Table of contents

SOP 1-003	**Division**	**Name**	**Date**	**Signature**
Created by:	Quality assurance	Ms Vantanakul		
Reviewed and approved by:	Qualified person urine	Dr Stieneker		
Reviewed and approved by:	Qualified person blood	Dr Anders		
Released by:	Pharmaceutical entrepreneur	Ms Kief		

1. Aim of this Standard Operating Procedure

This SOP describes the procedure for the collection of certain substances of human origin for drug preparation at commissioned facilities (collection facilities) according to sec. 14 para. 4 no. 4 AMG (German Pharmaceuticals Act).
The source materials obtained in these facilities (in this case, blood or urine) will be used for the preparation of drugs according to the AHIT procedure.
The exact procedure for the collection of blood and urine is strictly regulated. It describes the procedure for confirming the identity of the patient, for the collection of blood and/or urine as well as for the shipment of materials and documents to FBM-PHARMA.
Following the correct blood collection procedure is required for the preparation of high quality drugs free from impurities. The person carrying out the blood collection has to familiarize himself/herself with the procedure beforehand.

2. Scope of Application

Collection facilities, FBM-PHARMA Shipping Department

3. Terms/Abbreviations

Collection facility	Facility (such as a medical practice or hospital) where the collection of source materials is carried out
Medical person	Person present in the collection facility, who is responsible for carrying out the collection (e.g. physician at the medical practice)

4. Responsibilities

The physician at the respective collection facility (medical person) is responsible for the proper collection of blood and/or urine. Only trained personnel are allowed to carry out the collection. The medical person at the collection facility is responsible for the relevant staff training after initial training done by FBM-PHARMA GmbH.

5. Description

Blood collection for the preparation of AHIT products differs from normal blood collection for diagnostic purposes. After it is collected, the blood is used as a source material for the preparation of drugs, which must be **sterile**. All working steps are required to be implemented under aseptic conditions at the time of collection, so as not to contaminate the collected blood. In order to be approved as a facility commissioned by FBM-PHARMA GmbH, the collection facilities must be audited. This audit is carried

out by employees of FBM who are trained in the field of GMP and possess the required expertise or by a person with the required expertise commissioned by FBM.

5.1 General

The medical person receives a copy of this SOP. He/she must confirm that it has been received by signing the document (see Annex). The persons who carry out the collection of blood or urine in the practice are to be trained in accordance with this SOP. This training must be documented in writing.

The medical person at the collection facility is responsible for informing the patient and obtaining the relevant informed consent regarding blood collection for the preparation of an AHIT drug.

5.2 Request for and Control of Transport Boxes

5.2.1 Request for a Transport Box from FBM-PHARMA GmbH

The material required for blood collection is provided by FBM-PHARMA and sent to the respective medical practice on request. The material is contained in a styrofoam box, which is also used for returning patient material to FBM-PHARMA.
If the collection of blood or urine is planned at the medical practice, FBM-PHARMA GmbH must be contacted by telephone in a timely manner (no later than 7 days before the collection takes place) and a transport box must be requested.

Phone number for FBM-PHARMA GmbH: +49-621-669300

During this phone call, the following information must be given to FBM-PHARMA GmbH:

- Planned date of collection
- Material to be collected (blood or urine)

5.2.2 Receipt of the Transport Box at the Collection Facility

Upon receipt at the collection facility, the transport box must be checked for completeness. The following parts and documents must be contained in the transport box:

A) Transport box for blood and urine collection

- 1 insulation box (transport box)
- 2 thermal packs
- 1 vacuum bottle 250 ml with inserted Clexane
  (Note: to prevent coagulation, 5000 IU/100 ml low molecular heparin Clexane multidose has been inserted into the vacuum bottle. The date of the added

heparin as well as the allowed usage period are noted on the bottle. The heparin batch is documented on the production order form by the manufacturer (FBM-PHARMA).)

- G-Box 650 plastic box including Ultra-Sorb absorbent material and bubble wrap
- 2 name stickers (surname, first name, date of birth)
- 1 infusion holder
- 1 Urobox (urine collection container)
- 1 transfusion set with roller clamp
- 1 scalp vein set (Butterfly System)
- 1 address label
- 3 sterile swabs
- Documents:
    - Production order form for new orders
    - Instructions (with detailed pictures) for blood collection
    - Form FB 1-007-1 pharmacy shipping
    - Account information of FBM-PHARMA
    - FBM leaflet "*Did I forget anything?*"
    - Sticker UN3373

B) Transport box for urine collection

- 1 styrofoam box (transport box)
- 2 thermal packs
- 1 Urobox (urine collection container)
- Name labels (surname, first name, date of birth)
- Documents:
    - Production order form for new orders
    - Patient information sheet
    - Form FB 1-007-1 (Pharmacy Shipping Form)
    - Account information of FBM-PHARMA
    - FBM leaflet "*Did I forget anything?*"

FBM-PHARMA must be contacted immediately by phone if the box is not complete. The supplied cooling elements are to be stored at -18 ° C or lower (in a freezer) at the medical practice for at least eight hours before they are returned to FBM-PHARMA.

5.3 Requirements for Collecting the Transport Box

To ensure timely receipt of patient material by FBM-PHARMA, an appointment for picking up the material must be agreed with FBM-PHARMA **up to one day before** the planned blood or urine collection (**at the latest**).

A transport company commissioned by FBM-PHARMA will pick up the material at the practice. The shipment of the material is organized in such a way so that the time period between the collection of the material and its processing in the production area does not exceed 72 hours. In order to ensure direct further processing after transport, collection of the transport box is only possible from Monday to Wednesday. If the respective work week includes a holiday, FBM-PHARMA must be contacted before arranging an appointment with the patient.

5.4 Blood Collection

5.4.1 General Preparation prior to Blood Collection

Prior to blood collection, all materials must be checked again for completeness. The vacuum bottle must be checked in regards to the addition of heparin and the allowed usage period. The person taking the blood sample should make himself/herself familiar with the procedure in theory prior to the blood collection. This SOP must be kept at the workplace.

The transport box provided by FBM-PHARMA including its contents must be readily available.
The following material must also be readily available at the practice prior to the collection of blood:

- Sterile disposable gloves
- Suitable authorized or DGHM tested and approved skin disinfectant (e.g. Kodan, Cutasept (disinfectants that contain 1-propanol))
- Small patches
- I.V. pole

5.4.2 Establishing the Identity of the Donor prior to Blood Collection

Collection of personal data, labelling and blood collection must be carried out **by the same person**:

- Before collecting blood, the patient must be asked for his/her surname, first name and date of birth.
- Personal data must be noted down on the designated labels.
- The vacuum bottle must immediately be labelled with this data.

5.4.3 Carrying out the Blood Collection

It is important to ensure that the procedure is carried out under aseptic conditions. Any contamination of the blood with skin or airborne germs means that drugs produced from it cannot be manufactured!

For the preparation of an AHIT product, the following minimum amounts of blood are required:

Children aged 3-7	80 ml
Children age 7 and above and adults	100 ml
Patients with malignant diseases	150 ml

The blood collection process is described below.
Each step must be followed in the exact order presented.

- Measure the patient's body temperature and record it in the production order form.
- **When collecting blood, the person taking the blood sample asks the patient for his/her surname, first name and date of birth and afterwards must double-check his/her identity.**
- **The verification of identity shall be clearly documented by the person taking the blood sample. The type of documentation must be regulated internally within each practice.**
- Put on gloves and disinfect gloved hands.
- The preparation for the blood collection process is as follows:
  - Disinfect rubber plug on the vacuum bottle with disinfectant, pay attention to the exposure time according to the manufacturer's specifications.
  - Remove the transfusion set from packaging.
  - Close roller clamp of the transfusion set. The bottle's vacuum must be maintained in order to carry out the blood collection!
  - The roller clamp must remain closed until the start of the blood collection.
  - Quickly stab the transfusion set into the large circle of the vacuum bottle.
  - Prepare adapter with butterfly and adhesive tape.
- Choose a healthy skin area that is easy to disinfect for the venipuncture.
- Place a compression bandage on the upper arm of the patient and ask the patient to make a tight fist.
- Disinfect the designated puncture site. Generously spray the area of the puncture site and wipe dry with a sterile swab after 30 seconds of exposure.
- Spray again while taking into account the relevant exposure time of the disinfectant. The puncture site should not be touched after the 2nd spraying!
- Disinfect the gloved hands of the person taking the blood sample for a second time.
- Carry out venipuncture with butterfly, hold it in place with prepared adhesive tape.

- After the venipuncture, connect the transfusion set to the butterfly and ensure it is attached.
- Open the roller clamp and let the blood flow into the bottle.
- The bottle should have a deeper position than the puncture site.
- Gently shake the bottle in a circular motion to facilitate thorough mixing of the blood with heparin.

5.5 Urine Collection

The collection of urine is carried out independently by each medical practice by means of a Urobox (urine collection container) with screw cap. The patient must be informed that the insides of the urine cup must not be touched before, during and after filling. The container must be labelled with the patient's surname, first name and date of birth. Urine collected in the morning is preferable due to the increased concentration of ingredients.

Required minimum amounts of urine:

As an addition to the blood product	60 ml
As an independent drug	
Infants (up to 3 years)	60 ml minimum
Children (from the age of 3) and adults	80 ml minimum

5.6 Documents

Before shipment of patient material to FBM-PHARMA, the required documents must be checked for completeness:

- Prescription
- Fully completed and signed production order form

On the production order form, the following information is mandatory:

- Patient's personal data and diagnosis
- Patient's signature
- Body temperature upon blood collection
- Infectious diseases, if known
- Signature of medical person / therapist

As part of the identity confirmation process, the medical person confirms that the blood, without any doubt, comes from the patient with the information referred to respectively and that the blood was taken according to the provisions of this SOP by signing in the appropriate place on the production order form after blood collection.

5.7 Packaging and Shipping

The following aspects must be taken into account:

- All containers must be tightly closed.
- All containers (Urobox, vacuum bottle) must be checked again for correct and complete labelling to ensure that the identity of the donor is clearly identified.
- Unlabelled containers are not allowed to be used for preparation at FBM-PHARMA!
- Blood and urine must be shipped cooled (the appropriate cooling elements are to be frozen in the freezer at -18 ° C or lower for at least eight hours before shipment).
- The vacuum bottles must be placed into the G-Box 650 plastic box lined with absorbent material, and the lid of the box must be closed.
- All materials and documents must be checked for completeness by referring to the leaflet "Did I forget anything?"
- The transport box must be sealed with adhesive film.
- The adhesive label UN3373 must be placed on the outer packet.

Only packaging material provided by FBM-PHARMA (styrofoam box) can be used to ensure that the containers are shatter-proof. The documents are added to the patient material. The transport company commissioned by FBM-PHARMA will pick up the transport box from the practice.

6. Additional applicable Documents

Information brochure

7. Annexes

Receipt confirmation acknowledgment form for SOP 1-003
Informed consent (master copy)
Patient information sheet for urine collection
Image instruction booklet: "AHIT blood collection for the preparation of an individual drug"

8. Revision History

SOP 1-003	Changes	Valid as of:
01	Change of layout, complete revision, separate collection for infection serology no longer applies	15 June 2010
02	Revision of point 5 Change of the term medical practice to collection facility.	