

PSI Biobank Agreements



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1 Abbreviations

BBC	Biobank Code.
BED	Hereditary colorectal cancer (Dutch: erfelijke darmkanker).
CSF	Cerebrospinal fluid, liquor.
CVA	Cerebrovascular accident (stroke).
DIA	Diabetes.
IBD	Inflammatory bowel disease.
LML	Leukaemia, myeloma, lymphoma.
NDZ	Neurodegenerative diseases (Dutch: neurodegeneratieve ziekten).
NRF	Renal failure (Dutch: nierfalen).
PIM	String of Pearls Information Model (Dutch: Parelsnoer Informatie Model).
PSI	String of Pearls Initiative (Dutch: Parelsnoer Initiatief).
RAOA	Rheumatoid arthritis and osteoarthritis.
SOP	Standard operating procedure.
UMC	University medical centre (teaching hospital).

2 Introduction

Biomaterial for the String of Pearls Initiative is collected at all eight Dutch UMCs. It is then stored in a number of separate biobanks, although these ultimately serve as one common source for scientific research.

The collection process involves different UMCs, different Pearls and different UMC departments.

To guarantee the quality and consistency of collection, a series of joint agreements has been reached. They are set out in this document.

2.1 Harmonisation

String of Pearls has decided to adopt an approach based upon harmonisation rather than standardisation.

For each relevant topic, the crucial aspects and critical steps have been determined. This document covers the following subjects.

2.1.1 General biobank agreements

- Implementation of biobank agreements.
- Material to be collected.
- Data concerning the collection and storage of biomaterials.
- Quality assurance and control.
- Coding of biomaterials.
- Release of material.

2.1.2 Material-specific agreements

- EDTA plasma.
- Citrated plasma.
- Serum.
- Liquor.
- Urine.
- Acidified urine.
- Faeces.
- Tissues.
- DNA.
- Isolation from viable cells (LML).
- RNA isolation from intact cells (LML).
- DNA isolation from intact cells (LML).

3 General biobank agreements

3.1 Implementation

It is absolutely essential that the agreements described in this document be implemented at the UMCs.

Experience teaches us that SOPs and related matters can be influenced by interference from the Pearls – through the co-ordinator or local participant – by local opinion leaders or by personal practice and routine. This unintentionally introduces a variation which can result in problems of comparability within the String of Pearls collection. That, of course, is a highly undesirable situation. The biobank agreements described here have been reached after much consultation and consideration, with the predominant opinions prevailing. But such agreements are worthless unless everyone adheres to them.

Within the UMCs, the project leader is responsible for communicating the agreements. All those involved in the biobanking procedure must be familiar with them. Changes can be made only through the same process of finding a consensus as resulted in the original agreements. This approach ensures that modifications are recorded centrally, so that in future the origin of material being released is known.

This means that there is a strict policy in respect of amendments, which has to be observed at all times. That policy, too, should be known to all concerned.

3.2 Amendments policy

As long as they are properly justified, it is always possible to propose amendments to the biobank agreement.

Any suggestions should be submitted to the Pearl co-ordinator for tabling and discussion in the consultative forum.

Once consensus has been reached on any changes, this document is updated accordingly. The version number is then revised and the new draft is sent to each Pearl and to the PSI management team for approval.

If and when that approval has been received by e-mail from all parties, the new version enters force and is sent to the project leaders. They are then responsible for updating the underlying SOPs at the UMCs.

The intention is that this document be revised no more than once a year.

At least once every two years, it is reviewed and revised proactively.

4 Material to be collected

A special document has been compiled for each Pearl, describing what it is to do: what data and material to collect, when to do this and the expected patient numbers. This so-called "Pearl Document" also lists the biomaterial for collection. The table below summarises the materials covered. Specific details, such as frequency of collection and amounts, can be found in chapter 9 of this document.

PEARL	BED	IBD	Renal failure	RAOA	Diabetes	CVA	Neurodegeneration	Leukemia
Blood:								
EDTA plasma (9.1)	●		●		●	●	●	
Citrated plasma (9.2)			●		●			
Serum (9.3)	●	●	●	●	●	●	●	●
EDTA blood for DNA (9.10)	●	●	●	●	●	●	●	
Heparine blood for cells:								
Viable cells (9.11)								●
RNA from cells (9.12)								●
DNA from cells (9.13)								●
CSF (Liquor) (9.4)							●	
Urine (9.5)			●	●	●			
Acidified urine (9.6)					●			
Faeces (9.7)		●						
Tissue:								
Biopsy specimen (frozen) (9.8.1)	●							
Resection material (frozen) (9.8.2)	●	●						●
Biopsy specimen (paraffin-embedded) (9.9.1)	●	●						
Resection material (paraffin-embedded) (9.9.2)	●	●						
Bone Marrow:								
Viable cells (9.11)								●
RNA from cells (9.12)								●
DNA from cells (9.13)								●

5 Biomaterials collection and storage process data records

The autonomy of the biobanks is a key aspect of quality policy. Agreements exist only in respect of critical steps in the process. Biobanks are free to organise their processes and procedures as they wish, as long as they adhere to the following agreements.

- There are SOPs in place.
- Those SOPs comply with the relevant agreements (see section 9: Material-specific agreements).
- Local registration allows for control of the SOP agreements.

Data about the collection process can be recorded at three different levels.

5.1 Standard operating procedure

The technical specifications for individual tasks are set out in the SOPs. UMCs are required to have SOPs.

It is assumed that UMC personnel comply with the relevant SOP when carrying out the tasks covered by it.

Most aspects cannot be checked directly

- Techniques used.
- Methods of transportation.
- Storage temperature.
- Consistency of storage.

5.2 Local administration

Metadata which is important for quality control does not need to be recorded centrally. Tasks are recorded using a logging procedure, which or may not be incorporated into the laboratory information management system.

Instead, it can form part of the local process.

Since the local register is the source of the data published in the central database, the following information must be recorded locally.

- Equipment used; calibration data; maintenance details.
- Dates and times of the various steps in the collection process.
- Delay times (derived from date and time records).
- Specific deviations from the SOP.
- Storage location.
- Type of material.
- Quantity stored; number of units.

Local administration is the responsibility of the biobanks themselves (see section 6: Quality assurance).

5.3 Central administration (PIM)

Data which is important for the central organisation is recorded in PIM. Specifically, this is primary information about what has been collected, and how much of it.

In addition, PIM must be able to provide the details needed by researchers to select material for use in their projects.

PIM should contain the minimum possible amount of data.

Whenever possible it should refer to the SOPs.

- **Type** of material.
- **Amount** stored – for example, the number of units.
Central registration of amounts stored facilitates stock management.
- **Deviations** from the agreed SOP: a “yes/no” field.
Such deviations may be relevant to the selection of material.
- **List of deviations from agreed SOPs.**

No.	Deviation from agreed SOP	Remarks
1	Haemolytic material? (Yes/no)	Default: "no".
2	Lipaemic material? (Yes/no)	Default: "no".
3	Icteric material? (Yes/no)	Default: "no".
4	Different vessel used? (Yes/no)	Default: "no".
5	Citrate vial underfilled? (Yes/no)	Default: "no".
6	Different storage temperature prior to treatment? (Yes/no)	Default: "no".
7	Different storage time prior to treatment? (Yes/no)	Default: "no".
8	Deviation in mixing or homogenisation? (Yes/no)	Default: "no".
9	Deviation during centrifugation? (Yes/no)	Default: "no".
10	Storage problem? (Yes/no)	Default: "no".
11	Other (specify): ...	Free text

- Key **process information**, if applicable – for example, “Patient fasted – yes/no” or details of the collection technique.
- **Sample codes.** See section 7: “Coding of biomaterials”.
- **Biobank code.** See section 7: “Coding of biomaterials”.
- **Concentration.** DNA in µg/ml.
- **Quality.** DNA expressed as an OD 260/280 ratio.

6 Quality assurance

All the UMCs have begun collecting biomaterials. To this end, logistical processes have been implemented at the local level. For effective future use, it is extremely important that the material collected at different locations be comparable. In addition, the high quality of the material collected must be maintained. To achieve this, agreements have been reached centrally concerning the required parameters for the local logistics. Where possible, these allow sufficient scope for the use of existing infrastructure or for interfaces with it.

The central PSI organisation has initiated a programme to support the configuration of local collection and storage processes. Key to this is maintaining quality and comparability. The programme can be broken down into the following steps.

1. Consensus on minimum standards.

The consensus on minimum standards has been discussed and agreed in the consultative forum and is set out in the Biobank Document.

2. Implementation of PSI minimum standards at UMC biobank.

UMCs organise their own processes. In so doing, they are guided by the set minimum standards and the information requirements of the central database (formulated in PIM).

3. Initial check: consultation between PSI, the project leader and biobank management.

Once a UMC has organised its processes, "core PSI" discusses them with the project leader and biobank management.

4. Internal feedback.

The initial check may result in the local processes being refined.

5. External feedback.

Discussion within the UMC may generate proposals to modify the minimum standards.

6. Consultations concerning future use.

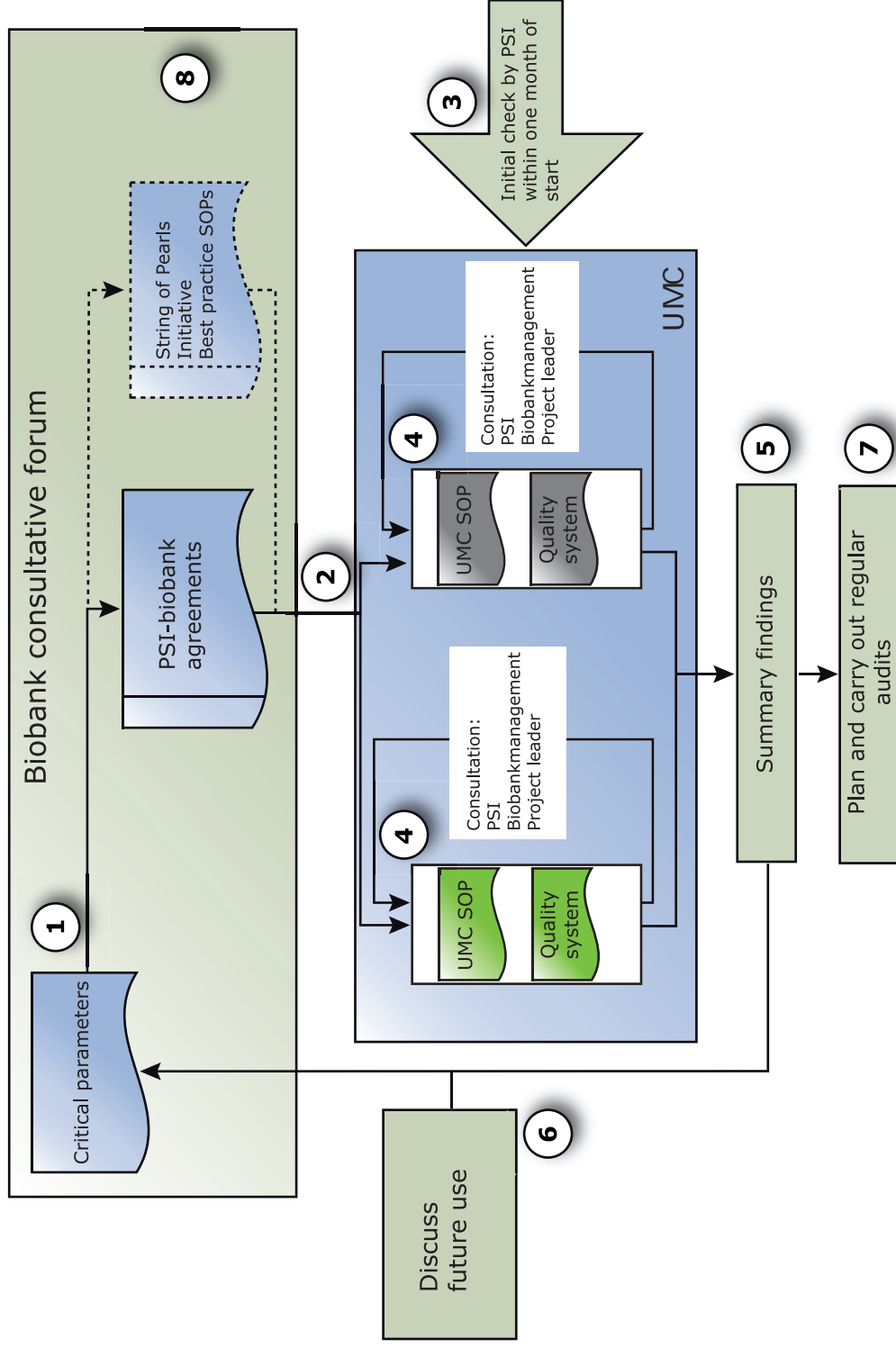
How the material is to be used in the future is a key factor determining the way it is collected and stored. A better understanding of that future use may therefore result in changes to the minimum standards.

7. Regular audits.

Once the collection process is under way, it is checked on a regular basis.

8. Compilation of best practices.

Information about the various UMCs' experiences may eventually lead to the compilation of best practices for PSI. These could be of use to new "pearls".



7 Coding of biomaterials

UMCs use their own systems to code the materials stored in the biobanks. Because no information that might identify an individual patient, either directly or indirectly, may be used in scientific research, a process of pseudonymisation is undertaken. Under exceptional circumstances and subject to strict conditions, this can allow the patient's identity to be traced.

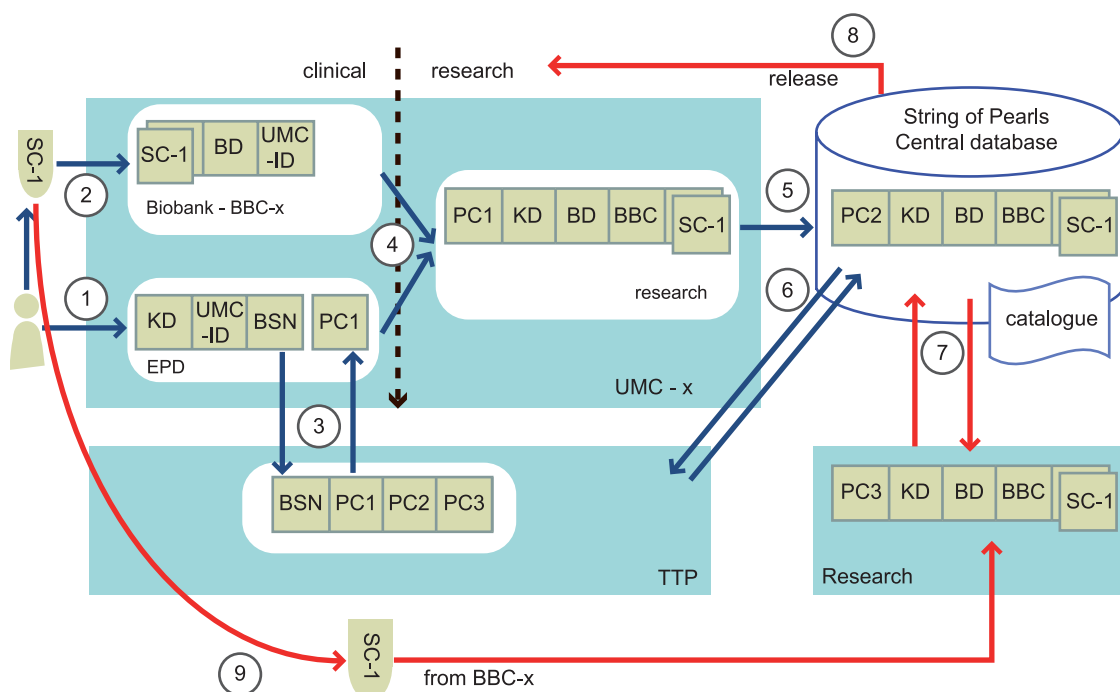
To allow for the consolidation of data concerning patients who attend more than one UMC whilst maintaining maximum information security, the pseudonymisation process consists of several defined steps. Once they have been completed, patient and biomaterial details held in the central database cannot be linked to the local biobank records at the UMCs. To facilitate the release of biomaterials, however, the sample codes must also be recorded in the central database.

The UMCs use a variety of coding techniques: 1D/2D barcodes or "readable" codes. In order to be able to recognise samples originating at other UMCs, they must bear a readable code as well as any barcode used.

Because there is a chance that biomaterial from different UMCs has the same locally defined sample code, an additional level of coding has been introduced. This so-called Biobank Code (BBC) is added to the record by the UMC and submitted to the central String of Pearls database with the rest of the information.

The diagram below illustrates the registration and release process.

7.1 Registration and release



7.2 Key to registration and release diagram

1. A patient is recorded in the hospital's administrative system (EPD).
This contains clinical data (KD) and the subject's Citizen Service Number (BSN).
2. Biomaterial is taken.
This is given a sample code (SC-x) and stored.
Information about the material stored (BD) is recorded in the biobank data system, together with the sample codes and a UMC identifier (UMC-ID).
3. In order to delink the KD and BD from any identifying information in the research environment, the BSN is converted into a pseudocode (PC1).
That code is generated by an independent trusted third party (TTP). Different encryption keys are used for each UMC. These activities take place "behind the scenes".
4. In the research environment, KD, BD and SC-x can be linked.
To prevent SC-x duplication, each biobank is allocated its own Biobank Code (BBC-x).
The resulting BBC-SC combination is unique.
5. The KD and BD are submitted to the central PSI database.
Part of this information is published in the catalogue.
6. The information in the central database is provided with a second pseudocode (PC2).
This enables information from a single patient who has attended multiple UMCs to be combined.
When material is released, it and the accompanying data are allocated a third, one-off pseudocode (PC3).
7. After a request for material and data is approved by the Scientific Assessment Committee, it is cleared for release to the applicant.
8. The biobank receives a message telling it which samples to release, based upon their BBC and SC-x.
9. The biobank sends the cleared samples to the researcher.
The researcher can check that the sample numbers are correct.
 - Only persons are pseudonymised, not samples.
 - PC1 can be used in the EPD, the research database and the biobank system.
 - Every biobank is unique. A UMC may have several different biobanks, and there may also be independent ones, each with its own numbering system.

UMC-x	UMC Code. Each hospital has its own code.
BBC-x	Biobank Code. Each bank has its own code; there may therefore be more than one BBC per UMC.
BSN	Citizen Service Number – equivalent to a social security number – or patient ID. (Dutch: Burger Service Nummer).
UMC-ID	Identification number for UMC use.
EPD	Electronic Patient Record (Dutch: Elektronisch Patiënten Dossier).
PC1	Patient pseudocode 1 for biomaterial, used by UMC and for submission to central infrastructure.
PC2	Patient pseudocode 2, used to combine material from different sources.
PC3	Patient pseudocode 3, used by PSI for the release of material.
BD	Biobank data: metadata for biosamples, such as volume and type of material. Some UMCs may record this as clinical data.
KD	Clinical data recorded locally using ProMISe, EPD or another solution (Dutch: klinische data).
SC-x	Sample Code, unique within each biobank and combined with BBC-x to form a totally unique number.

TTP Trusted Third Party, an independent body that converts a BSN into a PC1, PC2 and PC3 according to a fixed protocol but different algorithms.

8 Release of material

The String of Pearls Regulations include a procedure for the release of material. For the actual supply of biomaterials, the biobanks need to be provided with a logistical description.

8.1 Agreements

Once material has been released by a biobank, it must not be returned to it. To prevent thawing during the release process, frozen fluids are stored in release-ready units. When releasing a fragment of stored tissue, the section for release is excised and prepared for sending inside the biobank. The remaining material does not leave the biobank.

8.2 Future activities

Further details of the release process still need to be drawn up.

9 Material-specific agreements

9.1 EDTA plasma

Collection

Vial type	Standard vial; no gel, no protease inhibitors. Do not pool blood samples. When taking 10 ml, preferably use one 10 ml vial rather than two of 5 ml.
Needle type	No agreement; is not regarded as critical.
Patient fasted	Depends upon agreements specific to the Pearl.
Temperature	Prior to freezing, keep vials at room temperature or 4°C.
Time to freezing	Blood samples should be frozen as quickly as possible. Target: within two hours. Maximum: within four hours.

Centrifugation

RCF	2000g recommended; permitted range is 1500-2500g.
Time	10 minutes.
Temperature	Room temperature or 4°C.

Storage

Aliquoting	Store material as 0.5 ml aliquots. Keep at least five 0.5 ml aliquots. If there is additional material, create more aliquots rather than topping up existing ones beyond 0.5 ml.
Vial type	No agreement.
Temperature	Store at $\leq -80^{\circ}\text{C}$. Freeze slowly by placing in storage freezer.

9.2 Citrated plasma

Collection

Vial type	Standard vial, not glass unless siliconised; no gel, no protease inhibitors. Use BD model 366575 (6 ml), Greiner model 455322 (9 ml) or equivalent. Preferably use one vial only and do not pool blood samples.
Needle type	No agreement; is not regarded as critical.
Patient fasted	Depends upon agreements specific to the Pearl.
Temperature	Prior to freezing, keep vials at room temperature.
Time to freezing	Blood samples should be frozen as quickly as possible. Target: within two hours. Maximum: within four hours.

Centrifugation

RCF	2000g recommended; permitted range is 1500-2500g.
Time	10 minutes.
Temperature	Room temperature.

Storage

Aliquoting	Store material as 0.5 ml aliquots. Keep at least five 0.5 ml aliquots. If there is additional material, create more aliquots rather than topping up existing ones beyond 0.5 ml.
Vial type	No agreement.
Temperature	Store at $\leq -80^{\circ}\text{C}$. Freeze slowly by placing in storage freezer.

9.3 Serum

Collection

Vial type	Standard vial; no gel, no protease inhibitors. Use BD model 367896 or equivalent. Do not pool blood samples. When taking 10 ml, preferably use one 10 ml vial rather than two of 5 ml.
Needle type	No agreement; is not regarded as critical.
Patient fasted	Depends upon agreements specific to the Pearl.
Clotting time	Minimum 60 minutes, maximum 120 minutes. Clotting takes place at room temperature.
Temperature	Prior to processing, keep vials at room temperature.
Time to freezing	Blood samples should be frozen as quickly as possible. Target: within two hours. Maximum: within four hours.

Centrifugation

RCF	2000g recommended; permitted range is 1500-2500g.
Time	10 minutes.
Temperature	Room temperature or 4°C.

Storage

Aliquoting	Store material as 0.5 ml aliquots. Keep at least five 0.5 ml aliquots. If there is additional material, create more aliquots rather than topping up existing ones beyond 0.5 ml.
Vial type	No agreement.
Temperature	Store at $\leq -80^{\circ}\text{C}$. Freeze slowly by placing in storage freezer.

NB.

The use of gel vials is permitted when collecting serum for the NDZ and DIA pearls, as long as this deviation from the norm is documented fully and correctly.

9.4 Liquor

Collection

Vial type	Liquor must be collected in a polypropylene vial.
Needle type	For patient comfort, a thin needle is preferable.
Quantity	Minimum 3 ml. The ideal quantity is 20 ml.
Temperature	Prior to processing, keep vials at room temperature.
Time to processing	Maximum two hours.

Centrifugation

RCF	2000g recommended; permitted range is 1500-2500g.
Time	10 minutes.
Temperature	4°C.

Storage

Aliquoting	Store material as 0.5 ml aliquots. Keep at least six 0.5 ml aliquots. If there is additional material, create more aliquots rather than topping up existing ones beyond 0.5 ml.
Vial type	Liquor must be stored in a polypropylene vial.
Temperature	Store at $\leq -80^{\circ}\text{C}$. Freeze slowly by placing in storage freezer.

9.5 Urine

Collection

Vial type	No agreement; is not regarded as critical.
Urine type	Preferably midstream urine.
Temperature	Prior to processing, keep samples at 4°C.
Time to processing	Maximum four hours after collection (collect at UMC).

Centrifugation

Mixing	Mix sample before processing.
RCF	2000g recommended; permitted range is 1500-2500g.
Time	10 minutes.
Temperature	4°C.

Storage

Aliquoting	Store material as 0.9 ml aliquots. Keep at least six 0.9 ml aliquots. If there is additional material, create more aliquots rather than topping up existing ones beyond 0.9 ml.
Vial type	No agreement.
Temperature	Store at $\leq -80^{\circ}\text{C}$. Freeze slowly by placing in storage freezer.

9.6 Acidified urine

Collection

Vial type	No agreement; is not regarded as critical.
Urine type	Preferably midstream urine.
Temperature	Prior to processing, keep samples at 4°C.
Time to processing	Maximum four hours after collection (collect at UMC).

Ascorbic acid/EDTA solution

Weigh out 1.3 g of EDTA.
 Weigh out 1.3 g of ascorbic acid.
 Dissolve in purified water and top up to 100 ml using a calibrated flask.
 Pour into 1 ml vials (approximately 100 in all).
 Freeze to -20°C.
 Prepare a new batch weekly.

Acidification

Pipette 10 ml of well mixed and centrifuged urine, add 50 µl of EDTA/ascorbic acid solution and mix.
 The rest of the urine is divided up.

Centrifugation

Mixing	Mix sample before processing.
RCF	2000g recommended; permitted range is 1500-2500g.
Time	10 minutes.
Temperature	4°C.

Storage

Aliquoting	Store material as 0.9 ml aliquots. Keep six 0.9 ml aliquots.
Vial type	No agreement.
Temperature	Store at $\leq -80^{\circ}\text{C}$. Freeze slowly by placing in storage freezer.

9.7 Faeces

Collection

Vial type	No agreement; is not regarded as critical.
Temperature	No agreement.
Time to processing	Maximum twelve hours.

Processing

Homogenisation	Homogenisation is carried out at the UMC.
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Storage

Aliquoting	Store at least six 5 ml aliquots.
Vial type	No agreement.
Temperature	Store at $\leq -80^{\circ}\text{C}$. Freeze slowly by placing in storage freezer.

Comments

Faeces is collected only for the IBD Pearl.
 Given the current level of knowledge on this subject, at the present time it is not possible to make any useful agreements beyond what is described above.
 The IBD Pearl has pledged to compile a standard procedure as soon as possible, drawing upon String of Pearls collection experiences. Once ready, that procedure will be incorporated into version 5 of this document.

9.8 Frozen material

9.8.1 Biopsy specimens

Collection

Time to freezing Freeze immediately, at the point of collection.

Storage

Vial type No agreement.

Temperature Store at $\leq -80^{\circ}\text{C}$.
Freeze rapidly, preferably by placing in chilled isopentane.
The use of liquid nitrogen is also permissible.

9.8.2 Tissue

Collection

Temperature Freeze as quickly as possible, preferably at the point of collection.

Time to freezing Within 60 minutes.

Storage

Vial type No agreement.

Quantity Quantity should be indicated in number of units of approximately 0.5 cm^3 .

Temperature Store at $\leq -80^{\circ}\text{C}$.
Freeze rapidly, preferably by placing in chilled isopentane.
The use of liquid nitrogen is also permissible.

9.9 Paraffin-embedded material

9.9.1 Biopsy specimens

Collection

Time to fixation Fix immediately in formalin, at the point of collection

Processing

Embedding Embed the material in paraffin.

Storage

Temperature Store the material at room temperature.

9.9.2 Tissue

Collection

Time to fixation Fix in formalin as soon as possible after collection.

Processing

Embedding Embed the material in paraffin.

Storage

Quantity Quantity should be indicated in number of units of approximately 0.5 cm³.

Temperature Store the material at room temperature.

9.10 DNA from blood

Collection

Vial type	Standard EDTA vial; no gel, no protease inhibitors. Minimum 4 ml; preferably 7-10 ml.
Needle type	No agreement; is not regarded as critical.
Temperature	Depending upon the time to processing, the vials should be kept at either room temperature, 4°C or $\leq -20^{\circ}\text{C}$.
Time to processing	The DNA or buffy coat should be isolated as soon as possible. When stored at room temperature : process on day of collection. When stored at 4 °C : process within four weeks. When stored at <-20 °C : process within three months.

DNA isolation

Protocol	Given the variety of techniques available, requirements pertain only to the end product.
DNA concentration	The DNA concentration of the stock solution must be determined after isolation.

Storage

Aliquoting	Store the material in a stock solution. Divide the solution into at least two aliquots, and preferably three or four.
Vial type	No agreement.
Temperature	Store the material at 4°C or freeze it to $\leq -20^{\circ}\text{C}$. If freezing, do so slowly by placing in storage freezer.
PIM data	Submit the concentration in $\mu\text{g/ml}$ to the central database. Submit OD ratio 260-280 nm to the central database.

9.11 Isolation of viable cells (LML)

All the tasks below should be performed sterile.

Source material (blood)

Vial type	6 ml heparin vial, two to four units.
Needle type	No agreement; is not regarded as critical.
Temperature	Keep vials at room temperature prior to freezing.
Time to processing	Cells must be frozen within 24 hours of collection.

Source material (bone marrow)

Vial type	Heparin vial, maximum 30 ml.
Needle type	No agreement; is not regarded as critical.
Temperature	Keep vial at room temperature during transportation.
Time to processing	Cells must be frozen within 24 hours of collection.

Isolation of cells

Method	Cells are isolated from the blood by centrifugal density separation.
Medium	The density separation medium must be 1.077 g/ml.
Lysis	When isolating granulocytes, erythrocytes must be removed by lysis: 30 minutes in a 0.9% NH ₄ Cl solution at 4°C.
Time	Cells must be stored immediately after separation.

Storage

Medium	10% cryoprotectant (usually 10% DMSO).
Aliquots	Between one and eight 1 ml ampoules, each with 10x10 ⁶ cells/ml.
Vial type	No agreement.
Temperature	Store at ≤ -130°C.

9.12 RNA isolation from intact cells (LML)

Source material	Viable cells from blood or bone marrow, freshly thawed.
RNA concentration	The RNA concentration must be determined using spectrophotometry or NanoDrop technology.
Quality control	The quality of the RNA is determined by analysing the 18S and 28S rRNA using agarose gel electrophoresis or a BioAnalyzer or similar device.
Storage temperature	Store RNA as an ethanol precipitate at $\leq -80^{\circ}\text{C}$, so that multiple samples can be taken without repeated thawing and refreezing.

9.13 DNA isolation from intact cells (LML)

Source material	Viable cells from blood or bone marrow, freshly thawed.
DNA concentration	The DNA concentration must be determined using spectrophotometry or NanoDrop technology.
Quality control	It must be possible to perform a standard PCR on the DNA. If a laboratory routinely isolates DNA, this test is not required on every sample.
Storage temperature	Store the material at 4°C or freeze slowly to $\leq -20^{\circ}\text{C}$.
PIM data	Submit concentration ($\mu\text{g}/\text{ml}$) to the central database. Submit OD 260:280 ratio to the central database.

10 Changes compared with previous versions

Changes made in version 4.0, compared with 3.6 and 3.7, as a result of agreements reached during the Biobank consultations of 9 February and 20 April 2010, and from discussions between the PSI management team and Pearl co-ordinators.	
	IBD Pearl Co-ordinator changed.
2.1.2	Heparin plasma removed.
4	Table harmonised with Chapter 9. References added.
5.3	Added... <ul style="list-style-type: none"> ○ Concentration: DNA in µg/ml. ○ Quality: DNA as OD 260/280 nm ratio.
5.3	Added is the fact that, in the event of deviations from what has been agreed in this document, that should be justified by a list of possible SOP deviations.
7	Clarity of biomaterial coding text improved.
9	Wherever applicable, "Freeze slowly by placing in storage freezer" replaced with "Freeze slowly".
9	Wherever applicable, "a minimum of -80°C" replaced by "≤ -80°C".
9.2	Added under "Vial type": "Standard vial, not glass; no gel, no protease inhibitors. Use BD model 366575 (6 ml), Greiner model 455322 (9 ml) or equivalent." "When taking 10 ml..." replaced with "Preferably use one vial only and do not pool blood samples". Deleted: the sentence "The citrated plasma vial is not taken first."
9.2	"Standard vial, not glass" changed to "Standard vial, not glass unless siliconised".
9.3	Added: "Use BD model 367896 or equivalent".
9.3	Added: "NB. The use of gel vials is permitted when collecting serum for the NDZ and DIA pearls, as long as this deviation from the norm is documented fully and correctly."
9.6	"Acidified urine " replaced with "Urine with antioxidant".
9.7	Added: "Homogenisation is carried out at the UMC". Remark added by IBD co-ordinator concerning the lack of a procedure for collection and storage.
9.8 and 9.9	"Quantity should be indicated as follows ..." changed to "Quantity should be indicated in number of units of approximately 0.5 cm ³ ".
9.8.2/9.9.2	Tissue quantity indicators added.