Product standards

REV #9	Description and nature of change: Replacement of chapter introduction in SMeL description and organization, insertion of paragraph 5.2, MD4-5- 6-7-8 and Sibioc recommendations.			
Signature date	May 20, 2024 2025.01.23 12:47:18 +01'00'			May 20, 2024 2025.01.23 12:47:30 +01'00'
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	Preparation	Checked	Verified	Approved

Summary

1. SMeL description and organization

The Da Vinci Analytical Laboratory following the reclassification of SMeLs as DGR XI\7044|2022 provides the following organizational structure:

Organizational Unit	UO Code	Macro activities	Building	Macro code activities
Laboratory General Clinical with Specialty Areas	121	General Clinical Pathology Microbiology Virology	Via Isella No. 89 Gambolò (PV)	3507
		Collection Center 1	Via Isella No. 89 Gambolò (PV)	3500
		Withdrawal Point 2	Via Ciro Menotti n. 5 Garlasco (PV)	3500
		Withdrawal Point 3	Via Roma No. 88 Vellezzo Bellini (PV)	3500
		Withdrawal Point 4	Via del Commercio No. 2 Pavia (PV)	3500
Laboratory of Pathological Anatomy	125	Pathology Anatomy Specialist	Via Isella No. 89 Gambolò (PV)	3527

The two laboratories share the same structure and the same JLab management system described in the appropriate operating instruction, which provides for the use of separate modules for the acceptance phase without creating problems or overlapping data. Analytical data is handled in separate ways. Two different areas were identified for receiving biological specimens handled by two different operators. The number of cytology specimens is consolidated and predictable, this allows a more precise weekly organization of the reading of the preparations. Considering the guidelines that indicate the maximum number of slides to be read in order to contain the risk of error, daily activity has been organized in the following way for business efficiency:

- Early morning hours are devoted reading cytology preparations and staining them.
- After 11 a.m. finished the sampling activity at the sampling point present on the premises and with the arrival of samples from the EPPs, the activity of the General Clinical Laboratory begins, until the early afternoon hours.
- The cytology activity is resumed in the late afternoon. Ample time is left for collegial reading of the preparations and possible discussions arising from them.

This organization will be modified if the workload changes. The presence of at least one Executive Officer and one Biomedical Laboratory Health Technician (BBLT) is always guaranteed during business hours, see linked forms (STD MD7).

The laboratory activities are summarized in three stages:

- Pre-analytic phase: patient identification and acceptance.
- Analytical phase: careful handling of analyzers, execution of examinations.
- Post-analytical phase: storage and preservation of samples for one week for possible repetition or supplementation, acquisition of results, report management, and delivery of the report to the user.

The activities of collection, storage, and transport of biological samples must be scrupulously carried out according to the best practices in place for the control of critical points in order to obtain intact samples for subsequent processing and, at the same time, ensure the protection of operators. Their potential infectiousness constrains their handling to appropriate procedures that reduce the risk of dispersion of infectious agents or potentially so in case of spills with spillage of the material from the containers. Traceability of the process must be ensured at every stage.

2. Purpose

Define the operational methods for the safe handling of the collection, storage and transport of organic material ensuring the quality of performance and traceability of the entire process.

3. Scope of application

This procedure applies for any activity carried out by staff working at the SMeL site or at external pickup points.

4. Pre-analytical phase

All SMeL staff have been trained by taking single-topic FAD courses on:

- Criteria of Acceptability of Biological Sample.
- The preanalytic phase.
- The identification of the patient and biological specimen.

4.1 Patient identification

Reservations are not required for performance of laboratory tests. It is possible to
Request diagnostic laboratory investigations in three ways:

1- by going to a General Practitioner (GP) or Free Choice Pediatrician (PdLS) who will prescribe the tests on a National Health System prescription pad (SSN pink slip);
2- submitting the prescription to the of a Freelance physician on the personal prescription pad (white prescription);
3- directly requesting the analysis from the laboratory at time of acceptance (without no doctor's prescription).

The procedures acceptance are as follows:

- ✓ Respect the order of arrival;
- ✓ To ensure social distancing, only one person or the maximum two if cohabiting;
- ✓ Present the 'counter clerk with identification (health card) and prescription, if available;
- ✓ Make payment of the stipulated amount in cash or by Pos;
- ✓ the patient will then be invited to sit in the drawing room.

Using a bar code reader, the utility's tax code is recorded through the JLab management system, which assigns the patient a unique identification code (patient ID), while the master data (last name, first name, residential address) are entered by the operator. The master data will be available on further access. Consent to data processing is requested by signing the document produced at admission through graphometric signature on a tablet; this operation will take place only once a year after viewing the regulations available in the waiting room.

Analytes will be entered on the same management system and adhesive labels will be printed to be affixed to the tubes. The labels will state:

- the barcode;
- the sample ID;
- patient ID;
- The date of the withdrawal;
- date of birth;
- last name and first name;
- The type of tube (serum, hematology, coagulation, etc.).

If the patient only needs to hand in biological samples of various kinds (feces, urine, other organic materials), the secretarial staff, having completed the check-in phase, will invite the patient to enter the sampling room; the health worker will affix the label on the container and hand it over to the laboratory.

A receipt will be issued showing personal details, the examinations requested, the amount paid and the date of delivery of the report with the possibility of a proxy to be shown at the time of collection. In the case of a proxy, it is necessary to show up with one's own ID and a copy of the proxy's ID. The patient has the opportunity to choose whether to pick up the report in the traditional paper format or by email.

The administrative Iter will be concluded with the issuance of the invoice. The user will now be able to enter the withdrawal room where a health worker will be waiting for him/her to proceed the withdrawal operation.

For VAT-registered customers, the electronic invoicing program has been initiated; the J.Lab management software directly sends electronic invoices to the Digital Hub (electronic invoicing management software), which transmits them to the customer through the Interchange System (Sdl); these invoices will be digitally archived to store them in accordance with the law.

The patient identification methods described above will also be implemented at the external collection point; the only difference will be the management of access to the facility and the

Infection prevention mode related to the logistics of the building and the availability of different spaces.
For urgent examination requests, in order to optimize the organization of work, we proceed with differentiated modalities between the two workshops as detailed below.

- General Clinical Laboratory

Upon request made by the User, delivery of urgent reports is possible (excluding Saturdays) from 12 noon on the day of collection for examinations performed on the premises, from the
17.00 for those in service. At the time acceptance, the request is highlighted by entering Urgency (red writing) in the management system, which appears with the notation "U" on the worksheet. As a result, the operator will give priority to the sample in the analytical process and when signing the report.

- Pathologic Anatomy Laboratory

The request for urgency is indicated on the specimen accompanying form, and anticipated by telephone by the specialist who performed the collection. The operator in charge of receiving cytology specimens is pre-alerted verbally, and upon arrival of the specimens completes the "Urgent Examinations" form (STD MD 6), handing it to the person in charge of scheduling reading shifts. The report will be available within 24 hours of sample arrival.

4.2 Preparing the user for examinations

Venous blood sampling. General indications:
Before taking any blood sample, it is important to pay attention to some small but important rules so that the blood test is as correct as possible. Factors such as **fasting**, **diet, medication intake**, **exercise**, and **posture** can to varying degrees affect the success of the analysis. Therefore, here are some simple tips to simplify and facilitate the operation of the blood draw and analysis:

- FASTING: There is unanimous agreement that the patient should present at the blood draw at least 8-12 hours fasted. Only modest amounts of water may be taken during this period and sugary drinks, alcohol, coffee, and smoking must be absolutely excluded. In fact, these substances can make almost all hematochemical determinations inaccurate or even impossible.

- DIET: In the days leading up to the sampling, the diet should be as habitual as possible, avoiding abrupt changes in caloric intake either in excess or in deficit. In fact, following the drastic reduction caloric intake (300/600 calories/day), a 30% decrease in plasma volume was found. This alteration induces rapid changes in the blood which analysis reveals. The diet must also be habitual qualitatively i.e., with an intake of carbohydrates, proteins and fats that follows the normal personal diet.

    - DRUGS: There are numerous studies regarding the effect of drugs on the testing of laboratory. Interference can occur directly or indirectly to

analytical level. In the former case they are not always and completely predictable in their magnitude due to a wide range of individual variables that determine the absorption, metabolism and elimination of the drug. Not of all drugs on the market are the side effects sufficiently known, nor are any interferences analytically analyzed and indicated. The most correct preparation of the patient for hematochemical examinations should include the absolute and most prolonged absence of any drug treatment. This rule should adhered to without exception in the case of screening or metabolic profiling in healthy people and asymptomatic subjects.

- PHYSICAL EXERCISE: Changes in enzyme activities and some analytes from skeletal muscles as a result of intensive and prolonged exercise are expected phenomena and generally to be avoided immediately prior to sampling or in the 8 to 12 hours preceding it. This rule must absolutely be observed in case of urinalysis for determination of creatinine clearance.

- SMOKING: Tobacco smoking causes transient and/or stable alterations in many analytes. For example, one hour after smoking one to five cigarettes, there is an elevation in the blood concentration of fatty acids, free glycerol, aldosterone, cortisol, etc. The extent of these alterations is mainly a function age and smoking mode (cigarette, cigar, pipe). It is recommended, therefore, to abstain from smoking for at least 10 hours before the collection

For information and clarifications on preparation for collection, the patient can contact the secretarial staff either by phone or by going to the laboratory in person.

4.3 Mode of sample collection

- SAMPLE COLLECTION COMPLETE URINE EXAMINATION

It is necessary to collect morning urination in appropriate container, which can be purchased at the pharmacy or provided by the Laboratory; no different containers are accepted.

- 24-HOUR URINE COLLECTION

Urine from the night and day should be collected as follows:

– Eliminate the first morning urine and mark the time (example 7 a.m.);

– collect from this time onwards all urine from the day and night; the next morning finish the collection with urine issued at the same time as the previous day (e.g. 7 a.m.) in the same container; when the collection is complete, take the container to the laboratory. It is important to remember that urine should be stored in a cool place during the collection period.

- URINE COLLECTION FOR URINOCULTURE

Proceed with thorough cleaning of the external genitalia (wash with soap and water and rinse with plenty of water). Discard the first urine emitted and collect the next urine directly into the appropriate wide-opening sterile container that can be purchased at a pharmacy or

delivered by the laboratory, taking care not to touch its inner parts. Immediately close the container and check its closure.
For children, urine can be collected in special sterile adhesive plastic bags that can be purchased at pharmacies. The external genitals are cleaned then the bag is adhered to the pubic region where it should be left for a time not exceeding 40-45 minutes. If urination has not occurred during this time, the pouch should be replaced with another one after washing the external genitalia. The bag should be delivered to the Laboratory without transferring the urine.

- SEMINAL FLUID COLLECTION FOR SPERMIOCULTURE

Perform the examination at least 5 days after discontinuing any antibiotic therapy. After thorough genital and hand washing, collect the semen in a sterile container with a wide opening (e.g., urine container), taking care not to touch the insides.

- SPECIMEN COLLECTION FOR PERFORMING FECAL CHEMOPHYSICAL EXAMINATION, COPROCULTURE, PARASITOLOGICAL EXAMINATION, AND HP RESEARCH

Feces should be collected in the appropriate containers equipped with a scoop. The amount of feces to be collected is equal to the size of a walnut. The material can be stored at 2°C-8°C for 24 hours.

- SPECIMEN COLLECTION FOR FECAL OCCULT BLOOD TESTING

Preparation:

- Do not collect stool samples during menstrual flow or if in the presence bleeding hemorrhoids or blood in urine;
- Avoid taking excess alcohol, aspirin or other drugs that may cause gastrointestinal irritation and cause bleeding. If necessary, discontinue their intake at least 1 to 2 days before the test after consultation with the attending physician

Sample collection:

- Collect a stool sample in the appropriate container equipped with a dry paddle and clean.
- Unscrew the cap of the sample collection vial. Insert the paddle and collect small amounts from different areas until a volume equal to the size of a walnut is collected.
- Reinsert the paddle into the collection vial and screw the cap on.

Deliver the sample to the laboratory as soon as possible

- SAMPLE COLLECTION FOR PERFORMING THE SCOTCH TEST

The necessary materials are provided by the Analytical Laboratory.
Mode of performing the test:

The test should be performed in the morning upon awakening, before washing and defecating.
-Cut a piece of clear tape slightly shorter than the slide provided by the Laboratory.
-Apply the adhesive tape to the perianal folds (with the adhesive side facing the folds), compress well on the underlying skin for a few seconds.
-Tear off the tape and apply it tightly to the slide provided by the laboratory (avoiding the formation of air bubbles).
-Wash your hands well when the picking is completed.
-Insert the slide into the slide holder.
Deliver it to the Analytical Laboratory as soon as possible and no later than one day after collection.

- SPECIMEN COLLECTION FOR SPUTUM EXAMINATION

Sputum should be collected in a sterile container. This is done by first rinsing the oral cavity by gargling a few times with water then performing a deep expectoration and collecting the sputum directly into the container.
Deliver to the Analytical Laboratory as soon as possible and no later than one day after collection

- URINE COLLECTION FOR CYTOLOGICAL EXAMINATION

Discard the first morning urine and collect subsequent urine directly into the container provided by the Laboratory. It is necessary to collect one sample per day for three consecutive days by marking on the containers I, II, III. Samples collected in this way must be kept refrigerated until the day of delivery, which can be done for all three samples on the third day. The containers were prepared by adding an appropriate amount of 50° alcohol in order to ensure the preservation of the material.

WARNING:
The container where the collection takes place contains 50° alcohol: do not ingest, do not leave within reach of children. In case of accidental ingestion, contact the nearest emergency room. In case of skin contact, wash thoroughly with water, if contact is with the eyes:
Wash thoroughly with water and refer to the nearest emergency room. NB:
cytology examinations are not accepted on Saturdays.

The Laboratory makes itself available for the delivery of sample collection containers to your home. The user should not in any way implement operations to optimize the samples, as it will be the responsibility of the laboratory staff to carry out these procedures. No containers other than those delivered either directly by the Laboratory or by the pharmacy will be accepted.
Sample collection mode is available the user by going to the secretary's office.

4.4 Mode of withdrawal

4.4.1 Venous sampling

The phases into which this activity is divided are:

- Ascertaining the patient's identity: the first task the test taker is required to perform is to ascertain the patient's identity. This ascertainment is done by asking the patient to pronounce his or her last name and first name and verifying that they match on the label placed on the tubes.
- Preparing the patient: before taking the blood sample, the sampler should always ascertain the patient's physical condition by obtaining information on fasting, physical activity immediately preceding the sample, and emotional condition. If the patient is not in a suitable condition for the blood draw, it must inevitably be postponed to another date. The picker should try to reduce the patient's anxiety, one of the general factors of vosoconstriction. A calm atmosphere is an important requirement for accomplishing a good withdrawal, a goal easily achieved by reducing the waiting time from admission to withdrawal as much as possible. If the drawer deems it necessary or at the explicit request of the patient, it is possible to perform the draw in a lying position.
- Hand washing and use of gloves: prior to performing the sampling, the sampler must wash his or her hands as per WHO guidance implemented by the Ministry of Health. The operator should then wear latex-free gloves properly. Only if it is difficult to find a suitable sampling site is it acceptable to temporarily remove the gloves to increase the sensitivity of palpation.
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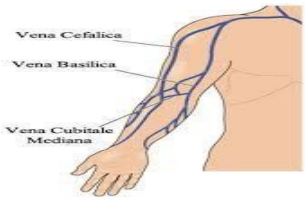
- Sampling point: The next step involves choosing the sampling point. The central veins of the forearm are preferred, alternatively the basilic vein and the vein of the back of the arm can also be used. The wrist and hand vein are to be used only if the previous sites are not accessible. Drawing from the dorsum of the foot is not considered because of possible complications that may occur.
- Techniques to identify the vein: first place the tourniquet about 10 cm above the chosen site, use enough pressure to generate venous stasis but not to cause pain or discomfort. Keep the tourniquet in place for about 1 minute and not for the duration of the sampling; once the suitable vein is identified,

release the tourniquet. Before proceeding with the puncture, it is best to disinfect the skin using a absorbent cotton pad soaked in alcohol solution; do not palpate the skin again after cleaning. Make the puncture with the needle at an angle of 10-20° to the skin and in line with the chosen vein. Insert the needle 10-15 mm until it reaches the lumen of the vein; move the plunger of the syringe taking great care not to move to prevent needle thrust from piercing the vein wall. Release the lace when the syringe is almost full; fill the tubes, discard the needle and syringe in the special waste container. Immediately place a cotton ball over the puncture site asking the patient to apply moderate pressure while keeping the arm extended and upward. In the event that a puncture fails, never use the same needle for repeat puncture, and after two attempts it would be a good idea to send the patient to another puncturer or in the absence of a colleague try again only after the patient has calmed down.



- Filling of tubes: during blood collection, the operator must verify that the amount of blood to be drawn is sufficient for the correct performance of the multiple tests; the amount of blood must respect the correct ratio with any anticoagulant present in the tube itself and the correct filling must be visually verified by the operator thanks to the filling line on the tube. Immediately after collection, tubes containing an anticoagulant (Na-citrate, EDTA) must be gently inverted 4/6 times order to ensure proper mixing of blood and anticoagulant. The first tubes to be filled are those containing anticoagulant and the serum tube last.

WARNING: In the event that the collection was particularly difficult to prevent the tubes from being completely filled, the patient will be notified, and the GP/PdLS will be contacted to prioritize the most urgent examinations.

<u>GLUCOSE LOADING CURVE</u>

The patient should present fasting to undergo an initial blood draw to exclude the presence of critical blood glucose values (< 126 mg/dl) prior to oral glucose intake. Subsequently, other blood samples will be taken, as prescribed by the physician, after taking a predetermined amount of glucose.

- Standard OGTT in pregnancy:

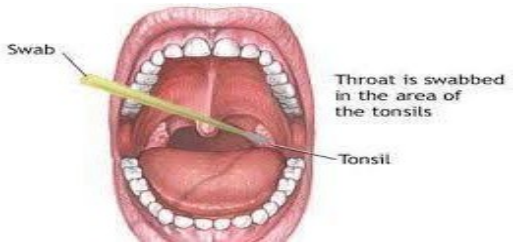
Basal sampling;
Administration of glucose solution (75 g glucose); Second draw
after 30'; Third draw after 60'.

Glucose is supplied by the Laboratory in the form of syrup contained in 150-mL bottles (Glucose Sclavo Diagnostics 75g/150 ml). It is recommended that the patient take the glucose drink within a maximum time of about 5 minutes after the basal blood draw and take small sips continuously to avoid the onset of vomiting. It is not possible to drink for at least 15 minutes after the glucose intake, so until the end of the examination take only a moderate amount of water at room temperature. During the entire time of the examination, the patient should remain at rest without eating and smoking, in an area controlled by health care personnel so that they can intervene in case of illness.

4.4.2 Microbiological sampling

Pharyngeal and nasal swab

- Patient preparation: the patient should be advised to present fasting, without having washed bodies and avoid the use of oral mouthwash; to have discontinued any antibiotic therapy at least 6 days prior to the examination.
- Collection: operator should wash hands and wear gloves; use sterile swabs with appropriately labeled transport medium. Invite the patient to bend his head back and open his mouth wide, warning him that he may gag during rubbing with the pharynx by inviting him to say "AH" for this; take the appropriate swab out of the case, insert it between the tonsillar pillars and behind the uvula. Begin rubbing the walls, avoiding contact with the tongue, cheeks, dental arches and saliva. Once this is completed, the swab should be placed in the appropriate transport by unscrewing the cap; the swab thus made is labeled and delivered to the laboratory.
- For the nasal swab, it is necessary to insert the swab into the roots and push it along the nasal cavity so that it reaches the posterior part of the nasopharynx; rotate it gently so that it becomes abundantly covered with nasal secretion. Repeat the same maneuver in the other root. When the collection is finished, it should be placed in the special tube containing the transport medium and broken up inside.



Eye swab

Remove the sterile specimen from its package only at the time of collection and immediately place it in its case, immersed in the appropriate transport medium (Amies) once collection is complete. Gently open the eyelid rhyme and absorb the material therein with the swab. If required repeat the same operation for the other eye taking care to indicate DX and SN on the swab label.

CAUTION: The patient must have ceased any antibiotic therapy for at least 7 days. Vaginal-

endocervical swab

Sampling should be performed by trained personnel according to the following procedure:

- Have the patient assume the gynecological position.
- Insert a sterile and possibly lubricated bivalve speculum into the vaginal canal only when performing endocervical swabbing.
- Insert the sterile swab into the vaginal canal, firmly rotate it 360° in one direction (clockwise or counterclockwise), wait 10 seconds, then take it out.
- Use one pad for each category listed below:

a) Common microorganisms: use a sterile swab in transport medium (Amies) and Store it at room temperature for up to 24 hours.

b) Mycoplasmas: clean the cervix with sterile swab and remove the cervical mucus, then introduce a sterile swab into the endocervical canal by performing gentle scraping of the mucosa. Immediately introduce the swab into the transport broth by removing the stick protruding from the vial with scissors and store it at room temperature for up to 24 hours.

c) Chlamydia: use a sterile swab without transport medium.

CAUTION: In all such cases, the patient must abstain from sexual intercourse in the 24 hours prior to the examination and have ceased any local/general antibiotic therapy for at least one week and must not be menstruating.

Storage use material: Speculum at room temperature, sterile swab with transport medium (Amies) at room temperature, dry swab at room temperature and transport broth in refrigerator 2-8° C until expiration date.

HPV research swab

The Molecular Biology technique is used to search for Human Papilloma Virus (HPV): after dilating the vaginal canal with the speculum and highlighting the cervix, gently insert the pipe cleaner (Cytobrush) into the endocervix making sure that the bristles remain visible; rotate the stick ¼ or ½ turn once then remove and extract. Place the cytobrush back in the container and identify it immediately.

CAUTION: In all such cases, the patient must abstain from sexual intercourse in the 24 hours prior to the examination and have ceased any local/general antibiotic therapy for at least one week and must not be menstruating.

Storage use material: Speculum at room temperature, sterile swab with transport medium (Amies) at room temperature, dry swab at room temperature.

4.4.3 PAP TEST cytology collection

Before taking the blood sample, make sure that the optimal conditions for taking the blood sample are met (having finished your menstrual cycle for at least 3 days, not having had sexual intercourse in the two days before the test, and not having used vaginal eggs or creams).

- Identification of the woman: each specimen must be accompanied by a special request in which the following data essential for proper performance of the examination must be included: first name, last name, date of birth, date of last menstruation, and medical history of the patient.
- Identification of the slide: the frosted part of the slide should be marked with the woman's first and last name using a pencil or glass pen; do not use markers, the ink dissolves in contact with fixative or alcohol.
- Withdrawal: properly positioning a suitable light source and properly calibrating the speculum size, introduce and position the speculum to visualize the portio. Use water to facilitate introduction of the speculum; the use of any other lubricant is not recommended because it can contaminate and alter the preparation. Carefully inspect the cervix and in case of abundant mucus or exudate gently cleanse with a gauze pad, possibly wet with saline. Do an exocervical, and an endocervical sampling in sequence; the exocervical sampling should always be done first to avoid contamination by bleeding that may follow the endocervical sampling. Take Eyre's spatula, insert the most elongated part at the beginning of the cervical orifice and rotate clockwise 360 degrees; take the cytobrusch spatula, insert it into the cervical canal and rotate 180-360 degrees.
- Preparation by traditional method: place the taken material in the two distinct areas of the slide, defined by convention, taking care not to overlap the material and applying gentle pressure to cellular integrity. Fix the preparation immediately to avoid cell degeneration phenomena resulting from drying; even a short wait can damage cells. (Photo 1) Spray fixative should be kept at a distance 15-20 cm from the slide to prevent cell displacement and air bubble formation. The slide thus prepared is left to dry in a horizontal position. (Photo 2)
- Preparation on "thin layer" method: this technique involves immersing the sample of cells taken in a preservation liquid contained in special jars, which must be opened and identified only before starting the sampling. The sampling technique is the same as that described for the conventional pap test. Then the preparation is set up not manually but using special machines, which will be stored at room temperature until staining. (Photo 3)

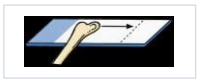


Photo 1

Photo 2

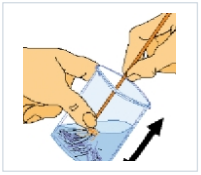


Photo 3

4.4.4 COVID-19 swab collection.

The preparation of operators is described in the procedure "PPE devices used" at the
to which we refer.
The steps of swabbing execution are as follows:

- Obtain the sterile swab specifically for Sars Cov 2 from the kit provided;
- Explain to the patient the maneuvers that are about to be performed so that he or she fully understands what will be performed and increases his or her cooperation;
- Explain to the patient that he or she may experience mild discomfort during the procedure,
- Ask the patient to open the mouth and expose the tongue; use a tongue depressor if necessary;
- Rub back of the pharynx and tonsil area on both sides
  Without touching the lateral mucosa of the mouth or the base of the tongue;
- Make the head recline backward;
- Insert the swab into the nostril and rub carefully against the turbinates and reach the posterior portion by this route. Repeat the operation in the other nostril;
- Insert the swab into the tube containing the appropriate buffer and proceed with performing the test.(See FAD Training course entitled "Swabs for the Diagnosis of Covid-19 in Adults and Children" Eureka Ltd.)

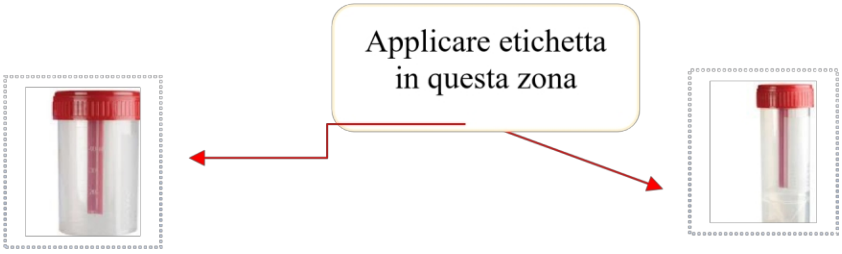
4.5 Identification of samples

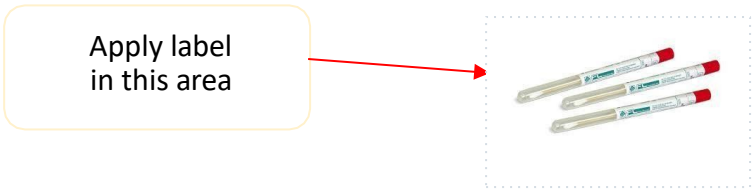
Tubes should be labeled before collection, never afterwards. All information necessary to uniquely identify the patient appears on the label, as made explicit above.

The barcode must be intact and central, the print crisp and smudge-free. Poor-quality printing of the labels will compromise the automatic instrumentation's reading of the barcode, causing continuous blockages in the analytical process resulting in the need to reprint the labels. Apply the labels vertically by placing them just below the cap (as shown in the image).

The barcode uniquely identifies the individual specimen for a specific patient. For the acceptance non-blood specimens e.g. urine or stool specimen collection, microbiological specimens such as pharyngeal swab, vaginal swab, etc., the following procedure is followed:

- ✓ Generally, **urine** is collected at home and delivered in the red cap container provided by the laboratory or bought at the pharmacy; it will be printed a label that will be attached to the wall of the container (see image below). The same procedure is applied to **stool** samples.





- ✓ For **microbiological samples**, (swabs) the label is always applied to the swab tube; the sample can be delivered directly because taken at another facility or performed at the SMeL.
- ✓ For **cervico-vaginal cytologic** sampling **(pap smears)**, exo- and endocervical material is swiped on a sandblasted slide previously identified with surname and name. This type of specimen can also be collected at the site and in EPPs in which a midwife is warranted or outside specialists (STD MD8).

- ✓ For **home** withdrawals**.** The front office staff after noting the master data on the STD MD1 form prints the labels for the analytes correctly
  communicated, alternatively some are printed for known examinations that will be supplemented later by having the prescription completed the acceptance of samples the front office will contact the user informing him/her of the cost, day and method of report collection.
- ✓ A form (STD MD8) will be filled out for sampling performed at the **farms** (STD MD2) with the details of the company, the list of employees to be subjected to health surveillance and analysis required by the Medical Officer. It is not possible in this case to prepare barcode labels in advance; each sample will be identified by reporting the worker's surname and name manually. Acceptance will be arranged at the headquarters as per close.

4.5.1 Type of test tubes

The choice of test tube cap color is far from random and is made according to the type of test that is to be performed on the blood. In fact, each blood draw is performed according to standard procedures, and it is essential for the sample to be suitable to choose the right anticoagulant, which does not interfere with the assay of the analytes. color table makes it very easy to associate each cap with a specific anticoagulant. Although there are differences between laboratories, worldwide efforts are being made to standardize interpretation criteria as much as possible to avoid training health care personnel each time.

- ✓ **Brown/White/Blue** Cap: Tubes with this cap are intended to be used for serological tests. These tubes in fact contain at their
  internal silica microparticles that activate coagulation at the time the tube is inverted, after the sample is taken. We can assay a wide range of analytes on this type of sample: liver enzymes, thyroid hormones, antibody titer. cannot be used for clotting tests, since the blood has already formed a clot and therefore the clotting factors have already been "consumed."

- ✓ **Purple cap (*ethylenediaminetetraacetic acid*)**: EDTA is able sequester Calcium ions, forming insoluble salts with it: the inability to use Calcium ions
  blocks the coagulation cascade. This tube can be used directly on automated analyzers to CBC examination (white blood cell count, red blood cell count, platelet count). In fact, EDTA does not alter the morphology of blood cells, and within 3 hours of collection, the sample can also be used to make blood smears for observation under a light microscope.

- ✓ **Blue Cap (Sodium Citrate)**: this anticoagulant, like EDTA, also sequesters the Calcium ions. Blood treated with sodium citrate is used for the determination of. of ESR (a test that measures the rate at which red blood cells settle to the bottom,

separating from plasma), for the study of coagulation factors (fibrinogen, PT, APTT) and for the determination of platelet function.

✓ **Grey Cap (Sodium Floride)**: this anticoagulant, in addition to sequestering Calcium ions, is a substance that stabilizes blood glucose concentration, inhibiting glycolysis. For this reason used at the time when it is necessary to determine blood glucose on the sample.

✓ **Green cap (Heparin)**. heparin, unlike other anticoagulants, does not act on calcium ions but prevents thrombin and fibrin formation. It is an anticoagulant "natural" since it is present at low levels in both blood and tissue. Heparin is used for plasma determinations in the clinical biochemistry laboratory. However, it cannot be used CBC examination since it alters the morphology of blood cells and causes platelet aggregation.

4.6 Mode of storage of samples

It is well known that the vast majority of errors in laboratory medicine are concentrated in activities that precede (preanalytical phase) or follow (postanalytical phase) sample analysis. In particular, a percentage ranging from 60% to 70% of errors are concentrated in the preanalytical phase, especially in activities where the human component is still crucial. If a sample taken is not stored at an appropriate temperature, e.g., too hot or too cold, the results provided by the laboratory may be altered. Some general information is provided below.

4.6.1 Venous blood samples

Samples should be delivered to the Laboratory as soon as possible to allow centrifugation. Routine testing can usually **be** considered **30' to 6 hours after collection**. Shaking of samples should be avoided because of the possibility of producing hemolysis. Tubes should be kept in an upright position to promote coagulation

in serum samples avoid activation in those for coagulation tests.

4.6.2 Urine samples

Ideally, urine sediment examination should take place within 1 hour of release (GR and GB are preserved differently depending on pH and osmolarity); delivery should therefore immediate. It is not always so easy to meet these tight delivery times; even for urine therefore, there is a margin of tolerance to be adopted in which the

possible changes occurred in the sample appear to be minimal. In agreement with published data in the literature, the **6-hour** time limit **from release** seems acceptable as an hourly limit for performing the test without significant interference with the results. In the case of analytes whose determination is required on the 24-hour collection, as a rule, the sample should not be kept refrigerated to avoid precipitation of crystals.

4.6.3 Stool samples

Only a small amount of feces will be delivered to the laboratory. The sample can be stored in a refrigerator while waiting for delivery.

4.6.4 Cytological specimens (Pap test)

The material should be stored at room temperature.

4.6.5 Histological specimens

The material submitted for histological examination consists of tissue fragments (biopsies). The mode of preservation of these specimens is critical to ensure the stability of the structural and biological components of the excised tissue. Formalin is the fixative par excellence for tissues taken for pathologic anatomy diagnosis because it maintains altered cell morphology. Small biopsies are collected in containers containing buffered formalin; the volume of fixative should be about ten times that of the specimen and stored at room temperature.

4.6.6 Sample storage at external sampling points

Biological samples taken or collected at the external collection point reach the SMeL site within 4 hours, so do not require special storage directions. Blood samples should not be centrifuged prior to their transport but kept at room temperature. At the end of the sampling activity and before departure, it should be verified that:

- No samples on the workstations in the sampling area;
- Let there be no unlabeled samples;
- Any patients accepted late are properly processed and samples added to the transport container;
- Be properly reported any failure to deliver samples of urine or feces the patient;
- All tubes are closed properly;
- All containers are closed properly.

4.7 Modes of transportation

4.7.1 Biological material transport (blood/urine/feces)

Transportation should be done using a **three-envelope system consisting of primary secondary and outer receptacle**:

✓ **Primary Receptacle**: understood as the container that holds the biological specimen retrieved: test tubes, tubes, ampoules, etc. Such a container must possess the

following technical features, in order to avoid and/or reduce, the potential exposure of the worker to Biological Agents:

- Be made for the specific use, in waterproof, labelable, leak-proof material Watertight, with closure.
- Allow easy introduction of biological materials to easy handling. The primary receptacle should be laid in test tube holders inside the secondary receptacle.

✓ **Secondary Receptacle**: is a container made of durable, waterproof, watertight material suitable for containing and protecting the primary receptacle. It can contain

multiple primary vessels as well.

The outside of the secondary receptacle must be affixed with the tabs showing the identifying and descriptive data of the contents; the data must be contained in a sealed envelope and in compliance with the standard protecting privacy.

Such a container must also possess the following technical characteristics:

- transparency and unbreakability to constantly display and thus ensure the integrity of the contained samples;
- be complete with absorbent support that can be used as a test tube holder or as a support base on which to lay bottles and test tube holders; - be lightweight because the minimal weight facilitates transport of the cases. - be chemically sterilizable.

✓ **Outer receptacle:** constitutes the outermost container in which to place the secondary receptacle to prevent damage caused by external factors such as physical agents or water.

Such a container can made a variety of materials: rigid cardboard, plastic, wood or other impact and weather resistant materials.

In the warmer months of the year, to prevent overheating of biological material, "siberini" are used, which should be placed outside the secondary container.

Used for a transport of numerous biological samples

Used for a transport a few biological samples

Vehicle transport

- Blood and biological samples (stool, urine)

Da Vinci Analytical Laboratory's sampling activities are conducted off-site only in the following cases:

- at home for both the inhabitants of the municipality where the laboratory is located and in the municipalities in which the sampling points are open.
- at companies in the area that are located within a maximum radius of 30 kilometers for health surveillance of workers.
- At the external sampling points.

Transportation is carried out using an air-conditioned passenger car; the outer container must be placed firmly, upright and securely in the vehicle itself.

Inside the transport vehicle is of a decontamination kit for use in case of accidental spillage of the biological material including: blotting paper, disinfectant, disposable gloves special waste container.
Verification that samples are transported correctly is done by filling out the MD3 form described in the chapter on traceability.

4.7.2 Transport of cervico-vaginal preparations

Three-layer packaging, consisting of primary, secondary and tertiary container, is provided for cytological preparations. The transport of these specimens takes place at room temperature, and it is recommended that the material smear on appropriate slides be completely dried before transport. Containers of the material sent in fixation fluids must be closed with great care, an indispensable precaution under pain of impossibility of any analytical continuation. The slides must be stored in the appropriate rigid containers, packed in envelopes containing the sender's/recipient's inscription and placed in the secondary container. The forms accompanying the preparation are placed outside the secondary container, again packaged in envelopes containing the sender/recipient inscription. The secondary container must then be placed in the tertiary container.

Vehicle transport

- Cytological specimens

For the transportation of cytology specimens (pap smears), the laboratory has entered into a contract with the company Co.Mi.Tras. The routes to be followed are established in advance according to the customer's needs, and the transporter is obliged to comply with the planned routes and to promptly inform the sender and consignee of any changes or unforeseen events that occur on the route. The package prepared by the sender's facility must always reach its destination intact and must under no circumstances be opened during transport. Again, transport must be carried out in compliance with current health regulations and the Highway Code. The vehicle must allow for the static and safe storage of the transported containers and must be equipped with a Kit for the treatment of any dispersion of biological material

4.7.3 Maintaining the cold chain

The cold chain is a temperature-controlled logistics chain; monitoring temperature means **measuring temperature at regular time intervals**. In this way, temperature trends can be kept under constant control.
Data loggers were created precisely for this: they record temperature at very short intervals (on the order of seconds, or even less depending on the case). This provides the most accurate measurement possible. Based on the model**, the** data loggers are able to autonomously detect temperature fluctuations and, through fully automated mathematical calculations, allow us to understand at a glance whether the temperature has remained at acceptable levels or not during the various stages of transport. The following steps are taken for the transport of biological samples:

- Biological samples are transported using a three-envelope system (primary, secondary, and tertiary vessel)
- The tertiary container arranges side pockets in which the siberines will be placed.
- The data logger will be placed inside the secondary container, setting an acceptable range between 0°C and +10°C.
- Upon arrival at the SMeL, the data logger is plugged into a pc through a USB port and the PDF file is downloaded, which will, after being checked, be saved on the SMeL server.

4.7.4 Recommendations in case of accidental spillage

In case the primary container lets out the contents due to uneven sealing of the cap or breakage as a result of dropping it, proceed as follows:

• Wear PPE. If the containers are placed in airtight bags, discard the bag directly into an infectious risk waste container; if the containers are placed in an airtight secondary container, remove any containers still intact and clean the container with sodium hypochlorite. Allow 5 minutes and. remove with disposable cloth to be disposed of as infectious-risk medical waste.

4.8 Non-compliance pre-analytical phase

The personnel in charge of receiving the sample, must:

- Check with the data logger for proper maintenance of the cold chain if the samples come from outside;
- Check the conformity of the sample as described below;
- Complete the STD MD3 form in case of noncompliance by indicating the patient ID for individual ineligible samples, or the number of samples received in case of transport for exceeding temperature range as verifiable from data logger graph.

Forms are completed in a computerized medium; and possible nonconformities are:

1. Hemolyzed or clotted sample;
2. Barcode labels not well readable on biological samples;
3. Insufficient material;
4. Absent or incorrectly filled out accompanying forms.

The corrective actions to be put in place will be:

- For NC 1 and 3, the draw must be repeated, and the secretarial staff contacts the patient by phone inviting her to come in to repeat draw;
- For NC 2the label is reprinted;
- For NC 4, reference is made to documentation issued by companies for health surveillance. In these cases, the Medical Officer in Charge is contacted to acquire the missing data.

The preventive actions to be put in place is the sensitization of personnel to comply with the correct procedures.

4.9 Summary tables conservation/transportation

The tables below summarize the methods of storage, transportation and the container to be used for the different materials to be analyzed.

TABLE 1 - MAIN HEMATOCHEMICAL INVESTIGATIONS.

MATERIAL	TEST	CONSERVATION	TRANSPORT	CONTAINER
Blood whole, serum, plasma	ACTH, Ammoniemia, Gastrin, Homocysteine, Somatotropic hormone, C Peptide, Calcitonin, Osmolarity Plasma, Parathormone, Vitamin D.	At refrigerated temperature (4-8 C°), up to 6 hours	Isothermal container + "siberino" within 3 hours	
Serum	All other chemistry-clinical tests	At room temperature up to 6 hours	Isothermal container within 3 hours	
Urine	Ex. Urine Full	At room temperature up to 6 hours	Isothermal container within 3 hours	

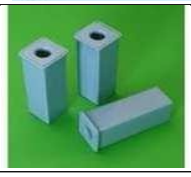
Whole Blood	All Hematology Tests	At room temperature up to 6 hours	Isothermal container within 3 hours	
Plasma	Routine Coagulative Testing	At room temperature up to 6 hours	Isothermal container within 3 hours	
Plasma	Special Coagulative Tests (Factors, LAC, etc.)	At room temperature up to 4 hours	Isothermal container+"sib erine" within 3 hours	
Stool	Chemical-physical examination	At room temperature up to 6 hours	Isothermal container within 3 hours	

TABLE 2 - MAIN MICROBIOLOGY INVESTIGATIONS.

MATERIAL	TEST	CONSERVATION	TRANSPORT	CONTAINER
Urine	Ex. culture (*urinoculture)*	At room temperature, up to 6 hours	Isothermal container; within 3h	
Tamp. earphone Pharyngeal Tamp. nasal Tamp. Cutaneous Tamp. Vaginal	Culture ex.	Ambient temperature in the its transport ground (8-10 h); at 4-8°C se si provide times of longer delivery (24-48 h).	Container isothermal; within 3h	
Seminal Fluid	Culture ex.	NO	Send immediately to the Laboratory	
Stool	Ex. culture *(co-culture)*	At room temperature, up to 12 hours	Isothermal container; within 3h	
Stool (parasitological examination)	Parasites in feces; egg search	Container with formalin 48-72 h	Isothermal container; within 3h	
Stool (examination parasitological)	Oxides (scotch test)	Room temperature.	Glass slide with scotch tape transparent	
Sputum	Culture ex.	Send immediately to Lab; (4-8°C up to **two** days)	Isothermal container; within 3h	

5. Analytical phase

SMeL guarantees in-house or by using the service to perform the services included in the Lombardy Region tariff schedule.

The proper execution of the analytical phase is guaranteed by:

- ⇒ Adherence to the instructions of the manufacturers of the routine maintenance plans, as per the manual located at each electromedical equipment, and the timely request for the intervention of technicians in case of extraordinary maintenance;
- ⇒ Internal Quality Controls (IQC) and External Quality Controls (EQC) as per IO CQ operational instruction.
- ⇒ Surveillance of the critical control point consisting of manual entry of examinations obtained from equipment not directly connected to Management due to double-checking before validation of results.
- ⇒ For examinations performed in-house, values found to be out of range are rechecked by repeating the session after verifying successful calibration and CQI. For regular users, for whom a historical record is available, data trend includes a critical evaluation related to the patient's history. When the value is confirmed, the user's referring physician is contacted.
- ⇒ Laboratories with which a collaborative relationship has been established for tests performed in service, in case of an out-of-range value, contact the facility by phone to share the patient's history if known, and still proceed to repeat the test.
- ⇒ Staff experience and mentoring for new hires coupled with ongoing training.

5.1 Analytical methods used

The analytical methods used are given below:

- ⇒ The two-step sandwich-type enzyme immunoassay method associated with a final fluorescent detection (ELFA) (Enzyme Linked Fluorescent Assay) is used for **enzyme immunoassays**.
- ⇒ For **chemistry-clinical**: enzymatic and colorimetric systems are used, for the **Coagulation** the Nephelometric method.
- ⇒ For **serum protein electrophoresis** migration on agarose gel.
- ⇒ For **hematology**, 24 parameters of a blood sample are detected. WBCs are analyzed by an optical detector block that is based on the semiconductor laser flow cytometry method. RBC values and platelets are analyzed by the RBC detector with the Hydro Dynamic Focusing method. Hemoglobin UHC is analyzed by the HGB detector with the SLS detection method for hemoglobin.
- ⇒ For **urine** and chemical and microscopic systems are used.
- ⇒ For **rapid** visual reading **tests**.

5.2 Management of critical values

Laboratory tests play an important role in clinical decision making. At a territorial SMeL, values requiring prompt communication are only rarely highlighted. This need was originally emphasized by Lundberg in 1972, who defined a critical (or panic) value as any laboratory result that shows an immediate danger to the patient's health and therefore requires appropriate and timely medical measures to be taken.

It should be emphasized that the critical value may be the result not only of a patient's pathological condition, but also of an error in the laboratory process, from sample collection to data reporting; therefore, potential errors in laboratory activity should excluded before defining a critical value.

The Italian Society of Clinical Biochemistry and Clinical Molecular Biology (SIBioC), the Italian Society of Laboratory Medicine (SIMeL), in concert with the Italian Committee for the Standardization of Hematological and Laboratory Methods (CISMEL), through the Intersociety Study Group (SG) on "Standardization of Extra-analytical Variability of Laboratory Data," have issued guidance, on the identification and management of critical values to which reference is made for the definition of those of the SMeL. The most representative analytes for the purpose of timely diagnosis have been identified, and the range of acceptability (STD MD4) has been defined for each one; for all others, they will be evaluated on a case-by-case basis. For examinations sent in service, the manner in which critical values are handled at reference laboratories has been asked, and we will follow these guidelines.

Criticality in data management emerges from cross-sectional comparison, with data chosen by the laboratory, and longitudinal comparison with previous data from the same patient, if available.

Laboratory personnel are aware of the main causes of error that can occur during a laboratory process, so they put in place all appropriate procedures to rule out that the data generated is the result of:

A. pre analytical error, the following checks should be made:
   - ✓ Verify the identity of the sample;
   - ✓ Correctness of sample collection, transport and storage.

B. analytical error, we proceed as follows:
   - ✓ Verification of proper operation of electromedical equipment;
   - ✓ Reconfirmation of the result with repetition of the analysis;
   - ✓ verification of reagent data sheets to rule out potential interference in the determination;
   - ✓ exclusion of a possible error in automatic data transfer from the instrument to the host or error in manual entry by the operator.

Once the criticality of the value is confirmed, the Laboratory Director, or his/her delegate, will promptly notify the result to the attending physician and, if not reachable or unknown, to the patient suggesting that the patient promptly contact his/her GP after collecting the report even if it is partial. If necessary, such a report will be emailed to the GP using the official email with extension .nome.cognome@crs.lombardia.it

It is verified that all information has been correctly received by the recipient (physician or patient), subject to a request for repetition by the interlocutor of all information communicated.
Communications are recorded on a form (STD MD5) in which the following information appears:

- Patient ID code
- Date and time of notification
- Identity of the person who received the information
- Identity of the operator who identified the value and the one who reported it (can also be the same person)
- Notes: any comments related to communication if necessary and important.

6. Postanalytic phase

After the analytical phase is finished, the report is made available both in paper format and on web-based portal. The paper can be picked up from the secretary's office directly by the person or a delegate from the day indicated on the receipt/collection form at the times indicated below.

Headquarters

Monday to Friday	**4:00 p.m. to 6:00 p.m.**
Saturday	**8 a.m. to 10 a.m.**

At the dedicated external collection point (Garlasco)

Monday through Saturday	**7:30 a.m. to 10:00 a.m.**

At the external collection point in social-health facility (Vellezzo Bellini)

On Tuesdays and Fridays	**4:00 p.m. to 6:00 p.m.**

At the external withdrawal point in social-health facility (Lainate)

Monday through Friday	**4:00 p.m. to 6:00 p.m.**
Saturday	**9 a.m. to 10 a.m.**

At the external collection point in social-health facility (San Martino Siccomario)

Monday through Friday	**2 p.m. to 7 p.m.**

The portal is accessed by following the directions provided by front office staff at the time of check-in with delivery of the facility card as detailed in the IO SI to which reference is made.

7. Related forms

Privacy policy Receipt/report form	
Home withdrawal form	STD MD1
On-farm withdrawal form	STD MD2
Noncompliance biological samples	STD MD3
Critical Values Table	STD MD4
Recording critical values	STD MD5
AP Urgent Exams	STD MD6
Weekly rostering	STD MD7
Facilities List	STD MD8
Check List for venous sampling	STD AL1
Urine collection	STD AL2
24H urine collection	STD AL3
Occult blood detection	STD AL4
Collecting co-culture	STD AL5
Sperm collection	STD AL6
Urine collection cytological examination	STD AL7
Scotch test collection	STD AL8
Sputum collection	STD AL9
Stool collection parasite search	STD AL10
User preparation for examinations	STD AL 11

External document "Covid Swab Fad Course"
External document "Recommendations for the identification and management of critical values in clinical laboratories," Clinical Biochemistry 2008, vol. 32, no. 3