Sourcing fresh human blood products for research:

Considerations and options

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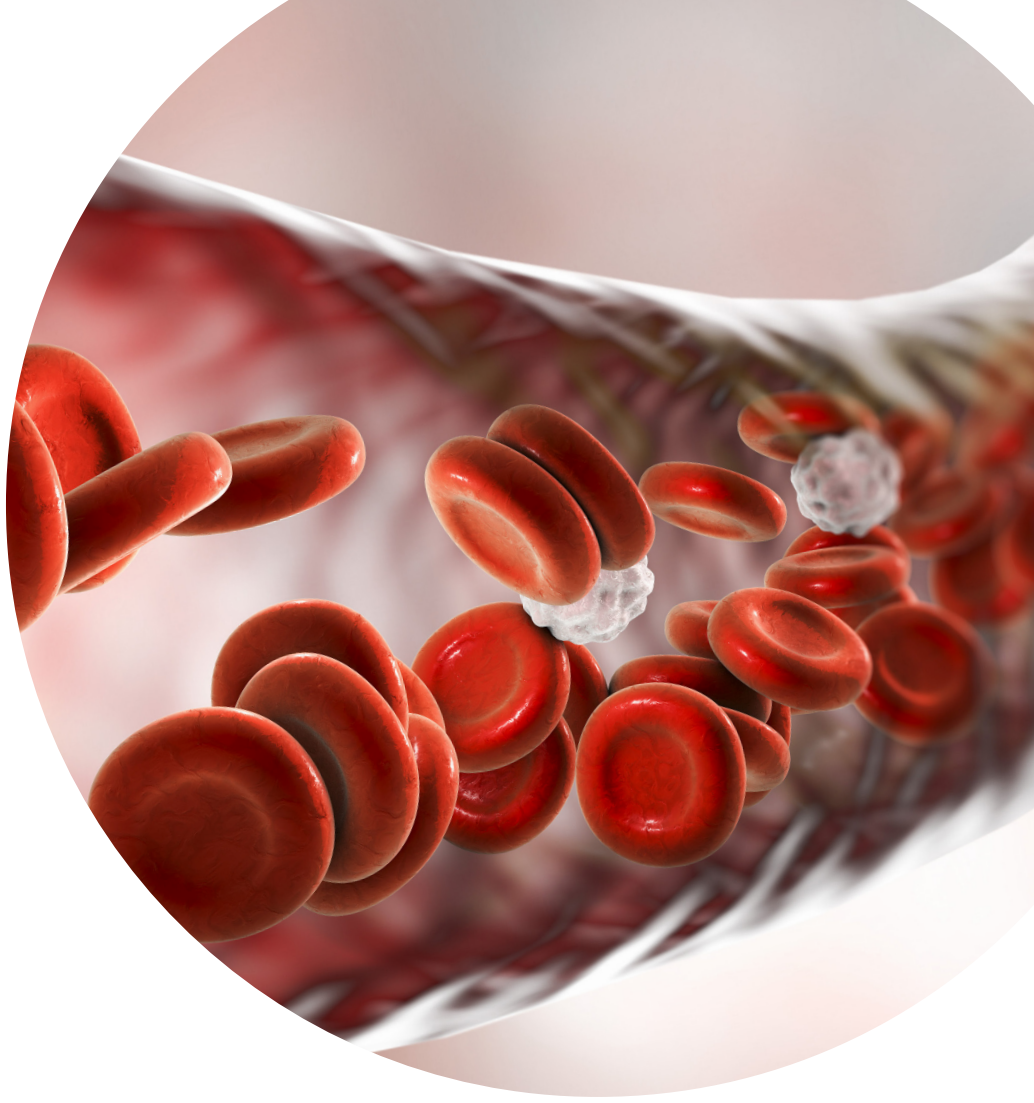
1. Introduction

Fresh, healthy blood products are crucial in a wide range of scientific disciplines, from immunology and genetics research to pharmacology and toxicology. For those working in these areas, having access to high-quality materials that can be used to generate reliable data is essential.

It is well known that securing a regular supply of high-quality human blood products is a challenge for most researchers. Indeed, if you work in these fields, you've probably felt the frustration of receiving dated blood samples or may have struggled to find the specific samples you need for your project. These issues often mean you have to work with cells that are suboptimal for your application, which can limit the transferability, accuracy and reliability of your data.

So, how can you avoid these frustrations and secure the best fresh blood products for your research? In this eBook, we explore why fresh blood products are essential for many research applications, how truly fresh blood can help overcome common research challenges, and how you can find the best supply source to meet your specific needs.



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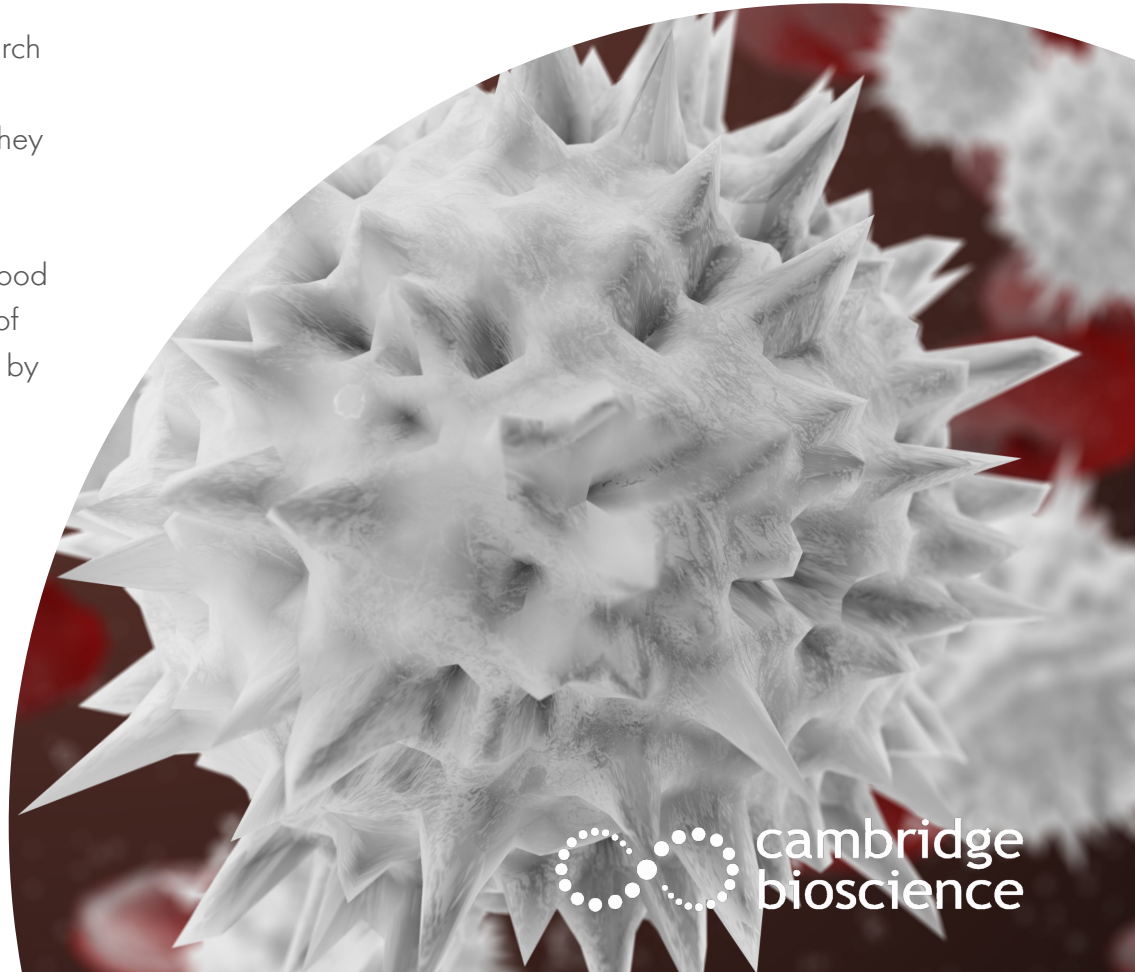
2. The different types of fresh blood products available

Before we delve into the importance of fresh blood for research applications, it is worth quickly reviewing the many different types of blood products that are available, as well as how they are usually collected and stored.

Table 1 on the next page highlights the range of different blood products available. As you can see from the table, the type of fresh blood product you should choose is heavily influenced by the goal of your research and the design of your study.

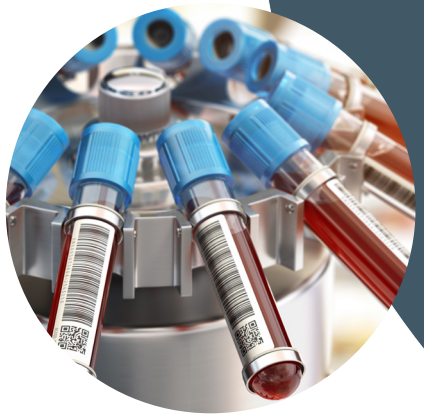


Blood product	Collection method	Application examples
Whole blood	Collected in tubes and bags with a choice of anti-coagulants.	Wide-ranging: the development and validation of analytical and diagnostic testing devices and kits measuring blood chemistry, blood gases, coagulation, as well as haematological, inflammatory, endocrinological, and cardiac biomarkers, and blood-borne infections.
Serum	Produced from whole blood using clot-activating tubes or in bags using the off-the-clot method.	Highly representative matrix, but blood clotting process will lead to presence of factors that may influence assay performance. Widely used in cell cultivation.
Plasma	Prepared by the centrifugation of anti-coagulated whole blood.	Essentially serum that contains fibrinogen. Will contain residual anticoagulant which may also impact assay performance. Widely used in bioanalytical and toxicology studies
Leucocyte reduction cones	An in-line filtration device used during blood or platelet collections to exclude leucocytes from the final blood product.	A rich source of PBMCs and other white blood cells. Leucocyte cones are used widely in research to isolate total leucocyte populations for functional assays on individual cell types of interest in disease.
Buffy coat	Prepared via the centrifugation of anti-coagulated whole blood and removal of erythrocytes and plasma. Contains most of the white blood cells and platelets.	A rich source of PBMCs and other white blood cells.
Peripheral blood mononuclear cells (PBMCs)	Produced by the centrifugation of whole blood or buffy coat over Ficoll-Paque density gradient media.	Widely used in immunology, cell therapy, toxicology and regenerative medicine applications. PBMCs are also used in the development of new immunotherapies, such as CAR-T.
Red blood cells (RBCs)	Isolated by centrifugation from whole blood.	Used widely for haematology research into conditions such as sickle cell anaemia, malaria and toxin exposure.
Leukopaks	Concentrated leucocytes isolated from whole blood by apheresis.	Very high numbers of cells from a single donor can be useful for experiments at large scale.

Table 1. Research applications of common blood products

3. The importance of using truly fresh blood for your research

Due to the speed at which cell functions can change following venepuncture, any delay in the processing and delivery of blood samples can affect how authentic the product's behaviour is. Ultimately, if cell function no longer accurately represents the *in vivo* environment, assay performance can be affected, which could impact any data generated. Therefore, as fresh blood products are often required for research that aims to improve human health, it's of the utmost importance that laboratories are using the freshest products possible.



Box 1. How fresh blood products have helped drive clinical advances

Fresh blood products have been used in many cutting-edge research programmes. In recent years, there have been two particularly noteworthy clinical advances that were first developed using fresh blood products from healthy patients.

The first is liquid biopsies. In 2016 the FDA approved the cobas® EGFR mutation liquid biopsy test for detecting lung cancer. This was a great step forward as these tests are safe, non-invasive and easy to repeat, providing a much better experience for patients compared to tissue biopsies.[1] Now, more companies are developing such tests, which requires the use of fresh blood products.

The second is CAR-T therapy, which has the potential to revolutionise cancer treatment. The process of modifying T-cells to produce chimeric antigen receptors on their surface was first developed using fresh blood products from healthy donors.

In both examples, fresh blood products were essential for generating relevant results that deliver true biological insights and advances.

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How fresh is fresh for blood products?

According to the International Society for Biological and Environmental Repositories (ISBER) Best Practices Guide, blood samples should be processed and stored within 1 to 24 hours of draw, depending on the analytical endpoint.[2] After this time, the functionality of the cells starts to decline, which could have substantial implications depending on your application.

For example, research exploring the effects of processing parameters on the immunological function of cells used in HIV vaccine trials showed that an increase in processing time after venepuncture from 8 to 24 hours had a modest effect on the viability of PBMCs (~8% decrease) and a greater impact on cell recovery which was down by ~32%. The greatest effect however was on T-cell functionality where a 36-56% loss in interferon gamma (IFN-y) frequencies, as detected by ELISpot, was observed.[3]

Given the potential ramifications of using suboptimal blood products, it is therefore not surprising that many scientists have been assessing how cell function is affected by processing times post-venepuncture. A number of studies have now been published that recommend the processing of products should ideally be carried out as soon as possible after blood has been drawn, with a maximum delay of eight hours storage at room temperature.[4-6]

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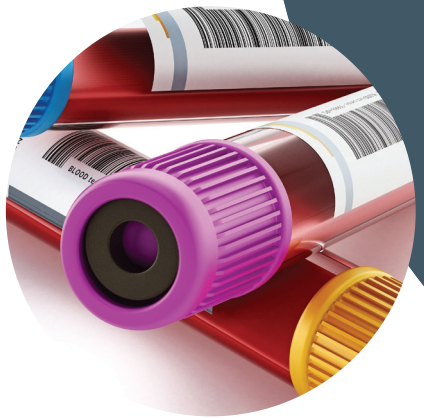
The importance of following best practices when processing fresh blood products

It is imperative that fresh blood products are processed appropriately. If best practices have not been followed, it is possible that the functionality of the cells you acquire will have been altered. For example, if not handled correctly, platelets in serum and plasma easily degrade. This results in platelet activation, which contaminates samples and results in inaccurate measurements.[7] It is therefore essential that your supplier can meet your specific processing and storage requirements.

Unfortunately, it's not always easy to determine which source of fresh blood products is the best for your research. In fact, the variation between products supplied from different companies and organisations can be unexpectedly large. In the next few chapters, we consider three main sources of fresh blood products and share tips on how you can identify the best source for your needs.



Box 2. Blood products from healthy vs non-healthy donors

Depending on the goals of the study, researchers might need to use samples from healthy donors and/or patients with a specific disease or condition. For the purposes of this eBook, please note that we are only focussing on the sources and applications of blood products from healthy donors.

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4. How to select the best source of blood products for your research

It is vital to understand which source of fresh blood will best meet the needs of your research. In the UK, there are three main sources of fresh blood products: national/regional public blood collection services, specialist commercial suppliers and the sourcing of blood directly from volunteers within your own organisation. Each has strengths and limitations that can impact the consistency and efficiency of your research.

When reviewing which supply option to choose, there are five main factors to consider:

- Supply timelines and consistency
- Donor characteristics and lifestyle
- Ethical/commercial requirements
- Range of blood product formats available
- Collection and processing methodologies

So, how can you assess and compare fresh blood product supply options against these factors? To help, we've collated a number of key questions that you should keep in mind (see Table 2 on the next page).

Box 3. Services outside of the UK

Please note, the information in this eBook is presented from a UK-centric viewpoint. While other national services might be similar, this should not be assumed. Instead, it is best to determine exactly how your local services operate if you are working in a country outside of the UK.

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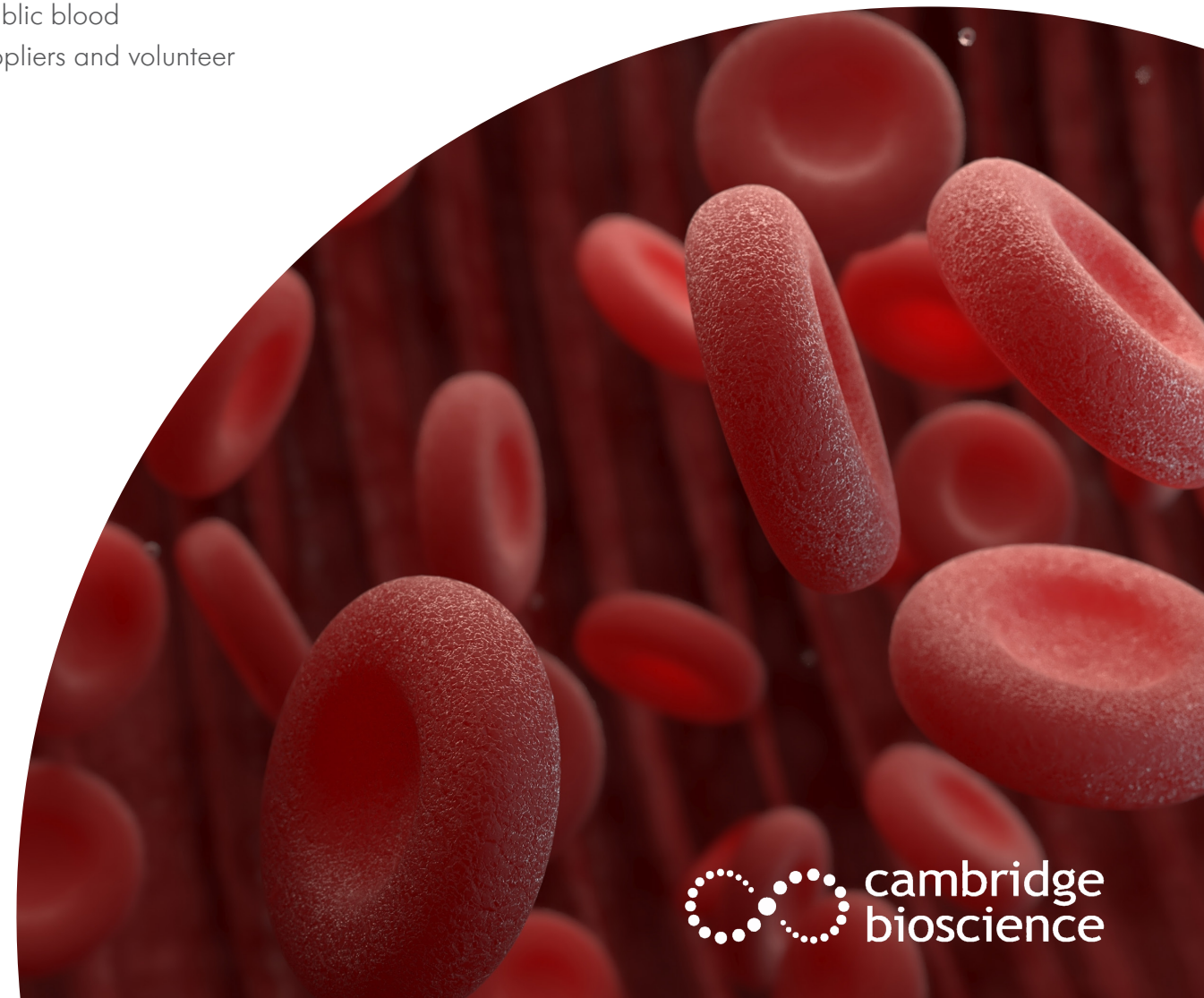
Supply timelines and consistency	Donor characteristics and lifestyle	Ethical/commercial requirements	Blood product formats	Collection and processing
How fresh do you need your blood products to be?	Does your study require (or would it benefit from) access to products with specific donor characteristics (e.g. gender, age, ethnicity, BMI)?	Do donors give specific consent for the blood to be used in commercial research and waive IP rights?	Which blood product format(s) will your research require?	Can the supplier provide details of how blood products will be collected and processed to ensure they meet your research needs?
Based on this, will the supply option be able to reliably supply these products when you need them for your experiment?	Do you require donors who have not taken drugs or medications that might interfere with your research?	Does the supplier guarantee ownership of data resulting from using the donor material?	Does the supply option offer the exact format you require, and does it offer additional formations should your needs change in the future?	If leveraging internal donors, what will be required to ensure your process will be consistent and ethically viable?
Will the supply option be able to consistently deliver them within the specified time frame?	Can the supply option consistently provide products against these characteristics?	Do donors know that their samples could be used for genetics or animal research?	Can the supply option consistently deliver the volume/amount of product you require?	
		Are donors compensated for their time?	Could the supply option continue to meet your requirements if you needed to scale-up your research?	

Table 2. Key questions to keep in mind when evaluating fresh blood product suppliers

To further explore some of the supply options available and help you make an informed choice, we will use the next few chapters of this eBook to review national/regional public blood collection services, specialist commercial suppliers and volunteer donors against these five factors.

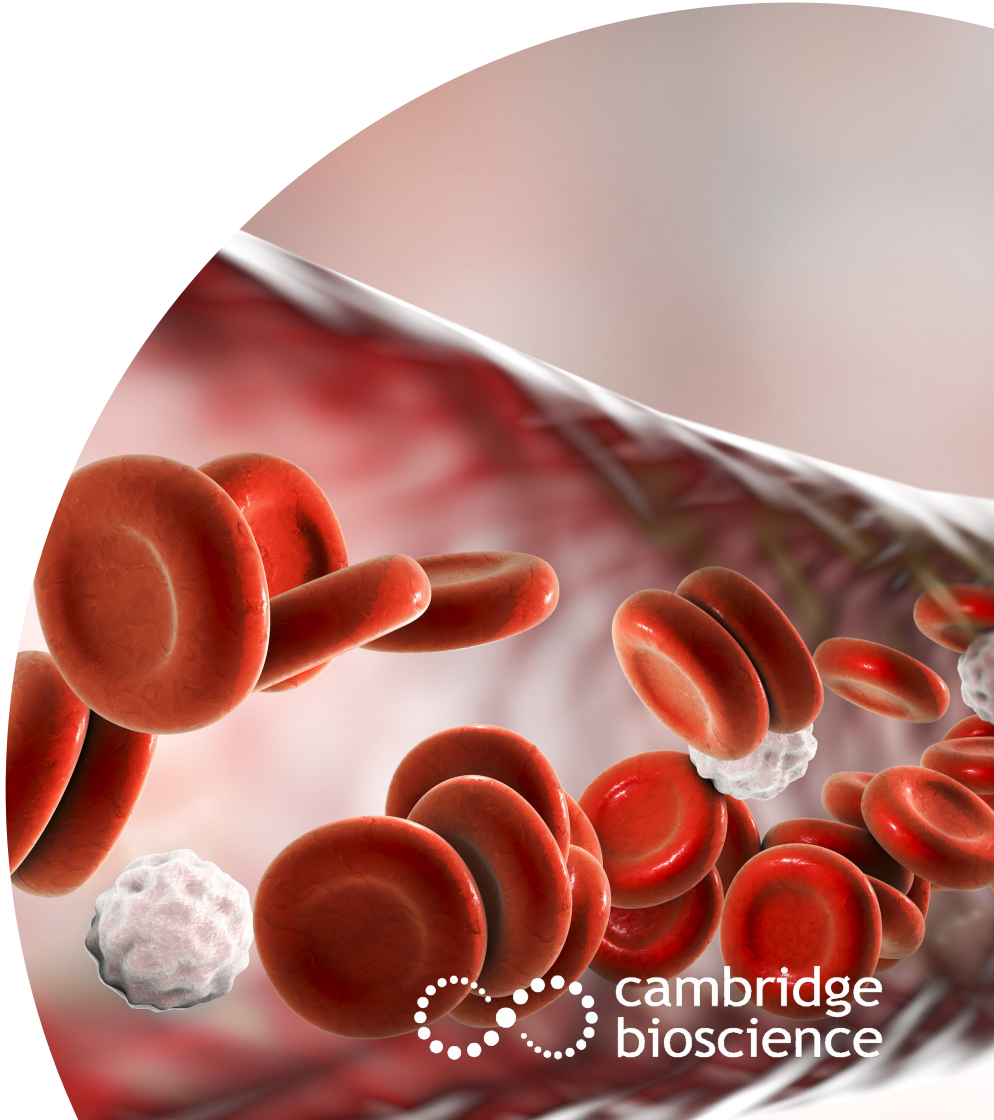


5. Supply option 1 – national/regional public blood collection services

NHS Blood and Transplant (NHS-BT) is a public voluntary donation service with the primary objective of supplying blood, organs, and tissues for transplantation. Where blood is unable to be used for clinical purposes, it can be released to certain organisations for approved non-clinical uses.

Supply timelines and consistency

As the primary focus of NHS-BT is to supply blood and organs for clinical use, they understandably cannot guarantee a steady supply of blood products for research. This is because if clinical demand is particularly high, more blood donations will be transported to hospitals, meaning there will be less blood available to supply for research. As a result, the availability of fresh blood products can fluctuate, and delivery times can be inconsistent. Ultimately, this could impact your project timelines if you don't build in contingency time when planning.



Donor characteristics and lifestyle

Due to the nature of the service, NHS-BT cannot control or limit its donor characteristics, as their priority is to ensure there are enough donations to meet clinical needs. This means that researchers are unable to preselect specific donor characteristics of relevance to their research. Instead, diversity is entirely dependent on those who choose to donate on a given day and whose samples are surplus to requirements at the donor centre. As a result, if donor characteristics such as age, BMI and smoking status are important to your research, it is possible that fresh blood products from NHS-BT will not be suitable for your project. In which case, it would be beneficial to find a supplier that can meet your specific needs.

Furthermore, there are no exclusion criteria for donors based on prior medication history, so there is a possibility of donor medication inadvertently interfering with an experimental assay. For example, NHS-BT donors may be taking commonly used medicines, such as ibuprofen or other anti-inflammatory drugs, which could interact with an immunological assay being run. Therefore, if the presence of such drugs and their metabolites could impact your research, it may be worth considering a supplier that can select donors based on medication usage history.

Another consideration here is that donated blood and blood components are anonymised with no systems in place to be able to recall donors. This means that it is impossible to secure repeat donations from specific individuals. Depending on your research application, this might not matter, but if your experiments require you to perform multiple tests or replicates using samples from the same donor this would be impossible using products provided by NHS-BT.

Ethical/commercial considerations

When using national/regional public blood collection services, there are also very important ethical and commercial factors to consider. Firstly, donors only give generic consent for their blood to be used for non-clinical use. As a result, they have not provided specific consent for their donations to be used in commercial research or waived their rights to IP. Depending on your organisation, before using NHS-BT blood products, you might need to engage with your legal team to ensure you are cleared to use these samples for your project.

Blood product formats

Depending on the focus of your research, it is worth noting that there is at least one unique and valuable product that the NHS-BT service can provide consistently – leucocyte cones. These are produced as a by-product of platelet donation, where a filtration device is used to remove leucocytes. However, while this cost-effective method provides a large number of leucocytes, the filtration systems used to create the cones may alter the functionality and viability of cells recovered from them. This is due to the interaction of cells with the cone membrane – a process that doesn't occur with leucocytes obtained from buffy coats.[8] Therefore, it is important to determine whether this change in functionality will impact your studies, which will depend on your application. If there is a risk that your research will be impacted, it could be best to find an alternative source of supply of leucocytes.

In addition to leucocyte cones, NHS-BT does also provide whole blood samples. Most labs have the resources available to process these samples, however, as the supply of blood products for research is not the primary focus of the organisation, NHS-BT cannot guarantee a specific delivery window. For many laboratories, being able to control how fresh the blood is and when it will be delivered is critical. If this consideration is key for your research, you might find it easier to work with a private supplier, as we will explore in chapter 7.

Additionally, as the primary focus of NHS-BT is to collect blood for clinical transfusions, specific devices are used for collection. Therefore, the organisation cannot offer flexibility on which collection devices or anti-coagulants are used or how the blood products are processed. Again, for some research applications this could have a detrimental effect, as collecting and processing blood in different devices can have a significant can affect assay results.

Collection and processing

Of course, it is imperative that donated blood used for transfusions needs to be disease-free. However, clinical-grade screening for viral infectious diseases can be a slow process, meaning that blood products used for preclinical research normally arrive at the receiving lab before testing is completed (in order to ensure they are delivered in a timely fashion). It's worth noting that it is possible that the presence of infection will only be recognised after you have run your assays (meaning you might have to repeat your experiments with an alternative supply of fresh blood, invalidating results and increasing safety risks).

A final consideration for the NHS-BT service is the limited control you have over blood collection procedures and processing methodologies. This ultimately means that you might have to change the design of your study to accommodate the format and quality of the products you receive.

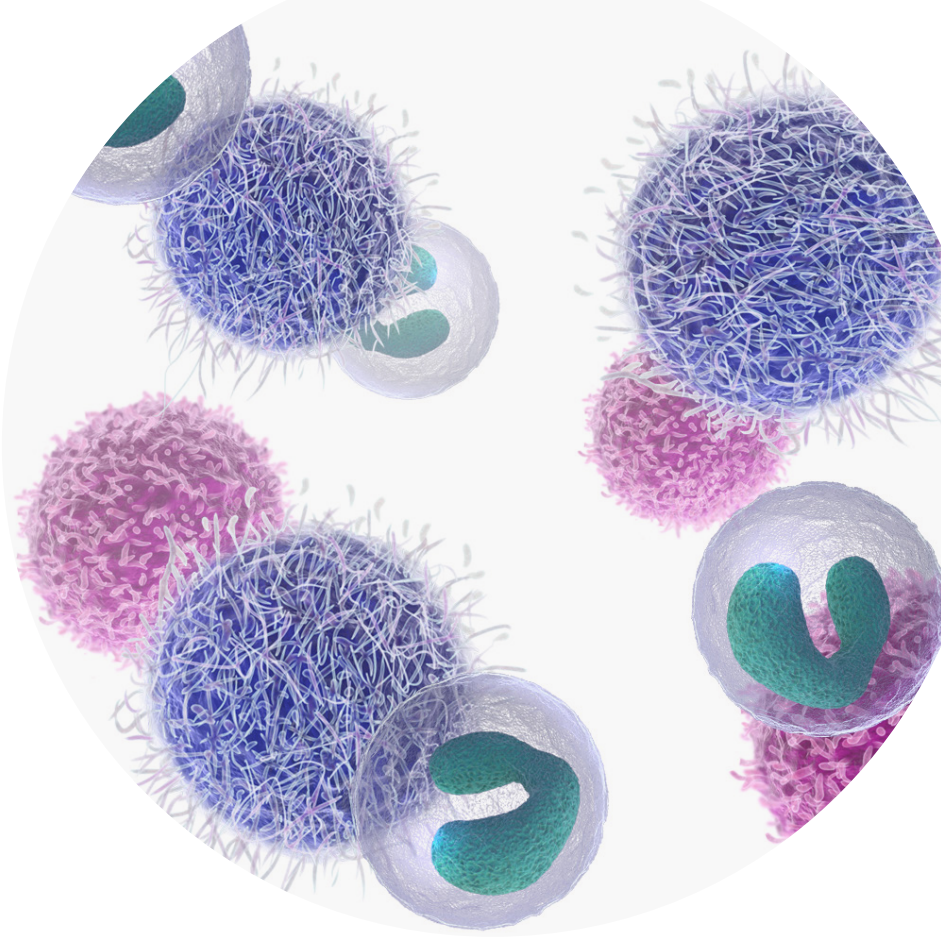
6. Supply option 2 – volunteer donors (e.g. colleagues)

Within certain research organisations and groups, it is not unusual for colleagues to donate blood to help support an internal programme. This route can often seem advantageous due to its low costs and rapid delivery, but there are other pros and cons to consider, as we explore in more detail below.

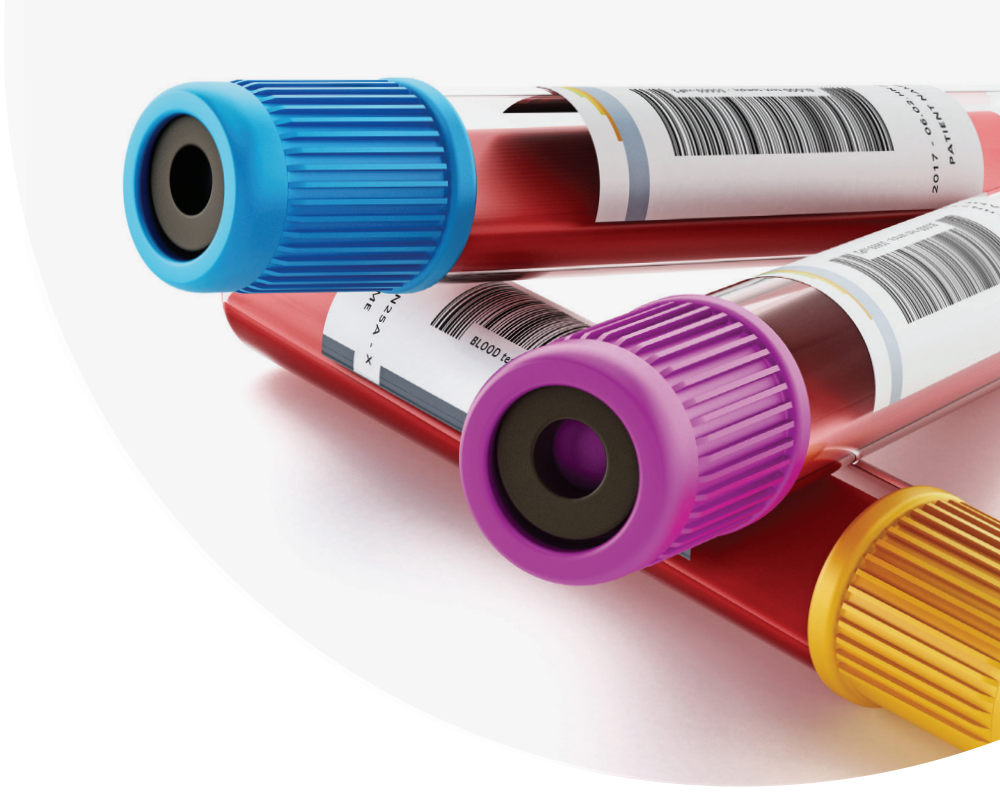
Supply timelines and consistency

As mentioned above, leveraging internal donors is cost-effective (often free) and the time between blood draw and experimental use can be very short. However, typically it is difficult to secure donors from within your organisation, resulting in a very small donor pool.

The volume of blood that can be collected is often limited too. This is because the collection processes often used internally only allow a small volume to be taken from each donor. Therefore, depending on your application requirements, you might find that your organisation's internal supply is unable to meet your needs.



Even if you do achieve the desired volume, you could struggle to anonymise your samples. Before collecting blood internally, it's of the utmost importance that systems are put in place to ensure that samples cannot be traced back to individual colleagues.



Donor characteristics and lifestyle

As you might imagine, the diversity of donors available to you and your research will depend on who is available to donate. As many lab groups are small and only a proportion of people will be willing to donate, this will further restrict the options available to you. If your experiment requires access to a certain number of donors with specific characteristics, such as a certain BMI index or whether they are a smoker, it is unlikely you will be able to source all the blood products you need through internal volunteer donors alone.

Ethical/commercial considerations

Using internal blood donors also raises some ethical considerations. For example, there is a risk that genetic or disease testing could reveal an undiagnosed condition of a donor. Even if you have systems in place that do effectively anonymise blood donations, it is still critical to plan for the possibility that your research could uncover an underlying health problem. In the worst cases, if samples aren't properly anonymised, then it is possible that the wider team will discover a diagnosis, raising confidentiality concerns.

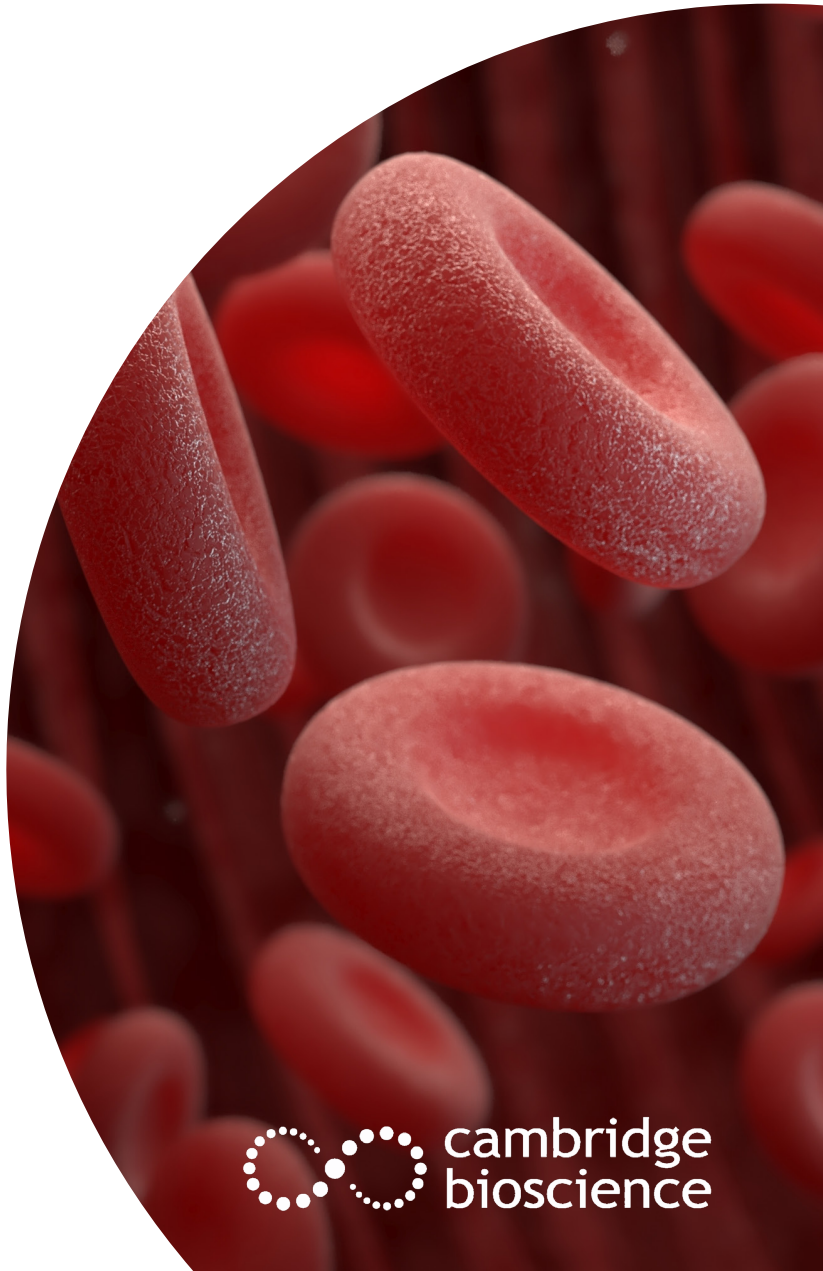
Labs using internal donors are also more likely to have rudimentary consent processes in place. Therefore, if you choose to use an internal supply, it is best to check if donors have waived their IP rights.

Blood product formats available

In theory, you can generate any type of product format you need from the blood drawn from internal volunteers. However, in order to do so, your team will need access to the reagents, technologies and expertise required to process the whole blood draws into the format needed for your research (e.g. PBMCs, buffy coat), as well as to perform QC on the resulting samples. While most labs do have these capabilities (especially for lower volume samples) these process steps still require the investment of time and resources.

Collection and processing

The ad-hoc approach to acquiring blood in-lab and relying on internal donors means that there is no guarantee that the collection and processing protocols specific to your needs are adequately followed. As a result, your experimental set-up could be compromised, which may have downstream repercussions such as inconsistent results or unreliable data.



7. Supply option 3 – specialist blood suppliers

In the UK, scientists can now secure samples from private companies that specialise in the supply of fresh blood products for research use only. Typically, these organisations can guarantee delivery within the same day locally, or 24-hours nationally, of venepuncture and can offer more flexibility in terms of how the products are collected and processed, better meeting your needs.

Supply timelines and consistency

To avoid the pitfalls associated with aged blood products, we recommend looking for a private supplier that has a large pool of donors and can guarantee rapid delivery to your location, preferably on the same day the blood is taken. Typically, such a supplier will have dedicated clinics where they collect donations in accordance to your specific needs (in terms of volume, choice of anticoagulant, shipment temperature and blood group etc.) before dispatching the products via a reliable courier. This means that you not only have a much greater control over donor characteristics, product formats and processing methodologies, but you also shouldn't experience project delays as a result of samples not being available or delayed in transit.

Donor characteristics and lifestyle

The large pool of blood donors often recruited by specialist suppliers means that you can request blood products from individuals that meet specific criteria, such as age, ethnicity, gender, tissue compatibility, BMI and whether they are medication-free. It can be particularly challenging to source a consistent supply of such samples, so specialist suppliers can be beneficial for researchers with precise requirements.

Ethical/commercial considerations

When using a commercial service you can be confident your IP is protected, as donors are fully informed as to how their blood will be used and give explicit consent for it to be used in a research capacity (and receive detailed information about the exact work and how their blood will be used).

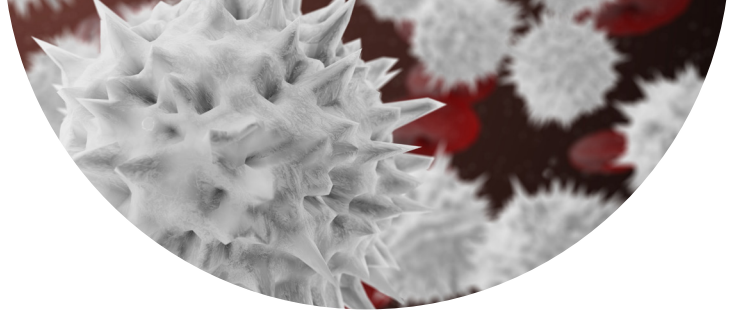
Blood product formats available

Many commercial providers go beyond just providing human whole blood, to offering a wider range of products. These can include LeukoPaks, PBMCs, plasma, buffy coat, serum, RBCs and more. By purchasing the formats you need, you can minimise any further delays and ageing of the blood products, while saving yourself time and resources (as you won't need to perform any downstream processing yourself). What's more, as most commercial suppliers adhere to robust processes, you can be confident that the products you receive will be as consistent as possible.

Collection and processing

The ability to customise how your fresh blood products are collected and processed is also advantageous. The storage time and conditions can be selected to meet your unique requirements, helping you avoid issues associated with lengthy storage and processing times. For example, some specialist suppliers can isolate PBMCs from blood samples within 5 hours after venepuncture, well within the recommended 8-hour time period.[4] Knowing that your fresh blood products have been collected within 24 hours and processed according to your requirements provides peace of mind that there will be less variation between samples, facilitating the reproducibility and consistency of your research.

Ultimately, since the sourcing of fresh blood products is the primary purpose of specialist suppliers, they're not restricted by collection formats or processing methods, as can be the case with other suppliers. This means your blood samples can be collected in a manner that suits your research. Before finalising your research plans, if you think a private supplier could be the best solution for you, it will be worth requesting cost estimates so you can build these into your budget from the beginning of your project.



8. Secure the right source of fresh human blood products for your needs

As we have explored in this eBook, there are a number of options open to researchers looking to use fresh blood as part of their research. The right option for you will depend on the specific needs of your study.

In most cases, you will need your blood products to arrive as fresh as possible, and ideally less than 24 hours after collection. If your research requires access to blood from donors with specific characteristics (e.g. age, ethnicity, gender etc.), it is important to find a supplier that can consistently deliver against these requirements. If you require a specific format (e.g. PBMCs), most traditional suppliers would provide you with whole blood that you can further process in your own lab ahead of downstream use in your experiments. Alternatively, you could directly purchase the format you need from a specialist fresh blood product supplier.

For scientists working in a commercial setting, it is imperative that products come from donors that have provided consent for their blood to be used for such applications, otherwise you could face legal risks further down the line. Therefore, we recommend building an internal process that covers this (when using internal volunteer donors) or select a supplier that offers this as part of its service.

Regardless of your application, to ensure you get the best possible results, it is important that you can trust your fresh blood supplier to deliver the quality products you need, when you need them. To learn more about the solutions offered by the team at Cambridge Bioscience, download our brochure today. Simply visit www.bioscience.co.uk/blood-sourcing-guide or click the button below.

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Authors

James Reed

James is the co-founder and Managing Director of Research Donors Ltd. With over 17 years' experience in the public health sector, he has an in-depth understanding of the operational and strategic management of medicine, pathology, surgery, therapies and theatres.

As an HCPC state-registered Biomedical Scientist, James also has considerable experience in haematology and blood transfusion and serves as a member of the NEQAS National Scientific Advisory Committee for blood cell morphology.

Dr Vashu Pamnani

Vashu is the Senior Business Manager for the Human Biospecimens Services at Cambridge Bioscience. Studying at the Max Planck Institute for Biochemistry and Psychiatry in Germany, he gained his PhD, focusing on novel ATPases in Archael bacteria in 1997.

Following this, Vashu undertook post-doctoral research at the Sealey Centre for DNA Repair at the University of Texas Medical Branch, USA, where he identified and isolated DNA repair mechanism proteins in yeast and humans. Vashu then went on to gain extensive experience of the commercial life science sector, before joining Cambridge Bioscience in 2007.

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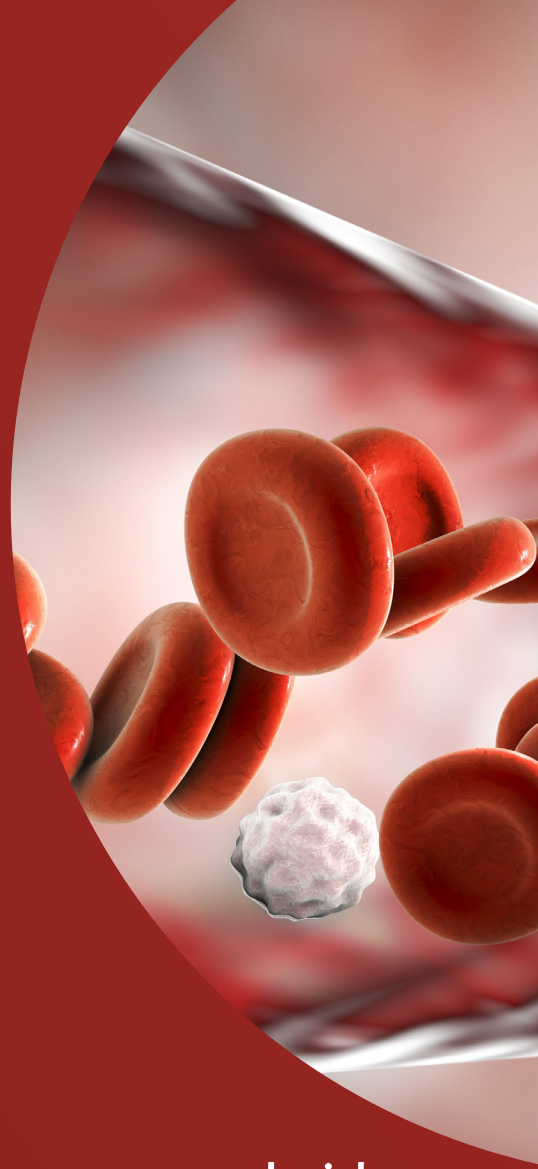

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