LETTER OF INSTRUCTION TO THE FRACTIONATION EXPERT GROUP

04.02.2021

Dr Paul Strengers and Dr Ruth Laub

Dear Dr Strengers and Dr Laub

Re: The Infected Blood Inquiry

1. I am writing on behalf of the Chair to the Infected Blood Inquiry, Sir Brian Langstaff, with instructions for the preparation of a report on matters relating to the fractionation of blood products.

2. The purpose of the report is to provide evidence about matters within your expertise that may assist the Chair in fulfilling the Inquiry's Terms of Reference. I set out in more detail below the topics and questions that the Chair asks you to address at this stage. The report will be provided to the Core Participants to the Inquiry and will be published on the Inquiry's website.

3. In due course, I may ask you to undertake further work to assist the Inquiry. This may include answering questions raised by Core Participants, preparing

further reports, conducting discussions with or providing opinions to other expert groups instructed by the Inquiry, giving oral evidence at the Inquiry's public hearings, and carrying out other duties appropriate to the role of an expert to the Inquiry as directed by the Chair through me.

Background

4. As you are aware, the Infected Blood Inquiry has been established to examine the circumstances in which people treated by the National Health Service in the United Kingdom were given infected blood and infected blood products. It is an independent public inquiry under the Inquiries Act 2005.

5. The provision of such blood and blood products led directly to people becoming infected with Hepatitis B virus ('HBV'), Hepatitis C virus ('HCV'), Human Immunodeficiency Virus ('HIV') and other diseases. Other people were indirectly infected. People have also been informed that they may be at risk of developing v CJD.

6. The Inquiry's Terms of Reference require it to consider and report upon a wide range of issues. These include:

"To examine the circumstances in which men, women and children treated by National Health Services in the United Kingdom (collectively, the "NHS") were given infected blood and infected blood products, in particular since 1970, including:

a. the treatment of men, women and children who were given infected blood or infected blood products through transfusion or other means;

b. the treatment of men, women and children with haemophilia or other bleeding disorders who were given infected blood products (recognising that the position of those with mild, moderate and severe

bleeding disorders may require separate consideration during the Inquiry);

c. *what was, or ought to have been known, at any relevant time about the risks of infection associated with blood donations and blood products, by Government (in particularly the Department of Health), pharmaceutical companies, any relevant licensing authorities, NHS bodies, the medical profession, and other organisations or individuals involved in decision-making in relation to the use of blood and blood products;*

d. *to what extent people given infected blood or infected blood products were warned beforehand of the risk that they might thereby be exposed to infection, and if so whether such warnings as were given were sufficient and appropriate;*

e. *the adequacy of the systems adopted for the screening of donors, and the collection, testing, licensing and supply of blood and blood products for use by the NHS;*

f. *the United Kingdom's failure to become self-sufficient in the production of blood products (and consideration of any relevant differences in terms of self-sufficiency between England, Wales, Scotland and Northern Ireland);*

g. *the actions of Government (in particular the Department of Health), pharmaceutical companies, licensing authorities, NHS bodies, the medical profession, and other organisations or individuals involved in decision-making in relation to the use of blood or blood products;*

h. *why people were given infected blood or blood products, including the nature and extent of any commercial or other interests which may have affected decision-making;*

i. *the extent to which the supply of infected blood or blood products could, and if so, should have been avoided or stopped earlier, and if so how best this might have been achieved".*

…

To examine:

a. *the nature, adequacy and timeliness of the response of Government (in particular the Department of Health), NHS bodies, other public bodies and officials, the medical profession, the UK Haemophilia Centre Doctors Organisation, the pharmaceutical industry and other organisations (including the Haemophilia Society), to the use of infected blood or infected blood products to treat NHS patients…"*

7. A full version of the Terms of Reference may be found on the Inquiry's website. The website also contains the Inquiry's List of Issues, which provides more detail of the matters that may be explored during the course of the Inquiry. I have sent links to both these documents to the group.

8. The Inquiry must report its findings to the Minister for the Cabinet Office, and make any recommendations, as soon as practicable.

Instructions

<u>Fractionated blood products</u>

9. Please provide an overview of the way in which fractionation is and has been used to provide blood products, and in particular cryoprecipitate and Factor VIII and Factor IX concentrates. To the extent that you consider it to be appropriate and within your knowledge and expertise to do so, please consider the following matters:

    a. The scientific principles involved in fractionation;

    b. The techniques developed to fractionate blood products, and in particular the techniques that were developed prior to and during the 1970s and 1980s to produce (i) frozen and freeze-dried cryoprecipitate, and (ii) Factor VIII and Factor IX concentrates;

c. The materials required for those techniques, including the resources, equipment and plant required;

d. An explanation of variables (such as purity, potency and yield) that affect the production of (i) cryoprecipitate, and (ii) Factor VIII and Factor IX concentrates;

e. The significance of inhibitors and the risk of allergic reactions to the production of (i) cryoprecipitate, and (ii) Factor VIII and Factor IX concentrates.

Heat Treatment

10. The Inquiry is examining the issue of viral inactivation of blood products through heat treatment. To the extent that you consider it to be appropriate and within your knowledge and expertise to do so, please consider the following matters:

a. The scientific principles that underlie viral inactivation by heat treatment;

b. The different methods of heat treatment available to fractionators, and how those methods, and knowledge of their effectiveness, developed over time;

c. How, if at all, those methods affected variables (such as purity, potency and yield) in the production of (i) cryoprecipitate and (ii) Factor VIII and Factor IX concentrates;

d. The materials required for those methods, including the resources, equipment and plant required;

e. Any technological advances that contributed to the development of heat treatment during the period of time of relevance to the Inquiry.

Other methods of viral inactivation

11. Please explain alternative methods of viral inactivation that have been used by producers of blood products against (i) HBV, (ii) HCV and (iii) HIV, including solvent/detergent methods and the use of virucides. To the extent that you consider it to be appropriate and within your knowledge and expertise to do so, please consider the following matters:

    a. The scientific principles underlying the method;

    b. The processes required to produce blood products using the method and the challenges involved;

    c. The materials required for those methods, including the resources, equipment and plant required;

    d. Any technological advances that contributed to the development of the technique during the period of time of relevance to the Inquiry.

Recombinant products

12. Please explain why, how and when recombinant products were developed for the treatment of haemophilia and other bleeding disorders. To the extent that you consider it to be appropriate and within your knowledge and expertise to do so, please consider the following matters:

    a. The scientific principles underlying such products;

    b. The processes required to produce the products and the challenges involved;

    c. The materials required for those methods, including the resources, equipment and plant required;

d. Any technological advances that contributed to the development of recombinant products during the period of time of relevance to the Inquiry;

e. Adverse events associated with the use of recombinant products, and when knowledge of such adverse events emerged.

Further Information

13. If there are issues on which you consider that you require further information before being able to reach a conclusion on some of the topics above, then please set that out in the report or in a separate letter to me. Where practicable, the Inquiry will seek to obtain such information as you require and provide it to you.

14. Where appropriate, you should provide provisional answers to the questions set out above, qualifying them as necessary with reference to further evidence or research that may be required to provide a more complete answer.

15. The manner in which you address the topics set out is a matter for you, as is the way in which you express your conclusions and any qualifications that accompany them.

16. The report should make clear if there are any matters on which it is not, or may not be, possible to provide an expert opinion, for example due to the lack of available information. The report should give the reasons for any such limitation.

17. If there is a range of professional opinion on a particular issue covered in the report that must be made clear and the range of opinions summarised. The report should explain why you have reached the particular conclusion that you have.

18. If there is a disagreement between you about any matter within the report, then this too should be made clear. The report should summarise the different opinions, attribute them to the relevant individual, and provide the reasons explaining the views expressed.

19. In the event that you consider it appropriate that certain sections of your response be prepared by part of the group, please indicate in the report by whom each section of the response has been prepared and why the division of the labour in this way was deemed appropriate

20. The Inquiry will be instructing other expert groups during the course of its work. You may consult freely with members of these other expert groups, as may help you, but should acknowledge in your report what, if any, material assistance their input has given you.

Expertise and Duties of an Expert

21. If having read this letter you feel that you do not have the appropriate experience or expertise then please let me know immediately. You should also notify me if you have any queries or require any further information.

22. As expert witnesses, you have a duty to exercise reasonable skill and care in carrying out your instructions and must comply with any relevant professional code of practice. Your overriding duty is to assist the Inquiry and to provide your unbiased opinion as independent witnesses in relation to those matters which are within your expertise.

Format of the Report

23. In preparing your report please make sure that:

a. It sets out details of your qualifications, and your respective academic and/or professional experience.

b. It gives details of any literature or other material which you have relied on.

c. It contains a statement setting out the substance of all facts and instructions which are material to the opinions expressed.

d. It makes clear which of the facts stated are within your knowledge.

e. It identifies who carried out any other work used for the report. The report should give the qualifications for the individual and indicate whether their work was carried out under your supervision.

f. Where there is a range of professional opinion on the matters dealt with in the report, it summarises the range of opinions and gives reasons for the opinion reached.

g. It contains a summary of your conclusions.

h. It sets out any qualification to an opinion or conclusion provided.

i. It contains a statement that you understand your duty to provide independent evidence and have complied with that duty.

24. The final report must be verified by statements from both of you saying:

"I confirm that in respect of those parts of the report to which I have contributed:

a. *I have made clear which facts and matters referred to in this report are within my knowledge and which are not.*

b. *Those that are within my knowledge I confirm to be true.*

c. *The opinions I have expressed represent my true and complete professional opinions on the matters to which they refer."*

25. You should let me know immediately if at any time after producing your report and before the conclusion of the Inquiry you change your views. It is also important that you notify me promptly if you feel it is necessary to update your report after it has been finalised, for example because new evidence has come to light.

26. The report should be reasonably concise and expressed as far as possible in straightforward language. Where technical or clinical terms are used, and their meaning may not be obvious, please provide a brief explanation as to their meaning, for example in a glossary.

Timetable

27. I would be grateful if you can provide a draft copy of your report by 30 June 2021.

28. I ask for the report to be provided in draft in the first instance so that I can approve its format, check that the formal requirements for an expert report mentioned above are fulfilled correctly and ask for any queries to be addressed before the report is signed.

29. You have indicated that you may be assisted by members of the Inquiry team in respect of the phrasing of your report, given that you will both be working in a language in which you are not native speakers. The Inquiry will provide such

support where requested, but on the clear and mutual understanding that the substance of your evidence is a matter for you alone. You should feel entirely free to reject any suggestions made to you by any members of the Inquiry team.

30. Once the report is finalised, a copy will be disclosed to the Core Participants and will be published on the Inquiry website. It may be that once Core Participants have reviewed this letter of instruction or your report they will identify further issues that I may wish to raise with you.

31. I may also provide you with further instructions at a later date in respect of any other matters on which we seek evidence from the group.

Fees

32. I will correspond with you separately about arrangements for your fees.

Next Steps

33. As I have indicated in this letter, and if you feel that it is appropriate, please write to me if you consider that the questions or topics should be amended or changed.

34. May I thank you for agreeing in principle to assist the Inquiry. If there is anything that I can do to assist or there are any aspects of these instructions that you would like to clarify then please do not hesitate to contact me.

Yours sincerely,

Michelle Secker

Infected Blood Inquiry, Secretariat