

Cytogenetics

Analytes/procedures in **bold** type are regulated for proficiency testing by the Centers for Medicare & Medicaid Services

ACMG/CAP Cytogenetics CY

Analyte	CY	Challenges per Shipment
Chromosome abnormality	■	5
Karyotype nomenclature designation	■	5
Modal chromosome number	■	5
Sex chromosome designation	■	5
Educational challenge, ungraded	■	1 per year

CYTOGENETICS VALIDATED MATERIAL (CYM)

Product Information

Survey CY is designed to provide educational opportunities for clinical cytogenetics laboratories. Participants are challenged to identify and denote chromosomal abnormalities in G-banded chromosome preparations, using the current *International System for Human Cytogenetics Nomenclature (ISCN)*.

Survey challenges will include prints of metaphase cells. A total of five challenges will be included with each shipment. For each challenge, two copies each of at least three metaphase cells that are representative of each case will be included. A brief case history will be included with each challenge. Challenges will vary with each Survey as follows:

- Two or three challenges will represent a constitutional chromosome disorder.
- One or two challenges will illustrate a neoplastic disorder.
- CY-B will include a print of G-banded partial karyotypes from different cases. Participants are challenged to identify whether the partial karyotypes are normal or abnormal and to identify the abnormalities noted.
- One shipment per year will include an educational challenge.

Each set of CYM ordered will consist of the same prints used in the Cytogenetics Survey CY.





ACMG/CAP Fluorescence In Situ Hybridization – Constitutional and Hematologic Disorders CYF

Procedure	CYF	Challenges per Shipment	
		A	B
FISH for neoplastic disorder	■	1	2
FISH for constitutional abnormality	■	2	1

Product Information

Survey CYF is designed for clinical laboratories that perform fluorescence in situ hybridization (FISH) using chromosome-specific DNA probes for cell suspension samples (for FISH in paraffin-embedded tissue, see CYP). Participants will use their own chromosome-specific DNA probes and FISH methodology to process and score a series of metaphase spreads and/or interphase nuclei for each specimen.

The first mailing will include one neoplastic disorder challenge (with two slides) for detection of rearrangement of the *PML* and *RARA* genes, one constitutional abnormality challenge (with two slides) for detection of a numeric sex chromosome abnormality, and a photopage challenge representing a constitutional abnormality.

The second mailing will consist of one challenge (with two slides) for detection of sex chromosomes in an opposite-sex bone marrow transplant specimen, one challenge (with two slides) for detection of a congenital abnormality involving the Smith-Magenis Critical Region, and a photopage challenge representing a neoplastic disorder.

ACMG/CAP Fluorescence In Situ Hybridization – Urothelial Carcinoma CYI

Procedure	CYI	Challenges per Shipment
FISH for urothelial carcinoma	■	2

Product Information

Survey CYI will consist of two shipments of two cell samples suspended in ethanol from two different specimens. Participants are to use FISH to detect chromosomal abnormalities associated with urothelial carcinoma using probes for the centromeres for chromosomes 3, 7, 17, and a locus-specific probe for 9p21.



ACMG/CAP Fluorescence In Situ Hybridization – Breast Cancer (*HER2* Gene Amplification) CYH

Procedure	CYH	Challenges per Shipment
<i>HER2</i> gene amplification for breast cancer	■	10

Product Information

Survey CYH is designed for clinical laboratories that perform fluorescence in situ hybridization (FISH) using chromosome-specific *HER2* DNA probes. Participants will use their own chromosome-specific DNA probes and FISH methodology to process and score a series of interphase nuclei for each specimen.

Each mailing will consist of two five-core tissue microarray slides that offer a combined total of ten paraffin-embedded breast tissues specimens. A duplicate set of H&E stained tissue microarray slides will be provided with the shipment.



ACMG/CAP Comparative Genomic Hybridization Microarray CYCGH

Procedure	CYCGH	Challenges per Shipment
CGH microarray analysis for constitutional abnormality	■	2

Product Information

Survey CYCGH is designed for clinical laboratories that perform comparative genomic hybridization testing (CGH) by microarray analysis for constitutional copy number changes. Extracted DNA will be provided for analysis using the same array platform and software analysis system used for clinical testing.

DNA will be obtained from individuals tested for a constitutional abnormality. Laboratories will assay specimens and interpret results for potential abnormalities of copy number representing phenotypes that have been characterized and reported in the general literature. Participants will be asked to identify gains or losses and the cytogenetic location of any abnormalities detected.





ACMG/CAP FISH For Paraffin-Embedded Tissue – CYJ, CYK, CYL

Gene/Region of Interest	CYJ (Glioma tissue)	CYK (Sarcoma tissue or pediatric neoplasm)	CYL (Lymphoma tissue)	Challenges per Shipment	
				A	B
1p/19q	■			1	1
<i>MYCN</i>		■		1	
<i>ALK</i>			■	1	
<i>CHOP</i>		■			1
<i>MYC</i>			■		1

Product Information

These Surveys are designed for clinical laboratories that perform fluorescence in situ hybridization (FISH) using chromosome-specific DNA probes in paraffin-embedded tissue (see CYF for FISH in cell suspension specimens). Participants will use their own chromosome-specific DNA probes and FISH methodology to process and score a series of interphase nuclei for each specimen. All specimens will be 4-micron tissue sections mounted on positively charged glass slides. One hematoxylin-eosin stained slide will also be provided with each challenge for reference.

The first mailing (CYP-A) will include one challenge each for CYJ, CYK, and CYL. CYJ-A will consist of four unstained slides from paraffin-embedded tissue representing a neurological cancer specimen (glioma). Participants are to use FISH probes for detection of deletions within 1p36 and 19q13 band regions. CYK-A will consist of two unstained slides from paraffin-embedded tissue representing a pediatric neoplasm. Participants are to use FISH probes to detect aberrations of the *MYCN* gene (2p24.3). CYL-A will consist of two unstained slides from paraffin-embedded tissue representing a lymphoma specimen. Participants are to use FISH probes to detect rearrangement of the *ALK* gene (2p23).

The second mailing (CYP-B) will include one challenge each for CYJ, CYK and CYL. CYJ-B will consist of four unstained slides from paraffin-embedded tissue representing a neurological cancer specimen (glioma). Participants are to use FISH probes for detection of deletions within 1p36 and 19q13 band regions. CYK-B will consist of two unstained slides from paraffin-embedded tissue representing a sarcoma tissue. Participants are to use FISH probes to detect aberrations of the *CHOP* (*DDIT3*) gene (12q13). CYL-B will consist of two unstained slides from paraffin-embedded tissue representing a lymphoma specimen. Participants are to use FISH probes to detect rearrangement of the *MYC* gene (8q24.1).

Product Fulfillment Group CYP

Biochemical and Molecular Genetics

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ACMG/CAP Biochemical Genetics BGL

Analyte/Procedure	BGL	Challenges per Shipment
Acylcarnitine (qualitative and quantitative)	■	1
Amino acids (qualitative and quantitative)	■	1
Mucopolysaccharides (qualitative)	■	1
Organic acids (qualitative and quantitative)	■	1
Educational specified metabolic disorder	■	1



Product Information

Survey BGL is designed for laboratories specializing in the biochemical testing of metabolic diseases. For acylcarnitine testing, a plasma specimen (approximately 100 lambda) will be provided. A 5.0 to 10.0-mL urine specimen will be provided for mucopolysaccharides and organic acids testing. For amino acid testing, either a plasma (up to 1.0-mL) or urine specimen (5.0 to 10.0-mL) will be provided. The last specimen will be provided for a specified group of metabolic disorders and will include plasma, urine, or other appropriate material.

Pharmacogenetics PGx

Analyte/Procedure	PGx	Challenges per Shipment
Allele detection	■	2




Product Information

Survey PGx is designed for laboratories performing genetic testing for predicting drug response. Each sample will include 25µg of extracted DNA. Interpretive challenges will also be included in the context of the clinical case scenario. Participants may perform testing for CYP2C19, CYP2C9, CYP2D6, UGT1A1, and VKORC1 on each sample.



ACMG/CAP Molecular Genetics MGL1, MGL2, MGL3, MGL4, MGL5

Disease/Gene	MGL1	MGL2	MGL3	MGL4	MGL5 
BRCA1/2			■		
Canavan				■	
Connexin-26			■		
Cystic fibrosis		■			■
DMD/Becker		■			
Factor V Leiden	■				
Familial dysautonomia				■	
Fragile X	■				
Friedreich ataxia		■			
Hemochromatosis	■				
Hemoglobin S/C		■			
Huntington disease		■			
Methylenetetrahydrofolate reductase (MTHFR)	■				
Multiple endocrine neoplasia type 2 (MEN2)			■		
Myotonic dystrophy		■			
Prader-Willi/Angelman Syndrome	■				
Prothrombin	■				
RhD		■			
Spinal muscular atrophy		■			
Spinocerebellar ataxia		■			
Tay Sachs				■	

Product Information

Surveys MGL1, MGL2, MGL3, MGL4, and MGL5 are designed for laboratories specializing in molecular testing for genetic disease. Each disease/gene will have three challenges per shipment with the exception of MGL5, which will have two challenges per shipment. Each shipment will include approximately 50 µg of extracted DNA.

Product Fulfillment Group MGL

Molecular Pathology

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Molecular Oncology MO, MO2, MO3

Procedure	MO	MO2	MO3	Challenges per Shipment
Molecular analysis (cells, frozen tissue, or DNA)	■			2
Molecular analysis, double volume (cells, frozen tissue, or DNA)		■		2
Molecular analysis (paraffin sections)			■	2

Product Information

Survey MO is designed for laboratories performing molecular analysis of leukemias and lymphomas. Survey MO2 contains additional sample vials to accommodate laboratories performing RNA testing in addition to DNA testing. Survey MO3 is for laboratories performing molecular analysis of leukemias and lymphomas on paraffin sections.

Note: Laboratories performing immunophenotyping on patients with leukemia and/or lymphoma should refer to Survey FL3 on page 151 and Survey MK on page 186.

Each shipment of Survey MO will include two sample vials containing a snap frozen cell pellet, frozen tissue specimen, or DNA. From each pellet or frozen tissue specimen, at least 100 µg of DNA can be extracted for Southern blot analysis and/or amplification of antigen receptor (B- and T-cell) gene arrangement or selected (B- and T-cell) translocations (eg, *bcr*). Survey MO2 will contain four sample vials (two per specimen). Each shipment of Survey MO3 will contain four 10-micron paraffin sections per specimen.

Product Fulfillment Group MO



In Situ Hybridization ISH

Procedure	ISH	Challenges per Shipment
<i>In situ</i> hybridization	■	1 per shipment
Kappa lambda	■	1 per shipment

Note: Brightfield in situ hybridization for HER2 is now offered in ISH2.

Product Information

Survey ISH offers laboratories performing clinical *in situ* hybridization tests the opportunity to objectively evaluate their performance for targets including human papillomavirus (HPV) and Epstein-Barr virus (EBV). Information including the conditions of slide pretreatment, probe type, hybridization conditions, and detection systems will be used to facilitate interlaboratory comparison of methods and standardization. Laboratories performing FISH for interphase chromosomal targets in paraffin sections should refer to CY Surveys.

Each shipment for *in situ* hybridization analysis will include a set of treated glass slides upon which are mounted one or more formalin-fixed, paraffin-embedded sections of either cell pellets or tissues containing the nucleic acid target of interest, along with appropriate information for direct testing. Each shipment will also contain one challenge for kappa and lambda mRNA. The kappa-lambda challenge will include a set of glass slides.

Product Fulfillment Group ISH



In Situ Hybridization, HER2 ISH2

Procedure	ISH2	Challenges per Shipment
<i>HER2</i> gene amplification for breast cancer	■	10

Product Information

Survey ISH2 is designed for clinical laboratories that perform brightfield *in situ* hybridization (ISH) for *HER2*.

Each mailing will consist of two five-core tissue microarray slides that offer a combined total of ten unique paraffin-embedded breast tissue specimens.

Product Fulfillment Group ISH

Minimal Residual Disease MRD

Analyte	MRD	Challenges per Shipment
Minimal residual disease	■	2

Product Information

Survey MRD is designed for laboratories that perform minimal residual disease testing in cancer patients. The Survey is specifically designed for laboratories monitoring chronic myelogenous leukemia by measuring the quantity of *BCR/ABL1* transcripts at diagnosis and during or after therapy. The MRD Survey is also applicable for monitoring acute leukemia for *BCR/ABL1*.

Each shipment of Survey MRD will arrive packed in dry ice and include three sample vials each holding a frozen cell pellet or extracted RNA. The first sample will typically be a baseline sample while samples two and three will represent follow-up samples.

Microsatellite Instability MSI

Analyte	MSI	Challenges per Shipment
Microsatellite instability (paraffin sections)	■	1

Product Information

Survey MSI is designed for laboratories performing microsatellite analysis of paraffin-embedded colorectal carcinoma (or other HNPCC-related tumors) by DNA amplification.

Each shipment will include one H&E slide and two or more 10-micron unstained sections on glass slides to be used to isolate DNA from tumor and normal tissue for microsatellite instability analysis.

Sarcoma Translocation SARC

Analyte	SARC	Challenges per Shipment
Sarcoma translocation	■	1

Product Information

Survey SARC is designed for laboratories performing molecular analysis of sarcoma translocations by RT-PCR. The participants may perform testing on the sample for any sarcoma translocation, including *EWS/EGR*, t(21;22); *EWS/FL11*, t(11;22); *EWS/WT1*, t(11;22); *FUS/CHOP*, t(12;16); *PAX3/FKHR*, t(2,13); *PAX7/FKHR*, t(1;13); *PDGFB/COL1A1*, t(17;22); *SYT/SSX1*, t(X;18); *SYT/SSX2*, t(X;18); and *SYT/SSX*, NOS.

Each shipment of Survey SARC will include one snap frozen cell pellet or extracted RNA from which the participant will be able to extract approximately 5 to 10 micrograms of RNA.