HIGH SECURITY BIOBANKING SOLUTION

Cryo Bio System
Groupe I.M.V. Technologies

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Biobanks and biosamples storage

Biobanks collect, process, store, and distribute biological samples and their related data for a therapeutic, research or traceability purpose

Definition

OECD *OECD 2007* " A biobank is a collection of biological material and the associated data and information stored in an organized system, for a population or a large subset of a population"

Main characteristics

- A biobank can store different type of biological samples…
  - Tissues
  - Blood and derivatives components
  - DNA/RNA
  - Cell lines
  - Other biological fluids
- … in different goals and end usages…
  - Traceability
  - Therapeutic use
  - Research on a specific pathology
  - Epidemiological research
- …and using different storage technologies…
  - Room temperature
  - Mechanical freezer
  - Nitrogen vessels

Biobanking techniques

For biosample storage, biobanks have mainly the choice between 2 types of technologies (mechanical freezer or nitrogen vessel) and 5 majors type of containers

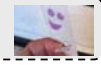
Storage temperature scale

-20°C -196°C

① ***Storage technology***

- Room temperature
- Mechanical freezer 
- Nitrogen vessel
  - *Vapor phase* 
  - *Liquid phase* 

② ***Type of Container***

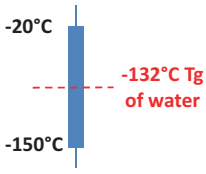
- Paraffin blocs (tissues) 
- DNA capsules 
- FTA Paper 
- **Microplate** 
- **Cryotube** 
- **Sealed, glass Ampule, tube** 
- **Sealed straw** 

Biobanking techniques

Freezers mostly enable -80°C storage temperature while nitrogen enables even lower storage temperature, from ~ -160°C in vapor phase to -196°C in liquid phase

① Storage technologies

Mechanical freezer 

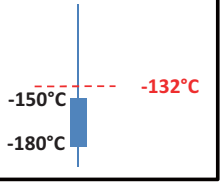


- **Mechanical freezers** work as classical freezers with often a back-up system
- Most freezers work at a **temperature of -80°C**
- Some new models reach -150°C, they are still rare

" Freezer is the basic equipment for cryostorage"

Nitrogen vessel (LN2)

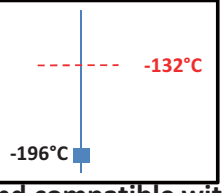
Vapor phase 



- Samples and their containers are **placed in LN2 vapor phase**
- To maintain the **vapor phase tanks** are continuously supply by LN2 gas line
- **Gradient temperature** depending on sample location

"Nitrogen is used for long term storage of critical samples"

Liquid phase 



- Samples and their containers are **immersed in the liquid nitrogen**
- **The temperature is uniform** in the entire tank at -196°C

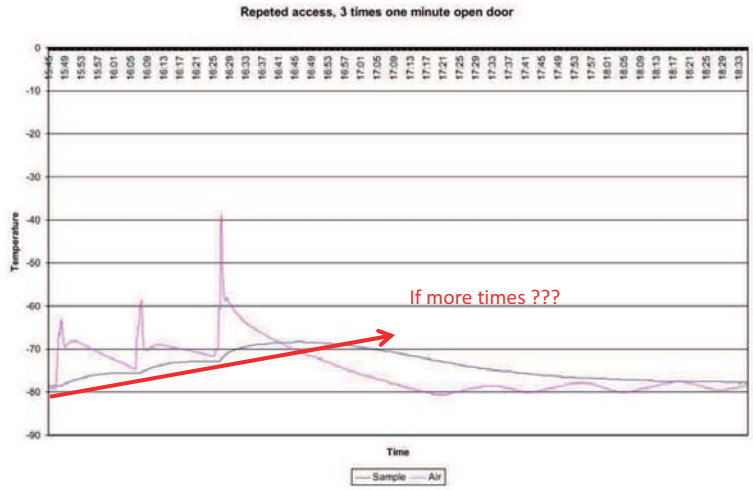
"Liquid nitrogen phase is the guaranty of sample stability and assure security even with LN2 supply disruption"

Freezers are easier to use and compatible with automated process, nitrogen offers a longer and more reliable conservation

Sample temperature evolution over working day

Storage technologies: Freezer

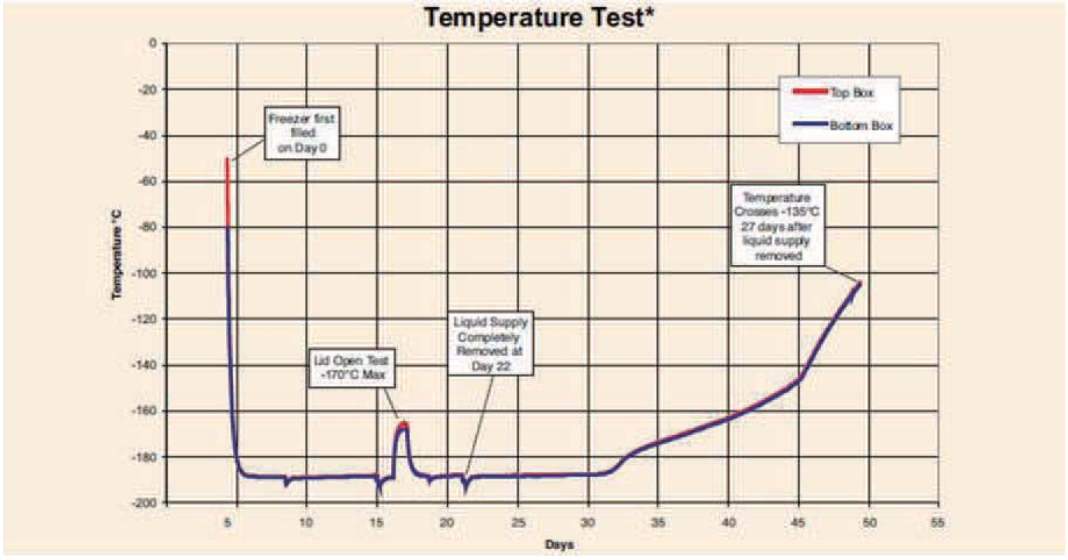
Working space temperature change over day



Front samples and back samples are not exposed to the same temperature over time

Autonomy of LN2 freezer after LN2 supply is stopped: 25 days

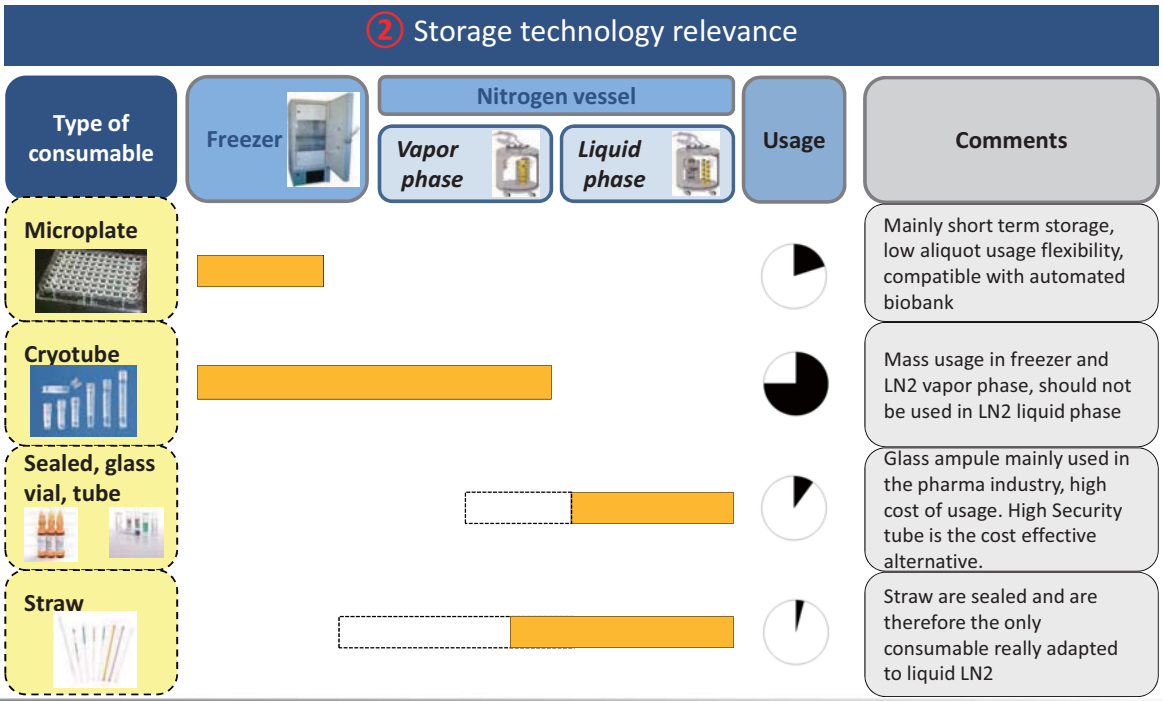
Storage technologies: LN2



Temperature homogeneity and maintenance over time are key parameters for samples

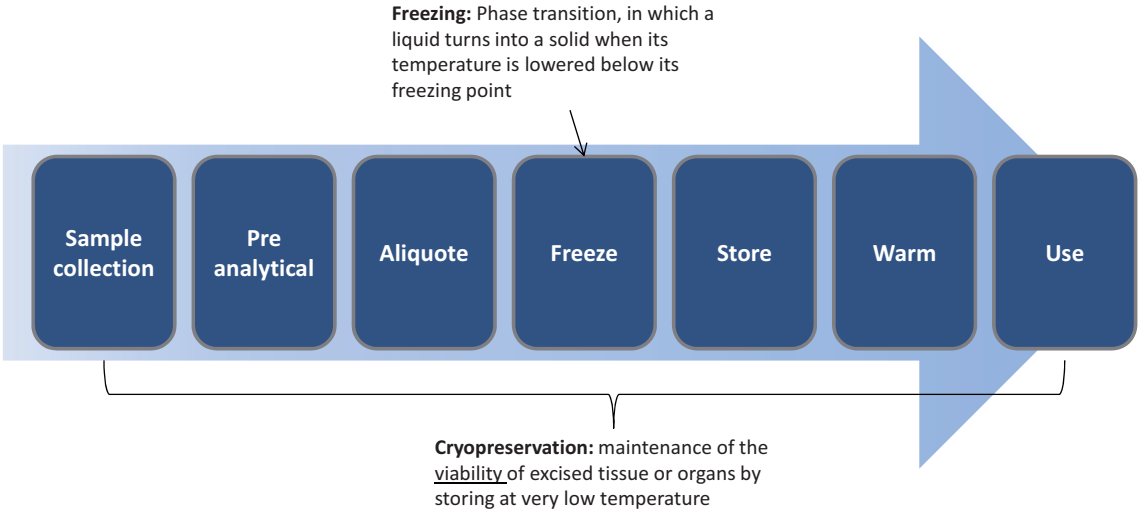
Biobanking techniques

Five type of consumables can be used in cryostorage , depending on the storage technology, with cryotubes, straws, high security tubes and sealed glass vials



Biobanking process

Biobanking quality chain is composed of 7 major key steps. Each step is supported by SOP's. Best practices have been developed and published by international organizations (BBMRI, ISBER, OECD,…)



STORAGE TECHNOLOGIE & QUALITY

"High – quality, data – rich samples are essential for future research. *But obtaining and storing these samples is not a straightforward as many researchers think"*

Alison Hubel Nature / vol. 486 / 7 June 2012

Sample quality drivers

- Quality of a biological sample
  - Preservation of initial qualities, representative
  - Preservation of capacities (development,…)
  - Absence of contamination (biological, chemical,…)
  - Identification and associated data
- For future use
  - Known
  - Unknown…
- The storage technology should always be based on the future use of the biological sample: if the future use is not (fully) determined the best preservation conditions should be selected

Sample quality value

- The value of a biological sample
  - Quality of preservation (container, environment)
  - Traceability
    - Of sample origin
    - Sample process handling
    - Link with data
  - Number of aliquots
    - Minimize temperature change exposure (microplate)
    - Analytical sensitivity change over time
    - Sample exchange from lab to lab
  - Size of collection the sample belongs to
    - Mirror site storage
    - Number of research team involved (specialties & sites)
- Value can be scientific, technical, personal (patient) and/or industrial

Quality Drivers & CBS Answers

"The lower storage temperature is the better": *Greater stability and long time before degradation*

The 4 key quality drivers

- **Quality**
  - Only few biomolecules are preserved well at **-20°C,** most samples must be stored below **-80°C** to stop degradative enzymes and definitely at **-196°C**, such as live cells, at which point enzymes are thought not to be able to function at all
- **Safety**
  - Sample container must assure an **absolute security for operator** and should **avoid any cross contamination risks** between sample within the storage space
- **Traceability**
  - Essential to link sample information (Patient data, analytical data,…) to the bio specimen itself, the **sample identification is a must**
- **Efficiency**
  - To maximize sample collection size and **minimize storage cost** research should select the **right sample container**

CBS solution

- **Packaging** and **sample management** solutions for preservation and storage of biological samples at variable low temperatures:
  - Liquid Nitrogen phase (-196°C)
  - Liquid vapor phase nitrogen (-132°C)
  - Ultra-low temperature electrical freezer (-80°C)
- To **preserve valuable** biological samples and **viable** cells **for future** use, ensuring **maximum sample viability** by assuring the:
  - **Quality:** preserving and maintaining a sample 's initial quality
  - **Safety :** ensuring the safety of the stored product, user, other stored samples
  - **Traceability:** enhancing traceability with tamperproof linear barcoding, or 2D barcoding
  - **Efficiency:** maximizing storage space by reducing foot print

Cryo Bio System's answer

CBS™ High Security Straw & Co-XStraw™

- **Storage space efficiency:** up to 4-fold more aliquots vs. cryovials
- **Sample quality:**
  - Higher surface/volume ratio for better and fast freezing
  - Chemically inert and biocompatible material, no plasticizers agents including paraben, bi phenol, phtalate
  - Dnase Rnase free
  - Cryogenic grade ionomeric resin
- **Security:**
  - Full seal to eliminate risk of cross-contamination of specimens or their environment
  - Guaranteed leak-proof and shatter proof container
  - Indestructible under normal conditions of use
- Sample **identification** and sample **inventory management**
  - CBS™ High Security Straws are available in three different volumes: 0.3mL, 0.5mL and 2 mL (7 different colors)
  - CBS™ High Security Co-X Straw™ available on 2 different volumes: 0.3mL and 0.5mL (8 different colors)
  - Linear barcoding (EAN 128), classic straw up to 11 characters CO-X up to 18 characters
  - Goblets with 8 different colors hosting internal subdivisions
  - Canister for up to 6 goblets or racks for up to 32 goblets

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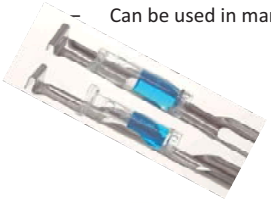
Cryo Bio System's answer

Lineage from High Security Straw, a fully-sealed container for direct storage in liquid nitrogen in a standard dimension cryogenic vial format, with a useful volume of 1.2 mL

CBS™ High Security Tube

- **Sample quality:**
  - Takes away the barriers and safety concerns around the long term packaging of cell
  - Chemically inert and biocompatible material, no plastifying agents (paraben, bi phenol, phtalate…)
  - Dnase Rnase free
  - Cryogenic grade, ionomeric resin
- **Security:**
  - Full seal eliminates risk of cross-contamination of the specimen or its environment
  - Guaranteed leak-proof and shatter-proof container
  - Indestructible under normal conditions of use
- Sample **identification** and sample **inventory management**
  - Colored inserts for easy primary identification
  - 2D data matrix coded inserts
  - Compatible with cryoresistant labels
  - RFID cryoresistant chips can be placed in inserts
  - Compatible with standard racks, boxes, and canes
  - Can be used in manual or automated filling system

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Cryo Bio System's answer

CBS™ Filling Sealing & Printing solutions

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Cryo Bio System's answer

Filling, Sealing, Printing and Sorting final aliquot from standard sample primary tube

DIVA – CBS Automatic process

- **Walk-away design**
  - XYZ pipetting arm and consumable management
  - Automated straw distribution and conveyor
  - Straw sorting system
  - Error management and traceability
- **Autonomy**
  - 3 automated loading racks with 32 positions each
  - 8 compartment straw hopper (8 x 60 straw)
  - 2 E-Tip racks and 2 Tecan tips racks on board
  - 2 sorting drawers
- **Easy to use**
  - Touch screen user interface
  - Administrator access control
  - Production file stored on board or exported to LIMS
  - Real time production progress
- **Assured full traceability and security of produced aliquots**
  - Operator
  - Primary sample
  - Produced aliquots
- **Reduces non added value laboratory tasks**

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Cryo Bio System's answer

Example of an upright freezer set-up with CBS racks (4 drawers) for daisy goblets, internal useful volume 680 liters: **86 016** CBS™ High Security Straw or **110 592** High Security CoX-Straw

CBS Storage solution

- CBS™ High Security Straw: **86 016 straws**
- CBS High Security CoX-Straw: **110 592 straws**

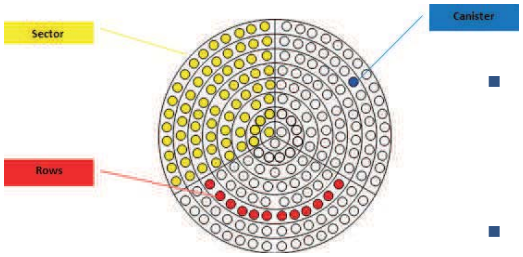
Specially designed racks for CBS Daisy goblets

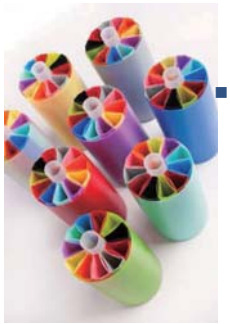
- 2 reference available
  - 022112 : **3** drawers (3 x 8); **24** goblets
  - 021998 : **4** drawers (4 x 8); **32** goblets
- **Straw capacity**
  - ✓ 022112:
    - CBS™ High Security Straw: **4 032 straws**
    - CBS High Security CoX-Straw: **5 184 straws**
  - ✓ 021998 :
    - CBS™ High Security Straw: **5 376 straws**
    - CBS High Security CoX-Straw: **6 912 straws**

Cryo Bio System's answer

Example of Liquid Nitrogen tank storage set-up with CBS canister in liquid phase, internal useful volume 1 000 liters: **211 680** CBS™ High Security Straw or **272 160** High Security CoX-Straw

CBS Storage solution





- **Daisy goblets specially designed to contain CBS High Security Straws**
  - **8** different goblet colors
  - **12** colored internal compartment, visotube
- **Straw capacity**
  - CBS™ High Security Straw: (12 x 14) **168 straws**
  - CBS High Security CoX-Straw: (12 x 18) **216 straws**
- **Canister designed to receive Daisy goblet equipped with lifter**
  - **5** different height, from **2** up to **6** goblet
  - **9** different color tab to be install on lifter

Cryo Bio System's answer

CBS Controlled Rate Freezer

- **Common Features**
  - Temperature range: -145°C to 45°C
  - Cooling rate: -0,1°C to -60°C per minute
  - Controller: 20 programs – 99 cooling rates – 450 segments
  - Structure 100% 304L stainless steel
- **Reliability**
  - Designed and manufactured by IMV Technologies since 1963
  - Eurotherm temperature controllers with quick release probes
- **Easy and practical use**
  - Special sample racks design (bags/tubes/glass ampules…) upon request
  - Easy to clean and disinfect
- **Traceability**
  - Automated recording of freezing curves for each cycle
  - Recordable and printable freezing process as required for GLP and SOP's
- **Security**
  - Chamber temperature alert for loading and unloading
  - Maintain -140°C at end of freezing cycle

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Cryo Bio System solution worldwide users

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Thank You

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