Impact of the Superior Health Council (SHC) report 9525 (pre-analytical variables of biological tests on human body material (HBM) donor samples) on your tissue bank

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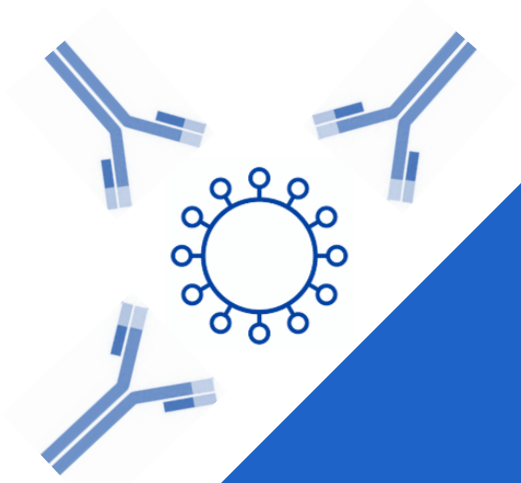

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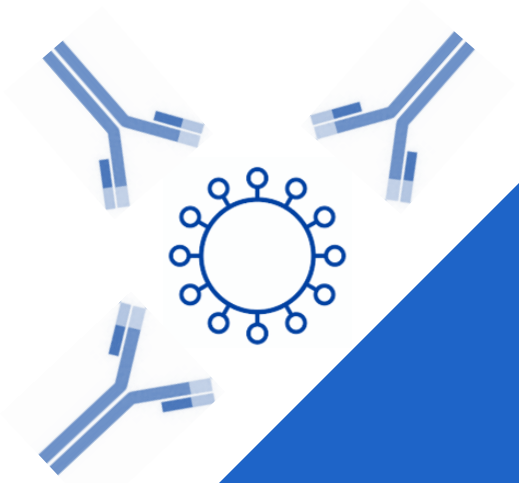

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Preanalytical phase

- Test: choice
- Test: order
- Patient preparation
- Sampling
- Transport
- Sample preparation
- Quality controls

Preanalytical variables

Patient-related

- ✓age, gender, race
- ✓menstruel cyclus, pregnancy
- ✓position
- ✓circadian rythme
- ✓season
- ✓hight
- ✓life style (diet, exercise, smoking, caffeine, alcohol)

Process-related

- ✓sample identification
- ✓anticoagulantia
- ✓temperature (collection, transport, storage)
- ✓delayed serum/plasma separation
- ✓delayed analysis
- ✓veneus occlusion

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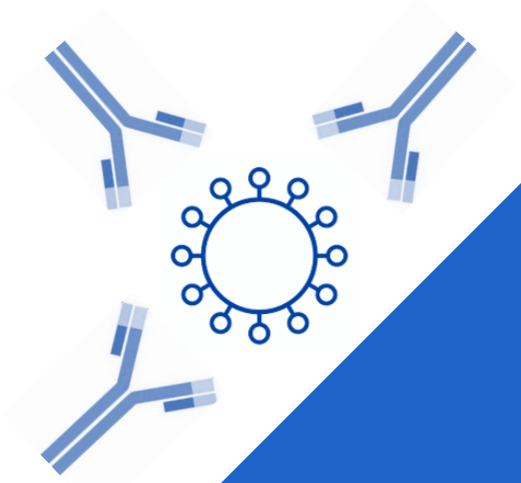

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Principles of viral diagnostics

Looking for virus or viral component

Looking for immune response

Viral culture

Antigen detection

Molecular methods

Viral serology

Direct approach in laboratory diagnosis of viral infections

Indirect approach in laboratory diagnosis of viral infections

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Preanalytical variables:
Viral Serology (1)

Broad use of commercially available, CE-marked kits

- Specimen Collection:
  - Proper timing
    - Clinical course
  - Sample type and quantity
    - Serum/plasma
    - Multiple aliquots
  - Collection/transport devices
    - Anticoagulantia **!**

Preanalytical variables:
Viral Serology (2)

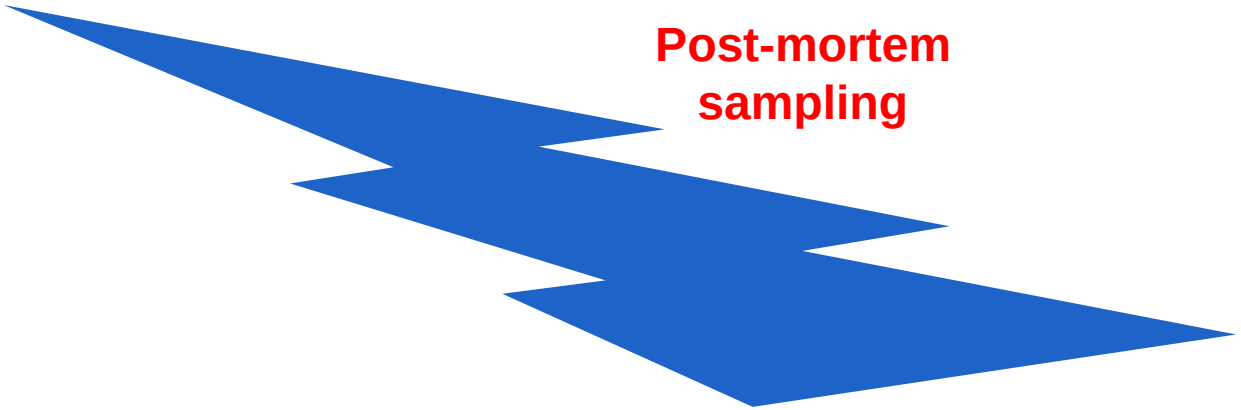
- Specimen Transport and Storage:
  - Proper instructions
    - Handling and transport conditions
      - At room t° for up to 7 days
      - At 2-8°C for up to 14 days
      - Frozen (-20°C) for extended periods
      - No influence of miltiple freeze-thaw cycli
  - Proper monitoring and registration
    - Collection date
    - Shipping date
    - Receival date

Preanalytical variables:
Viral Serology (3)

- Specimen Processing:
  - Rapid plasma/serum separation
  - Inhibitors/Interfering Substances
    - Lipemic/hemolyzed/icteric

Preanalytical variables:
Viral Serology (3)

- Specimen Processing:
  - **Rapid** plasma/serum **separation**
  - Inhibitors/Interfering Substances
    - Lipemic/**hemolyzed**/icteric



Principles of viral diagnostics

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Preanalytical variables: CLSI/NCCLS Molecular Methods

MM6-A: Quantitative Molecular Methods for Infectious Diseases; Approved Guideline (1)

- ***"Appropriate specimen handling, including controlled specimen collection and transport conditions, is critical to ensure specimen integrity and the accuracy of quntitative nucleic acid detection."***
- Specimen Collection:
  - Proper timing
    - Pretherapy for HIV viral load
  - Sample type and quantity
    - Multiple aliquots
  - Collection/transport devices
    - No irreversible binding of nucleic acids
    - No interference with amplification or detection
      - Heparin

Preanalytical variables: CLSI/NCCLS Molecular Methods

MM6-A: Quantitative Molecular Methods for Infectious Diseases; Approved Guideline (2)

- Specimen Transport and Storage:
  - Proper instructions
    - Handling and transport conditions
    - Rejection criteria
  - Proper monitoring and registration
    - Collection date
    - Shipping date
    - Receival date
    - ~ Approximate t° of specimen at receival

Preanalytical variables: CLSI/NCCLS Molecular Methods

MM6-A: Quantitative Molecular Methods for Infectious Diseases; Approved Guideline (3)

- Specimen Processing:
- ***"One of the most significant potential sources of inaccuracy and variability in quantitative molecular tests."*** !
  - Nucleic Acid Extraction
    - As simple as possible
      - Avoidance of specimen contamination
      - Avoidance of nucleic acids loss
    - Proper storage conditions of processed specimens
  - Inhibitors/Interfering Substances
    - Incorporation of an internal calibrator

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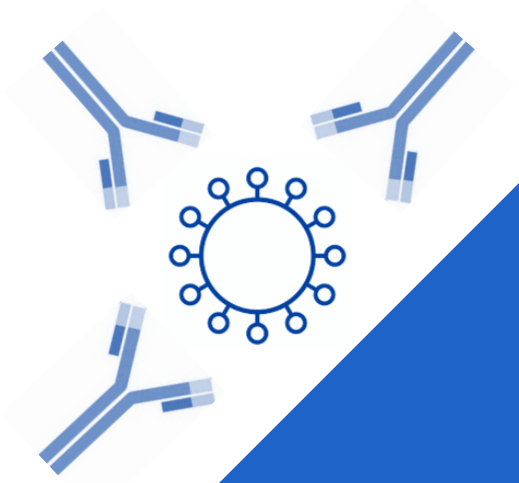

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1. **Sampling related variables**
   - 1.1. Type of samples
   - 1.2. Condition of the donor
   - 1.3. Collection of the samples
   - 1.4. Volume of the sample
   - 1.5. Choice of specific tubes
   - 1.6. Pre-mortem sampling
   - 1.7. Post mortem sampling
   - 1.8. Labelling of tubes (avoid mixing up of labels)

2. **Variables related to transport, storage and processing of blood samples**
   - 2.1. Transport
   - 2.2. Centrifugation and haemolysis
   - 2.3. Storage before and after centrifugation
   - 2.4. Serum versus plasma
   - 2.5. Serological tests versus NAT testing

3. **Variables related to dilution**
   - 3.1. Haemodilution
   - 3.2. Pooling of samples

4. **Available tests and validation**
   - 4.1. Available tests
   - 4.2. Validation

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Dilution: haemodilution

If transfusion or infusion of fluids (blood products, colloids and/or crystalloid) was performed shortly before donation, haemodilution may lead to a decreased detectability of the antibodies or antigens in the donor blood and possibly to false-negative results. An algorithm is applied to evaluate the degree of haemodilution (Kitchen et al, 2013). The EDQM states that it is current practice in a number of countries to consider 50 % calculated haemodilution to be the maximum allowable to minimize the risk of a false-negative test result due to serum dilution.

Exceptionally, a tissue establishment may accept tissues and cells from a donor with plasma dilution of > 50 %, but only if each required test has been validated appropriately for use with a diluted test specimen. In such cases, to help reduce risk, additional testing should also be performed using molecular tests (i.e. NAT) for HIV, HBC and HCV, and possibly for other viruses, depending on the donor's travel history, underlying disease or other factors.

Validation of the test(s) used

Dilution: pooling of samples

Pooling of samples cannot be used in the field of cell- and tissue banking. Also more in general, clinical diagnstic labs have to work on individual samples and that is also the case for molecular tests.

Pooling is only minimally[20] discussed in EDQM for tissues and cells, but the following statement is made for pooling of samples of the same donor: specimens of blood, serum or plasma from the same donor must not be mixed together for testing, whether collected at the same time or at a different time.

If cell- and tissue banks outsource their biological testing to blood establishments, they should stipulate in their agreement with the blood establishment that the serological as well as the NAT testing has to be performed on strictly individual, not pooled, blood samples.

Importance of mutual agreement between tissue bank and performing laboratory

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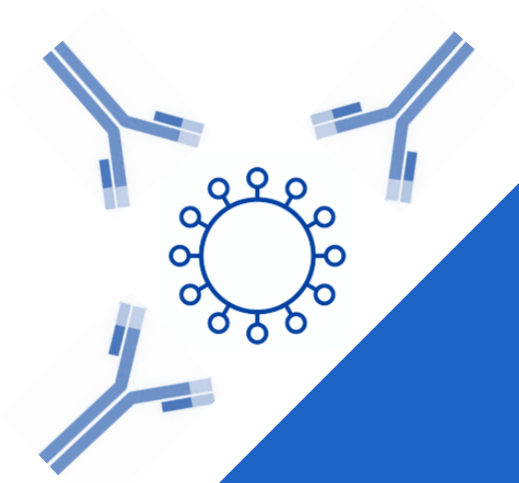

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As mentioned before, it is very important to have an agreement between the establishment for HBM and the laboratory that performs the serological and NAT testing, (regardless of whether the laboratory is internal to the institution or external to it). It may be useful to also involve the transplant centre in the agreement.

This agreement must include at least the following elements, but should not necessarily be limited to them:

- the type of tissue donor (living vs deceased),
- the fact that it is often not possible to obtain a new sample,
- the minimal sample volume required,
- the priority of the tests to be performed, in the event of reduced volume,
- the collection conditions (centrifugation, type of tubes, labelling (incl. anonymisation, …),
- the transport conditions (interval time, temperature, packaging, time of delivery),
- information about the performed tests, their CE marking, their validation, frequency of performance, time to response, …,
- performance of tests on individual samples, no pooling,
- formatting of the results (SHC 9314; e.g. results of microbiological cultures, etc.),
- the people who are responsible for selecting the tests to be performed,
- the necessity to notify the bank as soon as possible in the event of positive tests,
- the licensing/certification/accreditation of the lab according to the relevant regulatory frame,
- the cost and the billing of the tests,
- the transmission of (positive) tests to the establishment of HBM and/or other involved stakeholders (e.g. transplant center).

IT'S ALL HERE

Conclusions/take home messages

IT'S ALL HERE

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http://www.health.belgium.be/nl/advies-9525-pre-analytische-variabelen-van-biologische-tests-op-mlm-donormonsters

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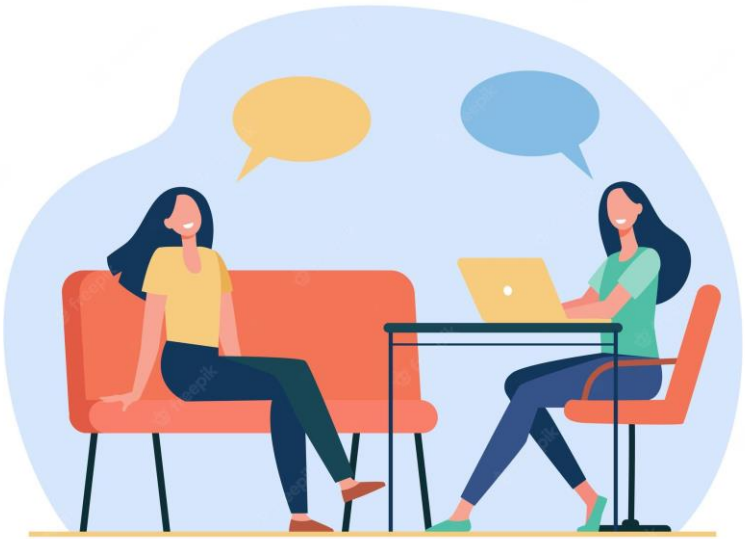


Contract Agreement Template

CONTRACT AGREEMENT

BY-Company Name Here

This Agreement is made on _____/_____/_____

BETWEEN

1. [The First Party Name Here]
2. [The Second Party Name Here]

RECITALS

1. _____
2. _____
3. _____
4. _____

AGREEMENTS

_____:

1. *Organization Information.*

_____
_____
_____
_____

2. *Services to be performed.*

2.1 _____
2.2 _____
2.3 _____

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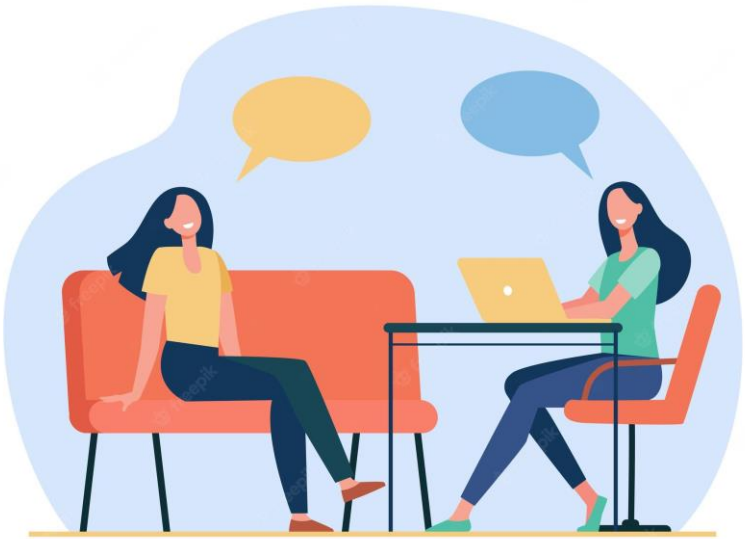


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