Subject Information Sheet and Informed Consent Form

Sponsor:	Biotest AG
Protocol No:	995
Protocol Title:	**A randomized, active-controlled multicenter, phase III study investigating efficacy and safety of intra-operative use of BT524 (human fibrinogen concentrate) in subjects undergoing major spinal or abdominal surgery (AdFIrst)**
Investigator:	PPD
Address:	PPD
	PPD
	PPD
Phone:	PPD
Fax:	PPD

1.0 General Information

You are being invited to participate in a research study. It is your decision if you wish to participate. Before you decide whether or not to take part in this study, we would like to explain why the research is being done and what it would involve for you. Your study doctor or member of the study staff will go through this Information Sheet with you and answer any questions you might have. Ask the study doctor or member of the study staff if there is anything you do not understand. You are free to talk to your family and friends about the study. Once you have a good understanding of the study, and if you agree to take part, you will be asked to sign the Consent Form. You will be given a copy to keep. You are free to withdraw at any time without giving a reason and this would not affect the standard of care you receive.

It is important to tell the study doctor everything regarding your health history otherwise you may harm yourself by participating in this study.

This study is being organized by the pharmaceutical company Biotest AG.

2.0 Purpose of Study

You have been asked to participate in this research study because you will undergo major spinal surgery and may experience major blood loss during the surgery.

The purpose of this research study is to find how well and how safe BT524 (human fibrinogen concentrate) is as a complementary treatment of severe blood loss in patients undergoing spinal surgery. Fibrinogen is one of the substances in the blood that helps with normal blood clotting.

BT524 (human fibrinogen concentrate) is an investigational drug. Investigational means that the drug is not currently approved by the regulatory authorities in your country for the treatment of severe blood loss during spinal surgery.

Another product that has been approved by the regulatory authorities in your country and is currently used to treat blood loss may also be administered to you. This product is called Fresh Frozen Plasma (FFP). FFP is the liquid part of blood that helps clotting and stops bleeding.

Approximately 200 adult subjects will participate in this research study in approximately 20 study centres in the EU and Switzerland.

Your participation in this study will last at least 36 days.

3.0 Description of the Procedures

In this study, the effectiveness of BT524 will be compared to the effectiveness of FFP in the treatment of severe blood loss for patients undergoing spinal surgery.

If you agree to participate in this study, you will be assigned to a group to receive either BT524 or FFP. To ensure the groups are comparable, each patient is assigned to a group by chance (randomly). The chances of you receiving BT524 are 50/50, i.e. like flipping a coin.

The study will be partially blinded which means that neither you nor your surgeon or surgical staff will know which treatment you have received (if needed for urgent medical reasons, your surgeon can be informed which treatment you received). The anaesthesiologist who administer the study drug will always know which treatment you received.

You will receive the study drug during surgery if your study doctor decides that you have experienced severe blood loss. In case treatment is needed during surgery you will receive either BT524 or FFP. The study drug will be given to you as an intravenous infusion – through a tube into a vein in your arm or hand.

4.0 Study Visits and Procedures

This section describes what will happen during the study.

Before any tests and exams can be initiated you are asked to sign and date this Informed Consent Form.

The following tests and procedures are performed during the study at the following time points:

a) Screening visit – prior to your spinal surgery to make sure it is safe for you to be in the study. This visit can happen anytime within 6 weeks before your surgery.

b) The day of your surgery (Day 1):
    - before your surgery (this can be done on Day 1 or 1 or 2 days before surgery)
    - during your surgery before the decision is made to treat you with BT524 or FFP for excessive blood loss (Day 1)
    - during your surgery after you have been given either BT524 or FFP (Day 1)
    - at the end of your surgery (Day 1)

c) Follow-up Visits during your hospitalization on Day 2, Day 3, Day 5, and Day 8

d) Closing Visit at least 5 weeks but not later than 10 weeks after your surgery

a) Screening visit

Before being eligible to receive BT524 or FFP as part of this research study you will undergo some tests and procedures. Having these tests and procedures will not guarantee that you will be able to receive BT524 or FFP. Your participation in the treatment part of the study (treatment with BT524 or FFP) will depend on the results of your laboratory tests, study guidelines, and the study doctor's judgment.

At the first visit, called the screening visit, the study doctor will ask some questions about you (including your date of birth, gender, and race), your general health, and your medical and surgical history. There will be a physical examination and assessment of your vital signs where your weight, height, heart rate, blood pressure, respiratory rate and body temperature will be recorded.

Blood (38 mL) and urine samples will be collected. These samples will be used to check your general health, if you are pregnant (if you are female and of child bearing potential) and to check how well your blood will clot.

The blood samples collected at screening visit will also be used to check if you are infected with human immunodeficiency virus (HIV) and hepatitis B and C (HBV and HCV). Depending on the local requirements, if your test is positive for HIV or Hepatitis B or C, these results will be reported to the Public Health Department. Additionally, it is possible that some insurance companies, employers, government agencies, or health care providers might also require you to report these tests results.

Some of the tests above may have been performed by your doctor as standard of care before you sign this informed consent form. If this test was done within 6 weeks before your first scheduled treatment with BT524 or FFP, your doctor may decide to not repeat this test and to use the result obtained from standard of care for the purpose of the study.Blood samples (5 mL) will be collected and stored in case you develop a viral reaction after you have been treated with BT524 or FFP, or for further analysis in case of future suspicion of a new virus not yet identified.

b) The day of your surgery (Day 1)

Before the surgery (Day 1, or 1 or 2 days before surgery), the study doctor will ask some questions about your medical and surgical history as well as your symptoms. There will be a physical examination and assessment of your vital signs where your weight, heart rate, blood pressure, respiratory rate and body temperature will be recorded.

Blood (44 mL) and urine samples will be collected. These samples will be used to assess your general health and to check how well your blood is clotting.

If you are female and of child bearing potential, prior to surgery you will have a urine pregnancy test.

During the surgery (Day1) your blood loss will be measured. Only in case your blood loss will be approximately 1 L and a treatment to control the bleeding is required, the study drug will be given to you. If you do not experience a major blood loss and your blood clotting is normal, a treatment with BT524 or FFP is not necessary. Your care during surgery will not be affected in any way.

During the surgery (Day1) and at the end of the surgery (Day1), the study doctor will monitor blood loss, vital signs including heart rate, blood pressure, respiratory rate and body temperature as well as medication you receive. After surgery you will be asked about your symptoms. Blood samples will be collected during (84 mL) and at the end of the surgery (38 mL). These samples will be used to assess your general health and to check how well your blood is clotting.

The following tests and procedures are only performed if either BT524 or FFP was given to you.

c) During your hospitalization on Day 2, Day 3, Day 5, and Day 8

There will be a physical examination and assessment of your vital signs where your heart rate, blood pressure, respiratory rate and body temperature will be recorded.

Blood (146 mL) and urine samples will be collected. These samples will be used to assess your general health and to check how well your blood is clotting.

You will be asked about your symptoms and the doctor will speak to you about how you feel.

d) Closing Visit at least 5 weeks but not later than 10 weeks after your surgery

There will be a physical examination and assessment of your vital signs where your heart rate, blood pressure, respiratory rate and body temperature will be recorded.

Blood (36 mL) and urine samples will be collected. These samples will be used to assess your general health and to check how well your blood is clotting.

Blood samples (5 mL) will be collected and stored in case you develop a viral reaction after you have been treated with BT524 or FFP or for further analysis in case of future suspicion of a new virus not yet identified. If the retention sample is not taken at the closing visit, your study doctor can schedule a follow-up visit to ensure that a sample for viral safety testing is available.

You will be asked about your symptoms and medication you have taken following your discharge from hospital and the doctor will speak to you about how you feel.

5.0 Subject Responsibilities

As a participant in this study, you have certain responsibilities to help ensure your safety. These responsibilities are listed below. It's your obligation to:

- Complete all required visits to the study centre;
- Report all side effects and medical problems to your study doctor or staff;
- Report if you (or your partner, if you are a man) have become pregnant; and
- Inform the study doctor or staff if you decide to no longer participate in the study. You may be asked to complete a close out visit.

6.0 Potential Benefits

We cannot promise the study will benefit you. The study drug may reduce the level of blood loss during surgery or may have no effect at all. The information we get from this study may help improve the treatment of people with excessive blood loss during major spinal surgery.

7.0 Potential Risks and/or Discomforts

In this study, you will receive either BT524 or FFP. There are benefits and risks associated with treatment in both groups, which your study doctor will discuss with you for both products BT524 and FFP.

You may have side effects from study drugs, or the procedures used in this study.

Side effects usually vary from person to person and can range from mild to very serious. If you have any side-effects as a result of taking part in this study, tell your study doctor right away, even if you do not think they may be due to BT524 or FFP.

Below you are informed about the potential risks (potential side effects) associated with BT524.

Potential General Risks

The study doctor will closely monitor your safety, and at every visit your study doctor and study staff will ask you about any side effects, you have experienced. If you have any problems, or any side effects during this study, you should let the study doctor know at once.

Known Potential Risks Associated with Fibrinogen Concentrate (Human)

The below side effects have been reported for other human fibrinogen concentrate products and therefore they can potentially occur in this study.

- **Allergic reaction**

Allergic reaction or anaphylactic type reactions such as generalised urticaria (hives over the whole body), rash, fever, chills, nausea, vomiting, abdominal or back pain, fall in blood pressure, dyspnoea (shortness of breath) is always possible. Serious allergic reactions that can be life-threatening may occur. If allergic or anaphylactic-type reactions occur, the injection/ infusion has to be stopped immediately. In case of a life-threatening allergic reaction such as difficulty breathing, low blood pressure, and/ or organ failure (anaphylactic shock), your doctor will start with standard medical treatment for shock to treat this reaction.

- **Increase in body temperature**

- **Blood Clot** (thrombosis/ thromboembolic events)

There is a risk of blood clot when patients are treated with human fibrinogen, particularly with high dose or repeated dosing. If you are given human fibrinogen, you will be closely observed for signs or symptoms of blood clots.

The blood clots may results in:

- Heart attack, the warning signs are sudden chest pain or shortness of breath.
- Stroke, the warning signs are sudden onset of muscle weakness, loss of sensation and/or balance, decreased alertness or difficulty in speaking.
- A serious condition called pulmonary embolism, the warning signs are chest pain, difficulty in breathing or coughing up blood.
- Clot in a vein (venous thrombosis), the warning signs are redness, feel warmth, pain, tenderness, or have a swelling of one or both legs.

For your safety please inform your study doctor, who will estimate the risk of having a thromboembolic event based on the individual medical history as mentioned below:

- If you have a history of coronary heart disease or myocardial infarction (heart attack), a liver disease,
- If you underwent or will undergo a surgery,
- If you are at risk of blood clots (thromboembolic events) or disseminated intravascular coagulation (a condition that is associated with uncontrolled clotting and bleeding in the body that can cause serious bleeding and organ damage),
- If you have family history of blood clot (thromboembolic events).

In case of over dosage, the risk of development of blood clots complications is enhanced. Pre-cautionary and close monitoring and appropriate measures will be put in place by your study doctor.

- **Transmission of infectious agents (Virus safety)**

BT524 is a fibrinogen concentrate made from human plasma (collected from blood). Products made from human plasma may potentially 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. The measures taken are considered effective for enveloped viruses such as human immunodeficiency virus (HIV), hepatitis B virus and hepatitis C virus, and for the hepatitis A and parvovirus B19 viruses.

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.

Known Potential Risks Associated with Fresh Frozen Plasma (FFP)

The side effects for the FFP listed in this Consent Form are derived from the Product Information of a reference FFP product.

Hypersensitivity reactions to this product may rarely be observed and are:

- Usually mild type of allergic reactions consisting of localised or generalised skin rashes, redness, hives, itching, and increased sweating.
- More severe forms can be complicated with a drop in the blood pressure and with swelling of the face, the tongue, and difficulty swallowing.
- Very rarely, some patients may experience severe allergic reaction that might have a rapid onset and is characterised with complications like low blood pressure, increased heart rate, or irregular heartbeats, constriction of the airways and difficulty breathing, wheezing, coughing,

breathlessness, nausea, vomiting, diarrhoea, abdominal or back pain. Such severe reactions may progress to shock, including unconsciousness, collapse of the circulation system, failure of breathing, heart failure, and in very rare occasions even to death.

Other side effects connected to the use of this medicinal product may include the following symptoms (frequencies cannot be estimated from the available data, as these side effects have been mainly observed during post-approval use):

- Reduced sense of touch, dizziness, flushing, chills (shivering with or without fever), local swelling (oedema), fever.
- Furthermore, there may be abnormal symptoms in the lungs with lack of oxygen, anxiety, agitation, restlessness, reactions of the application site, low or high blood pressure, and sometimes very rarely, a generalized predisposition to bleeding.
- Negative effects can be caused by citrate contained in FFP. You may experience symptoms like fatigue, tingling feelings (paraesthesia), tremor and low calcium levels.

FFP may increase the risk of blood clots which may result in:

- Heart attack, the warning signs are sudden chest pain or shortness of breath.
- Stroke, the warning signs are sudden onset of muscle weakness, loss of sensation and/or balance, decreased alertness or difficulty in speaking.
- A serious condition called pulmonary embolism, the warning signs are chest pain, difficulty in breathing or coughing up blood.
- Clot in a vein (venous thrombosis), the warning signs are redness, feeling warmth, pain, tenderness, or have a swelling of one or both legs.

In all patients that are at risk for increased clotting of the blood, special caution will be exercised, and appropriate measures will be considered.

In rare cases, an incompatibility between antibodies (natural chemicals in the body that fight infections) in FFP and antigens (a substance that, when introduced into the body, stimulates the production of antibodies against it) in your blood can result in haemolytic transfusion reactions with destruction of your red blood cells leading to low red blood cell count. The symptoms may include chills; fever; a non-productive cough; difficulty in breathing; rash; and bleeding within the body.

Infusion of FFP may give rise to specific coagulation factor antibodies.

High dosages or infusion rates may induce increased blood volume; oedema (fluid accumulation) in the lungs and/or heart failure.

Depending on type and severity of adverse reactions, the infusion rate must be reduced, or the administration must be stopped. Appropriate action will be taken by your doctor.

Please inform your doctor if you have any type of immune deficiency concerning the secretory IgA antibodies, a severe problem with your liver and possible diagnosed deficiency in the synthesis of Protein S, manifest or hidden heart diseases and decompensation, swelling of the lungs, as well as a previous reaction to this type of product. In these instances, the FFP used in the study should be administered with special caution under these conditions

Transmission of infectious agents (Virus safety)

Products made from human plasma may potentially contain infectious agents, such as viruses like hepatitis or HIV (the AIDS virus), that can cause disease.

Certain measures are put in place to prevent infections being passed on to patients. These include careful selection of the blood and plasma donors to make sure those at risk of carrying infections are excluded, and the testing of each donation and pools of plasma for signs of virus/infections. Manufacturers of these products also include steps in the processing of the blood or plasma that can inactivate or remove the viruses. Despite these measures, when medicines prepared from human blood or plasma are administered, the possibility of passing on infection cannot be totally excluded. This also applies to any unknown or emerging viruses or other types of infections.

Unknown/Unexpected Risks and Discomforts

There are adverse events that are not known or happen rarely when patients receive these study drugs. You will be told of any new information that might cause you to change your mind about continuing to take part in this study.

Other Study Procedures

In addition to the potential side effects listed above, you may also experience some discomfort, bruising, and possibly infection as a result of taking blood samples.

8.0 Pregnancy/Birth Control (Female Participants)

The risks of taking BT524 by pregnant women or to an unborn baby are unknown. For this reason, a negative pregnancy test at screening visit is mandatory. You must not become pregnant during this study. If you are a woman of childbearing potential, you are obliged to use an effective form of birth control during this study and for at least one month after the last administration of study drug. Acceptable methods of birth control include consistent use of an approved oral contraceptive (birth control pill), an implantable contraceptive, an injectable contraceptive, a double-barrier method (diaphragm with spermicide, condom with spermicide), or abstinence. True abstinence is only considered an acceptable method of birth control, if it is in line with your usual lifestyle. Oral, implantable (e.g. vaginal delivery system), or injectable contraceptives are only considered effective if used properly and started at least 30 days prior to the screening visit. Some drugs (e.g., antibiotics) may interact with hormonal contraceptives, making them less effective. Please inform your study doctor of all other medications you are taking. If you suspect that you may have become pregnant during the study, you must contact your study doctor immediately. Your study doctor may want to follow the progress of your pregnancy until the baby is born. The effects of BT524 on a nursing infant are unknown; if you are breastfeeding, you cannot participate in the study.

9.0 Male Reproduction/Birth Control

There are no specific birth control measures required, however the usage of condoms are strongly advised for male participants during the study.

If you suspect your female partner may be pregnant, you must contact the study doctor immediately. Your study doctor may want to follow the progress of your partner's pregnancy until the baby is born.

10.0 Reimbursement/Cost for Participation

There are no anticipated costs for you while participating in the study. The study medication will be provided to you free of charge. You will not be charged for any procedure performed for the purpose of this study.

You will not be paid for your participation in the study, but you will be reimbursed for any reasonable expenses incurred by taking part, for example travel to and from the study site for your visits and/or parking at the hospital.

11.0 Alternative Treatments

If you do not wish to participate in this study, your treatment will be continued by your regular doctor and your care during surgery will not be affected in any way.

Your study doctor will explain the standard treatments available for people who have acquired fibrinogen deficiency (blood clotting problems) caused by major surgery with excessive blood loss. Alternative treatment options are the use of cryoprecipitate, fresh frozen plasma or fibrinogen concentrates that might be available in your country to treat bleeding. There are benefits and risks associated with this medication, which your doctor will discuss with you.

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

12.0 Confidentiality and Data Protection

To participate in this study, it is necessary that you read and sign the data protection information and consent form attached in **Appendix 1**.

13.0 Injury Compensation – Information about Insurance

Before participating you should consider if this will affect any insurance you have and seek advice if necessary.

In the event of an illness or injury that is determined to be directly related to the administration of study drug or the properly-performed study procedures, the Biotest AG agrees to pay all reasonable and necessary medical expenses to treat such illness or injury provided that you have followed the directions of the study doctor, and that you have not otherwise been reimbursed by your personal insurance, a government program, or other third party coverage for such medical expenses. No other compensation will be offered by Biotest AG or the Institution. Financial compensation for such things as lost wages, disability, or discomfort due to any research-related injury has not been made available. By signing this form, you are not waiving any legal right to seek additional compensation through the courts.

In accordance with country regulation, Biotest AG has issued an insurance policy.

Name and address of the insurance company: PPD

Policy number: PPD

13.1 Who to Contact to Ask Questions or Report a Possible Research Related Injury or Reaction

If you have any questions concerning your participation in this study, or if you feel you have experienced a research-related injury or a reaction to the study drug, you should contact:

Dr. PPD at PPD

13.2 Who to Contact To Report a Breach of Confidential Information

If you feel that there has been a breach of your confidential information, you should contact the principal investigator for this study:

Dr. PPD at PPD

13.3 Who to Contact to Ask Questions about Your Rights as a Research Subject

This research project has been reviewed by the PPD. This committee or board is a group of individuals from the community responsible for the review and approval of research proposed to be conducted. If you have questions about your rights as a research subject, you may contact:

The PPD at PPD.

14.0 Voluntary Participation and Termination of Participation

Your participation in this research study is voluntary. You can choose not to participate in this study either at the beginning or at any time during the study. Your choice will not have a negative impact on your present or future health care. There will be no disadvantage or loss of benefits to which you are otherwise entitled. To ensure your safety, you will be asked to undergo a final evaluation visit. If you wish to withdraw from the study, you should contact:

PPD or study personnel at PPD.

Your participation in this study may be discontinued without your consent by the investigator or the sponsoring company if you fail to follow the investigator's instructions. You may also be withdrawn from the study if, in the investigator's opinion, the study drug is ineffective, harmful, or has medically unacceptable side effects, or for other reasons at the discretion of the Sponsor or investigator. If you are withdrawn from the study, you may be asked to have the appropriate medical tests and follow-up to evaluate your health and safety.

15.0 What if new information about the study drug becomes available

Sometimes new information about the study drug is received. You will be told if any relevant new information becomes available. If the information is available prior to surgery, it may affect your willingness to carry on taking part in the study. If this happens after surgery your study doctor will be available to discuss the impact of new information with you. In either case your study doctor will contact you as soon as possible. If you decide not to carry on in the study, your study doctor will make arrangements for your care to continue. If you decide to continue in the study, you may be asked to sign a new consent form.

Also, if new information becomes available, your study doctor may stop your participation without your consent. If this happens the reasons will be explained, and arrangements made for your care to continue.

Consent Form

Sponsor:	Biotest AG
Protocol No:	995
Protocol Title:	A randomized, active-controlled multicenter, phase III study investigating efficacy and safety of intra-operative use of BT524 (human fibrinogen concentrate) in subjects undergoing major spinal or abdominal surgery (AdFIrst)
Investigator:	PPD
Address:	PPD
	PPD
	PPD
Phone:	PPD
Fax:	PPD

- I have read the description of the clinical research study and have had it explained to me in words and terms that I understand. I understand that my participation is voluntary. I know enough about the purpose, methods, risks, and benefits of the research study.
- I voluntarily agree to participate in this study.
- The study doctor will inform me of any new findings developed during the course of this study, which may affect my willingness to continue participation.
- I authorize the release of my study-related medical records to Biotest AG, the regulatory authorities, and the Ethics Committee/IRB.
- I understand that I will be provided a copy of this signed consent.
- I understand that I am free to withdraw my consent and to stop my participation in this study at any time.
- By signing this consent form I understand that I have not waived any of the legal rights as a participant in a research study.

Subject
(or legally authorized representative as applicable)

_____

Subject Printed Name
(or legally authorized representative) Signature Date

Person Obtaining Consent

Printed Name & Title	Signature	Date

Witness (if applicable)

Witness Printed Name	Signature	Date

Appendix 1:
Data protection information and consent form

In connection with the conduct of the research study, certain personal data will be collected and processed. This document 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.

1.0 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

PPD

PPD

PPD

PPD

Contact details of [PPD]:

[PPD]

2.0 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, 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.

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

Your personal data will be collected by [PPD] and will be recorded on paper and/or on electronic data storage devices in/at [PPD] 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 [PPD]. 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 PPD , in accordance with applicable laws and the terms of this consent form. PPD and its authorized personnel have signed a non-disclosure agreement or are legally obliged to maintain secrecy. In addition, your personal data, including sensitive personal data, may be:

a) kept available in/at [PPD] 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 an agency 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 PPD . 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 some of your blood, which 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. If at all, they will receive pseudonymized personal data (e.g. 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 sensitive personal 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.

4.0 Will my personal data be transferred to a third party?

Qualified representatives of the Study Sponsor and its worldwide affiliates; and/or PPD and its worldwide affiliates; 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, PPD 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.

The disclosure of your personal data to the above-mentioned third parties, may include transferring your (pseudonymized) personal data to countries other than where you are based and outside the European Union (“EU”) / 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 the study doctor 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.

5.0 On which legal basis is the personal data processed?

The processing of your personal data, including any sensitive personal data, is based on Article 6(1) lit. a) and Article 9(2) lit a) of the GDPR in connection with [insert applicable national law].

6.0 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.

7.0 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.

8.0 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]

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

In case 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 which of your personal data collected and stored may still be necessary 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).

10.0 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 (see Article 17 of the GDPR) or restricted processing of your personal data (see Article 18 of the 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 in particular in the Member State of your habitual residence, place of work or place of the alleged infringement. 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.

11.0 Who can I contact if I have any questions?

You can contact Biotest's data protection officer using the following contact details:

PPD

You can also contact the study center's data protection officer using the following contact details:

[PPD
]

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.

Consent

I have read and understand the above data protection information concerning the processing of my personal data in connection with the conduct of the research study 995 (EudraCT number: 2017-001163-20).

By signing this consent form, I agree that:

(1) My personal data, including sensitive personal, is collected, processed and stored for the purposes of the research study as described above.

(2) My personal data, including sensitive personal data, can be transferred to and shared with third parties both within and outside of the EEA, including countries that may not have the same level of data protection as [insert country name], as described in the data protection information above.

(3) My health data may also be obtained from other treating physicians, in particular, whom I hereby release from the physician-patient confidentiality obligation.

_____
Print name of participant

_____ _____
Signature of participant Date (day, month, year)

Furthermore, I agree that my family doctor

_____
Print name of family doctor

will be informed of my participation in the researchResearch study.
(If this is not wanted, please leave in blank.)

_____
Print name of participant

_____ _____
Signature of participant Date (day, month, year)