Product Name: CellSave Preservative Tube
Model: 7900005/952820
Medical Device Registration Certificate No.: CFDA(I)20152413357
Product Technical Requirement No.: CFDA(I)20152413357
Legal Manufacturer Name: Janssen Diagnostics, LLC
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Customer Service Agent Contact Info: 8008201000
China Agent: Johnson & Johnson Medical (Shanghai) Ltd.
China Agent Address: Location C, 1/2/3 F, #439 Fu Te Xi Yi Road, Pilot Free Trade Zone, Shanghai, P.R. China
China Agent Contact Info.: 8008201000
Date of Manufacture: Refer to product package
Date of Expiration: Refer to product package
IFU Publish and Modification Date: 2015/10/13

Should any other Chinese or English IFU attached, CFDA version IFU shall prevail.

cellsave preservative tube

REF 7900005(100Tubes)
IVD 952820 (20 Tubes)

SYMBOLS

IVD	In vitro diagnostic medical device	REF	Catalog number
LOT	Batch code/ lot number		Use by YYYY-MM-DD
	Temperature limit		Manufacturer
	Caution, consult accompanying documents		Consult instructions for use
EC REP	Authorized representative in the European Community	STERILE R	Sterile, radiation
	Do not reuse		

INTENDED USE

The CellSave Preservative Tube is intended for the collection and preservation of circulating epithelial cells (tumor cells) in whole blood, to be used for enumeration and phenotyping.

INDICATIONS FOR USE

CellSave Preservative Tubes may be used for monitoring of circulating epithelial cells (tumor cells), which may aid in the management of cancer patients.

PRODUCT DESCRIPTION

CellSave Tubes are evacuated blood collection tubes that contain EDTA anticoagulant and a cell preservative. The vacuum is designed to draw approximately 10 ml of blood. The interior of the tube is sterile. CellSave Tubes are intended to be used in conjunction with Veridex instruments.

PRINCIPLE OF OPERATION

CellSave Tubes are evacuated blood collection tubes that are designed to be used with standard phlebotomy supplies for venous blood collection. The tube contains 300ul of a solution that contains Na_2EDTA and a cell preservative. The EDTA absorbs calcium ions, which prevents the blood from clotting. The preservative preserves the morphology and cell surface antigen expression of epithelial cells. Each tube is evacuated to withdraw 10.0 ml of venous whole blood when following standard phlebotomy procedures.

LIMITATIONS

- The volume of blood drawn varies with altitude, ambient temperature, barometric pressure, tube age, venous pressure and filling technique.
- Samples must be processed within 96 hours of collection.
- For rare cell analysis using the CELLTRACKS ANALYZER II®, check sample integrity as described in the User's Guide for the CELLTRACKS ANALYZER II®.

PRECAUTIONS

1. Storage of tubes at or below 0°C may result in tube breakage.
2. Do not remove rubber stopper by rolling with thumb. Remove stoppers with a twist and pull motion.
3. Do not use tubes if foreign matter is present.
4. Practice Universal Precautions. Use gloves, gowns, eye protection and other personal protective equipment, and engineering controls to protect from blood spatter, blood leakage and potential exposure to bloodborne pathogens.
5. All glass has the potential for breakage. Examine all glass for potential damage in transit before use and take precautionary measures during handling.
6. Handle all biological samples and blood collection sharps (lancets, needles, luer adapters and blood collection sets) according to the policies and procedures of your facility. Obtain appropriate medical attention in the event of exposure to biological samples (for example, through a puncture injury), since it might transmit viral hepatitis, HIV (AIDS), or other infectious diseases. Utilize any built-in used-needle protector, if the blood collection device provides one. Janssen Diagnostics does not recommend reshielding used needles. However, the policies and procedures of your facility may differ and must always be followed.
7. Discard all blood collection sharps in biohazard containers approved for their disposal.
8. Transferring a sample collected using syringe and needle is not recommended. Additional manipulation of sharps such as hollow bore needles increases the potential for needle stick injury.
9. Transferring samples from a syringe to a CellSave Tube using a non-sharps device should be performed with caution for the reasons described below. Depressing the syringe plunger during transfer can create positive pressure, forcefully displacing the stopper and sample, causing splatter and potential blood exposure. Using a syringe for blood transfer may also cause over or underfilling of tubes, resulting in incorrect blood-to-additive ratio and potentially incorrect

analytic results. CellSave Tubes are designed to draw a specific volume. Filling is complete when vacuum no longer continues to draw, though some tubes may partially fill due to plunger resistance when filled from a syringe.

10. If blood is collected through an intravenous line, ensure that line has been cleared of I.V. solution before beginning to fill CellSave Tubes.
11. Underfilling or overfilling of tubes will cause incorrect blood-to-additive ratio and can lead to incorrect analytic results.
12. Caution: Samples must be transported and stored at temperatures of 15-30°C. Refrigerating samples prior to processing could adversely affect sample integrity.

Prevention of Backflow

Since the CellSave Preservative Tube contains additives, it is important to avoid possible backflow from the tube, with the possibility of adverse reactions. To guard against backflow, observe the following precautions:

1. Place the patient's arm in a downward position.
2. Hold the tube with the stopper upmost.
3. Release the tourniquet as soon as blood starts to flow.
4. Make sure the solution inside the tube does not touch the stopper or end of the needle during venipuncture.

STORAGE

- Store tubes at 4-30°C with 18 months shelf life. Do not use if the additive is not clear and colorless. Do not use after the expiration date.
- **Store or transport samples at temperatures of 15-30°C. Proper insulation may be required for shipment during extreme temperature conditions.**

PROCEDURE

Materials Provided

CellSave Preservative Tubes. Contains: 300ul solution containing 4.6% Na_2EDTA and 36% cell preservative, 0.36% polyethylene glycol, 0.46% inert ingredients

Materials Needed, Not Provided

Blood collection needles and adapters, alcohol wipes, tourniquet

1. Perform venipuncture according to CLSI procedure H3-A6, *Procedure for the Collection of Diagnostic Blood Specimens by Venipuncture*. Draw the CellSave Tubes first, if multiple tube types are to be drawn.
2. Fill the tube until blood flow stops.
3. Remove the tube from the adapter and gently invert it 8 times to mix. Tube inversion prevents clotting. Inadequate or delayed mixing may result in inaccurate test results.
4. Process sample within 96 hours of collection. Store samples at temperatures of 15-30°C.

PERFORMANCE

Recovery

Recovery was evaluated by spiking samples with low tumor cell numbers (0, 50, 100 and 200 cells/7.5 ml) and high tumor cell numbers (0, 100, 1,000 and 10,000 cells/7.5 ml). Blood from 5 normal donors was collected into CellSave Tubes and spiked with SKBR-3 cells (a breast cancer cell line). Samples were processed and stained with a nucleic acid dye, anti-CD45- APC and anti-CK-PE using the CELLPREP™ Semi-Automated Sample Processing System and analyzed using the FACSCalibur flow cytometer with beads to enable calculation of absolute counts of cells. For the low spike experiment, the regression equation was y=0.8x+4.7 and the correlation coefficient was

R2=0.98. For the high spike experiment, the regression equation was y=0.9x+6.2 and the correlation coefficient was R2=0.99.

Table 1. Recovery data for low and high spikes of SKBR-3 tumor cells

	Low Spike				High Spike			
Donor	**0**	**50**	**100**	**200**	**0**	**100**	**1,000**	**10,000**
A	2	31	89	164	2	84	876	8,259
B	2	44	97	141	4	74	775	8,185
C	5	51	92	175	1	75	880	9,342
D	1	46	81	153	2	118	846	8,030
E	4	52	82	181	2	106	959	9,014
Mean	3	45	88	163	2	91	867	8,566
%Recovery		89.3%	88.2%	81.4%		91.3%	86.7%	85.7%

Interfering Substances

Blood from 5 normal donors was collected into EDTA and CellSave Tubes and spiked with approximately 800 SKBR-3 cells. CellSave Tubes were spiked with potential interfering substances (hemolysis 5+, lipemia 1.94-2.04% emulsified fat, icteris 7.0 mg/dl) to determine the effect on recovery and enumeration of tumor cells. Duplicate samples were processed using the CELLPREP™ Semi-Automated Sample Processing System and analyzed using the FACSCalibur flow cytometer. Hemolysis, lipemic and icteric whole blood samples collected into the CellSave Tube do not interfere with recovery and enumeration of tumor cells.

Table 2. Recovery of spiked tumor cells for 7.5 ml whole blood

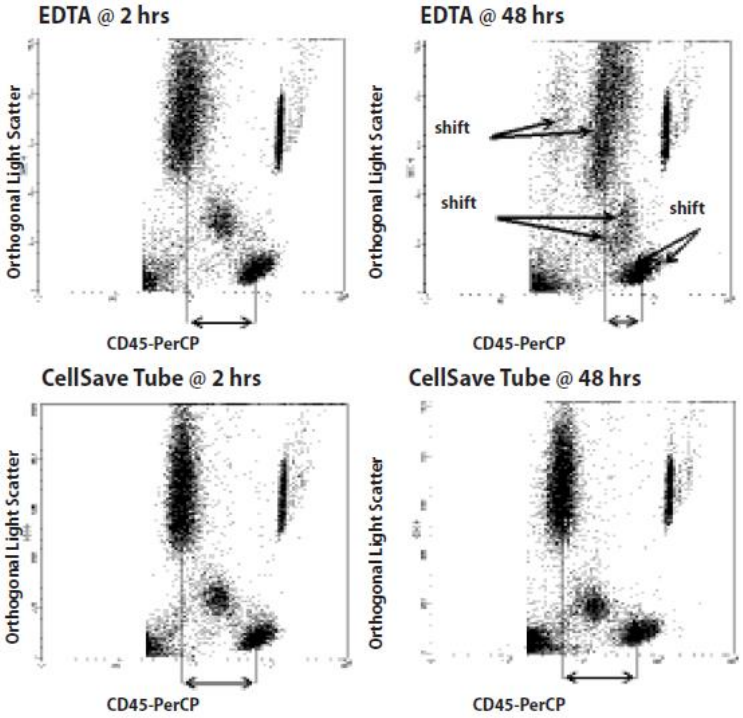
Donor	**EDTA Control**			**CellSave Control**		
	# Cells Recovered	# Cells Spiked	% Recovery	# Cells Recovered	# Cells Spiked	% Recovery
A1	452	828	55%	388	696	56%
A2	445	828	54%	486	696	70%
B1	802	749	107%	689	696	99%
B2	711	749	95%	690	696	99%
C1	580	771	75%	289	716	40%
C2	451	771	58%	272	716	38%
D1	571	771	74%	552	716	77%
D2	642	771	83%	636	716	89%
E1	610	771	79%	526	716	73%
E2	541	771	70%	535	716	75%
Mean	581		75%	506		72%
SD	117		17%	150		22%

	CellSave, Hemolysis			**CellSave, Lipemia**			**CellSave, Icteris**		
Donor	# Cells Recovered	# Cells Spiked	% Recovery	# Cells Recovered	# Cells Spiked	% Recovery	# Cells Recovered	# Cells Spiked	% Recovery
A1	482	696	69%	664	696	95%	638	696	92%
A2	502	696	72%	691	728	95%	612	728	84%
B1	514	696	74%	748	696	107%	678	696	97%
B2	571	696	82%	712	696	102%	679	696	98%
C1	499	716	70%	568	716	79%	561	716	78%
C2	470	716	66%	599	716	84%	514	716	72%
D1	582	716	81%	628	716	88%	651	716	91%
D2	551	716	77%	549	716	77%	589	716	82%
E1	571	716	80%	620	716	87%	554	716	77%
E2	499	716	70%	620	716	87%	584	716	82%
Mean	524		74%	640		90%	606		85%
SD	41		6%	63		10%	55		9%

Antigen Preservation for Phenotyping

The ability to discern the different cell populations clearly is affected by the age of the sample at the time of analysis, unless the sample is preserved. Leukocyte preservation is indicative of sample quality when performing analysis of circulating tumor cells. Figure 1 shows a typical example of the CD45 antigen density of the different cell populations of blood drawn in a standard EDTA tube and the CellSave Tube. Blood was analyzed within 2 hours of blood draw, then repeated at approximately 48 hours of blood draw. The degree of separation between lymphocytes and granulocytes is indicated by the length of the horizontal bars at the X-axis of each of the graphs. The separation between both cell populations is degraded over time with the EDTA tube. The separation is maintained with the CellSave Tube. The arrows in the figure pointing at the lymphocyte, monocyte, and granulocyte populations show the shift of these cell populations due to the aging of the blood samples. This makes it more difficult to discern these cell populations.

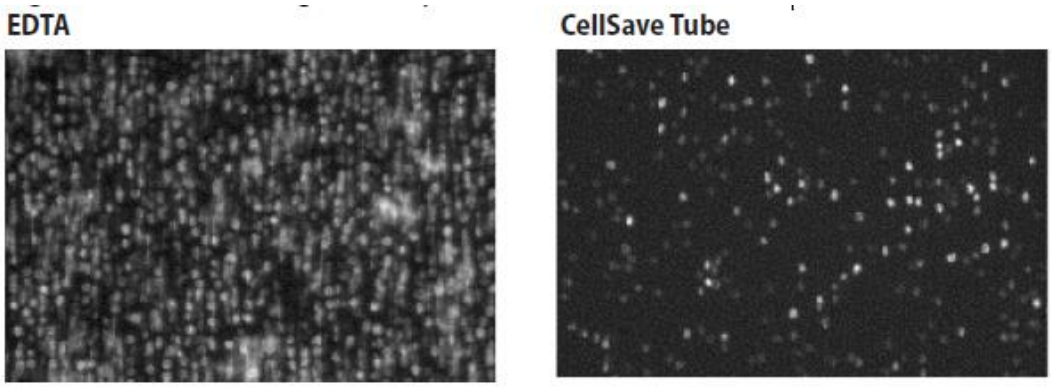
Figure 1. Separation of cell clusters during aging of blood collected in EDTA and CellSave Tubes.



Sample Quality

The quality of the sample is important for adequate detection of rare epithelial cells. Leukocyte integrity of blood samples immunomagnetically enriched for epithelial cells with the CELLPREP™ System is an excellent measure of this quality. Figure 2 shows images of nuclear staining (DAPI) of blood samples collected in EDTA and CellSave Tubes that were processed after 24 hours using a CELLPREP™ System. The images were taken using a 10x objective on a fluorescent microscope. Whereas an abundance of nuclear material is present in the sample collected in the EDTA tube, only round objects (leukocytes) are present in the sample collected in the CellSave Tube.

Figure 2. Nuclear staining of leukocytes in EDTA and CellSave Tubes.



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