

 (Web Link)	National Biobank Consortium of Taiwan Standard Operating Procedure		No.: NBCT SOP-011
	Title: NBCT Specimen Dispensing Process (1): Cold Chain Transport		Version/Total Pages: No. 1.1 / 13 pages
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1. Purpose

“National Biobank Consortium of Taiwan” (hereinafter referred to as the “Integration Platform”) primarily integrates domestic human biobanks and their biospecimens and data through a cloud-based system, and makes them available for application and use by medical, clinical, industry, and related biomedical research investigators nationwide. To achieve cross-institutional collaboration, maintain good quality of specimens and their data, and ensure consistency in the steps for dispensing specimens and their data, so as to facilitate future related research, this Standard Operating Procedure is hereby established.

2. Scope

This dispensing SOP applies to all specimens dispensed from Integration Platform biobanks that follow a cold chain (below -15°C) transport process. Such specimens include: serum, plasma, buffy coat, whole blood, DNA extracted from blood, DNA extracted from pleural fluid centrifugation sediment, DNA extracted from ascitic fluid centrifugation sediment, DNA extracted from frozen tissue, RNA, and small tissue fragments, among others.

3. Responsibilities

All human biobanks that have joined the Integration Platform, when dispensing frozen specimens, are recommended to follow this Standard Operating Procedure.

4. Description

The dispensing process for cold chain transport can be divided into two stages:

(1)Dispensing from Integration Platform human biobanks (hereinafter referred to as “Platform Biobanks”) to the Integration Platform Central Laboratory

- 1.Pre-Dispensing Preparation Process for Frozen Specimens
- 2.Frozen Specimen and Data Dispensing Process
- 3.Frozen Specimen and Data Receipt Confirmation Process

(2)Applicant Pickup of Specimens at Integration Platform Central Laboratory

1. Notification Process for Completed Application Case Frozen Specimens
2. Application Case Frozen Specimen and Data Pickup Process

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5. Operating Procedures

5.1 Platform Biobank Frozen Specimen Dispensing to Integration Platform Central Laboratory Consumables

1. 1.5ml microcentrifuge tubes (microcentrifuge tubes of different capacities may also be selected, depending on the volume or size of the specimen)
2. Freeze-resistant labels
3. Specimen storage box (9x9 grid)

5.1.1 Pre-Dispensing Preparation Process for Frozen Specimens

Procedure:

1. The Central Office shall, based on the order in which each Platform Biobank returns its approval letter, assign sequential numbers to the biospecimens for the application; the Platform Biobank that replies first shall be listed first. The numbering convention is NB-[application number]-[specimen sequence number].
2. The Central Office shall notify the Platform Biobank related to each application of the sequential number, number of cases, and specimen type.
3. Once the applicant has completed payment, the Central Office shall notify the Platform Biobank related to the application to dispense the specimens and data. The Integration Platform office shall provide the coding for each application's specimens and biological data, using sequential numbering.
4. The Platform Biobank shall use a label printer to print the Integration Platform case code and specimen code onto the freeze-resistant label; for example, for the NBCT No.43 application, case No.1's serum specimen would have its freeze-resistant label printed as: NB043-001S (see Attachment 1, Integration Platform Case Code Freeze-Resistant Label SOP). **See Frozen Specimen Dispensing Process Flowchart 1.**

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5. Aliquot the specimens to be dispensed, according to the needs of the application (e.g., DNA 2ug, RNA 5ug, or serum 200 ul, etc.), into 1.5 ml microcentrifuge tubes already labeled with the Integration Platform case code freeze-resistant label, and seal with parafilm. For this step, crushed ice must be prepared, and the aliquoted microcentrifuge tubes placed on the crushed ice to maintain a low temperature. Depending on the nature of the specimen, aliquoting
6. may need to be performed entirely without thawing, as with small tissue fragments (tissue fragments preparation). In that case, dry ice must be prepared, and the aliquoted microcentrifuge tubes placed on the dry ice.
7. In numerical order, place the aliquoted microcentrifuge tubes into a specimen storage box (9x9 grid). On the lid and side of the box, write the Integration Platform application case number, specimen number, specimen type, and specimen box number (if there is more than one box), and store in the -80 °C freezer until shipped. See Frozen Specimen Dispensing Process Flowchart 2.

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5.1.2 Frozen Specimen and Data Dispensing Process Procedure:

1. Once the application case specimens are prepared and ready for dispensing, a specimen list dedicated to each specimen type must be created according to the format established by the Central Office (see Attachment 2, Integration Platform Frozen Specimen List Format and Example).
2. Prepare in advance a foam box already loaded with a sufficient quantity of dry ice, then take the aliquoted frozen specimen storage box out of the -80°C freezer and place it in the foam box, once more verifying the specimen type and number of tubes. Confirm that the lid and side of the box have the Integration Platform application case number, specimen number, specimen type, and specimen box number (if there is more than one box) written on them.
3. Secure the verified specimen box with a rubber band, and place it in a foam box loaded with a sufficient quantity of dry ice; newspaper or bubble wrap may be used to cover the dry ice to slow its sublimation. Place the specimen shipping list for this shipment into a resealable bag, and seal the box. See Frozen Specimen Dispensing Process Flowchart 3.
4. Once the application case's specimens are prepared and ready for dispensing, notify the assistant at the National Health Research Institutes (NHRI) NBCT Central Laboratory responsible for receiving specimens in advance — by (1) e-mail; (2) telephone; (3) text message (using at least two of the three methods) — of when the specimens will be shipped and the expected delivery time. The Integration Platform Central Laboratory's specimen-receiving assistant's e-mail address is: (070925@nhri.edu.tw), telephone: 037-206166, ext. 33334, 33335.
5. Because no one is available to receive specimens at the NHRI on holidays, and shipments always take an additional day to arrive at the NHRI, cold chain specimen shipments must always be sent Monday through Wednesday, with adjustments made to accommodate holidays. Shipment on Thursday is permitted only under special circumstances. Before dispensing, each institution may check with the courier company whether current shipping

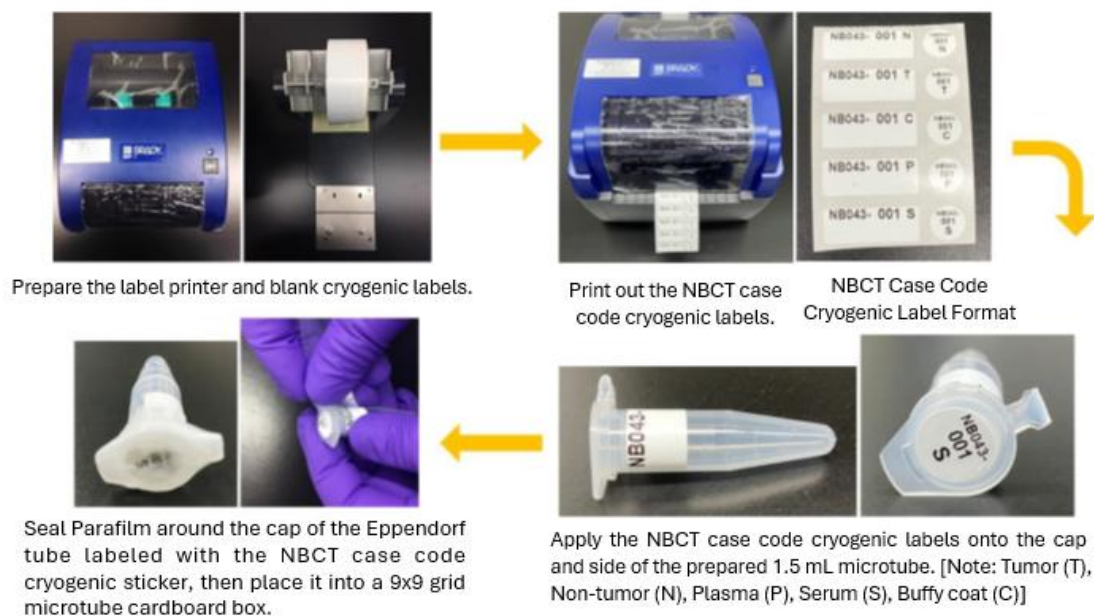
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volume is too high and likely to cause delays, and decide accordingly whether to postpone shipment.

6. Hand the packed foam box to the courier, using the NHRI's cash-on-delivery courier form, addressed to No. 35, Keyan Road, Zhunan Township, Miaoli County, NHRI R1-B1111, "National Biobank Consortium of Taiwan Central Laboratory," telephone: 037-206166, ext. 33334, 33335. Ship via "cold chain courier," which shall arrive within 24 hours. (Note: On the courier form, be sure to indicate: 1. Item: specimens for research use; 2. Select cold chain transport (circle "frozen"); 3. Check the box for delivery before noon.)
7. Send the electronic file of the specimen list for this shipment to the National Biobank Consortium of Taiwan Central Laboratory's specimen-receiving assistant (070925@nhri.edu.tw), with a copy to the Integration Platform Chief Executive (sfhuang@nhri.edu.tw). All laboratory correspondence must be copied to the Integration Platform Chief Executive.
8. After the specimens have been shipped, the Platform Biobank's information staff shall encrypt the de-identified and coded basic clinical data file, burn it to a disc, and send it by registered mail to the Integration Platform Central Office's information core staff. (Attachment 3: Basic Clinical Data Field Example). Information core telephone: 037-206166, ext. 33332, 33337.

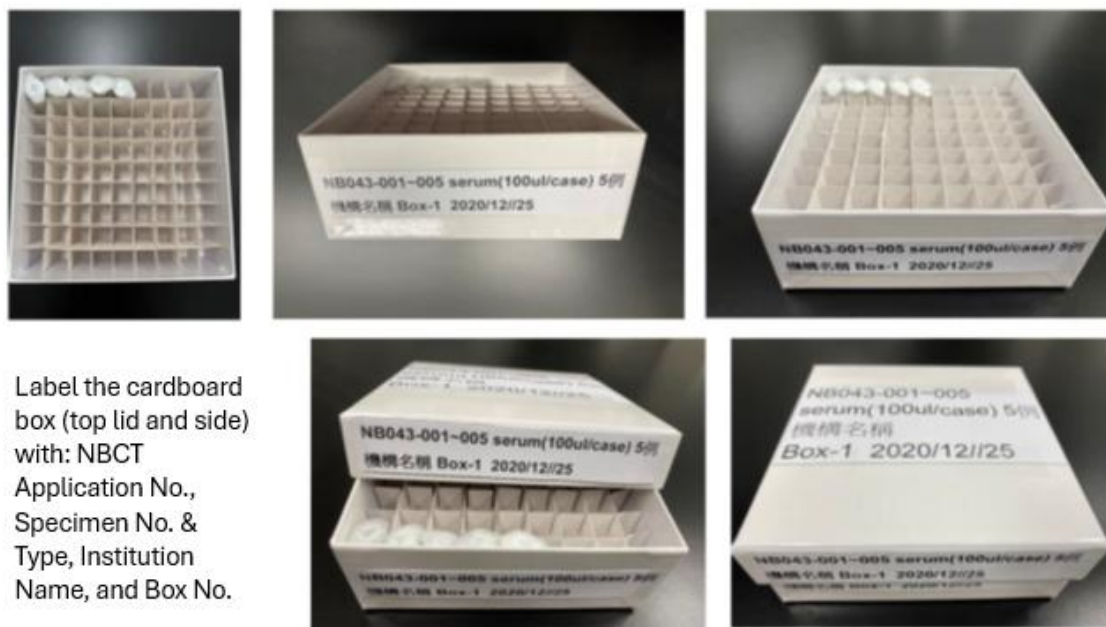
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Frozen Specimen Dispensing Process Flowchart 1:

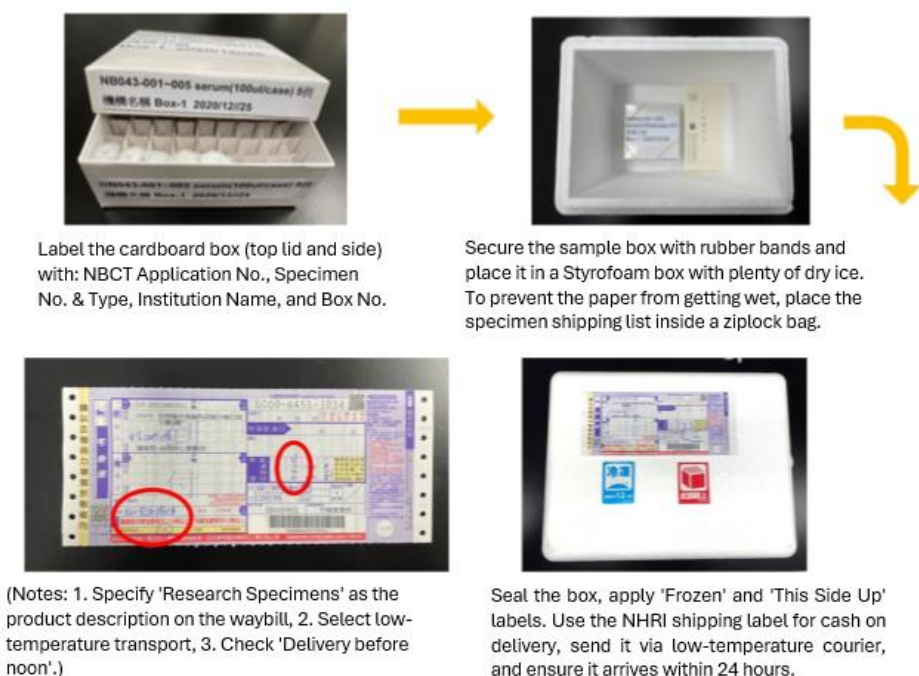


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Frozen Specimen Dispensing Process Flowchart 2:



Frozen Specimen Dispensing Process Flowchart 3:



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5.1.3 Frozen Specimen and Data Receipt Confirmation Process

Procedure:

1. When frozen biospecimens are transported under low-temperature conditions to the **Central Laboratory of the National Biobank Consortium of Taiwan at the National Health Research Institutes**, the laboratory assistant responsible for receiving the biospecimens shall first inspect the expanded polystyrene container to confirm that a sufficient amount of dry ice remains. This is necessary to ensure that the biospecimens have not thawed during transportation. While maintaining the biospecimens in a frozen state, the assistant shall verify their quantity and type. The biospecimen storage boxes shall then be placed in the Consortium's designated -80°C freezer. The assistant shall notify the submitting biobank by email that the biospecimens have been received and document the receipt in the biospecimen receipt log.
2. If the receiving assistant identifies any discrepancy in the quantity or type of the biospecimens, photographs shall be taken as documentary evidence. The assistant shall immediately contact the personnel of the submitting biobank to clarify the discrepancy, document the issue in the biospecimen receipt log, and report it to the Head of the Quality Division and the Executive Director. Further action shall be taken in accordance with the Executive Director's instructions.
3. If the receiving assistant finds that the dry ice in the shipping container has completely sublimated and that the biospecimens may have thawed, the condition shall be documented in the biospecimen receipt log. The assistant shall immediately report the incident to the Head of the Quality Division and the Executive Director of the Consortium and notify the personnel of the submitting institution that corrective improvements to the shipping procedure are required.

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4. Upon receipt of an encrypted compact disc containing de-identified and coded basic clinical data files, the Information Core personnel of the Consortium's Central Office shall notify the submitting biobank by email that the data have been received and record the receipt in the receipt log for the corresponding application.

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5.2 Collection of Biospecimens by Applicants at the Consortium's Central Laboratory

5.2.1 Notification Procedure for Completion of Frozen Biospecimen Preparation

Procedure:

1. Because biospecimens are extremely valuable and cannot be replaced or compensated for if damaged, they shall not be shipped directly to applicants. The Central Laboratory assistant shall therefore request that the applicant or a member of the applicant's research team personally collect the biospecimens from the Consortium's Central Laboratory at the National Health Research Institutes.
2. The Central Laboratory assistant shall first notify the applicant and the applicant's contact person by email that the frozen biospecimens for the application have been prepared and are ready for collection. The email shall include the available collection time, location, telephone number, contact person, and other relevant information. The Executive Director of the Consortium shall be copied on all email correspondence.
3. The Central Laboratory assistant shall subsequently contact the applicant or the applicant's contact person by telephone to confirm the collection arrangements and explain the precautions and requirements for collecting the biospecimens. The applicant shall be requested to reply by email with the date and time of collection, the name of the person collecting the biospecimens, and the collector's contact telephone number. The collector is not required to be the applicant personally. The Executive Director of the Consortium shall be copied on all email correspondence.

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5.2.2 Application Case Frozen Specimen and Data Pickup Process

Procedure:

1. The Integration Platform Central Laboratory assistant shall, on the day the applicant is to come to the NHRI to collect the frozen specimens, prepare in advance a sufficient quantity of dry ice and a foam box.
2. Once the applicant (or their designated representative) arrives at the laboratory, the Integration Platform Central Laboratory assistant shall then remove the frozen specimens from the -80°C freezer and place them into the foam box already loaded with dry ice, allowing the applicant's representative to inspect the condition and quantity of the specimens one by one.
3. Once everything has been verified correct, the Integration Platform Central Laboratory assistant shall then pack the frozen specimens. Secure the 81-well box with a rubber band around the outside, to prevent it from tipping over.
4. Place an appropriate amount of dry ice in the bottom of the foam box, place the 81-well box containing the specimens onto the dry ice, and fill the top and sides with dry ice; cover the top layer with newspaper to block air and slow the sublimation of the dry ice, then seal the foam box with wide tape to complete the cold chain specimen packaging.
5. Ask the applicant (or their designated representative) to sign the Specimen Pickup Receipt (Attachment 4, Specimen Pickup Receipt).
6. Once the cold chain specimens have been picked up, the Integration Platform Central Laboratory assistant shall provide the applicant and their contact person, by e-mail, with the electronic file of the application case's frozen specimen list showing only the sequential numbers, as well as a scanned copy of the Specimen Pickup Receipt signed by the applicant (or their designated representative), with a copy to the Integration Platform Chief Executive.
7. Once the cold chain specimens have been picked up, the Integration Platform Central Laboratory assistant must also notify the Integration Platform Central Office's information core staff that dispensing of specimens for the application has been completed.

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8. The Integration Platform Central Office's information core staff must first verify the application case's de-identified basic clinical information files (from different institutions). Once assembled in the original sequential order, a second information core staff member must verify and confirm correctness, after which the basic clinical information file for the application shall be provided to the applicant by e-mail; the cases in this file must be fully de-identified, containing only sequential numbers.
9. The application's de-identified basic clinical information file, if the application's case count exceeds one thousand cases, cannot be provided directly to the applicant; the applicant must instead go to the Central Office's information core independent workspace to use it on a one-time basis, and it cannot be downloaded or removed.

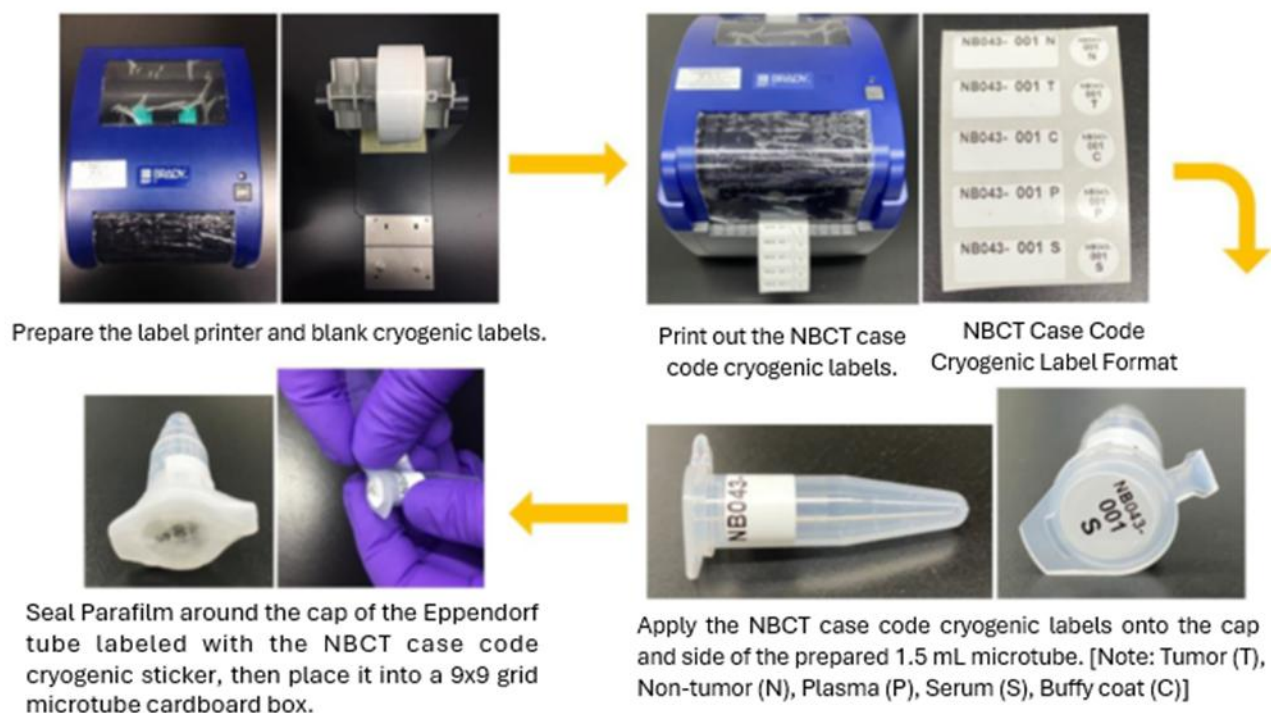
Precautions:

1. The applicant (or their designated representative)'s signed Specimen Pickup Receipt original, shall be retained by the National Biobank Consortium of Taiwan Central Laboratory; only a scanned copy of the Specimen Pickup Receipt need be given to the applicant.
2. In the cold chain transport process, specimens are, in principle, all packed in microcentrifuge tubes, which are relatively convenient to handle and use. However, applicants must be reminded that microcentrifuge tubes may only be stored in a -80°C low-temperature freezer; if the applicant wishes to store specimens in a liquid nitrogen tank, they must be transferred into cryovials, or they may burst.
3. If the applicant needs specimens packed in cryovials for transport, this must be indicated in advance at the time of application.

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6. Attachments

1. Integration Platform Case Code Freeze-Resistant Label SOP



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2. Integration Platform Frozen Specimen List Format and Example

Note: For consistency of data standards, please use the Thermo NanoDrop 2000 to measure DNA and RNA concentration whenever possible, and use an Excel file to prepare the list.

1. DNA Specimens (coded in black font):

Quantity No.	NBCT Sequential No.	Biobank ID No.	Tumor percentage	Concentration ng/uL	O.D 260/280	O.D 260/230	Volume Given (ul)	box
1	NB043-001 T		90%	1388	1.86	2.35	5.04	box-1
2	NB043-001 N			1140.9	1.89	2.06	6.14	box-1

2. RNA Specimens (coded in red font):

Quantity No.	NBCT Sequential No.	Biobank ID No.	Tumor percentage	Concentration ng/uL	O.D 260/280	Volume Given (ul)	box
1	NB043-001 T		90%	1278.4	1.9	3.9	box-1
2	NB043-001 N			1588.2	1.93	3.1	box-1

3. tissue fragments Specimens (coded in blue font):

Quantity No.	NBCT Sequential No.	Biobank ID No.	Tumor percentage	box
1	NB043-001 T		90%	box-1
2	NB043-001 N		--	box-1

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4. serum Specimens:

Quantity No.	NBCT Sequential No.	Biobank ID No.	Volume Given (μl)	box
1	NB043-001 S		50	box-1
2	NB043-002 S		50	box-1

5. plasma Specimens:

Quantity No.	NBCT Sequential No.	Biobank ID No.	Volume Given (μl)	box
1	NB043-001 P		50	box-1
2	NB043-002 P		50	box-1

6. Buffy coat Specimens:

Quantity No.	NBCT Sequential No.	Biobank ID No.	Volume Given (μl)	box
1	NB043 001 C		50	box-1
2	NB043 002 C		50	box-1

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3. Example of Basic Clinical Data Field Content

(The basic clinical data fields appropriate for each type of disease may be found in the Information Section of the Integration Platform website)

Clinical Data Fields for Oral Cancer Cases							
Sequential No.	Biobank ID No.	gender	Age	smoking history	betel nut chewing history		
CEA (ng/ml)	Hb (g/dL)	Platelet (10 ³ /uL)	Clinical stage:T	Clinical stage:N	Clinical stage:M	*Clinical stage	
Pathology Diagnosis	tumor size(cm)	tumor number	Tumor grade	Tumor site	vascular invasion	perineural invasion	Closest Tumor margin (cm)
Pathology stage:T	Pathology stage:N	Pathology stage:M	*Pathology stage	metastatic site			

*Clinical and Pathology staging according to AJCC, 8th edi.

Leave blank if there is no relevant data

Clinical Data Fields for Lung Cancer Cases						
Sequential No.	Biobank ID No.	gender	Age	smoking History	history of pulmonary tuberculosis	
Clinical stage:T	Clinical stage:N	Clinical stage:M	*Clinical stage	CEA	Hb	Platelet
Pathology Diagnosis	tumor size(cm)	Tumor site	treatment before surgery			
Pathology stage:T	Pathology stage:N	Pathology stage:M	metastatic site	*Pathology stage		
EGFR mutation	KRAS mutation	HER2 mutation	ALK mutation	other genes		
*Clinical and Pathology staging according to AJCC, 8th edi.						
Leave blank if there is no relevant data						

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4. Specimen Pickup Receipt

Customer No.:

Receipt No.:

Customer Name:

Date Completed:

Address:

Telephone:

Fax:

Valid for: 90 days

Additional Notes:

RECEIPT

Item	Description	Quantity	Unit
1			
2			
Customer Signature:		Date:	

Prepared by: National Biobank Consortium of Taiwan Central Laboratory / NHRI Human Biobank Laboratory

Handled by:

Telephone:

Ext.