Patient Information and Informed Consent Form [Master version in English]

Patient Information

Title of the study:

Double-blind, randomised, placebo-controlled, multi-centre phase III clinical study comparing the combination of ursodeoxycholic acid capsules plus budesonide capsules to ursodeoxycholic acid capsules plus placebo in the treatment of primary biliary cirrhosis

(BUC-56/PBC)

Dear patient,

You are invited to take part in the clinical study mentioned above. This clinical study compares the efficacy and tolerability of the combination of ursodeoxycholic acid (UDCA) capsules plus Budesonide capsules with the combination of UDCA capsules plus placebo for the treatment of primary biliary cirrhosis (PBC). This patient information sheet explains the purpose and the procedure of this clinical study. Please take your time to read the following text thoroughly. If you have any questions or are unsure about anything, please do not hesitate to ask the study doctor, i.e. the doctor who is taking care of you and conducts this study.

RATIONALE AND BACKGROUND

You were diagnosed with primary biliary cirrhosis (PCB) and the diagnosis was confirmed during the past 6 months with the analysis of liver tissue samples. Throughout the past 6 months you were treated with UDCA, but your liver continues to show signs of the inflammation.
Currently, UDCA is the only approved treatment for PBC. The therapy is most effective if treatment is initiated at an early stage of the disease. However, this study aims at enrolling patients for whom the UDCA therapy is not adequately effective.
The locally acting corticosteroid Budesonide appears to be suitable as concomitant therapy with the UDCA treatment. The efficacy of Budesonide for the inflammatory bowel disease (Crohn's disease) has been confirmed. In addition, Budesonide has been used for a number of liver disorders. Only two studies investigating the combination of Budesonide plus UDCA for the treatment of PBC have been conducted so far. Both studies showed that the combination treatment is superior to the UDCA monotherapy and Budesonide was well tolerated. Our goal is to continue investigating this outcome further.

PURPOSE OF THIS CLINICAL STUDY

The purpose of this study is to evaluate the efficacy of Budesonide as additional treatment to the common UDCA therapy. Therefore, one treatment group will receive UDCA plus Budesonide, while the other group will receive a combination of UDCA plus placebo. A placebo looks like the actual drug, but it does not contain any active ingredients.
In addition, every patient will be asked to evaluate the tolerability of the study drugs and to document the quality of life by means of a survey.

DURATION OF THE CLINICAL STUDY

The treatment duration will be 36 months for you. During this time, you will visit your study doctor 11 times. Because Budesonide is not approved for the treatment of PBC, it will likely not be prescribed to you at the end of the study period.

STUDY DESIGN

A total of about 144 patients from 14 different European countries will be enrolled in this study. The study will compare two treatment groups by means of a so-called "double-blind method". This means that neither you nor your study doctor knows which treatment you are receiving. You will be assigned randomly (i.e. "randomised") to one of the following two treatment groups. Neither you nor your study doctor will have any influence on the assignment to a treatment group:

The following drugs will be administered <u>daily</u>:

Treatment group A:	12-16 mg of UDCA/kg of body weight (Ursofalk® 250 mg capsules) 2 or 3 Budesonide capsules (Budenofalk® 3 mg capsules; the number of capsules depends on your "liver parameters")

Treatment group B:	12-16 mg of UDCA/kg of body weight (Ursofalk® 250 mg capsules) 2 or 3 placebo capsules (3 mg placebo capsules; the number of capsules depends on your "liver parameters")

A so-called 2:1 randomisation will be used, i.e. double as many patients will randomly be assigned to treatment group A (about 96 patients) as to treatment group B (about 48 patients).
The active ingredient Budesonide (Budenofalk® 3 mg capsules) used in this study is commercially available in the participating countries for the treatment of Crohn's Disease and chronic diarrhoea induced by collagenous colitis.
The active ingredient UDCA (Ursofalk® capsules) used in this study is commercially available in the participating countries for the treatment of PBC.
The drugs are packaged into boxes with a neutral look to ensure that neither you nor the study doctor is able to determine which of the two treatment groups you have been assigned to. In case of an emergency, your doctor is able to "unblind" your treatment, i.e. s/he is able to find out which study treatment you received.

SEQUENCE OF THE CLINICAL STUDY

Over the course of the study, you will visit your study doctor as follows:

Visit	Activities / examinations
Screening examinations (day -28 to 0) Eligibility examinations	Before the individual study activities start, the study doctor or his/her staff will discuss the study with you. You will be asked to read this patient information carefully before confirming your study enrolment by signing the declaration of consent. The study doctor will perform a number of tests and examinations to ensure that you are eligible to enrol in the study: • Your study doctor will document your general information (e.g. age, gender), the history of your PBC, whether you have any other disorders and whether you are taking any drugs. • The study doctor will perform a physical examination and measure your heart rate, blood pressure and body temperature. • In addition, the study doctor will ask you to see an ophthalmologist to perform an eye exam (see below). • If more than 6 months have elapsed since the last examination of your liver tissue, your study doctor will collect a new tissue sample (liver biopsy, see below). • If you agree, the study doctor can perform a FibroScan to examine the status of your liver (see below). • Your bone density will be measured by means of dual energy X-ray absorptiometry (DXA, see below). • You will be asked for a blood (approximately 20 mL) and a urine sample for routine laboratory tests and for serological analyses (hepatitis, HIV, see below). • Another blood sample (about 15 mL) will be drawn for additional laboratory analyses (see below). • A pregnancy test will be performed if you are a woman of child-bearing potential. • You will be asked to complete a quality of life questionnaire (PBC-40) and to rate the degree of your itchiness. • Finally, you and your study doctor will schedule an appointment for study visit 1.
Visit 1 (day 0) Randomisation	• The study doctor will review the results of the eligibility examination to make sure that you meet all the requirements for enrolling in the study. • S/he will be giving you a diary and explain how to complete it. • In addition, the study doctor will give you the study drugs and instruct you on how to take them. • You and your study doctor will schedule an appointment for the next study visit.

Visit		Activities / examinations
Visit 2 (day 14) **Visit 3** (day 28)	Follow-up examinations	• The study doctor will measure your heart rate, blood pressure and body temperature. • Blood (about 7.5 mL during each visit) and urine samples will be collected for routine laboratory tests. • The study doctor will ask you about possible discomforts or diseases you experienced and about any drugs you may have taken. • S/he will remind you to return the study drugs and the diary at visit 4. • You and your study doctor will schedule an appointment for the next study visit.
Visit 4 (month 3) **Visit 5** (month 6) **Visit 6** (month 9) **Visit 7** (month 12) **Visit 8** (month 18) **Visit 9** (month 24) **Visit 10** (month 30)	Follow-up examinations	• The study doctor will perform a physical examination and measure your heart rate, blood pressure and your body temperature. • In addition, the study doctor will ask you to see an ophthalmologist to perform an eye exam (at visit 7 and 9 only). • Blood and urine samples will be collected for routine laboratory tests. • An additional blood sample will be collected for additional laboratory and serological analyses (at visit 7 and 9 only). Overall, about 140 mL of blood will be drawn over the course of these follow-up examinations. • The study doctor will ask you about your opinion concerning the efficacy and tolerability of the study drug and to rate the degree of your itchiness. • You will be asked to fill out a quality of life questionnaire (PBC-40) (at visit 7 and 9 only). • Your bone density will be measured by means of X-rays (at visit 7 only). • The study doctor will document potential discomforts or diseases you experienced as well as any drugs you may have taken. • You will return the dairy and any used/unused study drugs. • The study doctor will give you a new diary and new study drugs and instruct you on how to use them. • You and your study doctor will schedule an appointment for the next study visit.

Visit	Activities / examinations
Visit 11 (month 36) Final visit (including after a withdrawal)	• The study doctor will perform a physical examination and measure your heart rate, blood pressure and body temperature. • In addition, the study doctor will ask you to visit an ophthalmologist to perform an eye exam. • The study doctor will collect a tissue sample of your liver (liver biopsy). • If you agree, your study doctor can perform a FibroScan to examine the condition of your liver more accurately. • Your bone density will be measured by means of X-rays. • You will be asked to provide blood (about 35 mL) and urine samples for routine laboratory tests and for additional (including serological) laboratory analyses. • A second pregnancy test will be performed if you are a woman of child-bearing potential. • The study doctor will ask you about your opinion concerning the efficacy and tolerability of the study drug and to rate the degree of your itchiness. • You will be asked to fill out a quality of life questionnaire (PBC-40). • The study doctor will document possible discomforts/diseases you experienced as well as any drugs you may have taken since the last visit. • You will be asked to return the dairy and any used/unused study drugs.

- **Eye examination:** the cornea, lens and intraocular pressure of your eyes are examined during the eye check-up. This examination is short and painless and can be performed by any ophthalmologist you know. If you do not know an ophthalmologist, the study doctor will recommend one for you.

- **Liver biopsy:** tissue samples of the liver (biopsies) will be collected during the screening examination (if more than 6 months have elapsed since the last liver biopsy) and during the final examination. The study doctor will insert a narrow hollow needle between 2 of your lower ribs. Before the procedure, s/he injects a local anaesthetic to numb the site where the needle will be inserted. Alternatively, the study doctor can decide to use a laparoscope (a thin illuminated tube with a camera attached). In this case, you will receive an anaesthetic that makes you fall asleep to prevent you from feeling pain. Next, the study doctor will make a small incision close to the belly button. Gas is slowly introduced through a needle to expand the abdominal cavity for better visibility. A laparoscope is then inserted through an additional incision to view the organs and to guide other devices used to collect the sample. The tissue samples are sent to a specialised pathologist for central evaluation. After the procedure, the study doctor will suture the incisions shut. The scars will be very tiny and often invisible.

- **FibroScan:** this method makes it possible to check whether cirrhosis of the liver is present without the need of performing a liver biopsy. The firmness of the liver tissue is examined, similar to an ultrasound examination. The examination is voluntary and will only be performed if the technical conditions at your study site are met and you provide your consent for the examination.
- **Bone density measurement:** your bone density will be measured by means of dual energy X-ray absorptiometry (also referred to as DXA). DXA is using X-rays aimed at your bones (neck of femur and lumbar spine). This method for the measurement of your bone density and for the early detection of osteoporosis is a very common procedure and is being performed for your own safety. The total radiation exposure associated with the study is about 0.03 mSv (unit for measuring X-ray irradiation; the average natural radiation in Germany is close to 2.1 mSv per year).
- **Serology:** a blood sample to test for hepatitis B and C (viral liver inflammation) will be collected during the screening examination. In addition, an HIV test will be conducted to check whether you are infected with the HI virus. Furthermore, the blood will be analysed for different antibodies associated with your PBC. The results of the hepatitis and HIV tests will be communicated to you personally and confidentially by the study doctor. You will be briefed about the far-reaching consequences affecting you in case of a positive test result.

  Other blood samples (about 5 mL each) will be collected at the start of the study, after 1, 2 and 3 years and stored. At the end of the study, the decision will be made whether these blood samples should be analysed for additional PBC-specific antibodies. In this case, you will be asked to provide your consent on a separate declaration of consent.
- **Routine laboratory tests** include blood cell count, blood chemistry (e.g. liver function values), electrolytes (acids, bases, salts), total protein, urine analysis and other examinations. These tests are being conducted for your own safety.
- **Other laboratory tests:** blood samples to check the bone density, function of the adrenal cortex and fibrosis of the liver will be collected during the screening examination, at visits 7 and 9 as well as during the final examination.
- **Dairy and questionnaire:** you will be asked to duly and completely fill out dairies and a quality of life questionnaire throughout the duration of the study and to return them during your visits. You will be asked to document any changes in the intake of the study drugs, the use of other medications (e.g. headache tablets) and any discomforts/diseases you experienced in the diaries. Your study doctor will show you an example dairy as well as a quality of life questionnaire when s/he explains the study to you.

POSSIBLE RISKS AND DISCOMFORTS

It is possible that your condition does not improve or even worsens during the course of the study. This can also be the case during regular treatment outside the clinical study. Because your study doctor evaluates your response to the treatment during every visit, any changes in your condition will be identified early.

Adverse reactions

Every drug has the potential to induce adverse reactions and we would like to inform you about them.

The evaluation of adverse reactions is based on the following incidence rates:

Very common: more than 1 of 10 treated subjects	**Common:** more than 1 of 100 treated subjects
Uncommon: more than 1 of 1‘000 treated subjects	**Rare:** more than 1 of 10‘000 treated subjects
Very rare: 1 case of 10‘000 subjects treated or fewer, including isolated cases	

Budesonide

The following adverse reactions of Budenofalk® 3 mg have been reported spontaneously:

In very rare and isolated cases:

- *Metabolic and nutritional disorders*: oedemas of the legs, Cushing’s syndrome (elevated levels of the hormone cortisol produced in the adrenal glands).
- *Adverse reactions involving the central nervous system:* pseudotumor cerebri (increased pressure of the brain), possibly accompanied with swelling of the eyeball in adolescents
- *Disorders involving the muscles and skeleton:* diffuse muscle pain and weakness, osteoporosis (disorder of the skeletal system with loss or reduction of bone mass and structure and increased fracture tendency)

Some of the undesired effects were reported after long-term use.

Occasionally, adverse reactions typical for systemic glucocorticosteroids (those acting throughout the entire body) may occur. These adverse reactions are dependent on the dose, the duration of the treatment, concomitant or prior therapy with other glucocorticosteroids and the patient’s individual sensitivity.
Clinical studies of patients with Crohn’s disease have shown that the incidence of glucocorticoid-associated adverse reactions under the administration of Budenoflak® 3 mg is almost 50 percent lower compared to the oral administration of Prednisolone doses with identical efficacy.

- *Disorders of the skin and subcutaneous tissue:* allergic reactions of the skin, striae rubra (stretch marks), petechiae and ecchymoses (small-scale and extensive bleeding of the skin), steroid acne, delayed wound healing, contact dermatitis (inflammatory alterations of the skin induced by contact with foreign materials)
- *Disorders of the skeletal musculature, connective tissue and bones:* aseptic bone necroses (thigh bone and head of humerus; decrease in bone tissue of the thigh and humerus)
- *Eye disorders*: glaucoma (green cataract), cataract (gray cataract)
- *Psychiatric disorders*: depression, irritability, euphoria

- *Gastrointestinal disorders:* upset stomach, duodenal ulcer, pancreatitis
- *Metabolic and nutritional disorders*: Cushing's syndrome: moon face, obesity around the trunk, impaired glucose tolerance, diabetes mellitus, inadequate sodium excretion with formation of oedemas (swelling), increased potassium excretion, inactivity or diminution of the adrenal cortex, impaired growth in children, impaired excretion of sex hormones (e.g. absent menstruation, excessive hair growth, impotence)
- *Vascular disorders:* high blood pressure, elevated risk of thrombosis, vasculitis (inflammation of the vessels; withdrawal syndrome after long-term therapy)
- *Disorders of the immune system*: impaired immune activities (e.g. elevated risk of infection)

Ursodeoxycholic acid (UDCA)

Possible adverse reactions of ursodeoxycholic acid include:

Adverse reactions affecting the gastrointestinal tract:
Pasty stools and diarrhoea were commonly reported in clinical studies under therapy with ursodeoxycholic acid.
In very rare cases, the treatment of primary biliary cirrhosis was associated with severe pain in the right abdominal region.
Disorders of the liver/bile:
In very rare cases, treatment with ursodeoxycholic acid can cause gallstone calcification.
In very rare cases, decompensation of the cirrhosis of the liver was observed under therapy of advanced stage primary biliary cirrhosis which was partially regressive after the discontinuation of the therapy.
Hypersensitivity reactions:
Urticaria (nettle rash) can develop in very rare cases.

Interactions with other drugs

Interactions between the study drugs and other medications may occur. Therefore, it is essential that you inform your study doctor of any medications you are currently taking or may be taking in the future.
Interactions with Budesonide have been described for the following drugs: cardiac glycosides, saluretic drugs (drugs promoting the excretion of salt in the urine), drugs affecting the Cytochrome $P_{450\ 3A}$ metabolism, Cimetidine- or steroid-binding synthetic resins (e.g. Cholestyramine and antacids).
Furthermore, interactions between Ursofalk® capsules and the following drugs are possible: Cholestyramine, Colestipol or aluminium hydroxide- and/or aluminium acetate-containing antacids, Cyclosporine, Ciprofloxacin and/or drugs metabolised by the enzyme Cytochrome $P_{450\ 3A}$.
The concomitant intake of Budesonide and Ursofalk® capsules is possible.

Prohibited concomitant medication

Some drugs are not permitted during the course of the study. Please discuss your other medications with your study doctor. The following drugs are not permitted: anti-inflammatory drugs (e.g. corticosteroids (except for inhaled corticosteroids such as anti-asthma sprays),

Mesalazine-containing drugs, immunosuppressant drugs), Colchicine, Chlorambucil, D-Penicillamine, Fibrates, CYP3A inhibitors (e.g. Ketoconazole, Itraconazole, Clarithromycin, Ritonavir) and CYP3A-inducing drugs (e.g. Carbamazepine, Rifampicin).

Liver biopsy

These days, a liver biopsy is considered a low-risk procedure. However, complications may arise in uncommon cases during the procedure in spite of caution being exercised:

- In very rare cases, biopsies can cause bleeding which normally stops automatically. Severe bleeding is extremely rare and may require blood transfusion or surgery.
- The intestines, gallbladder or kidney can be injured, requiring surgery.
- In very rare cases, the abdominal cavity may become inflamed, making treatment with antibiotics necessary.
- Allergic reactions to drugs used during the procedure (e.g. nausea, itchiness, rash) can occur in rare cases and do not require any treatment in the majority of cases.
- Breathing may be impaired in rare cases to the point of respiratory arrest. Cardiovascular malfunctions are very rare. They require intensive care and may lead to permanent damage (e.g. renal failure, brain damage, convulsions). These risks are significantly reduced because you will be monitored closely during and after the procedure.
- It is possible that you feel some degree of pain after the liver biopsy.

Additional information about the liver biopsy will be provided to you in a separate sheet.

Blood sampling

Blood sampling can cause discomfort such as e.g. blue spots, inflammation at the injection site, nerve injury and in very uncommon cases thrombosis (blood clot) of the vein at the sampling site. A total of about **225 mL** of blood will be collected throughout the study.

STORING THE STUDY DRUG

Do not store the Budesonide/placebo capsules at temperatures above 25°C. No special storage conditions are required for the UDCA capsules. Keep the study medication out of children's reach.

TAKING THE STUDY MEDICATION

Swallow the Budesonide/placebo capsules without chewing with plenty of fluid 30 minutes prior to meals. The Budesonide/placebo dose depends on your "liver parameters". Your study doctor will instruct you on how to take the drugs.
Swallow the UDCA capsules without chewing with some fluid independent of the meals. The recommended UDCA dose depends on your body weight. Therefore, please take the UDCA capsules as prescribed by your study doctor.
Avoid taking the study drug together with grapefruit juice (pomelo juice).

PREGNANCY DURING THE CLINICAL STUDY

Pregnant women may not be enrolled in the study. Female patients must not become pregnant during the course of the clinical study, must not breastfeed and are required to use a reliable method of contraception such as e.g. a hormonal contraceptive (pill), intrauterine device (spiral) or diaphragm. Please keep in mind that an additional method of contraception, e.g. a

condom is required for the remainder of the menstrual cycle if you are taking the pill and experience vomiting and/or severe diarrhoea. Other acceptable options include abstinence or a vasectomised partner. If you are unsure about the reliability of your method of contraception, please discuss it with your study doctor. If a woman becomes pregnant during the course of the study, she must immediately notify her study doctor and withdraw from the study for safety reasons.

POSSIBLE BENEFITS

The treatment you receive during the study may improve your health condition. Regular follow-up examinations and blood tests will be conducted during the course of the study. This has the advantage that you are always informed about your current health condition during your enrolment in the study. Compared to the standard treatment, you will be subject to closer and as a result better medical monitoring.

ALTERNATIVE TREATMENT OPTIONS

UDCA monotherapy is the only approved treatment for PBC. No alternative treatment options are currently available for patients at risk of progressive illness.

COSTS

The sponsor of the study will cover the costs for all study-related procedures as well as the study drugs. Consequently, you will not incur any costs for taking part in the study. Travel costs may be reimbursed upon presentation of the corresponding receipts.
Study-related procedures include any activities or examinations that are different from the standard treatment you would receive without participating in the study.

CONFIDENTIALITY

This clinical study is being conducted in compliance with the statutory data privacy provisions applicable in your country. Any personal information collected during the clinical study will be documented in a non-identifiable manner (only your birth month and year will be recorded, no names or initials), evaluated scientifically and forwarded to the sponsor. In order to make sure that the study is being conducted in compliance with the statutory provisions, it is necessary that authorised representatives of the sponsor (Dr. Falk Pharma GmbH), representatives of the national and local health authorities or representatives of the ethics committees have permission to inspect your patient records and any other information collected during the course of the study. These persons are bound by confidentiality. Your personal information is handled strictly confidential and will not be disclosed publicly. You have the right to view your medical records and to ask for corrections, if applicable.

VOLUNTARY PARTICIPATION AND WITHDRAWAL OF THE CONSENT

It is important for you to understand that your participation in the clinical study is voluntary. If you do not wish to participate, you are not obligated to do so. You have the option of withdrawing from the clinical study any time without experiencing any penalties concerning your further medical care or the relationship with your study doctor or the hospital. If you wish to withdraw from the study, please discuss this decision with your study doctor first.
Before signing the declaration of consent, you should have asked the study doctor any questions you may have.

Your study doctor may discontinue the treatment within the scope of the clinical study any time if this is in your best interest (e.g. in the event of extreme adverse reactions) or if this is necessary for the proper conduct of the study (e.g. if you do not abide by the instructions concerning the study). The decision to terminate the study as a whole will be made by the sponsor and their medical advisor.
You are not eligible to enrol in this clinical study if you participated in a different clinical study within the past 30 days, if you intend to participate in another study simultaneously or if you have previously participated in this clinical study.

INSURANCE

Pursuant to the German Medicines Act (AMG section 40 subs. 3) and the Radiation Protection and X-Ray Ordinance, the sponsor of this study (Dr. Falk Pharma GmbH) has taken out a subject and radiation liability insurance for the study subjects with [redacted] (maximum coverage per insured: 500‘000 Euro). Your study doctor will provide you with a copy of the written insurance terms and conditions.

To assist with the determination of a potential damage to your health, you are required to follow the instructions from your study doctor and to refrain from seeking any other medical treatment during the course of the study without consulting your study doctor first (except in case of emergency in which case you are asked to notify your study doctor as soon as possible). Furthermore, you are required to inform your study doctor and the insurance company promptly about any damage to your health [redacted]. Intentional or gross negligent violation of the insurance conditions may result in the loss of insurance coverage.

CENTRAL CONTACT POINT

Additional information about any circumstances that are significant for this clinical study is available from the central contact point: Federal Institute for Drugs and Medical Devices, Kurt-Georg-Kiesinger-Allee 3, 53175 Bonn, ph.: 0228-207-4318.

NEW INFORMATION THAT BECOMES AVAILABLE OVER THE COURSE OF THE STUDY

New information about the study drugs that becomes available while you are enrolled in the study and which may affect your decision to remain in the study will be communicated to you promptly by the study doctor (i.e. during the next study visit at the latest).

Thank you for your co-operation!

For more information about this study, to clarify legal questions and in case of emergency, please contact:

Name, address and phone number of the study doctor

Declaration of consent

A double-blind, randomised, placebo-controlled multi-centre clinical phase III study to compare the combination of ursodeoxycholic acid capsules plus Budesonide capsules with the combination of ursodeoxycholic acid capsules plus placebo capsules for the treatment of primary biliary cirrhosis

(BUC-56/PBC)

My study doctor has extensively briefed me about the nature, significance and consequences of this clinical study and about the possible adverse reactions of the investigational drugs. I had the opportunity and time to ask questions and to make a decision about the enrolment in the study. I know that I am entitled to revoke my consent for the participation any time without any penalties with respect to my medical care. I have also received this information in written format.

I have been informed that I am covered during the course of this clinical study by an insurance policy (as outlined in the patient information) pursuant to the German Medicines Act (AMG section 40 subs. 3) and the Radiation Protection and X-Ray Ordinance against possible damages to my health as a consequence of my enrolment in the study which are not covered otherwise. I have been briefed about my duties with respect to this insurance, in particular to the effect that I may only undergo a different medical treatment after consulting with my study doctor (except in case of a medical emergency). I am required to inform my study doctor and the insurance company promptly about any damage to my health which may potentially have been caused by my enrolment in this study.

I have been given a copy of the insurance policy and the insurance terms and conditions.

I am aware that personal information, in particular medical findings about me will be collected, archived and evaluated during this clinical study. The use of the information about my health is based on statutory provisions and requires the following voluntary declaration of consent before my participation in the clinical study, i.e. I am unable to participate in the clinical study without providing the following consent.

Declaration of consent regarding data privacy

1. I agree that information collected within the scope of this clinical study, in particular information about my health will be documented in paper format and on electronic data storage media. To the extent required, the collected information may be disclosed in pseudonymised (encoded) format as follows:
   a) to the sponsor of the study (Dr. Falk Pharma GmbH, Leinenweberstr. 5, 79108 Freiburg) or to an office appointed by the sponsor for the scientific evaluation, assessment of adverse events or to submit an application for approval
   b) to the involved contract research organisation (Aptiv Solutions GmbH, Robert-Perthel-Str. 77a, Cologne)
   c) to the competent supervisory authority/authorities (regional authorities or district council), the higher federal authority (Federal Institute for Drugs and Medical Devices), the European database or the ethics committee to review the proper conduct of the clinical study, to evaluate the study outcomes and adverse events or to submit an application for approval.

2. In addition, I agree that authorised representatives of the sponsor (Dr. Falk Pharma GmbH, Leinenweberstr. 5, 79108 Freiburg) bound by secrecy as well as the competent domestic and foreign supervisory authorities are entitled to view my personal data, in particular my health records kept by my study doctor to the extent this is required to review the proper conduct of the study. For this purpose, I am releasing the study doctor from the patient/doctor confidentiality.
3. I agree that the radiation exposures contained in the X-ray applications are irrevocably disclosed to the competent authority.
4. The consent to collect and process my pseudonymised personal information, in particular the information about my health is irrevocable. I have been told that I have the right to withdraw from the clinical study any time. In the event of this withdrawal I agree that the information archived up to this time may be used further without mentioning my name, to the extent this is required to
   a) determine the effects of the investigational drug,
   b) ensure that my interests worthy of protection are not being impaired,
   c) comply with the requirement of presenting complete approval documents.
5. I agree that my information will be kept for at least ten years after the end or termination of the study, such as set forth in the provisions governing the clinical study of drugs. After that time, my personal information will be deleted as long as this does not conflict with any legal, statutory or contractual storage periods. The contractually agreed period is 15 years.
6. I have been informed about the following legal provision: in the event that I revoke my consent to participate in the study, any offices where my personal data, in particular my health records have been archived are required to check immediately to what extent the archived data is still required for the purposes mentioned in no. 4.a)-c). Data that is no longer required shall be deleted immediately.

I agree that my general practitioner is informed about my enrolment in the clinical study:

O Yes **O No**

The following line must be completed personally by the patient!

I am herewith providing my explicit consent to enrol in this clinical study.

_____	_____	_____
Patient's name (please print)	Date	Patient's signature

I herewith confirm that I have informed the patient about the clinical study as set forth in the GCP and the statutory requirements.

_____	_____	_____
Study doctor's name (please print)	Date (added by the study doctor)	Study doctor's signature

Original for the study doctor's binder, copy for the patient.