SAPIENS	TEST GUIDE

CONTENTS

1. INTRODUCTION

In this guide, the operation of Sapiens Genetik ve Sağlık Hizmetleri A.Ş., the tests, the process from examination entry to sending the results, analytical quality studies of the laboratory, working methods of the tests, running times, selection of sample type / sample container according to the test, acceptance / rejection of samples. Information about the criteria, reporting times of the results, normal values, panic values if any, and briefly the clinical benefits of the tests were included.

2. LABORATORY OPERATION

2.1. TEST REQUESTS AND ENTRIES

For outpatients coming to our center, after the patient is examined by our genetic specialist, a test request is made by marking the test deemed appropriate by the doctor on the test request form and entering the necessary information. For samples coming from outside, it can be done by the relevant doctor at the sending center by marking them on the test request form, or samples marked on the test request form are taken.

For test entries, the patient is selected from the patient list in the GENETIS system and the "sample information" menu is selected. The name of the test(s) requested will appear here and tests can be added from the Add Test option. After the test materials taken from the patients or the test samples from outside arrive at the laboratory, they are received by the sample acceptance personnel. Samples arriving at the center by cargo from outside are delivered by filling out the cargo delivery form. After the necessary preliminary procedures, the relevant personnel accepts or rejects the sample according to the rejection/acceptance criteria.

2.2. RULES FOR TAKING SAMPLES OF THE STUDY TESTS

2.2.1. Preliminary Preparation Rules for Tests Before Sample Collection

It is stated if preliminary preparation is required for the tests performed in the laboratory.

2.2.2. Patient Preparation Rules Before Sample Collection

1. For the blood sample, the appropriate sample tube is selected according to the tests, and the patient's name and surname, the desired test, laboratory number and date of birth are written on the selected tubes.

2. While the patient is resting on the blood collection chair, the requested tests are checked and a brief anamnesis is taken from the patient. If there is no inappropriate situation, blood collection is performed.

3. Before blood collection, the baby is placed on a stretcher, the baby is waited to calm down and adapt to the environment, and the family is informed about the blood collection process. It is tried once and if it is not successful, the baby is directed to a center with a nurse to have blood drawn.

2.2.3. Labeling of Samples

Laboratory number and test name are written on all samples taken.

2.2.4. Rules Regarding Sample Collection

2.2.4.1. Taking Samples

The aim is to collect samples of patients applying to the laboratory under the most appropriate conditions and prepare them for the study.

A) Taking Blood Samples - Venous Blood Collection

1. The patient should be in a lying or sitting position during blood collection.

2. Upper extremity veins should preferably be chosen for blood collection.

3. The needle tip should be chosen as wide as possible.

4. The tourniquet should not remain tight on the arm for more than 30 seconds.

5. The tourniquet should be released after the needle is inserted into the vein.

6. During blood collection with a syringe, strong aspiration of blood into the tube should be avoided.

7. When taking blood into vacuum tubes containing anticoagulant, care should be taken to fill the blood up to the marked line.

8. Immediately after collecting blood into tubes containing anticoagulant, the tube should be gently inverted and mixed carefully. Shaking should be strictly avoided.

1) Whole blood with EDTA

1. Blood is collected into 2 ml K3 EDTA glass tubes with purple caps.
2. To prevent clots from forming in the tubes, the blood is mixed by gently inverting it 5-6 times as soon as it is taken. During blood collection, care should be taken to fill the blood up to the marked line. Samples should be kept refrigerated until studied.

2) Whole Blood with Heparin

1. The blood sample is collected into green-capped tubes with lithium heparin.
2. In order for the blood sample to be mixed with lithium heparin, it must be filled completely up to the marked line and gently inverted 5-6 times to ensure full contact of the blood with the anticoagulant.

B. Amniotic Fluid

1. At least 15-20 ml of amniotic fluid should be taken.
2. The sample should be delivered to the laboratory immediately and studied immediately. If not possible, it can be stored at 2-8 °C for a maximum of 3 days.

C. Chorionic Villus Sampling

At least 20 -30 mg of chorionic villus biopsy sample should be taken.

The sample should be delivered to the laboratory immediately in a tube containing sterile transport medium and studied immediately. If not possible, it can be stored at 2-24 ° for a maximum of 3 days.

D. Discharge Material

Examples of abortion materials that can be sent:
Placental biopsy: A piece of at least 1 cm3 should be taken from the area close to the umbilical origin (fetal origin).
Skin biopsy: Approximately 5 mm2 should be taken from the back, leg or hip.
Cord biopsy: Approximately 2 cm piece should be taken.
Amnion biopsy: At least a 2 cm2 piece should be taken from the area closest to the umbilical cord.
The sample should be delivered to the laboratory immediately in a tube containing sterile transport medium or in a sterile falcon and processed immediately. If not possible, it can be stored at 2-24 ° for a maximum of 3 days.

E. Bone Marrow

Approximately 2-3 ml of bone marrow sample is taken into EDTA purple capped tubes.

In order for the bone marrow sample to be mixed with EDTA, it must be filled completely up to the marked line and gently inverted 5-6 times to ensure full contact of the blood with the anticoagulant.

F. Fibroblast skin biopsy

At least 1 cm3 biopsy sample should be taken.

The sample should be delivered to the laboratory immediately in a tube containing sterile transport medium and studied immediately. If not possible, it can be stored at 2-8° for a maximum of 3 days.

G. Paraffin block sections

For molecular tests;

4-5 sections with a thickness of approximately 10 µm prepared from approximately 15 mg (17 µl) paraffin blocks should be prepared.

Samples should be sent spread on glass or placed in a 1.5 ml Eppendorf tube.

Samples should be shipped at room temperature (2-24°).

For molecular cytogenetic tests;
For the FISH test, sections taken from paraffin block sections with a thickness of approximately 4-6 µm, taken on a slide and fixed with formaldehyde will be accepted.

At least 2 slides should be sent.

Samples should be shipped at room temperature (2-24°).

Samples in which non-formaldehyde fixatives were used during the preparation of the blocks and samples in insufficient quantities will not be included in the study.

2.3. TRANSFER OF SAMPLES

SAMPLE TYPE	QUANTITY (Minimum)	METHOD	SHIPPING METHOD	TRANSPORT TEMPERATURE	REJECTION CRITERIA
Peripheral Blood	2-5ml	cytogenetics (conventional, FISH) molecular genetics (DNA/RNA)	Heparin tube (green cap) EDTA tube (purple cap)	2-24 °C 2-24 °C	*•Samples where the request paper and consent form are not available or not fully filled out, •The amount of sample is not sufficient, •Coagulated blood samples, •Samples that come in a broken tube, •Samples that do*

					not reach the laboratory in the appropriate time, •Samples that come without a name, •The sample is not transported within the appropriate temperature range. •Samples sent within 72 hours of receipt.
Bone marrow	2-5ml	cytogenetics (conventional, FISH) molecular genetics (DNA/RNA	Heparin tube (green cap) EDTA tube (purple cap)	2-24 °C 2-24 °C	*•Samples where the request paper and consent form are not available or not fully filled out, •The amount of sample is not sufficient, •Coagulated blood samples, •Samples that come in a broken tube, •Samples that do not reach the laboratory in the appropriate time, •Samples that come without a name, •The sample is not transported within the appropriate temperature range. •Samples sent within 72 hours of receipt.*

Amniotic Fluid	15-20ml	cytogenetics (conventional, FISH) molecular genetics (DNA/RNA)	Sterile fit syringe Sterile 15 ml falcon	2-24 °C 2-24 °C	*•Samples where the request paper and consent form are not available or not fully filled out, •The amount of sample is not sufficient, •Coagulated blood samples, •Samples received in broken tubes, •Tissue samples such as abortion and CVS material have been taken in alcohol or formalin, •They have not reached the laboratory in the appropriate time. samples, •Samples received anonymously, •Prenatal diagnosis samples for which maternal blood was not sent for maternal contamination control, •The sample was not transported within the appropriate temperature range, •Samples sent 72 hours after collection.*

Chorionic Villus Sampling	20-30mg	cytogenetics (conventional, FISH) molecular genetics (DNA/RNA)	Container or falcon containing sterile transport medium	2-24 °C	*•Samples where the request paper and consent form are not available or not fully filled out, •The amount of sample is not sufficient, •Coagulated blood samples, •Samples received in broken tubes, •Tissue samples such as abortion and CVS material have been taken in alcohol or formalin, •They have not reached the laboratory in the appropriate time. samples, •Samples received anonymously, •Prenatal diagnosis samples for which maternal blood was not sent for maternal contamination control, •The sample was not transported within the appropriate temperature range, •Samples sent 72 hours after collection.*
Evacuation (Abort) Material	1-2 cm3	cytogenetics (Conventional, FISH) molecular genetics (DNA/RNA)	Container or falcon containing sterile transport medium Tube or falcon containing sterile transport medium	2-24 °C	*•Samples where the request paper and consent form are not available or not fully filled out, •The amount of sample is not sufficient, •Coagulated blood samples, •Samples received in*

					broken tubes, •Tissue samples such as abortion and CVS material have been taken in alcohol or formalin, •They have not reached the laboratory in the appropriate time. samples, •Samples received anonymously, •Prenatal diagnosis samples for which maternal blood was not sent for maternal contamination control, •The sample was not transported within the appropriate temperature range, •Samples sent 72 hours after collection.
Paraffin Block Or cross sections	30-50µm Or paraffin block	Cytogenetic FISH molecular genetics (DNA/RNA)	Sections taken on the slide are 5-10 µm and 4-5 pieces In addition, tumor sections Section with marked area	2-24 °C	*Samples where non-formaldehyde fixative was used during the preparation of the blocks, samples without patient information and insufficient quantity*
Peripheral Blood (RNA Obtaining)	4-10ml	molecular genetics (DNA/RNA)	2-5 EDTA tubed blood samples	2-24 °C	*•Examples where the request paper and consent form are missing or not fully filled out, • Insufficient sample quantity, • Clotted blood samples, • Samples received in broken tubes, • Samples*

					that did not reach the laboratory in the appropriate time, • Samples arriving without anonymity, • The sample not being transported within the appropriate temperature range. •Samples sent within 72 hours of receipt.
Serum	2-5ml	molecular genetics (DNA/RNA)	15ml sterile falcon	2-24 °C	*•Samples where the request paper and consent form are not available or not fully filled out, •The amount of sample is not sufficient, •Coagulated blood samples, •Samples that come in a broken tube, •Samples that do not reach the laboratory in the appropriate time, •Samples that come without a name, •The sample is not transported within the appropriate temperature range. •Samples sent within 72 hours of receipt.*
Vaginal/Cervical Samples	swap	molecular genetics (DNA/RNA)	Special tube for swab, in transport solution or dry	2-24 °C	*•Samples where the request paper and consent form are not available or not fully filled out, •The amount of sample is not sufficient, •Coagulated blood samples, •Samples that come in a broken tube, •Samples that do not reach the laboratory in the*

					appropriate time, •Samples that come without a name, •The sample is not transported within the appropriate temperature range. •Samples sent within 72 hours of receipt.
Throat Swabs	swap	molecular genetics (DNA/RNA)	Special tube for swab, in transport solution or dry	2-24 °C	*•Samples where the request paper and consent form are not available or not fully filled out, •The amount of sample is not sufficient, •Coagulated blood samples, •Samples that come in a broken tube, •Samples that do not reach the laboratory in the appropriate time, •Samples that come without a name, •The sample is not transported within the appropriate temperature range. •Samples sent within 72 hours of receipt.*
Liquid Biopsy	10ml	molecular genetics (cfDNA)	Stretch tube	2-24 °C	*•Samples where the request paper and consent form are not available or not fully filled out, •The amount of sample is not sufficient, •Coagulated blood samples, •Samples that come in a broken tube, •Samples that do not reach the laboratory in the appropriate time, •Samples that*

					come without a name, •The sample is not transported within the appropriate temperature range. •Samples sent within 48 hours of receipt.
NOTE	In addition to the patient's identity and indication information, the INFORMED EXPRESS CONSENT CONSENT FORM and GENETIC TEST INFORMATION FORM regarding the procedure to be performed must be filled out by the patient and the physician and delivered to our department along with the sample. Samples without patient consent will not be reported until the consent form reaches our center.				

2.4. DELIVERY, ACCEPTANCE, REJECTION AND SEPARATION OF SAMPLES TO THE LABORATORY

2.4.1. Preliminary evaluation in sample delivery/acceptance areas

Samples arriving at the laboratory are evaluated and recorded in the Sample Acceptance Unit according to the Sample Rejection Acceptance Criteria List. The recorded samples are delivered to the laboratory personnel responsible for the sample in the relevant Laboratory Department. During this process, the samples are reviewed according to the Sample Rejection Acceptance Criteria List and received from the sample delivery area by laboratory personnel. In preliminary evaluation; By looking at the test requests made from GENETIS, the suitability of the sample container, sample amount, labeling, etc. control is done. Unsuitable samples are rejected from the system and a new sample is requested. If the rejected samples are requested to be returned, they are returned with the Faulty Sample Return Report.

2.4.2. Sample Rejection/Acceptance Criteria

SAMPLE ACCEPTANCE CRITERIA:

Peripheral Blood Sample; For cytogenetic and molecular cytogenetic analyses, at least 2-5 cc of peripheral blood sample should be collected into a heparin green cap tube. For these tests, samples must be transported at a transport temperature of 2-24 ° and to reach the laboratory within 72 hours after collection. For molecular genetic (DNA/RNA) analyses, at least 2-5 cc of peripheral blood sample should be collected in a purple capped tube. For molecular genetic tests, it must be transported at 2-24 ° transport temperature (room temperature) and reach the laboratory within 72 hours after receipt.

Bone Marrow Sample;For cytogenetic and molecular cytogenetic analyses, at least 2-5 cc of bone marrow sample should be collected in a heparin green cap tube. For these tests, samples must be transported at a transport temperature of 2-24 ° and to reach the laboratory within 72 hours after collection. For molecular genetic (DNA/RNA) analyses, at least 4-10 cc of bone marrow sample should be collected in a purple capped tube. For molecular genetic tests, it must be transported at 2-24° transport temperature (room temperature) and reach the laboratory within 72 hours after receipt.

Amniocentesis Example; Approximately 15-20 cc amniocentesis sample sent for cytogenetic, molecular cytogenetic and molecular genetic examination should be placed in a suitable sterile injector. Injectors with black seals should not be used. The sample must be transported at 2-24 ° transport temperature (room temperature) and reach the laboratory within 72 hours after collection.

Chorionic Villus Biopsy Sample;Approximately 20-30 mg of the chorionic villus biopsy sample sent for cytogenetic, molecular cytogenetic and molecular genetic examination should be placed in sterile transport medium. The sample must be transported at a transport temperature of 2-24 ° and to reach the laboratory within 72 hours after collection.

Biopsy Sample from Evacuated Material;Approximately 1-2 cm3 of the biopsy sample from the discharge material sent for cytogenetic, molecular cytogenetic and molecular genetic examination should be placed in a sterile transport medium. The sample must be transported at 2-24 ° transport temperature (room temperature) and reach the laboratory within 72 hours after collection.

Examples of abortion materials that can be sent:

Placental Biopsy:A piece of at least 1 cm3 should be taken from the area close to the umbilical origin (fetal origin).

Skin Biopsy: Approximately 5 mm2 piece should be taken from the back, leg or hip.

Cord Biopsy: Approximately 2 cm piece should be taken.

Amnion Biopsy: At least a 2 cm2 piece should be taken from the area closest to the umbilical cord.

Skin Biopsy Sample; Approximately 1 cm3 of the sent skin biopsy sample for cytogenetics, molecular cytogenetics and molecular examination should be placed in sterile transport medium. The sample must be transported at 2-24 ° transport temperature (room temperature) and reach the laboratory within 72 hours after collection.

Solid Tissue Biopsy (Tumor) Sample;Approximately 5-10 mg of the skin biopsy sample sent for cytogenetics, molecular cytogenetics and molecular examination should be placed in sterile transport medium. The sample must be transported at 2-24 ° transport temperature (room temperature) and reach the laboratory within 72 hours after collection.

Paraffin Block Sections;For molecular cytogenetic tests, sections taken on a slide or in Eppendorf should be taken as at least 5 sections, and in tumor sections, an additional section should be taken as a section stained with hematoxylin and with the tumor area marked. The sample must be transported at 2-24 ° transport temperature (room temperature) and reach the laboratory within 72 hours after collection.
Obtaining RNA from Peripheral Blood;To obtain RNA, at least 4-10 cc of peripheral blood sample should be collected into a purple capped tube. Samples must be transported at 2-24 ° transport temperature (room temperature) and reach the laboratory within 72 hours after collection.
Vaginal/Cervical Examples: It should be sent with dry swap or special transport solution.
Swabs Taken from the Throat:dry swap
Serum: 2-5 ml falcon tube 2-24 °C

In addition to the patient's identity and indication information, the Informed Explicit Consent Approval Form regarding the procedure to be performed must be filled out by the patient and the physician and delivered to our department along with the sample.
Sample acceptance hours; Monday-Friday (weekdays) between 09:00-17:00. Samples that reach the laboratory at the appropriate time and conditions are accepted.
A sample with a test selection appropriate to its indication is accepted.
Samples in which the patient's identification information, request form and consent form are filled out accurately and completely are accepted.

SAMPLE REJECTION CRITERIA

1. Samples sent in the wrong sample container/tube will not be accepted.
2. Samples arriving at the laboratory more than 72 hours later (48 hours for liquid biopsy samples) will not be accepted.
3. Clotted blood samples will not be accepted in studies performed from peripheral blood.
4. Samples with damaged sample tubes/sample containers will not be accepted.
5. Frozen samples will not be accepted.
6. Samples not taken in the quantities recommended above will not be accepted.
7. If samples to be placed in sterile media (amniocentesis, chorionic villus biopsy, evacuation material, solid tissue, skin biopsy) are taken and sent under non-sterile conditions, the samples will not be accepted.

8. If tissue samples (chorion villus biopsy, evacuation material, solid tissue, skin biopsy) have been placed in alcohol or formalin, the samples will not be accepted.
9. Samples using fixatives other than formaldehyde will not be accepted in studies to be performed from paraffin block sections.
10. Samples sent with the wrong indication will not be accepted (decided by discussing with the doctor).
11. Samples in which the patient's identification information, request sheet and consent form are filled in incorrectly or incompletely will not be accepted.

2.4.3. Statistical analysis of rejected samples

If the sample is requested to be returned, through the Faulty Sample Return Report; If no sample return is requested, the Nonconforming Sample Registration Form is used. The laboratory monitors monthly faulty samples.

2.4.4. Initiating corrective and preventive actions

Sample taking and transportation training regarding the Laboratory Preanalytical Process are basic corrective and preventive activities.

2.5. ANALYSIS OF TESTS

2.5.1. Internal quality control studies

Internal quality control studies are carried out in accordance with the quality control rules defined in the Test Working Instructions for the relevant method.

2.5.2. Studying tests

Each test is carried out in accordance with the relevant Device Use and Maintenance Instructions and Test Working Instructions.

2.5.3. Reporting panic values

Tests with panic values are stated in the Panic Value List. These are the detection of pathological results in samples taken for prenatal diagnosis and preimplantation diagnosis (amniocentesis, chorionic villus sampling, cordocentesis, balstomer/trophoectoderm biopsy). In these cases, if pathological results are detected, the clinician who requested the test is contacted and more information about the patient's clinic is obtained, the doctor is informed about the test result and the report is approved. Panic value notification is recorded after consulting with the relevant physician, and the result is immediately sent to the relevant doctor and institution via e-mail.

2.5.4. External quality control studies

External quality control samples are studied together with patient tests for the tests within the program on the calendar days determined by the external quality control program of which we are a member. External quality control studies are carried out according to the Quality Control Program Procedure.

2.6. SAMPLE STORAGE PHASE

one. Samples are stored according to the periods and conditions specified in the Test Operating Instructions. It is also stated in the List of Storage Periods of Samples.

2.For molecular genetic tests, DNA samples are stored at <+4 ºC, RNA at <-80ºC, and the patient's primary sample is stored under appropriate conditions for the period specified in the List of Storage Periods of Samples. After the procedures are completed, blood samples are destroyed in accordance with the instructions.

3.For molecular infection tests, DNA is stored at <+4ºC and the patient's primary sample is stored at +4-+24ºC under appropriate conditions for 1 month. After the procedures are completed, blood samples are destroyed in accordance with the "Waste Management Procedure" by filling out a "Destruction Report". DNA samples of stored samples (sick child, ex-patient child) are kept indefinitely for the possibility of establishing advanced genetic tests.

4.For cytogenetic and molecular cytogenetic tests, primary samples such as heparinized blood, bone marrow sample, cell pellets, preparations and CDM images of the patient are stored indefinitely until the genetic diagnosis report is written. If there is a leftover primary sample in the tissue cultured samples, it is stored according to the List of Storage Periods of Samples.

2.7. CONFIRMATION OF RESULTS

The findings obtained are evaluated by the relevant personnel and the results are presented to the Medical Geneticist. After the result is approved, a report is prepared by the Patient Admission and Reporting Personnel.

2.8. REPORTING RESULTS

one. After the tests studied in the laboratory are analyzed, they are approved by the responsible physician and after approval, the Patient Admission and Reporting staff prepares a report. Approved reports are directed to the attention of the relevant patient/institution/doctor and shared via LIMS.

2.Urgent FISH test requests for prenatal diagnosis samples are processed and approved within 3-4 days.
3.In laboratory result reports, patient name and surname, Lab No/Protocol No, TR ID number, Age and gender, Department Name, Doctor's Name, Institution Name, Request Date and Time, Laboratory Acceptance Date and Time, Approval Date and Time, Report Date and Time. , Test Name, Result, Unit, Reference Values, Approving doctor and hospital address and contact information.
4.Reports of the results included in the panic value list are sent immediately after informing the doctor.
5.Pathological results are reported with detailed information about possible risks and consequences.
6.In accordance with the Genetic Diseases Evaluation Centers Regulation, gender is not specified in prenatal (before birth) and preimplantation genetic diagnosis reports, except for defects in sex chromosomes and sex-linked diseases.
7.It is updated immediately whenever the kit, method or device used changes. Reference ranges are always determined and updated by following national and international literature and reviewing prospectus information.
8.Patients can receive their test results in writing from our institution. If they wish, they can also access their results via e-mail.
9.In accordance with genetic diagnosis legislation, reported patient data (reports and analysis images) are archived and stored for 30 years.

2.9. STORAGE OF RESULTS

In accordance with genetic diagnosis legislation, reported patient data (reports and analysis images) are archived and stored for 30 years.

3. ALL TEST LIST

Annex.1 SG.LS.06 Test List

REVISION INFORMATION		
Revision date	**Revision Number**	**Revision Description**
26.05.2022	01	Rejection Criteria have been rearranged. Obtaining a Genetic Test Information Form has been added to the identity and indication information of the patients.

PREPARER	APPROVED BY