# INFORMATION FOR ADULT PATIENT AND CONSENT TO PARTICIPATE IN A CLINICAL RESEARCH STUDY

**Protocol Title:** **A prospective, open-label, phase I/III study investigating pharmacokinetic properties of BT524 and efficacy and safety of BT524 in the treatment and prophylaxis of bleeding in patients with congenital fibrinogen deficiency**

**Protocol Number:** **984**

**Sponsor:** **Biotest AG**

**Investigator:** _____

**Address:** _____

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**Phone:** _____

**Email:** _____

## ***A. Patient Information***

We are asking you to be a subject in a research study. If you agree to participate in this study, we would like to ask you to sign this informed consent document. Informed consent is a written agreement that you sign indicating your willingness to participate in this research.

Before you agree (consent) to participate in this study, it is important that you read (or have read to you) and understand the information contained in this informed consent document. This document describes your rights as a research patient and the study's purpose, procedures, risks, discomforts, precautions, alternate procedures and possible benefits. It is important for you to understand that no guarantees or assurances can be made regarding the study results. You should consent only after you have received all the necessary information and have had enough time to decide whether you wish to participate. Your signature on this form is voluntary and does not waive any of your legal rights or make any institutions or persons involved in this research any less

responsible for your well being. Also after having signed you can decide to withdraw your agreement at any time.

In this consent form, 'you' always refers to the study patient. If you are a legal representative, please remember that 'you' refers to the study patient.

***Review of the Study***

This clinical study will be conducted in accordance with the principles of the World Health Organization, as stipulated in the Declaration of Helsinki, and in accordance with the requirements of the drug approval agencies in Middle East and North Africa (MENA) region, and the European Union. Prior to study start an Independent Ethics Committee ***<country specific designation>*** favourably evaluated the conduct of the clinical study. This organization is an independent body of experts whose responsibility is to ensure the protection of the rights, safety, and well-being of patients involved in a study. In particular, the Ethics Committee reviewed whether the participants are adequately protected and their rights are safeguarded.

***Why am I being asked to be a part of this study?***

This research study is being done by the pharmaceutical company Biotest AG (Biotest). This study is evaluating how BT524, a Fibrinogen Concentrate (a medicine containing human fibrinogen) is handled by your body and how well it controls bleeding. Fibrinogen is normally made by our body and plays an important part in stopping bleeding.

You are being asked to take part in this study because you have a congenital fibrinogen deficiency that may result in severe bleeding events.

***Do I have to participate in this study?***

No, you do not have to participate in this study. Your participation is voluntary. Even if you decide today that you will participate, you can drop out of the study at any time. You do not have to give any reasons, and there will be no penalty. You will not lose any benefits or medical care to which you are otherwise entitled. If you decide to withdraw from the study before it ends, you will be asked to visit your study doctor for a final study visit/examination in order to make some final assessments and have an orderly end to your participation.

If new information becomes available about this study product during the study, we will tell you about it. If this happens, you can also leave the study at any time.

In certain circumstances, it may also happen that the study doctor decides to stop the study.

Your participation in the study could also be terminated by the study doctor without your consent, if the study doctor decides that this is in your best medical interest. Your participation may also be terminated without your consent by Biotest if you fail to comply with the requirements of the study or if Biotest decides to discontinue the study.

***Who is responsible for the data collected in this study?***

***<Insert Name and Address of Principal Investigator.>***

***Where will this study be done?***

This study is being conducted at approximately 5-7 centres in Middle East and North Africa (MENA) region and in the European Union. You will be one of approximately 40 subjects who will receive this study treatment.

***Introduction and Study Rationale***

Fibrinogen is made by our body and plays an important part in stopping bleeding. It does this by helping to thicken the blood (blood clotting) at the site of the bleed. Enough quantity of fibrinogen needs to be available in our body in order to achieve this, otherwise bleeding may continue. Some people are born with too little fibrinogen (congenital deficiency).

Congenital fibrinogen deficiency is a rare inherited bleeding disorder that is passed from parents to their children. It induces moderate to severe bleeding after injuries or surgical procedures. In the most severe form of this disease, fibrinogen levels are undetectable or extremely low.

Today, Fibrinogen Concentrate preparations are available in some countries. These preparations are derived from human donor blood and are used as a replacement therapy, providing fibrinogen to people with fibrinogen deficiency for the treatment and prevention of their bleeding. These Fibrinogen Concentrates are licensed (doctors can prescribe them to their patients) in several European countries and in the United States.

Biotest has also developed a Fibrinogen Concentrate, BT524, derived from human donor blood, which will be used in this study. BT524 is manufactured in Germany under very strict guidelines according to international regulations, to ensure that it is safe for patients. BT524 is not licensed and only available in clinical studies.

Patients with severe fibrinogen deficiency will be included in this clinical study, which is designed to follow the outcome of BT524 in their body and to demonstrate its efficacy and safety in their bleeding situations.

***Study Overview and Procedures***

The study will be conducted in two parts. In Part 1 you will receive a single infusion of BT524. Blood samples will be taken before and after the infusion to analyse what happens to BT524 and how long it stays in your body. In Part 2 you may receive BT524 as treatment in case of a bleeding event or as treatment prior to surgery to prevent a bleeding event. Only those who meet the study entry requirements can participate.

Part 1 of the study will last approximately up to 66 days. You will have a Screening Visit which will allow the study doctor to make sure you are eligible to take part in the study. Various examinations will be done and blood samples will be collected during the Screening Visit. Then within the next 17 days you will be admitted to the hospital and will receive one treatment with BT524. Each infusion of BT524 lasts an average of 45 minutes to one hour. You will have blood samples collected and undergo various examinations. You will stay in the hospital for 48 hours. During the time you are in the hospital, you will be encouraged to be active (spend time walking) to reduce the risk of clots that can sometimes form when patients are immobile. Each day additional blood samples will be taken and examinations will be done. Then you will need to come to the study centre about once every three days for the next two weeks for additional blood sampling and examinations. There will be a final check up on Day 49.

Part 2 of the study will begin after Part 1 and will last for at least 13.5 months, dependent on the timepoint when you will be included into the study. During Part 2, you may be treated with BT524

if you have a bleeding event or prior to any surgery you may need. After every BT524 treatment you will have one or two follow-up visits. You will be hospitalised during Part 2 if you are undergoing surgery or if the bleeding event requires it. The total duration of the study, for Part 1 and Part 2, will be at least 15.5 months.

It is very important that throughout the study period, you note and remember any illness and any medication you will be taking (please note their dates and their dosage also), because your study doctor will ask you about them at each of your visits to the hospital.

***Study Part 1: Measuring the fibrinogen and how long it stays in your body***

Before anything is done in the study you must give your written informed consent to participate. Then you will have a screening examination. First your study doctor will need to check that you have a severe fibrinogen deficiency (plasma fibrinogen level less than or equal to 50 mg/dL). He or she will consult your medical records to do this. If the study doctor treating you today is not your regular doctor, he or she may need to contact your regular doctor to check that you can participate in the study.

The study doctor will also perform a physical examination, take a detailed medical history (including what medications you are currently taking), ask about any allergies you may have and check that you will not be having any vaccinations within the 3 weeks before you have your BT524 infusion. You will also have the following procedures done as Screening assessments:

- measurement vital signs (temperature, blood pressure, pulse rate) and weight
- a urine pregnancy test, to ensure you are not pregnant (if applicable)
- an electrocardiogram (ECG) which makes a “picture” of the electrical activity of the heart, to check for heart problems
- an ultrasound of your lower limbs to ensure there are no blood clots
- a urine laboratory test
- blood samples taken from your arm for testing of routine laboratory parameters, specific clotting parameters, confirmation of fibrinogen levels, and to see if you have any antibodies to fibrinogen.

Then within the next 17 days you will be admitted to the hospital to begin the study; this will be Day 0. You are asked not to perform excessive physical exercise (extreme sports activities, sauna) during the 72 hours before you go to the hospital. You should not drink any alcohol and should limit your caffeine intake (for example, coffee, tea, chocolate, etc.) during the 24 hours before you go to the hospital.

On Day 0, the doctor will again confirm that you meet the criteria for entry into the study. If so, you will receive one infusion of BT524 through a needle into a blood vessel (vein) in your arm. Before you receive the infusion the study doctor will perform most of the examinations that were done at the Screening Visit, and collect blood samples for measurement of your fibrinogen levels and for routine and specific clotting laboratory parameters. Some samples will also be stored for further analysis, in case it becomes necessary to check for any viral infection.

Additional blood samples will be taken from the opposite arm. A sample will be collected as soon as the infusion is complete, and at the following time points after the infusion:

- 30 minutes
- one hour
- two hours

- four hours
- eight hours.

These blood samples will be analysed to measure your fibrinogen levels. The study doctor will also check your vital signs during and after the infusion and evaluate if you have had any unpleasant reactions (side effects) from the BT524 infusion. You will have a physical examination done by your study doctor 2 hours after the end of the infusion, and an ECG six hours after the end of the infusion.

On Day 1 and Day 2 you will remain in the hospital. Each day you will have blood samples collected to check routine and specific clotting parameters and to measure your fibrinogen levels. You will also have a physical examination, your vital signs will be measured and a urine laboratory test (Day2 only) will be done. The doctor will continue to check if you have had any side effects from the BT524 infusion. An ECG will be done on Day 1. The doctor will decide if an ultrasound is needed to check for any blood clots.

You will be discharged from the hospital on Day 2 after all the tests have been completed.

You will return to the hospital on Day 4, Day 7, Day 10 and Day 14 for a check up. At each visit the following procedures will be done:

- blood samples will be taken to measure your fibrinogen levels and for routine and specific clotting laboratory parameters
- a urine laboratory test (D14 only)
- a physical examination
- measurement of your vital signs and
- a check to see if you have had any side effects from the BT524 infusion.

A urine pregnancy test will be done on Day 14, if applicable.

If you have no bleeding events after the Day 14 Visit, or if you do not need any surgery, you will return to the facility on Day 49 (49 days after the infusion of BT524) for the last visit in Part 1. At this time the study doctor will do the following procedures:

- collect blood samples for specific clotting laboratory parameters and to see if you have developed any antibodies to fibrinogen. Some of the blood will be stored in case analysis is needed for viral infection.
- perform a physical examination
- measure vital signs
- check to see if you have had any side effects from the BT524 infusion.

IT IS VERY IMPORTANT THAT YOU COMPLY WITH THE EXACT DATES AND TIMES WHERE YOU SHOULD BE PRESENT IN THE HOSPITAL IN THIS PART 1 OF THE STUDY.

***Study Part 2: Treating or preventing a bleeding event***

Part 2 of the study will begin with the first bleeding event for which you receive treatment after your Day 14 follow up visit in Part 1. This may be a bleeding event that happens because of an injury, or it may be to prevent a bleeding event if you are going to have surgery (including dental surgery), If this occurs before your Day 49 Visit, the Day 49 Visit will be postponed.

The BT524 treatment you receive (dosage, number of infusions and length of infusions) will be based on how severe the bleeding is, the location and extent of the surgical procedure or bleeding, and your condition at the time of the event. If the study doctor decides it is necessary, you may have more than one infusion for a single bleeding event.

In Part 2, the BT524 infusion, and the blood sampling that will be done 1 hour after the infusion is done, will always be done in the hospital. However, you will only be hospitalised if the study doctor decides it is necessary. Otherwise, you will be discharged from the hospital or the dentist's office on the same day you came in.

Prior to the infusion of BT524, the study doctor will confirm that you meet all the requirements to participate in Part 2 of the study, and will carry out the following procedures:

- a physical examination
- measurement of your vital signs
- collection of blood samples to measure routine and specific clotting laboratory parameters, fibrinogen levels, and for storage, in case it become necessary to check for any viral infections
- a urine pregnancy test, to ensure you are not pregnant (if applicable)
- an ultrasound of your lower limbs.

1 hour after the end of the infusion, you will have blood sampling for determination of your fibrinogen level and of specific clotting laboratory parameters. Your vital signs will be measured regularly.

You may receive more than one infusion of BT524 for each bleeding event, if the study doctor decides it is necessary, and/or if after each infusion your blood samples show that your fibrinogen levels are too low. The study doctor may also decide that you need to stay overnight in the hospital, or that you need to come back to the hospital for your follow-up visits.

Follow up assessments performed in the hospital will include a physical examination, measurement of vital signs and blood sampling for the measure of routine and specific clotting laboratory parameters. If you have been hospitalised, these assessments will be performed at the following times:

- 24 hours after the last infusion of BT524
- at the day of your hospital discharge (if you stayed overnight)
- and anytime during your hospitalisation period when your study doctor decides it is needed.

At any time, the doctor may decide to do an ultrasound of your lower limbs.

If the doctor has decided it is not necessary for you to stay in the hospital, or return to the hospital, he or she will call you on further days to check your condition.

If the doctor decides it isn't necessary for you to return to the study facility, he or she will call you to check on your condition. After every infusion and at every visit or phone call, the doctor will ask you about any possible side effects from the BT524 infusion.

You will have a visit at Day 49 after the last infusion you receive for each bleeding event. The only exception is if you have another bleeding event prior to the Day 49 Visit. If this happens the Day 49 Visit will be postponed. At the Day 49 Visit you will undergo the following procedures:

- physical examination
- measurement of vital signs
- an ultrasound of your lower limbs (in case of thromboembolic event)
- collection of blood samples to for specific clotting laboratory parameters, for storage, in case it become necessary to check for any viral infections, and to see if you have developed any antibodies to fibrinogen
- and the doctor will ask you about any possible side effects you may have experienced since the last visit.

***Alternative Treatments***

Your study doctor will explain to you the standard treatments available for people who have congenital fibrinogen deficiency. Alternative treatment options are the use of cryoprecipitate, fresh frozen plasma or fibrinogen concentrates that might be available in your country to treat bleeding.

If the treatment with BT524 ever seems to be insufficient in controlling your bleeding events, the study doctor can use another available alternative treatment.

***Possible Benefits For You***

By participation in this study you will be treated with the Fibrinogen Concentrate BT524 when needed, and this may provide a direct benefit to you in terms of treating your bleeding. Your participation could also help advance medical research. Information learned may benefit future subjects who have congenital fibrinogen deficiency.

***Possible General Risks***

The risks and side effects of BT524 are expected to be in line with the safety profile of authorised fibrinogen concentrates. These are described in the next section. But as with any other treatment BT524 and study procedures in this investigation may cause unknown risks. All drugs, in theory, can have both temporary and permanent side effects or discomfort and can cause unforeseen adverse reactions, including death. A lot of measurements are done in this study to closely monitor your safety, and at every visit your study doctor and study staff will ask you about any side effects you may have experienced. If you have any problems, or any side effects you think might be related to this study or the study treatment, you should let the study doctor know at once.

***Known Possible Risks Associated with Fibrinogen Concentrate (Human)***

The safety of authorised fibrinogen concentrate (human) has been evaluated in clinical studies and by collecting reports of possible side effects since it was originally approved for use in Europe in 1986. The following side effects have been reported after market authorisation or in the scientific literature:

- Allergic or anaphylactic type reactions such as generalised urticaria (hives over the whole body), rash, fall in blood pressure, dyspnoea (shortness of breath)
- Increase in body temperature
- Thromboembolic episodes, including myocardial infarction and pulmonary embolism (episodes of formation or presence of a blood clot inside a blood vessel that may break off and damage some body organs such as the heart (heart attack) or the lungs (possible failure to breathe))

If allergic or anaphylactic-type reactions occur, the injection/ infusion has to be stopped immediately. In case of anaphylactic shock (life-threatening allergic reaction, such as difficulty breathing, low blood pressure, and/ or organ failure), your doctor will start with standard medical treatment for shock to treat this reaction.

There is a risk of thrombosis when patients with congenital fibrinogen deficiency are treated with human fibrinogen, particularly with high dose or repeated dosing. If you are given human fibrinogen, you should be observed closely for signs or symptoms of thrombosis.

If you have e.g. a history of coronary heart disease or myocardial infarction (heart attack), a liver disease, if you are having or just had a surgery, or if you are otherwise at risk of thromboembolic events or disseminated intravascular coagulation (blood clots form throughout the body's small blood vessels, which can reduce or block blood flow through the blood vessels, and can damage the body's organs), the potential benefit of treatment with human plasma fibrinogen should be weighed against the risk of thromboembolic complications. Caution and close monitoring should also be performed by your doctor.

BT524 is a Fibrinogen Concentrate made from human plasma (collected from blood). Products made from human plasma may contain infectious agents, such as viruses like hepatitis or HIV (the AIDS virus), that can cause disease. The risk that BT524 will transmit an infectious (viral) agent has been reduced by screening plasma donors for prior exposure to certain viruses, by testing for the presence of current viral infections, and by inactivating and/or removing certain viruses during the manufacturing process. Despite these measures, such products may still potentially contain infectious agents, including those not yet known or identified. Thus, the risk of transmission of infectious agents cannot be totally eliminated.

***Collection of blood samples***

Blood samples will be collected during this study. A needle is put into a vein in the arm and a blood sample is taken. Although one blood draw is usually sufficient, a second one may be necessary if the first is not successful. Blood drawing does not usually have any risks, but in rare cases it can cause pain, bleeding, burning, dizziness, fainting, or a bruise or an infection at the site where the needle was inserted to take the blood.

In each part of the study, blood samples will be drawn to study the effects of treatment with BT524 on blood fibrinogen and other measures of blood clotting, and for other laboratory tests related to general health (safety measures). Estimates of the amount of blood that will be taken are shown in the table below:

| | |
|---|---|
| **Part 1** | |
| Screening | 35.2 mL |
| Day 0 | 167,3 mL |
| Days 1-to-14 | 160,3 mL |
| Day 49 (Final visit) | 51,2 mL |
| **Part 2 :On-demand prophylaxis / treatment without hospitalisation** | |
| Days 0 | 85.9 mL |
| Optional visit | 14,7 mL |
| Day 49 (Final visit) | 45.2 mL |
| | |

| **Part 2 : On-demand prophylaxis / treatment with hospitalisation** | |
|---|---|
| Days 0 | 85.9 mL |
| 24h after end of last infusion and Discharge Day | 17.4 mL |
| Optional visit | 8,7 ml |
| Day 49 (Final visit) | 45.2 mL |
| | |
| **Total for**<br>Screening; Part 1; one bleeding event in Part 2; and two Day 49 visits (one in Part 1 and one in Part 2) | 559.8 mL or 571.2 mL in case of hospitalization |

For each additional bleeding event in Part 2, approximately 145.8 mL or 157.2 mL of blood will be collected over the 49 day treatment period. This is approximately 29 or 31 teaspoons.

The total amount of blood drawn during the study will vary according to how many bleeding events or surgeries take place during Part 2 and how many times you are examined for a “Day 49” follow-up. If you experience symptoms that seem like they might be an allergic reaction, the study plan calls for several additional samples. Many of the blood tests planned during Part 2 are blood tests that would likely be drawn as part of regular clinical care. If a bleeding or surgery event in Part 2 requires hospitalisation, other blood samples may be drawn by your doctors, including additional samples that measure the blood clotting at timepoints other than those named in the study plan. If this happens, the results will be recorded as part of the study.

The estimated blood requirement for the whole study as shown above is 559.8 mL or 571.2 mL in case of hospitalization. This is based on participation in Parts 1 and 2 with a Day 49 follow-up visit after each part. For purposes of comparison, when volunteer donors give blood to a blood bank for use in transfusion of patients, the blood volume taken is approximately 500 mL at one day.

A portion of the blood from the blood samples will be kept frozen to test for any viral infections in the future, if needed.

***Electrocardiogram (ECG)***

The ECG test that will be used to monitor your heart rhythm at different times during the study is a non-invasive, standard medical procedure performed routinely at medical centres. There are no direct risks from a diagnostic ECG but please ask your doctor if you have any questions.

***Ultrasound***

Ultrasound is another standard imaging method that is performed routinely at medical centres. Ultrasound uses low power sound waves to produce relatively precise images of structures within your body. The ultrasound examinations done during this study are also a non-invasive procedure, and will use a sonar device outside of your body. There are no direct risks from a diagnostic ultrasound exam but please ask your doctor if you have any questions.

***Pregnancy***

There is no information about the risks of Fibrinogen Concentrate on pregnancy or breast feeding. Therefore, if you are a woman, you will not be allowed to participate in the study if you are pregnant or breast feeding, and you are not allowed to get pregnant while participating in this study (until the final study visit has been done). During the study and at least one month after the last administration of BT524, women will have to use an approved contraceptive method: oral/ injectable/

implantable/insertable/topical hormonal contraceptives, intrauterine devices, female sterilization, partner's vasectomy or condoms. If you become pregnant during your participation in this study, you will be withdrawn from the study but representatives from Biotest will follow the progress and outcome of your pregnancy, to monitor your safety and the safety of your baby. In order to achieve this, Biotest will need to collect information from the physician following up your pregnancy.

***New Findings***

If new information becomes available during your participation in this study that may influence your willingness to participate, your study doctor will communicate this to you and/or your legal representative promptly.

***Costs to You***

The study treatment BT524, hospital stays, and any tests or procedures associated with the study (for example, blood tests) will be provided to you free of charge by Biotest. You will be responsible for paying all other charges associated with your treatment and follow up not related to this study. ***<to be adapted to country specific requirements and needs>***

***Compensation***

***<to be adapted to country specific requirements and needs.>***
***<As per Biotest, patients in Lebanon to receive the equivalent of US$80.00 per day. To be paid after Screening for patients who are Screening failures and after completion of Day 49 assessments for patients who are enrolled.>***
You will not receive payment for your participation in this study. You will receive full reimbursement for study-related expenses e.g. necessary travel and overnight stays, or they will be pre-arranged by Biotest. Your doctor and the institution will receive payment for the testing and data collection associated with this study.

If you have a planned or elective surgery during the course of the study, you or your insurance company will be responsible for the costs of the surgery, and all costs associated with your hospital stay. Biotest will only be responsible for the costs of the study treatment BT524 and any procedures required for this study.

***Research Related Injury – Information about Insurance***

For any costs directly resulting from health problems caused by the study treatment you are covered by Biotest's insurance during the clinical study.

Under the insurance ***<to be adapted as needed for each country: Name of Insurance Company>***, participants are obliged to report to the study doctor immediately any change (especially worsening) of the state of health, which might be connected to study participation. The study doctor also has to be informed about additional treatment (whether medical or non-medical) which is initiated while the patient is taking part in the study. After informing the study doctor you should also inform the insurance company. Otherwise insurance coverage cannot be guaranteed. In cases where you are not able to inform the insurance company by yourself, a relative should do this. The details of the insurance conditions will be provided to you by your doctor.

If you are injured as a direct result of receiving BT524 while following your study doctor's instructions, you should immediately contact _____ ***<insert study doctor and study coordinator names>*** at _____ ***<insert primary and back up telephone numbers for emergency contacts>*** and emergency medical treatment will be

provided. You will be reimbursed for the reasonable cost of your treatment not covered by your health or other insurance. By signing this form, you will not give up any of your legal rights that you may have under federal or state laws and regulations (as a research patient).

The insurance company for this study is:

***<to be added>***

Insurance No.: ***<to be added>***

In case of a claim to the insurance please contact:

***<to be added>***

Phone: ***<to be added>***

Fax: ***<to be added>***

Please note that any damages occurring during your travels to or from your study doctor/study hospital (e.g. accident, theft) are not covered by the above mentioned insurance and you are responsible for any consequences.

***Treatment after the End of the Study***

After study is completed, you can either return to your prior treatment or ask your doctor to continue on another Fibrinogen containing product that may be available in your country for the treatment of future acute bleeding.

***Source of Funding***

Biotest will provide funding for this study.

***Confidentiality and Data Protection***

In connection with the conduct of the research study, certain personal data will be collected and processed. This section aims at informing you on how the collection and processing of your personal data is handled in connection with the research study.
Please read this data protection information carefully. To confirm that you have read and understood its content and that you agree with the processing of your personal data as described herein, please provide your signature at the end of the document.

***Who is responsible for the data processing?***

As the sponsor, Biotest AG ("Sponsor") determines the purposes and means of the processing of your personal data in the context of the research study together with study center and/or the study doctor. Therefore, both the Sponsor and the study center/study doctor are considered data controller under applicable data protection laws.

Contact details of the Sponsor:

Biotest AG
Landsteinerstraße 5
63303 Dreieich
Germany
Tel.: 0049 6013 801 0

E-Mail: datenschutz@biotest.com

You can also contact our data protection officer at the e-mail address provided if you have any questions about data processing concerning you or if you wish to exercise any rights to which you are entitled.

Contact details of [study center and study doctor]:
[Insert name and contact details, including telephone number and e-mail address as necessary]

***What types of personal data are processed?***

In connection with your participation in the research study, the following personal data, including sensitive personal data, will be processed: your name/initials, sex, month, year of birth, contact details, information needed for reimbursement purposes, body weight and height, racial and ethnic origin, health data, including medical records and information on how you respond to the treatment, as necessary for the purpose of the research study, including blood and urine samples.

***How and for what purpose will my personal data be used?***

Your personal data will be collected by [the study doctor and the study center staff] and will be recorded on paper and/or on electronic data storage devices in/at [insert Clinical Site Name & Address] to run the research study and to monitor your safety as a study participant. In addition, some of your health data may be obtained from other treating physicians, provided you have released them from their obligation to maintain medical confidentiality.
The personal data collected will be processed in a manner that ensures appropriate security and confidentiality of your data. The Sponsor and its representatives (e.g. Clinical Research Organisation - CRO), as well as the study center and the study doctor will take all reasonable steps to protect your privacy as is required by applicable laws and regulations. These include, e.g., measures to prevent unauthorized access to or use of your personal data and the equipment used for the processing, e.g. by limiting access to the rooms and equipment where your personal data is stored and by pseudonymizing your personal data. Specifically, for the purpose of this research study, your name will be replaced by a code (study patient number) at the beginning of the trial, in order to rule out that you can be directly identified or to make your identification significantly harder. The list with patient names and their respective codes will be kept in a secure place, separate from the research study documentation. Only your study doctor and the study center staff/persons explicitly authorized by the study doctor have access to the list and can link your study patient number to your name in case of emergency in/at [insert Clinical Site Name & Address]. The analysis and usage of the data obtained during the research study by the study doctor and the study center staff takes place exclusively in pseudonymized form.
Your pseudonymized personal data may be disclosed to and processed under supervision of [insert CRO Name & Address], in accordance with applicable laws and the terms of this consent form. [insert CRO Name] and its authorized personnel have signed a non-disclosure agreement or are legally obliged to maintain secrecy. In addition, your personal data, including your ethnicity and health data can be:

a) kept available in/at [insert Clinical Site Name & Address] and disclosed to competent supervisory authorities for inspection or monitors appointed by the Sponsor to verify the proper conduct of the research study;

b) transferred, in pseudonymized form, to the Sponsor or to a service provider (Clinical Research Organization) commissioned by the latter for scientific evaluation,

c) transferred, in pseudonymized form, to the Sponsor and the competent authority for the marketing authorization if an application for a marketing authorization is filed;

d) transferred, in pseudonymized form, to the Sponsor and the competent authority and subsequently by the latter to the European database in the event of adverse events in connection with the investigational medicinal product,

e) transferred to the responsible health authority in case of a positive test result for hepatitis B and/or C, as far as the test result indicates an acute infection and to the Robert-Koch-Institut Berlin in case of a positive test result for HIV.

The blood and urine samples collected from you during the research study will be pseudonymized and shipped to, temporarily stored and tested by SYNLAB, SYNLAB Analytics & Services Germany GmbH, Bayerstr. 53, 80335 Munich / Germany.

The blood samples for Fibrinogen activity and antigen analyses will be shipped to, temporarily stored and tested by Institute for clinical Chemie and Lab Diagnostics at University Hospital Duesseldorf Moorenstraße 5, 40225 Duesseldorf, Germany.

The samples will only be used for research purposes and no analyses except those specified in the Patient Information for the research study will be performed without your prior consent and the approval of the competent Ethics Committee. Your identity is kept confidential as the laboratory will only receive your study patient number. All data gained through the analysis of the samples will be transferred in pseudonymized form to the Sponsor or to a site commissioned by the Sponsor for the purposes of further analysis within scope of the research study. Following the completion of the research study all samples will be destroyed except for those blood samples that will be frozen and stored in case you develop a viral reaction after you have been treated with BT524, or for further analysis in case of future suspicion of a new virus not yet identified. The frozen blood samples will be kept up to six months following the completion of the research study, or longer if required by applicable laws. The Sponsor will be responsible for storage and record keeping after completion of the research study. Subsequent to the six months period, the samples will be destroyed.

Neither the Sponsor, nor its CRO or any other company supporting the Sponsor in conducting the research study will be able to identify you directly, as these parties will receive pseudonymized personal data (e.g. month, year of birth, gender, race and health data relevant to the research study). This, however, does not apply to monitors, who are appointed by the Sponsor to ensure the appropriate implementation of the research study and that your rights and well-being is protected. They will verify that you have provided informed consent prior to participating in the research study and that the source documents and other trial records are accurate, complete, kept up-to-date, and maintained. For that purpose, these monitors require direct access to your personal data, including your health data. Further, your personal data may be disclosed in response to lawful requests by public authorities, including those to meet national security or law enforcement requirements. For this purpose, you have to release the study doctor from the obligation to maintain medical confidentiality. All other individuals or companies acting on behalf of the Sponsor for the purpose of conducting the research study have been sworn to confidentiality.

Your personal data will be processed for the purposes of analyzing and reporting the results of this research study; to develop future study protocols; for product performance monitoring and scientific research investigating new treatments, interventions and management procedures so that patient

outcomes are continually improved; and for ensuring compliance with medical, ethical and medical device laws and regulations.
If the Sponsor or the study doctor makes public any study results your identity will remain confidential, as the study results will be published in a form that does not allow your re-identification. With your permission, the study doctor will tell your family doctor about your participation in this study.

***Will my personal data be transferred to a third party?***
Qualified representatives of the Study Sponsor and its Clinical Research Organization, [insert CRO Name], and/or national and foreign regulatory authorities (including the Paul-Ehrlich-Institute (PEI) and /or the Food and Drug Administration (FDA); and/or independent auditors may look at your medical notes (including un-coded personal data), to check the information collected in this study, to check how the study was conducted and to monitor participant's safety. Further, [insert CRO Name] may be required to disclose your personal data in response to lawful requests by public authorities, including those to meet national security or law enforcement requirements.

***Will my personal data be transferred abroad?***
The disclosure of your personal data to the above-mentioned recipients, may include transferring your (pseudonymized) personal data to countries other than where you are based and outside the European Economic Area ("EEA"), such as the USA. The laws protecting personal data in third countries may not be not as strict as those applicable in Germany. However, the Sponsor will ensure that your personal data is transferred in compliance the provisions of the General Data Protection Regulation (GDPR). You may contact Biotest's data protection officer to get more information about the safeguards used to protect your personal data transferred to third country. Some ways in which your personal data is kept safe includes having study sites put the appropriate arrangements for the security of your personal data, removing some direct identifiers of your personal data or key-coding it so that it is not identifiable and collecting only the personal data needed. You may also ask the study doctor for a copy of those safeguards.

***On which legal basis is the personal data processed?***
The processing of your personal data, including your health data, is based on Article 6(1)(a) and Article 9(2)(a) of the GDPR in connection with [insert applicable national law].

***For how long will my personal data be stored?***
Your personal data will be kept as long as necessary for the purpose of conducting the research study, unless longer periods are provided by applicable laws. The code to link your study patient number to your name will be deleted by the study doctor as soon as the purpose of the research study allows for it. However, applicable laws may provide for a longer retention period of the personal data. In that regard, your personal data may be stored for at least

- 10 years following the completion or discontinuation of the research study, or
- 2 years following the investigational medicinal product has received its last approval for a marketing authorization, or
- 2 years after the development of the present investigational medicinal product has been stopped,

depending on whichever period is longer.

Absent other statutory or contractual retention periods, your personal data will be deleted afterwards.

***Do I have to agree to the processing of my personal data?***

No, your consent to the processing of your personal data is voluntary. However, you will not be able to participate in the research study without giving the consent for the processing of the above-mentioned personal data.

***Do I have the right to withdraw my consent to the processing of personal data?***

No, your consent to the processing of your personal data is irrevocable pursuant [insert applicable national law]. However, you are free to revoke your consent to participate in the research study at any time pursuant to [insert applicable national law]

***What happens with my personal data if I revoke my declaration of consent to participate in the research study?***

If you withdraw your consent to participate in the research study, the Sponsor and its representatives (e.g., CRO), as well as the study center and the study doctor will determine without undue delay whether the stored data is still required to:

a) determine effects of the investigational medicinal product,
b) ensure that those of your interests which are worthy of special protection are not prejudiced,
c) satisfy the obligation to provide complete marketing authorization documents.

Personal data that is no longer necessary for the above-mentioned purposes will be deleted immediately or anonymized (e.g., by destroying the key code linking your name with your study patient number). Only the study doctor is able to restore the personal reference.

***Which rights do I have in connection with my personal data?***

You have the right to gain access to your personal data stored by the Sponsor, the study center or the study doctor (Article 15 of the GDPR). You also have the right to request the rectification of inaccurate personal data without undue delay according to Article 16 of the GDPR. Under certain conditions, you can also request deletion of your personal data without undue delay (Article 17 GDPR) or restricted processing of your personal data (Article 18 GDPR). You may also have the right to receive the personal data concerning your person, in a structured, commonly used and machine-readable format and to transmit those data to another controller without hindrance (Article 20 GDPR).

If you believe that the processing of your personal data violates the provisions of the GDPR, you have the right to lodge a complaint with the competent data protection supervisory authority. Further information regarding competent supervisory authorities can be found on the website of the Federal Commissioner for Data Protection and Freedom of Information: www.bfdi.bund.de.

***Who can I contact if I have any questions?***

If you have any questions regarding the handling of your data, you can contact Biotest's data protection officer using the following contact details:

SPIE GmbH

Lyoner Straße 9
60528 Frankfurt, Germany
Phone : 0049 (0)69 6649-6921
E-Mail: datenschutz@biotest.com

As the Sponsor usually only receives pseudonymous information and, therefore, cannot always respond to all requests, please contact the study center's data protection officer with your questions. Please use the following contact details:
[insert contact details (address, telephone number and email address) of the study center's data protection officer]
Finally, a description of this research study will be available on http://www.ClinicalTrials.gov as required by U.S. Law and on the European Clinical Trials database at https://www.clinicaltrialsregister.eu as required by European Law. This website will not include information that can identify you. At most, this website will include a summary of the results. You can search this website at any time.

***Opportunity to Ask Questions***

At any time you are permitted and are encouraged to ask the study doctor ***<name & phone number>*** any questions about the treatment, the study, your rights as a patient, etc. In addition, to gain more information about this study and/or your rights as a patient, or if you feel that your questions have not been sufficiently addressed, contact _____ ***<name, address and telephone number of IEC contact person, human research office and/or hospital patient advocacy group>*** at this facility.

***B. Consent to Participate in the Study titled***

**Protocol Title: A prospective, open-label, phase I/III study investigating pharmacokinetic properties of BT524 and efficacy and safety of BT524 in the treatment and prophylaxis of bleeding in patients with congenital fibrinogen deficiency**

Please initial the box if you agree with the following:

☐ I confirm that I have read and understand the information sheet dated 02Aug2018 (Version 6.0) for the above study. I have had the opportunity and enough time to consider the information, ask questions and have had these answered satisfactorily.

☐ I have read the above explanations and I agree to participate in Part 1 and Part 2 of this study, if I am eligible. I understand that I should comply with the exact dates and time of my scheduled visits to the hospital in Part 1 and I will do so.

☐ If I have any question about this study, I realise that I am encouraged to ask them now or at any time during the study by contacting:

***<Principal Investigator's name, address, office number phone, fax, and email. Include possible alternate contacts too.>***

☐ I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.

☐ I agree to use or have my partner use an acceptable method of birth control (as defined in the consent form) from the beginning of the screening period until the final study visit.
*(Write a cross in the box if you are a male.)*

☐ I understand the pharmaceutical company carrying out this study, Biotest, has contracted an insurance policy to cover my participation in this study.

☐ I understand that I must not participate in the study if I am pregnant or breastfeeding or if I intend to become pregnant between the time that I have signed this consent form and until 30 days after my last dose of BT524.
*(Write a cross in the box if you are a male.)*

☐ I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals or representatives of Biotest, auditors, Independent Ethics Committee/Independent Review Board or from Regulatory Authorities in order to verify the conduct of the study and the protection of my rights and welfare. I give permission for these individuals to have access to my records.

☐ I am willing for my anonymous research data, and the results arising from the study, to be used as appropriate.

☐ I am willing for my anonymous research data to be sent to a country where the same level of data protection may not apply.

☐ I am willing for my general practitioner to be informed about my participation and progress in this study.

☐ I realise that I may report any objections to this study, either orally or in writing, to:

**< Insert country specific contact information, including address, email and phone>**

☐ I understand that, in signing this consent form, I give Biotest and ***<Principal Investigator>*** permission to present the results of this study, with my personal data being anonymised. The results may be presented in written and oral form, without further permission from me.

☐ I understand that I will receive a signed and dated copy this informed consent form for my records.

| **Patient's first name and family name (printed)** | **Signature of Patient (18 years and older)** | **Date** |
|---|---|---|
| **Legally Authorised Representative's first name and family name (printed) (if applicable)** | **Signature of Legally Authorised Representative (if applicable)** | **Date** |
| **Investigator's first name and last name (printed)** | **Signature of Investigator who conducted the Informed Consent Discussion** | **Date** |

*1 copy for the patient; 1 (original) to be kept in the Investigator File*

N.B The patient/patient authorized representative must date his/her own signature (or affix his/her thumb print if illiterate)

***Statement of an impartial witness in case of an illiterate patient/patient legally authorized representative:***

*I certify that the patient/patient legally authorized representative was given full information about the study as described herein, and agrees to participate to the study*

| **Impartial Witness first name and last name (printed)** | **Signature of Impartial Witness** | **Date** |
|---|---|---|