product or component has been prescribed and collected. The MHRA accepts reports from UK Blood Services, and laboratory errors which don't involve a named patient'* [SHOT0000032] (8). Thus, there appears to be some complexity in the reporting system that might detract from reporting. A unified approach might help. At present, SaBTO receives the annual report from SHOT, then it is discussed at the meeting of SaBTO, and this review is included in the annual work plan of SaBTO. SaBTO is also made aware of any unexpected adverse event that requires review.

3.33. Review of the SHOT report also allows one route for the Committee to evaluate the consequences of its recommendations. One example of this is the impact of implementing SaBTO's recommendation for the introduction of testing for Hepatitis E virus ("HEV") which has led to the discard of a number of donations,

as these were found to contain the HEV even though the donor was asymptomatic. However, a few cases of transfusion-related HEV infections still occurred, so we recommended changes in the testing of donations.

Yellow card system

3.34. I understand that the role of the Yellow Card system is to report suspected side effects to medicines, vaccines, e-cigarettes, medical device incidents, defective or falsified (fake) products to the MHRA to ensure safe and effective use.

3.35. At present and as far as I am aware, the Yellow Card system does not cover transfusion-related infections although, there is a facility to include an adverse event from something not on their list, so this could include adverse events from transfusion, but I suspect this is rarely used for this purpose.

Record keeping

3.36. I note that the Inquiry has received some evidence to suggest that the standards of record keeping following treatment by blood or blood products was variable and that there is evidence to suggest that either no record was made in medical records setting out what treatment was given, or that inadequate records were kept.

3.37. SaBTO has no role in monitoring these standards and therefore I am unable to comment in my capacity as Chair. However, we fully recognise the importance of accurate and complete records, and this is emphasised in the SaBTO's guidelines on consent, as discussed in paragraph 3.8 above, which appears on our website along with the papers and minutes, reports and guidance [WITN7001044].

3.38. I understand that the GMC, JPAC and the NHS have individually published guidance on record keeping.

3.39. The GMC's guidance, entitled '*Good Medical Practice'* recommends medical practitioners to:

'Record your work clearly, accurately and legibly

19 Documents you make (including clinical records) to formally record your work must be clear, accurate and legible. You should make records at

the same time as the events you are recording or as soon as possible afterwards.

20 You must keep records that contain personal information about patients, colleagues or others securely, and in line with any data protection law requirements.

21 Clinical records should include:

a relevant clinical findings

b the decisions made and actions agreed, and who is making the decisions and agreeing the actions

c the information given to patients

d any drugs prescribed or other investigation or treatment

e who is making the record and when' [RLIT0001283] (11).

3.40. JPAC issued guidance on the '*documentation required at each stage of the transfusion process*' and that this should '*be kept to an essential minimum, and whether hard copy or electronic, be 'user-friendly' to encourage compliance by busy clinical teams… Documentation in the clinical record should include:*

Pre-transfusion:

- *The reason for transfusion, including relevant clinical and laboratory data.*
- *The risks, benefits and alternatives to transfusion that have been discussed with the patient and documentation of consent (see below).*
- *The components to be transfused and their dose/volume and rate.*
- *Any special requirements, such as irradiated components.*

During transfusion:

- *Details of staff members starting the transfusion.*
- *Date and time transfusion started and completed.*
- *Donation number of the blood component.*

- *Record of observations made before, during and after transfusion.*

Post-transfusion:

- *Management and outcome of any transfusion reactions or other adverse events.*
- *Where the transfusion achieved the desired outcome (e.g. improvement in symptoms, Hb increment)'* [RLIT0001287].

3.41. Finally, the NHS' *'Record Management Code of Practice 2021'* is a '*guide… in relation to the practice of managing records*' and '*provides a framework for consistent and effective records management based on established standards. It includes guidelines on topics such as legal, professional, organisational and individual responsibilities when managing records. It also advises on how to design and implement a records management system including advice on organising, storing, retaining and deleting records. It applies to all records regardless of the media they are held on. Wherever possible organisations should be moving away from paper towards digital records… All organisations and managers need to enable staff to conform to the standards in this Code. This includes identifying organisational changes or other requirements needed to meet the standards, for example, the people, money and correct tools required'* [RLIT0001284] (3).

Transfusion database

3.42. At present and as far as I am aware, there is no national transfusion database which records all instances where blood or blood products are transfused to a patient. There would be some potential advantages of such a system in determining traceability and patient outcome. However, to be of value from the point of view of haemovigilance, this database would need to interact with clinical information and results of blood tests.

3.43. Of the recorded adverse reactions from transfusion of blood and its components, TTIs are a very small component. Last year, SHOT reported no new TTIs. As indicated above, this is not a cause for congratulation or complacency, as we know that there is a residual risk of TTI from blood and its components and we are certain that TTIs are not always recognised or

reported. Furthermore, the onset of an infection in a transfused patient does not necessarily mean that the infection was acquired as a consequence of that transfusion. Thus, I am uncertain how effective such a database would be in the recognition of possible TTIs. These administrative issues can be overcome but will undoubtedly add complexity.

3.44. Overall, I believe that for any such database to be comprehensive and workable, input to the database would need to be through existing platforms. I also believe it would be important for primary care health care professionals including the bio-scientists, as well as secondary care professionals, to be able to access the database; previous experience has shown that while this can be done, there are many regulatory and technical issues to be addressed. As with all databases, there would need to be agreed data and definitions, appropriate oversight, analysis and assured, identified funding and, of course, proper governance. All these and other issues are not insuperable, and a full cost-benefit analysis would need to be undertaken.

Section 4: The future of the lookback exercise

4.1. The acceptance of the recommendations about occult Hepatitis B virus infection, ("OBI") led to discussions by the OBI Working Group and by SaBTO as to how a lookback exercise should be done. Please see the minutes of a SaBTO meeting held on 28 October 2021 [NHBT0203835].

4.2. In an article entitled, '*Update of the statements on biology and clinical impact of occult hepatitis B virus infection*' by Giovanni Raimondo, Stephen Locarnini, Teresa Pollicino, Massimo Levrero, Fabien Zoulim, Anna S. Lok, OBI '*… is defined as the presence of replication-competent HBV DNA… in the liver and/or HBV DNA in the blood of people who test negative for hepatitis B surface antigen (HBsAg) by currently available assays'* [WITN7306005].

4.3. It was agreed that for large scale exercises, it would be useful to have some clear guidelines as to the conduct of the exercise (see paragraph 4.5 below). OBI occurs when the donation carries enough Hepatitis B virus DNA to infect the recipient but the level is below the limit of detection by the approved assay.

4.4. I wrote a letter dated 18 November 2021 informing Sir Brian of the latest developments of SaBTO and the intention to:

> *'… set up a working group to agree principles for lookback investigations in such cases where newer technologies and other scientific and clinical advances have taken place. The working group will advise on the conduct of lookback studies in the UK, where there is concern that treatments may have inadvertently transmitted disease to patients. When agreed by the committee, the recommendations will be made to Ministers'* [JPAC0000230].

4.5. The proposal for guidelines for lookback studies arose from the recommendations of SaBTO consequent to our recommendations that there should be additional testing for donations to reduce the risk of transmission of Hepatitis B virus from those few donors with OBI. Discussion between SaBTO and the four national Blood Services indicated uncertainty about several aspects of lookback, including how far back the lookback should include, how to contact recipients, and whether to contact the partners of recipients who have died. Initially, discussions suggested it might be possible to draw up guidelines for consultation based on meetings between myself and the medical directors of the blood services, but it became clear that there would need to be wider input and so, I asked Professor Susan Brailsford, Consultant in Epidemiology and Health Protection, NHS Blood and Transplant, to form a fixed-term working party to provide recommendations to SaBTO. This explains, in part, the delay between the decision to form a group to develop guidelines for consultation and the setting up of the working party. I should note that the lookback exercise for those who might have been affected by the risk of OBI donations is being currently carried out by the UK blood services. Areas of uncertainty arising from this exercise will be fed back to the working party.

4.6. I have included the minutes of SaBTO meetings from February 2022 and May 2022 – both of which discuss the lookback exercise: [WITN7306006; WITN7306007]. The February 2022 minutes includes '*paper 4*' – the SaBTO Code of Practice referred to therein. Please note that the May minutes are due to be ratified at our forthcoming meeting on 27 September.

4.7. In regard to the draft Terms of Reference for the Working Group (to be ratified at our SaBTO meeting to be held on 27th September, 2022), the group will review:

a. why a national lookback exercise may be required and who has responsibility for initiating such a lookback;

b. determine the general principles of the lookback and how these should be approached by the UK blood services;

c. identify the roles and responsibilities of all interested parties including national Departments of Health and other national bodies, regulators, Blood Services, hospitals, primary care providers and patient organisations and associated resources;

d. consider the ethical issues of notifying both donors and recipients identified in the lookback; and

e. consider closure of lookbacks and associated communications and outputs and produce a report to SaBTO.

The Working Group will meet ad hoc, either in person or by teleconference, during the review. Any administrative issues will pass on to the SaBTO Secretariat who will also maintain a document library.

4.8. Regarding the proposed membership, we would need: -

a. representation from the devolved administrations;

b. an ethicist;

c. a hospital clinician with expertise in transfusion;

d. representatives from the four UK blood services clinical/microbiology screening;

e. a public health specialist with expertise in incident management/patient notification;

f. a virologist with expertise in blood borne infections;

g. representatives including blood donor representative(s), patient representative(s) including multi-transfused individuals;

h. JPAC director;

i. SaBTO nurse member;

j. an epidemiologist;

k. any additional expertise including legal and regulatory expertise; and

l. the Chair of SaBTO will attend as an observer.

4.9. As there will be a need for wide consultation before SaBTO can make any recommendations, it is anticipated that the Working Group would report within 12 months. The Working Group will first meet shortly after the Terms of Reference have been agreed and discuss to: -

a. reach a conclusion on the circumstances in which different types of lookback would be appropriate;

b. reach a conclusion on the approaches necessary to identify patients at risk;

c. reach a conclusion on how long blood samples from both donors and patients should be retained;

d. reach a conclusion on how to obtain informed consent from both donors and recipients of donations;

e. discuss how lookback exercises may be undertaken in the future; and

f. discuss electronic systems that may assist in future lookback exercises and in particular, what, if any, consideration is being given to a database recording all instances where blood or blood products are transfused to a patient.

4.10. The Blood Services from all four UK nations will be involved with the making of the recommendations for a large-scale look back exercise and it is hoped that all four nations will agree to a common approach, although that decision will be with the relevant Minister.

4.11. I am not currently aware of any detailed guidance from other international bodies in regard to the development of the lookback investigation rules.

Statement of Truth

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

Signed…… GRO-C ……

Dated……29th September 2022……

Section 5: Table of exhibits

Date	Description	Exhibit number
18/11/2021	Letter from Professor James Neuberger to Sir Brian Langstaff, Infected Blood Inquiry	JPAC0000230
Undated	Transfusion handbook update - 5.1: Haemovigilance	WITN7306002
05/08/2022	Independent report entitled, 'SaBTO: Advisory Committee on the Safety of Blood, Tissues and Organs annual report 2019 to 2020.	WITN7306003
17/12/2020	Independent report entitled, 'Guidelines from the expert advisory committee on the Safety of Blood, Tissues and Organs (SaBTO) on patient consent for blood transfusion.	WITN7001044
Undated	Article entitled, 'Consent for blood transfusion: summary of recommendations from the Advisory Committee for the Safety of Blood, Tissues and Organs (SaBTO)' by Professor Michael F Murphy, Ms Andrea Harris and Professor James Neuberger.	WITN7001045
01/12/2021	The Blood Safety and Quality Provisional Common Framework.	WITN7306004

Undated	'A guide to establishing a national haemovigilance system' published by the WHO.	RLIT0000992
01/07/2022	A report entitled 'Annual SHOT report 2021'	SHOT0000032
Undated	User guide for mandatory and professionally mandated haemovigilance reporting in the UK.	NHBT0203834
25/03/2013	Guidance on Good Medical Practice by GMC	RLIT0001283
Undated	Transfusion Handbook Update - 4.2: Administration	RLIT0001287
01/08/2021	Records Management Code of Practice 2021	RLIT0001284
28/10/2021	Minutes of the 44th SaBTO meeting	NHBT0203835
Undated	Article entitled, 'Update of the statements on biology and clinical impact of occult hepatitis B virus infection' by Giovanni Raimondo, Stephen Locarnini, Teresa Pollicino, Massimo Levrero, Fabien Zoulim, Anna S. Lok, and the Taormina Workshop on Occult HBV Infection Faculty Members	WITN7306005
01/02/2022	Minutes of the SaBTO meeting	WITN7306006

24/05/2022	Minutes of the SaBTO meeting	WITN7306007