

# The Interreg NWE Project **Codex4SMEs**:

## Webinar rules

1. Switch off your camera and your microphone.
2. During the whole webinar, only the speakers will be allowed to talk.
3. Ask questions via the CHAT.
4. **If you cannot hear the speaker please inform us via CHAT. Alternatively, use the dial-in number:**



# Interreg NWE Project Codex4SMEs Introduction

Webinar, 9<sup>th</sup> of March, 2021

Pablo Zardoya-Laguardia, PhD

Biobank Graz (Medical University)

# Interreg North-West Europe

EUROPEAN UNION

## Interreg NWE Programme

European Territorial Cooperation programme with the ambition to make the North-West Europe area a key economic player and an attractive place to work and live, with high levels of innovation, sustainability and cohesion.

# Codex4SMEs Project

## Codex4SMEs

= **Companion diagnostics expedited for (4) Small and Medium Enterprises**

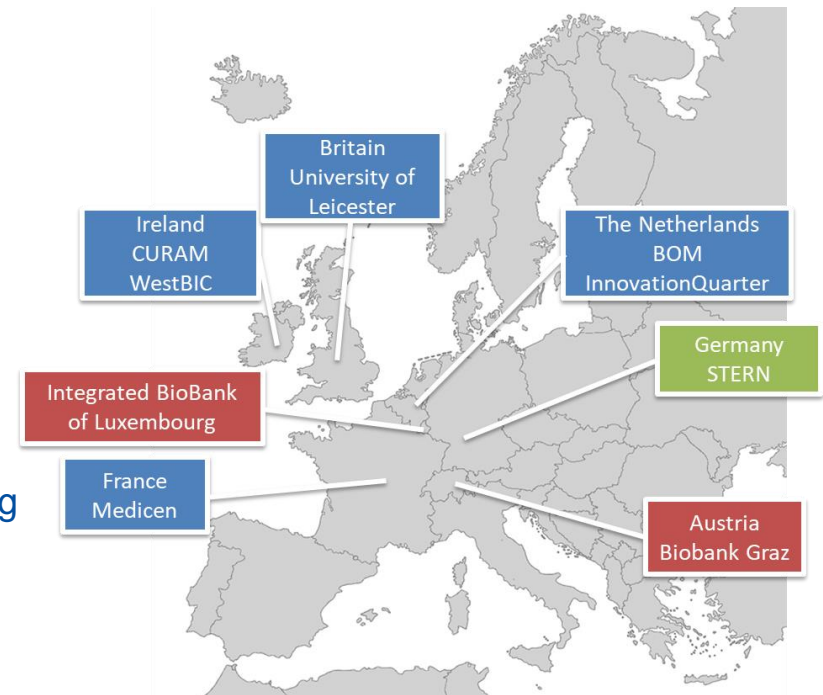
**Total budget:** 3 M €  
**ERDF budget:** 2 M €  
**Project period:** 51 months

### Objective of the project:

- Improve healthcare by enhanced adoption of Personalized Medicine
- Establishing a network which supports SMEs along the value chain of Companion diagnostics (Cdx) development

### Associated Partner:

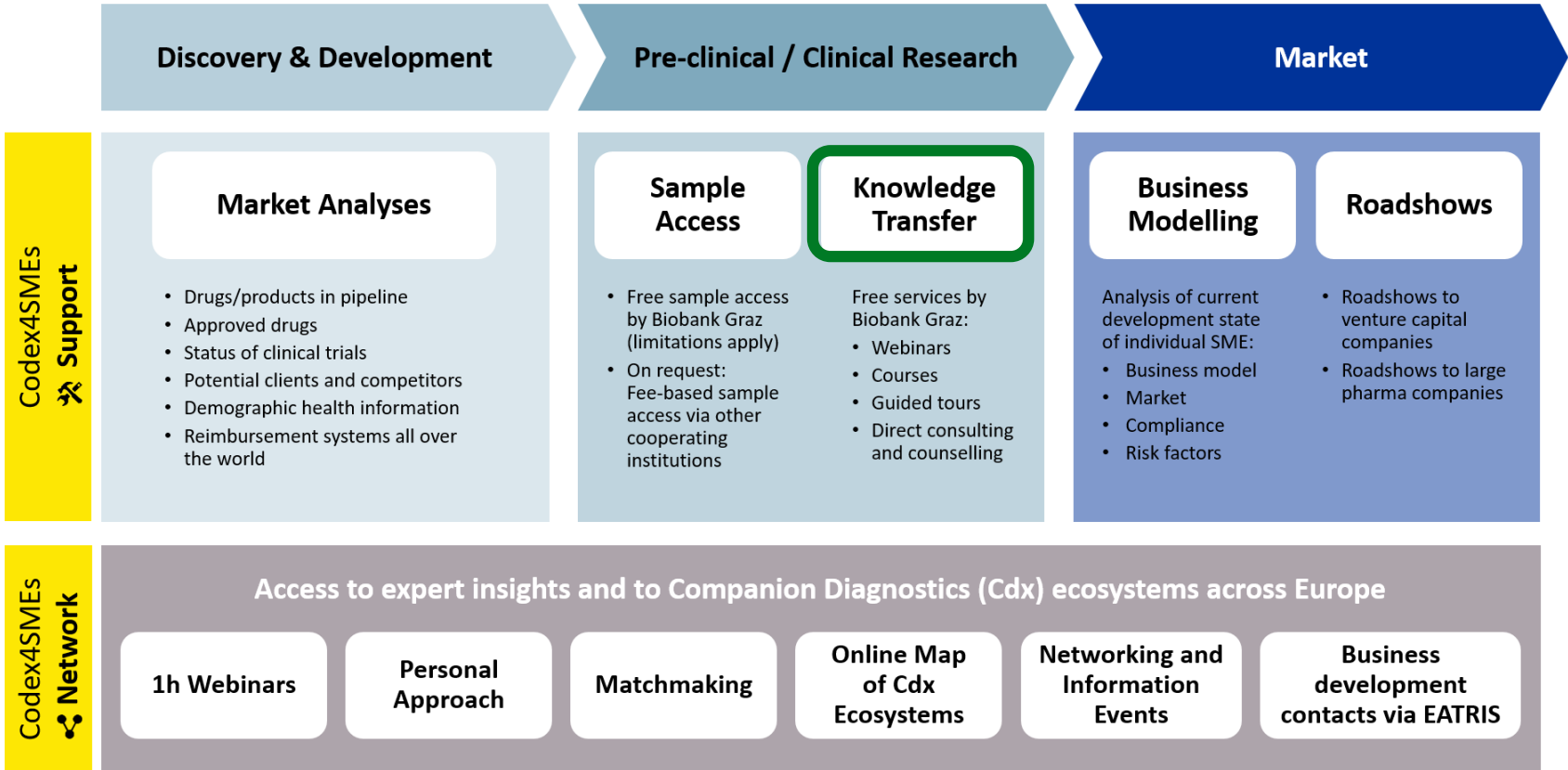
EATRIS European Infrastructure for Translational Medicine, NL



# Codex4SMEs project introduction

## What is in for you?

Our services for your path towards the market



# Codex4SMEs Project – Free Sample Access Service

to boost your research in the diagnostics' sector

## Samples for Pilot-projects (no ethics vote required)

- ◆ To test or establish a new method
- ◆ Clinical samples from a max. number of **5 patients**

## Samples for Research-projects (valid ethics vote mandatory)

- ◆ Sample access for research projects/biomarker research
- ◆ Clinical samples from a max. number of **20 patients**

- Open for any European SME working in the Diagnostics' sector
- Samples are provided by the Biobank of Graz
- Ask for sample availability at [codex4smes@medunigraz.at](mailto:codex4smes@medunigraz.at)
- More Info: <https://www.nweurope.eu/codex4smes>

# Biological Samples in Biobanks – Types, Quality, Management and Gains for your Business/Research

Webinar, March 9<sup>th</sup>, 2021

Pablo Zardoya-Laguardia, PhD

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# Biobanks – The Basics

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## Definition

“biorepository that accepts, processes, stores and distributes biospecimens and associated data for use in research and clinical care”

## Goal/Importance

Collect, store and disseminate specimens and related data

Maintenance standards in different processes: collection, processing, storage, tracking and shipment of biospecimens are key to the outcome of a multitude of studies

**What type of tissue samples?**

Yvonne G. De Souza and John S. Greenspan. 2013. Biobanking Past, Present and Future: Responsibilities and Benefits. AIDS. 28; 27(3): 303–312.



# Types of Biological Samples – Tissue Sampling

## 1. Tissue Sampling

Tissue sampling refers to various procedures to obtain body fluids or tissue (e.g. bone, muscle, etc.) for analysis.

### 1.1. Frozen tissue/samples

- Long term preservation
- Native state
- Stored at  $-20^{\circ}/-80^{\circ}\text{C}$  (equipment)
- Less common source of archived material



### 1.2. Formalin-Fixed Paraffin-Embedded (FFPE)

- Long term preservation
- Denatured state
- Stored at RT
- Most common source of archived material



# Types of Biological Samples – Tissue Sampling

## 1. Tissue Sampling

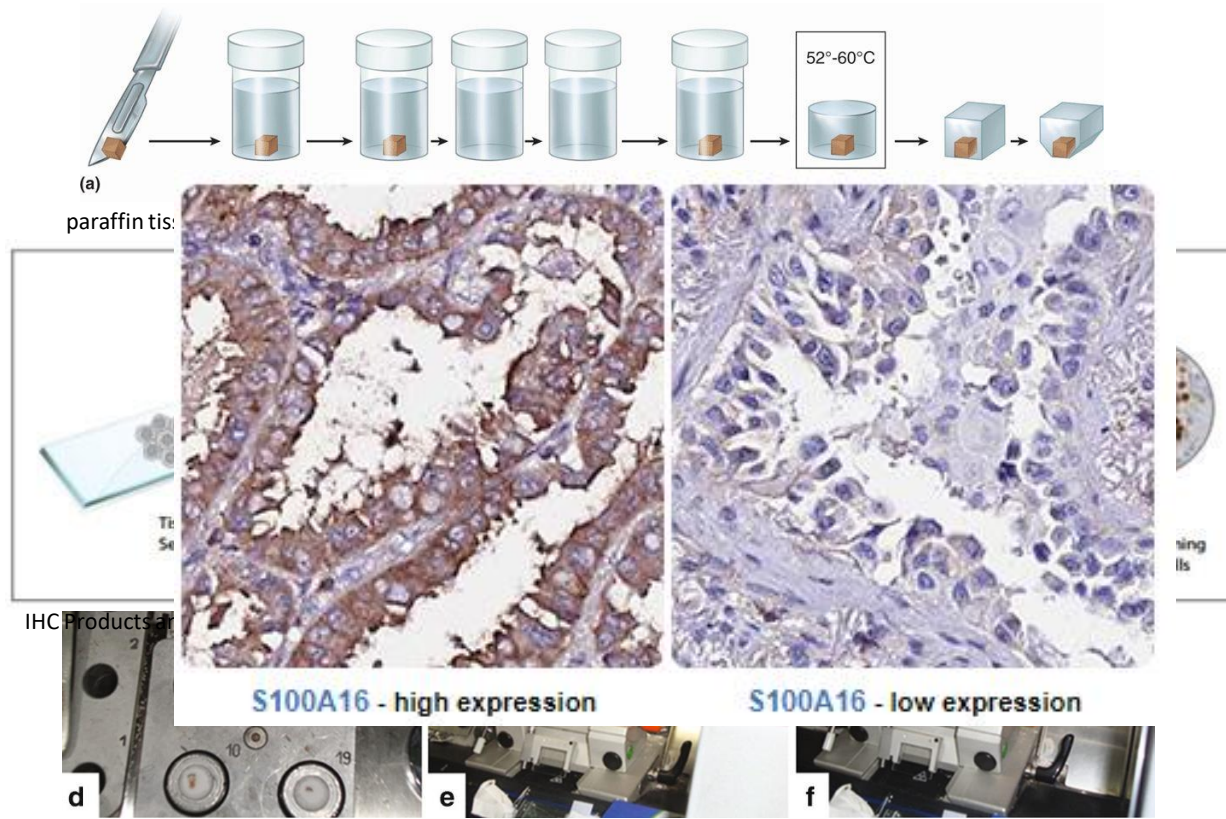
### Comparison between the sample 2 types

Frozen Tissue	FFPE
Ultra low T° freezer required ( <b>more expensive</b> )	Stored at RT in a cabinet ( <b>cheaper</b> )
No dangerous handling ( <b>safer</b> )	Formalin: volatile & toxic ( <b>riskier</b> )
<b>Less laborious &amp; quicker</b>	<b>Laborious &amp; time consuming</b>
<b>Vulnerable</b> power/mechanical failures	<b>Stable</b> for decades
<b>Structural integrity compromised</b>	<b>Good cell/tissue morphology</b>
Protein native state ( <b>biochemical analysis</b> )	Protein denatured ( <b>no biochemical analysis</b> )
DNA/RNA well preserved ( <b>genetic analysis</b> )	DNA/RNA damaged ( <b>limited genetic analysis</b> )
More standardised ( <b>less interlab variability</b> )	Less standardised ( <b>more interlab variability</b> )
<b>Not familiar</b> for pathologist	<b>Established method</b> for diagnosis

# Types of Biological Samples – Tissue Sampling

## 2. Methods for analysis

### 2.1. Immunohistochemistry

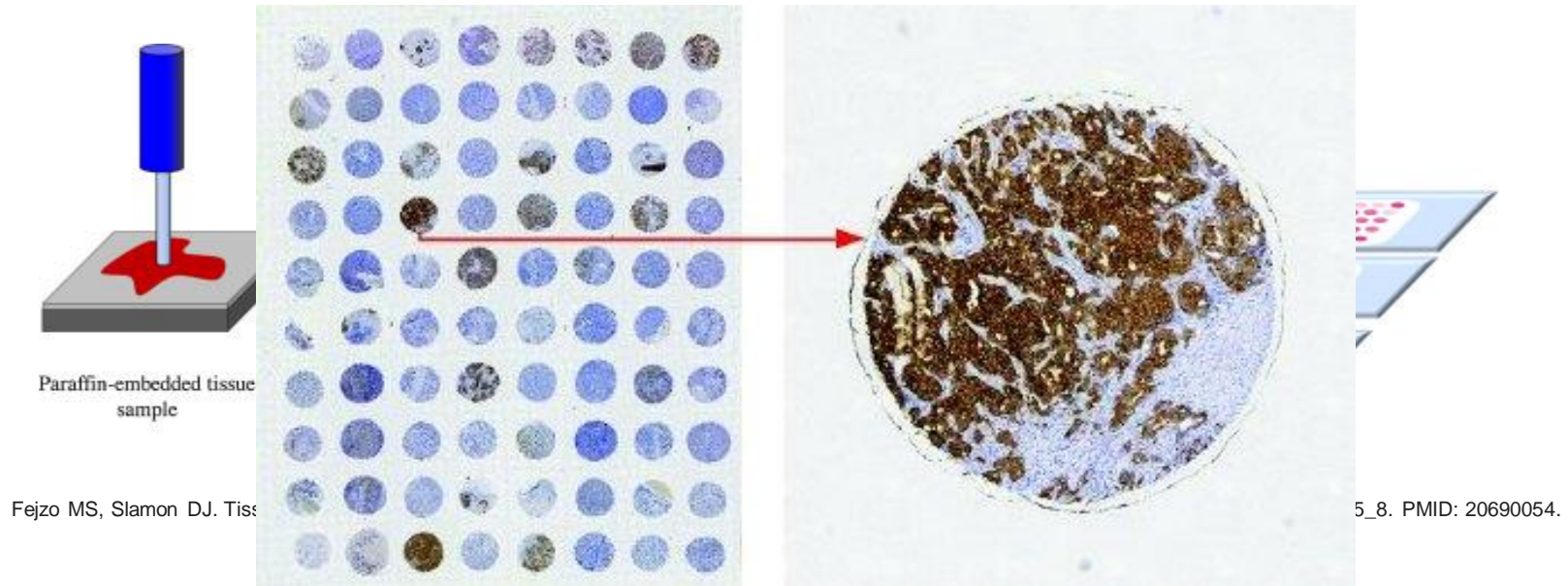


Frozen Section: Principle and Procedure | SpringerLink

# Types of Biological Samples – Tissue Sampling

## 2. Methods for analysis

### 2.2. Tissue Microarrays



# Types of Biological Samples – Tissue Sampling

## 2. Methods for analysis

### 2.3. PAXgene



[PAXgene Tissue FIX Container \(50 ml\) - QIAGEN Online Shop](#)

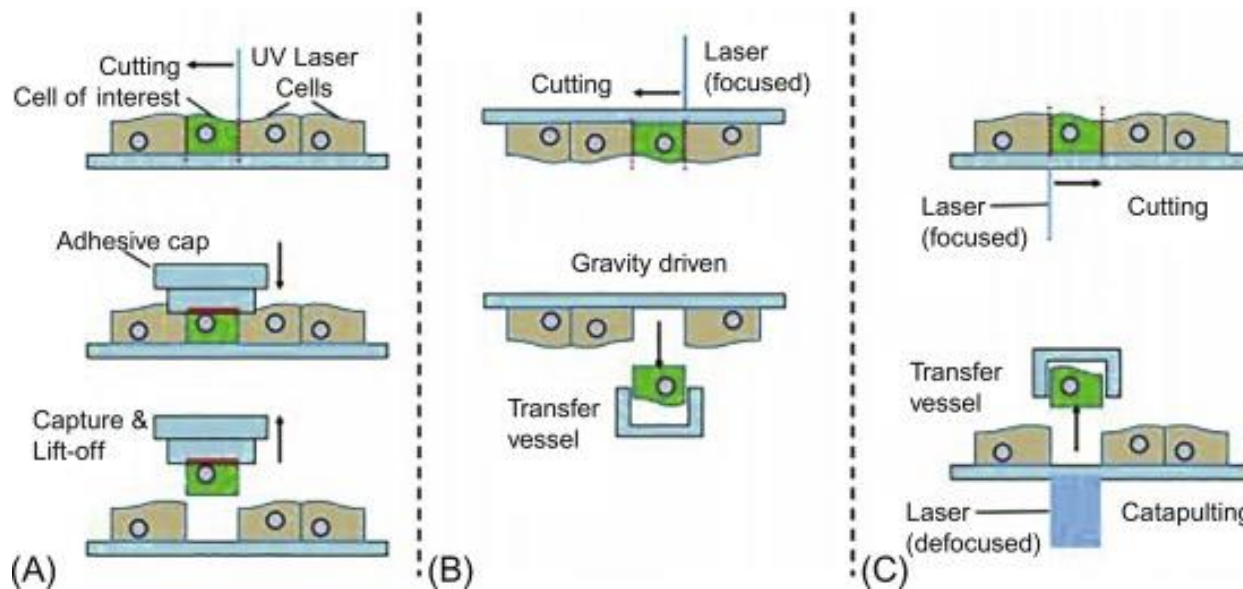


[EU GDPR Update - Please check back shortly \(thomassci.com\)](#)

# Types of Biological Samples – Tissue Sampling

## 2. Methods for analysis

### 2.4. Laser Capture Microdissection



Chandrakant Tayade, Andrew K. Edwards, Mallikarjun Bidarimath. Laser Capture Microdissection. 2014. Academic Press. 567-575

# Types of Biological Samples – Tissue Sampling

## 3. Tissue Samples

### 3.1. Body Fluids

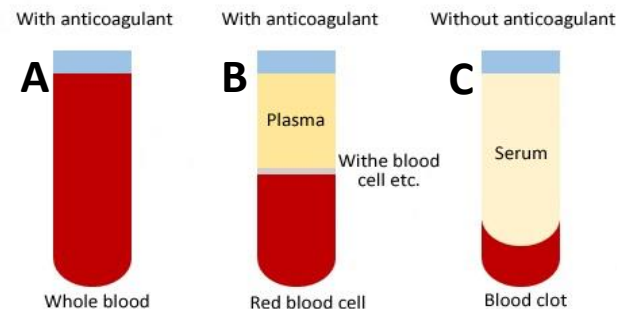
#### I. Blood samples

- Research (biomarkers) & diagnosis
- long-term storage:  $-80^{\circ}\text{C}$

A. Whole Blood → tube + anticoagulant (EDTA, heparin or citrate)

B. Plasma, buffy coat and haematocrit → tube + anticoagulant + centrifugation

C. Serum → tube + 10-30 min (no anticoagulant!) + centrifugation (after clotting)



Blood Collection Methods of Mice and Rats - Mouse Serum

# Types of Biological Samples – Tissue Sampling

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## 3. Tissue Sample

### 3.1. Body Fluids

#### II. Urine

- Metabolic diseases, drug or microbiome analysis
- Short-term storage:  $\sim 4^{\circ}\text{C}$ ; long-term storage:  $-80^{\circ}\text{C}$

#### III. Saliva

- DNA/RNA extraction, hormone or microbiome testing
- long-term storage:  $-20^{\circ}\text{C}$

#### IV. Synovial fluid (SF)

- Specific diseases (arthritis)
- Samples frozen promptly ( $-80^{\circ}\text{C}$ )



# Types of Biological Samples – Tissue Sampling

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## 3. Tissue Sample

### 3.1. Body Fluids

#### V. Cerebrospinal fluid (CSF)

- Diagnosis of several neurological diseases
- long-term storage: -80°C

#### VI. Liquid samples – reproductive medicine

- Metabolic diseases, infertility and stem cell therapy
- Supernatant of the fertilised egg cell (♀), semen (♂), seminal plasma, follicular fluid (♀), cumulus cell (♀) and cord blood (placenta)
- long-term storage: -80 to -160°C

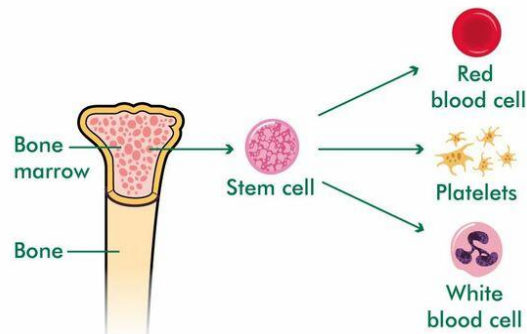
# Types of Biological Samples – Tissue Sampling

## 3. Tissue Sample

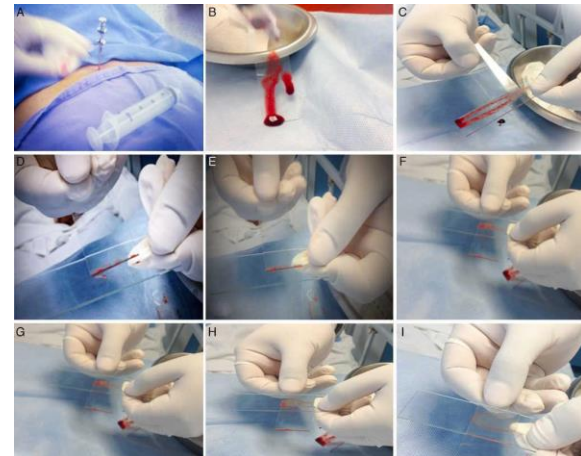
### 3.1. Body Fluids

#### VII. Haematological samples

- Blood disorders, spread infection/cancer to the bone marrow & stem cell therapy
- Bone marrow biopsy (solid) and aspiration (liquid)
- Peripheral blood smear
- long-term storage:  $-80^{\circ}\text{C}$



[What are stem cells and bone marrow? - Macmillan Cancer Support](#)



R.A. Trejo-Ayala, M. Luna-Pérez, M. Gutiérrez-Romero. Bone marrow aspiration and biopsy. Technique and considerations. 2015. 78;4; 196-201

# Types of Biological Samples – Tissue Sampling

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## 3. Tissue Sample

### 3.1. Body Fluids

#### VIII. Stool Samples

- Fecal occult blood test or microbiome analysis
- long-term storage: -80°C

#### IV. Hair, nail clippings and teeth

- Testing of drugs, nutrition, poisons/toxicity and stem cell therapy
- long-term storage: from RT to -80°C

# Types of Biological Samples – Tissue Sampling

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## 3. Tissue Sample

### 3.1. Body Fluids

#### X. Non-human samples: microorganisms (bacteria/fungi)

- Research & diagnosis
- Freezing → Bacteria + cryoprotectant + snap-frozen (from -20 to -190°C)
- Freeze-drying → freeze-dried in medium and then freeze-drying suspension (from 4 to -20°C)

#### XI. Post-mortem samples – autopsies

- Different reasons
- Before or during an autopsy (blood, urine, liquor, bile, gastric contents, tissues, etc.)
- Specific ethical guidelines

# Types of Biological Samples – Tissue Sampling

## 4. Biobank Graz – Sample Collections Overview

### Healthy Control

- Citizens of Graz - Healthy aging study
- Healthy control

### Endocrinology

- Diabetes mellitus
- Morbid obesity
- Rheumatic diseases
- PCO - Polycystic ovarian disease
- Osteoporosis

### Dermatology

- Psoriasis
- Fibrosis of skin
- Scar conditions
- Other skin diseases

### Gynecology

- Disorders of cervix uteri
- Pre-eclampsia
- Diabetes mellitus in pregnancy
- In vitro fertilization - Follicular fluid
- Placenta disorders



### Oncology and Hematology

- Head and Neck
- Mamma
- Prostate
- Colorectal
- Gynecological
- Leukemia
- Others (pancreas, esophagus,...)

### Cardiology

- Ischemic heart diseases
- Hypertension
- Other heart diseases

### Pulmonology

- COPD/Asthma
- Other pulmonary diseases

### Orthopedics

- Osteosarcoma
- Cartilage
- Bone /Soft tissue tumors
- Other bone diseases

[Specific Collections & Cohorts \(medunigraz.at\)](https://medunigraz.at)

# Types of Biological Samples – Tissue Sampling

## 4. Biobank Graz – More Detailed Sample Material

### Paraffin material

Paraffin block
Original paraffin section
Paraffin section
Paraffin shavings
Tissue microarray

### Cryopreserved tissue

Cryo tissue
Cryo section

### Body fluids and other samples

EDTA whole blood	Cumulus cells	Liquor
Serum	Follicular fluid	Liquor cells
Buffy coat (= EDTA buffy coat)	Fertilized egg supernatant	PAXgene® Blood RNA
Plasma: - EDTA plasma - Na citrate plasma - LI-HEP plasma	Supernatant control	Saliva
		Synovial fluid
		Stool sample
Urine: - Spontaneous - 24-hour urine	Seminal plasma	Other: [redacted]

Blood samples

IVF samples

other

Urine

# Quality of Biological Samples

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## Preanalytical Phase

- Mostly meet Biobanks
- Anything that comes before the analysis phase
- All factors in handling that affects integrity of the samples

## Analytical Phase

## Postanalytical Phase

# Quality of Biological Samples

## 1. Preanalytical Phase

### 1.1. Biological/environmental Factors



Time of Day/  
season



Alcohol/  
coffee



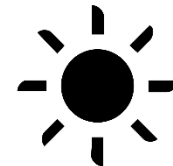
Weight



Smoking



Medicine

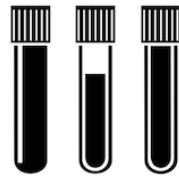


Sunlight

### 1.2. Technical Factors



Collection



Processing



Transportation



Storage

Ellervik C, Vaught J. Preanalytical variables affecting the integrity of human biospecimens in biobanking. Clin Chem. 2015 Jul;61(7):914-34. doi: 10.1373/clinchem.2014.228783. Epub 2015 May 15. PMID: 25979952.



# Quality of Biological Samples

## 2. Processes Involved in Sample Quality

### 2.1. Collection



- Obtaining tissue or fluids which represents the kind and quality of the whole sample for clinical (diagnosis, treatment and recovery) and research purposes
- Biopsies, blood draws or donations, saliva, urine, needle punctures, etc. Blades, scalpels, scissors, lancet, tubes with additives, needles, plastic containers
- Forgotten, incorrect, duplicate, type and age of devices, contamination of specimen, insufficient sample volume, diluted samples, short-term storage
- Example: first blood draw order is the most representative (blood composition depends on blood draw); using a too-thin needle might produce hemolysis

# Quality of Biological Samples

## 2. Processes Involved in Sample Quality

### 2.2. Processing



- Process of keeping the biospecimens free from damage or decay over the time
- Automated systems (bar-code reading, decapping, fractioning, aliquoting), T°-controlled centrifuges, labels (unique, adhesive, cryostable, etc.), material (tubes, swabs, etc.)
- Processing duration, aliquot volume, rough handling and pipetting, mislabelling (unlabelling), wrong ID pairing of primary and secondary tubes.
- Example: processing time reduction increases DNA yield (blood); aliquot volume help reducing freeze-thaw cycles; smooth handling avoids analytes degradation

# Quality of Biological Samples

## 2. Variables Involved in Sample Quality

### 2.3. Transportation



- Act, process, or activity of taking biospecimens from one place to another either by foot or in a vehicle trying to limit the degradation of the sample.
- Transportable coolers, refrigerators or freezers, special packing, dry ice
- Environmental exposures (season, distance, duration, method of transportation), receiver not on duty, wrong packing-labelling, sent to wrong laboratory
- Example: wrong packing or labelling might cause delays (sample integrity); tubes transported vertically/ smooth handling-transport (hemolysis)

Ellervik C, Vaught J. Preanalytical variables affecting the integrity of human biospecimens in biobanking. Clin Chem. 2015 Jul;61(7):914-34. doi: 10.1373/clinchem.2014.228783. Epub 2015 May 15. PMID: 25979952.

# Quality of Biological Samples

## 2. Variables Involved in Sample Quality

### 2.4. Storage



- Process of long-term preservation for biospecimens; ideally they remain equivalent to freshly-collected specimens for the purposes of research
- Fridges, freezers, cabinets and drawers, tanks and LN<sub>2</sub>
- Time from processing to storage, storage duration, T°, and facility, environmental factors (humidity, moisture, dehydration, evaporation, etc.), no labelling/destroyed labelling, microbiological contamination, missing aliquots, freeze-thaw cycles
- Example: thaw and freezing cycles might affect stability of analytes; high humidity might lead to microbiological contamination

Ellervik C, Vaught J. Preanalytical variables affecting the integrity of human biospecimens in biobanking. Clin Chem. 2015 Jul;61(7):914-34. doi: 10.1373/clinchem.2014.228783. Epub 2015 May 15. PMID: 25979952.

# Management of Biological Samples

## 1. Labelling/Coding of Samples

### 1.1. Barcode labels/QR codes

- Method of representing data in a visual, machine-readable form
- Unique identifiers standard in sample management
- Barcode labels (1D or 2D) → represented data by varying the widths and spacings of parallel lines or using rectangles, dots, hexagons and other geometric patterns; QR code → especial and more secure type of 2D barcode

#### 1D barcodes:



#### 2D barcodes:



#### QR code:



# Management of Biological Samples

## 1. Labelling/Coding of Samples

### 1.1. Barcode labels/QR codes

Tissue pieces or fluids:



FFPE blocks or slides:



# Management of Biological Samples

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## 2. Documentation

### 2.1. Collection

- Sender information: hospital, institution, department, physician's name, etc.
- Patient information: name & surname, birth date, case number, PID, etc.
- Date and time: site of sample localization, tentative diagnosis, etc.

### 2.2. Processing/Storage

- Analog
- Digital



# Management of Biological Samples

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## 3. Data Management

Processes related to managing data as a valuable resource

Sample storage + clinical data

### 3.1. IT System

- Organizational system designed to collect, process, store and distribute info
- Directly related to sample management
- Efficient IT system → supports sample management + data management



# Advantages for your Business

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## 1. Standardised quality

- Quality control/assurance procedures compliant with applicable European and International standards
- SOPs should be established and made publicly available
- ISO 9001:2015, ISO 20186:2019, CEN 16945:2016
- Sample quality is guaranteed

# Advantages for your Business

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## 2. Clinical data from samples

- Access to clinical data from the patients (when possible)
- Related clinical data from the biospecimens
- Find correlation or even causality between your results and the clinical data obtained
- Reasons for outliers or strange results, new correlations or hypothesis, etc.
- Quality & reliable results

# Advantages for your Business

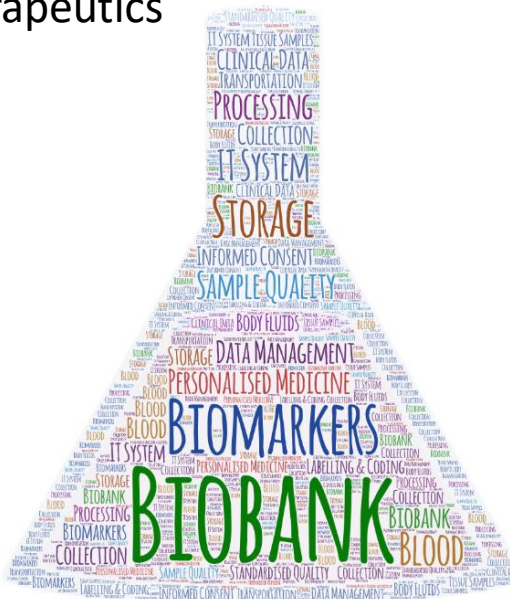
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## 3. Social and ethical issues

- **Use of medical samples** that are **no longer required for your treatment**. Samples can be used for current research projects or stored for future research projects.
- Every project requires a **favorable opinion** from the **ethics committee**.
- **Samples & data only used** for research if the donor has been **fully informed and has positively signed** an informed consent.
- **No more** or different **tissue** will be **removed** from the donor **than is necessary** for the **diagnosis/treatment** of the disease (blood up to max 20 mL).
- Due to data protection, **samples/data** are **used in coded** (pseudonymised) **form**.
- **Right to revoke** consent to the **sample use at any time** and without giving reasons.

# Biomarker Development

- Biomarker development is a multistep and iterative process beginning with biomarker discovery in disease and non-disease samples.
- Biobanks increase the success rate of biomarker development strategies by providing **high quality samples and data** and thereby accelerate the availability of new therapeutics



# Thank You !

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## Biobank Graz Team



# Biological Samples in Biobanks – Types, Quality, Management and Gains for your Business/Research

Webinar, March 9<sup>th</sup>, 2021

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