We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists



185,000

200M



Our authors are among the

TOP 1% most cited scientists





WEB OF SCIENCE

Selection of our books indexed in the Book Citation Index in Web of Science™ Core Collection (BKCI)

Interested in publishing with us? Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected. For more information visit www.intechopen.com



Chapter

Harmonized and Quality Sample Handling in Biobank-Supported Multicenter Prospective Studies

Verónica Valdivieso-Gómez, Javier Garrancho-Pérez, Inés Aroca-Siendones and Rocío Aguilar-Quesada

Abstract

In the frame of multicenter research studies, biobanks ensure the harmonization and traceability of the prospective collection of quality samples. This is significant because pre-analytical variables must be carefully considered to guarantee the integrity of biomarkers to be tested and to avoid bias affecting the validity of the analytical results. According to a quality management system, biobanks contribute with documents and records; consumable preparation for collection, processing, and conservation; sample quality controls; and centralized management of sample handling, storage, and distribution. Traceability of samples is based on unique standard codes and the use of pre-assigned, pre-coded, and pre-labeled materials for sample collection, processing, and conservation. By using these supporting tools, quality derivatives are obtained based on common and evidence-based standard operating procedures (SOPs), with associated traceability information in relation with their collection, processing, conservation, and distribution. The biobank-supported workflow, specifically designed and implemented for each project, allows obtaining harmonized quality samples contributing to the quality of large and complex research projects and the corresponding validity of the analyses.

Keywords: multicenter prospective project, sample handling, traceability, workflow harmonization, quality-assured biobanking

1. Introduction

Professionalism is the current hallmark of biobanks [1], which are driven by standards and best practices. A biobank is "an entity that receives, stores, processes, and/or distributes specimens, as needed. It encompasses the physical location as well as the full range of activities associated with its operation [2]." Different types of biobanks have been proposed [3], although the definitive model will be the result of the activities performed in support of the particular needs of attended projects, including real or virtual collection, processing, conservation, and distribution.

Biobanks have been involved in large quality-assured prospective studies based on validated and standardized sample handling and storage protocols [4, 5]. When a prospective multicenter research project is designed, multiple variables must be considered such as the number and type of donations, recruitment sites and analytical laboratory locations, pre-analytical requirements of samples and derivatives obtained, and processing and storage facilities. Attending to the complexity of the project, a specific workflow is implemented after process definition identifying every factor involved in (site, staff, equipment, method, materials, samples and transferences) and their corresponding checkpoints.

2. Harmonization of sample collection and derivative preservation

To guarantee the integrity of biomarkers to be tested and to avoid bias, pre-analytical variables must be carefully considered [6]. In fact, many studies are being conducted to elucidate the effects of pre-analytical variables on analytical profiles. In this sense, a study has been recently published to determine acceptable delays to fixation for formalin-fixed paraffin-embedded (FFPE) tissue samples [7]. In order to mitigate their impact in the complex frame of multicenter projects, biobanks contribute through supervised materials and sample handling and continuous and overlapped checkpoints.

2.1 Centralized preparation of consumables for sample collection, processing and preservation

With the objective to ensure the consistency in sample collection, stabilization, and preservation, specific kits with the consumables necessary for only a donation are defined in function of pre-analytical requirements of obtaining samples and derivatives (**Figure 1**). A careful selection of collection devices is critical here since differences in biomarker testing have been reported [8, 9]. Consumables such as modified cards (IsoCode cards or FTA cards) for blood spot collection, in addition to multibarrier pouches with desiccant packs for room-temperature transportation and future conservation, could be also included for traceability purposes [10]. For

	Sample	Collection material	Stabilization material	Preservation material	Derivatives	Protocols
		1 K2 EDTA tube of 10 ml		10 Pre-coded tubes of 1,4 mi	10 Whole blood aliquots of 1 ml	
COLLECTION KIT (at the recruitment site)		1 K2 EDTA tube of 10 ml	1 Tube of 15 ml	10 Pre-coded tubes of 0,65 ml	10 Plasma (EDTA) aliquots of 0,5 ml	Protocol
LECTION KIT (at recruitment site)	Blood			Initial K2 EDTA tube of 10 ml	Blood cells in the K2 EDTA tube	
LECTIC		6 Serum separator tubes of 8,5 ml		20 Pre-coded tubes of 0,65 ml	20 Serum aliquots of 0,5 ml	
COL				14 Pre-coded tubes of 1,4 ml	14 Serum aliquots of 1 ml	Protocol
		1 Sterile container of 100 ml	1 Tube of 50 ml	25 Pre-coded tubes of 1,4 ml	25 Urine supernatant aliquots of 1 ml	
me)	e			5 Pre-coded tubes of 1,4 ml	5 Urine pellet aliquots of 1 ml	
(at ho	Urine		1 Tube of 50 ml	25 Pre-coded tubes of 1,4 ml	25 Urine supernatant aliquots of 1 ml	Protocol
NORS				5 Pre-coded tubes of 1,4 mi	5 Urine pellet aliquots of 1 ml	
COLLECTION KIT FOR DONORS (at home) COLLECTION KIT FOR DONORS (at home) COLLECTION KIT FOR DONORS (at home) recruitment site)	Stool	2 Sterile specimen tubes with an integral spoon		1 Specimen bag with 2 sterile specimen tubes with an integral spoon	2 Stool aliquots	Protocol
LECTION		1-2 Specimen bags		1-2 Specimen bags		
COL	Nails			AB	Nails	Protocol

Figure 1.

Consumables included for sample collection, stabilization, and preservation in representative kits, classified by the corresponding protocol and derivatives obtained.

noninvasive samples (nails, stool, etc.), kits targeted to donors may be designed for a more accessible collection at home, with the appropriate consumables to guarantee the integrity of samples until they are receipted by the biobank or analytical laboratory. When processing is performed by a different center from the recruitment site, two kits are prepared in independent boxes for collection and processing, especially when the sample collection is made by the donor on his own.

Materials included in the kits are classified in several bags according with the downstream protocol. Expiration date and batch numbers for consumables must be considered during the purchasing process in relation with the recruitment rates and the validity of the results, respectively. Additionally, expiration date is identified for each kit according to the most recent expiration date from the consumables, and it is used as a reference to track and replace expired consumables by the biobank when the recruitment rate is not the expected.

2.2 Sample processing and quality controls

Evidence-based standard operating procedures (SOPs) are elaborated for sample processing taking the sample requirements provided by the testing laboratories into consideration. The number and volume of samples necessary for analytical assays and the type of derivative, anticoagulant or preservative must be identified in order to choose the most appropriate and approachable option of prospective collection of samples providing high-quality biomarkers useful for downstream applications [11]. Additional requirements from guides [12] or previous scientific publications [13] are also taken into account in relation with specific sample collection and derivative stabilization. Preservation delay and resources available for long-term storage will influence the selection of the collection device as well. In fact, roomtemperature storage alternatives have been proposed [14]. When the same sample allows obtaining different derivatives (i.e., blood for plasma, buffy coat, and RBCs), protocols will adjust the number and type of collection tubes or devices to minimize the quantity of sample collected from the donor. On the other hand, the number of aliquots of liquid samples must be set in function of the different analyses to be performed avoiding unnecessary freeze-thaw cycles.

These pre-analytical conditions of samples and derivatives will determine where each process (collection, initial sample processing, provisional cryopreservation of derivatives, long-term storage, testing) will be performed depending on the recruitment site, the biobank, and the analytical laboratory locations and facilities. Accordingly, transportation of samples at the corresponding temperature should be organized [15] following the international recommendations.

Obtaining of specific derivatives such as nucleic acid isolation may be centralized in the biobank or testing laboratories in order to avoid bias. In the same sense, reactive batches must be controlled. When possible, automation of processes must be implemented to avoid traceability errors and decreasing hands on time. Samples should be handled following validation of standard operating protocols by using samples not belonging to the particular project, specifically collected and approved for this purpose by an ethical committee.

The quality of samples must be evaluated after processing by means of a comprehensive analysis of quality indicators [16]. Because of the current lack of qualification tools for each type of derivative and pre-analytical variable, numerous studies are trying to identify new markers to assess the fitness-for-purpose of samples. Thus, new scores and indicators have been proposed for the quality of samples in relation with the impact derived from the pre-analytical phase [17–23]. In the same way, participation in external quality assurance (EQA) schemes like the EQA program developed by the International Society for Biological and Environmental

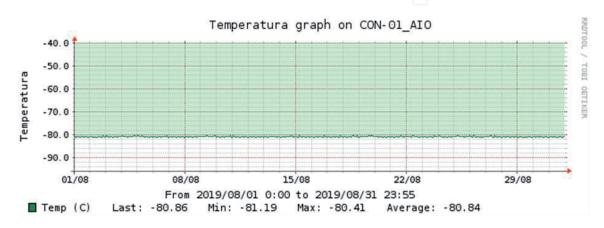
Repositories (ISBER) focused on sample processing and testing evaluation [24]; it is a highly recommended complementary tool for the internal quality control (IQC). Biobank collaboration through international working groups focused on standardization of sample processing, and biological sample quality control will contribute to the implementation of the last innovations in the field as well.

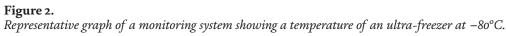
2.3 Monitored storage of biological samples and distribution

In relation with sample conservation, derivatives are long-term stored in the most appropriate conditions to maintain their original characteristics, being very important for the sample stability the selection of the temperature storage [15]. When samples are receipted in the storage facilities, aliquots are immediately revised to check the shipment temperature; the number, integrity, and volume of each aliquot regarding the expected; and incidents reported, maintaining the cold chain. Racks and boxes are previously prepared to directly store the derivatives in a reduced and optimized space within the conservation equipment classified by the type of container. In addition, derivatives are preferably stored separately in different equipment and preservation rooms as a safety measure.

So, long-term storage facilities may be located in one or more rooms or buildings and may even be assumed by several institutions when transportation of samples and temperature variations are minimized. In any case, sample handling and positions must be under control and restricted access. Both the preservation rooms and storage equipment are constantly controlled through a monitoring system that records critical parameters such as temperature, humidity, CO₂, and O₂ levels (where necessary) and the proper functioning of equipment (compressors, battery power, display) (**Figure 2**). The system triggers an alarm when any parameter is out of the established range, thus activating an emergency plan. Briefly, warnings are received by specifically dedicated staff available for 24 h who analyze and classify the failure to initiate the defined corrective actions. In case it could not be repaired, samples are evacuated to backup equipment.

If previous instructions are followed, samples could be preserved in good conditions for a long time. However, the specific period of time will depend on the type of sample but, most importantly, on the biomarker to be detected by a particular methodology, with a range from minutes to years [15]. In this sense, fitness-for-purpose procedures should be validated and established when a prospective workflow is designed, taking into consideration the general good practices that do allow the most use of samples [2, 12]. Independently, other approaches have been reviewed for the conservation of samples at room temperature by biobanks [25].





Before sending of samples to analytical laboratories from the storage facilities, a checkpoint is introduced to guarantee that each aliquot is compliant with the corresponding study or with the necessary volume of sample to thus supplement with additional aliquots. Additional quality controls should be performed when incidents during the sample conservation occur or after a non-validated long-term storage. The remaining precious samples may be again received for long-term storage from the testing laboratories followed by a new quality control.

3. Traceability of biological samples

3.1 Electronic database

The electronic database used by biobanks allows the integral management of multicenter prospective projects with a maximum level of security through restricted access. Donors, biological samples, and associated information, as well as the ethical-legal documentation associated to the project, are recorded. In detail, the system allows an exhaustive control of collaborating centers and researchers, preparation of sample collection kits maintaining the traceability of all materials used, donor and clinical information, informed consent forms, ethical and scientific committees' approvals, agreements, sample handling by different sites (reception, processing, storage and shipments), quality incidents, and even the project monitoring by using any recorded information, for example, the recruitment rates from each clinical site. The electronic database may be also connected to external databases incorporating additional information such as temperature information from storage equipment. So, traceability is achieved from all the processes.

				4 4								
				1		-	ation code	Sample	Catal Catal	. Steres	anumeric co	ode
1	-			D. D. Marine		INVN	02519A001	SAN	1	A00	01	
/			Sample	ecoue	Pie	-coded tub	6					
					1.		-					
AAA 0000		2	3	• /	5	6	7	8	9	10	11	12
AAA 00001	NVN02519A0013	NVN02519A0015	IN VN025 19A0015	INVN0251940015	IN VN 0251 9A0015	INVN02519A0015		IN VN02 519 A0015	INVN02519A0015	IN VN025 19A0015	INVN02519A0015	IN VN025 19400
	IN VN02 51940013	NVN02519A0015 ANA002	IN VN025 19A0015 AN A003	INVN0251940015	IN VN 0251 9A0015 AN A005	INVN02519A0015 ANA006	ANA007	IN VN02 519A0015 ANA008	INVN02519A0015 ANAD09	NVN02519A0015 ANA010	UEA011	UEA012
AAA 00003	IN VN02 519A0019 ANA001 AAA00000101	NVN02519A0015 ANA002 AAA0000102	IN VN025 1940015 AN 4003 AA 40000103	INVN0251940015 ANA004 AAA0000104	IN VN 0251 9A0015 AN A005 AAA0000 105	INVN02519A0015 ANA006 AAA0000106	ANA007 AAA0000107	IN VN02 519A0015 ANA008 AAA0000108	INVN02519A0015 ANAD09 AAA0000109	IN VN02519A0015 ANA010 AAA0000110	UEA011 AAA0000111	IN VN02519A0 UEA012 AAA000011
	NVN02519A0013 ANA001 AAA0000101 NVN02519A0015	NVN02519A0015 ANA002 AAA0000102 INVN02519A0015	IN VN025 1940015 ANA003 AAA0000103 (IN VN025 1940015	INVN0251940015 ANA004 AAA0000104 INVN0251940015	IN VN 0251 9A0015 AN A005 AAA0000 105 IN VN 0251 9A0015	INVN02519A0015 ANA005 AAA0000105 INVN02519A0015	AN A007 AAA0000107 5 IN VN 02519 A0 015	IN VN02 519A0015 ANA008 AAA0000108 IN VN02 519A0015	INVN02519A0015 ANA009 AAA0000109 INVN02519A0015	NVN02519A0015 ANA010 AAA0000110 NVN02519A0015	INVN02519A0015 UEA011 AAA0000111 INVN02519A0015	IN VN0251940 UEA012 AAA000011
A	ANA001 AAA0000101 NVN02519A0015 UEA013	NVN02519A0015 ANA002 AAA0000102 INVN02519A0015 U EA014	IN VN025 1940015 ANA003 AAA0000103 IN VN025 1940015 UE401 5	INVN0251940015 AN4004 AA40000104 INVN0251940015 U EA016	IN VN 0251 9A0015 AN A005 AAA0000 105 IN VN 0251 9A0015 UEA017	INVN02519A0015 ANA005 AAA0000105 INVN02519A0015 UEA018	AN A007 AAA0000107 5 IN VN 02519 A0 015 UEA019	IN VNO2 519AD015 ANADOS AAAD000108 IN VNO2 519AD015 U EA020	INVN02519A0015 ANA009 AAA0000109 INVN02519A0015 UEA021	N VN02519A0015 AN A010 AAA0000110 N VN02519A0015 U EA022	INVN02519A0015 UEA011 AAA0000111 INVN02519A0015 UEA023	NVN0251940 UEA012 AAA0000112 NVN0251940 UEA024
	NVN02519A0013 ANA001 AAA0000101 NVN02519A0015	NVN02519A0015 ANA002 AAA0000102 INVN02519A0015	IN VN025 1940015 AN4003 AA40000103 (IN VN025 1940015	INVN0251940015 ANA004 AAA0000104 INVN0251940015	IN VN 0251 9A0015 AN A005 AAA0000 105 IN VN 0251 9A0015	INVN02519A0015 ANA005 AAA0000105 INVN02519A0015	AN A007 AAA0000107 5 IN VN 02519 A0 015	IN VN02 519A0015 ANA008 AAA0000108 IN VN02 519A0015	INVN02519A0015 ANA009 AAA0000109 INVN02519A0015	NVN02519A0015 ANA010 AAA0000110 NVN02519A0015	INVN02519A0015 UEA011 AAA0000111 INVN02519A0015	NVN02519A0 UEA012 AAA000011 NVN02519A0 UEA024 AAA000012
A	N VN02 51940015 AN4001 AA40000101 IN VN02 51940015 U E4013 AA40000113	NVN02519A0015 ANA002 AAA0000102 INVN02519A0015 UEA014 AAA0000114	N VN025 1940015 AN4003 AA40000103 C N VN025 1940015 UE4015 AA40000115	INVN 0251940015 ANA004 AAA0000104 INVN 0251940015 U EA016 AAA0000116	IN VN 0251 9A0015 AN A005 AAA0000 105 IN VN 0251 9A0015 UEA017 AAA0000 117	INVN02519A0015 ANA005 AAA0000105 INVN02519A0015 UEA018 AAA0000118	ANA007 AAA0000107 5 INVN02519A0015 UEA019 AAA0000119	IN VN02 519A0015 ANA008 AAA0000108 IN VN02 519A0015 U EA020 AAA0000120	INVN02519A0015 ANA009 AAA0000109 INVN02519A0015 UEA021 AAA0000121	IN VN025 19A0015 ANA010 AAA0000110 IN VN025 19A0015 U BA022 AAA0000122	INVN 02519A0015 UEA011 AAA0000111 INVN 02519A0015 UEA023 AAA0000123	NVN02519A0 UEA012 AAA000011 NVN02519A0 UEA024 AAA000012
A	NVN02519A0013 AAA0000101 NVN02519A0015 UEA013 AAA0000113 INVN02519A001	NVN02519A0015 ANA002 AAA0000102 INVN02519A0015 UEA014 AAA0000114 INVN02519A001	IN VN025 19A0015 ANA003 AAA0000103 IN VN025 19A0015 UEA015 AAA0000115 INVN02519A001	INVN0251940015 AN4004 AAA0000104 INVN0251940015 UEA016 AAA0000116 INVN025194001	IN VN0251940015 ANA005 AAA0000105 IN VN0251940015 UEA017 AAA0000117 IN VN025194001	INVN02519A0015 ANA006 AAA0000105 INVN02519A0015 UEA018 AAA0000118 INVN02519A001	AN A007 AAA0000107 IN VN 02519 A0015 UEA019 AAA0000119 IN VN 02519 A001	IN VNO2 519A0015 ANA008 AAA0000108 IN VNO2 519A0015 UEA020 AAA0000120 INVN02519A001	INVN02519A0015 ANA009 AAA0000109 INVN02519A0015 UEA021 AAA0000121 INVN02519A001	N VN02519A0015 AN A010 AAA0000110 N VN02519A0015 U EA022 AAA0000122 INVN02519A001	INVN02519A0015 UEA011 AAA0000111 INVN02519A0015 UEA025 AAA0000123 INVN02519A001	 N VN02519A00 UEA012 AAA0000112 N VN02519A00 UEA024 AAA0000124 N VN02519A00 ORIA035
A	NVN02519A0019 ANA001 NVN02519A0015 UEA013 AAA0000113 INVN02519A001 OR W025 AAA0000125 INVN02519A001	NVN02519A0015 ANA002 AAA0000102 INVN02519A0015 UEA014 AAA0000114 INVN02519A001 CR1A026 AAA0000126 INVN02519A001	N VN025 19A0015 ANA003 AAA0000103 N VN025 19A0015 AAA0000115 INVN025 19A001 ORIA027 AAA0000127 INVN025 19A001	INVN0251940015 <u>ANA000104</u> INVN02519A0015 UEA016 <u>AAA0000116</u> INVN02519A001 ORIA025 <u>AAA0000128</u> INVN02519A001	IN VN 0251 9A0015 AAA000 105 IN VN 0251 9A0015 UEA017 AAA0000 117 IN VN 0251 9A001 ORIA029 AAA0000129 IN VN 0251 9A001	INVN02519A0015 ANA000 AAA0000106 INVN02519A0015 UEA018 AAA0000118 INVN02519A001 ORIA030 AAA0000130 INVN02519A001	AN A007 AAA0000107 IN VN02519 A0015 UEA019 AAA0000119 IN VN02519A001 ORIA031 AAA0000131 IN VN02519A001	IN VN02 519AD015 ANAD08 AAA0000108 IN VN02 519A0015 U EA020 AAA0000120 INVN02519A001 ORIA032 AAA0000132 INVN02519A001	INVN02519A0015 ANAD09 AAA0000109 INVN02519A0015 UEA021 AAA0000121 INVN02519A001 ORIA033 AAA0000133 INVN02519A001	IN VN025 19A0015 ANA010 AAA0000110 IN VN025 19A0015 UEA022 AAA0000122 IN VN02519A001 OR IA034 AAA0000134 IN VN02519A001	INVN02519A0015 UEA011 AAA0000111 INVN02519A0015 UEA023 AAA0000123 INVN02519A001 CR1A035 AAA0000135 INVN02519A001	 NVN02519A00 UEA012 AAA0000112 NVN02519A00 UEA024 NVN02519A00 ORIA036 AAA0000124 NVN02519A00 ORIA036 NVN02519A0
A B C	NVN02519A0019 ANA001 AAA000101 NVN02519A0015 UEA013 AAA0000113 INVN02519A001 OR IA025 AAA0000125 INVN02519A001 OR IA037	INVN02519A0015 ANA002 AAA0000102 INVN02519A0015 UEA014 AAA0000114 INVN02519A001 CRIA025 AAA0000126 INVN02519A001 CRIA038	N ∨N025 19A0015 ANA003 AAA0000103 VN025 19A0015 UEA015 AAA0000115 INVN02519A001 ORIA027 AAA0000127 INVN02519A001 ORIA029 ORIA039	INVN0251940015 ANA0001 AAA0000104 INVN02519A0015 UEA016 AAA0000116 INVN02519A001 ORIA028 AAA0000128 INVN02519A001 ORIA0259A001 ORIA040	IN VN02519A0015 AAA0005 AAA0000105 IN VN02519A0015 UEA017 AAA0000117 BV VN02519A001 ORIA029 AAA0000129 IN VN02519A001 ORIA041	INVN02519A0015 ANA005 AAA0000106 INVN02519A0015 UEA018 AAA0000118 INVN02519A001 OR M030 AAA0000130 INVN02519A001 OR M042	ANA007 AAA0000107 UNVN02519A0015 UEA019 AAA0000119 INVN02519A001 ORIA031 INVN02519A001 ORIA043	IN VN02 519AD015 ANA005 AAA0000108 IN VN02 519A0015 UEA020 AAA0000120 INVN02519A001 OR M032 AAA0000132 INVN02519A001 OR M032 AAA000132	INVN02519A0015 ANA009 AAA0000109 INVN02519A0015 UEA021 AAA0000121 INVN02519A001 ORIA035 AAA0000133 INVN02519A001 ORIA045	IN VN025 19A0015 ANA010 AA0000110 IN VN025 19A0015 UEA022 AAA0000122 IN VN02519A001 OR IA034 AAA0000134 IN VN02519A001 OR IA046	INVN02519A0015 UEA011 AAA0000111 INVN02519A0015 UEA023 AAA0000123 INVN02519A001 CR1A035 AAA0000135 INVN02519A001 CR1A047	IN VN02519A00 UEA012 AAA0000111 IN VN02519A00 UEA024 AAA0000124 IN VN02519A0 ORIA036 AAA0000137 IN VN02519A0 ORIA045
A	NVN02519A0019 AAA000101 NVN02519A0015 UE4013 AAA0000113 INVN02519A001 OR IA025 AAA0000125 INVN02519A001 OR IA037 AAA0000157	NVN02519A0015 ANA002 AAA0000102 INVN02519A0015 UEA014 NVN02519A001 CR1A025 AAA0000126 INVN02519A001 CR1A025 AAA0000138	IN VN025 1940015 AN 4003 AAA0000103 UEA015 AAA0000115 INVN025194001 ORIA027 AAA0000127 INVN025194001 ORIA029 AAA0000139	INVN0251940015 ANA004 AAA0000104 INVN02519A0015 UEA015 AAA0000116 INVN02519A001 ORIA025 AAA0000128 INVN02519A001 ORIA020 AAA0000140	IN VN0251940015 AAA0005 AAA0000105 IN VN02519A0015 UEA017 AAA0000117 IN VN02519A001 ORIA029 AAA0000129 IN VN02519A001 ORIA041 AAA0000141	INVN02519A0015 ANA006 AAA0000106 INVN02519A0015 UEA015 INVN02519A001 OR M030 AAA0000130 INVN02519A001 OR M042 AAA0000142	ANA007 AAA0000107 VIVV02519A0015 UEA019 AAA0000119 NVV02519A001 ORIA031 AAA0000131 NVV02519A001 ORIA043 AAA0000143	IN VN02519AD015 ANAD08 AAA0000108 IN VN02519A0015 UEA020 AAA0000120 IN VN02519A001 OR IA032 AAA0000132 IN VN02519A001 OR IA044 AAA0000144	INVN02519A0015 ANA009 AAA0000109 INVN02519A0015 UEA021 AAA0000121 INVN02519A001 ORIA035 AAA0000133 INVN02519A001 ORIA045 AAA0000145	IN VN025 19A0015 ANA010 AAA0000110 IN VN025 19A0015 UEA022 AAA0000122 IN VN02519A001 OR IA034 AAA0000134 IN VN02519A001 OR IA046 AAA0000146	INVN02519A0015 UEA011 AAA0000111 INVN02519A0015 UEA023 AAA0000123 INVN02519A001 CR14035 AAA0000135 INVN02519A001 CR14047 AAA0000147	IN VN02519400 UEA012 AAA000111 IN VN02519400 UEA024 AAA0000121 IN VN02519400 ORIA036 AAA0000121 IN VN02519400 ORIA036 AAA0000124 IN VN02519400 ORIA036 AAA0000124 AAA00001340 ORIA048 AAA0000144
A B C	WVN02519A0019 ANA001 AAA0000101 INVN02519A0015 UEA013 AAA0000113 INVN02519A001 OR M025 AAA0000125 INVN02519A001 OR M025 AAA0000125 INVN02519A001 OR M037 AAA0000137 INVN02519A001	NVN02519A0015 ANA002 AAA0000102 UEA014 AAA0000114 NVN02519A001 ORIA025 AAA0000126 NVN02519A001 ORIA025 AAA0000128 NVN02519A001 ORIA035 AAA0000138	NVN025 19A0015 ANA003 AAA0000103 C NVN025 19A0015 UEA015 AAA0000115 INVN02519A001 ORIA027 AAA0000127 INVN02519A001 ORIA039 AAA0000139 NVN025 19A0025	INVN0251940015 ANA000 AAA0000104 UEA016 AAA0000140 UEA016 AAA0000140 INVN02519A001 ORIA025 AAA0000128 INVN02519A001 ORIA040 AAA0000140 INVN02519A0025	NVN02519A0015 ANA005 NVN02519A0015 UEA017 AAA0000107 PVVN02519A001 ORIA029 AAA0000129 NVN02519A001 ORIA01 AAA0000141 NVN02519A0025	INVN02519A0015 ANA006 AAA0000106 INVN02519A0015 UEA018 AAA000018 INVN02519A001 OR IA030 AAA0000130 INVN02519A001 OR IA042 AAA0000142 INVN02519A00242	ANA007 AAA0000107 IN VN02519A0015 UEA019 AAA0000119 IN VN02519A001 ORIA031 AAA0000131 IN VN02519A001 ORIA043 AAA0000143	NVN02519A0015 ANA008 AAA000108 NV02519A0015 UEA020 AAA000120 INV02519A001 ORIA032 AAA000120 INVN02519A001 ORIA032 AAA0000120 INVN02519A001 ORIA044 AAA0000144 NVN02519A0014	INVN02519A0015 ANA009 AAA0000109 INVN02519A0015 UEA021 AAA0000121 ORIA033 AAA0000135 INVN02519A001 ORIA045 AAA0000145 INVN02519A00145	IN VN025 19A0015 AAA0000110 IN VN025 19A0015 U BA022 AAA0000122 IN VN025 19A0013 OR IA034 AAA0000134 IN VN025 19A0013 IN VN025 19A0013 IN VN025 19A0025	INVN02519A0015 UEA011 AAA0000111 INVN02519A0015 UEA023 AAA0000123 INVN02519A0015 ORIA035 AAA0000135 INVN02519A0015 ORIA035 AAA0000135 INVN02519A0015 ORIA03519A001 ORIA03519A00135 INVN02519A00135 INVN02519A00137	IN VN02519A00 UEA012 AAA0000112 IN VN02519A00 UEA024 AAA0000122 IN VN02519A00 ORIA036 AAA0000134 IN VN02519A00 ORIA036 AAA0000144 IN VN02519A00
A B C	КVN02 51940019 Ал400000101 Ал400000101 NVN02 51940015 U E4013 AA40000113 INVN02 5194001 OR IA025 AA40000125 INVN02 5194001 OR IA037 AA40000125 INVN02 5194001 OR IA037 AA4000137 INVN02 519400 OR IA037 AA4000137 INVN02 519400 OR IA037 AA4000137 INVN02 519400 OR IA049	NVN02519A0015 AAA0000102 URA014 AAA0000102 URA014 AAA000014 MVN02519A001 ORIA026 AAA0000126 RI VN02515A001 ORIA026 AAA0000158 AAA0000158 AAA0000158	NVN02519A0015 AAA00000103 NVN02519A0015 UEA015 AAA0000115 INVN02519A001 ORIA027 AAA0000127 INVN02519A001 ORIA039 AAA0000199 AAA0000199 AAA0000199 AAA0000199	INVN0251940015 AAA0000104 INVN0251940015 UEA016 UEA016 AAA0000116 INVN025194001 ORIA028 AAA0000128 INVN025194001 ORIA040 AAA000140 AAA0003 AAA0003	NVN0251 9A0015 AAA0000105 NVN0251 9A0015 UEA017 AAA0000179 NVN02519A001 ORIA029 AAA0000129 NVN02519A001 ORIA041 AAA0000141 NVN02519A000141 AAA000141 AAA000141	INVN02519A0015 AAA0000106 UNN02519A0015 UA015 AAA000018 UA000018 AAA0000130 INVN02519A001 OR IA042 AAA0000140 INVN02519A001 OR IA042 AAA0001402 AAA0001402 AAA0001402	ANA007 AAA000107 INV02519A0015 AAA0000119 INVV02519A001 ORIA031 AAA0000131 INVV02519A001 ORIA033 AAA0000143 SINVV02519A002 ANA006	IN VN02 519A0015 AAA0000108 UN02 519A0015 UEA020 AAA0000120 INVN02519A001 ORIA032 AAA0000122 INVN02519A001 ORIA042 AAA000144 INVN02519A002 AAA000144 INVN02519A002 AAA000144	INVN02519A0015 AAA0000109 INVN02519A0015 UEA021 AAA0000121 RNN02519A001 ORIA033 AAA0000133 RNN02559A001 ORIA045 AAA000145 AAA000145 AAA000145	NVN02519A0015 ANA010 AAA0000110 NVN02519A0015 UEA022 AAA0000122 INVN02519A0015 OR M034 AAA0000134 INVN02519A001 OR M034 AAA0000134 NVN02519A001 OR M034 AAA0000134 NVN02519A001 OR M046 AAA0000134	INVN02519A0015 UEA011 AAA0000111 INVN02519A0015 UEA023 AAA0000123 INVN02519A0015 AAA0000135 INVN02519A0013 INVN02519A001 OR IA035 AAA0000135 INVN02519A001 OR IA047 AAA0000147 INVN02519A001	IN VN02519A00 UEA012 AAA0000112 IN VN02519A00 UEA024 AAA0000122 IN VN02519A0 ORIA036 ORIA036 ORIA036 IN VN02519A0 ORIA048 AAA0000144 IN VN02519A0 UEA011
A B C	WVN02519A0019 AAA000000101 NVN02519A0015 UE4013 AAA0000113 INVN02519A001 OR IA025 AAA0000125 INVN02519A001 OR IA025 AAA0000125 INVN02519A001 OR IA025 AAA0000125 INVN02519A001 OR IA037 AAA0000137 INVN02519A001 OR IA039 AAA0000137	INVN02519A0015 AAA0000102 UEA014 AAA0000102 UEA014 AAA0000114 BIVN02519A001 OR IA026 AAA0000128 BIVN02519A001 OR IA038 AAA0000138 AAA0000150	NVN02519A0015 AAA00000103 < NVN02519A0015 UEA015 AAA0000113 INVN02519A001 ORIA027 AAA0000127 INVN02519A001 ORIA039 AAA0000159 NVN02519A0025 AAA0000151	INVN0251946015 AnA000 AAA0000101 INVN02519A0015 UEA016 AAA0000118 INVN02519A001 ORIA028 AAA0000128 INVN02519A001 ORIA020 AAA0000140 INVN02519A0025 AAA000140	NVN02519A0015 ANA005 AAA0000105 NVN02519A0015 UEA017 AAA0000117 NVN02519A001 ORIA029 AAA0000129 NVN02519A001 ORIA041 AAA0000141 NVN02519A0025 ANA004 AAA0000155	INVN02519A0015 ANA006 AAA0000106 INVN02519A0015 UEA018 AAA0000118 INVN02519A001 OR IA030 AAA0000130 INVN02519A001 OR IA042 AAA0000142 INVN02519A002519 AAA000142	ANA007 AAA000107 IN W02519 A0015 AAA000019 IN VN02519 A0011 ORIA031 AAA0000131 IN VN02519 A001 ORIA031 AAA0000143 IN VN02519 A0025 ANA006 AAA0000155	IN VN02 519A0015 AAA0000108 IN VN02 519A0015 U EA020 AAA0000120 IN VN02 519A001 OR IA032 AAA0000132 IN VN02 519A001 OR IA034 AAA0000144 IN VN02 519A0025 ANA007 AAA000156	INVN02519A0015 ANA009 AAA0000109 INVN02519A0015 UEA021 AAA00001251 RVN02519A001 ORIA033 AAA0000135 INVN02519A001 ORIA045 AAA0000145 INVN02519A00215 ANA005	INVN02519A0015 AAA0000110 INVN02519A0015 UBA022 INVN02519A0015 ORIA034 AAA0000132 INVN02519A001 ORIA036 AAA0000145 INVN02519A0025 ANA009 AAA0000155	INVN02519A0015 UEA011 AAA0000111 INVN02519A0015 UEA023 AAA0000123 INVN02519A001 CR IA035 AAA0000135 INVN02519A001 CR IA047 AAA0000147 INVN02519A0025 AAA0000147	IN VN02519A00 UEA012 AAA0000111 IN VN02519A00 UEA012 AAA0000121 IN VN02519A00 ORIA036 AAA0000121 IN VN02519A00 ORIA036 AAA0000121 IN VN02519A00 ORIA036 AAA0000121 IN VN02519A00 UEA011 AAA0000141
A B C	WVN02519A0019 AAA0000101 RVN02519A0019 WEAD3 AAA0000113 INVN02519A0019 OR IA02519A0019 OR IA02519A001 OR IA02519A001 OR IA02519A001 OR IA02519A001 OR IA0500149 NVN02519A001 NVN02519A001	NVN02519A0015 AAA0000102 INVN02519A0015 UEA014 AAA00000114 INVN02519A001 OR IA025 AAA0000128 INVN02519A001 OR IA025 AAA0000138 INVN02519A0001 AAA0000150 INVN02519A000150 INVN02519A000150	RVN02519A0015 AAA00000103 UEA015 AAA0000103 UEA015 AAA0000113 INVN02519A001 ORIA027 AAA0000123 INVN02519A0025 AAA0000139 RVN02519A0025 AAA0000151 RVN02519A0025	INVN0251940015 AAA0000104 INVN02519A0015 UEA016 AAA0000116 INVN02519A001 ORIA025 AAA0000125 INVN02519A001 ORIA020 AAA0000140 INVN02519A0025 AAA0000152 INVN02519A0025	NVN02519A0015 ANA005 AAA0000105 NVN02519A0015 UEA017 AAA0000117 PVVN02519A001 ORIA029 AAA0000129 NVN02519A001 ORIA021 AAA0000141 NVN02519A0025 ANA004 AAA0000155 NVN02519A0025	INVN02519A0015 ANA006 AAA0000106 INVN02519A0015 UEA015 AAA0000115 INVN02519A001 OR IA032 AAA0000130 INVN02519A001 OR IA042 AAA0000142 INVN02519A0025 ANA005 AAA0000154 INVN02519A0025	ANAGO7 AAA0000107 IN VN02519A0015 UEA019 AAA0000119 NVN02519A001 AAA0000131 NVN02519A0013 AAA0000143 AAA0000143 AAA0000155 AAA0000155	IN VNO2 519A0015 AAA0000108 NV NO2 519A0015 U EA000 AAA0000120 INV NO2 519A0015 OR IA032 AAA0000132 INV NO2 519A001 OR IA032 AAA0000144 NV NO2 519A00156 INV NO2 519A00156 INV NO2 519A0025	INVN02519A0015 ANA009 AAA0000109 INVN02519A0015 UEA021 AAA0000121 INVN02519A001 ORIA035 AAA0000135 INVN02519A001 ORIA045 AAA0000145 INVN02519A0025 ANA005 AAA000157 INVN02519A0025	NVN02519A0015 ANA010 AAA0000110 NVN02519A0015 UEA022 AAA0000122 INVN02519A001 DR M034 AAA0000134 INVN02519A001 DR M034 AAA0000134 INVN02519A001 DR M046 AAA0000134 INVN02519A001 DR M046 AAA0000145 NVN02519A002 AAA0000158	INVN02519A0015 UEA011 AAA0000111 INVN02519A0015 UEA023 AAA0000123 INVN02519A001 CRIA035 AAA0000133 INVN02519A001 OKIA045 AAA0000133 INVN02519A001 OKIA047 AAA0000147 INVN02519A001 AAA00000147 INVN02519A0025 AAA0000159 INVN02519A0025	IN VN02519A00 UEA012 AAA000011 IN VN02519A00 UEA024 IN VN02519A00 UEA024 IN VN02519A0 ORIA036 AAA0000134 IN VN02519A0 ORIA036 AAA0000134 IN VN02519A0 UEA011 AAA0000164 IN VN02519A00 UEA011 AAA0000164 IN VN02519A00
<u>А</u> В С D	WVN02519A0029 AAA0000101 RVN02519A0015 UE4013 AAA0000113 INVN02519A0015 OR IA025 AAA000125 INVN02519A0015 OR IA025 AAA000125 INVN02519A001 OR IA037 AAA0000137 INVN02519A001 OR IA039 AAA0000149 NVN02519A001 UE4012	INVN02519A0015 AAA0000102 UEA014 AAA0000102 UEA014 AAA000012519A001 ORIA02519A001 ORIA02519A002 AAA0000138 INVN02519A0025 AAA000138 AAA0000150 INVN02519A0025 UEA013	RVN02519A0015 AAA00000103 VN02519A0015 UEA015 AAA0000115 INVN02519A0015 INVN02519A00127 INVN02519A00127 AAA0000139 RVN02519A0025 AAA000151 RVN02519A0025 AAA000151 RVN02519A0025 AAA000151	INVN0251540015 AAA0000104 UEA016 AAA0000104 UEA016 AAA0000116 INVN025154001 ORIA025 AAA000125 AAA000125 AAA000125 AAA000152 INVN0251540025 AAA000152 INVN0251540025 UEA015	NVN02519A0015 AAA0000105 NVN02519A0015 UEA017 AAA0000107 ORIA02519A0015 ORIA002519A0025 AAA0000129 NVN02519A0025 AAA000141 NVN02519A0025 AAA000151 NVN02519A0025 UEA015	INVN02519A0015 AAA0000106 INVN02519A0015 UEA018 AAA000016 INVN02519A001 ORIA030 AAA0000130 INVN02519A002 AAA0000142 INVN02519A0025 AAA0000154 INVN02519A0025 AAA000154 INVN02519A0025 AAA0000154	AN AGO7 AAA0000107 IN W02515 A005 AAA000019 IN VN025 15A001 ORIA031 AAA0000135 IN VN025 15A001 ORIA033 AAA0000145 IN VN02515A002 AAA0000155 IN VN02515A0025 AAA0000155 IN VN02515A0025 AAA0000155 IN VN02515A0025 AAA0000155	NVN02519A0015 AAA0000108 NVN02519A0015 UEA020 AAA0000120 INVN02519A0012 OR A0032 AAA0000121 NVN02519A0025 AAA0000144 NVN02519A0025 ANA000156 NVN02519A0025 UEA019	INVN02519A0015 ANA008 AAA0000109 INVN02519A0015 UEA021 AAA0000121 NVN02519A001 ORIA035 AAA0000135 INVN02519A0025 AAA0000145 INVN02519A0025 AAA0000157 INVN02519A0025 UEA020	NVN02519A0015 ANA010 AAA0000110 NVN02519A0015 UBA022 AAA0000122 INVN02519A0015 ORIA0034 AAA0000134 NVN02519A001 ORIA0034 AAA0000134 NVN02519A002 AAA0000145 NVN02519A0025 ANA000 AAA0000158 NVN02519A0025	INVN02519A0015 UEA011 AAA0000111 INVN02519A0015 UEA023 AAA0000123 INVN02519A001 ORIA03 AAA0000137 INVN02519A002 AAA0000147 INVN02519A0025 ANA010 AAA0000159 INVN02519A0025 UEA022	IN VN02519A00 UEA012 AAA0000111 UEA012 AAA000012 UEA024 AAA000012 IN VN02519A00 ORIA036 AAA000012 IN VN02519A00 ORIA035 AAA000014 IN VN02519A00 UEA011 AAA000164 IN VN02519A00 UEA011 AAA000164 IN VN02519A00 UEA011
A B C	WVN02519A0013 AAA0000101 RVN02519A0013 WVN02519A0013 AAA0000113 INVN02519A001 OR IA02519A001 OR IA02519A001 OR IA02519A001 OR IA02519A001 OR IA0519A00 OR IA050137 AAA0000137 AAA0000158 NVN02519A0001 OR IA049 AAA0000137	NVN02519A0015 AAA0000102 INVN02519A0015 UEA014 AAA0000114 INVN02519A001 CR1A025 AAA0000136 INVN02519A001 CR1A035 AAA000136 INVN02519A0025 UEA013 AAA0000150	RVN0251940015 AAA0000103 C AAA0000103 C RVN0251940015 AAA0000137 AAA0000137 AAA0000137 RVN0251940025 AAA000139 RVN0251940025 AAA000151 RVN0251940025	INVNO251940015 AAA0000103 UEA015 AAA0000103 UEA015 AAA0000118 INVNO2519A0015 AAA0000102 AAA0000102 AAA0000152 INVNO2519A0025 UEA015 AAA000154	NVN02519A0015 AAA0000105 NVN02519A0015 UEA07 AAA0000117 NVN02519A0017 ORIA029 AAA0000141 ORIA041 AAA000141 NVN02519A0025 NVN02519A0025 UEA015 AAA0001055	INVN02519A0015 AAA0000106 INVN02519A0015 AAA0000108 INVN02519A0015 AAA0000130 INVN02519A001 OR IA042 AAA0000142 INVN02519A0012 AAA000154 INVN02519A0025 AAA000154	ANAGO7 AAA000107 IN W02519A005 AAA000019 NVW02519A001 ORIA031 AAA0000131 NVW02519A001 ORIA033 AAA0000143 AAA0000145 IN W02519A002 AAA0000155 UUEA018 AAA0000157	IN VNO2 515A0015 AAA0000108 IN VNO2 515A0015 UEA020 AAA0000120 IN VNO2 515A0015 OR IA044 AAA0000144 IN VNO2 515A0015 AAA000158 IN VNO2 515A0025 UEA019 AAA000168	INVN02519A0015 ANA009 AAA0000169 INVN02519A00121 UEA021 AAA0000137 RVN02519A001 ORIA045 AAA0000145 INVN02519A0025 ANA008 AAA0000157 INVN02519A0025 UEA020 AAA0000169	NVN02519A0015 ANA010 AAA0000110 NVN02519A0012 UEA022 AAA0000120 INVN02519A001 OR IA034 AAA0000140 OR IA034 AAA0000150 OR IA034 AAA0000158 NVN02519A001 OR IA045 AAA0000158 NVN02519A0025 AAA000158 NVN02519A0025 UBA021 AAA000170	INVN02519A0015 UEA011 AAA0000111 INVN02519A002 UEA023 AAA0000123 INVN02519A001 CR (A035 AAA0000147 INVN02519A002 AAA0000157 INVN02519A0025 UEA022 AAA0000171	IN VN02519400 UEA012 AAA000011 IN VN02519400 UEA024 AAA000012 IN VN02519400 ORI4036 AAA0000124 IN VN02519400 UEA011 AAA0000144 IN VN02519400 UEA011 AAA000016 IN VN02519400 UEA013 AAA000016 IN VN02519400 UEA013 IN VN02519400 UEA013 IN VN02519400 UEA013 IN VN02519400 UEA023 IN VN0251940 IN
<u>А</u> В С D	WVN02519A0029 AAA0000101 RVN02519A0015 UE4013 AAA0000113 INVN02519A0015 OR IA025 AAA000125 INVN02519A0015 OR IA025 AAA000125 INVN02519A001 OR IA037 AAA0000137 INVN02519A001 OR IA039 AAA0000149 NVN02519A001 UE4012	INVN02519A0015 AAA0000102 UEA014 AAA0000102 UEA014 AAA000012519A001 ORIA02519A001 ORIA02519A002 AAA0000138 INVN02519A0025 AAA000138 AAA0000150 INVN02519A0025 UEA013	RVN02519A0015 AAA00000103 VN02519A0015 UEA015 AAA0000115 INVN02519A0015 INVN02519A00127 INVN02519A00127 AAA0000139 RVN02519A0025 AAA000151 RVN02519A0025 AAA000151 RVN02519A0025 AAA000151	INVN0251540015 AAA0000104 UEA016 AAA0000104 UEA016 AAA0000116 INVN025154001 ORIA025 AAA000125 AAA000125 AAA000125 AAA000152 INVN0251540025 AAA000152 INVN0251540025 UEA015	NVN02519A0015 AAA0000105 NVN02519A0015 UEA017 AAA0000107 ORIA02519A001 ORIA001 ORIA001 AAA0000129 NVN02519A0025 AAA000141 NVN02519A0025 AAA000151 NVN02519A0025 UEA015	INVN02519A0015 AAA0000106 INVN02519A0015 UEA018 AAA000016 INVN02519A001 ORIA030 AAA0000130 INVN02519A002 AAA0000142 INVN02519A0025 AAA0000154 INVN02519A0025 AAA000154 INVN02519A0025 AAA0000154	AN AGO7 AAA0000107 IN W02515 A005 AAA000019 IN VN025 15A001 ORIA031 AAA0000135 IN VN025 15A001 ORIA033 AAA0000145 IN VN02515A002 AAA0000155 IN VN02515A0025 AAA0000155 IN VN02515A0025 AAA0000155 IN VN02515A0025 AAA0000155	NVN02519A0015 AAA0000108 NVN02519A0015 UEA020 AAA0000120 INVN02519A0012 OR A0032 AAA0000121 NVN02519A0025 AAA0000144 NVN02519A0025 ANA000156 NVN02519A0025 UEA019	INVN02519A0015 ANA008 AAA0000109 INVN02519A0015 UEA021 AAA0000121 NVN02519A001 ORIA035 AAA0000135 INVN02519A0025 ANA008 AAA0000157 INVN02519A0025 UEA000	NVN02519A0015 ANA010 AAA0000110 NVN02519A0015 UBA022 AAA0000122 INVN02519A0015 ORIA034 AAA0000124 NVN02519A005 ORIA034 AAA0000146 NVN02519A0025 AAA0000145 NVN02519A0025 AAA0000158 NVN02519A0025 UEA021	INVN02519A0015 UEA011 AAA0000111 INVN02519A0015 UEA023 AAA0000123 INVN02519A001 ORIA03 AAA0000137 INVN02519A002 AAA0000147 INVN02519A0025 ANA010 AAA0000159 INVN02519A0025 UEA022	IN VN02519400 UEA012 AAA0000111 NVN02519400 UEA024 NVN02519400 UEA024 NVN02519400 ORIA036 AAA0000134 NVN02519400 ORIA036 AAA0000146 NVN02519400 UEA011 AAA0000146 NVN02519400 UEA011 AAA0000146 NVN02519400
<u>А</u> В С D	NVN02515840013 AAA0000101 NVN02515840013 UE4013 AAA0000113 INVN0251584001 OR k037 INVN0251584001 OR k037 INVN0251584001 OR k037 INVN0251584001 OR k037 INVN0251584001 OR k042 AAA0000137 INVN0251584001 OR k049 AAA0000137 INVN0251584001 OR k049 AAA000135 UE4012 AAA0000161 NVN0251584021 UE4012 AAA0001615	NVN02519A0015 AAA0000102 INVN02519A0015 UEA014 AAA0000116 ORIA02519A001 ORIA02519A001 ORIA02519A001 ORIA055 AAA0000156 INVN02519A0025 AAA000156 INVN02519A0025 AAA0000150 UEA013 AAA0000150 UEA013 AAA000150 ORIA02519A0025 ORIA02519A0025 ORIA02519A0025 ORIA02519A0025 ORIA02519A0025 ORIA02519A0025 ORIA02519A0025 ORIA02519A0025 ORIA02519A0025 ORIA02519A0025 ORIA02519A0025 ORIA02519A0025 ORIA02519A0025 ORIA02519A0025 ORIA025 ORIA02519A0025 ORIA05 ORIA05 ORI	RVN0251940015 AAA0000103 C RVN02519A0015 UEA015 AAA0000137 INVN02519A001 ORIA025 AAA0000139 RVN02519A0025 AAA000139 RVN02519A0025 AAA000151 RVN02519A0025 UEA014 AAA000151 INVN02519A0025 UEA014 AAA000151 INVN02519A0025 UEA014 AAA000151 INVN02519A0025 INVN02519A005 INVN02519A05 INVN02519A05 INVN02519A05 INVN02519A05 INVN02519A05 INVN0250 INVN0250 INVN0250 INVN0250 INVN0250 INVN0250 INVN0250 INVN0250 INVN0250 INVN	INVN0251946015 AAA0000164 UEA016 AAA0000161 INVN02519A0015 INVN02519A001 INVN02519A00140 INVN02519A0025 AAA0000140 INVN02519A0025 AAA000152 INVN02519A0025 AAA000152 INVN02519A0025 AAA000152 INVN02519A0025 AAA000152 INVN02519A0025 AAA000154 INVN02519A0025 INVN02519A0025 AAA000154 INVN02519A0025 AAA000154 INVN02519A0025 INVN02519A0025 AAA000154 INVN02519A0025 INVN02519A0025 INVN02519A0025 INVN02519A0025 AAA000154 INVN02519A0025 INVN02519A0025 INVN02519A0025 INVN02519A0025 INVN02519A0025 INVN02519A0025 INVN02519A0025 INVN02519A0025 INVN02519A0025 INVN02519A0025 INVN02519A005 INVN02519A05 INVN02519A05 INVN02519A05 INVN02519A05 INVN02519A05 INVN	NVN02519A0015 AAA0000105 NVN02519A0015 UEA07 AAA000017 PVVN02519A0017 ORIA021 AAA0000128 ORIA021 AAA0000141 NVN02519A0025 AAA000155 AAA000155 AAA000155 AAA000155 AAA000155 AAA000155 AAA000155	INVN02519A0015 AAA0000106 INVN02519A0015 UEA015 AAA0000106 INVN02519A001 OR IA030 AAA0000130 INVN02519A001 AAA0000134 INVN02519A0025 AAA0000154 INVN02519A0025 AAA0000154 INVN02519A0025 OR IA022 UEA017 AAA0000156 INVN02519A0025 OR IA022 INVN02519A0025 OR IA022 INVN02519A0025 OR IA022 INVN02519A0025 INVN02519A005 INVN02519A05 INVN05	ANA007 AAA0000107 UEA019 AAA0000131 AAA0000131 NVN02515A001 ORIA031 AAA0000131 NVN02515A001 ORIA033 AAA0000143 INVN02515A0025 INVN02515A0025 UEA018 AAA000167 NVN02515A002 ORIA030	NVN02515A0015 AAA0000168 NVN02515A0015 UE4000 AAA0000120 INVN02515A001 OR IA044 AAA0000134 NVN02515A001 AAA000144 NVN02515A00158 NVN02515A00158 INVN02515A00158 UE4019 AAA000168 INVN02515A00258	INVN02519A0015 AAA0000169 INVN02519A0015 UEA021 AAA0000121 NVN02519A001 ORIA033 AAA0000135 INVN02519A001 AAA0000145 INVN02519A0025 AAA0000157 INVN02519A0025 AAA0000157 INVN02519A0025 AAA0000159 INVN02519A0025 ORIA032	NVN025 1940015 ANA010 AAA0000110 NVN025 1940021 UEA022 AAA0000120 NVN025 19400120 OR K045 AAA0000120 NVN025 194000145 NVN025 194000145 NVN025 194000145 NVN025 194000158 NVN025 194000120 AAA0000138 NVN025 1940025 AAA0000170 NVN025 1940025 AAA0000170	INVN02558A0015 UEA011 AAA0000111 INVN02518A0015 UEA023 AAA0000123 INVN02519A001 OR14047 AAA0000137 INVN02519A001 OR14047 AAA0000147 INVN02519A0025 AAA0000147 INVN02519A0025 AAA0000159 INVN02519A0025 AAA0000171 INVN02519A0025 AAA0000171	N-VN025-ISA00 UEA012 AAA0000113 N-VN025-ISA00 UEA012 AAA0000113 N-VN025-ISA00 AAA0000124 N-VN025-ISA00 N-VN025-ISA00 AAA0000125 N-VN025-ISA000145 AAA0000145 AAA0000155-ISA00 UEA013 AAA0000155-ISA00 UEA015 N-VN025-ISA000165 N-VN025-ISA000165 N-VN025-ISA000177
А В С С С С	WVN025154001 AAA000101 AAA000101 NVN025154001 UE4013 AAA000013 NVN025154001 OR IA025 INVN025154001 OR IA035 AAA0000137 INVN025154001 OR IA035 AAA0000147 INVN025154001 OR IA049 AAA0000147 NVN025154025 UE4012 AAA0000147 NVN025154002 UE4012 AAA0000147	INVNO2519A0015 AAA0000102 UE4014 AAA0000102 INVN02519A0015 QEA005 AAA0000128 AAA0000128 INVN02519A002 AAA000018 AAA000019 AAA000018 AAA0000152 BINVN02519A00	RVN02519A0015 AAA0000103 VEA015 AAA0000103 VEA015 AAA0000125 AAA0000112 RVN02519A002 AAA0000127 RVN02519A002 AAA0000139 RVVN02519A002 AAA0000155 RVN02519A002 AAA0000155 RVN02519A002 AAA0000155 RVN02519A002	INVNO251940015 AAA0000104 UEA016 AAA0000104 UEA016 AAA0000118 INVNO2519A0025 AAA0000128 INVNO2519A0025 AAA0000128 INVNO2519A0025 AAA0000150 INVNO2519A0025 AAA000154 INVNO2519A0025 AAA000154 INVNO2519A0025	NVN02519A0015 AAA0000105 NVN02519A0015 UE4017 AAA0000107 NVN02519A0025 AAA0000129 NVN02519A002 AAA0000141 NVN02519A0025 AAA0000141 NVN02519A0025 AAA0000165 NVN02519A002	INVN0251880015 AAA0000166 INVN025184001 UEA015 AAA0000186 INVN025184001 OR IA030 AAA0000130 INVN025184001 OR IA030 AAA0000134 INVN0251840021 AAA0000142 INVN0251840021 AAA0000142 INVN0251840021 AAA0000142 INVN0251840021 AAA0000142 INVN0251840021 AAA0000145 INVN0251840021 AAA0000145 INVN0251840021 INVN02518402 INVN02518402 INVN02518402 INVN02518402 INVN02518402 INVN02518402 INVN02518402 INVN0251840 INVN02518402 INVN0251840 INVN02518402 INVN0251840 INVN0251840 INVN0251840	ANA007 ANA000107 AAA0000107 UEA019 UEA019 NVN02519A001 NVN02519A001 ORIA031 AAA0000131 AAA0000145 ANA000145 ANA000145 ANA0001519A002 UEA018 AAA000167 NVN02519A002	NVN02515840015 ANA008 AAA000108 NVN0251584001 NVN0251584001 NVN0251584001 OR A032 AAA0000120 INVN0251584001 OR A032 AAA0000120 INVN0251584001 OR A032 AAA0000156 NVN0251584001 AAA0000156 NVN0251584002 OR A032 AAA0000156 INVN0251584002 OR A031 AAA0000156 INVN0251584002 OR A031 AAA0000156 INVN0251584002 OR A031 AAA0000156	INVN02519A0015 ANA009 AAA0000109 INVN02519A0015 UEA021 AAA000012519A002 ORIA033 AAA0000133 RVN02519A002 AAA0000145 INVN02519A002 AAA0000157 INVN02519A002 AAA0000169 RVN02519A002	NVN02519A0015 ANA010 AAA0000110 NVN02519A0012 UEA022 AAA0000122 INVN02519A0012 INVN02519A0012 INVN02519A00134 AAA0000136 INVN02519A002 ANA0000146 NVN02519A002 ANA000 INVN02519A002 UEA021 ANA000 INVN02519A002 UEA021 INVN02519A002	INV/N02558A0015 UEA011 AAA0000111 INV/N02518A0015 AAA000013 INV/N02558A001 OR1A035 AAA0000135 INV/N02558A001 AAA0000147 INV/N02518A000147 UEA0000159 UEA021 AAA0000159 INV/N02518A002	IN VN02519A0 UEA012 AAA000011 IN VN02519A0 UEA024 AAA000012 IN VN02519A0 ORIA036 AAA000013 IN VN02519A0 ORIA036 AAA000013 IN VN02519A0 ORIA036 AAA000013 IN VN02519A0 UEA011 AAA00013 IN VN02519A0 UEA012 AAA000137 IN VN02519A0 UEA012 AAA000175 IN VN02519A0
А В С С С С	NYN0251584001 AAA000101 AAA000101 NVN0251584001 NVN0251584001 NVN0251584001 OR M025 INVN0251584001 OR M025 INVN0251584001 OR M025 INVN0251584001 OR M025 INVN0251584001 OR M025 AAA0000145 NVN0251584002 U E4012 AAA0000161 NVN0251584002 U E4012 AAA0000161 NVN0251540002 U E4012 AAA0000161	NVN025158A0015 AAA0000102 INVN025158A001 ORIA025 NVN025158A001 ORIA025 AAA0000118 NVN025158A001 ORIA025 AAA0000150 INVN025158A002 AAA0000150 INVN025158A002 ORIA025 AAA0000152 BVVN0025158A002 ORIA025 AAA0000152	RVN02519A0015 AAA0000103 NVN02519A0015 UEA015 AAA0000135 UEA015 AAA0000117 NVN02519A0021 ORIA029 AAA0000127 INVN02519A0025 AAA0000155 NVN02519A0025 AAA0000165 INVN02519A0025 AAA0000155	INVN025158/6015 AAA0000163 UEA016 AAA0000161 INVN02519A0011 INVN02519A001 ORIA028 AAA0000182 INVN02519A0021 ORIA029 AAA0000182 INVN02519A0025 AAA0000164 INVN02519A0025 AAA0000164 INVN02519A0025 AAA0000164	PLVN0251 5A0015 AAA0000 105 NLVN0251 5A0015 UEA017 AAA0000117 PLVN0251 5A001 ORIA025 AAA0000129 NLVN0251 5A002 ORIA021 AAA0000145 NLVN0251 5A002 AAA0000155 NLVN0251 5A002 ORIA021 AAA0000155	INVN025158A0015 AAA0000166 INVN02515A0015 NNVN02515A001 OR IA030 AAA0000135 INVN02515A001 OR IA030 AAA0000154 AAA0000154 AAA0000154 INVN02515A002 OR IA030 AAA0000158 INVN02515A002 OR IA030 AAA0000158	ANA007 ANA000107 IAA0000107 UEA019 UEA019 AAA000019 NVN02515A001 ORIA051 AAA0000131 NVN02515A002 AAA0000135 INVN02515A002 UEA018 AAA0000157 NVN02515A002 UEA018 AAA0000157	NVN02515840015 ANA008 AAA000108 NVN0251584001 NVN0251584001 NVN0251584001 OR A032 AAA0000120 INVN0251584001 OR A032 AAA0000120 INVN0251584001 OR A032 AAA0000156 NVN0251584001 AAA0000156 NVN0251584002 OR A032 AAA0000156 INVN0251584002 OR A031 AAA0000156 INVN0251584002 OR A031 AAA0000156 INVN0251584002 OR A031 AAA0000156	INVN02516840015 ANA009 AAA0000109 INVN0251984001 UE4021 AAA0000121 INVN0251984001 ORIA033 INVN0251984001 ORIA045 AAA00001457 INVN0251984002 AAA0000169 INVN0251984002 ORIA032 AAA0000169	NVN02519A0015 AAA000110 NVN02519A0051 UEA022 AAA0000120 NVN02519A001 OR IA034 AAA0000134 INVN02519A001 OR IA045 AAA0000145 NVN02519A002 AAA0000145 NVN02519A002 OR IA045 AAA0000170 INVN02519A002 OR IA035 AAA0000170	INVNO25158A0015 UEA011 AAA0000111 INVNO25158A002 AAA0000133 INVNO2519A001 OR1A035 INVNO2519A001 OR1A045 AAA0000147 INVNO2519A002 AAA0000147 INVNO2519A002 AAA0000171 INVNO2519A002 OR1A044 AAA0000159	NVN02519a0 UEA012 AAA00011 NVN02519A0 UEA014 AAA00013 NVN02519A0 ORIA03 AAA00013 NVN02519A0 ORIA03 AAA00013 NVN02519A0 ORIA03 AAA00014 NVN02519A0 ORIA035 AAA00017

Figure 3.

Identification of samples and materials with structured codes and representative box map with pre-coded tubes.

3.2 Identification of materials and samples

Unique standardized codes are generated by the electronic database to identify each donation, sample, and material included in its corresponding collection kit, thanks to label printing (**Figure 3**). Therefore, samples (and associated information) are de-identified in compliance with applicable laws. Records included in the kit are also identified in relation with donations.

Commercially available pre-coded tubes are selected to prepare derivative aliquots so that specific pre-coded tubes are pre-assigned to each type of sample for a donation during the kit preparation by using the electronic database, supporting the traceability of samples (**Figure 3**). Similarly, racks for the pre-coded tubes included in the kits are identified as well. The process of generation of a new donation code to the positions of aliquots within the storage equipment is recorded in the electronic database. Code generation and identification also accompany manual or automated sample processing to identify the samples by using code readers.

4. Quality management system

A variety of quality standards can be implemented by laboratories, being requirements from ISO 9001 for the quality management system (QMS) the most widely used [26]. Briefly, ISO 9001 is characterized by a process-based approach following the plan-do-check-act cycle, not only focused on the quality of a product or service or the satisfaction of its users but on the way to obtain them. This QMS involves the definition and systematic management of the processes and the interactions between them in order to meet the legal, regulatory, and users' requirements and to achieve the expected results by continuously improving efficiency. Specifically for biobank activities, the ISO 20387:2018 Biotechnology-Biobanking-General Requirements for Biobanking has been launched under which other more specific standards will be additionally developed [27]. Next, quality assurance tools related with the harmonization and traceability of samples in multicenter prospective studies are shown.

4.1 Protocols, records, and other documents

The definition of processes (strategic, key, and support) involves identifying every factor involved (staff, equipment, method) with the objective of describing them through procedures and keeping them well controlled. Strict adherence to procedures by each stakeholder involved in the multicenter projects is mandatory to avoid pre-analytical deviations. A scheme summarizing the project workflow may be useful to clearly represent the responsibilities of all the stakeholders (**Figure 4**).

Clear and schematic protocols are developed for each type of collection device included in the kits in order to make easier the procedure interpretation (**Figure 5**). This action is especially critical when kits are targeted to donors for collection at home. The protocols include associated records to be filled with pre-analytical information of donations or samples, to report any incident that occurred during collection and preservation, even rack maps as guide for derivatives aliquoting into the specific tubes.

After centralized derivatives are obtained, a technical report specifying the sample processing features is accompanied in the shipments to analytical laboratories. Once all the samples for a study are sent from storage facilities to analytical laboratories, a final report is prepared with the missing samples, because of insufficient quantity of aliquots or any incident reported, and with the remaining

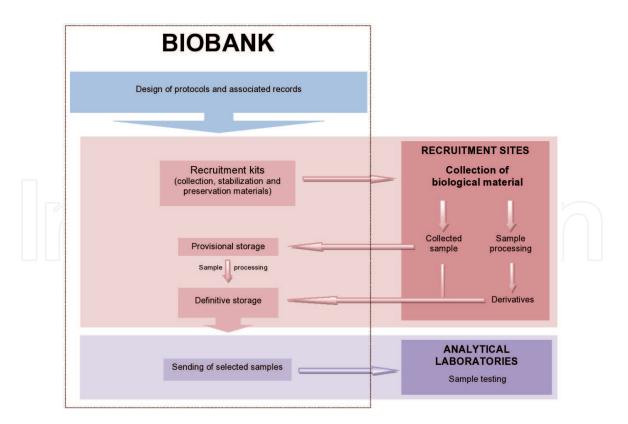


Figure 4.

Biobank-supported workflow for sample handling.

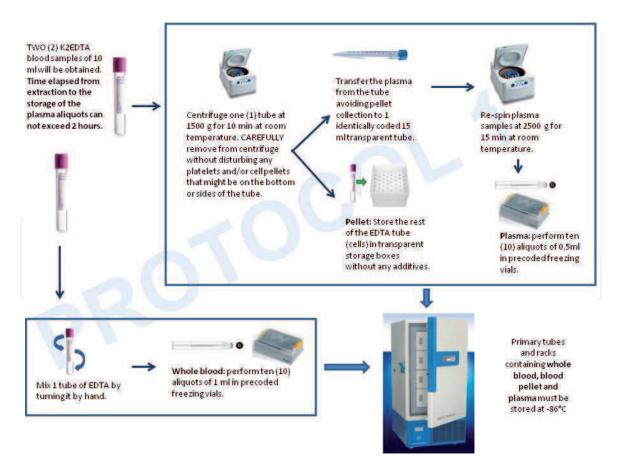


Figure 5.

Representative schematic protocol for derivative stabilization and preservation.

material for the study. Transaction forms specifying the samples included are necessary to declare the derivative shipment to the next facility involved in the project workflow.

4.2 Risk management tool

As part of the quality assurance tools, the processes of prospective sample collection, stabilization and processing, conservation, and distribution in multicenter research studies are managed under a global approach based on risk analysis, aimed at preventing undesired results. Since incidents are treated in the format of corrective and preventative action (CAPA) and root cause analysis (RCA) documentation, these records are used as reference.

So, the implementation by the biobanks of a comprehensive quality control for sample collection kits before shipment to recruitment sites is a result from this risk analysis. The potential consequences (inadequate preservation of samples due to inappropriate devices, containers, or additives, lower amount of derivatives for analysis, or loss of traceability) and costs of this process (new shipment of replacement kits and time of technician dedicated to kit checking), in addition to the number of nonconforming kits detected, have been evaluated. Quality control of kits is performed with a checklist, and follow-up of kit preparation and shipments is made with a specific record. Similarly, a checklist for the recruitment sites is included to track the reception of kits.

In addition, a training activity for the staff from the recruitment sites is organized before initializing the donors' recruitment to present the procedures for sample handling and the kit composition and usage. On the other hand, a pilot in a recruitment site is necessary to validate the model designed and to propose improvement measures.

5. Conclusions

The biobank-supported workflow, specifically designed and implemented for each research study, allows obtaining prospective, harmonized, and quality samples avoiding pre-analytical bias and contributing to the validity of the analytical results. Through biobanking processes and continuous and overlapped checkpoints, quality derivatives are obtained based on common and evidence-based standard operating procedures and supervised materials, with associated traceability information in relation with their collection, processing, conservation, and distribution. The effective workflow established is valid for large and complex multicenter projects.

Acknowledgements

This work was supported by Consejería de Salud y Familias-Junta de Andalucía, Ministerio de Economía y Competitividad-Gobierno de España, and Instituto de Salud Carlos III (grant number PT17/0019/0004 co-financed by FEDER). Thanks go to the staff from the Andalusian Public Health System Biobank for their continuous effort and improvements that make these supporting activities possible. Several projects have been satisfactorily attended following the previous premises.

Conflict of interest

The authors have declared no conflict of interest.

IntechOpen

Intechopen

Author details

Verónica Valdivieso-Gómez, Javier Garrancho-Pérez, Inés Aroca-Siendones and Rocío Aguilar-Quesada^{*} Andalusian Public Health System Biobank, Coordinating Node, Granada, Spain

*Address all correspondence to: rocio.aguilar.quesada@juntadeandalucia.es

IntechOpen

© 2020 The Author(s). Licensee IntechOpen. This chapter is distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/3.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

References

[1] Simeon-Dubach D, Kozlakidis Z. New standards and updated best practices will give modern biobanking a boost in professionalism. Biopreservation and Biobanking. 2018;**16**(1):1-2. [Epub 2018/02/03]

[2] International Society for Biological and Environmental Repositories (ISBER). Best Practices: Recommendations for Repositories [Internet]. 4th ed. 2018. Available from: https://www.isber.org/page/BPR. [Accessed: September 26, 2019]

[3] Riegman PH, Morente MM,
Betsou F, Blasio P, Geary P. Marble arch international working group on biobanking for biomedical research.
Biobanking for better healthcare.
Molecular Oncology. 2008;2(3):213-222.
DOI: 10.1016/j.molonc.2008.07.004.
Epub 2008/07/30

[4] Elliott P, Peakman TC. The UK biobank sample handling and storage protocol for the collection, processing and archiving of human blood and urine. International Journal of Epidemiology. 2008;**37**(2):234-244. Epub 2008/04/03

[5] Haumann R, Verspaget HW. Qualityassured biobanking: The Leiden University Medical Center model. Methods in Molecular Biology.
1730;2018:361-370. [Epub 2018/01/25]

[6] Ellervik C, Vaught J. Preanalytical variables affecting the integrity of human biospecimens in biobanking. Clinical Chemistry. 2015;**61**(7):914-934. Epub 2015/05/17

[7] Jones W, Greytak S, Odeh H, Guan P, Powers J, Bavarva J, et al. Deleterious effects of formalin-fixation and delays to fixation on RNA and miRNA-Seq profiles. Scientific Reports. 2019;**9**(1):6980. DOI: 10.1038/ s41598-019-43282-8 [8] Kozaki T, Lee S, Nishimura T, Katsuura T, Yasukouchi A. Effects of saliva collection using cotton swabs on melatonin enzyme immunoassay.
Journal of Circadian Rhythms.
2011;9(1):1. DOI: 10.1186/1740-3391-9-1

[9] Häntzsch M, Tolios A, Beutner F, Nagel D, Thiery J, Teupser D, et al. Comparison of whole blood RNA preservation tubes and novel generation RNA extraction kits for analysis of mRNA and MiRNA profiles. PLoS One. 2014;**9**(12):e113298. DOI: 10.1371/ journal.pone.0113298. eCollection 2014

[10] Parrish RS, Garafalo AV, Ndifor V,
Goetz KE, Reeves MJ, Yim A, et al.
Sample confirmation testing: A
short tandem repeat-based quality
assurance and quality control procedure
for the eyeGENE biorepository.
Biopreservation and Biobanking.
2016;14(2):149-155. DOI: 10.1089/
bio.2015.0098. [Epub 2016 Feb 18]

[11] Lucena-Aguilar G, Sanchez-Lopez AM, Barberan-Aceituno C, Carrillo-Avila JA, Lopez-Guerrero JA, Aguilar-Quesada R. DNA source selection for downstream applications based on DNA quality indicators analysis. Biopreservation and Biobanking. 2016;**14**(4):264-270. [Epub 2016/05/10]

[12] International Agency for Research on Cancer (IARC). Common Minimum Technical Standards and Protocols for Biobanks Dedicated to Cancer Research. IARC Technical Publication No. 44 [Internet]. 2017. Available from: https://www.google.es/ search?source=hp&ei=uWaMXciFNIuaM33IJAN&q=Common+Minimum+T echnical+Standards+and+Protocols+fo r+Biobanks+Dedicated+to+Cancer+Re search&oq=Common+Minimum+Tech nical+Standards+and+Protocols+for+B iobanks+Dedicated+to+Cancer+Resear ch&gs_l=psy-ab.3..0i19.595.595..1380...

0.0..0.150.150.0j1.....0....2j1..gws-wiz. mQHl2WGrdAg&ved=0ahUK EwiIxuXT-e3kAhULHxo KHc07BdIQ4dUDCAk&uact=5 #spf=1569482428652. [Accessed: September 26, 2019]

[13] Bernini P, Bertini I, Luchinat C, Nincheri P, Staderini S, Turano P.
Standard operating procedures for preanalytical handling of blood and urine for metabolomic studies and biobanks.
Journal of Biomolecular NMR.
2011;49(3-4):231-243. [Epub 2011/03/08]

[14] Lou JJ, Mirsadraei L, Sanchez DE, Wilson RW, Shabihkhani M, Lucey GM, et al. A review of room temperature storage of biospecimen tissue and nucleic acids for anatomic pathology laboratories and biorepositories. Clinical Biochemistry. 2014;47(4-5):267-273. DOI: 10.1016/j.clinbiochem.2013.12.011. Epub 2013 Dec 18

[15] Hubel A, Spindler R, Skubitz AP.
Storage of human biospecimens:
Selection of the optimal storage
temperature. Biopreservation and
Biobanking. 2014;12(3):165-175. DOI:
10.1089/bio.2013.0084. [Epub 2014
Jun 11]

[16] Betsou F, Bulla A, Cho SY, Clements J, Chuaqui R, Coppola D, et al. Assays for qualification and quality stratification of clinical biospecimens used in research: A technical report from the ISBER biospecimen science working group. Biopreservation and Biobanking. 2016;**14**(5):398-409. [Epub 2016 Apr 5]

[17] Ammerlaan W, Trouet J, Sachs MC, Guan P, Carithers L, Lambert P, et al. Small nucleolar RNA score: An assay to detect formalin-overfixed tissue. Biopreservation and Biobanking. 2018;**16**(6):467-476. DOI: 10.1089/ bio.2018.0042

[18] Kofanova O, Bellora C, Quesada RA, Bulla A, Panadero-Fajardo S, Keipes M, et al. IL8 and EDEM3 gene expression ratio indicates peripheral blood mononuclear cell (PBMC) quality. Journal of Immunological Methods. 2019;**465**:13-19. DOI: 10.1016/j. jim.2018.11.012. [Epub 2018 Nov 26]

[19] Schwarz N, Knutti N, Rose M,
Neugebauer S, Geiger J, Jahns R, et al.
Quality assessment of the preanalytical workflow in liquid biobanking: Taurine as a serum-specific quality Indicator for preanalytical process variations.
Biopreservation and Biobanking.
2019;17(5):458-467. DOI: 10.1089/ bio.2019.0004

[20] Mathieson W, Mommaerts K, Trouet JM, Mathay C, Guan P, Carithers LJ, et al. Cold ischemia score: An mRNA assay for the detection of extended cold ischemia in formalinfixed, paraffin-embedded tissue. Journal of Histochemistry and Cytochemistry. 2019;**67**(3):159-168. DOI: 10.1369/0022155418819967. [Epub 2018 Dec 18]

[21] Neumeister VM, Parisi F, England AM, Siddiqui S, Anagnostou V, Zarrella E, et al. A tissue quality index: An intrinsic control for measurement of effects of preanalytical variables on FFPE tissue. Laboratory Investigation. 2014;**94**(4):467-474. DOI: 10.1038/ labinvest.2014.7. Epub 2014 Feb 17

[22] Trezzi JP, Bulla A, Bellora C, Rose M, Lescuyer P, Kiehntopf M, et al. LacaScore: A novel plasma sample quality control tool based on ascorbic acid and lactic acid levels. Metabolomics. 2016;**12**:96. [Epub 2016 Apr 27]

[23] Kofanova O, Henry E, Aguilar Quesada R, Bulla A, Navarro Linares H, Lescuyer P, et al. IL8 and IL16 levels indicate serum and plasma quality. Clinical Chemistry and Laboratory Medicine. 2018;**56**(7):1054-1062. DOI: 10.1515/cclm-2017-1047 [24] Shea K, Betsou F. Development of external quality assurance programs for biorepositories. Biopreservation and Biobanking. 2012;**10**(4):403-404. DOI: 10.1089/bio.2012.1044

[25] Muller R, Betsou F, Barnes MG, Harding K, Bonnet J, Kofanova O, et al. Preservation of biospecimens at ambient temperature: Special focus on nucleic acids and opportunities for the biobanking community. Biopreservation and Biobanking. 2016;**14**(2):89-98. DOI: 10.1089/ bio.2015.0022. [Epub 2016 Feb 17]

[26] Valdivieso-Gomez V, Aguilar-Quesada R. Quality management systems for laboratories and external quality assurance programs. In: Zaman GS, editor. Quality Control in Laboratory. London: IntechOpen; 2018. DOI: 10.5772/intechopen.73052

[27] Furuta K, Allocca CM, Schacter B, Bledsoe MJ, Ramirez NC.
Standardization and innovation in paving a path to a better future: An update of activities in ISO/TC276/ WG2 biobanks and bioresources.
Biopreservation and Biobanking.
2018;16(1):23-27. DOI: 10.1089/ bio.2017.0117. [Epub 2018 Feb 2]

IntechOper